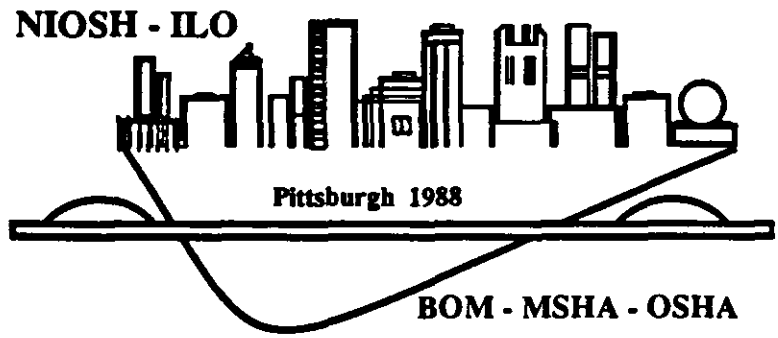
Proceedings of the VIIth International Pneumoconioses Conference | *Part* **I**
Transactions de la VIIe Conférence Internationale sur les Pneumoconioses | *Tome*
Transaciones de la VIIa Conferencia Internacional sobre las Neumoconiosis | *Parte*



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PREFACE

It is truly an honor and privilege to provide this preface to the Proceedings of the Seventh International Pneumoconioses Conference which was conducted in Pittsburgh, Pennsylvania during August 23–26, 1988. This symposium, only the seventh such conference since 1930 and the first to be held in the United States, was conducted under the joint sponsorship of the International Labour Office (ILO), the National Institute for Occupational Safety and Health (NIOSH), the Mine Safety and Health Administration (MSHA), the Occupational Safety and Health Administration (OSHA), and the Bureau of Mines (BOM).

The Pittsburgh Conference was attended by over 1000 participants from 50 countries. The symposium call for papers was issued in 1987 and invited submission of abstracts focusing on research and scientific expertise on the pneumoconioses and other occupational respiratory disease. The response was truly gratifying and resulted in the acceptance of over 275 papers for presentation in various scientific sessions and workshops and 124 papers for presentation at poster sessions. The Proceedings (Part I) now in your hand contains over half of those presented at the Conference.

It is my pleasure to acknowledge with gratitude the invaluable assistance of the many individuals and organizations which contributed to the planning, conduct and follow-up of this Conference. The International Organizing Committee was extremely helpful in developing the framework of the Conference. Special thanks to the National Organizing Committee who generously gave of their time and talents so that this Conference was truly representative of an event of its preeminent stature. I wish to publicly thank Mr. John Pendergrass, Assistant Secretary of Labor, OSHA and Mr. David Taylor, Deputy Director General, ILO for their inspiring keynote presentations; to Dr. J. Donald Millar, Assistant Surgeon General, Director of the National Institute for Occupational Safety and Health, Mr. Lynn Williams, International President, United Steel Workers of America and Dr. Bruce Karrh, Vice President, Safety, Health and Environmental Affairs, E.I. Dupont de Nemours Co., USA for their incisive overview presentations; and to the many staff of NIOSH who worked tirelessly in the conduct of the Conference. All were important partners in this enterprise.

But there could have been no successful venture without the enthusiastic and committed support of two people. Dr. Jack Berberich who when called upon at a critical time served both as Executive Secretary-General of the Conference and Editor-in-Chief of these Proceedings and Mr. Georg Kliesch, ILO.

On behalf of the International and National Organizing Committees, the five sponsoring organizations, these Proceedings (Part I) are presented with the hope that you will find them as rewarding as your participation in the Conference. We look forward to completing Part II within the next 12 months so that you will have a complete chronology of the program.

Edward L. Baker, M.D., M.P.H.
Chairman
VIIth International Pneumoconioses Conference

Georg Kliesch
Vice Chairman
VIIth International Pneumoconioses Conference

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SEVENTH INTERNATIONAL CONFERENCE ON THE PNEUMOCONIOSES

JOHN A. PENDERGRASS

Assistant Secretary of Labor
Occupational Safety and Health Administration
U.S. Department of Labor

It is my privilege to be one of several to welcome you to Pittsburgh, and for many of you to the United States and to all of you to this Seventh International Conference on the Pneumoconioses. This is the first of the conferences to be held in the United States and we are honored. The importance of the conference and the breadth of interest is indicated by the number of countries represented by the participants in the conference. It is my understanding that over 50 nations are represented. The speakers, workgroup leaders and presenters are world authorities in the pneumoconioses. These diseases of the lungs have held the attention of scientists for well over 400 years. Agricola discussed the consequences of dusty trades in his 1556 publication De re Metallica. He emphasized the poor prognosis for workers who developed asthma and ulceration of the lungs due to dust exposure of miners. He stated that in the Carpathian Mountains many women married seven husbands all of whom died of diseases of the lungs, pneumoconioses. A term unknown at Agricola's time. It is credited to Zenker who in 1866 suggested it as a generic designation for dust deposits in the lungs.

When I began my industrial hygiene career 40 years ago I soon learned about dust exposure and the lung conditions caused by exposure to asbestos, silica, talc, bauxite, diatomaceous earth, coal dust, carbon, calcium and iron. The program for this week includes sessions on many of these same materials. Not for a moment should we or those who report on this conference think that we are gathered to rehash old topics or assume that progress has been lacking. To the contrary, this conference, as its six predecessors, is a continuance of knowledge. Current data, built on the past, using modern techniques and technologies permit the industrial hygienists, the physiologists, physicians, toxicologists and engineers to challenge the future.

As a government regulatory official I am acutely aware of the need for quality scientific information. If our regulations are to be effective and acceptable to those we regulate, we must have information that can generate a consensus. Such information stems from scientific data that stands up to peer review, peers from around the world. No nation and no single group of scientists can afford to isolate themselves nor ignore the work of others.

Perhaps more than ever before in the history of science, your work has direct effect on how business is conducted regardless of the country of origin or country of application. Multinational corporations adapt to the countries in which they produce and market but they do not leave the knowledge, practices and policies of the home country behind. As you exchange scientific information on health effects you are also affecting how businesses will be conducted and trade carried out. Physiological response to occupational exposure knows no national boundaries.

Dust particles take many shapes and sizes and have almost unlimited chemical compositions. Agricola understood that lethal lung diseases resulted from working in the mines. The South Africans developed instruments to measure the concentration of dust particles in the gold mines. Particle size and lung retention are important in the causes of pneumoconioses. We are currently struggling with the definition of a fiber, only because we are learning that fiber length and diameter are important to what happens in the lungs. Are these properties of more concern than the chemical composition? Some day you will be able to tell us why silica in different combinations has decidedly different physiological responses. Today questions are being raised about particles that at one time, not so long ago, were thought to be benign.

The demise of asbestos as a satisfactory insulating material created markets for man made fibers. This has created a need for better understanding of what, when, and how these fibers affect the human body. We, as scientists, employers, government administrators and professors are challenged as to what we should be doing to protect workers' health and not unduly restrict innovation in the workplaces and the markets of the world.

You will not leave Pittsburgh with all of the answers. You will not have all of the answers when the Eighth International Conference on the Pneumoconioses ends. But we and all who depend on us for guidance and knowledge will be closer to the answers.

In addition to the scientific sessions that are planned I hope you will have time to take advantage of what the Pittsburgh area has to offer. Among these is the Department of Labor Mine Safety and Health Administration laboratories.

Thank you for allowing me to be a part of your conference and I wish you continued success in your search for scientific truth.

DAVID P. TAYLOR

Deputy Director-General, International Labour Office, Geneva

Mr. Chairman, Ladies and Gentlemen:

On behalf of Mr. Francis Blanchard, Director-General of the International Labour Office, I extend a hearty welcome to all of you who have come from all over the world to attend the VIIth Pneumoconioses Conference. I should also like to thank our hosts, the City of Pittsburgh, in the person of the Assistant Executive Secretary to the Mayor, who is honouring this session with his presence, as well as the institutions in the United States which have joined forces together and with the ILO to organise the Conference. Those who have not organised an international scientific conference of this magnitude cannot possibly imagine the amount of planning, both technical and practical, that is entailed. Most grateful thanks are due, and it is my pleasure to give them, to the National Institute for Occupational Safety and Health, the Occupational Safety and Health Administration, the Mine Safety and Health Administration, the Bureau of Mines, and the very many institutions, such as the American College of Radiology, a number of universities, hospitals, employers' organisations and trade unions, which participated actively in the work of the national and international organising committees. I am most grateful—as I am sure you all are—to these institutions for their commitment, and to their individual members for the dedicated, intensive work they put into prepare the Conference. I am sorry that I cannot thank them individually—that would take us well into the afternoon—and I will ask you, Mr. Chairman, to convey my Organisation's most sincere appreciation to each and every one whose efforts enabled us to meet today for discussions which I am sure will prove to be stimulating, rewarding and effective.

Pneumoconioses are ugly diseases, and I, for one, always thought that the word itself was a bit of a nuisance to bring out. I am glad there are plans to find a more manageable title for the next Conference, something along the lines of "International Conference on Occupational Lung Diseases." This Conference is the seventh of its kind, the first one dating back to 1930. In those days, the title reflected the basic concern, which was with diseases induced by mineral dusts, mainly in mines. Over time, the Conference has come to consider the identification and prevention of lung impairments due to exposure to various contaminants, so the time may have to come to find a broader title. There is yet another reason for change. The "miners' disease"—to revert to the old popular term—is not only the concern of physicians and the affected persons or their families; like all occupational hazards, it is the concern of policy-makers and indeed of the general public. Of course, the dedication of medical practitioners, engineers and other technical specialists will continue to be required to fight lung diseases; indeed the skills of these professionals will need to become ever more sophisticated. At the same time, the involvement of governments and representatives of employers and workers is going to become keener as time goes on. We believe there is now a need to use simple words that all concerned can understand.

If I harp on this somewhat, it is not for concern about semantics. To me, the use of the layman's language is as important as an illustration of one of the major features of the current approach to occupational hazards; I refer to tripartite participation in the assessment of problems, as well as in the design and implementation of effective policies and action programmes.

The emergence, in the mid-seventies, of a new approach to occupational safety and health led the ILO to reorient its activities in that field, while remaining constant in their aim: when the ILO was created, in 1919, in the wake of the first World War, the right of workers to safe and healthy working conditions was established in the Constitution of the Organisation. At the end of a later world conflict, the Declaration adopted in this very State, in the city of Philadelphia, gave the ILO the "solemn obligation to further among the nations of the world programmes which will achieve adequate protection for the life and health of workers in all occupations."

This is the mandate of the ILO for the world of work. We can truly say that the International Labour Organisation has been successful, as evidenced, for example, by the drop in the incidence of occupational accidents in industrialised countries. But much more needs to be done to take into account the growing complexity of labour problems and the high sophistication of new work processes. The ILO programmes feature a multi-disciplinary and integrated approach that has proved well-suited to tackling occupational safety and health problems in developing and industrialised countries alike, in a manner designed to promote both the well-being of workers and the productivity of enterprises.

In the Conclusions which it adopted in 1984 concerning future action in the field of working conditions and environment, the ILO Conference stated that improved working conditions and environment were a positive contribution to national development and a measure of the success of economic and social policy. I believe that good, safe working conditions must be promoted by international as well as national solidarity. If I think of miners, as one does in the context of lung diseases, I am struck by the fact that they often are migrant workers. If they have not been properly protected, if they are affected by the time they return to their home

countries, I am appalled to think of the burden that is placed on those countries, which may not have the infrastructure required to monitor the health status of those workers or the resources needed to compensate disabilities incurred abroad.

It is indeed very true, the U.S. Secretary of Labor made the point at the past session of the International Labour Conference in Geneva last June, that "in some developing countries, compliance with what would be considered human working conditions is not always easy—not because of a lack of concern, but because of a lack of resources to implement measures necessary to upgrade working conditions." This indicated that we still have a long way to go, and if I may again quote the Secretary of Labor, that "the ILO needs to promote the understanding that its labour standards are beneficial to long-term growth and development." I hope that the present Conference will contribute to fostering such an understanding.

The approach which underlies the recent international labour standards on occupational safety and health is dynamic and promotional. We recognise that occupational hazards are man-made hazards and as such can—and must—be controlled. Occupational injury and disease cannot be considered to be the inevitable tribute to progress. We see that, as socioeconomic development progresses, there is a wider acceptance of the fact that a worker's physical integrity and health are assets for the nation and the undertaking. Of course, work continues to maim and kill, sometimes with a vengeance, as in the recent North Sea oil platform catastrophe, at other times more insidiously. The miners or foundry workers who are suffering today from a disease they contracted unawares some twenty years ago are thus the victims of past conditions. Nevertheless, the International Labour Office estimates a total of approximately 40,000 new cases of occupational lung diseases each year. The fight goes on, in the safety and health administrations of member States of the International Labour Organisation, and through the work of the ILO and other specialised agencies of the UN system. I should like to mention here the excellent cooperation we maintain with the World Health Organization. We plan to continue that cooperation in order to avoid duplication of efforts and mobilise maximal resources for the promotion of occupational health.

I understand from a recent report of the U.S. National Institute for Occupational Safety and Health that the "black lung" compensation programme has grown over ten years into an 18-billion dollar programme. This shows that the American miner is well protected, but at the same time highlights the importance of early action. The priority throughout the world must therefore be prevention, through the regular assessment of work places and work practices, regular health monitoring, early detection and reassignment to other duties as required. To give but one example, I would mention that at its 1988 meeting, the ILO's Coal Miners Committee called for the establishment of specialised occupational health services concentrating essentially on preventive functions, to advise employers and workers, and stressed the need for prevention and control measures to be fully integrated in machinery and working processes.

A few years back, the member States of our Organisation made an important statement: they noted that "the improvement of working conditions and environment must be pursued in times of economic recessions as well as in times of economic upturns." A clear political commitment is therefore required at national level, and the ILO will continue to promote and support the efforts made in its member States to devise realistic policies for the protection of workers' health and well-being. Over a number of issues, and lung diseases are clearly among those, technical expertise is of paramount importance in the implementation of action programmes. Your Conference provides an ideal forum for a broad exchange of scientific knowledge and practical experience, and I wish it every success.

INDUSTRY OVERVIEW—VIITH INTERNATIONAL CONFERENCE ON THE PNEUMOCONIOSES

BRUCE W. KARRH, M.D.

Vice President, Safety, Health and Environmental Affairs
E.I. duPont de Nemours & Company, Inc., Wilmington, DE 19898, USA

It is certainly a pleasure for me to be here and participate in this timely conference on such an important subject as the pneumoconioses. I am particularly glad to be able to give the industry overview to the issue and to be with such distinguished fellow participants in the opening session.

One may ask why a health and safety manager from a chemical company is presenting the industry overview to this topic. That is a good question, but it hits right at the central issue in dealing with the pneumoconioses. These conditions can occur, and usually do, in almost any industry and any group of workers. As it happens, though, the duPont Company, my employer, has more than a passing interest in the pneumoconioses. We own a large coal company, Consolidation Coal Company, headquartered right here in Pittsburgh. We also, though, on the chemical side of the company, have many heat sensitive processes and have been a user of insulation materials, some of which in the past has been, or has contained, asbestos.

Some of our processes have used silica and other similar process materials. We also are the manufacturer of asbestos-substitute materials, such as keular aramid fiber. So, as you can see, we have more than a passing interest in the pneumoconioses.

The pneumoconioses are an excellent illustration of some of the issues that industry, and society, face when dealing with chronic illnesses.

Industry has a responsibility to accept those health conditions it caused or contributed to. And this is a responsibility that my company, at least, willingly accepts and carries out. Industry can't, and shouldn't be expected to, however, accept all the ills of our society. We need different, more equitable, means for fulfilling that societal need. Some examples of where various efforts have been put forth which could possibly have industry begin to accept more than it's fair share of some illnesses have been seen in the high risk worker notification legislation which has been introduced, the victime compensatgion aspects which were a prominent part of the superfund reauthorization debate a few years ago, and others. Industries opposition to these measures was not because we didn't want to properly care for those we may have harmed but because of the never-ending nature of the obligation to a poorly defined group.

Another significant issue industry faces is the never-ending litigation that is an integral part of our doing business, especially in the U.S. And again, this is not a desire on our part to not appropriately compensate those we have harmed, but to be able to have some semblance of fairness and equity between the magnitude of the harm we may have inflicted and the compensation which is awarded.

Industry has a sizeable effort to test the toxicity of materials which we handle and make as part of our programs to avoid creating needless societal risks. These efforts are costly, but needed. And we, at least in duPont, are proud of the work we have done and are doing to help assure we can control the risks we may impose.

At duPont, we have, for many years, had an extensive medical surveillance program for workers who may be exposed to asbestos. As newer technologies have come along, we have upgraded that program and added newer capabilities. In spite of this, however, we have had several cases of asbestosis and many more cases of pleural thickening from asbestos exposure.

Our consolidation coal company subsidiary has had some experience with the United States black lung legislation. While we don't have a great many cases of black lung disease, from a medical standpoint we have many current and former workers drawing financial benefits because they are included in the legislative definition of black lung. The issue is distinguishing between coal workers pneumoconioses and "black lung." The former is a disease and a medical issue. The latter is a program and a political/legal issue.

Medical, industrial hygiene and management people are well on the way to eradicating coal workers pneumoconiosis as a disease from American mining. "Black lung" will disappear more slowly as laws and regulations are adjusted to respond to political realities.

Simple coal workers pneumoconiosis was once common in U.S. coal miners but radiographic studies have shown a progressive decline in both its prevalence and its severity. The U.S. "black lung" legislation has gone through several revisionss but, since those of 1981, seem to be more realistic and more capable of appropriately addressing the need for which it was designed.

Another issue that manufacturing industry is increasingly facing is the removal of old asbestos-containing insulation. And industry is not alone. Many of our schools and public and private buildings are faced with the difficult task of removing old, worn, and friable insulation that contains asbestos. This is a significant problem in the U.S. now. How to remove the insulation without creating additional risk.

There is a great need for health professionals to be more knowledgeable in all work-related health and safety conditions, but especially in the area of the pneumoconioses. Conferences such as this provide the opportunity for development of the state-of-the-art and some general concensus around what is known, what isn't and what can be done to both know more and do more. We certainly are proud to be a part of this conference and to participate in the international effort to be better at what we do and hopefully play a part in eliminating, or at least controlling, the preventable diseases.

Thank you again for letting me be with you.

REMARKS TO THE VIIth INTERNATIONAL CONFERENCE ON THE PNEUMOCONIOSES

LYNN R. WILLIAMS
International President, United Steelworkers of America

Mr. Taylor, Mr. Pendergrass, Dr. Millar, Dr. Karrh, colleagues and friends in the fight against occupational disease:

It gives me great pleasure to address this Seventh International Conference on the Pneumoconioses. I am especially proud that, for the first time, the conference takes place in North America. Certainly the conference will spotlight some of the important research under way in the United States and Canada. At the same time, I hope it will give North Americans a better appreciation of importance of the International Labour Organization in the cause of worker health and safety and worker rights generally.

I suspect that many American occupational health researchers, when they think about the ILO at all, have a profound misimpression. The ILO may be seen as a rather ineffectual organization, bound by its own bureaucracy, spending a lot of money to publish a few monographs and reports. And yet in August 1980, when the Solidarity Trade Union was being born in the Gdansk shipyard in Poland, the very first demand of the strikers was that the government comply with a convention of the ILO.

ILO conventions and recommendations are a source of hope for oppressed workers everywhere. ILO Codes of Practice can be tools in the hands of trade unions struggling to improve working conditions. Of course the ILO can be bureaucratic; its documents can be bland. After all, the organization has to reconcile the views of workers, employers and governments; developed and developing countries; the Socialist Bloc, industrial democracies and the Third World. But it is that very diversity, and the need to balance differing views and interests, that give ILO instruments and codes such force. Nor are they only a matter for underdeveloped or undemocratic countries. The United States has ratified only a handful of ILO conventions; despite lip service to the principles of ILO, the United States has not always been in compliance with them.

This is a research conference. Its immediate purpose is to collect and report scientific data, not to debate political issues. But I hope you will keep in mind that the ultimate purpose of this conference is not research in the abstract, but research in the service of worker health. The right of every person to a safe and healthful working environment is, at base, the reason this conference exists. The ILO was not created merely to provide funding to scientists, or impressive studies for our bookshelves. The fundamental mission of the ILO is human welfare—in this case the eradication of occupational disease. Of course the same is true of NIOSH.

It is especially gratifying to be in the presence of so much expertise, from so many parts of the world. With us this morning are occupational physicians, epidemiologists, toxicologists, industrial hygienists, and public health officials. Individually, and collectively through the ILO, NIOSH and other organizations, you are a tremendous resource in the fight against occupational disease. The great gains we have made in understanding and controlling workplace hazards would not have been possible without your technical knowledge and professional dedication. You have much to be proud of.

But in your daily work, I hope you will remember and join with those who have another kind of expertise, another source of dedication. Workers who face hazards every day on their jobs are also experts in occupational health and safety. They know firsthand the dangers of work and the practical problems of control. Frequently they are the first to identify an occupational disease. It was, for example, the miners of uranium-bearing ores in the Erz Mountains of Ventral Europe who first described radiation-induced lung disease to Georgius Agricola more than 400 years ago.

And I should not have to remind you that effective control of occupational hazards has usually come only through political action by workers themselves and the unions which represent them. I sometimes hear it said that occupational health and safety is a new issue for the trade union movement. Nothing could be further from the truth.

One example comes from the early textile industry in Massachusetts. The workers were mostly women. They were represented by one of the first North American unions, and led by a remarkable labor leader named Sarah Bagley. In 1845, they marched, agitated, and petitioned the state legislature for shorter hours and better ventilation in the mills in order to combat a "wasting sickness" they correctly attributed to cotton dust. Of course, the legislature did nothing, citing a possible competitive disadvantage with Connecticut and Rhode Island if Massachusetts attempted to regulate, and suggesting that the real solution was to be found in the wider spread of Christian principles among the mill owners.

It took more than 60 years for the medical profession to catch up to the Massachusetts women by identifying their disease as byssinosis. The British Factory Inspectorate began to look

at the problem in about 1908. Effective regulation in the United States did not come until 1978.

Safety and health concerns were also evident in the early labor struggles in mining, steel, and other industries, sometimes in the context of shorter hours, or union-sponsored benefit programs for injured members—sometimes more directly, in demand for improved working conditions. For example, the first effective dust controls in the Quebec mines came only after a 5 month strike in 1949. In short, workers have always cared about health and safety. But despite their best efforts, and the efforts of a few enlightened health professionals and government officials, it took the rise of strong trade unions to bring real reform. Even then, it took decades of hard work through collective bargaining and political agitation to achieve the protection workers now enjoy.

That is not just the lesson of history, it is a lesson we must learn every day. In countries where worker rights are recognized and a strong trade union movement exists, working conditions are safer and more healthful. But the inverse is also true. I ask you to consider whether a country or a company which denies its workers the right to a decent wage, the right to organize a trade union, the right to speak out about unfair practices, will voluntarily provide a safe and healthful workplace. You cannot believe in occupational health unless you also believe that workers should have the right to do something about the hazards they face.

Perhaps the most important development in occupational health in the past decade is the right-to-know movement. That movement has a simple goal—that workers should have the right to all information affecting their health and safety. In the United States we have mostly achieved that right through the OSHA Hazard Communication Standard, EPA regulations, state and local laws, and many collective bargaining agreements. Canada and the European Communities have adopted new chemical information systems. Worldwide, the phrase "right-to-know" is coming into general use.

Achieving the right to know has not been easy. In the United States, the attitude of many companies and some health professionals was that workers didn't need, couldn't understand, and might even misuse specific chemical information. It took years of effort by unions and environmental groups to get effective laws on the books. It required public education, lobbying, legal action, extensive participation in rulemaking, and plain hard work. I hope you will understand that effort for what it was—a profound complement to the research community you represent. What we wanted was the right to know the results of your research as it applies to our workplaces, the right to know chemical names so we could effectively use the knowledge you helped gain. If there was ever any doubt about the importance of your work, not as abstract research, but as a tool for eliminating hazards, surely that should dispel it.

I hope the right-to-know movement can point the way to a more effective coalition between scientists and those who depend on scientific research to improve the workplace. For our part, the trade union movement will work to ensure that occupational health research enjoys the funding it deserves. Without us, such agencies as NIOSH would never have been created. But we can do more.

What workers need from you in return is, quite simply, the truth. First and foremost, the research you do must be thoughtful and objective. But we hope you can do more. We hope you will choose your research objectives, not solely on the basis of scientific interest or available funding, but by asking what we need to know to best protect workers. And we hope you will add your voice to the effort to win worker rights and establish safer conditions around the globe. That is the mission of the ILO; that is the tradition of public health. You stand in a long line of researchers who fought for public health, from the early epidemiologist John Snow, who in 1854 identified and then destroyed the Broad Street cholera pump in London, to Alice Hamilton who early in this century established occupational medicine in the United States. Such scientists are objective researchers, but they are not "disinterested"—they are passionately committed to human welfare.

That passion, indeed, should motivate us all. Safety and health in the workplace must be a shared commitment, a common concern. We ask only that you work with us to ensure it.

A GOVERNMENTAL PERSPECTIVE ON THE PREVENTION OF OCCUPATIONAL LUNG DISEASES

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INTRODUCTION

Thank you. I am very proud that the ILO asked NIOSH to co-sponsor this VIIth International Conference on the Pneumoconioses.

This summer in the United States we have had exceptionally warm weather. Almost every day we have been setting new records for high temperatures. It seems this Conference has followed the trend and has also proven exceptional. We have over 1,000 participants here from 50 countries; both are new records for The International Conference on the Pneumoconioses!!

Thanks to each of you for coming. As I traveled in many of the countries represented here, I always received the finest hospitality. I would like to say "Thank You" to each of you in your own language; instead I will simply welcome you and wish for you the same fine hospitality in my country that you have shown me in yours.

It is fitting that the VIIth International Pneumoconioses Conference should meet this week, in this place. This week, 124 years ago, delegates from 16 European nations met in Geneva, Switzerland, and founded the International Red Cross. The new organization had one clear purpose—to alleviate human suffering. We gather here committed to a similar noble purpose—alleviating the suffering of workers by preventing death, disease, and disability caused by the pneumoconioses.

It is also fitting that we meet here in Pittsburgh, Pennsylvania. For in 1869, almost 120 years ago, Pennsylvania was the first U.S. State to pass a law providing for the inspection of coal mines.

BACKGROUND

I have been asked to provide you with a brief overview of The Prevention of Occupational Lung Diseases, from the perspective of the U.S. Government. As you no doubt have realized from listening to my predecessors at this podium, there are several agencies of our federal (central) government who are involved with this problem; it would be difficult for any one of us to delineate a *single* U.S. governmental perspective. However, a month ago, I began my 8th year as Director of one of those agencies, the National Institute for Occupational Safety and Health (NIOSH). So, I can share with you a personal professional perspective based on my experience in that assignment.

But first, those of you from other countries may appreciate some brief explanation of the various U.S. agencies active in this field whose names, or rather initials, you have heard or seen in the Program. I will attempt a brief orientation to the principal federal governmental agencies involved.

In 1970, the U.S. Congress passed a law, the Occupational Safety and Health Act, which is fundamental to the subject of this conference. It created two of the agencies from whose Directors you have already heard. The "Occupational Safety and Health Administration" or "OSHA" is directed by Mr. John Pendergrass. "The National Institute for Occupational Safety and Health" or "NIOSH" is in my charge. As Mr. Pendergrass told you, OSHA, which is part of the U.S. Department of Labor, is responsible for promulgating and enforcing standards for the workplace. NIOSH, which is part of the U.S. Department of Health and Human Services, is responsible for conducting laboratory research and field investigations, for training professionals, and for recommending standards.

As regards mining specifically, there are two other agencies at work. These are the "Mine Safety and Health Administration" or "MSHA", created by the Federal Coal Mine Safety and Health Act of 1969 (and its amendments of 1977), and the oldest federal agency in this field, the "Bureau of Mines" or "BOM". "BOM" was created in 1907 in response to a major mine disaster in Monangah, West Virginia, where 400 miners, mostly non-English speaking immigrants, were killed. MSHA, which is part of the U.S. Department of Labor, is responsible for setting and enforcing standards in mines; the Bureau of Mines, which is part of the U.S. Department of the Interior, conducts research on problems related to mining.

To oversimplify then, OSHA and MSHA are agencies which regulate the workplace, while NIOSH and BOM are agencies which principally conduct research and disseminate information. Please note that we have all joined happily together with the ILO to co-sponsor this conference!

National Perspective Rooted in Heritage

Our central governmental perspective on any subject reflects the traditions of our culture and history as a nation. In this

regard, America has traditionally emphasized the sanctity of human life in its fundamental governing principles. Our first national document—the "Declaration of Independence" of 1776, depicted Life (along with Liberty) as an "inalienable right" of each citizen.

Hence, a governmental perspective on the prevention of occupational lung disease begins with a reaffirmation of the right of workers to *live*. By their very nature as human beings, the lives and health of workers should take priority over all else that concerns us in the workplace. These same principles were later reflected in the Constitution of the United States, and even later in the Occupational Safety and Health Act which seeks "safe and healthful working conditions for every working man and woman." So whatever we do as a nation that affects workers should be measured first and foremost against one standard—the prevention of harm, (i.e., the prevention of disease, injury, and death) caused by work.

Are we meeting the standard? You be the judge. In the U.S. each year about 8,000 workers are killed, 10 million others suffer significant injuries, and perhaps 400,000 suffer occupational diseases.

Perspective Guided by Analysis

As part of a national Institute focusing on occupational safety and health, we in NIOSH see our principal role as one of exercising professional leadership to assure that our citizens understand the burden and the nature of occupational disease and injury. We also feel obligated to assure that they understand what can be done to prevent these problems. In exercising this leadership, we, NIOSH, in 1982 began to delineate and prioritize the occupational health problems of our country. For the first time in the U.S., we developed a list of the ten leading occupational diseases and injuries using the following criteria: (1) frequency of the problem; (2) severity in the individual case; (3) amenability to prevention.

As most of you know, we reached the conclusion that occupational lung diseases deserve first place on the list; i.e., these occupational diseases of the lungs constitute the most important occupational disease problem in the United States.

Our view of our role as a national leader demanded also that we describe a strategy by which each of the 10 leading occupational problems could be prevented. To accomplish this, we convened two National Symposia at which proposed strategies for preventing each problem were developed. This process has resulted in an unprecedented, broad-based, understanding of what we as a nation can and need to do to reduce the burden of our most important occupational diseases. These ten proposed prevention strategies are now published. The *words* exist, the actions to fulfill the words are another matter.

Perspective Inspired by Experience

Being here with you in such a "melting pot" of professionals from all over the world seems to compel me to reflect on "how it was" 20 years ago. At that time I was working hard in the beginning stages of the global smallpox eradication campaign. It was a difficult, frustrating, and yet exhilarating time. Many apparently wise people said smallpox eradication could not be done and that we were deranged even to try. Yet smallpox eradication *was* done. In the process, East and West, the industrially developed and the industrially developing, the aligned and the non-aligned, all joined hands in pursuit of a common goal. No barriers to eradication were so great that they could not be solved.

As a result, smallpox has been extinct now these 10 years. Even in India where smallpox was thoroughly entrenched for thousands of years, young people recognize "smallpox" only as a vague historical entity without contemporary relevance. Smallpox is gone because smallpox eradication was an idea whose time had come.

Perspective Provokes a Challenge

Now, I will gently ask this audience two questions, (1) are the pneumoconioses—any of them—eradicable? (2) Is their eradication an idea whose time has come? I believe the answer to the first question is "yes". The pneumoconioses *are* eradicable. While eradicating smallpox we learned that in order for a disease to be eradicated, it should have the following characteristics: (1) The source of the hazard is obvious; (2) Those at risk are predictable; (3) An intervention is available that protects those at risk from the hazard.

With the pneumoconioses, (1) the source of the hazard is obvious. As was written in the Proposed National Strategy for the Prevention of the Occupational Lung Diseases, "occupational lung disease is caused by inhalation of toxic substances present in the work environment." Work-related lung diseases may "be further complicated by cigarette smoking and its independent or synergistic effects on the lungs." (2) Those at risk are predictable, namely workers exposed to the airborne toxic substances. For the most part, workers who smoke are at greater risk. (3) A specific intervention is available which protects those at risk from the hazard, namely eliminating inhalation of the toxic substance. This can be done by eliminating the toxic substances in the environment, and/or by preventing their inhalation from the environment. This process is greatly abetted by not smoking cigarettes.

Those are the reasons why I believe that the pneumoconioses are eradicable.

Is This the Time?

Now, is eradication of the pneumoconioses an idea whose time has come? Ah, there's the rub. Smallpox vaccine was introduced 200 years before global smallpox eradication was initiated. Yet when the time came, after 200 years of preaching, eradication was accomplished through a major outpouring of international cooperation, and national commitments by many countries. Here, I think we have a problem. Eradication of smallpox required that we *exceed* the ordinary effort and do more than was minimally necessary, to assure the outcome. And this rule is generalizable. After all, to achieve victory in any field requires a sacrificial commitment. In fighting smallpox there was an international willingness to use every weapon, maximally, to reach zero cases. It meant going on a "wartime footing." And here, I'm afraid we face a formidable problem. In the field of oc-

cupational safety and health, we are far too accustomed to doing the *minimum*, not the maximum. Rather than doing all that we can conceive in prevention, we are much more likely to do as little as we can get away with. Instead of overwhelming our occupational health problems with a noble extremity of effort, we often settle for a marginal token contribution. In this field we are much too infatuated with the "small, economy model;" far too prone to compromise.

(As an aside regarding sound investment, I would point out that the total financial commitment of the United States to global smallpox eradication, is recovered *every four months* in savings of the costs of the programs on vaccination and quarantine we previously *had* to maintain in order to keep smallpox out!)

Like all conferences, this one ultimately will be a Conference of words. But may we now add a new word—the word "eradication"? Unless the word is spoken, the outcome will never happen. And what better group to begin to speak this word and to probe its requirements, than this group, which knows more about The Pneumoconioses than any other group in the world.

Is it possible that the next one of these international conferences might be titled "The VIIIth International Conference on the *Eradication* of Pneumoconioses?" Think about it.

Thank you.

WELCOME ADDRESS OF THE INTERNATIONAL SOCIAL SECURITY ASSOCIATION

ROLF HOPF

Member of the Bureau of the International Social Security Association

Ladies and Gentlemen:

It is an honour and a pleasure for me to extend to you the greetings of the International Social Security Association on the occasion of this Conference of such long-lasting tradition. For the seventh time, specialists from the entire world have gathered here in order to exchange their experiences on the protection of the health of workers against the risks of exposure to dust in the workplace. The new knowledge acquired here will be applied to measures for workers' protection and thus contribute to the prevention of pneumoconioses and mitigate and cure the effects of these diseases.

The struggle against pneumoconioses is not only a task confronting medical science. On the contrary, together with medical care, there must be an assurance that adequate measures are taken to ensure that sick workers are provided with social compensation. The International Social Security Association has set itself the target of supporting and improving measures for the protection, promotion and development of social security through its specialized activities. Today, the ISSA works in an advisory capacity on a voluntary collaboration basis in more than 159 countries throughout the world. The ISSA attaches particular value to the protection of workers against lung diseases caused by dust. This is exemplified by the fact that the ISSA has established a special section for the mining industry, which is one of the nine sections towards which the ISSA has oriented its focal activities.

The worldwide collaboration of all occupational safety and health institutions has led to a coordinated struggle against pneumoconioses. The declining figures for these occupational diseases demonstrate that the common effort has produced fruitful results. On the international level, social security institutions or governments, ensure that workers are guaranteed social security as well as protection at work through national regulations. To us it seems evident that workers suffering from dust-related lung diseases should benefit from financial compensation, although the principles for this were only established a few decades ago.

Around 20 years ago, specifically in the year 1969, our friendly host country decreed a federal programme for the protection of miners. As a result, it was guaranteed that miners suffering from lung diseases would receive a monthly cash payment, or, in the event of death, their relatives or heirs would receive a pension.

It is to the credit of specialists in medical science and practice that their work has established the link between the causes and development of pneumoconioses and that today, there are not only possibilites for their prevention and early detection, but also for curative treatment. Although we can look back with pride on the past success in health protection, problems still remain which demand urgent answers. We cannot yet affirm that the problems have been satisfactorily solved. This is precisely why it is so important that we remain in contact, in order to jointly seek solutions.

The ISSA has set itself the target of encouraging and supporting international exchanges, to provide guidelines and inspiration, and of promoting further development. Besides other activities, the ISSA, in collaboration with the International Labour Office, organises a world congress on occupational safety and health every three years. The next one, the XIIth World Congress on Occupational Safety and Health, will take place in my homeland in the city of Hamburg in May 1990. Its theme is "A Safe and Healthy Working Environment—a Task for the Enterprise and for Society." The hosting associations for statutory accident insurance are expecting about 2,000 participants. The Congress will provide the most recent information on the development of workers' health protection for all specialists in the field of occupational safety and health. Regular contacts and exchanges can contribute to the improvement of the working environment all over the world and to the reduction of the burden placed on the community by a constantly rising number of accidents at work and occupational diseases. In this context, the World Congress provides an appropriate forum for discussion. As President of this Congress, may I already today invite you and tell you how delighted I will be to greet you in Hamburg.

I hope that this Pneumoconioses Conference will be a successful experience and that you use the information you acquire here for the benefit of workers in your native land.

ADDRESS TO THE VIITH INTERNATIONAL CONFERENCE ON THE PNEUMOCONIOSES ON BEHALF OF THE INTERNATIONAL COMMISSION ON OCCUPATIONAL HEALTH

PREMSYL V. PELNAR, M.D.

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It is an honor and privilege for me to address this distinguished assembly on behalf of the International Commission on Occupational Health. The ICOH, under its original name Permanent Commission, was founded by a private group of scientists in 1906 and thus it is the most senior of international organizations working in the field of occupational health. It was already 13 years old when International Labour Organization and Office were created. The birth of ILO was accepted by the Permanent Commission with great satisfaction as it was seen as a great ally with official standing in protection of the workers' health. Indeed the first Secretary General of the Permanent Commission, Dr. Luigi Carozzi, was appointed Head of the Industrial Hygiene Section of the ILO and served in this capacity for full 20 years. In various periods of time such personal unions between the ILO and the Permanent Commission—ICOH were successfully repeated. Let us just mention the ILO periods of later President of ICOH Dr. Robert Murray, and the ILO period of the present Secretary Treasurer of ICOH, Dr. Luigi Parmeggiani. For many years now the ICOH has enjoyed a special position with ILO. Our representatives at many occasions were allowed to actively participate in the ILO meetings. Some members of ICOH were invited for working in the ILO institutes of occupational health in developing countries. Many others were called as experts in preparing international recommendations and other ILO legal instruments. On the other hand, members of ICOH come from a great number of countries in which they frequently occupy important positions. They can effectively encourage the implementation of the ILO instruments and guidance in practice of occupational health in their countries.

A good example of cooperation for mutual benefit is the field of pneumoconiosis. Silicosis and coal-workers' pneumoconiosis have been a common concern for many years and many conferences. Asbestosis appeared prominently on the scene later, in 1960. The UICC/Cincinnati Classification of radiograms covering more specifically asbestosis was developed by an international group of scientists many of whom were members and leading personalities of ICOH. The ILO accepted it, gave it its official sanction as "the ILO Classification" and provided its world wide dissemination accompanied with valuable standard films. Up-date of the Classification prepared by an ICOH Task Force is on the agenda of this Conference. Another example: Several ILO Meetings of Experts at which the ICOH was always represented addressed the question how to use asbestos safely. On the basis of this work eventually the ILO Convention Concerning Safety in the use of Asbestos was passed and accepted in 1986.

The present status of ICOH as a non-governmental cooperating organization with the United Nations gives us a particular privelege to be close allies of ILO in its endeavors toward protection of workers' safety and health. Let me thank ILO for accepting us in this capacity, and let me wish ILO and this conference the best success.

OPENING ADDRESS BY THE REPRESENTATIVE OF THE WORLD HEALTH ORGANIZATION

BERNICE GOELZER

Office of Occupational Health, World Health Organization

On behalf of the Director-General of the World Health Organization, I would like to greet the organizers and sponsors of this VIIth International Pneumoconiosis Conference, as well as all the participants, and wish for a very successful exchange of knowledge and experiences with the objective, not only of improving our skills for the prevention of pneumoconioses and other occupational lung diseases, but, more important even, of finding ways to put these skills into practice. So much is known about the etiology of silicosis and other pneumoconioses, so much is known about evaluations and control of exposures to dust in the work environment; however, pneumoconioses still claim countless victims, everyday, all over the world, as exemplified by the Representative of the International Labour Organization. I believe that, on a world-wide basis, the greatest challenge for us, occupational health professionals, and for all concerned with the health of workers, is to apply the vast knowledge which is already available in our field.

Work is necessary. Each piece of work accomplished, each pound of ore extracted, each pound of steel produced, each item manufactured, constitutes an essential link in a chain which allows the survival of the human race. All work is important, and the greatest injustice is that, in order to accomplish it, human beings may lose their health, and even their life, or may have an unacceptable quality of life. Scientists, occupational health professionals, technical personnel, international organizations, scientific institutions, governments, enterprises, workers organizations, all should join hands in the fight against such injustice. Keywords for this are collaboration and commitment.

The Director-General of the World Health Organization has been requested by Member States, on many occasions, through a number of resolutions, to give special attention to the health of working populations, as can be exemplified by the following extract from Resolution WHA33.31 (May 1980):

> "... to support the developing countries in ensuring safe working conditions and effective protective measures for workers' health in agriculture, in mining and in industrial enterprises which already exist or which will be set up in the process of industrialization, by using the experience available in this field by both industrialized and developing countries,...".

Through its Office of Occupational Health, and in collaboration with the International Labour Organization, the World Health Organization aims at the prevention of occupational diseases and at health promotion in the workplace. The main approaches are to collaborate with countries in the development of their own capabilities to establish and operate occupational health programmes, and to prepare supporting documentation and educational materials. In its activities, the Office of Occupational Health focuses both on the workers, for example, the development of guidelines for the early detection of health impairment, or the development of educational materials for workers, and, on work environment, for example, the development of guidelines for the evaluation and control of occupational hazards.

Only a multidisciplinary approach, by which medical, environmental and required sciences complement one another in an integrated effort, can lead to the prevention of occupational diseases and, beyond, to the promotion of health through the workplace. We should not forget what Alice Hamilton, a very eminent occupational physician, once wrote, with reference to silicosis: "... obviously, the way to attack silicosis is to prevent the formation and escape of dust, ...". While the formation and escape of dust in the work environment is not prevented, nothing is achieved in terms of protecting workers from pneumoconioses; the recognition of a dust hazard, the diagnosis of a pneumoconiosis, the accomplishment of accurate dust evaluations, the establishment of correlations between dusty occupations and lung diseases, are all necessary steps, but which have real meaning only, if and when, they serve as the basis for an adequate control strategy. In fact, the goal of occupational health practice should be to anticipate and control hazards before they can even occur. Control technology for the prevention of occupational diseases comprises the planning and design of control measures, both environmental and personal, as well as their implementation and continuous operation. Therefore, the immense and essential task of protecting the health of workers can only be accomplished through close collaboration and joint efforts by occupational health professionals, such as occupational hygienists, physicians, nurses, ergonomists, and workers, managers, administrators and governments. That we may all work together for the protection of workers' health.

EVALUATION OF RESPIRATORY HAZARDS IN THE WORKING ENVIRONMENT THROUGH ENVIRONMENTAL, EPIDEMIOLOGIC AND MEDICAL SURVEYS

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HISTORICAL AND CURRENT CONTEXT

Respiratory disease consequent on work in dusty trades has been recognized since ancient times when man first turned to tools to help him to exploit the riches at the earth's surface. In the past, distinctions have been blurred between various disease processes involved (fibrotic, infectious, malignant), all of which may follow occupational exposures.[1] The term pneumoconiosis was introduced in the 19th century to describe the rather specific nature of the lung's fibrotic reaction to inorganic dusts, such as silica, coal and iron. In keeping with its Greek roots, the term is currently defined by the World Health Organization as the "accumulation of dust in the lung and tissue reactions to its presence."[2] Over the past century, industrialization, the growth of populations, and the increased demands for the raw materials of the earth's crust have led to an increase in the number of workers whose jobs expose them to mineral dusts.

In consequence, the early years of this century saw an increase in the burden of dust diseases in industrialized countries, and post World War II in the newly industrializing countries. There are no global estimates of the number of workers currently at risk; Table I refers to the 1970's[3-5] and is mainly based on information furnished to the International Labour Office by those countries which report on their mining, tunnelling and quarrying operations.[3] The considerable between country differences in rates are no doubt largely due to differences in methods of reporting. Nor is the coverage comprehensive.

Not only the distribution but also the nature of some of the pneumoconioses may be changing. For instance, since the first International Pneumoconiosis Conference held in Johannesburg, in 1930,[6] the profile of diseases such as silicosis appears to have changed, at least in the large controlled industries.[7,8] Whereas in the early decades of this century, these were diseases which disabled young and killed prematurely, they are now increasingly diseases of primarily radiologic manifestation with little morbidity or impact on longevity. Reasons no doubt include improved living standards, better medical care and tuberculosis control in addition to improved environmental controls at the workplace.[8]

*Career Investigator, Medical Research Council of Canada.

However, outbreaks of acute disease continue to appear, usually in new processes or small uncontrolled industries, even in the technologically advanced countries.[1,8-12] The mid-century epidemic of asbestos-related disease is another example of the failure to apply known control technologies to commercial exploitation, in this instance due perhaps in part to the exigencies of World War II.[13]

The perspective envisaged for the VIIth International Pneumoconiosis Conference as reflected in the themes selected for discussion is considerably broader than that of the First Conference, held in Johannesburg in 1930. The players are also different. Clinical, engineering and industrial hygiene scientists were the major contributors at the First Conference, with the major contributing laboratory sciences being pathology and microbiology. Today all branches of the clinical laboratory sciences are represented, in particular, epidemiology. This is a late comer on this scene and has become increasingly important as it adapted the techniques developed for the study of epidemic infectious disease to the study of chronic noninfectious disease of multifactorial etiology. It is well accepted that environmental and medical surveys can be used to evaluate hazards in the working environment. However, today I wish to indicate how they may be combined using the approaches and methods of epidemiology, and statistics which together offers 3 powerful tools: i) a basis for sampling when numbers to be studied exceed resources; ii) a means of estimating power when sample size is limited (workforces are after all finite) and iii) the methods of analysis which enable the simultaneous consideration of more than one factor in these diseases of multifactorial etiology. The examples chosen to illustrate this presentation are from my own field of endeavour.

ROLE OF EPIDEMIOLOGY

Epidemiology is defined as the study of the "distribution and determinants of health related states or events in specified populations and the application of this study to the control of health problems."[14] I agree with those who argue that it is a discipline rather than a science, i.e., a field of learning or practice applicable to the study of natural phenomena (biological, sociologic or other), rather than a science, i.e., a systematized theoretical body of knowledge about a particular category of natural phenomena.[15] As such, it is a

Table I

Selected Information on Dusty Occupations in Various Countries: Number of Current Workers at Risk, Reported Prevalences of Pneumoconiosis (total cases) and Incidences (new cases each year) per 1000 Exposed Workers

Continent /country	Sources of exposure	Years	Number at risk	Total cases/ 1000	New cases/yr 1000
Europe					
France	mines, pits, quarries	1977	89,391	51.1	5.1
Germany	coal mines,	1977	111,992	228.9	7.5
	other	1977	c.7,000	116.9	2.4
Poland	mines, other	1978	c.90,000	34.4	3.7
UK	coal mines,	1977	252,600	119.1	2.1
	other	1977	5,800	103.4	9.4
America					
US	coal	1973-78	118,579	'20.0	na
Ontario	mining	1970	17,355	na	1.4
Quebec	mining	1967-77	12,556	na	1.8
Mexico*	mining	1973	4,815	8.9	8.9
Peru	not stated	1976	56,819	c.36.0	na
Australia					
NSW	coal	1973-76	15,970	28.8	na
	other	1976-78	4,484	10.6	0.5
Queensland	coal	1968-72	1,387	na	6.4
	other mines	1968-72	3,903	na	8.1
W Australia	mines	1978	6,923	27.0	2.6
India	mines,other	1973-77	c.600,000	c.25.0	
Africa					
Kenya	small mines	1977	3,359	0.0	na
S Africa	hard	1977	19,504	na	11.1
	rock	1977	300,357	na	1.6

Table shows information derived mainly 3 countries reporting to ILO on the number of subjects exposed in dusty occupations as well as pneumoconiosis rates: (ref 3): figures for Ontario, Quebec, and for S Africa were derived from ref 4.

* refers to 1 company only; each company keeps its own statistics

discipline which must be of interest and of use to all participants here today, whatever our branch of science.

Epidemiology can be used to address in populations the same issues which a clinician addresses in the management of a single case: namely, the description and recording of its features (the history, examination and laboratory tests); the explanation contained in the diagnosis and the formulation of prognosis, and in light of the above the planning of the management and the evaluation of its success. Thus population based (epidemiologic) studies may have as their objective, description (prevalence or incidence of disease) and/or explanation (who in a population is affected and why: who is not and why not). These findings can then be used to formulate corrective measures, and once in place, their effectiveness can be evaluated by further studies. The key in the clinical as well as the public health management of occupational disease is how to establish the link between the biologic outcome of interest (abnormality, dysfunction or disease) and the pertinent exposure.

ESSENTIAL ELEMENTS OF AN EPIDEMIOLOGIC SURVEY

These can be summarized in four interrogative adverbs: why (the objectives of the survey), how (its design), who (the target population or workforce(s)) and what is to be studied (referring to the measurements made of dependent and independent study variables).[13] Most important is the first, what McDonald calls the "fundamental ingredient of any scientific endeavour," namely, "an obtainable objective or answerable question ... clearly and unambiguously defined."[16] He also recommends that a subsidiary question be asked: "and what will I do with the answer?" Thus an epidemiologic study is neither "a data gathering exercise with a nebulously defined purpose and no hypothesis to test;" nor is it a study "which misses a truth because it is buried in a mass of data." These are both popular misconceptions which relate to the false belief that the key characteristic in epidemiological study is that it is based on large numbers of subjects.[17] Indeed some of the most effective epidemiologic studies are very economical in this regard.

Design

At the heart of the scientific method is the experimental design. In its complete form it requires that the researcher have control of all aspects of the study including the option of testing the entire target population (or sampling at random from it); control of the assignment of test units to intervention (exposure) or not, as well as the opportunity to examine all test units before and after the intervention with no loss to follow-up.[16] When study units are cells, or plants or animals, this is possible; when the subjects are human, and exposure the result of natural experiment, this is rarely so. Indeed, the definition of a survey (the word used in the title of this presentation) is "an investigation in which information is systematically collected but in which the experimental method is not used."[14]

Other than randomized control trial, for instance, of tuberculosis drug therapy, most occupational health surveys must of necessity use a less-than-complete experimental design. While the strongest designs include measurements before and after exposure (i.e., are longitudinal or cohort in concept), prevalence (i.e., cross-sectional) designs are often all that is feasible, and are most frequently used for chronic non-malignant diseases such as pneumoconiosis whose onset is difficult to pinpoint. Indeed, the prevalence study has been not inappropriately dubbed the "workhorse" of chronic disease epidemiology.[17]

By contrast, the case control design is an elaboration of the traditional clinical case series, in which clinical case experience is described without reference to the population from which they were derived. The case control study also starts with identification cases of the disease under study; persons without the disease (controls) are then selected from as far, as can be determined, the same population as generated the cases, and the past of cases and controls are compared for evidence of exposure. Hybrid designs, using the case-control approach within a cohort, have been creatively exploited in establishing relationships between occupational exposure and malignant diseases,[18] and they are now increasingly being used in the study of non-malignant diseases such as the pneumoconioses.[17] Nor does the case series study necessarily merit the scorn often accorded it by editors and reviewers: it was after all such a clinical case series reported by a missionary doctor, the surgeon to whom his cases were referred, and the pathologist on the surgical pathology service which first drew the attention of the medical community to the link between mesothelioma and asbestos exposure.[19] Indeed, it has been pointed out that shrewd clinical observation remains the most powerful tool in detecting new disease patterns linked to workplace exposure,[20] also in identifying recognized disease patterns in workplaces or associated with exposures not previously thought to be at risk.[17]

Dose Response Relationships

Dose response relationships form the scientific basis of pharmacology (which deals with desired responses) and toxicology (which deals with undesired responses). In both, dose refers to the amount of the agent delivered to the target organ and retained for a period of time sufficient to evoke a response. In occupational surveys of chronic diseases like pneumoconiosis and chronic obstructive pulmonary disease, dose-response relationships are important in establishing causality.[16,17,21] However, estimates of exposure have until recently, been the only available indicator of dose; obviously a very poor substitute given the low deposition rates and highly efficient clearance of so much of what we breathe in. What is surprising, given the impossible task of represent ing exposure over a working lifetime accurately, is that exposure-response relationships are usually demonstrable in workplace surveys even using quite simple indicators of exposure.

The development of new methods, such as the quantitative measurement of lung dust residue represent a quantum advance in the study of the dose variable and these have already contributed to our understanding of why exposure response relationships differ between workforces. For instance, there is now evidence in support of mass rather than fiber number being the determinant of fibrosis scores for asbestosis.[22] This topic is rightly one of the key themes of this Conference.

New technologies of this sort to obtain the most precise estimates of dose possible may not however always be available, and the value of what is surely the simplest estimate of exposure, the worker's personal assessment, should not be overlooked. Thus several recent community-based studies have shown clear evidence of association between indicators of chronic obstructive pulmonary disease (COPD) such as FEV_1 and occupational exposure to dusts at work, evaluated subjectively by study participants.[23,24] Subjective estimates of personal exposure have also proved as useful as objective dust exposure measurements in demonstrating exposure response relationships in workforce based studies, an observation of relevance in situations where resources for objective environmental control measurements do not exist, for instance in certain industrializing countries.

Modelling Exposure Profiles

Whether or not lung responses are influenced by exposure profiles (such as the occurrence of peaks or gaps in exposure versus steady level exposure) remains a matter of concern, with implications for setting control levels. However it is not an easy matter to investigate. One approach is to use mathematical modelling based on biologically plausible models.[26,27] For instance, in Quebec asbestos miners, temporal patterns of exposure appeared to influence the different respiratory responses;[27] thus for asbestosis, the strongest predictor was cumulative exposure; for pleural change exposure, peaks and residence time of dust in the lung; for airway reactivity, both with early and recent exposure, and for airflow limitation and bronchitis, dust level and dust load over time as well as smoking.

MEASUREMENT TOOLS OLD AND NEW: APPLICATIONS AND EXAMPLES

The effect of measurement error, whether of exposure or response, is attenuation of exposure response relationships. This has led to concerted efforts to improve standardization and reduce measurement error. In the case of the chest radiograph, the traditional health measurement tool in pneumoconiosis surveys, the ILO has taken the lead in standardizing techniques of film reading.[28] Subsequently, respiratory questionnaires and lung function tests have been included in most workplace surveys,[1,17] originally in support of the diagnosis of pneumoconiosis, but subsequently as outcome measurements in their own right to characterize among other things airway function and standardization procedures for their use in surveys has been developed by various professional bodies.[29,30] Despite its modest status (it is cheap and despised by clinicians as inaccurate), the respiratory questionnaire has proved a surprising but powerful measurement tool. For instance, exposure-response relationships for the complaint of shortness of breath when hurrying on the flat are readily demonstrated in asbestos exposed workers, consistent with the clinical conviction that shortness of breath is an early, characteristic and essential feature of asbestosis.[8,13] Recently there has been a resurgence of interest in this and other symptoms such as wheezing as response variables coinciding with the increasing appreciation of the fact that acute and chronic airway responses occur following a wide range of occupational exposures.[31]

Pulmonary Function Tests

Obsession with the importance of reproducibility of lung function tests for epidemiology studies often led researchers to exclude subjects whose results failed to meet specified criteria for acceptability.[29] A careful analysis by one research group of subsequent health experience in subjects with and without test failure brought to light a very interesting source of bias, namely, that test failure in itself carries a greater chance of a less unfavourable outcome.[32] This observation has now been confirmed in several cohorts and the underlying mechanism(s) are under investigation.

The "healthy worker effect" is a term originally coined to describe the lower mortality experience of employed workers compared to the general population,[14] presumably due to their better than average health status. There may be a similar explanation for the better than average lung function often seen in workers engaged in physically demanding jobs. For instance, in a survey of Paris workers employed in a number of plants, younger workers with pollutant exposure had consistently better (not worse) values for FEV than those whose jobs did not involve exposure; in older workers the situation was reversed.[33] Nor is this experience unique.[34] It is also biologically plausible: dusty jobs are traditionally heavy jobs likely to attract those of above average performance. This potential source of bias has implications for analysis as well as for interpretation, and suggests that cross-sectional studies of older workers are likely to underestimate exposure effects on lung function even when external reference values are used to take account of confounders.[35]

Complex Health Measurements as Tools in Epidemiologic Studies

The laboratory measurements now available to characterize pulmonary abnormality, dysfunction and disease are remarkable for their variety and precision, but also for their complexity and cost and their optimal integration into research into pneumoconiosis and other diseases of occupation can be challenging. This is often possible through the use of hybrid study designs, such as case-control within a cohort or within a prevalence study. This allows the target population to be described by low-technology measurements (e.g., questionnaire, job, and if necessary lung function or x-ray), and within this framework, stratification by exposure, or response, or both can be done prior to sampling. In this way it is possible to address well formulated objectives by comparison of selected but small groups of subjects using high technology tools. Note the population description should respect basic epidemiologic principles including a complete definition of the target population with an assessment of selection bias into and out of the workforce (respectively the "healthy worker" effect and the "survivor" effect). For example, it was possible to use questionnaire, x-ray and lung function data gathered in a cross-sectional study of the Quebec asbestos miners and millers[36] to select smaller subsets of subjects in whom further measurements were carried out to address additional questions on the early effects of exposure,[37] and whether lung geometry was a risk factor for the development of asbestosis.[38]

UNRESOLVED ISSUES, FUTURE RESEARCH AND DIALOGUE

A conference like this brings to light many unresolved issues, and perceptions vary as to their importance. One which deserves careful scrutiny is how best to evaluate the effectiveness of current pneunoconiosis control measures including health surveillance and environmental control levels. Most current survey research is descriptive (for instance, health hazard identification or evaluation) or etiologic (examining exposure response relationships), little is evaluative (determining the effectiveness of controls). Despite the probably billions of chest radiographs, and the probably millions of spirometric test records carried out in health surveillance programs, it is still not clear whether medical surveillance and/or current environmental control levels for silica[12] and asbestos[35] if respected, do indeed protect human health.

A second and related question concerns the links between pneumoconiosis and tuberculosis, an issue of great importance in those countries of Africa and Asia with both high tuberculosis infection rates, and extensive mining operations.[4] Under such circumstances, mine medical services may be responsible for extensive surveillance and treatment programs which could provide the framework for important research. For instance, a recently completed study in goldminers in the Orange Free State evaluated several short tuberculosis treatment regimens, and in a subset of the data showed that continued mining exposure while on treatment did not affect the outcome unfavourably.[39] This important finding went contrary to the current practice which precluded miners on treatment for tuberculosis from further underground service, in the belief that continued silica dust exposure diminished the chance of treatment success. Nor was outcome unfavourably influenced by the presence of silicosis. As a result of these findings, regulations now permit miners to continue in underground service, while under treatment, without loss of income, an important consideration in a largely migrant and rurally based workforce.

A third issue is how better to exploit the many existing data banks (including case registries and health surveillance data) for research and health control purposes. For instance, the Swedish silicosis case registry,[40] set up in 1933, has been used to study i) progression (shown to be greater if cases continued in a job with exposure after the earliest radiologic manifestation); ii) the relationship to lung cancer (silicosis cases have a greater risk than non-cases); iii) tuberculosis rates (still a frequent complication in cases of silicosis, even after the introduction of drug therapy in 1951). The PATHAUT data file, another registry containing machine readable autopsy reports on some 33,000 South African miners,[41] has also been used as a data base for a case control study which showed hard rock mining to be a risk factor for emphysema.[41] Other uses of case registries will be reported at this meeting.

Finally there is the issue of dialogue, within and between disciplines, within and between researchers, and within and between professionals. Each of us tends to believe the other is ignorant of what we have to offer. Dialogue is less difficult in the context of a conference such as this, when participants are free of daily tasks; dialogue is also less difficult perhaps in institutes dedicated to a common theme "Dialogue" should also include user-responsiveness: those who are in the workplace on a daily basis are often the first to perceive the unexplained or the unexpected and yet their comments are often not sought or heard. Finally, research into the diseases of occupations (whether it be basic laboratory research, cellular biology, environmental or clinical research) should always and only be driven by hypotheses which have biologic credibility as well as user plausibility, in the context of good study design. In addition, if there is a sound answer to Dr. McDonald's question: "and what will I do with the information" before starting a survey, then the survey is likely to be one which will furnish a useful evaluation of respiratory hazards in the working environment.

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PROGRESS IN ETIOPATHOGENESIS OF RESPIRATORY DISORDERS DUE TO OCCUPATIONAL EXPOSURES TO MINERAL AND ORGANIC DUSTS

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INTRODUCTION

Thank you for giving me the honour of introducing the theme on progress of Etiopathogenesis of Respiratory Disorders due to Occupational Exposures to Mineral and Organic Dusts.

In the first place, I would like to say how pleased I am to follow Margaret Becklake in the setting of these themes. We both did our Graduate and Postgrauate training in Johannesburg which was the scene of the first of these conferences in 1930. Of course, we were both too young to attend.

Secondly, I have been given a vast field to cover in a very short time. I will paint with a very thick brush on a large canvas. I will concentrate on my personal experiences and views to offer a provocative base to the further sessions of this conference. I trust this will stir up sufficient controversy to satisfy our sponsors.

I note that my remit covers both mineral and organic dusts. On organic dusts my experience is brief—I do not believe that there is such a disease as byssinosis. The biological effects of cotton dust are part of the vast new field of study covered by the term "Industrial Asthmas," which is now a separate field from pneumoconiosis.

SILICOSIS

There are two facets of silicosis research in which we have developed new ideas since the 1930 conference. One is positive and requires explanation, the other I feel is a false lead which requires most serious scrutiny.

Although historical evidence goes back to neolithic times, it was in the industrial revolution that it was realized that exposure to mineral dust could have fatal consequences. By 1912 South African workers had shown that quartz was responsible for these lesions and by the Johannesburg conference it was proved that tuberculosis was the main killer of silicotics. The problem is how does silica do the damage and why is there this promotion of tuberculosis? My views are now considered simplistic and I hope that at a later stage of this conference someone will produce a more scientific hypothesis. I believe that silicosis is a disease of the monocyte macrophage system and the destruction of numerous macrophages by the inhaled quartz crystals produces a local milieu promoting infection from the mycobacteria when they are present. As far as I will go in explaining this are the studies of Tony Allison and Jack Harington. Briefly the quartz crystal is taken up by the macrophage forming phagosomes with the relevant lyzosomes which are released, but fail to digest either the quartz crystal or the wax coat surrounding the tubercle bacillus. The quartz crystal then by some means disrupts the membrane of the phagosome releasing the "enzyme soup" which destroys the macrophage: the unscathed quartz crystal is freed to destroy further macrophages and the bacillus to reproduce.

The other facet which disturbs me is the suggestion that quartz is an important carcinogen. We have as pathologists studied numerous cases of silicosis and exposed a vast number of animals to quartz dust. In all the human cases I know of where carcinoma does occur in silicotics it is either associated with cigarette smoking or much more rarely with radon release. In the experimental evidence only two series of experiments are quoted in which malignancy occurs. I am responsible for one of these studies and our results have been incorrectly interpreted. In 1960 I inoculated quartz into the pleural cavity of Wistar rats. Some of these rats subsequently died of tumour which were not mesotheliomas. In 1962 the experiment was repeated with two further strains of Wistar rats in which a much higher incidence of these tumours occurred. These tumours were subsequently studied by my wife who showed that these tumours were in fact histiocytic lymphomas of macrophage origin. She was unable to produce a significant number of these tumours by using different routes of exposure. It is unlikely in human exposure that silica would reach the pleural cavity.

The other study was carried out by Dave Smith at Los Alamos where Fischer rats were exposed to very heavy clouds of quartz and developed severe pulmonary fibrosis. Some of these animals subsequently died of peripheral carcinomata. These peripheral tumours occur in the animals with severe pulmonary fibrosis and these lesions are not specific for silica exposure.

COAL WORKERS PNEUMOCONIOSIS

When I first became involved in the study of coal workers pneumoconiosis I was informed that the disease could be divided into simple and complicated forms. The simple form did not cause disability; the complicated form did because

of the production of massive pulmonary lesions consisting of vast chunks of fibrous tissue. All these facts have been disproved. The majority of coalworkers do not develop any pathological change apart from having excessive coal dust blackening their lungs. About 10% of these then develop pulmonary nodulation, so at this stage the disease becomes "complicated," and with further exposure, these nodules tend to form vast coalescent masses if exposure is sufficient. The main disease in these men is not the nodulation *per se*, but the associated emphysema and interstitial fibrosis in some cases. In the massive lesions, the lumps are not fibrous tissue. In fact, the amount of collagen and pre-collagen amino-acids present in them is the same as in the non-involved lung tissues. Working with Dr. F. Wusterman of the Biochemistry Department of the University College of Wales in Cardiff and Professor P. McGee at Oxford, we were able to show that the main constituent of these lesions is fibronectin, a glycoprotein which occurs as 3% of the normal serum proteins.

ASBESTOS AND ASSOCIATED DISEASES

There are as we all know, a group of fibrous minerals that can be split longitudinally and have commercial uses. These are chrysotile, crocidolite, amosite, tremolite / actinolite and anthophyllite. The term "asbestos" was originally used for chrysotile. If this had been maintained and the other materials referred to as the amphibole fibres, the present confusion in assessing the risk hazard would not have occurred. In the amphiboles the risk hazard depends on the ultimate length diameter ratio of the fibre and this has been clarified with the studies of the biological effects of tremolite, an amphibole with a widespread occurrence in the earth's crust, usually as a contaminant of chrysotile, talc, anthophyllite, and other minerals. It also occurs in small deposits and is frequently used all over the world as a soil conditioner in agriculture.

The physical features of tremolite vary in all forms from thick flakes to very fine fibres. The electron microscopic appearance of some fibres is shown. Under the transmission electron microscope it can be seen that the finest and straightest of the fibres is crocidolite followed by amosite and the coarse anthophyllite. Now tremolite covers this whole spectrum. By far the finest of all fibres are chrysotile fibres particularly when they break up into fibrils, one chrysotile fibre having the equivalent diameter of at least 100 chrysotile fibrils. However, due to the coiled wave-like configuration the aerodynamic efficiency of chrysotile depends upon that of the full coil. Before venturing into an account of the biological effects of these different fibres, it is necessary to state the hypothesis of selective retention of fibres in the lungs. This contends that it is the fibres retained in the lung parenchyma which are significant in the causation of the disease.

Now I will briefly state our belief in the correlation of disease with fibre type. I am sure this will be contended and defended during this conference.

Asbestos Bodies

Asbestos bodies develop around amphibole and other straight mineral fibres and are seldom on chrysotile fibres.

Pleural Plaques

All types of asbestos are associated with development of pleural plaques particularly tremolite, amosite and anthophyllite. The incidence of environmental plaques is extremely high in agricultural situations and these are usually associated with tremolite.

Asbestosis

All forms of asbestos dust if inhaled in excessive quantities will cause asbestosis.

Carcinoma of the Lung

Initially carcinoma of the lung occurred in people with severe asbestosis with long term survival. Since the 1950's the incidence of carcinoma of the lung has greatly increased due to the association with cigarette smoking. We still contend, and will present supporting evidence, that the association is between cases of definite asbestosis and carcinoma.

Diffuse Pleural Mesotheliomas

Diffuse pleural mesotheliomas are associated with exposure to crocidolite, very fine tremolite, very fine amosite; and if associated with pure chrysotile this must be an extremely rare occurrence. These associations have been occupational, para-occupational or familial.

In 30% of cases of diffuse mesotheliomas in adults, there is no evidence of an association with actual asbestos exposure as defined above. The amount of asbestos in the lungs of these cases is similar to that seen in the the general population living in the same environment.

Diffuse Peritoneal Mesotheliomas

These tumours are not as common as those originating in the pleural cavity.

Experimental Mesotheliomas

We have produced these tumours by the intrapleural inoculation of various types of asbestos dust, including chrysotile. In the majority of the chrysotiles used there was tremolite contamination. The exception to this was the chrysotile that gave the highest rate of experimental tumours. This was a specially prepared preparation containing numerous long straight fibrils and the actual dosage was at least one thousand million times greater than occurs in human exposures. When we used this dust in an inhalation study the tumour rate was similar to that seen in the controls.

Significance of Fibre Body Burden

Chrysotile

Chrysotile fibres are difficult to count as they tend to form clumps, and fibres break up into a myriad of fibrils, so that amphibole fibre is equivalent to about 100 chrysotile fibrils. The present opinion is that exposure to chrysotile has a much milder effect than the amphiboles, and that the association with mesotheliomas is minimal.

Amphiboles

The total amphibole count, a mixture of fibre types, with different length and diameter, can be used in the assessment

of effect, taking 5×10^6 fibres per gram dried weight of lung as the absolute upper limit of non-occupational exposure.

In significant asbestosis there are 100×10^6 fibres and in severe asbestosis 1000×10^6 fibres.

Significant Fibre Size

Mesotheliomas Diameter <0.25 μm, length >8.0 μm
Pulmonary Fibrosis Diameter <3.0 μm, length >8.0 μm

Diffuse Mesotheliomas

Crocidolite—1 million fibres probably minimal but there have been familial cases with counts of 500,000.

Other Amphibole Fibres

Again, only fibres in the size range of less than 0.25 μm and greater than 8.0 μm in length are regarded as significant. The tremolite and amosite are probably equivalent to crocidolite.

It must be borne in mind that these studies are in a developmental stage and the criteria recorded above are those of our present state of knowledge. Further modifications will be reported as the studies continue.

The number of fibres recorded as millions per gram weight of dried tissue depend on the technique developed by Fred Pooley in Wales in collaboration with Patrick Sebastien in France. There have been modifications of their methods which I understand can be made comparable in some circumstances.

MAN-MADE MINERAL FIBRES (VITREOUS)

I have used the above title deliberately as we have only undertaken extensive studies on samples of rockwool, slag wool, glass wool and sub-micronic glass fibre. I am not in the position to report on detailed studies of the other synthetic fibres such as the ceramic fibres; but hope that later in the conference others will give reports.

In our extensive studies with fibres given to us by both European and American industries, we were only able to produce significant tumour incidents following the intrapleural inoculation of the sub-micron glass fibre. No increased incidence of tumours or significant fibrosis was seen following inhalation experiments.

It should be recorded that in the numerous specimens of lung extracts from tumours that Professor Pooley has studied, only a handful have contained commercially prepared man-made mineral fibre. If the material does not get retained in the lung it is unlikely to cause disease.

ABSORBENT CLAYS

These clays are part of the palygorskite group and are used for cat litter and containing spills on factory floors. Another use is in the preparation of drilling mud for the oil industry. Our detailed studies have been confined to the attapulgite and sepiolite produced in Spain. In our experimental studies only fibres from a small deposit in western Spain were shown to be of a length/diameter ratio to be regarded with suspicion. These fibres produce mesothelioma following intrapleural inoculation into rats. On our advice, the production of this fibre has been discontinued. Other attapulgite fibres and sepiolite fibres did not produce tumours following both intrapleural and inhalation studies. Later in this conference Dr. Kathryn McConnochie will report on a clinical and radiological study of the workers who produce the sepiolite.

ERIONITE

The most fascinating new development in the fibre studies are those on erionite. We all know of Professor Baris' fascinating studies in which erionite was shown to produce a higher incidence of mesotheliomas than any other fibre.

From our experimental studies we obtained fibres from one of the houses in Karain and also from other sources in Oregon State and following intrapleural inoculation it was shown that the sample from Oregon produced 100% tumours and only a slightly lower rate was found in the dust from Karain although it had a lower fibre content.

In inhalation studies the Oregon fibre produced mesotheliomas in 27 out of the 28 animals exposed, 1 animal dying of leukaemia. In repeated experiments tumours rose to 100%.

In comparison to this in our much larger experiments in which animals inhaled asbestos dust, we were only able to produce a very low incidence of mesotheliomas.

Therefore, as I retire from this field, I leave you with a fibre which is a very potent carcinogen and must be of value in unraveling the mineral fibre mesothelioma mystery.

.....oOo.....

ADIEU!

PROGRESS IN PREVENTION: EARLY DIAGNOSIS AND MEDICAL CONTROL OF OCCUPATIONAL LUNG DISEASE

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I would like to touch the old—nevertheless very interesting—history of dust-related lung diseases very briefly. I will concentrate more on later results and on data available for further research and strategies for dust-exposed persons, especially miners.

PARACELSUS already mentioned the miners' disease, and he called it consumption of miners ("Bergsucht"). In this term, the relationship to tuberculosis is obvious. At this time and till the early fifties of this century, silico-tuberculosis was one of the main problems of complications of miners' dust-related lung disease. This is more or less history but not in all parts of the world.

RAMAZZINI of Padua (1780) described bakers' asthma for the first time which was caused by the organic flour dust as an asthma-like disease.

The term "pneumoconiosis" was introduced by ZENKER (1867) for the first time, and at this time pathologists showed us all the changes of the structures in the lungs caused by dust, mainly by quartz and coal mine dust. In Germany, mostly the term "silicosis" was used for "coal workers' pneumoconiosis" as it is called in English speaking countries. At present, coal workers' pneumoconiosis is still the most important dust-related disease from the sociomedical point of view. Many of us may remember the tremendous basic contribution given by pathologists and some may remember that for physicians' better understanding of this disease radiology was the key to a new era. These different pictures led to different X-ray classifications. The first internationally used classification was that of Johannesburg (1928) followed by the classification of the International Labour Office (ILO 1980/81). With one set of standard films edited by ILO we have an instrument world-wide available to control the development of pneumoconiosis by the X-rays and for comparative studies.

We leave history now and we move on to the present time.

The development during the last 30 years has shown tremendous progress not only on behalf of our knowledge. Our improved understanding of this disease "coal workers' pneumoconiosis" and very similarly of pneumoconiosis caused by organic dusts like bakers' asthma have had important progress for the expectation of life as well as for the quality of life of dust-exposed and disabled persons due to exposure to harmful dust.

The development of new methods in basic research work was followed by much better insights in the etiology and pathogenesis of these diseases. At the same time, new drugs, very efficient drugs, were developed which could not prevent these diseases till now, but could control the complications responsible for disablement and early death. Both early disablement and early death were terrible facts connected with most of the pneumoconiotic disorders and with the complications related to the different forms of pneumoconiosis.

To remember some of these steps, it may be useful to understand our plans and projects for the future.

There is no doubt that the improvement of dust control at all levels is a very important step for the control of dust-related diseases, but besides the improved dust control tremendous medical progress took place. All the coal workers who really develop problems in relation to coal workers' pneumoconiosis have obstructive airway diseases. This kind of airway obstruction starts on the basis of chronic bronchitis and is followed by obstructive bronchitis. In case of less strong X-ray changes, the obstructive airway disease is not more frequent than in non-dust-exposed men (REICHEL et al., 1969).

In categories B and C of the ILO classification this means large massive fibrotic lesions the incidence of which is twice as high as in non-dust-exposed men (the smoking habits of miners agree with the control group of non-dust-exposed men) (Figure 1).

Like patients with idiopathic obstructive bronchitis, the obstructive bronchitis of coal miners dictates the clinical situation of these patients. Fortunately, the obstructive bronchitis of coal workers with coal workers' pneumoconiosis can be treated in the same way with the same success as the idiopathic form of chronic obstructive bronchitis (Figure 2).

We control our coal workers with coal workers' pneumoconiosis very carefully. This means, coal workers with coal workers' related obstructive bronchitis stay under a controlled regime of treatment. Under the long-term treatment the expectation of like of our miners with large opacities and fibrotic lesions on the X-ray is now at least as long as that of the general population (Figure 3).

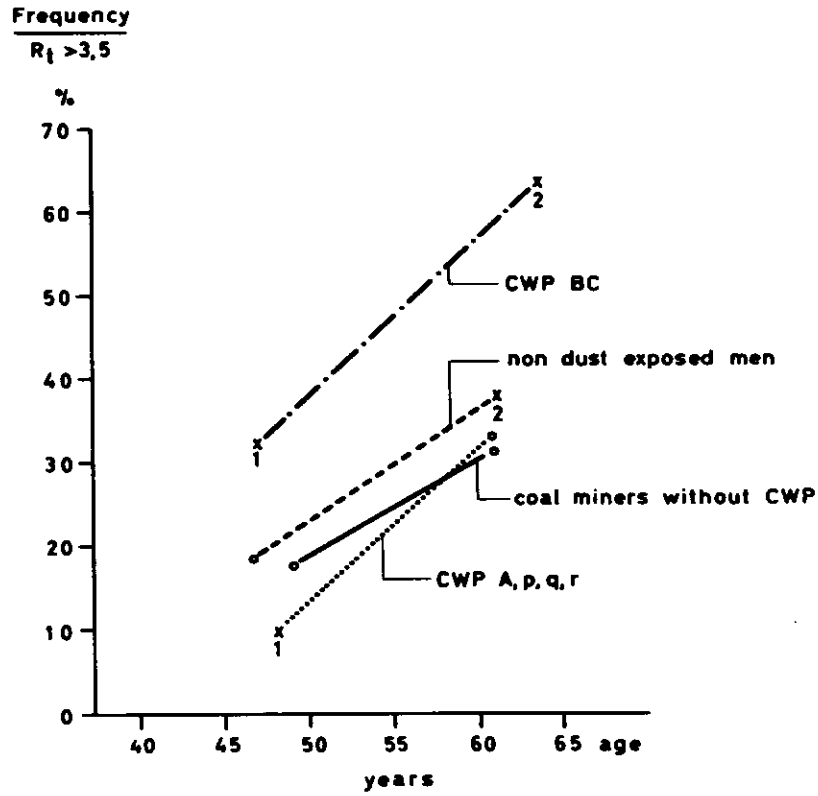

Figure 1. Age dependency of patients with obstructive airway diseases at different stages of coal workers' pneumoconiosis and of non-dust-exposed men (obstructive airway disease = R_{aw} >3.5).

At first glance, the situation may give satisfaction, but we have to realize that the age at which the coal workers develop obstructive bronchitis is nearly the same as 20 years ago. The mean age of the manifestation of obstructive bronchitis is 57 years. In the fifties the expectation of life after airway obstruction was 3.5 years on the average, and now the expectation of life is 16 years on the average. But during this time, coal workers with coal workers' pneumoconiosis and obstructive bronchitis are disabled and have more or less dyspnea, and some even develop cor pulmonale.

Therefore, for the future we have to avoid the development of coal workers' pneumoconiosis and we have to learn to avoid manifestations of chronic obstructive airway diseases.

First the development of coal workers' pneumoconiosis on the X-ray: The correlation between the ILO 12 step classification (from −/0 to 3/+) is relatively linear. Figure 4 shows the results of one mine in W.-Germany as mean value and also the progression of the worst and the best case (Figure 4).

From these curves we can calculate the ILO classification step time: it is the time in years necessary to get from one classification step to the next one (e.g., 0/1–1/0). In the example in Figure 4, the ILO classification step time is 8 years on the average. These curves allow an extrapolation at a relatively early time. From such curves we may learn more about the causes of the different ILO classification step times for different individuals as well as for different mines.

There are clear differences between different mines as Figure 5 shows (Figure 5).

We proposed that:

a) the X-ray development of coal workers' pneumoconiosis should be documented for each coal worker on ILO classification step times/exposure times curves;
b) an interval of 4 years for X-ray examination of coal miners is adequate and without any risk for coal miners at present exposure levels.

In order to prevent the pneumoconiosis due to obstructive airway disease the prevention of airway obstruction is the most important factor as already mentioned above. Today, we dispose of sensitive methods to detect early signs of lung function changes related to airway obstruction. In W.-Germany, we examined in 4 mines the miners by careful lung

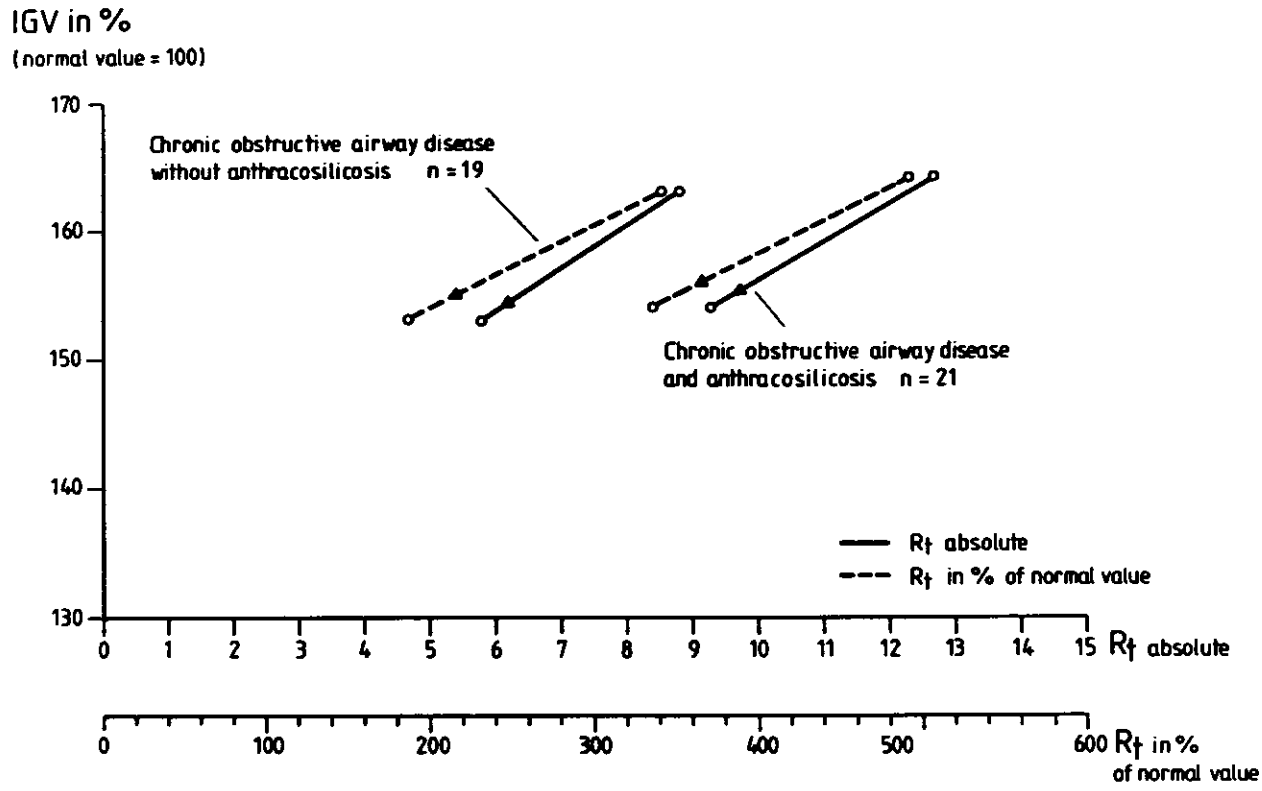

Figure 2. Decrease of airway resistance (R_t) and of intrathoracid gas volume (IGV) under typical treatment with bronchodilators and glucocorticoids in patients with pneumoconiosis-related obstructive bronchitis (n = 21) and of patients with idiopathic obstructive bronchitis (n = 19).

function tests. Among the miners is a relatively high percentage still at work who has obstructive airway disease, and there is quite a number of miners with oversensitivity (hyperreagibility) of the airways.

It is very important to detect persons with signs of obstructive airway disease as early as possible to control the development of the lung function of these persons:

1. to start with an adequate treatment at adequate time and
2. to avoid progression of this disease. It is very likely that an early treatment can control this disease and can avoid progression.

We have to control the lung function of dust-exposed persons with adequate methods. Time intervals for re-examination could be 4 years but not longer.

Dust concentration decreases in the inhaled air are most important for prevention. The very effective dust masks are normally worn for short times only. The acceptance of normal light masks depends on the isolation, and therefore on the development of sweat under the mask. The loss of the possibility of communication is also important and problems of increased airflow resistance may be a factor, too.

The light masks (Figure 6) comparable to those masks worn in hospitals, have in this respect many advantages, although they decrease the dust concentration only for about 70%.

1. They allow communication with other persons without effort;
2. They soak up the sweat around the mask;
3. The decrease of dust concentration in the inhaled air is about 70%, and therefore the ILO classification step time increases so that during the life time coal workers' pneumoconiosis responsible for dust-related obstructive airway disease will not develop (Figure 7).

CONCLUSION

In addition to the best available dust suppression we should emphasize that the light (one-way) masks will be used continuously. With this strategy, coal workers' pneumoconiosis could be controlled so that dust related obstructive airway diseases never will occur.

These results shown mostly for coal miners and coal workers' pneumoconiosis can be transferred more or less to other types of pneumoconiosis.

Our knowledge about the development of pneumoconiosis increased tremendously. During the last decades we could dispose of strategies which are able to slow down the development of coal workers' pneumoconiosis suddenly and which can avoid the coal workers' pneumoconiosis-related obstructive airway diseases. Furthermore, we can improve the health situation of the miners we are responsible for.

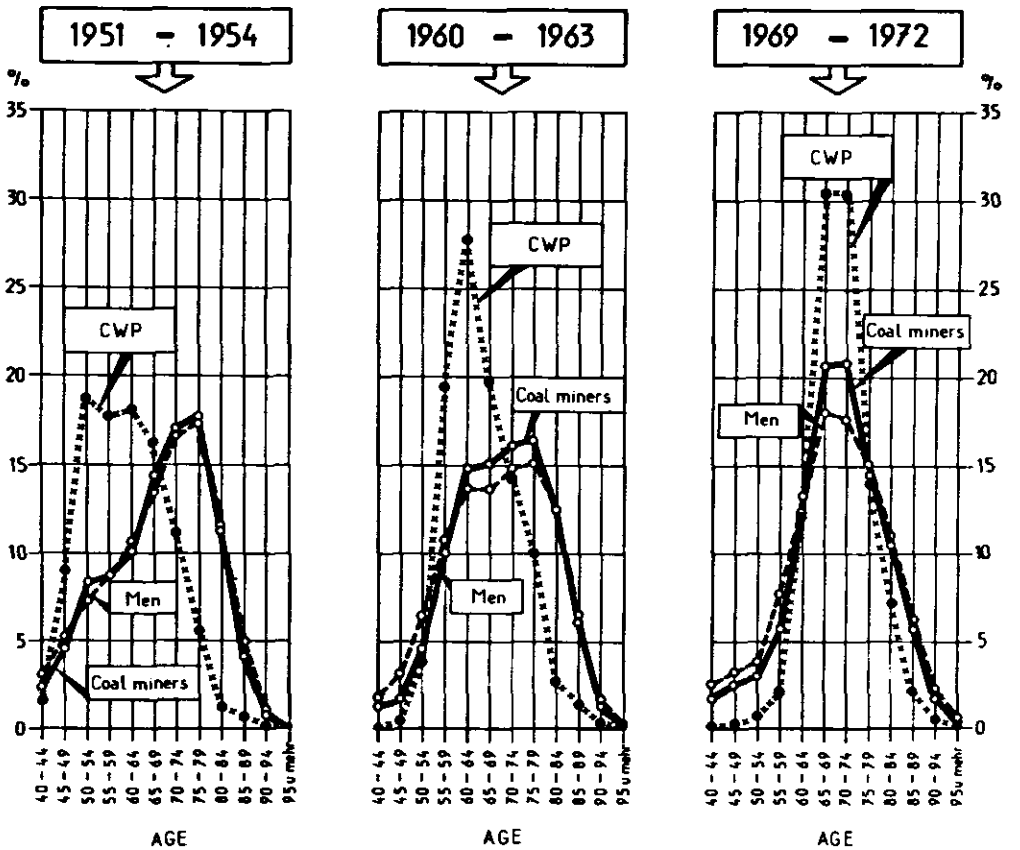

Figure 3. Expectation of life of coal workers with obstructive bronchitis and of miners without coal workers' pneumoconiosis and of non-dust-exposed men in the years 1951–1954, 1960–1965, 1969–1972.

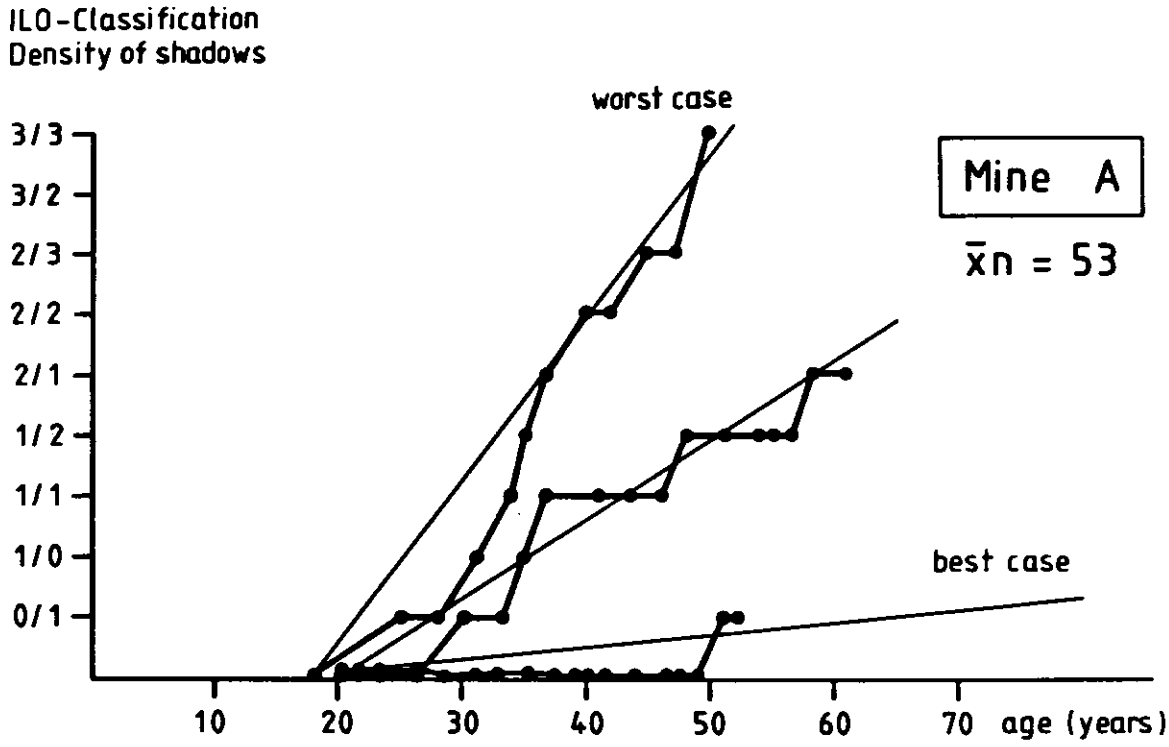

Figure 4. Correlation between ILO classification and exposure time (mean values of 53 miners and the best as well as the worst individual case).

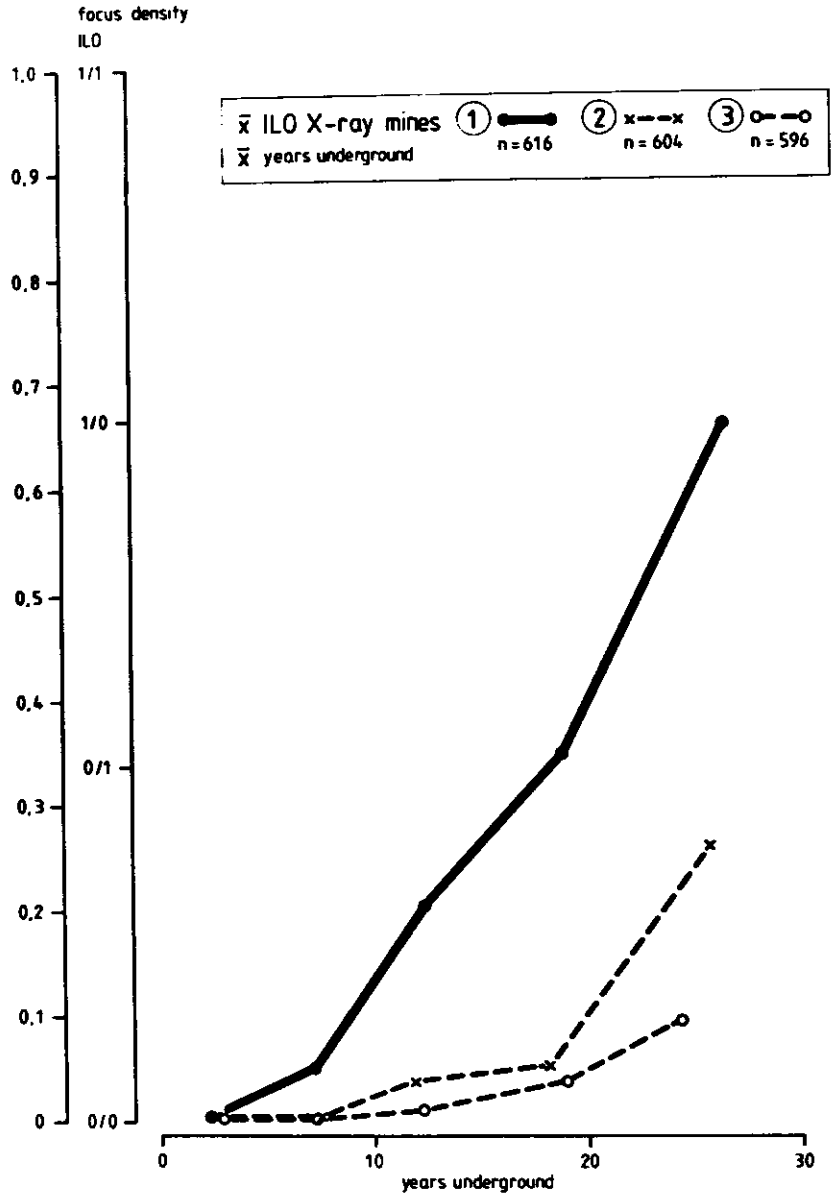

Figure 5. Correlation between ILO classification steps and exposure time on 3 different mines in W.-Germany (mine 1 n = 616, mine 2 n = 604, mine 3 n = 596).

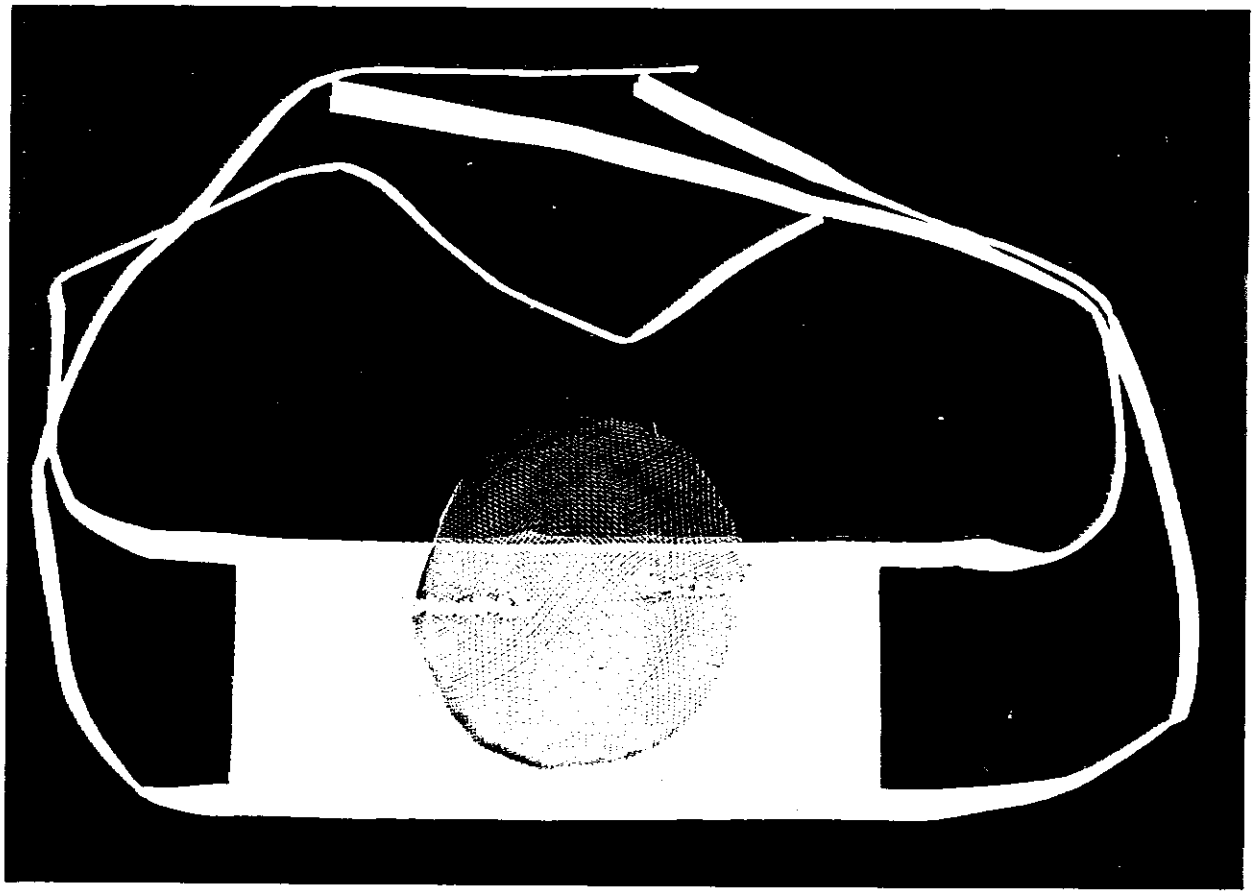

Figure 6. Light mask with very good acceptance and many advantages protecting against the development of coal workers' pneumoconiosis (decrease of dust concentration in the inhaled air ~ 70%).

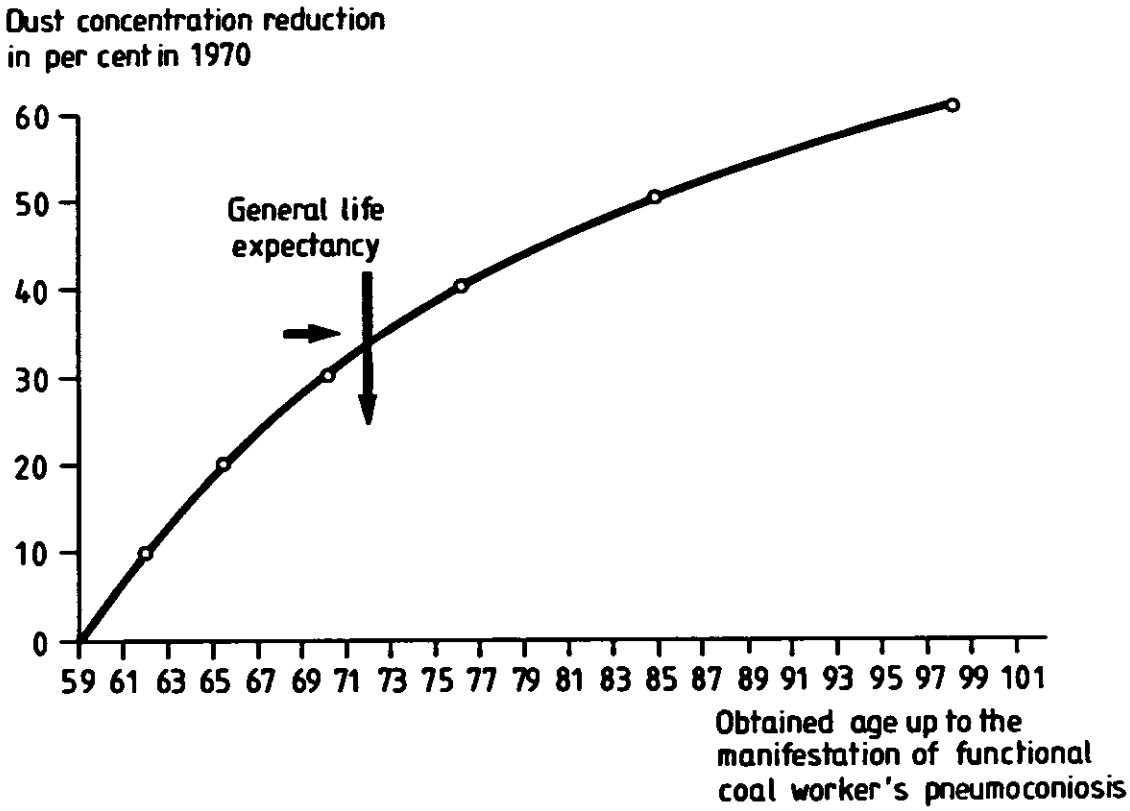

Figure 7. Relationship between decrease of dust concentration in percent of the values from 1970 and the age at which X-ray changes take place which could be responsible for coal workers-related obstructive airway diseases (a decrease of about 35% would be enough to prolong the manifestation time to the values of the normal expectation of life).

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REFLECTIONS ON PROGRESS WITH MINE DUST CONTROL AND DUST CONTROL TECHNOLOGY

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INTRODUCTION

It is obviously impossible to provide a detailed historical or even present-day account of the control of dust in mines and dust control technology in the brief time allotted to me. Therefore, as a compromise this theme paper highlights major selected subject areas of scientific and technical knowledge that have culminated in the current degree of dust control and control technology in U.S. mines. What were the historical understandings and emphases; what types of knowledge were gained through laboratory and applied research that permitted us to effectively implement dust control strategies through either voluntary or regulatory societal mechanisms? In different nations there has been a shared concern with this occupational problem, and the contributions to understanding have been multinational. Bear with me if I tend to oversimplify; it is my belief that at times we must sit back and take a long look at what has been called the "drum roll of history." This enables us to discern "the big picture" from the many necessary and essential details that punctuate progress in any field of human endeavor. It also enables us to better consider where we are at present and to define further, needed progress.

CONTROL OF MINE DUST

Recognition of Coal Workers Pneumoconiosis as a Disease State

The report by Bedford and Warner[1] in Great Britain in 1943 must be regarded as a major turning point in our understanding of the impact of inhaled coal dust and of dust control in mines in Great Britain. This report stimulated the adoption of airborne dust standards for "approved dust conditions" in conjunction with employment underground. No specific dust concentration limits or standards were set by law, but the adopted standards in the attainment of dust suppression continued for almost 30 years. The standards were the result of extensive studies of pulmonary disease in South Wales coal miners conducted by the Medical Research Council. These studies were conducted in five mines; they associated dust with x-ray abnormalities. The British later extended these studies to a larger number of mines, i.e., the so-called 25 Pit Studies.

The proposal for a standard was that not more than 10 milligrams per cubic meter of anthracite dust or 1 milligram per cubic meter of minerals other than coal for particles 5 microns or less in size, should be achieved. Note that the particle number standards for approved mine dust conditions introduced in Britain in 1949, remained basically the same until 1970, when gravimetric standards were introduced, again resulting from epidemiologic studies relating dust and pneumoconiosis. Thus, in Great Britain there was recognition of the disease state and adoption of standards for approved dust conditions.

In the United States, a major 1936 report by the Public Health Service[3] indicated that the term anthracosilicosis, as used, was a descriptive title for the form of pneumoconiosis commonly called miners' asthma. It was diagnosed by occupational histories, clinical examination and x-ray exams. The report indicated that the correlations "between exposure to dust and the evidence of constitutional changes left little doubt as to the etiological significance of the dust in the air breathed." Similar correlations were found between the silica exposure and the extent of pulmonary changes. Investigators concluded that employment in an atmosphere containing less than 50 million dust particles per cubic foot would produce a negligible number of cases of anthracosilicosis when the quartz content of the dust was less than 5%. This report was also an extraordinarily important one in that it lead to adoption of the standards for free silica in the United States, which are in effect to this day under our Occupational Safety and Health Act, if the user chooses to utilize midget impinger sampling and dust counting methods to evaluate dustiness.

My point in citing these two reports is to indicate that acknowledgement of the correlation between the disease state and the etiological agent is essential before control efforts can take place. In the 1950s the Commonwealth of Pennsylvania pioneered in studies of coal miners that lead to the recognition of the disease state of coal workers pneumoconiosis in bituminous coal miners, as contrasted to anthracite miners. Thus, the 1930's U.S. investigations resulted in differentiation between free silica in the dust causing silicosis, and miners' asthma occurring in hard coal mines. We spent another 25 years in the United States

debating legitimacy of the disease state of coal workers pneumoconiosis, which seriously hampered efforts at dust control. In this regard, the British reached consensus on this point before we did.

The Physics of Dust

In order to control the dust associated with a disease, one must know a great deal about dust physical and chemical properties. Although there were scientific treatises on dust properties as early as 1934,[2,37] these volumes were very limited in the technical information provided that could be translated to the measurement and control of mine dust. The dust measurement techniques in effect during the 1930's were the midget impinger[16] developed in the United States, and the Kotze' Konimeter,[26] developed in South Africa. Gravimetric techniques were not extensively utilized to assess airborne dust for disease prevention until the late 1940's and 1950's. In fact, calibration of the impinger for coal dust particles (the only particles for which, to my knowledge, the instrument was ever calibrated) was reported by C.N. Davies in 1951.[9] The concept of aerodynamic particle size remained to be elucidated. However, even without these understandings enormous progress in mine dust reduction could be, and was made, as evidenced in South Africa in the 1930's through the 1950's.

The ability to advance beyond the qualitative understanding that inhalation of dust is dangerous to your health and that dust concentrations measured as described correlate with disease prevalence in exposed workers, also depends upon insights into the hygienically significant sizes of inhaled particles. The development of this area of understanding is my third selected critical area of knowledge for effective dust control.

Dust Deposition in the Human Respiratory Tract

Drinker and Hatch[11] traced the examination of particles in exhaled air to studies by Tyndall in 1882, and also cite a hygienic study by Saito in K.B. Lehmann's laboratory in 1912. Studies in the 1930's on nasal filtration by normal men were performed by Lehmann and by Torangeau and Drinker. The studies by Brown in 1931 were the first major studies on dust retention in man.[5] Experimental investigations by Davies,[8] Landahl and Hermann,[23] Van Wijk and Patterson[36] and Wilson and LaMer,[38] supplemented by theoretical calculations by Findeisen,[13] all advanced the state-of-the-art of particle size deposition in the human respiratory tract. The particle inhalation study that dictated U.S. views on deposition for two decades was that by Brown, et al., in 1950.[6] It was the major source of definitions for respirable dust in the U.S. and Europe, and for the very important report on dust deposition and retention in the human respiratory tract by the International Congress on Radiological Protection in 1966.[35]

These were the first of a long series of experiments, still continuing, to define the particle sizes of significance for chronic disease developing in the pulmonary compartment of the respiratory tract. The studies have been refined and there has been international agreement on the deposition curves in healthy men after inhalation at standard volume. The subject was reviewed by Lippman[24] and the new definitions of compartmental deposition in the human respiratory tract have been published.[27]

The significance of this work was that it provided a target in terms of the spectrum of particle sizes of hygienic importance in dusty environments, and enabled those interested in control to take aim at that target.

It should be noted that during all of this work the characteristic "size" of a particle was the projected area diameter, because the predominant instrument for viewing collected dust particles was the light microscope. In the light microscope one observes a silhouette, a two dimensional representation of a three dimensional object, the dust particle. Work performed at a later date would differentiate between the aerodynamic size of a particle and the silhouette size of the particle that one observes in the microscope. While this may appear to be a minor physical differentiation, it is of the utmost significance. It explains why we observe fibers 200 microns in length in the human pulmonary compartment; their aerodynamic size is equivalent to a less than 10 μm diameter sphere of unit density which could penetrate to that region of the respiratory tract. It took many years for the significance of the aerodynamic size to be recognized.

The understanding of dust aerodynamic behavior and deposition in the lung required decades to crystallize. The control of dust could progress, but there was great uncertainty if one was capturing the sizes appropriate to the disease state. An analogy is use of a shotgun versus a target rifle. The standardization of so called "respirable dust" and the development of an instrument to simulate that dust size waited until 1954 when B.M. Wright in England introduced the horizontal elutriator.[39] Dust control efforts were proceeding in all industrialized nations, but it is fair to say that permissible dustiness was far above the concentrations we have today in mines of industrialized nations. There was also great uncertainty in the long term benefits associated with the control efforts, because the largest particles have the greatest weight associated with them. There could be extensive reductions in dust measured in terms of weight per unit volume; there could, however, still be only conjectural impact on the disease state, because the smallest particles reaching the pulmonary compartment are associated with the least weight per particle.

West Germany began a series of epidemiologic studies in their mines in the search for the dust parameter that would best correlate with disease. They concluded that the surface area of the dust was an appropriate parameter and developed their dust measurement techniques accordingly. At a later date, they too would recognize the respirable dust concept with cyclone precollector sampling to determine respirable dust weight. During all the years of the 1950s and 1960s the British counted particles using a thermal precipitator instrument and reported their dust concentrations in numbers of appropriately sized particles per cubic centimeter of air.

Instruments to Measure Respirable Dust

It is interesting to peruse the first volume of air sampling instruments entitled "The Encyclopedia of Instrumentation for Industrial Hygiene."[40] The volume is concerned with many different types of air sampling instruments. The cas-

cade impactor, the midget impinger, and the electrostatic precipitator were the major instruments available for particulate sampling in 1956. Indeed, at a Governor's Conference in the Commonwealth of Pennsylvania in 1964 a leading U.S. industrial hygienist who was director of industrial hygiene for our major steel firm, and a previous President of the American Industrial Hygiene Association, stated publicly that the respirable dust concept then in vogue in England and Germany was not applicable to United States mines. Thus, one reason that efforts to develop instruments that would apppropriately sample respirable dust in coal mines did not rapidly progress in the U.S. was because the respirable dust concept was not readily accepted.

Subsequently, appropriate instruments were developed in the 1960s, utilizing a United States Atomic Energy Commission cyclone preseparator and the definition of the United States Atomic Energy Commission for respirable dust. It approximates the BMRC respirable dust acceptance curve defined by the horizontal elutriator.[20] These instruments approximated the accepted pulmonary deposition curve at that time, mainly based on the data of Brown et al.[5]

The dust standards in mines enforced in Great Britain during the period 1949 to 1970 were summarized by Chamberlain et al.[7] The British abandoned the particle counting standards in 1970 and adopted gravimetric standards. The introduction of gravimetric standards in the United States accompanied the Coal Mine Health and Safety Act of 1969.

The Mine Health and Safety Act of 1969 required that beginning June 30, 1970 the operator of each coal mine was required to maintain the average concentration of respirable dust in the active working at or below 3.0 milligrams per cubic meter. The standard was reduced to 2 milligrams per cubic meter after December 30, 1972 and has remained at this level.[32] Because of the difficulty of adapting to this standard an Interim Compliance Panel was authorized to issue a permit for non-compliance for a dust concentration as high as 4.5 milligrams per cubic meter while the standard was 3 milligrams per cubic meter, and for 3 milligrams per cubic meter when the standard was 2 milligrams per cubic meter. However, by December 30, 1975 the 2 milligrams per cubic meter was to be met. In the U.S. we are still not meeting that standard in all mines. The Mine Safety and Health Administration has developed an elaborate sampling procedure to insure compliance with this standard. The procedure involves sampling key occupations or key locations in the mine. The progress in dust control in mines has been achieved with a regulatory inspectorate for approximately 275,000 miners that equals the inspectorate of the U.S. Occupational Safety and Health Administration, which has responsibility for over 75 million workers at all types of worksites. Mine Safety and Health Administration inspectors in the United States visit every mine many times in a given year; the probability for a visit by an OSHA inspector to a workplace are, on the average, less than one in 50 for most businesses.

RISK LEVEL OF PRESENT STANDARD

Since 1982, there has been major emphasis on risk assessment in the regulatory process in the U.S.[30] The 1969 U.S. standard for permissible dustiness in mines was keyed to the British standard. It is interesting to review the risk level estimated to be associated with that standard. The interpretation of risk level can be derived from the British and the German epidemiological studies. In England the 25 pit study provided the data base.[22] In the British studies the quartz in the coal dust varied from 0.8% to 7.8% (respirable dust), with an average of 4.1%. The progression of the disease seemed to be associated with the quartz content of the respirable dust. Nonetheless, the probability of occurrence of 0/1 ILO classification x-ray for mean dust concentration of 2 milligrams per cubic meter for 35 years of exposure, is approximately 4%. The probability that a man starting with no pneumoconiosis (category 0/0) will be classified into 2/1 or higher after 35 years exposure to 2 milligrams per cubic meter is about 1 1/2% for low rank coal; 3% for high rank coal.[31] The U.S. estimate of CWP category 1 at 2 mg/m^3 is 9%; category 2 is 1–2%. In terms of current risk levels being discussed in the United States for other airborne contaminants, this is a somewhat high risk level. For example, the current estimate of risk at 0.2 fibers per cc for 35 years asbestos exposure is 0.7% for lung cancer and mesothelioma, with virtually zero risk of asbestosis. The 35 year time base for estimate of the risk is the same as that for respirable coal mine dust.

The German epidemiological studies occurred in 10 coal mines over a 10 year period.[29] A cumulative dust index was utilized based on light scattering measurement of the dust. Thus, the dust measurement was dependent on some function of the dust surface area. The German investigators related the Tyndallometric fine dust concentrations to the gravimetric fine dust concentrations measured with a cyclone/filter collecting device. They concluded that the ratio varied with coal rank; therefore, there was considerable uncertainty in a general correlation, but they did correlate by high, medium and low ranks of coal. Using the index developed, a cumulative dust value of 50,000 was associated with definite pulmonary change. The parameters influencing the conversion from light scattering to gravimetric measurements were a dirt concentration factor and the fineness factor of the dust, which influences the degree of forward scattering of light in the instrument. The concentration range of 0.9 to 1.5 milligrams per cubic meter as measured by the cyclone, was estimated to correspond to a cumulative fine dust concentration measured by light scattering of about 125,000. If I correctly interpret the publication describing these results, there would be a risk of about 5% of light to medium pulmonary changes with a 6,000 shift exposure to approximately 1.5 milligrams per cubic meter, indicating a risk level about that encountered in Great Britain and the U.S. These estimates are very intimately associated with the rank of coal and my conversions are therefore a rough estimate.

Chemical Composition of Dust and Coal Miners' Pneumoconiosis

The pathophysiology of coal miners pneumoconiosis is still not well understood. The presence of quartz in the dust is a confounding factor. The present tools for disease diagnoses, namely x-ray and pulmonary function testing, cannot dif-

ferentiate in the living miner between silicosis and coal workers pneumoconiosis. There is considerable disagreement at the lowest ILO classifications re: the disease state. Promising efforts to understand the disease state, as reflected in the present research emphasis, appears to be correlation of residual dust components for dust retained in the lungs and analyzed post mortem, with components of the exposure dust.[34] In particular, there seems to be increasing emphasis in the United States on free silica content of mine dust. MSHA is increasingly stressing the silica content of the dust. The classification in 1986 by the International Agency for Research on Cancer of crystalline free silica as Class 2A gives further impetus to the emphasis on free silica.[33] The inability to estimate the free silica of the airborne dust on the basis of settled dust has long been known.[12] It is now possible to measure free silica in respirable dust samples with a sensitivity of 1–10 micrograms, depending on technique, and it is anticipated that with the IARC classification there will be a change of the current U.S. silica standard, which is presently stated as a sliding scale for permissible dustiness based on free silica content.

In summary, the control of dust in mining has witnessed enormous progress during the past 20 years, stimulated by increased regulation in many countries, including the U.S., and innovative development of standards in South Africa, Germany and England, standards preceded by extensive epidemiological investigations that provided an estimate of the risk levels associated with adopted numbers. Areas of knowledge that required development to efficiently implement dust reduction in mines were the deposition of dust in the respiratory tract and the physics of dust, the latter required for instrument development and sensitive analytical techniques to measure the dust collected. Different nations took different approaches to the evaluation of dustiness but almost all now utilize gravimetric methods, for both feasibility and for scientific reasons. When compared to risk levels associated with standards now being adopted for other airborne contaminants in the United States, there is need to further consider the airborne respirable mine dust standard. Recent classification by IARC of crystalline free silica as a Class 2A carcinogen strongly suggests the need to better understand the exposure to and impact of free silica in coal mine dust, in particular. Having discussed selected topics in the control of mine dust, I will now briefly look at the progression of dust control techniques in mines. What are the technologies that have brought about this progress and how much further can we exploit these technologies, or are other "understandings" needed to make further progress?

DUST CONTROL TECHNOLOGY

Ventilation

The Office of Technology Assessment in its 1984 report Controlling Hazards in the Workplace[27] introduced the terminology of the "hierarchy of controls," with engineering controls at the top of the hierarchy and administrative procedures and work practices following; personal protective equipment is the last intervention to control exposure. Among the engineering controls are control at the source and control by substitution. The seven engineering controls listed by OTA are shown in Table I. In 1950 in a review of literature on dusts,[14] the authors quote Harrington, a 1934 reference[18] with regard to the control of dust in mines. Harrington indicates that ventilation, fire protection and prevention, health, safety and efficiency are very closely interlocked in mines. He indicates that ventilation is perhaps the major route for control of hazards in mining, both in metal and nonmetal mines, permitting the worker to exert himself in comfort at maximum physical capacity without endangering his health. He focuses very heavily on "the best remedy for the dust menace in mines, other than preventing its formation, is the universal coursing of currents of air to remove the dust, as it has been proved that the very fine, most dangerous dust in metal mines remains suspended..." Harrington indicates that spraying devices available to reduce dust while drilling may be effective if used intelligently. However, they may even intensify the air dustiness if used without intelligence and, unfortunately, the latter is generally the case. He points to the availability of efficient water drills. Harrington also indicates that while finely divided dust "in mines is probably the chief cause of miners consumption, it is now recognized that there may be other factors of almost equal influence, such as high temperatures and humidities, harmful gases, and lack of air movement; all of these defects are readily remedied by ventilation." Table II is a summary of approaches or "lines of attack" for dust control in mines, as presented by Hamilton in 1972.[17] It differs little from Harrington's approach.

Table I

OTA Hierarchy of Controls: Engineering Controls

Elimination
Substitution
Isolation
Enclosure
Ventilation
Process Change
Product Change

Table II

"Lines of Attack" for Dust Control in Mines[17]

1. Removal and dilution of dust by ventilation.
2. Contol of the formation and dispersion of dust by attention to the method of mining and the way in which machines are operated.
3. Application of water, either to limit the dispersion of dust into the air, or to suppress airborne particles.
4. Use of exhaust ventilation to contain dust sources, followed either by ducting the dusting air to unoccupied parts of the mine, or by filtration before returning it to the main ventilation current.

The use of water in drilling and in mining has a long history. The British Coal Mines Act of 1911 required that a drill worked by mechanical power "shall not be used for drilling in ganister, hard sandstone, or other highly siliceous rock, the dust from which is liable to give rise to fibroid phthisis, unless a water jet or spray or other means equally efficient is used to prevent the escape of dust into the air."[21]

Water

Water has also been used, particularly in Western Europe to infuse the coal seam prior to drilling. Coal piles have been wetted after blasting and after cutting. Permanent use of water is not possible because moisture can be detrimental to certain processes in minerals and in some mines limited quantities of liquid must be used if the product is to be marketed. Wetting agents have been added to water and in recent years droplets have been electrified during spraying to increase contact with the dust. Foams has also been utilized, the theory being that dust particles will be trapped in the individual cells of the foam and subsequently wetted by the liquid as the cells collapsed.

The development of our understanding of aerosols and particles owes much to the concerns of mining. In particular, the work of the Safety in Mines Research Establishment in Sheffield, England and the Bergbaustaubsverein and the Silicosisforscungs Institut in the Ruhr were major contributors to the pool of knowledge of the physical properties of dust as reflected in compendium volumes such as that by Green and Lane.[15] Other summaries of particulate knowledge also reflect the contributions of investigators at these institutes who, although they were pursuing applied research, recognized the necessity for basic contributions on the physics and chemistry of dust. The names of Cartwright, Hodkinson, Davies, Robock, Hamilton and Timbrell immediately come to mind. It is not my purpose here to dwell on the specific research investigations that lead to progress in the control of mine dust. Rather, I believe it is possible to discern the trends in this area, as reflected in comparing a 1980's review published in the United States with the earlier literature on dust control in mines.

The review by Breslin and Niewiadomski[4] of the United States Bureau of Mines was published in 1984 and reviews progress in dust control technologies for U.S. mines from 1969 to 1982. In this report the authors stressed the control of dust formation, primarily. The relationship of coal cutting to the generation of airborne dust is highest on the priority list of the Bureau's dust control "understandings" for control technology. This is an extension of the innovative work by Hamilton in England.[17] The type of cutting bit, the depth of cut, the possibility for injecting water through the bit, the number of bits used, are all aspects of this research program. Because the mining methodology in the U.S. is shifting very rapidly to longwall production the applications of these techniques to the longwall operation both at the cutting site and upstream are focused upon. As indicated in the earlier statements by Harrington, the dust movement caused by the application of water is of great concern in these investigations. Ventilation is still our major workhorse in the dilution and removal of dust through both blowing and exhaust, but a substantial gain is achieved through the use of water injection and control of cutting.

The Bureau also focuses upon the use of dust collectors for trapping the dust; these operate both on scrubbing and filtration principles. The trapping of the dust after generation permits the use of the air without its burden of respirable mine dust. The largest fraction of work performed by the Bureau in these years was for in situ testing of these techniques after laboratory evaluation. A great deal has been learned about the equivalent volume of air cleaned versus water pressure as a function of different types of spray nozzles in the wet type scrubbers. Wetting agents have also been tested and there is some reported incremental gain due to their use. In the course of advancement of this technology the Bureau lists the following basic "understandings" which have come from this work.

- Laboratory studies showing the relationship between dust generation and the specific energy used to cut coal.
- Studies of deposition of aerosol on electrostatically charged surfaces.
- Experimental research on the dynamics of water drops impacted on surfaces.
- Development of laboratory apparatus for generating water drops of uniform size and for measuring drop size.
- Measurement of the adhesion force between dust particles and surfaces.
- Characterization of the physical and chemical properties in mine dust.
- Development of technology for automatic measurement of particle size, shape and composition using a scanning electron microscope.
- Studies of the efficiency of dust sampling inlets.
- Development of apparatus for generation of laboratory aerosols.
- Studies on the effect of water sprays on air movement and dust suppression.

The Bureau indicates that fundamental research was done with the ultimate long term goal of improving technology for control of dust in mines and that meant many of these areas of knowledge have applications in areas other than mining. The National Academy of Sciences in 1980 issued a report[25] in which the Academy directed the Bureau towards research which "should be directed more toward obtaining fundamental understanding of the origin, transport and characteristics of respirable coal mine dust." One could say this is expected from an Academy report, but I prefer to think that there is finally broad recognition of the need to understand fundamentals in order to develop technology.

The future goals of the dust control technology in the Bureau are also of interest. They are stated as:

- Optimization and in mine application of the new water spray system ("Shearer/Clearer") for longwall dust control.
- In-mine evaluation of new and emerging longwall dust control technology.
- Determination of the applicability and effectiveness of water powered scrubbers at longwall operations and on continuous miners.
- Completion of field evaluation and application of a mine worthy twin scrubber system for continuous miners.

- Development and testing of optimal ventilation systems for dust control during continuous miner operations.
- Redesign, testing, and application of an improved canopy-air curtain system in underground as well as surface operations.
- Development of a basic understanding of the formation of transport of dust during the cutting cycle for development of more effective controls.
- Development and testing of improved bagging machine dust controls, bag ceiling, cleaning and disposal techniques for the mineral processing industry.
- Development of dust suppression systems for cutter machines and other equipment used in conventional mining operations.
- Development of improved dust controls for conveyors, transfer points and stage loaders.
- Determination of cutting force in coal seam for use in development of deep cutting machines.
- Development and testing of improved personal dust exposure.

It would be interesting to compare these research goals for control of dust in mines with those of other nations committing significant expenditures to development of dust control technology at the national level. As one reviews progress in this field over the past 50 years, it is striking that the impetus for sharing of information has come from the professionals and the professional associations and not through their governments. Thus, the first International Pneumoconiosis Conference was held in South Africa, very much due to the efforts of Dr. Beadle, who was preeminent in development of a dust control and medical surveillance program in South Africa. The inhaled particles and vapors series of conferences, a major stage for sharing of information by investigators and practitioners, was sponsored by the British Occupational Hygiene Society. The overlapping of many research program areas is apparent in the past. One wonders if we can become more efficient in our approaches to development of these new technologies. The scientific community will always share results, but the planning of research could greatly benefit by such an international effort.

It is impossible to not be struck by our utilization of the same workhorses for making progress with dust control in mines. We have reached the limit for bringing air to the face and diluting the generated dust. We are probably on the asymptotic portion of the curve for extracting greater efficiency from the application of water, either through the cutting tool or after the cut. We are in need of some new, innovative approaches. In view of the enormous progress over the last 2–3 decades with our understanding of disperse systems and aerosols, it would appear there is opportunity for introducing new and innovative ideas into dust control technology. There are analogies in other fields to this need. The treatment of hazardous waste is receiving major impetus because the major workhorse heretofore has been burial and storage in the ground, which has run its course and is associated with great risks for the future. New technologies are appearing and will undoubtedly have a major impact on the quantities of materials disposed of to ground by 1995. The Superfund Act and its recent renewal have stimulated this work. While the impression in England and perhaps also in the United States is that we have "solved" the problem of coal workers pneumoconiosis and dust in mines, in general, it is incumbent upon us to make clear that this is by no means true. We have made enormous progress, but it remains to bring our risk levels in concordance with those accepted for other work environments. Doing this efficiently requires knowledge and knowledge requires investment of funds.

On this note I would like to end. The story of dust control in mines has some logical development. It is troubling that the current perception is that the job is done, and that diversification of scientific effort and funds from this subject area is occurring in many countries. We must correct this erroneous perception in order to maintain and continue the hard won gains to date.

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SCIENTIFIC PAPERS

OVERVIEW OF RESPIRABLE DUST CONTROL FOR UNDERGROUND COAL MINES IN THE UNITED STATES

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ABSTRACT

Control of respirable dust is an important consideration in the design of the production cycle of an underground coalmine. In order to create an effective and efficient system, the mining engineer must integrate the regulatory requirements with the specific conditions that exist in a coal mine. Typical mine development is by room and pillar. Second mining is by mining rooms, extracting pillars or by retreating longwalls. Each of the mining systems can have specific constraints depending on the type of equipment used. Continuous miners and conventional mining systems (cut, shoot and load) are used for room and pillar application. Single and double drum shearers primarily are used for retreating longwall systems. This paper provides a review of the specific federal regulations affecting dust control and description of the various dust control systems commonly used to supplement those regulations for the various mining systems.

INTRODUCTION

There are over 2,000 mechanized mining sections in underground coal mines in the United States. Each of these sections must utilize a dust control system capable of maintaining their dust levels below the specified standard.

The purpose of this paper is to provide an overview of the specific federal regulations affecting dust control and a description of various respirable dust control systems currently used in underground coal mines. Utilization of these systems has been successful in controlling workers exposure to coal mine dust.

FEDERAL REGULATIONS

Current authority to establish and enforce a respirable coal mine dust standard was given to the Mine Safety and Health Administration (MSHA) of the Department of Labor through the Federal Mine Safety and Health Act of 1977. Primary responsibility of enforcing the respirable dust standard rests at the federal level as state laws generally do not specify a respirable dust standard. Specific regulations pertaining to the dust standard and dust control are contained in Title 30, Code of Federal Regulations.

Part 70—Mandatory Health Standards—Underground Coal Mines, contains the dust standards and the sampling procedures that must be followed by the coal mine operators. Part 70 establishes a respirable coal mine dust exposure standard of 2.0 milligrams per cubic meter (mg/m^3. If the dust contains more than five percent quartz, the dust standard is computed by dividing the percentage quartz into the number 10. Additionally, Part 70 establishes a dust standard for intake air of 1.0 mg/m^3. Part 70 also requires mine operators to collect and submit five dust samples from a designated occupation during each bimonthly sampling period.

Part 75—Mandatory Safety Standards—Underground Coal Mines, contains various ventilation regulations that pertain to the control of respirable coal mine dust. Part 75 contains various regulations pertaining to the design and performance of a mine's ventilation system which also have an impact on dust control. Specifically, each mechanized mining unit must be ventilated on a separate split of intake air. This prohibits series ventilation of working sections so that the return of one section cannot be used to ventilate another section.

To provide dilution, the ventilation system must deliver 9,000 cubic feet of air per minute (cfm) to the last open cross cut of a set of developing entries and to the intake entries of a retreating section. The system must also supply 3,000 cfm to each working face where coal is being cut, mined or loaded.

Unless otherwise approved by the local enforcement official, the line brattice or face ventilation device must be maintained within 10 feet of the face. For exhausting face ventilation systems, the minimum mean entry air velocity in working places where coal is being cut, mined or loaded is 60 feet per minute (fpm).

Each coal mine operator must also submit for approval a ventilation system and methane and dust control plan. The plan must show in detail the methane and dust control practices along all haulageways and travelways, at all transfer points, at underground crushers and dumps, in all active working

places and in any other areas which may be required by MSHA's local enforcement official.

Prior to approval, dust samples are collected by inspection personnel to verify system performance. The dust control plan concept was developed to provide flexibility, yet ensure that appropriate measures were being taken to control respirable dust. The following discussions provide more information on specific dust control systems used for various mining systems.

DUST CONTROL ON CONTINUOUS MINER SECTIONS

Approximately two-thirds of the mining sections in the United States utilize continuous mining machines. Continuous miners are used to both develop and retreat room and pillar mining sections. Dust generated on a drum type continuous miner is controlled by two primary means, ventilation and water. The two basic types of face ventilation are exhausting and blowing. In an exhausting ventilation system, air is brought to the face at a lower velocity, captures the dust cloud and then extracts it from the face at a higher velocity. For a blowing face ventilation system the return air passes over the mining machine. This situation necessitates the use of additional controls such as machine mounted dust collectors (scrubbers) to maintain adequate dust control.

Water sprays are used in addition to ventilation to suppress and direct the dust cloud generated at the face. Typical suppression sprays are mounted on the miner as close to the cutting drum and gathering arms as possible. These systems are designed to deliver water to strategic dusty locations around the machine. Directional sprays (spray fan systems) are mounted on the body of the miner up to 10 to 15 feet from the face. These sprays are designed to use the momentum of the water to direct the dust cloud away from the machine operator. Spray fan systems are normally used in conjunction with exhaust line brattice.

Each continuous mining section utilizes one or more roof bolters to install roof support in the entries mined. Dust control on roof bolters is especially important because the drilled strata can contain high levels of quartz. The two primary methods of controlling dust generated during roof bolting operations are through proper use and maintenance of the machine dust collection system and proper ventilation of the working place.

DUST CONTROL ON CONVENTIONAL MINING SECTIONS

In a conventional mining system the coal is extracted in a series of operations each performed in proper sequence. The operations in a conventional mining system are: cutting, drilling, blasting, loading and hauling. Each operation in the cycle employs a specialized piece of equipment to perform that operation.

The cutting operation is performed with a mobile cutting machine which most nearly resembles a large chain saw on wheels. Dust from the cutting operation is controlled by the use of a "wet" cutter bar and external water sprays mounted above the cutter bar as well as proper ventilation. The wet cutter bar is made by plumbing a water pipe inside the cutter bar which terminates in a small opening at the end of the bar. The movement of the cutting chain around the bar distributes the water along the length of the cut. External water sprays should be directed towards the ingoing and outgoing bits and also toward the pile of cuttings being deposited on the mine floor.

The drilling operation employs a mobile drilling machine with a single movable drill capable of drilling to the same depth as the cutting machine. The number of holes drilled depends on the height of the coal seam, width of the face, hardness of the coal and the desired size of the coal lumps. The period of highest dust concentration is when the drill is first sumped into the coal. Once the drill has penetrated the coal, the hole itself helps contain the dust. The use of a wet auger (drill steel) is the preferable method of controlling dust on a coal drill. Water is directed through the hollow auger to the bit and is then forced out of the hole after it has mixed with the cuttings and dust. The coal cuttings and dust are thoroughly wet and come out of the hole in the form of a slurry, thus producing very little dust.

Blasting is done chiefly with permissible explosives. An explosive charge is placed in each hole and then stemmed with an inert material (either water or clay dummies). The charges are wired together and then detonated. The rapid release of energy by the explosives breaks the coal and also generates a large amount of dust. However, the dust is rapidly dissipated if the face is properly ventilated. If the blasting is done on the return air side of the other mining operation, then personnel will not be exposed to the dust generated by blasting. The next operation is the loading of the coal by either a loading machine or a scoop. Loading machines have mechanical gathering arms which pull the coal onto a chain conveyor located along the centerline of the machine. The movement of the gathering arms and chain conveyor produces dust. This dust is controlled by the face ventilation system and by external water sprays mounted on the body of the loading machine. Prior to loading, the coal pile should be thoroughly wetted. Wetting the coal pile is particularly important since subsequent loading of the coal is done with scoops that are not equipped with water spray systems.

DUST CONTROL ON LONGWALL MINING SECTIONS

In general longwall mining systems in the United States use single or double drum shearers to retreat mine a block of coal. Longwall faces range from 400 to 1,000 feet wide with total panel length often in excess of 4,000 feet. There are approximately 100 operating longwalls which produce approximately 15 percent of the underground coal mined. Normally seven people are required to operate the longwall face equipment.

When identifying and attempting to control a longwall system's dust source(s), the longwall can be divided into three primary sources of dust generation. These sources are the machinery in the headgate area, the shearer and the shields.

The dust generated in the headgate area affects personnel on the entire longwall face since it contaminates the intake air before it traverses the face. The headgate sources are the

stageloader, crusher and product transfer points. The common practice employed for dust control is to enclose the stageloader and crusher on the sides and top and to install flat jet water sprays across the product inlet and outlet. To assist the water sprays in creating a tighter enclosure on the product inlet and outlet, a strip of mine conveyor belting or brattice is installed on both ends. Usually flat jet water sprays are located in the crusher and along the length of the stageloader. To control dust at transfer points, various types of water sprays are used.

The shearer's primary dust source is the cutting of the coal by the bits on the drum(s). To combat this dust source, four control methods are normally used. The four dust control methods are: internal water sprays, external water sprays, remote control and work practices.

Internal water sprays are the water sprays in/on the shearer cutting drum. The internal sprays are used to suppress the dust at the source and provide a cooling effect for the cutting bits. The number of sprays range from 25 to 45 with the orifice ranging from 1/8 to 3/16-inch. The operating water pressure measured at the spray nozzle ranges from 40 to 100 pounds per square inch (psi).

The external water sprays are the water sprays located on the shearer body or on any attached bar and/or arm. The best practice is to use these sprays to direct the dust laden air over the shearer body so that the shearer operator is maintained in a clean split of intake air not contaminated by the dust generated by the shearer. The operating water pressure measured at the spray nozzle ranges from 40 to 120 psi. To assist the external water sprays in directing the dust, passive barriers (usually made of mine conveyor belting) are sometimes attached to the shearer body, bars and/or arms.

A remote control unit(s) is a device that allows the shearer operator(s) to control the shearer from various locations. It is used to remove the shearer operator(s) from the dust being generated by the shearer. Radio control or umbilical cord are the two types of remote control units available. Radio control is more versatile but not as durable as an umbilical cord unit. Approximately 50 percent of the shearers are equipped with a remote control system.

Administratively controlled work practices are also used on longwalls to lower the dust exposure of personnel. The most common work practice employed to lower exposure is to reduce the amount of time personnel spend on the face. This is accomplished by having personnel move to the upwind side of the shearer after they have completed their primary tasks. Also changing the cutting sequence of the shearer can reduce the exposure of face personnel. A common practice employed is to cut unidirectional, cutting two-thirds of the face height in one direction and cutting the remaining one-third coming back. The shields (roof supports) are then pulled on the upwind side of the shearer. This practice keeps the shield setters out of the dust that is created by the shearer. However, the shearer operators are exposed to the dust generated by the shields. Bidirectional cutting, cutting fullface height in both directions, exposes shield setters to the dust generated by the shearer for half the mining cycle and the shearer operators to the shield dust for half a mining cycle.

The movement of the shield top creates a dust problem because the crushed and ground material on top of the shield falls. The severity of the dust problem will vary depending on the amount of this falling material. The dust problem can range from negligible to very severe. To circumvent this problem, the industry is phasing in electrohydraulic shields. The electrohydraulic shields have controls connected to a computer on the shields that allow a set of shields (1 to 15) to be electronically controlled. This allows shield setters to achieve an upwind position from this dust source.

SUMMARY

Prior to the 1969 Act respirable dust levels of 9 mg/m^3 were commonly reported. Today the industry average exposure for the designated occupation is approximately 1.0 mg/m^3. These dust levels have been mainly achieved through the application of the various dust control methods previously discussed which include:

1. A supply of uncontaminated intake air.
2. Suppression through the use of machine cutting head design and water.
3. Containment through the use of properly designed and maintained face ventilation systems, water sprays or barriers.
4. Dilution from an adequate supply of fresh air.
5. Avoidance through the use of remotely operated cutting and loading machines.
6. Administratively controlled work practices.

With continued application of these techniques, respirable dust levels can be maintained at acceptable limits.

EXTRACTION DRUMS AND AIR CURTAINS FOR INTEGRATED CONTROL OF DUST AND METHANE ON MINING MACHINES

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INTRODUCTION

Over the past 30 years British Coal has expended a considerable amount of research effort on solving the problems of environmental control at and around the production machines in coal mines. That effort has borne much fruit in the field of respirable dust control, with the levels of pneumoconiosis falling from over 10% of the workforce in 1970 to the current level of 0.9% for mineworkers of all ages. This improvement has been achieved despite a doubling of productivity at the coalface. However, the current rapid rise in output demands even more efficient dust control systems for the future.

The other major environmental hazard at the production machine is the frictional ignition of methane, caused by cutting tools striking quartzitic or pyritic strata in the presence of explosive mixtures of methane. There has been little reduction in the incidence of frictional ignitions over the last 20 years, with an average of 14 ignitions reported each year,[1] despite improvements in the ventilation of the cutting zone to dilute dangerous concentrations of methane and the more recent use of water sprays to cool the ignition source.

There is often a conflict between the requirements for good dust control and those for effective dilution of methane in the cutting zone or dispersal of methane layers in the roof of drivages. Excessive amounts of dust are often dispersed by the high air velocities blown into the cutting zone or roof area to get rid of methane. On longwall shearers the hollow-shaft ventilator does this job,[2] while in drivages where exhaust ventilation is used to control dust, machine-mounted fans can be fitted to disperse methane layers. The high air velocities these fans produce can result in roll-back (or back-up) of dust to the operator's position on the machine.

To overcome the conflicting requirements for dust and methane control, and also to provide the improvements needed to ensure that the vital productivity increases being gained by British Coal are not jeopardized by dust sanctions or increasing numbers of ignitions, two new control technologies have been developed at Headquarters Technical Department, the Extraction Drum for longwall shearers, and Air Curtains for use in exhaust ventilated drivages.

DUST EXTRACTION ON SHEARERS

Numerous attempts have been made in various countries to provide effective dust extraction systems on shearers, using fans and dust collectors. All failed, because of problems with blockage of ducting by coarse material, or the large size of equipment needed to supply adequate extracted airflows. However, work on small, water-powered dust capture tubes in the early 1970's[10] led to the development in the UK of effective dust extraction systems for use on shearers with cutting drums well shielded from face ventilation.[8] In these systems the non-blocking, open-ended tubes were integrated with the coal loading doors or cowls around the cutting zone. Efficient dust control on ranging-drum shearers and those with unshielded drums was not possible until the concept of the extraction drum was devised in 1981.[7]

Description of Extraction Drum

The extraction drum was developed after laboratory tests showed that the best place to extract dust was from the face side of the drum. A number of dust capture tubes are built into the drum barrel, with the tube inlets at the face side remote from face ventilation. Dusty air is drawn from the cutting zone, cleaned by the tubes, and blown out at the goaf side, from where it is turned back into the cutting zone, together with the water spray and debris, by an angled deflector plate fitted to the gearhead. Figure 1 shows a version commonly used on medium-sized drums. It has nine, 100 mm diameter, tubes which extract 1.5 m^3/s of air using 60 l/min of water, released from hollow-cone, wear-resistant spray nozzles at a pressure of 100 bar. Even though up to 70% of the air is recirculated, nearly 0.5 m^3/s of fresh air is provided to dilute methane. On smaller drums rectangular section tubes are used to minimize drum diameter, while up to twelve 100 mm tubes have been fitted to drums above 1.5 m in diameter in order to maintain air velocities across the cutting zone.

High pressure water is fed through the drum shaft to nozzles on the face-side spray ring by a dual pressure water distribution system, which also delivers up to 45 l/min of water, at approximately 7 bar pressure, to sprays on the drum to wet the cut coal before it is loaded out. It is essential to

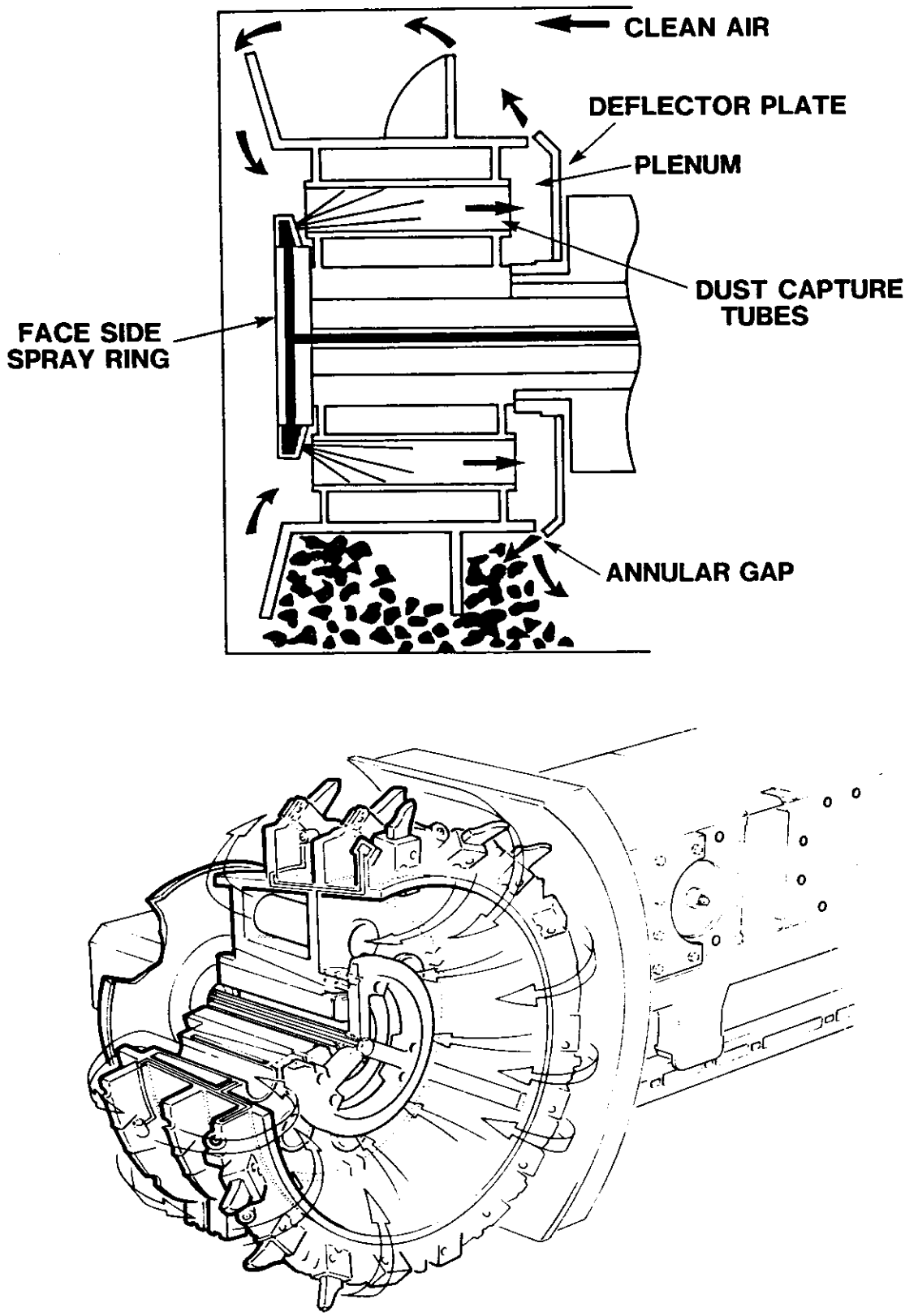

Figure 1. Schematic view and cross-section of a 9-tube extraction drum.

operate the tubes at high water pressures to provide high airflows and freedom from blockage, together with a respirable dust capture efficiency exceeding 95%.[5]

Operational problems experienced with the extraction drum have primarily resulted from inadequacies in the water supply. It is therefore essential to install water pumps with sufficient capacity, together with the correct water control and monitoring equipment. The high pressure water pump can be sited in the roadway at the end of the face, or integrated with the shearer. These pumps are expensive (for a double-drum machine, £32,000 for a roadway pump and £14,000 for a shearer-mounted pump) and represent the major cost for a system. The additional cost of fitting the two extraction drums, water distribution equipment, and deflector plates is only about £5,500.

Dust Control Efficiency

Results from underground trials on a range of shearers, see Table I, have indicated dust reductions during cutting operations of between 40% and 80% when extraction drums replaced drums incorporating the normal pick-face-flushing water spray systems. In most cases water flows were similar for each system. At one site in the UK, installation of extraction drums enabled output to be raised from 1000 to 1600 tonnes per shift without exceeding the statutory dust limits. This result shows the size of the benefits to be gained from the use of the extraction drum.

Results quoted are for dust levels in the face return air. Evidence from the USA[11] indicates somewhat less improvement at the operator's position, possibly due to the effect of the high air velocities leaving the exit annulus of the drum.

Effect on Methane Dilution

Extensive surfaces and underground trials[3] have shown that at least 30% of the air drawn in by the extraction drum is fresh air which dilutes methane in the cutting zone. Thus, for a nine-tube drum approximately 0.5 m^3/s of fresh air is provided for methane dilution, which is more than twice the airflow given by the hollow-shaft ventilator normally used at ignition risk sites. In laboratory tests on a shearer in an artificial coalface,[4] a hollow-shaft ventilator prevented frictional ignitions up to a methane emission rate of 5.5 l/s. Using the extraction drum ignitions did not occur until methane emission reached 15 l/s, which is above the emission rate on most UK coalfaces.

Measurements taken during the underground trials,[3] of methane emission rates at the shearer and methane concentrations in the cutting zone, confirmed the superiority of the extraction drum for ventilation. Consequently, British Coal now considers the extraction drum to be the best device for methane dilution, and is installing them at a number of sites primarily for ignition control. In such cases, attempts are being made to continuously monitor the extracted airflow by measuring the air pressure developed across the outlet annulus between the edge of the drum barrel and the deflector plate.[5] Alarms are activated when the airflow falls below a preset level. Systems have been fitted to a number of machines, and development is continuing to improve their reliability.

Utilization of Extraction Drums

Since 1985, when 15 drums were in use, there has been a rapid increase in numbers, with more than 85 drums in operation on some 20% of faces in the UK. In addition, drums

Table I

Reduction in Dust Produced During Cutting with Extraction Drums as Compared to Normal Water Sprays

Machine Type	Drum Diameter m	Number of Tubes	Face Air Flow m^3/s	Reduction in Dust %
Fixed Height	1.3	9	12	80
	1.5	9	15	78
	1.8	9	5	62
Single-Ended Ranging Drum	1.4	9	14	40
	1.4	9	18	72
Double-Ended Ranging Drum	1.5	10	18	53
	1.7	10	12	60
	1.8	12	13	55

have been installed both in the USA and Australia. The drums have been fitted to most types of shearer, operating on faces ranging from 1.07 m to 3.0 m in height.

HQTD have produced a comprehensive training package on the extraction drum system to aid the transfer of this technology to the collieries. This includes interactive video to cover the fault-finding and maintenance aspects.

Future developments include the use of higher water pressure to increase efficiency.

AIR CURTAINS FOR DRIVAGE MACHINES

Exhaust ventilation gives effective dust control in drivates, providing the exhaust duct entry is kept in front of the machine operator and a forward air velocity of 0.5 m/s is maintained around the machine. In practice, these requirements are often not met, and even when they are, exhaust ventilation alone cannot provide high enough air velocities to disperse methane. The air curtain system was developed to generate these velocities without dispersing dust, and also to increase dust control efficiency at sites where the ventilation criteria for preventing dust back-up were not being met.[6]

Air Curtain System

The air curtain system directs 'sheets' of fast moving air forward from the top and side of the machine body into zones of the drivage where air velocities are low and dust therefore backs up, as illustrated in Figure 2. An additional tube is usually fitted above the machine's conveyor to prevent dust from being pulled back to the operator's position by the outgoing debris. Air curtains are produced from 100 mm diameter steel tubes, fitted with cover plates from which the air is released tangentially to the tube surface through 2.5 mm deep slots running the length of the tube. The 'Coanda Effect' causes the discharged air to cling to the tube surface until directed off in the required direction by a 'splitter' bar on the tube, as shown in the tube cross-section illustrated in Figure 3.

Air is fed to the tubes at pressures of between 0.75 and 2.0 kPa by a small centrifugal fan powered from the machine's hydraulic supply at a flow of 40 l/min. The total airflow to a system depends on the length of air curtain tube used. It ranges from 0.15 m^3/s on a small boom-type machine, like the Dosco 2A, to about 0.30 m^3/s on a continuous miner, such as the BJD/Dresser Heliminer.

On some machines the exhaust duct can be installed on either side of the heading, whilst on others, aircooled motors are fitted which draw dust back beneath the exhaust duct. For such cases, tubes are sited on both sides of the machine, and the air pressures in the tubes are balanced to provide the correct flow of air around the front of the drivage towards the duct inlet.

At present systems are available for ten different boom-type machines, and three continuous miners, with equipment for a further two of the latter soon to follow. Figure 4 shows a typical system, fitted on a Dosco LH1300 machine. Prices range from £4,500 to £7,500 for a complete system, dependent upon the number and complexity of the air curtain tubes.

Airflow monitoring systems are currently under development to ensure that adequate airflows are provided for methane dispersal whenever the machine starts to cut. A new technique is at present also under development as an addition to the air curtains, to give integrated ventilation of the cutting zone for continuous miners. Air for this system would be taken from the same fan as the air curtain, and it is hoped that use of both systems will provide effective ventilation of the cutting zone and the roof, whilst maintaining effective dust control.

Dust Control Benefits

Underground trials[6] have shown that the air curtains significantly reduce dust back-up, see Figure 5. Over the range of forward airspeeds and duct entry positions used, the proportion of dust from cutting that reached the operator was reduced by at least 70% when the air curtains were

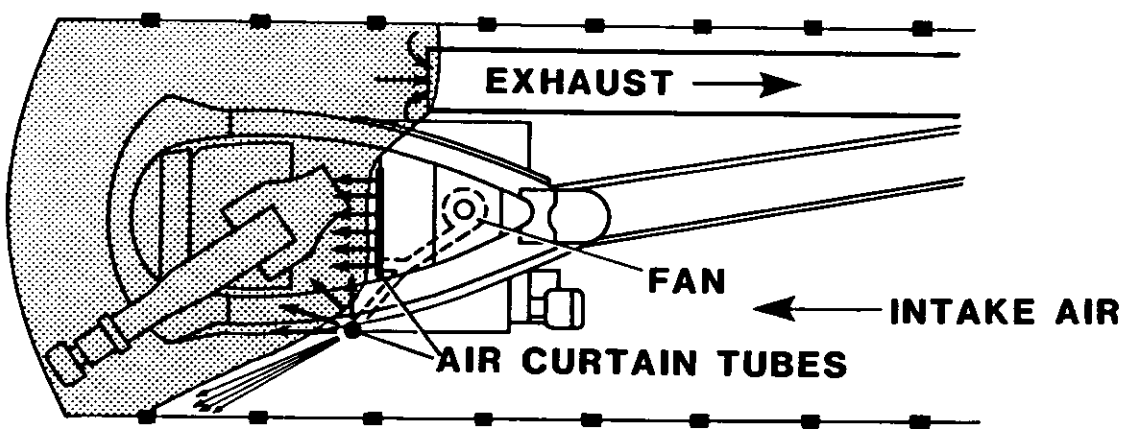

Figure 2. Plan view of drivage showing air curtains containing dust cloud.

switched on. The visual improvements when using air curtains are dramatic on most types of machines, and operators are loath to work with them turned off. Time lost in waiting for dust to clear is reduced, with consequent improvement in production. As a consequence, to date more than 80 systems have been installed.

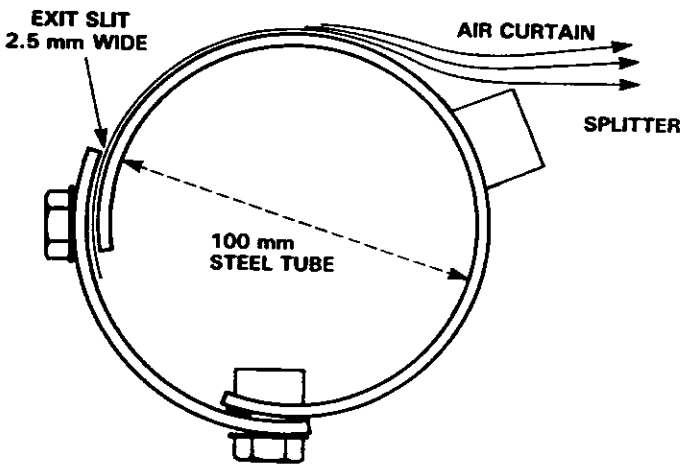

Figure 3. Cross-sectional view of air curtain tube.

Effectiveness of Methane Layer Dispersal

Full-scale laboratory tests were carried out to ascertain the air velocity profiles around Dosco 2A and LH1300 machines in an arched section drivage.[9] These tests showed that the air curtains directed air into the roof area at velocities well above the 1 m/s required for the dispersal of methane layers. In addition, they were just as effective as a machine-mounted blower fan for removing the 'dead zones' present at the front of the drivage when exhaust ventilation was used alone. Underground evaluation confirmed these results. It is now British Coal policy to fit air curtains to all drivage machines.

CONCLUSIONS

The extraction drum and air curtain systems both provide effective control of dust and methane on longwall coalfaces and in exhaust ventilated drivages respectively. Each system can be easily integrated with mining machines without detriment to operational performance, and offer solutions to the problems of environmental control on high performance coalfaces and in rapidly advancing drivages.

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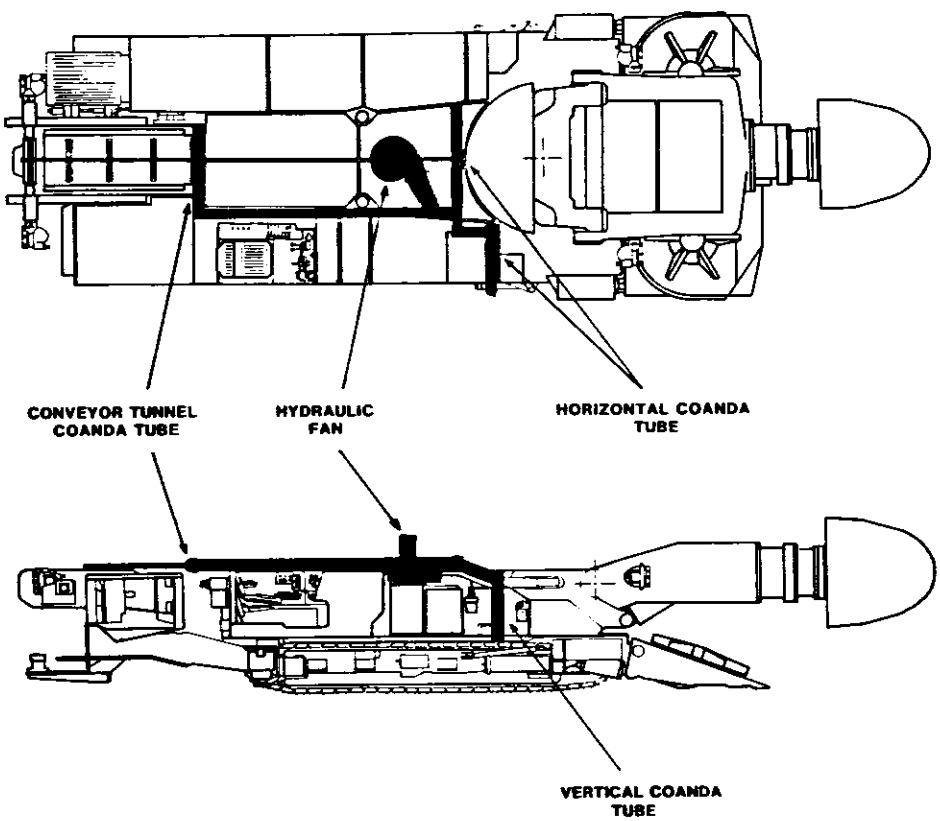

Figure 4. Air curtain system for Dosco LH1300 Drivage Machine.

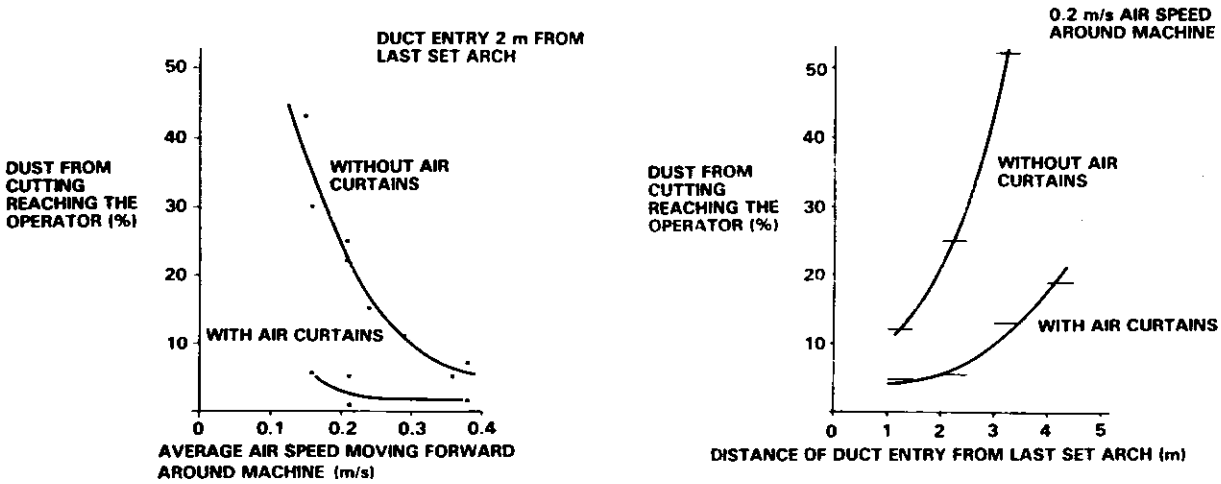

Figure 5. Underground results with air curtains on Dosco MK2A Machine.

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INCREASING COAL OUTPUT WILL REQUIRE BETTER DUST CONTROL

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BACKGROUND

In 1969, the Federal Coal Mine Health and Safety Act (FCMHSA) was passed for the purpose of reducing the incidence of Coal Workers' Pneumoconiosis (CWP), or black lung, a chronic lung disease caused by coal dust inhalation. The FCMHSA limited the average exposure of coal miners over an eight hour working shift to 3.0 mg/m^3 (milligrams of respirable dust per cubic meter of air); this maximum dust level was reduced to 2.0 mg/m^3 in late 1972, effective in 1973. Additionally, in order to reduce the incidence of silicosis, a lung disease caused by the inhalation of silica dust, the FCMHSA requires that the Mine Safety and Health Administration (MSHA) enforce a more stringent standard if dust samples contain silica in excess of 5.0 percent. (Dust standard = 10/(percent SiO_2 in sample); the standard is less than 2.0 mg/m^3 if the silica content of the sample exceeds 5.0 percent.)

The annual costs of the black lung program, which include compensation payments to retired miners or their survivors and the program costs of the Departments of Labor and Health & Human Services, have leveled off in the $1.6–1.7 billion range since 1979. The cumulative cost of the program from 1970 through 1985 is estimated at $18.4 billion.[2,5] In constant 1970 dollars using the Consumer Price Index (CPI) to adjust for inflation, however, the cumulative cost of the program was $10.0 billion, and annual costs have declined every year since 1979, from $834 million to $585 million in 1985.

Due to the time lag between initial exposure of miners to respirable coal dust and the filing of black lung claims, sometimes as long as 25–30 years, it is likely that future compensation payments will decline, if compliance with the standard is maintained, as miners who worked in dustier conditions prior to passage of the FCMHSA leave the compensation rolls. Based on a British study predicting the incidence and progression of CWP over a ten year period as a function of mean dust concentration and assuming compliance with the 2.0 mg/m^3 dust standard, Attfield forecasted the future incidence of CWP Category 1, a less debilitating form of the disease, to be about 9 percent of the underground work force and the incidence of CWP Category 2/Progressive Massive Fibrosis, a disabling form of the disease, at 1–2 percent.[1,10]

Throughout the remainder of this analysis, it is accepted as given that there is a direct relationship between lower dust levels and reduced worker morbidity and mortality. Therefore, this paper evaluates the relationship between dust control and mine worker health indirectly through its impact on mine dust levels rather than directly on incidence of dust related disease.

UNDERGROUND COAL MINING METHODS

The three major underground mining methods employed by the domestic coal industry are conventional, continuous, and longwall mining. Since conventional mining currently accounts for only 11.7 percent of underground coal production and is predicted to decline to 4.2 percent by 1995 it will not be further considered in this analysis.[3,8,11,17]

Longwall mining is more productive than continuous mining and generates more coal dust.[12,13] The silica dust problem, however, is currently almost entirely restricted to continuous mining due to the cutting pattern used in this mining method.

DUST LEVELS AND COMPLIANCE

Due to improvements in dust control technology, average dust levels of continuous and longwall mining sections are currently at or below the required dust levels (Figure 1). These data are average values, implying that not all mines operate in compliance with the dust standard. This is evident when the standard deviations of these average data are examined (Table I). Furthermore, compliance data indicate that the problem is far from having been solved—through May 1987, 70 percent of longwall sections were in compliance and only 59 percent of continuous mining sections could comply with more stringent dust standards due to the presence of silica in excess of 5 percent (Figure 2). As an example of the remaining problem, several U.S. longwall mining sections having the highest output per shift recorded an average dust exposure value of 3.8 mg/m^3, more than two standard deviations above the longwall average.[15]

The costs to the underground coal mining industry of the decline in the average dust level fall into two categories: (1) direct costs, and (2) opportunity (i.e., lost production) costs. In fiscal year 1986, for example, mine operators submitted 83,985 samples at a cost of $10.3 million.[14] The General

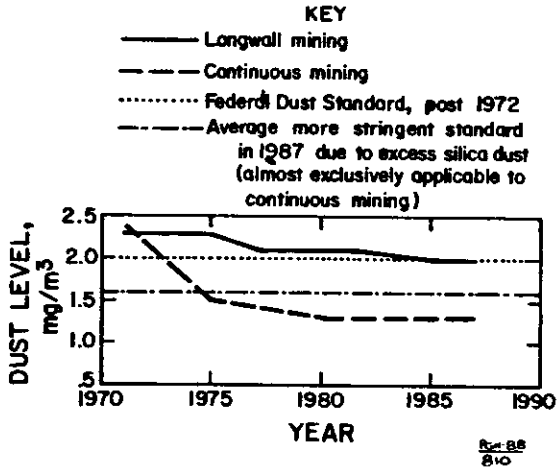

Figure 1. Average dust levels of operator samples from selected underground mining methods.

Table I

Dust Levels, by Underground Mining Method (mg/m^3)

Year	Continuous Mining		Longwall Mining	
	Ave.	Std. Dev.	Ave.	Std. Dev.
1975	1.5	0.62	2.3	1.40
1980	1.3	0.53	2.1	0.71
1985	1.3	0.42	2.0	0.52
1987	1.3	0.48	2.0	0.87

Source: (16); Bureau of Mines records

accounting Office cited a National Coal Association claim in 1977 that 15–20 percent of the total payroll in large underground coal mines is paid to employees involved with MSHA-related tasks; it is uncertain whether this figure is still accurate.[9]

The opportunity costs associated with lowering dust levels include: (1) the present value of production lost due to reductions in production rates to generate less dust per eight hour shift and thereby maintain compliance, and (2) the present value of production lost as a result of closure of mines unable to meet the standard. Longwall operators employ unidirectional cutting methods instead of bidirectional cutting solely to comply with dust regulations, resulting in an estimated production loss of 12 percent per working face. (Estimated based on personal communications with Consolidation Coal, Old Ben Coal, Jim Walters Resources, and Island Creek Coal Corp.) In 1985 this translated into a loss in potential revenues of approximately $200 million. (Revenue Loss = {[(350.8 million tons mined underground in 1985) × (14.7 pct longwall mining underground)/(100−12 pct)]—[(350.8 million tons) × (14.7 pct)]} × {$28.18 per ton average underground coal price in 1985} = $198.2 million.)

EFFECT OF COAL OUTPUT ON DUST LEVELS

A fundamental fact of coal mining is that as coal is mined at a faster rate, more dust is generated. Coal producers must balance increased production per eight hour shift against the reduction of average dust levels per eight hour shift.[4] This has become more difficult in recent years since: (1) the use of longwall mining, a more productive yet dustier mining method than continuous mining, has increased from only 3.6 percent of underground coal production in 1975 to 20.8 percent in 1987 (Figure 3), and (2) longwall mining technology has advanced dramatically. The average production of longwall sections per shift was approximately 850 short tons in 1978 and has increased to 1,968 short tons in early 1987, an increase of 132 percent.[14]

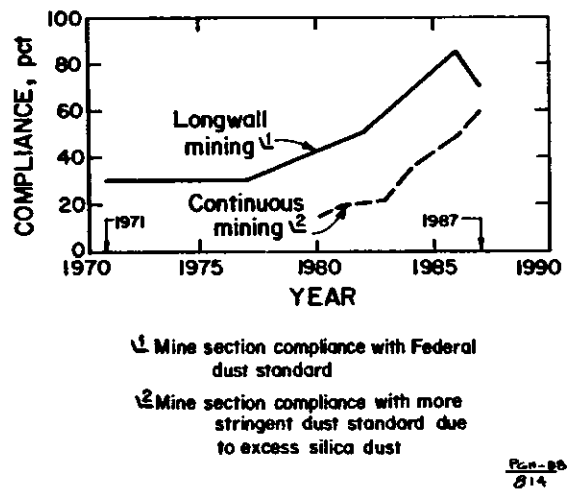

Figure 2. Compliance of selected underground mining methods with dust standards.

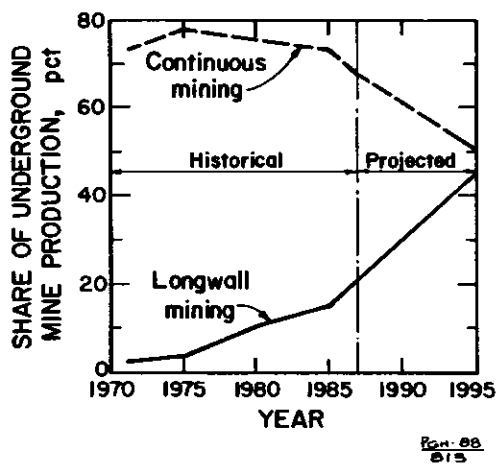

Figure 3. Production by underground mining type.

Due to the direct positive relationship between output and dust generated by longwall mining and its growing share of underground coal production, plots of dust levels against time (Figure 1) are extremely misleading. It is evident that for a given amount of dust control technology, dust levels will rise as coal output per eight hour shift rises. Average dust levels have decreased through time despite the fact that coal output per hour has increased considerably, but not as much as they would have, given the dust control technology implemented, if output per hour had remained constant. In Figure 4, the observed path of dust reduction is indicated by the round markers. Had output per shift remained at "output level 1," dust would have been reduced even further, as indicated by the square markers.

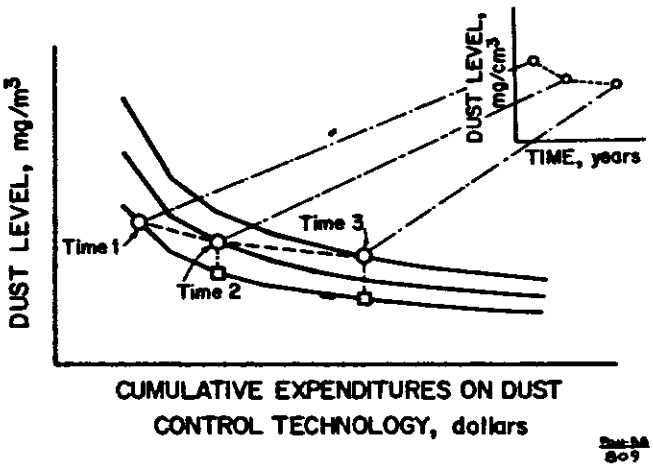

Figure 4. Effect of shifting output level on dust versus expenditures on control technology.

Dust levels of longwall and continuous mining sections adjusted for output per hour are presented in Figure 5. These adjustments were made as follows: output per hour data for the years 1970, 1978, and 1986 were indexed to 1986 levels and these ratios were used to adjust the raw dust data. The adjusted curves, then, show the dust level assuming output per hour had been held constant at the 1986 level, ceteris paribus. The adjusted average dust level in longwall sections declined from 7.29 mg/m³ in 1970 to 5.50 mg/m³ in 1978 to 2.0 mg/m³ in 1986. Raw data indicate a decrease from 2.3 mg/m³ to 2.1 mg/m³ to 2.0 mg/m³ in these years, respectively. Thus, these curves indicate that, particularly in longwall sections, average dust levels have been lowered more drastically since 1970 than is apparent from the raw data.

The 1986 average dust level was then adjusted to the year 1995 given forecasted output per hour of the two mining methods. Output per hour data for 1986 were indexed to forecasted 1995 levels and these ratios were used to adjust the 1986 dust data. (Output per hour is forecasted to increase by 28 percent for longwall mining and by 25 percent for continuous mining by 1995.) Under this scenario, if output per hour were allowed to increase to the forecasted values, by 1995 dust levels would exceed the current dust standards by 28 percent in longwall sections and by 2 percent in continuous mining sections (Figure 5).

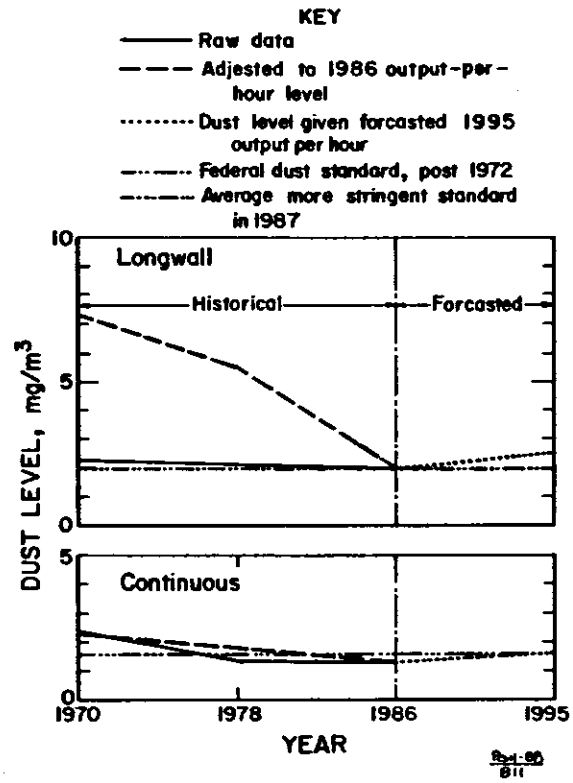

Figure 5. Dust levels of longwall and continuous mining sections adjusted for output per hour.

Unless new dust control technology is developed which enables compliance to be reached at these higher production rates, it is likely that output per hour will be significantly constrained in the future due to required compliance with the dust standard. Indeed, because the average dust level of longwall mining sections is already at the 2.0 mg/m³ standard, future increases in output per hour are already constrained, on average.

Barring the introduction of new dust control technology, the lost 28 percent increase in longwall mining output per hour forecasted for 1995 translates into a loss in potential revenues in 1995 of $584 million from currently existing longwall sections. (Coal production from longwall mining is expected to total 74 million tons in 1987 (based on calculations from data in 3, 8, 11)). Revenue Loss = {[1.28 × (74 million tons)] − [74 million tons]} × {$28.18 per ton average underground coal price in 1985} = $583.9 million.) This estimate is a maximum figure because even if no new dust control technology is developed by 1995, it is expected that more of the existing technology will be implemented by the industry before 1995.

COMPETITIVENESS

The United States is a major coal exporting nation; exports totalled 85.5 million short tons in 1986, 50 percent going to Europe and 17 percent to Canada.[6] There are numerous indications, however, that the U.S. is losing market share to foreign competitors despite the transition to more efficient

underground mining technology. Coal exports have dropped significantly from the 1981 high of 112.5 million tons. The Energy Information Administration reported that the U.S. share of the European market declined from 42 percent in 1981 to 31 percent in 1985; Australia and South Africa appear to have gained market share at the expense of the U.S.[7]

The reason for this loss in competitiveness is apparent from a comparison of the price of delivered coal to Europe (Figure 6)—the U.S. price is by far the highest of the major coal exporting nations to this market. The U.S. has been losing market share even though European coal imports have been rising. And European coal imports have been forecasted to increase from 139 million tons in 1985 to 174 million tons in 1995. Thus, unless the U.S. is able to improve its competitiveness, a continued loss of market share in Europe can be expected.

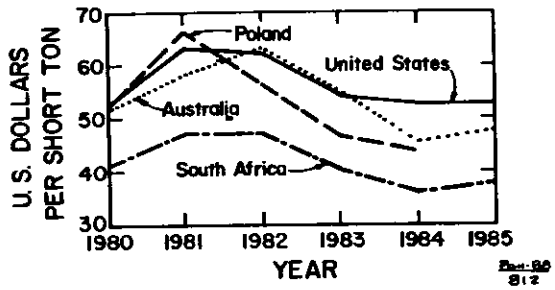

Figure 6. C.I.F prices of non-EEC coal delivered to Europe.

CONCLUSION

To reduce unit costs and thereby ameliorate its competitive position in world markets, the domestic coal industry must continue to increase output while holding the line on production costs. Output from longwall mining sections is forecasted to increase to 45.0 percent of underground coal production, from 20.8 percent currently as the industry attempts to achieve this goal.

The silica dust problem, presently uncommon in longwall sections, is anticipated to become more prevalent as a consequence of increased longwall production because continuous mining machines are used to develop coal panels for extraction by longwall methods. In addition, due to geological conditions—mining of thinner and more heavily faulted and fractured coal seams—the amount of silica dust in airborne respirable dust is expected to increase.

In light of the industry trend toward longwall mining, advancement of dust control technology is necessary to enable associated increases in production while maintaining compliance with the mandated standard. If no new control technology is made available, the dust standard will act as a binding constraint on future output per hour. This is especially pertinent to longwall mining where the average dust level is already 2.0 mg/m^3.

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ON THE TRANSPORT OF AIRBORNE DUST IN MINE AIRWAYS

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ABSTRACT

One of the primary means of control of health hazards from respirable contaminants in mine atmospheres is through design and operation of mines to meet mine health and safety regulations and recommended practices. A U.S. National Academy of Sciences study concluded that for significant progress in coal mine dust control, research should be directed more toward obtaining fundamental understanding of the origin, transport and characteristics of respirable coal mine dust. Theoretical and experimental studies on transport of dust in mine airways, particularly coordinated efforts to validate theory with practice, are scarce. Some empirical models, developed on the basis of experimental data, are available but these models cannot be applied to new conditions. The purpose of this paper is to present the results of theoretical and experimental studies on the transport and deposition of dust in mine airways. This study is a part of an ongoing research project in the Generic Mineral Technology Center on Respirable Dust.

In the paper, the assumptions of the modeling phase of the project and the development of a convection-diffusion equation for dust transport in mine airways are outlined. The important aspect of the modeling effort is the capture of the deposition phenomenon. The experiments performed under controlled conditions in a typical mine airway, as well as under normal mine operating conditions, are discussed. The comparison of the model predictions with experimental results are made to identify critical areas of agreements and deviations. The implications of the findings and areas for further research and development are presented.

LIST OF SYMBOLS

- b class of size distribution
- c concentration at center of duct
- d particle diameter
- D_p Brownian diffusivity
- K_{ij} collision frequency function
- L length of airway under consideration
- n_k number of particles in size class k
- N deposition rate
- r_i radius of particle in i^{th} class
- R radius of dust
- Sc_i molecular Schmidt number
- Sc_t turbulent Schmidt number
- $u_\star$ friction velocity
- v_t terminal velocity
- V deposition velocity of particles
- y distance from surface of deposition
- ε eddy diffusivity
- σ dimensionless particle

INTRODUCTION

The objective of this study was to aid in the control of dust in underground mines through an improved understanding of the behavior of dust clouds in mine airways. The results of the study presented in this paper span three phases. Phase I involved the development of a mathematical model; Phase II related to experimental studies in underground mine airways; and Phase III dealt with comparative analyses of the mathematical model predictions with experimental data. A summary of the three phases is presented in this paper.

MATHEMATICAL MODEL

The dispersion and deposition of dust in underground mine airways was modeled as a convective-diffusion problem. To achieve this, the constituents of the model were identified, relationships developed, and assumptions made that closely approximate the physical conditions in a mine airway. A brief description of the major components are presented in this section.

PARTICLE DEPOSITION

The three major mechanisms of deposition in turbulent airflow in mine airways are Brownian diffusion, convective diffusion, and sedimentation. Deposition due to other mechanisms such as electrostatic and thermal force, and inertial impaction were considered not significant compared to the mechanisms considered.

The equation for the turbulent diffusion of particles to the sides of the airways may be written as (Friedlander, 1977):

(equation 1)

$$N = (D_p + \varepsilon) \frac{dc}{dy}$$

while the flux towards the floor and roof are (Sehmel, 1973): (equation 2)

$$N = (D_p + \varepsilon) \frac{dc}{dy} \pm v_t c$$

The value of the eddy diffusivity ε varies within the boundary layer. Therefore, different values of ε have to be used when integrating the flux equation from the deposition surface to the core of the airflow.

An empirical relation is used for describing deposition due to turbulent diffusion in the inertial range, given by (Wood, 1981): (equation 3)

$$v^+ = \frac{N}{cu_*} = 0.13 \quad \text{for} \quad 17 < \sigma < 265$$

and: (equation 4)

$$v^+_{Skyrme} = \frac{2.6}{\sigma} \left(1 + \frac{50}{\sigma}\right) \quad \text{for} \quad \sigma < 265$$

The total deposition due to all mechanisms is given by: (equation 5)

$$\frac{N}{u_*} = \int_0^{r_1} n(r)\, dr\, v^+_{diff} + \int_{r_1}^{r_2} 0.13\, n(r)\, dr + \int_{r_2}^{r_3} v^+_{Skyrme}\, n(r)\, dr$$

The deposition due to gravity is a function of the terminal velocity and can be written as: (equation 6)

$$v_{gravity} = v_t$$

COAGULATION

Coagulation of airborne particles was represented in the mathematical model by a modified rate equation (Chung, 1981) and is given as: (equation 7)

$$\frac{dn_k(t)}{dt} = \frac{1}{2} \sum_{\substack{i=1 \\ i+j=k}}^{k-1} K_{ij} n_i n_j + n_k \sum_{i=1}^{b} K_{ik} n_i - n_k \sum_{i=b+1}^{\infty} K_{ik} n_i$$

where the first term represents the gain in particles in size class k due to the collision of particles of size i and j. The second term represents the loss of particles from size class k due to collision of class k particles with other particles. The last term represents those k class collisions occurring with particles of class less than b, the resultant size being less than the upper boundary of size class k. K_{ij} is the collision frequency term that takes into account the motion of the particles with the air, relative motion due to the air and relative motion due to sedimentation. The formula proposed by Saffman and Turner (1956) was used in the model.

The governing equation is a convective-diffusion equation. A one-dimensional equation was adopted and is represented by the relation: (equation 8)

$$\frac{\partial c}{\partial t} = \varepsilon_x \frac{\partial^2 c}{\partial x^2} - u \frac{\partial c}{\partial x} + \text{sources} - \text{sinks}$$

The equation was solved for a range of particle sizes obtained by discretizing the particle size distribution of the source dust. The behavior of the total dust cloud is a weighted average of the contribution from the various sizes. The initial condition to solve the equation is of the form: (equation 9)

$$c(x, t) = 0 \text{ for } t = 0,\ 0 < x < L$$

where L is the length of the region of interest. The boundary condition was developed by assuming that the concentration of the dust becomes asymptotic at the end of the region of interest. It is represented as: (equation 10)

$$\frac{dc}{dx} = 0$$

The source term (S(t)) was developed as a step function and is given as: (equation 11)

$$S(t) = \sum_{i=1}^{n} A_i (\delta(t - t_i)$$

when n = the number of operating modes, A_i is the amount of dust released in mode i, and δ is the dirac delta function. The model was solved numerically, using an implicit scheme (Bandopadhyay, 1982) and programmed in WATFIV.

EXPERIMENTAL STUDIES

To obtain a better understanding of the spatial and temporal behavior of dust clouds in underground mines and data to compare with the predictions of the mathematical model, a set of mine experiments were conducted. They were performed in the Lake Lynn Laboratory of the U.S. Bureau of Mines. The laboratory was formerly a limestone mine. Six experiments were conducted. The salient parameters are listed in Table I. The experiments provided data on ambient concentration, floor deposition, particle size distribution, and cross-sectional variation of dust at various stations along the length of the airway. In addition, two experiments were performed in the return airway of a longwall section.

Table I
Salient Data on Controlled Experiments

	Dust Type	Velocity, m/s
Experiment 1	Semianthracite	0.838
Experiment 2	Bituminous	0.838
Experiment 3	Semianthracite	1.855
Experiment 4	Bituminous	1.855
Experiment 5	Semianthracite	1.525
Experiment 6	Bituminous	1.525

The sampling plan for airborne concentration and deposition is shown in Figure 1. Centerline and cross-sectional airborne dust samples were collected as shown in the figure. Twelve samples were collected at each of the three cross-sectional sampling stations. The sampling systems were designed for isokinetic sampling, using specially shaped sharp-edged nozzles. Corrections as suggested by Belyaev and Levin (1974) were applied to those data for which isokinetic sampling conditions were not achieved.

Floor samples were collected at about 13 stations, 100 feet apart, along the airway. Samples were collected along the center and across the width of the airway. Flat deposition plates covered with preweighed, lightweight, "sharkskin" filter papers were used to collect the dust.

The dust was dispersed by a fluidized bed-type trickle duster through a four-port system of tubes. Each port was located at the center of the four quadrants of the airway cross-section. Semi-anthracite and bituminous dust, with top size of 25 μm and median size in the 4.96 to 7 μm range were used as source dusts.

COMPARISON OF MODEL OUTPUT WITH EXPERIMENTAL DATA

The experimental data were compared with the output from the mathematical model for similar physical conditions. Comparisons were made for ambient concentration, deposition, particle deposition rates, dispersion coefficient and cross-sectional concentration of the dust. The inputs to the model were based on the physical conditions prevailing during the experiments. These included the airway, source dust characteristics, and airflow conditions. For reasons of brevity, comparisons for only a select set of experiments are presented.

The results of comparison of model output and experimental data for experiments 1 and 6 are presented in Figures 2 and 3 for ambient concentration, and in Figures 4 and 5 for deposition.

The comparison of predicted and actual concentrations for experiment 1 (Figure 2) shows that predicted concentration falls rapidly with distance from the source tending to an asymptote towards the end of the region of interest. The experimental data also shows a rapid decrease in concentration from the source, in fact, more than that predicted by the model. However, part of this decrease may be due to agglomeration induced increase in deposition rate. The two data sets closely follow each other after 120 m from the source. The respirable dust data show that while the predicted and experimental data are generally in agreement, the experimental data show a more consistent deposition along the airway.

The concentration data for experiment 6 (Figure 3) shows a closer match between the predicted and experimental data up to 180 m, after which the experimental data tends to assume a less steeper decline in concentration. This pattern is also true in the case of respirable dust data for the experiment. The experiment was conducted at 1.55 m/s. It appears that some of the differences between the concentration data sets may be due to the greater sensitivity and scope for errors in concentration data measurement. The deviation between predicted and experimental data at the first two stations near the source may possibly be due to inadequate dispersion of the source dust.

The deposition data for experiment 1 is presented in Figure 4. The data shows good agreement between the predicted and experimental data. The agreement is especially close between 60 and 400 m. The deposition data for experiment 6 (Figure 5) also show good correlation between the two data sets between 100 and 420 m.

In addition to comparison of the predicted and experimental ambient concentration and deposition, comparisons were also made between the deposition rate per unit concentration, per unit time, and the dispersion coefficient of the dust cloud. The comparisons could be made for floor deposition only, as the amount of dust deposited on the sides and roof could not be collected with an acceptable degree of accuracy. Very little dust, compared to floor deposition, could be collected on the sides and roof.

The theoretical deposition rate was assumed to be dependent on only the physical parameters relating to the particle and flow properties. The volume concentration of the dust was assumed to be low enough to be considered a 'dilute' flow. Therefore, the particles were assumed not to affect the fluid flow properties and the theoretical deposition rate was considered to be independent of concentration or location of the dust cloud in the mine airway. However, the experimental data showed that deposition rate decreased with distance from the dust source, becoming fairly constant towards the end of the airway (Figure 6).

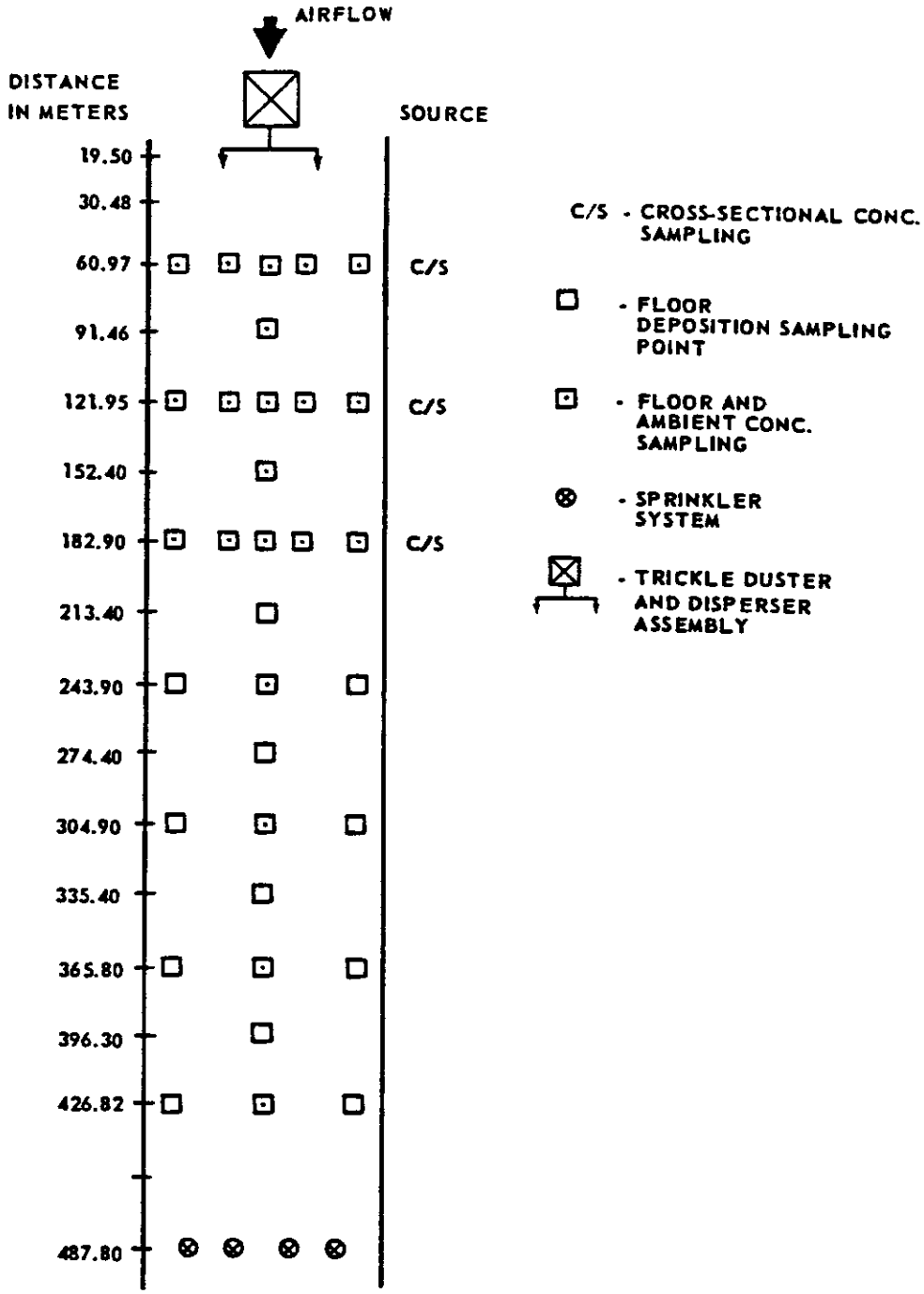

Figure 1. Ambient concentration and deposition sampling plan (Controlled Experiment 6).

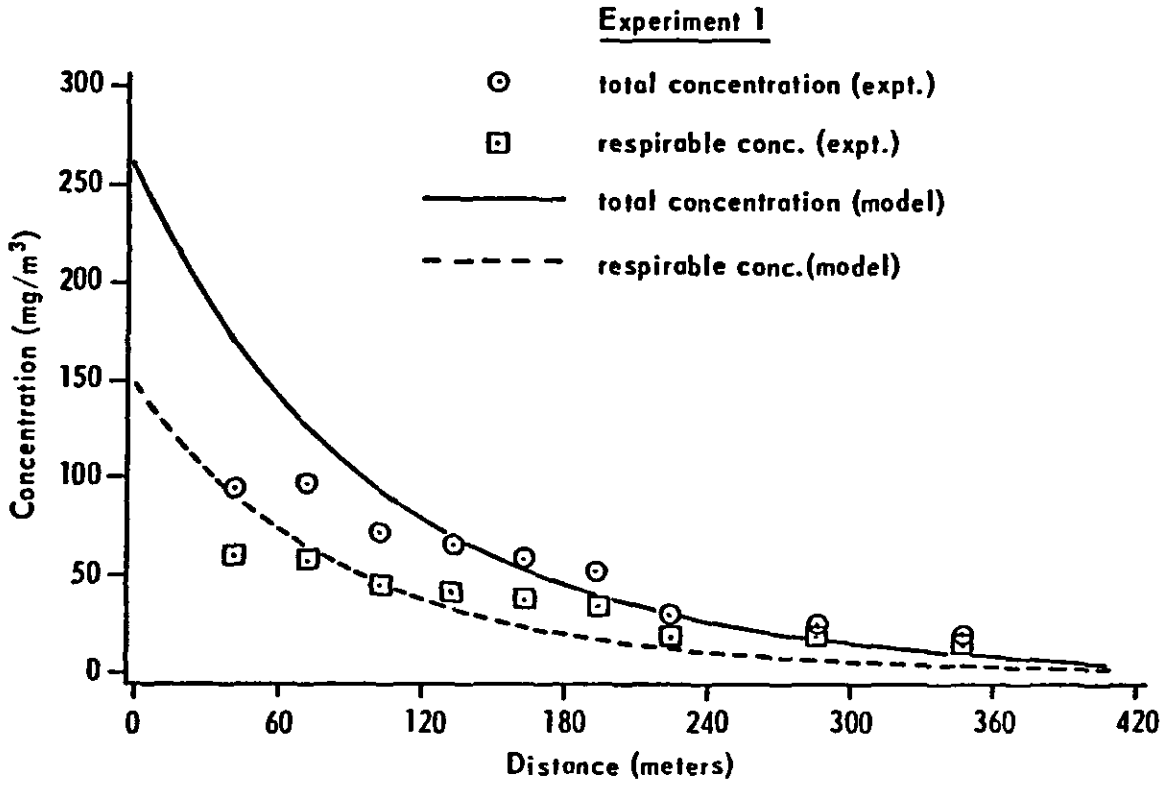

Figure 2. Comparison of model predicted concentration with experimental data (Controlled Experiment 1).

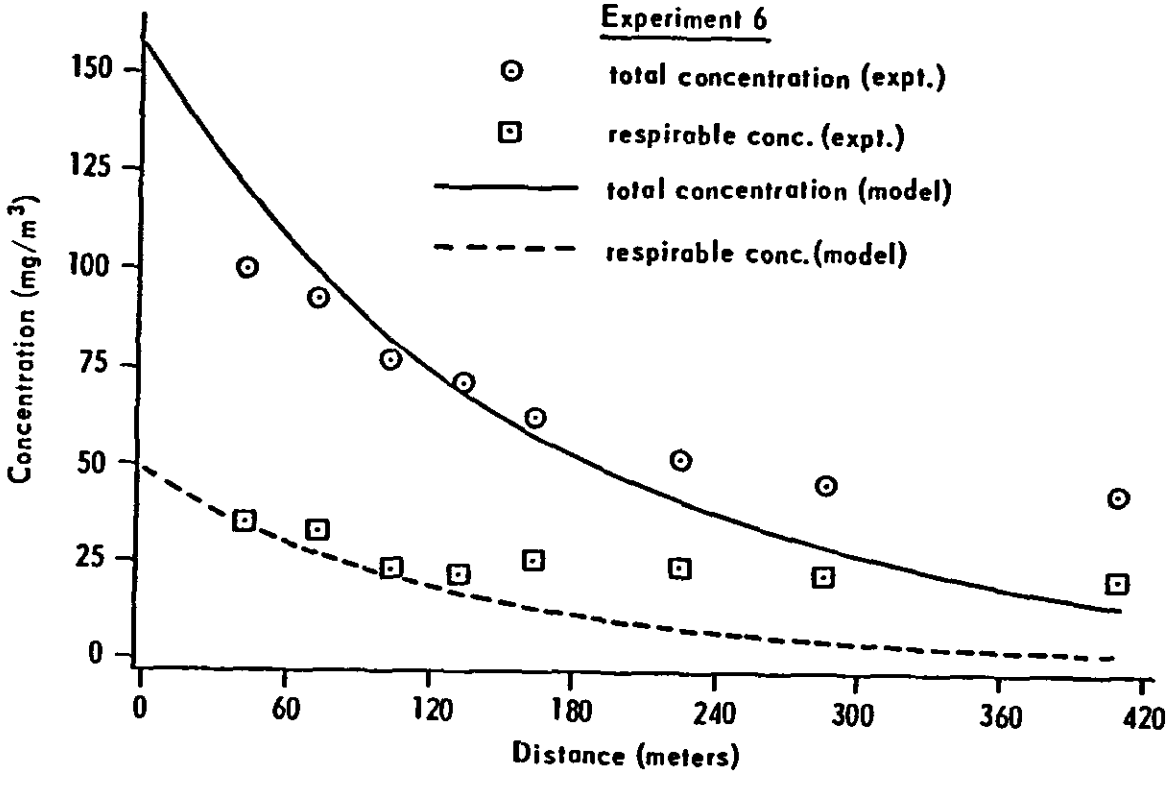

Figure 3. Comparison of model predicted concentration with experimental data (Controlled Experiment 6).

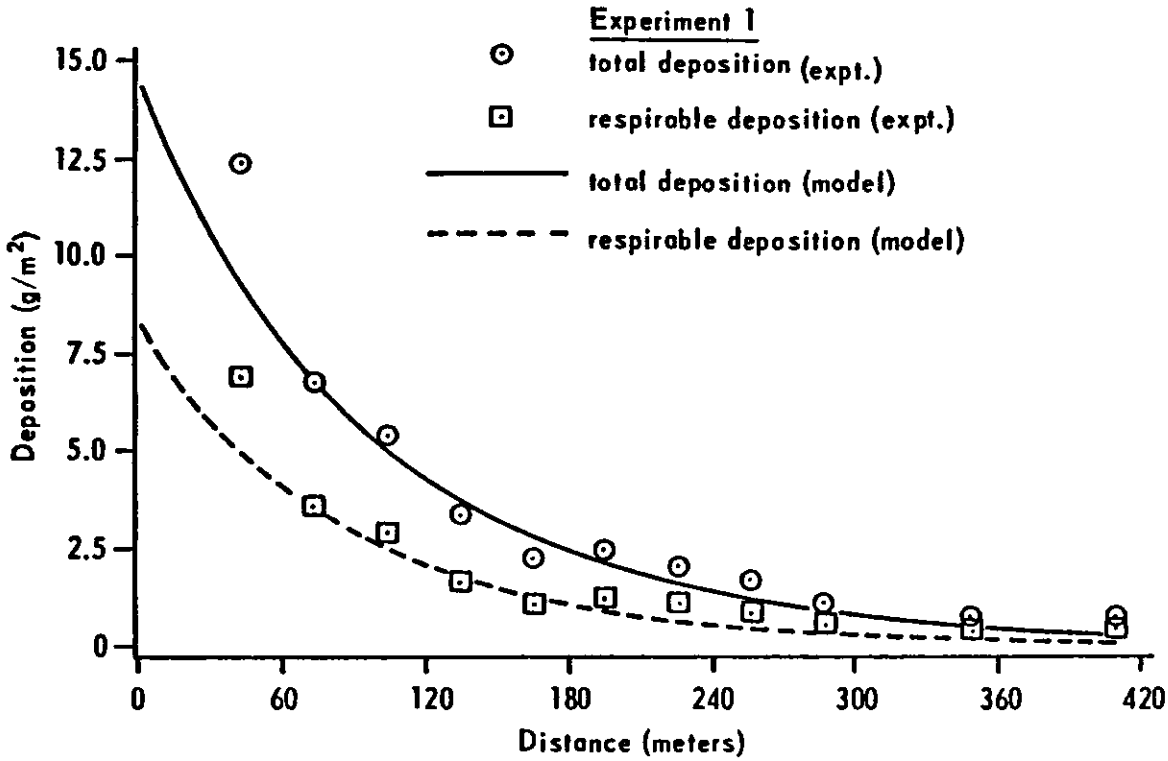

Figure 4. Comparison of model predicted floor deposition with experimental data (Controlled Experiment 1).

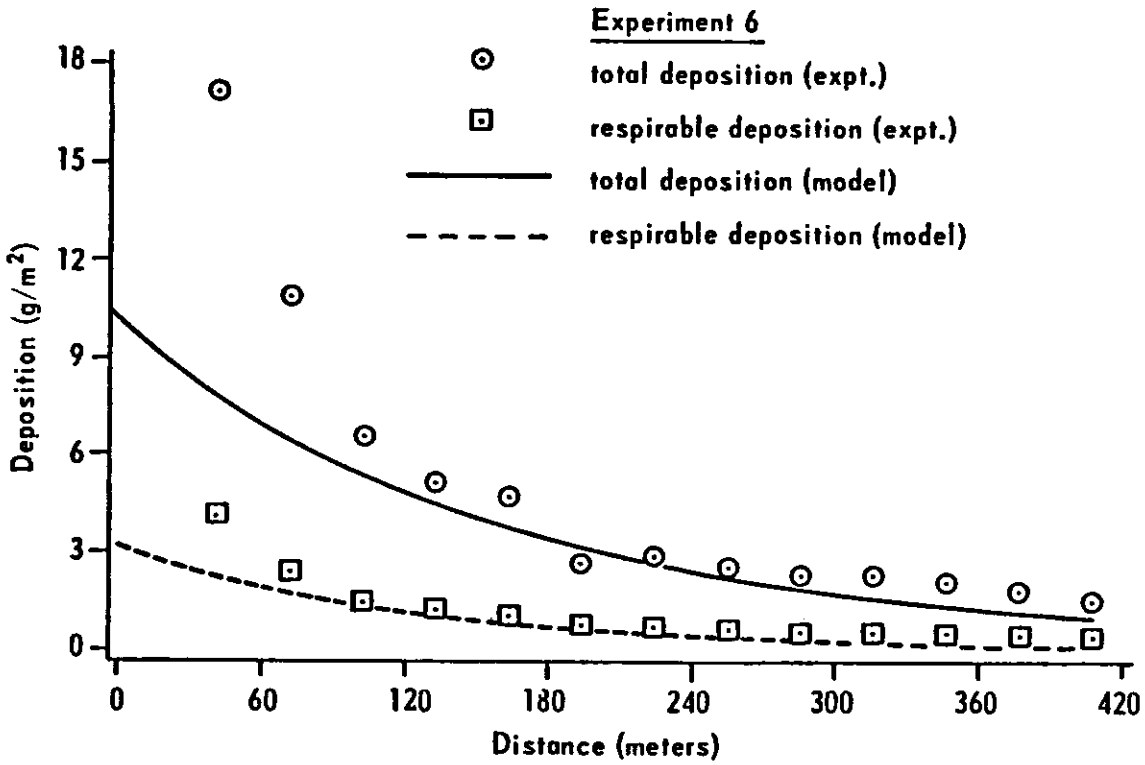

Figure 5. Comparison of model predicted floor deposition with experimental data (Controlled Experiment 6).

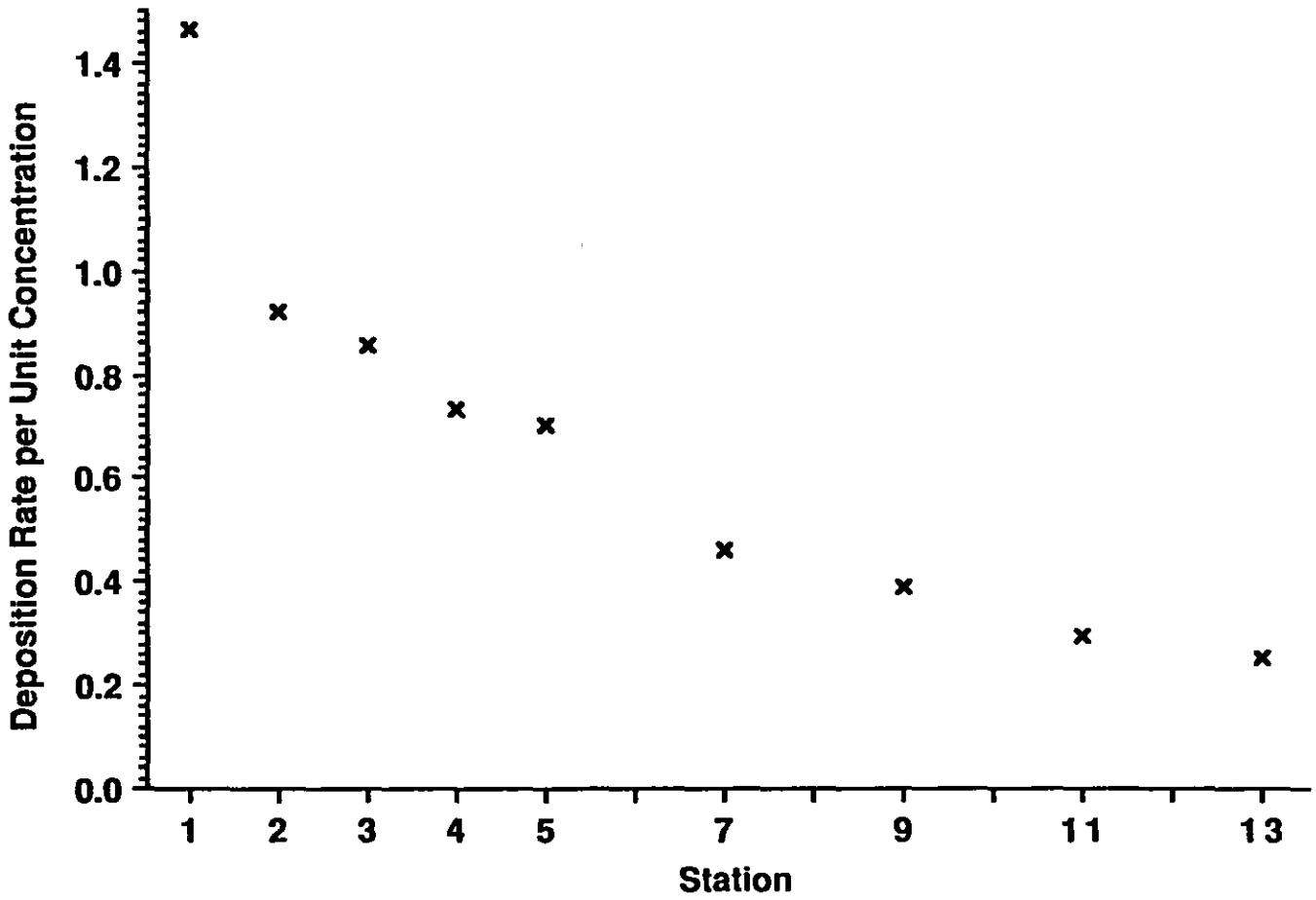

Figure 6. Normalized deposition rates of dust along mine airways (Experiment 5, size 3.73 microns).

The dispersion coefficient relationship used in the model was developed by Skubunov (1974) and is given by: (equation 12)

$$E_x = 15.8\ UDSc_i^{-0.6}\ Sc_t\ \sqrt{\lambda/\lambda_r}$$

The values obtained by this relation was compared with the experimental data. The experimental dispersion coefficient was calculated using the procedure outlined by Klebanov and Martynyuk (1974). The results are presented in Table I. The comparison of the calculated and experimental data show that both are in the same order of magnitude. The experimental values vary from 11.79 to 45.06 m^2/s while the model assumed value was 61.46 m^2/s.

Cross-sectional concentration data were also collected during the experiments. The data showed that the average concentration across the cross-section is 75% of the concentration at the center of the airway, with all the points in the cross-section given equal weights. The concentration decreases from the roof to the floor, with the top third of the airway having a concentration 72% of that in the lower third, while the concentration in the middle third being 89% of that in the lower third of the airway. Complete details of the theoretical and experimental study are presented in Bhaskar (1987).

SUMMARY

A mathematical model describing the behavior of dust clouds in mine atmospheres was developed with special reference to the condition prevailing in a mine. The model was programmed for the computer and outputs ambient concentration and deposition data as a function of time and location. The output includes both the total and respirable size ranges. In addition to mathematical modeling, experimental studies were performed in mine airways for two types of dust at three velocities. The experimental data were compared with the output of the mathematical model for similar conditions.

The results show that there are areas of agreement and deviation between the two data sets. The comparison highlighted areas, such as deposition rate, reentrainment and diffusion coefficient, where additional studies have to be performed. Studies in these areas have been initiated and are continuing.

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DUST CONTROL ON LONGWALL SHEARERS USING WATER-JET-ASSISTED CUTTING

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INTRODUCTION

Since 1977 the number of U.S. longwall mining sections using double-ended ranging-arm shearers has more than doubled. Improved productivity is a primary reason for using the longwall mining method. Average U.S. longwall production is 700 to 1,200 tons/shift compared with 300 to 400 tons/shift for room and pillar mining. However, in some cases, production on longwall sections must be limited because the levels of airborne respirable dust exceed the mandatory standard.

The best way to suppress dust generated by the shearer is to add water to the coal at a location near the cutting bit. The most effective way to accomplish this is to supply water through the rotating drum and distribute it to nozzles located in the bit block. All longwall shearers operating in the United States are equipped with this type of water spray system for dust control. Typically the water pressure measured at the nozzle is 100 to 200 psi. Increasing the water pressure delivered through the drum-mounted sprays will usually decrease dust levels.

Water-jet-assisted cutting uses moderately high pressure, 2,000 to 10,000 psi (13.5 to 67.5 MPa), solid streams of water, called water jets, that are directed to strike near the cutting bit tip. The Bureau of Mines and others have evaluated the potential advantages of using high-pressure streams of water for water-jet-assisted cutting. Water-jet-assisted cutting was used with a roadheader. Energy supplied by the water jets enabled the roadheader to cut hard rock that could not be cut when operating dry.[1] Results of an earlier laboratory test program showed that airborne dust formed during cutting could be reduced by using water-jet-assisted cutting.[2] The objective of this research program was to determine what effect use of water-jet-assisted cutting has on respirable dust levels generated during cutting with a longwall shearer.

Testing was conducted on the surface at a simulated longwall face and on an operating underground longwall section. The initial study took place at the Bureau of Mines' surface test facility in Pittsburgh, PA. Operating parameters could be controlled more precisely at the surface site than underground. A 60-ft-long (18.5 m) by 6-ft-high (2 m) coalcrete block, composed of coal, fly ash, and concrete, was used to simulate a longwall face. Because coalcrete has a higher silica content, it is more abrasive than coal; however, when using conventional drag bits, its cutting properties are similar. Overall the coalcrete face was homogeneous.

The shearer used to cut the coalcrete was a Joy 1-LS1* double-drum machine (Figure 1). For each test the shearer cut from right to left. Only the left hand, or leading drum, was supplied with high-pressure water and used for cutting during the tests. The right-hand drum was positioned so that it traveled within the cut made by the left-hand drum. A longwall face conveyor, located adjacent to the coalcrete block, provided continuous removal of the cut material, as well as functioning as a support along which the shearer moved. The diameter of the cutting drum (bit tip to bit tip) was 54 in. (137 cm), and the drum width was 28 in. (71 cm). During the tests, web width (thickness of the cut) varied from 25 to 29 in. (63.5 to 73.5 cm). The machine tram rate was maintained at approximately 5 ft/min (1.5 m/min). Drum rotation speed was 46 r/min with a bit tip speed of 650 ft/min (200 m/min). Thirty-two radial attack bits were mounted on the drum.

The site for the underground work was a longwall section in the Auguste Victoria Mine, which is located in Marl, West Germany. The face was 7.54 ft (2.3 m) thick, 919 ft (280 m) long, and mined on retreat. During the tests, one single-drum and one double-drum shearer were operated on the face. Figure 2 shows the relative locations of the shearers on the longwall face. The single drum machine, an Eickhoff model EW-200/170-L shearer, was supplied with high-pressure water (Figure 3). This shearer operated within 164 ft (50 m) of the longwall tailgate. While making dust measurements, the shearer cut only in the upper part of the face. Shearer tram rate and web width were maintained as constant as possible.

Underground testing at low pressure was conducted using the cutting drum that was originally supplied with the shearer. This drum was not designed for use with high-pressure water and a new drum had to be designed and built for the water-jet-assisted cutting tests. Table I compares features of the original and new drums. Included with the high-pressure

*Reference to specific products does not imply endorsement by the Bureau of Mines.

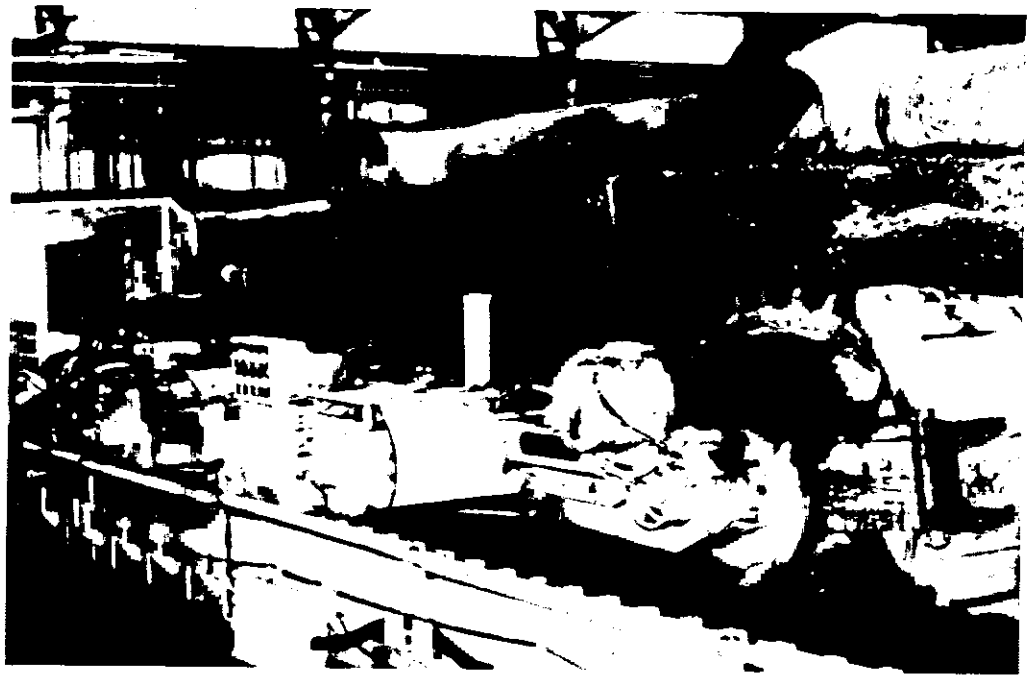

Figure 1. Shearer use for surface testing.

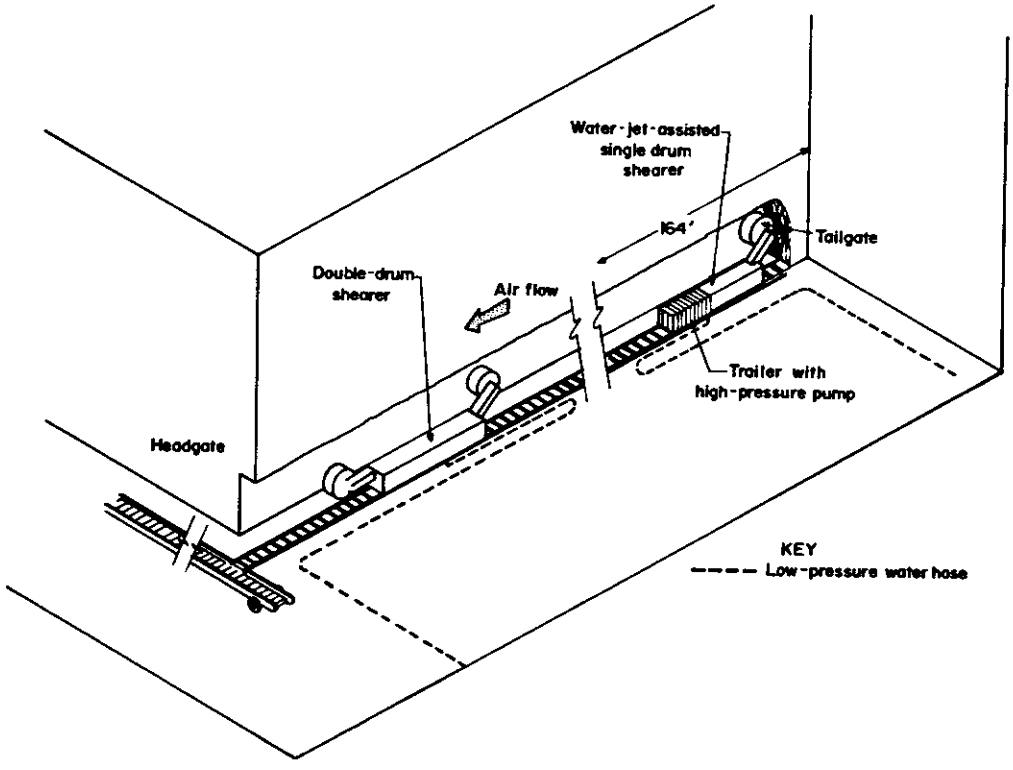

Figure 2. Underground test area.

Table I

Comparison of Cutting Drums Used During Underground Tests

	High-Pressure Drum	Low-Pressure Drum
Diameter(in).....	67	63
Web depth(in).....	33.4	33.5
R/min.....	23.6	48
Bits (No./type).....	51/conical	55/radial
Bit tip speed (ft/min)..	413	791
Spray nozzles (No./type)	50/Sapphire	41/conical
Flow rate(gal/min).....	10 to 21	10

Figure 3. Shearer operating underground.

drum was a newly designed ranging arm with double planetary gearing that provided a drum rotational speed of 23.6 r/min. The slower rotational speed allowed a more efficient distribution of fluid energy, i.e., more energy could be supplied per length of cut. However, another consequence of slower rotation speed was a deeper depth of cut. The bit lacing was modified to provide more efficient cutting and loading at deeper cutting depths.

SURFACE WATER DELIVERY SYSTEM

A 200-hp (112-kW) Aqua-Dyne triplex pump was used to supply the desired water pressures to the shearer. The pump was placed adjacent to the coalcrete face and water was transported to the shearer through a 2-in (5.1 cm) flexible hose. Water pressure during the low-pressure tests was maintained at 190 psi (1 mPa). During each water-jet-assisted cutting test the pressure was maintained constant. High pressures between 1,000 and 6,000 psi (7 to 40 MPa) were used. Water entered the cutting drum through a high-pressure Aqua-Dyne rotary seal, located in the drum hub. Six hoses were attached to the rotary seal. Each one of the six hoses carried water to a sector of the cutting drum which contained approximately 1/6 of the water jet nozzles. A water jet nozzle was located in front of each of the 32 cutting bits on the left cutting drum (Figure 4). All water nozzles in the drum operated continuously during the surface tests.

Each nozzle used for these tests had a 13 degree Leach and Walker configuration (Figure 4). To maintain approximately the same flow rate during the high- and low-pressure tests, 0.024 in. (0.6 mm) and .07 in. (1.78 mm) orifices, respectively, were used. Nozzle flow rates for each test pressure are given in Table II. Each nozzle delivered a solid stream of water to a location about 0.1 in. (3 mm) in front of the bit tip. Distance from the nozzle to the bit tip averaged about

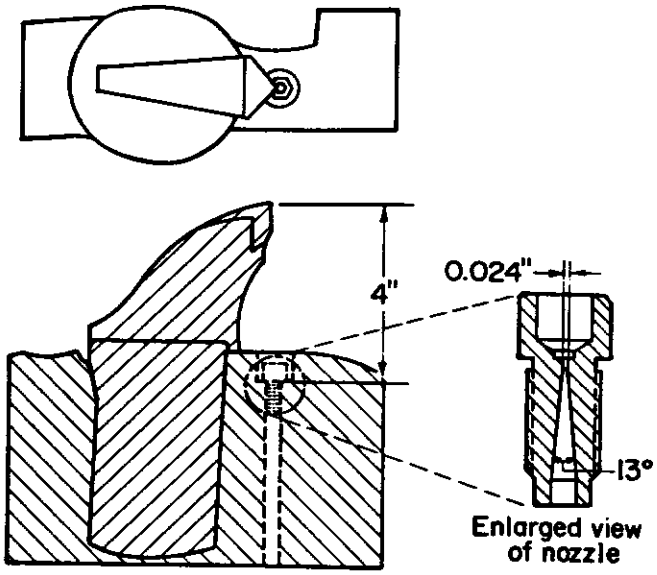

Figure 4. Bit block and nozzle configuration for surface testing.

Table II
Flow Rate versus Water Pressure for Surface Tests

Pressure, psi	Flow rate gal/min
High-pressure:[1]	
6,000.....	1.26
5,000.....	1.15
4,000.....	1.03
3,000.....	.90
2,000.....	.75
1,000.....	.54
Low-pressure:[2]	
190.....	.90

[1]0.024-in orifice [2]0.071-in orifice

4 in (10 cm). The water lines in the cutting drum were flushed frequently, and the water passed through 10 micron filters to reduce the possibility of nozzle blockage.

UNDERGROUND WATER DELIVERY SYSTEM

Normal head pressure provided water to the shearer at 340 psi (2.4 MPa). Forty-one conical spray nozzles mounted in the cutting drum were used for dust control. Total flow rate for this normal operating pressure was approximately 10 gal/min (38 l/min).

To provide the high-pressure water needed for water-jet-assisted cutting, a five-piston pump was mounted on a trailer that was pulled by the shearer. The maximum capacity of the pump was 34 gal/min at 10,000 psi. Fifty of the 51 bit blocks were equipped with jet nozzles (Figure 5). Blockage of the 0.6 sapphire nozzle orifices was reduced by installing a 10 micrometer filter in the water line.

The drum built for the high-pressure tests, was divided into 10 sectors. Water was directed to each sector through manifolds and high-pressure hoses (Figure 6). A phasing system was designed to feed the water to five of the ten sectors at a time. The average angle of the arc of rotation that was supplied with water was 195 degrees (see Figure 7). Using this phasing system reduced the water required by about 50 pct.

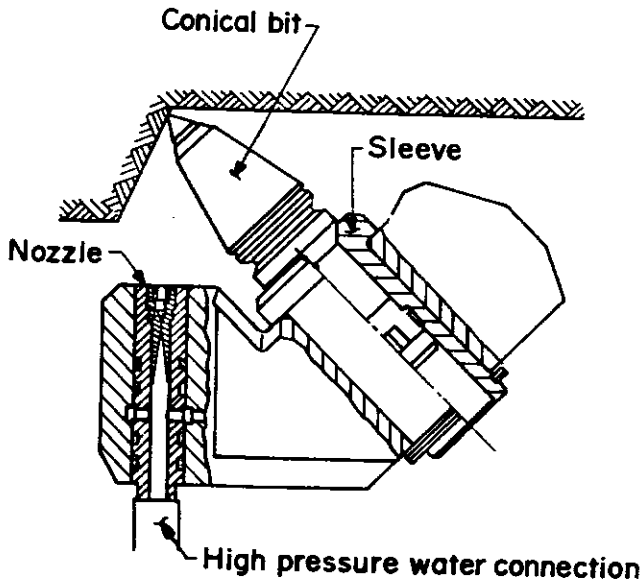

Figure 5. Bit block and nozzle configuration for underground testing.

TEST PROCEDURE

Cuts made in the coalcrete block were 5 to 40 feet (1.5 to 12.3 m) in length. Water pressure was monitored during each test cut to assure the water pressure did not vary.

Dust levels were measured at two locations near the shearer.

1. About 6 ft (1.8 m) from the cutting drum at approximately the same height as the top of the cut.
2. About 24 in. (0.6 m) from the bottom of the lead drum.

Real-time aerosol dust monitors (GCA RAM 1's) and strip chart recorders were used to track the levels of airborne respirable dust. Dorr-Oliver 10 mm-nylon cyclones were used to separate the respirable dust from the larger particulates.

Underground, one location upwind, and another downwind of the shearer were sampled. As much as possible, during underground testing, no other work that produced dust, such

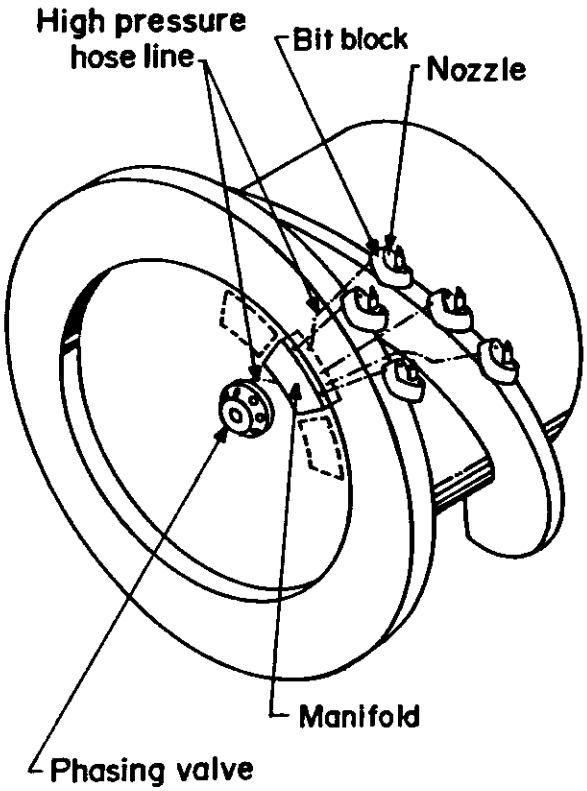

Figure 6. High-pressure water supply to cutting drum.

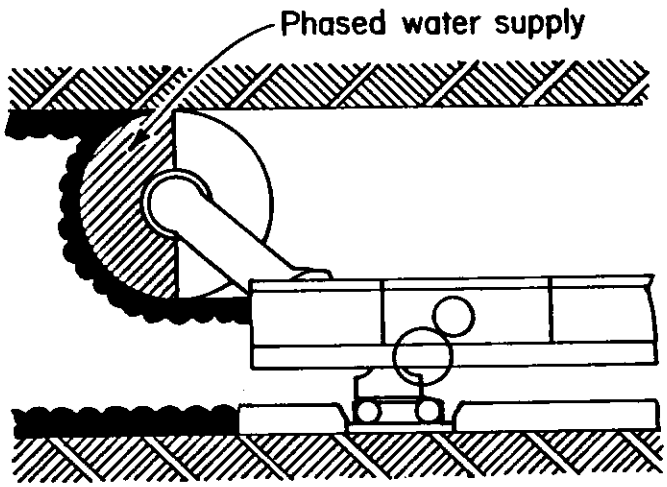

Figure 7. Phasing system for underground testing.

as moving the roof supports, was carried out upwind of the shearer. The dust generated by the second shearer, which operated on the headgate side of the test shearer, did not influence the dust readings, because airflow was from tailgate to headgate.

RESULTS

For the surface tests, the average dust levels measured while using high-pressure water (1,000 to 6,000 psi) were compared with dust levels generated while operating at 190 psi (1 MPa). The percentage dust reductions achieved by using the higher water pressures are shown in Table III. At a water pressure of 3,000 psi (20 MPa), the dust levels were 79.2 pct less than when operating at 190 psi (1 MPa). Raising the pressure further from 3,000 to 6,000 psi (20 to 40 MPa) resulted in only small additional dust reductions.

Table III

Comparison of Dust Reduction During High- and Low-Pressure Operation

Pressure, psi	Dust reduction, pct
High-pressure:[1]	
6,000.....	80.4
5,000.....	84.8
4,000.....	80.4
3,000.....	79.2
2,000.....	63.9
1,000.....[2]..	4.2
Low-pressure:[2]	
190.....	0

[1]0.024-in orifice [2]0.071-in orifice

The underground respirable dust results are shown in Figure 8. At a water pressure of 1,800 psi (12 MPa) and a water flow rate of 10 gal/m (38 l/min), average dust levels were reduced almost 80 pct compared to dust levels measured while operating at 340 psi (2 MPa) and 10 gal/min (38 l/min). Maintaining the water pressure at 1,800 (12 MPa) and increasing the flow rate to 21 gal/min (80 l/min), by increasing the nozzle orifice size, resulted in no further reduction in dust. Additional reductions in dust level due to increasing the pressure to 7,200 psi (50 MPa), with a flow rate of 21 gpm, (80 l/min) were not significant.

DISCUSSION

Dust Levels

Use of water during longwall mining reduces the levels of airborne dust by:

1. Capturing airborne dust particles.
2. Wetting the dust particles before they can become airborne.

The surface study results showed that increasing the water pressure from 190 to 1,000 psi (1 to 7 MPa) did not significantly reduce dust levels. Dust levels decreased rapidly as the water pressure was raised from 1,000 to 3,000 psi (7 to 20 MPa). Any further decrease in dust level, as the water pressure was raised from 3,000 to 6,000 psi (20 to 40 MPa), was small.

Raising the water pressure underground from 340 to 1800 psi (2 to 12 MPa) reduced airborne dust levels 70 to 80 pct. There was no significant additional reduction in dust level when the pressure was raised from 1800 to 7,200 psi (12 to 50 MPa). The fact that there is a maximum pressure above

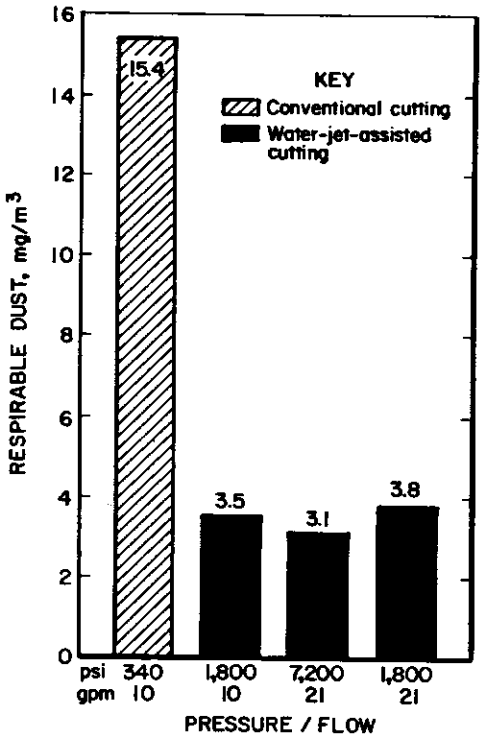

Figure 8. Underground respirable dust results.

which no further dust reductions take place further confirms the results of the surface longwall shearer study and the work performed by other researchers with roadheaders.[3]

The operation of the shearer during surface cutting of the coalcrete was similar to the operation of a shearer on an underground longwall section. However, the airflow patterns on an underground longwall face, which have a significant effect on the distribution of the airborne dust near the shearer, could not be simulated during surface testing. Also, the amount of dust generated by cutting coalcrete and coal would not be the same, due to physical differences between the two materials. Therefore, the dust levels measured during surface testing cannot be directly related to the amount of dust generated underground. However, the underground study results verify that the relative reductions in dust resulting from use of the high-pressure sprays are typical of what can be achieved underground.

Mining conditions during underground testing were representative of a typical longwall operation although the amount of dust generated was extraordinarily high. This may have been due to cutting in a faulted zone. The same reductions in respirable dust obtained underground cannot be expected for all faces. Use of high-pressure water directed through drum mounted jet nozzles would be effective for dust suppression on all longwall faces.

Interpretation of the underground dust data is complicated by the fact that during the high-pressure tests, a different cutting drum was used and the drum r/min was reduced. Cutting depth was increased because the tram rate was kept constant. Reduced drum r/min and increased cutting depth has been shown to reduce airborne dust levels.[4] It is not possible to determine how much each factor, reduced r/min, deeper cutting, or water-jet assist, contributed to the reduction in dust levels. For optimum dust control, it is recommended that high-pressure water be used with reduced drum speed and deeper depth of cut.

Supplying high-pressure water for water-jet-assisted cutting requires a large amount of fluid energy. The quantity of energy can be reduced if water is supplied only to that part of the cutting drum where the bits are in contact with the rock. Although a phasing system was used for the underground study, a suitable system wasn't available for the surface study. To more accurately reflect the amount of energy directed to the bits that were cutting during the surface tests, the total fluid energy supplied was divided by two. Using these calculations, at 190 psi (1 MPa) operating pressure, the fluid energy accounted for less than 2 pct of the total energy used during cutting. At 6,000 psi (40 MPa), almost 33 pct of the total energy supplied during cutting was provided by the water jets. During underground testing a similar proportion of the total energy was supplied by the water jets.

CONCLUSIONS

The results of the surface and underground studies showed that use of water-jet-assisted cutting significantly reduces airborne dust generated by a longwall shearer. Optimum dust suppression was achieved using pressures between 1,000 and 3,000 psi (7 to 20 MPa). These reductions in respirable dust were obtained without increases in water flow rate. Underground a phasing system, used to direct water to only those bits that were cutting, reduced water flow rate by 50 percent. The second underground trial called for under this research project will be conducted on a longwall face in the United States. During this test a double ranging arm shearer will be equipped with a high-pressure water supply system.

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TECHNICAL DUST SUPPRESSION METHODS IN COAL MINES IN THE FEDERAL REPUBLIC OF GERMANY DEPENDING ON THE CONDITIONS OF THE DEPOSITS AND THE MINING DEVELOPMENT

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In the Federal Republic of Germany, mining techniques and dust suppression measures must take into consideration the following important characteristics of the deposits:

- Great depth
- Simultaneous mining in several seams
- Mining in level and inclined formations and the occurrence of rock strata in the seams.

Conditions of the Deposits and of the Mining Technique and Dust Suppression Measures

The average mining depth in West German coal mines in 1986 was 902 m. By the year 2000, an increase in depth to around 980 m is anticipated.

The control of high temperatures requires large volumes of mine air. The results is an increased inlet of dust into the ventilating air current at the dust generation point and hinders dust sedimentation. An important planning principle in all mines is to have both the coal and the ventilating air moving in the same direction (homotropal ventilation) wherever possible. Antitropal ventilation must be avoided.

In order to avoid dust raising in the transport area, transfer points and crushers in particular must be carefully surrounded. Where the belt conveyors have to pass through air locks, covering belts (see Figure 1) are a good method of preventing the dust swirling at these points of high ventilation air velocity.

In some cases, an increasing gas content has been observed with increasing mining depth. In these cases too, large quantities of ventilation air are required in order to keep the CH_4 concentrations within permissible limits. Homotropal ventilation here is an important precondition for preventing dust raising.

Figure 1. Covering belts at air locks.

The depth of the mining operations and the associated overburden pressure demand special measures for roof control at the faces. All faces in level and inclined formations are fitted with shieldtype supports.

Cushions of rock on the shield canopy are the primary causes of dust development at the support and of the dust concentration in the mine air. A further reduction in dust can be achieved with slide bars moving in the same direction (see Figure 2) and dampening of the cushions of rock using water under high pressure (see Figure 3).

A face with a roof which is difficult to control can be effectively improved by a high rate of face advance. All the faces

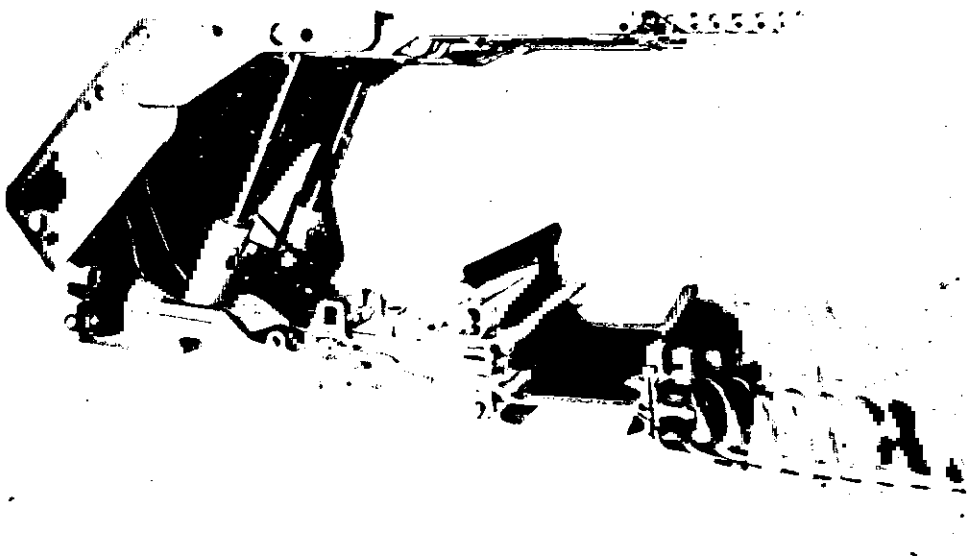

Figure 2. Shield-type support with slide bars.

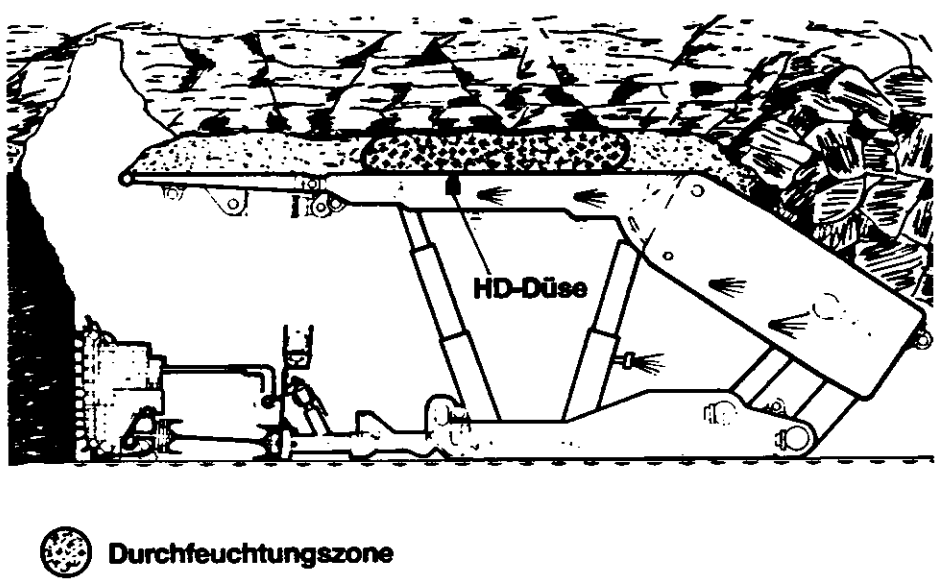

Figure 3. Dampening of the rock cushion with high-pressure water.

are operated in several coaling shifts. This multiple shift mining means, however, that only a limited time is available per night for coal face infusion from the face area, demonstrably the most effective method of dust suppression in West German coal mines. "Longwall face infusion" is therefore becoming more widespread. "Longwall face infusion" can be performed as a process of advance infusion through long boreholes from one or both gate roads. The infusion of 3–4 l/min of water with the necessary pressure is commenced several months before the actual start of mining.

High rates of face advance and the consequent demands for gate roads require a high-performance road heading system. In 1987, 100 cutting head machines and 36 impact rammers were used for this purpose (see Figure 4). The high level of dust created by the cutting head machines necessitates the use of dedusters with high extraction rates.

Mining depth and overburden pressure require special measures to maintain the cross-sections in the gate roads. These measures include back-filling of roadway supports and production of roadside packs using hydraulically bonding materials to increase the strength of the roadway supports on the side of the worked seam. The materials are transported pneumatically in pipelines. Dusts can be created if these materials are sprayed with the incorrect water content. This problem can be avoided, however, by applying the material hydro-mechanically.

These great mining depths and increasing overburden pressures have, however, also resulted in convergence-reducing road heading methods being more widely used. This has led in some cases to a move away from the gate roads being headed in front of the coal face so that the gate roads are now kept with or kept behind the line of the coal face. In 1986, 59 gate roads were kept with and 6 gate roads kept behind the line of advance of the coal face. With this method of road heading, impact rammers (see Figure 5) have proven to be effective, since they show clearly the benefit of reduced cutting into the surrounding rock and thus less dust development. In gate roads headed with the advance of the coal face, face conveyors with supporting sheave curves (see Figure 6) are used. This provides for a sliding transfer of the material conveyed during the deflection through 90°. A free fall of the material from one means of transport to the next is thus avoided.

In the vast majority of pits in West German coal mines, several seams with differing thickness are mined simultaneously in level, gently sloping and sharply sloping formations.

During this multiseam working, the horizontal development is primarily effected by excavations in the surrounding rock of the deposits. In 1986, in addition to the widely practiced heading by blasting, seven full-thickness headers were used for developing hardheads (see Figure 7). During this year, 14 km of roadway were developed. The dust production is controlled by the use of high-performance dedusters.

In the majority of cases, *headings parallel to the face* have to be developed by overcutting and undercutting due to the lack of seam thickness or the non-horizontal position of the seams in the heading area.

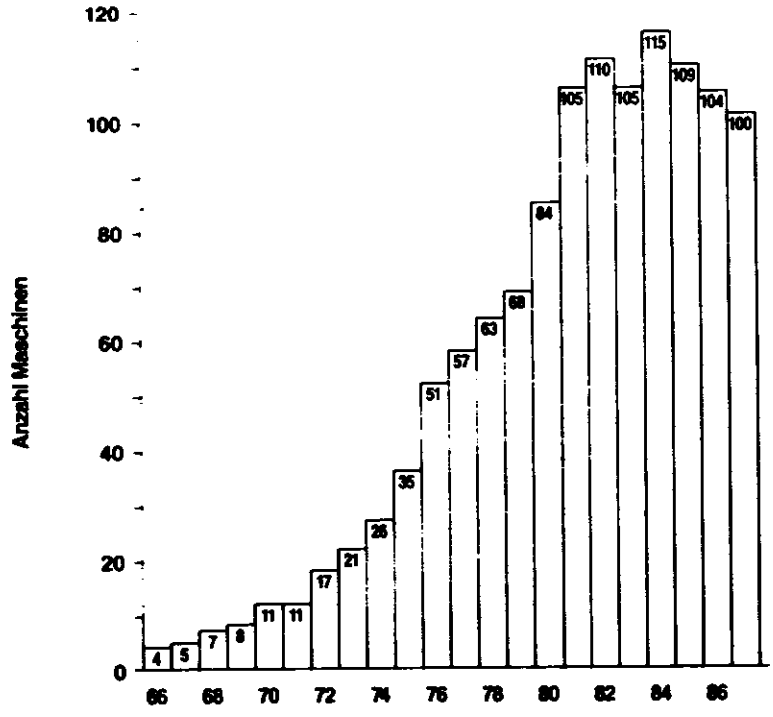

Figure 4. Use of road headers.

Figure 5. Impact rammer.

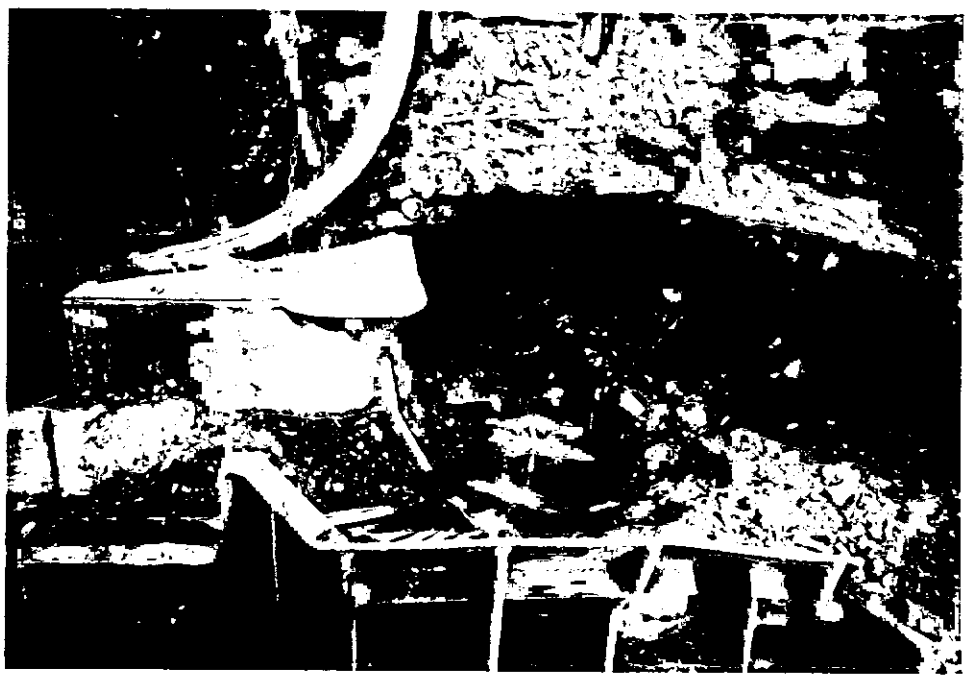

Figure 6. Face conveyor with supporting sheave curvers in the coal haulage road.

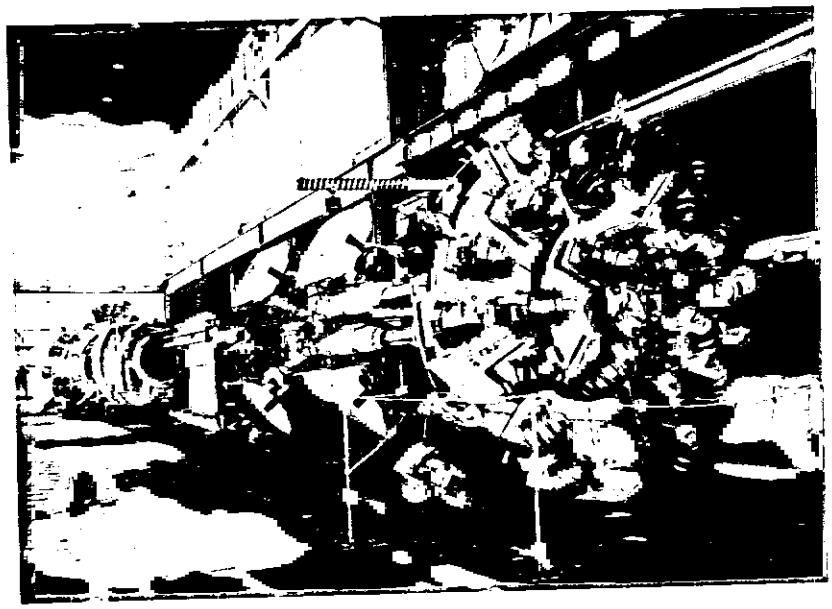

Figure 7. Full-thickness header.

Seams of greater thickness frequently contain intercalated rock materials. Coal dust and rock dust are produced when these intercalations are cut. This creates particular problems for the dust suppression. Since it is not possible to suppress the rock dust separately, the aim must be to make dust suppression so intensive that the total respirable dust content of the mine air is kept as low as possible.

Both plough-type and shearer-type machines are in operation for *mining*. The percentage of the production from 93 faces employing shearer-loader operation in 1986 was approx. 40 million tv = 48%. Shearer operation is used primarily in seams with solid coal with a thickness of greater than 1.90 m. Drum speed and pick lacing, pick length and cutting depth, drum shape, spray jet position and an adequate water distribution to the leading and trailing drums with the necessary pressure are among the most important preconditions for minimizing dust creation.[1] In 1987, good results were obtained during trials using the "coarse grain drum" (see Figure 8).[2]

In mines with gently sloping formations or mines with geological faults and high percentages of surrounding rock which is cut with the coal, no acceptable degree of dust suppression can be achieved using the measures described above. In such cases, the installation of separating elements between the conveyor track and the mining area ("dust flow separation") has proven to be an effective solution.[3,4] An effective deduster for 2/3 of the face air volume in the return air road is necessary.

In seams of lesser thickness and with soft coal, plough operation is employed. In 1986, approx. 37 million tv = approx. 45% of the total coal production came from plough-operated faces. Development of the sliding plough has now made it possible to extend the use of the plough to the tough/hard, thin and gently undulating seams of h.v. bituminous and long-flame coal. At plough-operated faces, sectional plough track spraying has been successfully used under automatic remote control for several years. In two of the mines, trials have been performed with a programmable track spray system which simultaneously monitors the pressure and volume of the spray water.

Optimization of the cutting depth, the number, shape and line of contact of the picks and, of course, the choice of the plough speed are important criteria for minimizing the respirable dust production.[5]

Applying the dust suppression measures described above, a high degree of success has been achieved in West Germany since 1952. The industrial health demands have been regularly increased since the beginning of systematic measurements of the respirable dusts. The annual number of new cases of compensation due to silicosis has decreased noticeably.[6] In order to achieve further successes in the reduction of total respirable dust concentrations, I would like to conclude by formulating a number of demands to be made on future development work on improving technical dust suppression:

1. Increased use of water under high pressure.
2. Planning of all dust suppression facilities as a complete system from the outset.
3. Greater use of remote control systems.
4. Research into the other physical properties of the dusts which would allow the dusts to be bound as a replacement, for the use of water.
5. Research into the surface physics and specific harmfulness of the individual particles.

These new developments in dust suppression measures must be put into practice as soon as possible in order to achieve a further reduction in the total respirable dust content in the mine dusts, and thus to improve the health-related working conditions of the coal miner.

Figure 8. Coarse grain drum.

SUMMARY

In the Federal Republic of Germany, the particular conditions of the deposits—average mining depth of 902 m, high overburden pressures, multiseam mining, sloping formations, developing of roads in the surrounding rock, mining of rock strata in the seam, etc.—and the mining techniques—mining using plough systems, shearer-loaders, use of road heading machines in the coal and in the surrounding rock, use of hydraulically bonding construction materials, etc.—demand intensive efforts in the development of technical dust suppression measures.

Specific planning principles, e.g., ensuring that both the coal and the ventilating air are moving in the same direction, must be observed wherever possible. Effective techniques, e.g., coal face infusion, programmable plough track spraying systems and shearer-loader spraying systems at the face, pick spraying systems on the road heading machines, must be applied.

In research and development, projects are being pursued which are aimed at extending our understanding of the surface characteristics of dust particles. The knowledge of these characteristics can then be used for even more effective dust suppression and for an assessment of the specific harmfulness of the dust particles.

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CHARACTERISTICS OF CHRONICALLY DUSTY LONGWALL MINES IN THE U.S.

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INTRODUCTION

Concentration of respirable coal mine dust in underground mines in the U.S. has been analyzed as industry wide averages and in relation to specific mining technologies.[2,7,12,13] Industry wide averages do not consider important differences between mines and analyses of exposure classified by mining technologies do not consider differences and associations within mines.

The proportion of sections in or out of compliance with the 2.0 mg/m^3 dust standard is also a common method of measuring performance. This type of analysis usually does not consider performance over longer periods of time. Since most lung diseases caused by dust require chronic exposure, it would be more appropriate for the task of disease prevention to assess patterns of violation over longer time periods than is done with measures at one point in time. And since the principal focus of enforcement is a mine, we should analyse performance of mines.

Therefore, the principal analytical unit considered in this paper is individual mines whose performance is assessed over a four year period, from FY 1984–1987. The purpose of this analysis is to describe a method for identifying chronically dusty mines and to consider characteristics of these mines that may provide insight into achieving improved dust control.

Feasible engineering controls for conventional, continuous, and longwall mining methods have been developed and described.[3,6,9] The principal methods for having these controls adopted in mines include enforcement of regulations adopted by the Mine Safety and Health Administration (MSHA), and providing technical assistance by MSHA and the U.S. Bureau of Mines (BOM).

Exposure to respirable dust has been significantly reduced since 1969 when the Federal Coal Mine Health and Safety Act was enacted.[4] However, in recent years, progress in controlling dust exposure in mines, particularly those that use longwall methods, has ceased. (Table I) Therefore, it is appropriate to question what additional opportunities exist or may be created for continuing progress in controlling exposure to dust. This analysis is limited to mines that have one or more longwall sections.

The question remains which mines have the poorest records and what do these mines have in common. The Bureau of Mines has identified some engineering problems at mines with excessive dust concentration.[5] I wish to describe some characteristics that may provide additional opportunities for intervention.

MATERIALS, METHODS

Data were gathered from three sources. First, measurements of dust exposure by mine operators were obtained from MSHA. Operators in the U.S. are required to monitor exposure to respirable dust for five consecutive production shifts six times each year.[11] High exposure personal or quasi-personal samples are taken for specified workers or "designated occupations" at each mechanized mining unit (MMU) or mine section.

The purpose of this monitoring program is to assess compliance with the statutory limit of 2.0 mg/m^3. If the average of five samples exceeds the limit, the operator is issued a citation for non-compliance and is required to continue sampling and make adjustments to reduce exposure.

This sampling program generates approximately 100,000 individual dust samples each year—an exceptionally large data base that can be used to consider a wide variety of issues. This data set includes the mine identification number (including a state code), MMU number, mining method, occupation code, date the sample was taken, and dust concentration.

The dust analysis program at the United Mine Workers of America acquires and analyzes this data on a regular basis in order to identify those mines with the most persistent dust exposure problems. Annual average dust exposure is calculated for each MMU taken at each mine. Those mines that have one or more MMUs with annual averages above 2.0 mg/m^3 are considered "dusty mines." Industry-wide average dust exposure for each mining method and the proportion of mine sections with averages over 2.0 mg/m^3 are also calculated.

Certain mines appear regularly on this list. Chronically dusty mines are those that have appeared on the dusty mines list for at least three out of the past four years.

Second, we acquired additional information about mines with active longwall sections from annual census data published in industry trade publications.[10] This includes the dimensions of longwall panels (length, width, thickness), and number of entries, and the average depth for each mine.

Third, since diesel powered equipment generates respirable

Table I
Percent of Longwall Sections with Annual Average Concentration of Respirable Dust Over 2.0 mg/m³

FY	%
1982	33.7
1983	35.5
1984	32.8
1985	37.7
1986	32.7
1987	38.4

particulates, it is possible that excess exposure to dust is associated with use of this equipment. At the present time, personal respirable dust sampling units cannot distinguish between diesel particulate and respirable coal mine dust generated by coal cutting and transport.[8] Therefore, we obtained from MSHA a census of diesel powered equipment currently used in underground mines.

None of these data sources is perfect. Operator samples of respirable dust may systematically underestimate concentration.[1] The industry census was incomplete, is dependent on voluntary contributions, and could not be independently confirmed. MSHA's census of diesel equipment also could not be independently confirmed and was a measure only at one point in time.

We compared characteristics of chronically dusty longwall mines with other longwall mines and with the remainder of the industry. Variables examined include geographic distribution, dust exposure at non-longwall sections (Without exception, these are all continuous mining sections) at these mines, number of entries, use of diesel powered equipment, and dimensions of the longwall panels.

RESULTS

Included among all longwall mines are 19 that are chronically dusty. While they occur in most mining regions, they are concentrated in the west. Out of 16 longwall mines in the west (Utah, Colorado, New Mexico, and Wyoming), 9 are chronically dusty. (Table II) Both the proportion and the number of chronically dusty longwall mines is greater than that in the mid-west, northern Appalachia or southern Appalachia.

Chronically dusty mines are somewhat more likely to use diesel powered equipment than not, though the difference is not significant (Table III). They are four to five times more likely to employ two entries for their longwall panel as other mines. This association is highly significant statistically ($p=0.002$) (Table IV).

Use of diesel powered equipment and two-entry mining are also concentrated in the west. (Tables V, VI) These three characteristics—geographic distribution, use of two entries, and use of diesels—are almost completely confounded, making it difficult to separate independent associations.

The length, width and cutting height of chronically dusty longwall panels are slightly but not significantly larger than that of other longwall panels. (Table VII) Moreover, they are also, on average, under deeper cover, especially for mines in the west. (Table VIII) Taken together, these factors may contribute to dust problems. Wider panels and larger cutting height may be associated with dust generation by increasing cutting time per shift and increased contact between cutting bits and the coal seam. Greater depth of cover puts greater pressure on the coal seam which could result in less stability and increased friability.

It is not only longwall sections at these mines that have greater dust exposure; there is greater dust exposure on continuous mining sections at these same mines. Average dust exposure (for FY 1987) and proportion of MMUs with annual averages over 2.0 mg/m³ at continuous mining sections at chronically dusty mines are both significantly greater than those at other longwall mines and greater than the remainder of continuous mining sections throughout the industry. (Tables IX, X) This is consistent with findings we have reported before.[14]

DISCUSSION

Annual average dust concentrations based on operator samples taken in order to assess compliance is a conservative measure of exposure. Because of institutional incentives, operator samples may underestimate exposure to dust. Furthermore, an annual average based on measurements taken for the purpose of assessing compliance may also underestimate exposure. After a determination of noncompliance, the operator must take additional samples until the average is reduced. In the analysis presented here, we included all measurements, including those taken for the purpose of demonstrating compliance.

By limiting attention to those mines with longwall sections that generate averages over 2.0 mg/m³ for at least three of the past four years, we miss considering those mines that

Table II

Geographic Distribution of Chronically Dusty Mines

	Number of LW Mines	Chronically Dusty Mines	(%)
West (CO, UT, NM, WY)	16	9	(56)
Mid-West (IL)	5	0	(0)
No. Appalachia (MD, OH, PA)	12	3	(25)
So. Appalachia (AL, KY, VA, WV)	44	7	(16)
Total	77	19	(25)

Table III

Chronically Dusty Mines Classified by Use of Diesel Powered Equipment (percent) 1987

	Number of LW Mines	Chronically Dusty Mines	
Using Diesel Powered Equipment	31	10	(32)
Not Using Diesel Powered Equipment	46	9	(20)
Total	77	19	

Chi Square = 1.61, 1 d.f., NS

Table IV

Chronically Dusty Mines Classified by the Number of Support Entries (percent)

	Number of LW Mines	Chronically Dusty Mines
Number of Support Entries		
2	6	5 (83)
3	27	7 (26)
4 +	39	6 (15)
Unknown	5	1

*P=0.002 Fisher's Exact Test for 2 entries v. others

Table V

Geographic Distribution of Longwall Mines that Use Diesel Powered Equipment (percent)

	Number of LW Mines	Number Using Diesels	
West (CO , UT, WY)	16	16	(100)
Mid-West (IL)	5	0	(0)
No. Appalachia (MD, OH, PA)	12	1	(8)
So. Appalachia (AL, KY, VA, WV)	44	14	(32)
Total	77	31	(40)

Table VI

Geographic Distribution of Longwall Mines by Number of Support Entries

	Number of Mines by Number of Support Entries			
	2	3	4+	Unknown
West (CO, UT, WY)	6	5	1	1
Mid-West (IL)	0	4	0	0
No. Appalachia (MD, OH, PA)	0	6	8	2
So. Appalachia (AL, KY, VA, WV)	0	12	30	2
Total	6	27	39	5

Table VII

Average (SD) Panel Dimensions and Depth of Longwall Sections

	Chronically Dusty Mines N=19	Others N-58
Cutting Height (inches)	85 (27)	74 (21)
Panel Width (feet)	632 (113)	622 (95)
Panel Length (feet)	5028 (1247)	4949 (1311)
Depth (feet)	1131 (697)	965 (533)

(None of the differences are statistically significant , p > .05, t test.)

Table VIII

Average Depth of Longwall Mines Classified by Geographic Location

	Average Depth (feet)	(SD)	N of mines
West (CO, NM, UT)	1492	(704)	16
Mid-West (IL)	620	(60)	5
No. Appalachia (MD, OH, PA)	598	(179)	12
So. Appalachia (AL, KY, VA, WV)	1084	(535)	44

p < .01 one-way ANOVA

have only recently developed longwall sections or that have temporarily stopped production. Dust exposure at these mines (the number is unknown and assumed small) may be similar to that of the mines shown here.

It is likely that several factors could contribute, independently or in combination, to the concentration of chronically dusty mines in the west. These include development of two entries, increased depth, and panel dimensions. Assessing the contribution of these factors would require more detailed examination. It is also possible that mine management or regulatory agency practices unique to this area may be contributing factors.

The relatively poor performance in continuous mining sections (in addition to longwall sections) at chronically dusty mines suggests that dust control problems at these mines may be mine-wide rather than confined to any one section or mining method. Excess dust exposure in continuous mining sections shows no geographic association and therefore, no association with any of its correlates—use of diesel powered equipment or two support entries.

We have described and demonstrated a method for identifying mines that exhibit a pattern of excess concentration respirable dust. This method could be employed more efficiently to use resources throughout the industry for the pur-

Table IX
Continuous Mining Sections With Annual Averages Over 2 mg/m³

	Total Number of Continuous Mining Sections	Number with Annual Averages > 2.0 mg/m3 (%)
Longwall Mines:		
Chronically Dusty	74	8 (11)
Other	281	8 (3)
Non-Longwall Mines	1,659	60 (4)
Total	2,014	

p < .01, Chi Square, 1 d.f., Chronically Dusty Longwall Mines v. all others.

Table X
Average Dust Exposure on Continuous Mining Sections

	Average (SD) (mg/m3)	N of samples
Chronically Dusty Mines	1.38 (1.25)	1,685
Industry-Wide Average	0.98 (1.11)	44,773

pose of achieving better dust control and thereby, to reduce the risk of chronic occupational lung disease.

We have shown that mines in the west have the poorest performance, that chronically excessive dust concentration is associated with use of two entries, and that excessive dust concentration is not limited to longwall sections. Chronic excessive dust concentration is weakly associated with increased panel dimensions and depth of cover.

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MONITORING AND CONTROLLING QUARTZ DUST EXPOSURE IN U.S. COAL MINES: CURRENT MSHA PROGRAM AND EXPERIENCE

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ABSTRACT

On December 1, 1985, the U.S. Department of Labor's Mines Safety and Health Administration (MSHA) implemented a fully computerized, revised quartz exposure monitoring program that among other features, enables coal mine operators to participate for the first time in the coal dust standard-setting process when more than 5 percent quartz is found in active workings. In addition, the improved program also provides for automatic reevaluation of work areas or occupations on a reduced dust standard on a biannual basis.

In the 22 months since its inception, 7418 MSHA, 1349 operator, and 455 operator 6-mo. samples were analyzed for respirable quartz. As a result, 1740 areas or occupations were identified as having excessive quartz dust and thus were required to comply with a reduced respirable dust standard. An additional 304 operations on reduced respirable dust standards continued to operate under stricter dust standards because of quartz reevaluations.

During this period, approximately 42 percent of the coal mining operations given the opportunity to participate in the dust standard-setting process elected to do so. Despite the lower than expected participation rate, the improved program has enabled more effective identification and more frequent monitoring of areas or occupations experiencing high levels of quartz dust exposure.

This paper will discuss the key features of the improved MSHA quartz dust exposure monitoring program, how reduced respirable dust standards are currently set, and the performance of the program since its inception.

INTRODUCTION

During the seventeen years following passage of the Federal Coal Mine Health and Safety Act of 1969, exposure to airborne quartz dust has been controlled by reducing the allowable dust standard when coal mine dust contains more than 5 percent quartz. One of the significant milestones in the Federal quartz enforcement process occurred in early 1981, when MSHA began to use the low-temperature ashing, infrared (IR) method for the determination of quartz in coal mine dust samples.

Unlike the earlier direct IR procedure, which required a number of samples to be combined to obtain a sample containing sufficient dust for analysis,[1,2] the upgraded IR method allows individual samples weighing as little as 0.5 mg to be analyzed for quartz. By using this method, the number of quartz determinations per year increased dramatically as illustrated in Table I. Consequently, this has resulted in a corresponding rise in the number of designated entities on a reduced respirable dust standard (entities that are required to be sampled bimonthly by coal mine operators), from 155 in 1980 to over 1360 in 1985.

The increase in the number of reduced standards, especially on roof bolters, coupled with growing operator concern about MSHA's longstanding policy of establishing a dust standard based on the analysis of a single inspector sample prompted the agency to reexamine its quartz enforcement strategy. In December of 1985, MSHA instituted the current quartz program, one that not only provides for more frequent monitoring of quartz dust exposure, but, for the very first time, enables coal mine operators to participate in the dust standard-setting process.

Table I

History of Inspector Coal Mine Dust Samples Analyzed for Quartz, FY 1978–FY 1987

Fiscal Year	Number of Analyses	Number with >5% Quartz
1978*	876	311
1979*	1257	528
1980*	1619	721
1981*	3937	2188
1982*	4342	1881
1983	4774	1896
1984	5134	2135
1985	4380	1712
1986	4484	1482
1987	3848	1181

* Calendar Year

MSHA's CURRENT QUARTZ PROGRAM

The implementation of the revised quartz enforcement program marked the successful culmination of three years of effort to make the dust standard-setting process more effec-

tive. Its aim was to expand the level of health protection of the miner through more frequent monitoring and timely dust-standard adjustments.

Specific Features

The current quartz enforcement program was designed to achieve these objectives:

1. Consider day-to-day variations in environmental quartz levels.
2. Allow use of limited number of operator dust samples to set the dust standard when over 5 percent quartz is found.
3. Provide for subsequent monitoring of entities (i.e., jobs, areas, or work positions) placed on a reduced standard.
4. Provide for automatic biannual reevaluation of entities placed on a reduced standard.

As before, the sample that triggers the dust standard-setting process is an MSHA sample. However, the resulting dust standard is now based on up to three samples, a combination of MSHA and operator samples. The background and development of this dust standard-setting strategy will not be discussed as it is beyond the scope of the paper.[3,4]

Adjusting a Dust Exposure Standard

The specific procedures for setting a respirable dust standard differ somewhat depending on whether an entity is (a) on the normal 2.0 milligrams per cu. meter of air (mg/m^3) dust standard; (b) already on a reduced respirable dust standard; or (c) on a reduced standard and being automatically reevaluated.

Entities on the Normal Dust Standard

Whenever an MSHA dust sample from an entity is found to contain over 5 percent quartz (or more than 10 percent quartz from a Part 90 miner already on a 1.0 mg/m^3 dust standard), the mine operator is notified by computer message of the option to collect a sample from the entity in question and submit it to MSHA for quartz analysis within a prescribed time frame. Since optional samples require minimum weight of 0.5 mg for analysis, dust collection over several shifts is permitted to obtain the required weight gain. These optional samples are used for quartz analysis only—not for compliance determination.

If the percentage of quartz found in the optional sample is within ±2% of the MSHA sample, the two values are averaged, and the result is used to determine the allowable standard by dividing it into the number 10. Should the percentage of quartz differ by more than 2%, the operator is asked to collect a second sample. The three quartz values, MSHA plus two operator, are then averaged, and the result determines the standard for the entity. All quartz percentages are truncated to a whole percent. If the hundredths position in the calculated standard is greater than 0, the standard is raised to the next highest 0.1 mg.

In the event the operator fails to submit an optional sample containing enough dust for analysis within the prescribed time frame, the standard is based on the MSHA sample alone. If the first optional sample is sent in, but not the second, the sample with the highest quartz percentage—be it MSHA's or the operator's—is used to set the standard.

Entities on a Reduced Respirable Dust Standard

When an MSHA sample is collected from an entity already on a reduced respirable dust standard, the percentage of quartz in the MSHA sample is compared to the quartz value that was used to set the standard currently in place. If the two values differ by 2% or less, they are averaged and the standard adjusted accordingly. If the difference exceeds ±2%, the operator is notified of the option to collect a sample from the entity in question. The same procedures used for entities on a normal dust standard are then followed.

Whenever a second optional sample is requested, submitted, and utilized, the preestablished quartz value is no longer used; only the three most recent samples (MSHA's plus two operator samples) are used to determine the average percentage of quartz and the applicable standard.

Automatic Reevaluations

Once an entity is placed on a reduced respirable dust standard, approximately every six months the Information System Center's computer, in Denver, CO, selects the first valid operator bimonthly sample taken on that entity. The entity, however, must be in compliance, and the sample must have sufficient weight for quartz analysis. If no valid sample can be found, the computer continues searching the incoming bimonthly samples until it finds one. This sample is retrieved and analyzed for quartz.

If the percentage of quartz in this sample is within ±2% of the quartz value used to set the current standard, the two values are averaged and the standard adjusted accordingly. If the difference exceeds 2%, the operator is notified of the option to collect another sample; the three values are then averaged to determine the standard. Should the operator not submit an optional sample with sufficient dust for analysis, the previously established standard stays in effect until the next automatic reevaluation or until an MSHA sample is submitted for quartz analysis.

Once a dust standard has been established, the operator is notified about whether bimonthly sampling will be required, the date of the first sampling cycle, and the applicable dust standard for the entity.

PROGRAM STATUS

As of the end of FY 1987 (Sept. 30, 1987), 7418 MSHA, 1349 operator optional and 455 operator 6-month samples have been analyzed for respirable quartz dust. Thirty-three percent of the MSHA, 36% of the operator optional, and 31% of the 6-month samples were found to contain more than 5 percent quartz. Roof bolter and surface highwall drill operators continue to have the highest quartz exposure. Over 23% of the roof bolter and 55% of the highwall drill samples that were submitted for analysis contained more than 10 percent quartz. Some 22% of the highwall drill samples had more than 20 percent quartz.

Of the entities given the opportunity to submit the first optional sample, only 42% elected to do so. The data appear to suggest that the operator's decision may be influenced,

in part, by the amount of quartz found in the MSHA sample. This is most apparent when the MSHA sample contains less than 8 percent quartz, a level below which an operator, if given the option, is less likely to participate in the program. The data also show that, when submitted, 33% of the samples where found to contain insufficient weight for analysis and, therefore, had to be voided. As a result, the majority of the reduced dust standards established during this period were solely based on the quartz content of the MSHA samples.

Some 1740 separate entities were required to comply with more stringent standards during part of the period. An additional 304 established entities already on a reduced standard continued to operate under such standards as a result of biannual reevaluations. Of the 2044 entities, 42% were roof bolters. At the end of FY 1987, there were 1526 or 12% more established entities (in producing status) on a reduced standard than in FY 1985, before the current program took effect. However, the number of standards at or below 1.0 mg/m^3 declined by 18%, while the mean of the reduced standards remained relatively unchanged at 1.2 mg/m^3 (Table II).

Table II

Number and (Pct) of Producing Entities on Reduced Standard

Fiscal Year	Range of Reduced Standards, mg/m^3 1.8-1.5	1.4-1.1	1.0-0.7	0.6-0.1	Avg
1985	227 (31)	218 (30)	199 (27)	90 (12)	1.1
1987	304 (42)	180 (25)	186 (26)	50 (7)	1.2

According to the quartz data, over 70% of the time the MSHA samples contained more quartz than operator first-optional samples for the same entity. And only in 31% of the instances, the quartz content of first-optional samples was within ±2% of the MSHA value (Table III). This is considerably lower than the 58% found in an earlier study which looked only at operator samples.[4]

In 74% of the biannual reevaluations, the quartz content of the 6-month sample was lower than the previous quartz percentage used to set the standard. The difference in % quartz between the previous value and the 6-month sample exceeded 5 percent 38% of the time. As shown in Table IV, only 25% of the 6-month samples were found to contain percentage of quartz that was within ±2% of the previous quartz value.

Finally, to determine the level of impact, if any, of operator participation in the program, a comparison was made of the percentage quartz in the MSHA sample and the final quartz value used to set the allowable dust standard. These show (Table V) that 77% of final quartz values were within ±2% of the MSHA value. Specifically, 56% of the time the two values were found to be equal, 31% of the time the MSHA quartz value was greater, and 13% of the time it was less than the value used to set the standard. This appears to suggest that selective operator participation can influence the final outcome of the dust standard-setting process.

Table III

Cumulative Distribution of Differences in % Quartz: MSHA* vs. Operator 1st Optional Samples

Diff. (±) % Quartz	Cumulative % ≤ Stated Diff.
0	5
1	17
2	31
3	41
4	53
5	62
>5	100

* 71% of the time MSHA samples contained more quartz.

Table IV

Cumulative Distribution of Differences in % Quartz: Previous Value* vs. 6-Month Samples

Diff. (±) % Quartz	Cumulative % ≤ Stated Diff.
0	7
1	17
2	25
3	38
4	47
5	56
>5	100

* 74% of the time Previous quartz value exceeds the 6-mo. value.

Table V

Cumulative Distribution of Differences in % Quartz: MSHA* vs. Final Value Used to Set Std.

Diff. (±) % Quartz	Cumulative % ≤ Stated Diff.
0	56
1	73
2	77
3	82
4	87
5	90
>5	100

* MSHA % quartz vs. Final % value
(=) 56% of the time
(>) 31% of the time
(<) 13% of the time

SUMMARY

Since early 1970, exposure to airborne quartz dust has been controlled by reducing the allowable dust standard when coal mine dust contains more than 5 percent.

The rise in the number of reduced standards, especially on roof bolters, and operator concerns about the use of a single MSHA sample to adjust the standard has led to the development and implementation on December 1, 1985, of a fully computerized, revised quartz enforcement program. The pro-

gram not only speeds up the dust standard-setting process to control exposure to quartz dust, but enables coal mine operators to be actively involved in this important process.

During the first 22 months of the program's operation, only 42% of the coal mining operations elected to participate in the standard-setting process. As a result, the reduced standards on the majority of the 2044 separate entities, that were found to contain more than 5 percent quartz during this period, were established based on the quartz content of the MSHA sample only.

When operator samples were submitted, over 70% of the time MSHA samples contained more quartz, and only 31% of the samples had a quartz content that was within ±2% of the MSHA value. In 74% of the biannual reevaluations, the quartz content of the 6-month sample was lower than the previous quartz percentage used to set the standard.

A comparison of the percentage quartz in the MSHA sample and the final quartz value used to set the allowable standard, revealed that in 56% of the instances the values are equal, in 31% the inspector quartz value was greater, and in 13% the inspector quartz value was less. This appears to suggest that the final outcome of the standard-setting process may be influenced by selective operator participation.

Through more frequent monitoring of exposure to airborne quartz dust, the current quartz enforcement program has had a positive impact on enhancing the level of health protection of U.S. coal miners.

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THE CHANGING FOCUS OF THE U.S. BUREAU OF MINES RESPIRABLE DUST CONTROL RESEARCH PROGRAM

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ABSTRACT

Since it was established in 1910, the Bureau of Mines, U.S. Department of the Interior, has been concerned with the problems of dust in mines. Early research focused on the explosion hazard of coal dust. Following the passage of the Federal Coal Mine Health and Safety Act of 1969 (amended by the Federal Mine Safety and Health Act of 1977) research has also focused on controlling the respirable-sized coal dust that contributes to lung diseases. Research accomplishments, along with the cooperation of the mining industry, have provided the technology and procedures that have resulted in mines in the United States being among the least dusty operations in the world.

The Bureau's dust control research has experienced three major thrusts since 1969. From 1969 to 1976, emphasis was on developing technology to comply with the newly enacted Federal dust standard of 2.0 mg/m^3. With the increasing trend in extracting coal by longwall methods, emphasis from 1976 to 1983 was on controlling the dust in these operations. Since 1983 emphasis has been on technology to reduce the silica dust component of the respirable-sized dust. Current Federal standards are based on the amount of silica dust found in the mine air. The standard becomes more stringent (less than 2.0 mg/m^3) when silica is present in the mine atmosphere.

No Paper provided.

REDUCING QUARTZ DUST WITH FLOODED-BED SCRUBBER SYSTEMS ON CONTINUOUS MINERS

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ABSTRACT

The use of scrubber systems for respirable dust control in continuous mining sections has been found to be a relatively effective approach over the last few years. However, with the implementation of more stringent dust standards due to quartz, the efficacy of some of these systems has been found to be less than optimal. In response, the Bureau of Mines has undertaken field studies to characterize quartz dust, and to determine the effectiveness of scrubber systems on quartz dust.

One underground evaluation for quartz dust suppression involved the doubling of scrubber panel to capture the quartz particles entrained in the ventilation system. The second evaluation consisted of modifying the mining sequence to include a curtain at the end of a blowing tube. Results of these tests indicate that the median diameter of quartz dust is likely to be smaller than that of coal dust. Results also indicate that quartz dust can be suppressed as effectively as coal dust by the doubling of the scrubber panel. A modified mining sequence will help to reduce the operator's exposure to quartz dust. Modified control techniques such as these will be required in mine sections where more stringent dust standards are in effect.

INTRODUCTION

One of the important methods of dust suppression in coal mine sections using blowing face ventilation is the use of machine-mounted scrubbers. They are usually of the flooded bed type, with a capacity of 5,000 to 7,000 cfm, and utilize 6 to 8 gpm of water. Differences exist in the number and location of nozzles upwind of the scrubber panel. The dust reduction efficiency at the machine operator location also varies, and for any scrubber system, depends on face air quantity blowing towards the machine. The operator exposure to dust also depends on whether a tube or a brattice is used to deliver the air to the face. Most scrubber systems do an adequate job of suppressing the dust, so that most of the coal mines using them are in compliance with the 2-mg/m^3 standard for respirable dust exposure. However, some continuous miner sections with scrubber systems are on more stringent quartz standards. It is, therefore, necessary to identify the reasons for the high quartz levels at the machine operator location, and to develop techniques that are more effective on respirable quartz dust.

To achieve the objective of quartz dust control, a knowledge of the source and character of respirable quartz in mine dust is necessary. Taylor et al.[1] indicate that the major source of quartz dust is the continuous miner mining the roof, floor, or middleman (a rockband in the middle of the coal seam). Laboratory testing by Conoco[2] indicates that approximately 65 pct of the respirable dust from a sandstone block (cut by bits on a shaping machine) was less than 2 µm in size. Stobbe et al.[3] have investigated dust from the return of a continuous miner face for size fractions. The results indicate that about 40 pct of respirable quartz dust is between 1 and 3 µm in size.

This paper deals with the nature of quartz dust and explains the methods to suppress it in sections using machine-mounted scrubbers. Quartz size and percentage evaluation was carried out in a mine with a rockband near the top of the coal seam. Evaluation for dust suppression took place in a mine that utilized two panels, instead of one, to capture the quartz particles in the scrubber system. The second evaluation for dust suppression was completed in a mine that used a modified mining sequence with a curtain at the end of the blowing tube.

EVALUATION OF CONTINUOUS MINER DUST FOR SIZE AND QUARTZ PERCENTAGE

Experimental Procedure

The procedure consisted of collecting respirable dust samples using a 10-mm nylon cyclone and a 2-lpm Dupont* pump. The samples were collected from the face return of a continuous miner in a three-entry section in Virginia. The sampling location selected was approximately 40 ft from the face, in the dust cloud raised by the continuous miner while cutting the coal seam and roof rock. An impaction device and filter cassette sampled the same dust cloud at the same location for a different size fraction. Figure 1 shows the impaction device and cassette filter arrangement.

*Reference to specific products does not imply endorsement by the Bureau of Mines.

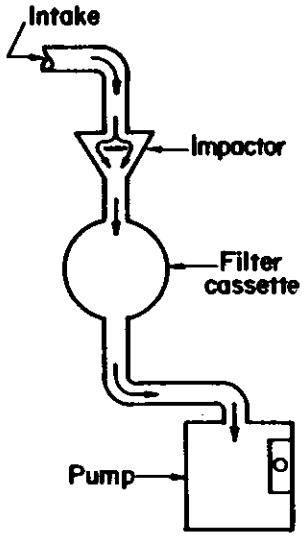

Figure 1. Collection of dust sample through an impactor.

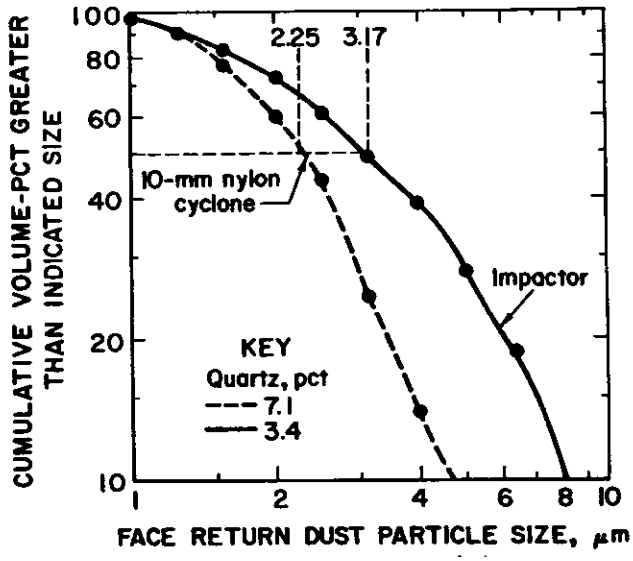

Figure 2. Results of particle size analysis for cyclone and impactor samples.

Analysis Results

The analytical method used to determine quartz content was the standard P-7 method approved by MSHA for these types of samples. Table I shows results of quartz analysis for the two sets of samples. The size distribution of the samples was determined by a Coulter Counter. Table II shows results of particle analysis, and Figure 2 compares the impactor and cyclone results graphically. It can be seen that the median particle size for the regular respirable sample was 2.25 μm, while that for the impactor was 3.17 μm. This means that, in general, the impactor sample consisted of larger size particles than the cyclone sample. However, the quartz percentage in the regular cyclone sample was almost twice that of the impactor sample. This indicates that there is more quartz dust in the smaller size fraction (cyclone sample) of the dust in the face return of the continuous miner. It can also be interpreted that the quartz dust, in general, is finer than coal dust.

CONTROL OF QUARTZ DUST AT A CONTINUOUS MINER SECTION IN MINE *A*

The first underground test was carried out in a coal mine section in Illinois. Two Joy 14 CM continuous miners with flooded bed scrubbers were operating in a 6.5-ft-high coal seam. Electric shuttle cars hauled away approximately 1,200 tons of coal every shift. The entries were 16 ft wide, and a 20-ft cut was usually taken. Face airflow was 8,000 cfm through a blowing curtain. The scrubber airflow was approximately 5,000 cfm, and the miner was equipped with a conventional water spray system. Twenty hollow-cone nozzles, each discharging about 0.7 gpm at 100 psi, were being used. No wetting agent was in use at the mine. Figure 3 shows the ventilation layout and sampling points for scrubber evaluation.

Experimental Procedure

Filter samples were primarily taken to identify the fraction of quartz in the samples, while the light-scattering instruments were used to determine where in the mining cycle dust was being generated. Filter samples were collected using MSA filter holders and compliance-type cassette filters. A 10-mm nylon cyclone sized dust into the respirable range, and air was sampled at a rate of 2 lpm using a flow-controlled Dupont pump. Filters were pre- and post-weighed at Bruceton, PA. Filter samples were collected in packages of three or four, and results were averaged to minimize sampling errors. Filter packages were located as follows:

1. Intake: Located in the last open crosscut and hung from a roof bolt to a distance of 12 to 18 in. from roof.
2. Return: Located in the immediate return of the entry being mined, approximately 80 ft from the face. This was hung 6 to 18 in. from the roof, such that it was representative of face return.
3. Hinge point: Located less than 24 in. from the right rear side of the scrubber inlet, on top of the miner frame. It was protected by a steel enclosure to prevent it from being damaged by falling coal or rock.
4. Operator: Located in the cab, 12 to 18 in. to the left side, and about the same height as the operator's head.

All filter samples were taken only during a portion of the shift and do not represent full-shift samples.

Sampling procedure for scrubber efficiency consisted of drawing air into cans, as shown in Figure 4. One isokinetic probe was introduced into the airstream to sample the dirty air in the intake duct, and another probe to sample clean air coming out of the scrubber fan. The velocity of the air, in inlet and discharge of duct, was measured using a pitot tube.

Table I
Results of Quartz Analysis

Sample No.	Sample type	Dust weight micrograms	Quartz weight micrograms	Quartz pct
1.....	Cyclone	1,220	85	6.9
2.....	Cyclone	1,305	102	7.8
3.....	Cyclone	2,773	187	6.7
4.....	Impactor	2,586	72	2.8
5.....	Impactor	3,006	120	4.0

Table II
Results of Subsieve Particle Size Analysis on Dust Samples

Size in micrometers	Cumulative vol pct > indicated size	
	Impactor	Cyclone
0.79.....	100.0	100.0
1.00.....	95.9	95.8
1.26.....	90.3	88.6
1.59.....	83.3	78.6
2.00.....	74.1	63.5
2.52.....	62.8	43.8
3.17.....	50.8	25.5
4.00.....	39.8	14.2
5.04.....	28.7	8.8
6.35.....	8.5	5.9
8.00.....	9.3	4.2
10.08.....	4.5	2.8
12.70.....	1.5	2.0
16.00.....	.0	1.2

To determine the efficiency of a double panel, a second single panel was placed next to the existing one. No cutting or welding was necessary to install the second panel.

Results of Testing

To determine the total efficiency of the system from the face area to the face return, dust concentrations and quartz percentages were determined, as shown in Table III. There was a reduction in total respirable dust of about 40 pct between the face area and face return. However, there was only a 15-pct reduction in the quartz fraction of respirable dust, with the result that the percentage of quartz dust in the sample increased. In other words, the water sprays and dust collection system on the continuous miner selectively suppressed the coal dust in preference to the quartz dust. Isokinetic sampling to determine the efficiency of the scrubber (single filter panel) showed that there was a total reduction of 50 pct in respirable dust when the downstream sample was compared to the upstream sample. However, there was virtually no reduction in quartz dust, indicating that the scrubber let the quartz dust through. Table IV shows the results.

When the double filter was used, the collection efficiency was found to be 72 pct for all respirable dust. The same collection efficiency was found for quartz dust also. This indicates that the double filter scrubber panel was equally efficient on coal and quartz dust. Table V shows the results.

Discussion of Filter Performance

The flooded-bed panel has the advantage of a constant dust collection efficiency and pressure drop during service because dust particles are continuously flushed away from the cleaning elements. It operates very well at about 4 gpm of water and 2,000 fpm face velocity. Normally, there are 20 double layers of stainless steel mesh. Pressure drop is about 4 to 5 in. W.G. across the panel. Pressure drop in the ducting is 7 to 8 in. W.G.

An important requirement for using a flooded bed scrubber panel is that it must be, at all times, wetted with evenly distributed water sprays. Although some mines use just one spray nozzle upwind of the panel to wash out the dust, a minimum of two nozzles is necessary to cover the entire surface area of the panel. The spray patterns should preferably be of solid cone type, and each nozzle should discharge about 1.3 gpm of water. Increasing the water flow rate will increase dust collection efficiency marginally, but will overload the scrubber fan and mist eliminator. The fan may begin to stall, and performance will deteriorate rapidly.

Once during each shift the panels should also be removed, washed down with water, and allowed to dry out over a warm place. The dried-out dust particles can be vacuumed, and the filter put back in service. A few spare panels should be available at all times. The mist eliminator acts as a trap for water droplets carried with the airstream and is very efficient at about 2,000 fpm velocity. Some dust particles are also knocked down, making it a second scrubber. The mist eliminator should be cleaned once a week for optimum performance.

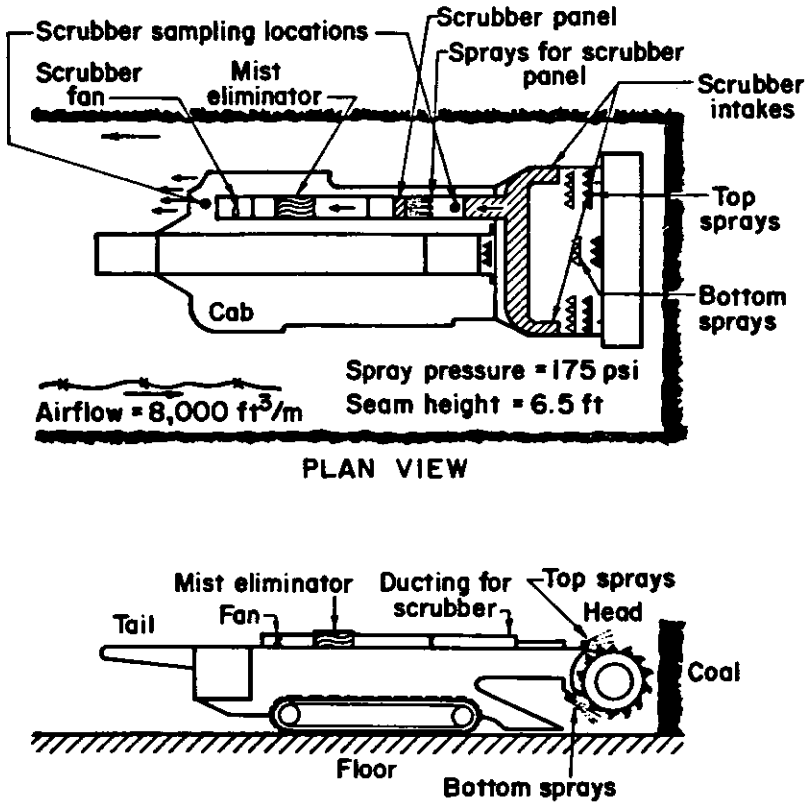

Figure 3. Face ventilation layout and scrubber sampling locations.

Table III

Behavior of Quartz Dust in Face Area

Location	Time, min	Dust mass, mg	Dust conc., mg/m3	Quartz mass, µg	Quartz, pct
Face intake..	311	0.21	0.34	82	12.3
	311	.22	.35		
	311	.23	.36		
Face return..	311	1.26	2.03	219	15.7
	311	1.32	2.12		
	311	1.40	2.24		
Face area left hinge..	321	2.44	3.80	274	11.0
	321	2.51	3.91		
	321	2.45	3.81		
Face area right hinge.	319	1.58	2.47	183	11.6
	319	1.88	2.95		
	319	1.74	2.73		

Table IV
Scrubber Efficiency Results—Single Filter Panel

Location	Time, min	Dust mass, mg	Dust conc., mg/m3	Quartz mass, µg (composite)	Quartz, pct
Intake can...	51	0.832	8.16		
	51	.861	8.44		
	51	1.121	10.99	288	10.2
Return can...	51	.263	2.58		
	51	.809	7.93		
	51	.314	3.08	275	19.9

Table V
Scrubber Efficiency Results—Double Filter Panel

Location	Time, min	Dust mass, mg	Dust conc., mg/m3	Quartz mass, µg (composite)	Quartz, pct
Intake can...	103	0.672	3.26		
	103	.836	4.06		
	103	.977	4.74	311	12.5
Return can...	102	.205	1.00		
	102	.283	1.39		
	102	.226	1.11	87	12.2

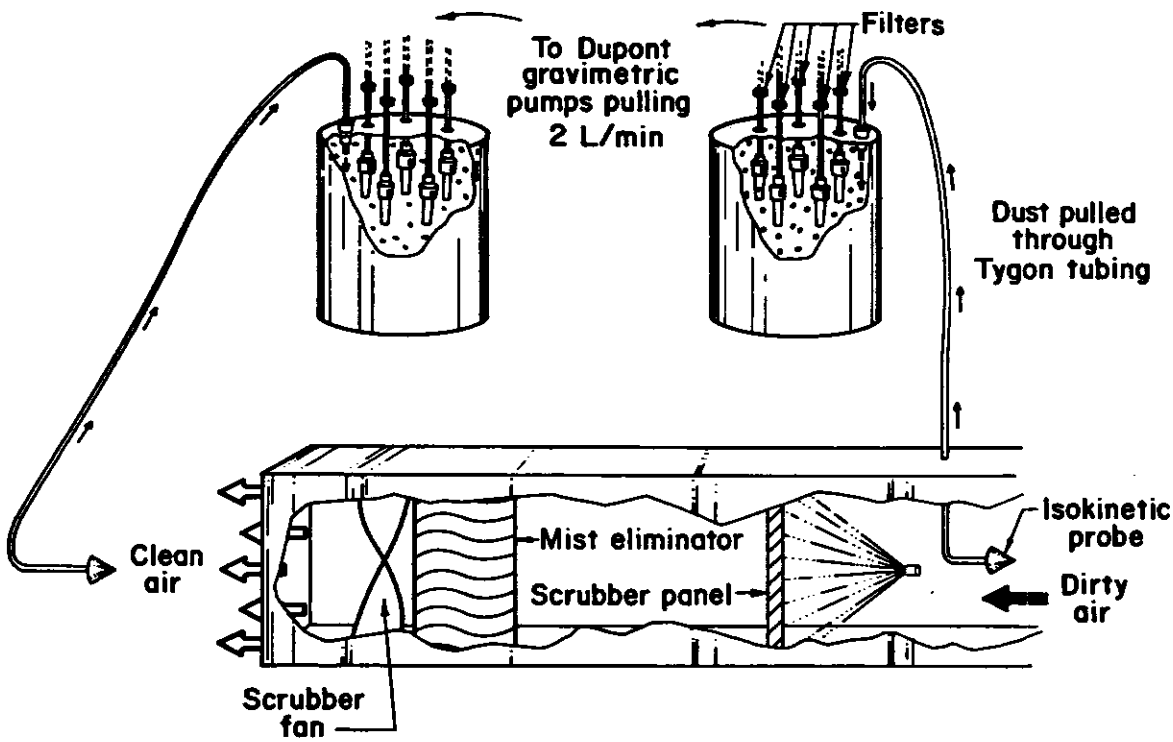

Figure 4. Sampling diagram to determine scrubber efficiency.

CONTROL OF QUARTZ DUST AT A CONTINUOUS MINER SECTION IN MINE *B*

The second underground test was carried out in a mine in Utah. One Joy 12CM continuous miner, equipped with a flooded-bed scrubber, was operating in an 8.5-ft-high coal seam. Diesel ram cars hauled away the coal, as shown in Figure 5. The entries were 18 ft wide, and a 20-ft cut was usually taken. Face airflow of 7,500 cfm was through a blowing tube with a diffuser. The scrubber airflow was about 5,000 cfm, and the airflow in the last open crosscut was 12,000 cfm. One point that should be made here is that the air in the last open crosscut did not go towards the face, but went directly to the face return. The face was totally supplied by the blowing tube, and this air quantity ranged from 6,000 to 10,000 cfm, depending on the length of the tube from the fans located far away from the face. Water spray pressure was approximately 145 psi, and scrubber nozzles operated at 60 psi. A jet pump pumped the slurry from the scrubber discharge on to the coal conveyor. The water pressure at the jet pump was also 60 psi. The mine did not use any wetting agent in the water supply. Section intake had an airflow of 43,500 cfm.

Sampling Procedure

This was similar to the one conducted at Mine *A* where filter samples were primarily taken to identify the fraction of quartz in the samples, while the light scattering instruments, called Real-time Aerosol Monitors, were used to determine short-term fluctuations in dust concentrations. The Real-time Aerosol Monitors (RAM-1's) are manufactured by Monitoring Instruments for the Environment, Inc., at Bedford, MA. The RAM-1's were connected to DL 331 data loggers (Metrosonic Co., Rochester, NY), which stored the data signal from the RAM 1 at 10-s intervals. At the end of each day, data were transferred from the logger to a personal computer and stored on floppy discs for further analysis. All data were time-synchronized with digital watches, and voice tape recorders were used to record mining activities in detail.

Air quantity was determined from velocity measurements taken with a vane anemometer. The collapsible tubing had a diameter of 24 in. when operating. The end of the tubing was initially set at a distance of 15 ft from the face and was not advanced along with mining. Water pressure for the sprays was measured on a gauge located in the operator's cab.

Procedure for Testing

Preliminary tests with the scrubber indicated that the scrubber fan was operating under a significant pressure drop and would not handle any increased resistance through the scrubber circuit. If any additional resistance is added, aerodynamic stall will occur. The addition of a second panel will not, therefore, improve the dust concentration at the operator location because of increased resistance to airflow and greatly decreased capture efficiency.

A modified cutting sequence, in which the operator would sump at about 6 in. from the floor and shear upwards,

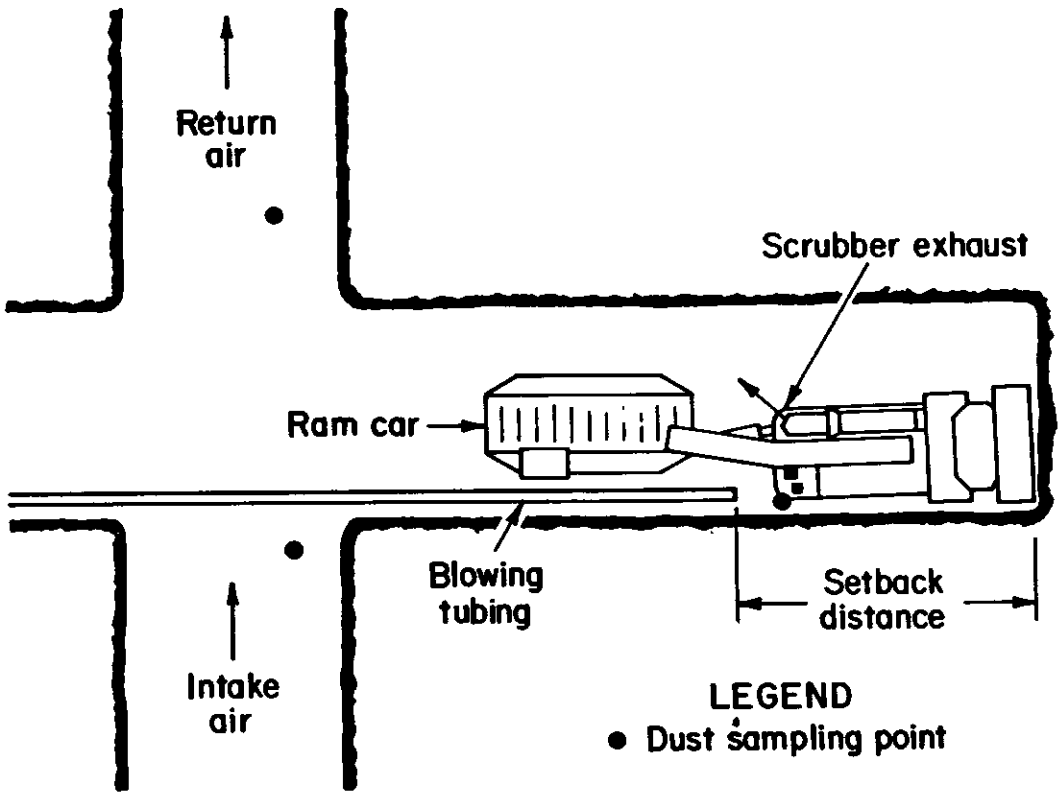

Figure 5. Mining plan with blowing ventilation tube.

was adopted. This eliminated the grinding of the sandstone floor, which was the main source of high quartz levels. Visual inspection of the dust cloud indicated that the dust capture efficiency of the scrubber system was much greater during the box cut. During the box cut, the mining machine prevented the main airflow from reaching the face by blocking the entry. The scrubber inlets, being located near the dust source, were thus able to vacuum a highly concentrated dust cloud before it was diluted by the main airstream.

During the slab cut, however, the large open volume created by the box cut provided an outlet for the dust to disperse and significantly reduced the dust capture efficiency. To eliminate this effect, a curtain was hung to the right side of the machine from the last set of roof bolts when the machine was taking a slab cut. The curtain isolated the dust source from the main airflow and let the scrubber inlets operate effectively on the dust cloud. The curtain layout is shown in Figure 6.

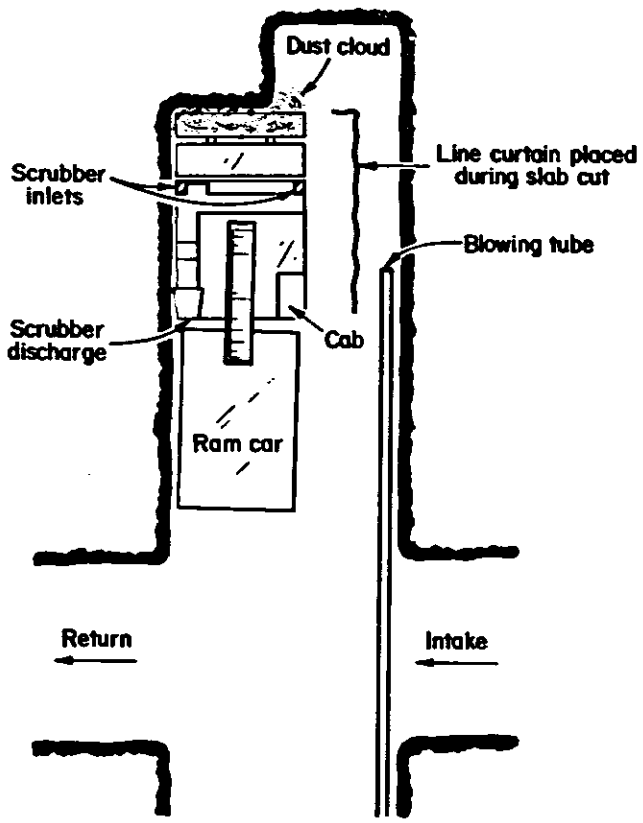

Figure 6. Curtain layout for mining during a slab cut.

Results of Testing

The respirable dust concentrations with and without the modified cutting sequence (together with curtain) are shown in Figure 7. There is a reduction of approximately 50 pct in respirable dust concentrations at the operator location and in the face return. Quartz percentages were also determined to see if there is any reduction at the operator's position. Figure 8 shows that there was a reduction of 60 pct in the quartz content due to the modified operation.

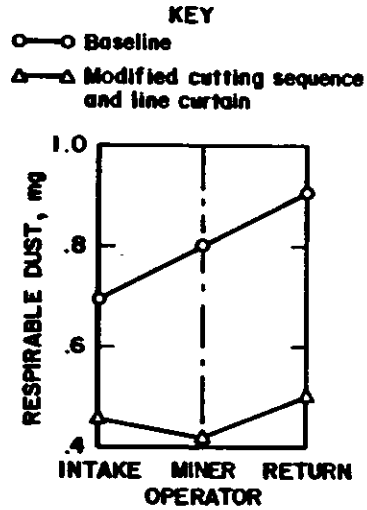

Figure 7. Respirable dust concentrations with and without modified cutting sequence.

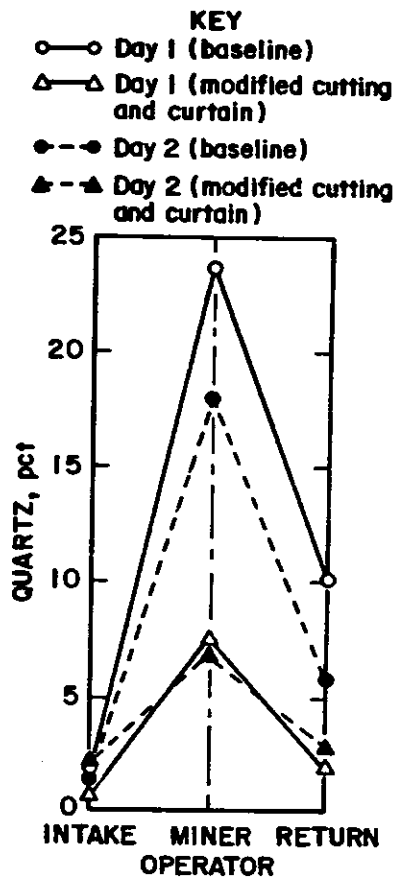

Figure 8. Quartz percentage with and without modified cutting sequence.

CONCLUSIONS

1. The quartz percentage for samples collected by a 10-mm nylon cyclone (median diameter 2.25 μm) was higher than for samples collected by an impactor with a cutoff of 3.7 μm. This leads us to believe that the median diameter for the quartz dust is smaller than that of coal dust. This will affect the planning for dust control technology in coal mines.
2. The results of underground testing show that a machine-mounted scrubber system can be used to reduce the respirable dust, as well as its quartz content, by doubling the scrubber panel.
3. Research indicates that a modified cutting sequence will reduce the operator's exposure to quartz dust.

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RESPIRABLE DUST TRENDS IN COAL MINES WITH LONGWALL OR CONTINUOUS MINER SECTIONS

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INTRODUCTION

In 1970 a mandatory respirable dust standard of 3.0 mg/m^3 was established for underground Coal mines under the Federal Coal Mine Health and Safety Act of 1969. This standard was lowered in 1972 to 2.0 mg/m^3. Mandatory dust standards for surface work areas of underground coal mines and surface mines also became effective in 1972. These regulations were continued under the Federal Mine Safety and Health Act of 1977,[6] which amended the 1969 act and merged coal and noncoal regulations into one law. In the 1969 act, "concentration of respirable dust" was defined as a measurement made with a Mining Research Establishment (MRE, Casella 113A) instrument or such equivalent concentration measured with another device. The 1977 act changed the definition of "concentration of respirable dust" to be the "average concentration of respirable dust measured with a device approved by the Secretary and the Secretary of HEW." The device approved for measuring respirable dust uses a Dorr-Oliver 10-mm nylon cyclone to remove the nonrespirable fraction of dust sampled. Measurements made with this device are converted to equivalent MRE concentrations by multiplying by a constant factor of 1.38.[3] A more rigorous standard is used if the sample contains more than 5 pct quartz. Specific regulations detailing the collection of respirable dust samples by mine operators are found in the Code of Federal Regulations, Title 30.[5]

Since 1970 more than 6.5 million respirable dust samples have been collected by coal mine operators and Mine Safety and Health Administration (MSHA) inspectors to determine compliance with the 2.0 mg/m^3 standard, or with the more rigorous standard due to the presence of excessive levels of quartz. Each year MSHA provides the Bureau with copies of these records to update the Mine Inspection Data Analysis System (MIDAS). MIDAS is a computerized, industrial hygiene data base developed by the Bureau with the assistance of MSHA to statistically analyze environmental compliance data collected by MSHA inspectors and coal mine operators.[7-8] These analyses provide information that is used to determine trends in exposure, to prioritize problem areas requiring special emphasis, and to evaluate the impact of proposed standards. Data are stored on the Bureau's mainframe computer in Denver, Colorado, but portions of the data base may be analyzed on personal computers. MIDAS is available, on-line, via the Bureau's telecommunications network to Bureau, MSHA, and National Institute of Occupational Safety and Health personnel involved in mining research.

Each record of coal mine respirable dust exposure stored in MIDAS contains coded information which identifies the state, mine, type of mine, sample date, occupation code, tons of coal mined, dust concentration, and other information. These records are edited, sorted, stored, and statistically analyzed using software developed by the Bureau.

It was previously reported[8] that the highest mean concentrations of respirable coal dust reported by MSHA inspectors were measured in coal mine sections with longwalls. These sections also had the greatest percentage of samples exceeding the 2.0-mg/m^3 standard (35 pct). Many more samples were collected at mines using continuous rippers, with 11 pct of the samples exceeding the Federal standard. However, a single sample exceeding the 2.0-mg/m^3 standard does not place a mine section out of compliance with the Federal standard. A mine is only out of compliance if the arithmetic average of five operator respirable dust samples collected over consecutive normal production shifts exceeds the standard, or if the average of two or more MSHA inspector samples exceeds statistically determined levels.

MSHA inspectors and coal mine operators regularly sample miners or areas known to have high dust exposure, but mine operators collect many more samples. In underground mines, certain occupations are referred to as designated occupation (DO) and are sampled bimonthly by coal mine operators and annually by MSHA inspectors. Examples of DO's include the continuous miner operator and the longwall shearer operator.

The objective of this paper is to summarize the recent trends in respirable dust levels in sections using longwalls or continuous ripper miners. The analysis includes the large amount of compliance data collected by coal mine operators and MSHA inspectors. Recent data will be compared to data reported for FY 78 to determine the changes that have occurred in dust levels and coal production. Data from mines using both methods of mining will also be compared. In addition, operator data will be compared to inspector data to determine if different trends exist.

Continuous Mining

Continuous mining is a system that allows coal to be ripped from a seam and loaded in the same operation. It was developed in the 1940's to replace the conventional mining cycle of undercutting, drilling, shooting, and loading. Continuous rippers are commonly found in room-and-pillar mines. In these mines, multiple entries are cut parallel to the main haulage lane and reached by cross tunnels, resulting in a checkerboard of alternating rooms and pillars. Pillars are left to support the mine roof; as mining is extended to greater depths, larger pillars must be left behind. This results in reduced mining efficiency.[1]

Longwall Mining

Longwall mining is the most recently introduced mechanized method of mining. Coal is cut by either a shear or a plow from a coal face that is typically 350 to 600 ft in width and 1,000 to 6,000 ft in length. Cut coal drops onto a chain conveyor that lies along the bottom of the face and is hauled to one end. Here it is transferred to the stage loader, which loads it onto a conveyor belt. The roof is supported by hydraulic roof supports which extend support over the walkway, thus creating space for mining to take place. As the coal is cut, the roof supports move forward to cover the newly exposed face, allowing the unsupported roof to fall behind and eliminating the need for permanent roof supports or pillars. Longwall sections are generally developed by continuous ripper miners,[4] and most longwalls operating in the United States are retreat operations using three or more entries on either side of the longwall panel.[2] Though fairly new to the United States, longwall mining has been used in Europe for many years, because mines there have reached greater depths, making it safer and more efficient to use longwall roof-support methods.

RESULTS OF ANALYSIS

From FY 83 through FY 87, mine operators collected 260,370 respirable coal dust samples on continuous miner operators. These samples had a mean dust concentration of 1.0 mg/m^3, with 12.2 pct of the samples exceeding the standard. This compares to 12,622 samples collected on longwall operators on the tailgate side, which had a mean concentration of 2.0 mg/m^3, with 36.8 pct of the samples exceeding the standard.

FY 87 MSHA data show that more than 65 pct of the mine sections in the United States use continuous ripper machines (about 1,750 sections). This mining method typically produces between 300 and 400 tons of coal per shift (Figure 1). Ripper sections have had a small increase in production since FY 78. Table I shows the trends in FY respirable coal dust mean concentrations for continuous ripper operators. The 0.4-mg/m^3 reduction in mean dust concentration from FY 78 to FY 87 is statistically significant and is accompanied by 11.8 pct fewer samples exceeding the 2.0-mg/m^3 standard. In FY 87, 439 ripper sections were cited for noncompliance once, and 120 were cited two or more times.

There were about 128 longwall sections operating in the United States in FY 87. This is approximately a 30-pct increase in the number of longwalls since 1978. However, only about 85 to 90 longwalls are in operational status at any given time. Most of these sections use longwall shearers, primarily of the double drum type. Since FY 78, longwall operators have experienced increases in median production from 500 tons/shift to 2,200 tons/shift, as shown in Figure 1. At the same time, respirable dust levels have also changed, as evidenced by Table II, which shows the trends in respirable coal dust mean concentration for tailgate side shearer operators. The 0.5-mg/m^3 reduction in mean dust concentration from FY 78 to FY 87 is statistically significant and is accompanied by 13.0 pct fewer samples exceeding the 2.0-mg/m^3 standard. In FY 87, 58 longwall sections were cited for noncompliance once, and 31 were cited two or more times.

Table I

Respirable Coal Dust Trends for Continuous Ripper Operators[1]

FY	N	Concentration, mg/m^3		
		Pct of N >2.0	AM	ASD
78	78,765	23.5	1.4	1.5
83	56,742	13.5	1.1	1.3
84	60,273	12.8	1.1	1.3
85	49,716	11.6	1.0	1.1
86	48,996	11.3	1.0	1.1
87	44,643	11.7	1.0	1.1

FY fiscal year. N number of samples.
AM arithmetic mean.
ASD arithmetic standard deviation.
[1]Data collected by coal mine operators

Table II

Respirable Coal Dust Trends for Longwall Operators, Tailgate Side[1]

FY	N	Concentration, mg/m^3		
		Pct of N >2.0	AM	ASD
78	2,747	51.6	2.5	1.9
83	2,392	33.7	2.0	2.0
84	2,782	37.1	2.1	2.0
85	2,234	36.5	2.0	1.6
86	2,668	38.0	2.0	1.5
87	2,546	38.6	2.0	1.5

FY fiscal year. N number of samples.
AM arithmetic mean.
ASD arithmetic standard deviation.
[1]Data collected by coal mine operators

Mines With Both Longwall and Ripper Sections

Respirable coal dust concentrations may be compared at mines having both longwall and ripper sections. The comparison was made by selecting the 10 mines with the greatest number of operator coal dust samples for the continuous miner and longwall operator on the tailgate side covering the period FY 83 through FY 87. These mines are identified as mines A through J in Table III, which summarizes the respirable coal dust concentrations. One mine is in Virginia, two mines each in Alabama, Ohio, and Pennsylvania, and the remaining three mines are in West Virginia.

The mine average respirable coal dust concentrations for the continuous miner and longwall operator samples in Table III are 1.2 and 2.1 mg/m^3, respectively. These means approximate the overall means for the two occupations over the same time period, which were 1.0 and 2.0 mg/m^3, respectively. Mines C, D, E, and J had the highest mean respirable coal dust concentrations for both the continuous miner operator and the longwall operator on the tailgate side. Mine H had the highest median longwall production (2,230 tons/shift) and the second lowest mean longwall operator dust concentration (1.4 mg/m^3).

Comparison of Mine Operator and MSHA Inspector Data

Figures 2 through 4 compare data collected by mine operators to data collected by MSHA inspectors on continuous miner operators and longwall operators on the tailgate side. The arithmetic mean (Figure 2), the percent of samples <0.2 mg/m^3 (Figure 3), and the percent of samples >2.0 mg/m^3 (Figure 4) are used because these measures cover a wide range of exposure. The only measure of the three to show a remarkable trend is the percent of samples <0.2 mg/m^3 (Figure 3), which clearly shows that operators are more likely to submit a sample with a low dust concentration. Approximately 27.4 pct of the operator samples collected on continuous miner operators had concentrations <0.2 mg/m^3, compared to approximately 16.1 pct of the MSHA samples. The trend is also apparent for samples collected on the tailgate side longwall operator, where 6.6 pct of the operator samples and only 1.5 pct of the inspector samples are <0.2 mg/m^3. Possible explanations for this difference are that operators collect five samples over consecutive work shifts during which operating conditions may change and affect dust levels, and since operators sample far more frequently, there is a

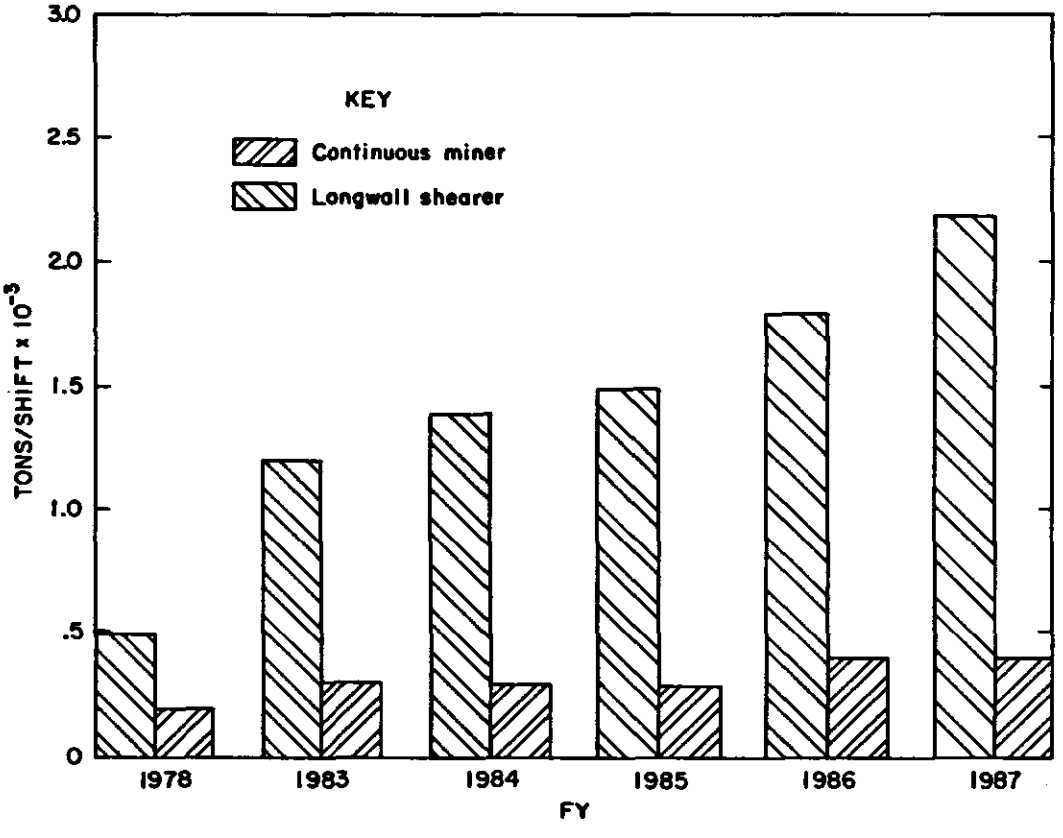

Figure 1. Underground median production as reported by mine operators for longwall shearers and continuous miners.

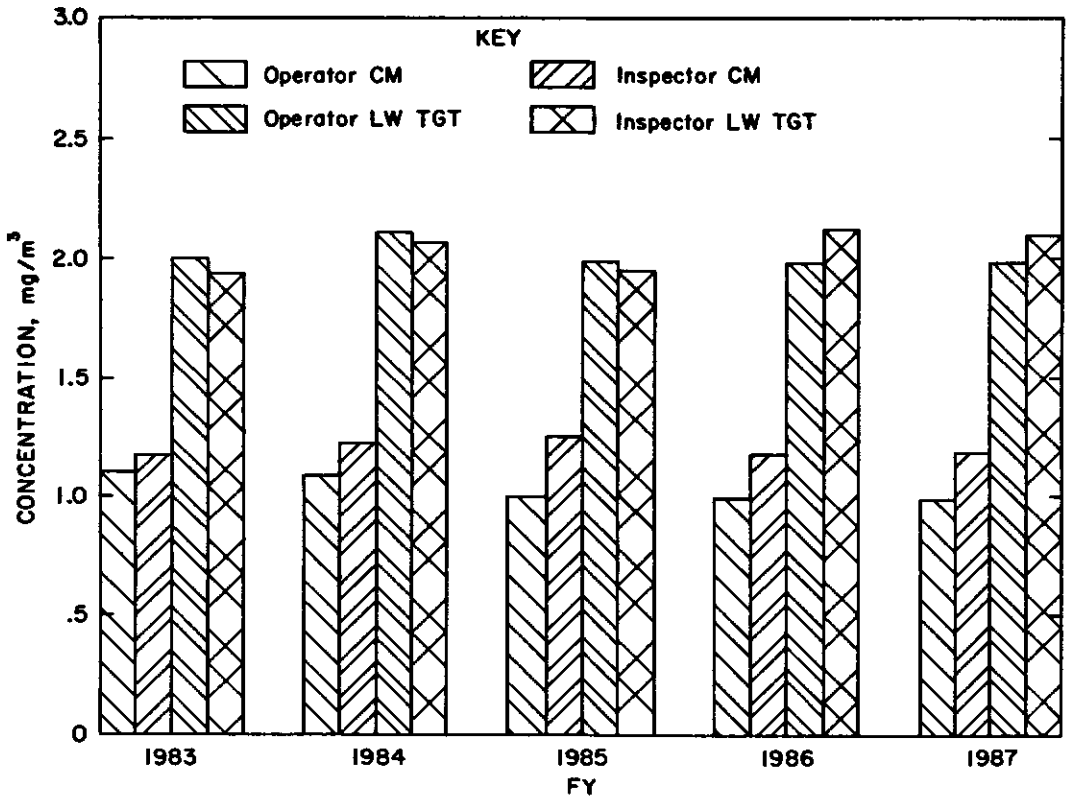

Figure 2. Arithmetic mean concentration for operator and inspector samples collected on continuous miner and tailgate side longwall operators.

Table III

Respirable Coal Dust Concentration, mg/m³ at Mines Using Continuous Rippers and Longwalls[1]

Mine	Continuous miner operator			Longwall operator tailgate side		
	N	AM	ASD	N	AM	ASD
A	970	1.0	1.0	464	2.1	1.8
B	1,222	1.0	0.7	371	2.0	1.5
C	1,437	1.8	1.8	566	2.7	2.1
D	1,172	1.7	1.7	573	2.5	1.8
E	870	1.3	1.1	201	2.6	1.7
F	1,369	0.5	0.7	165	1.8	1.3
G	517	1.0	0.7	139	1.4	1.3
H	681	1.1	1.1	289	1.4	1.2
I	966	0.9	0.9	338	1.3	1.0
J	902	1.4	1.7	173	3.1	2.9

N number of samples. AM arithmetic mean.
ASD arithmetic standard deviation.
[1]Data collected by coal mine operators.

greater chance of collecting samples with low dust concentrations. In addition, MSHA results could be higher because no prior announcement of arrival is given to the mine operator; thus, these samples may be indicative of truer day-to-day conditions.

SUMMARY

Over the past 5 years, operators of longwall shearer sections reported increases in median production from 1,200 to 2,200 tons/shift. This increase in production was accompanied by a continuing problem with respirable dust despite the significant decrease in mean dust levels that has occurred since FY 78. A number of longwall sections still experience difficulty in maintaining continuous compliance with the Federal standard. Longwall sections have arithmetic mean respirable dust concentrations that are more than double the concentrations reported by continuous ripper sections (2.0 mg/m³ vs. 1.0 mg/m³). In FY 87, 45 pct (58) of the longwall sections were found to be in noncompliance once, and an additional 24 pct (31) were cited two or more times. Thus, 69 pct of the longwall sections in operation during FY 87 experienced compliance problems. It is evident from these data that dust problems continue to plague longwall mining operations as longwall production continues to rise. If more high-producing longwalls are to be brought on-line to realize the full potential of this mining method, additional effective dust

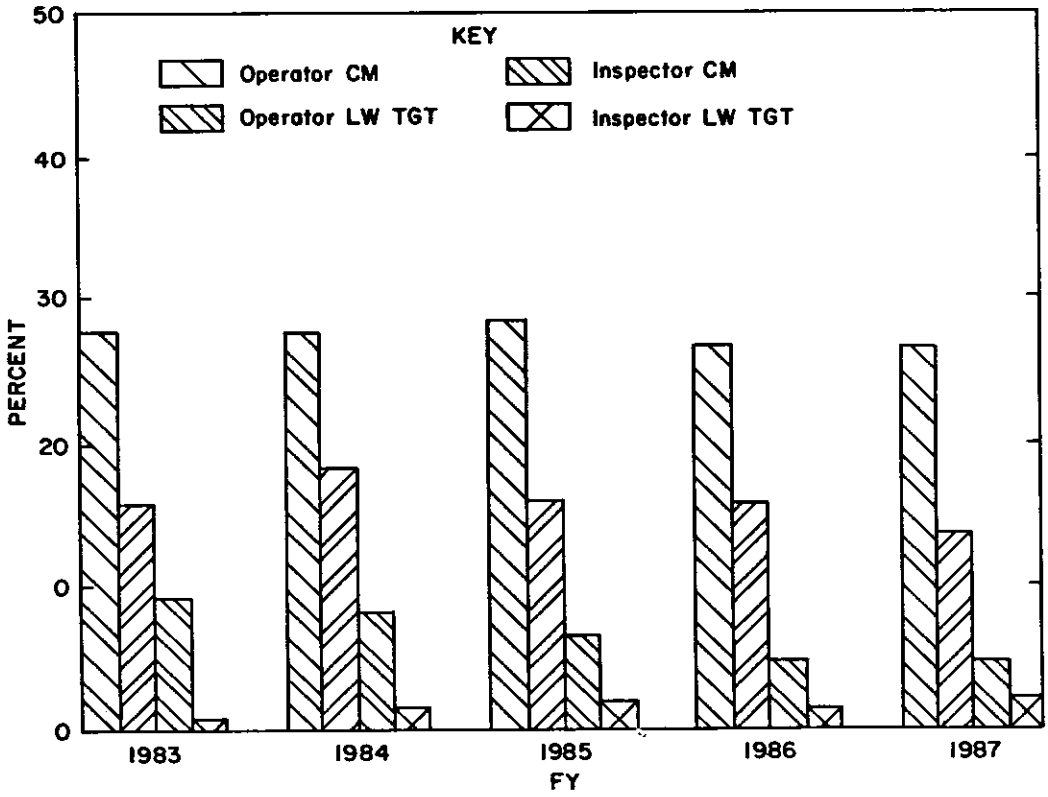

Figure 3. Percent of samples <0.2 mg/m^3 for operator and inspector samples collected on the continuous miner and tailgate operator.

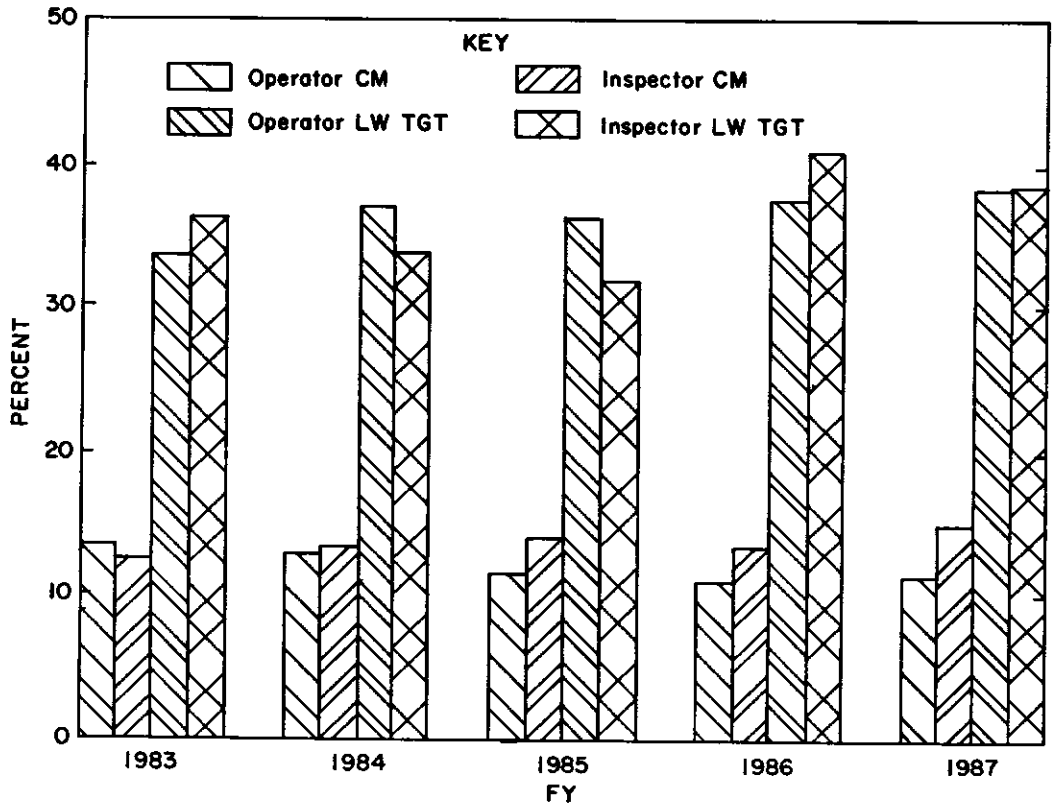

Figure 4. Percent of samples >2.0 mg/m³ for operator and inspector samples collected on the continuous miner and tailgate side longwall operator.

control measures must be put into place and maintained to more consistently control dust levels on a continuous basis.

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NEUMOCONIOSIS DE LOS MINEROS DEL CARBON: ESTUDIO EPIDEMIOLOGICO LONGITUDINAL

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INTRODUCCION

A pesar de los indudables avances que, a nivel europeo, se están obteniendo en la lucha contra la "Neumoconiosis de los Mineros del Carbón" y que sin duda son consecuencia de la disminución de los niveles de polvo al aplicar eficaces sistemas de prevención técnica en las minas, existen casos, como es el de la minería del carbón en España, donde las peculiaridades muy especiales de sus yacimientos, generalmente formados por capas muy estrechas, con numerosas intercalaciones de roca y alto porcentaje de sílice libre y explotadas manualmente, dificultan enormemente la eliminación del polvo, lo que se traduce en una mayor incidencia de la Neumoconiosis de los Mineros del Carbón, comparada con otros paises de la Comunidad Europea, a pesar de los grandes esfuerzos que se hacen para disminuir dicha enfermedad profesional.

Precisamente, entre las acciones planificadas a largo plazo para combatir la Neumoconiosis de los Mineros del Carbón, figura un proyecto de investigación Epidemiológico Longitudinal, consistente en controlar la aparición y evolución de la enfermedad en un colectivo de 3.000 mineros de la empresa nacional Hulleras del Norte, S.A. (HUNOSA), relacionando a su vez aquellos parámetros de tipo médico con los niveles y características mineralógicas del polvo que, individualmente, los mineros inhalan durante su vida laboral. El proyecto se plantea a lo largo de la vida del colectivo estudiado, lo cual incluye el seguimiento médico de aquellos trabajadores que, por alguna causa (accidente, jubilación, etc.) abandonan la actividad minera.

OBJETIVO

El objetivo del proyecto es doble. Por una parte, y en base a la correlacción enfermedad-niveles de polvo, se pretende llegar a conocer la verdadera peligrosidad del polvo existente en nuestras minas (generalmente con altos contenidos de sílice libre), y así poder fijar unos límites de riesgo que estén muy en consonancia con la realidad. Por otra parte, los reconocimientos médicos, a los que, como se indica más adelante, se someten los trabajadores estudiados, permiten valorar periódicamente "el estado de salud" de los mineros del carbón en relación con otros colectivos profesionales.

METODOLOGIA

El proyecto, realizado por un equipo médico-técnico perteneciente al Instituto Nacional de Silicosis y a HUNOSA, comenzó su trabajo en el año 1.983, seleccionando y reconociendo médicamente a un colectivo de unos 3.000 mineros que habían iniciado su actividad laboral en la mina, entre los años 1.972 a 1.980, sin que anteriormente hubieran estado sometidos a ningún riesgo en relación con la Neumoconiosis de los Mineros del Carbón. Posteriormente, cada 4 años se repiten los reconocimientos médicos, a la vez que, mensualmente, se les asigna a cada uno de los mineros estudiados—los índices de polvo relativos a los mg/m^3 y % de sílice libre.

Simultáneamente, desde el Instituto Nacional de Silicosis y de análoga manera, se estudia un grupo control formado por trabajadores no mineros, pertenecientes a la industria del transporte, con quien se comparan los resultados obtenidos en el proyecto de los mineros del carbón.

El estudio se realiza en dos etapas o escalones.

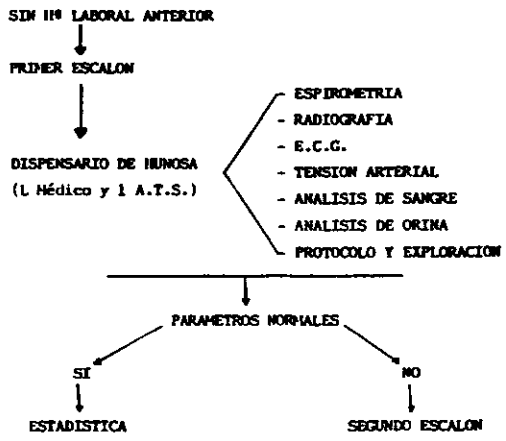
El primer escalón incluye a todo el personal seleccionado. Los reconocimien tos tienen lugar en los Dispensarios Médicos situados en la propia mina, con revisiones periódicas cada 4 años. Se realizan por un médico y un asistente técnico sanitario, puestos por la empresa exclusivamente para éste estudio. Asi mismo, existe un ingeniero de minas que dirige el control pulvígeno de los distintos puestos de trabajo.

A todo trabajador en el primer escalón se le realiza una encuesta cubriendo un protocolo, una exploración clínica, radiografía de tórax, electrocardiograma, espirometría, toma de tensión arterial y analisis de sangre y orina. Si presentan alguna anormalidad pasan al segundo escalón, donde se les hacen todas las pruebas necesarias para llegar a un diagnóstico. Una vez obtenidos todos los datos, se le envía informe al trabajador comunicando los resultados y si presenta alguna enfermedad se le aplica tratamiento o se le orienta hacía un servicio especializado. Posteriormente, el médico coordinador del Instituto Nacional de Silicosis envía los datos obtenidos al Servicio de Estadística (Tabla I).

Cuando los parámetros obtenidos en el primer escalón no son normales pasan a un segundo escalón, bien sea en el

Tabla I

PRIMER ESCALON



Instituto Nacional de Silicosis o en los propios laboratorios de las minas. En el primer caso, un médico coordina el paso de los trabajadores por los distintos Servicios del Instituto, al objeto de estudiar las diferentes patologías. Asi, en el Servicio de Medicina Preventiva, Diagnóstico y Valoración se controla la hipertensión arterial, Neumoconiosis simple y Neumoconiosis complicada (Tabla III). En el Servicio de Neumología se estudian el carcinoma pulmonar, efusión pleural, artritis reumatoide, esclerodemia o tuberculosis pulmonar (Tabla IV). En Cardiología: el cor pulmonale y la cardiopatía isquémica (Tabla V). Finalmente en el Servicio de Fisiología Respiratoria la obstrucción crónica al flujo o el síndrome restrictivo (Tabla VI).

Tabla II

SEGUNDO ESCALON

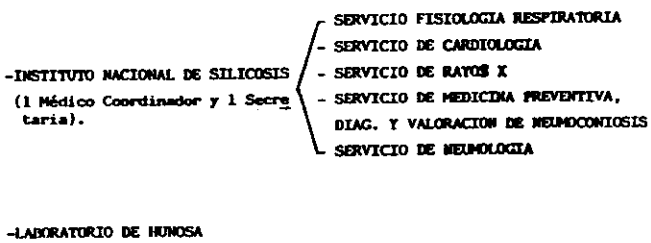


Tabla III

PATOLOGIA A ESTUDIAR EN EL SEGUNDO ESCALON

- SERVICIO DE MEDICINA PREVENTIVA, DIAGNOSTICO Y VALORACION DE LAS NEUMOCONIOSIS.
  - HIPERTENSION ARTERIAL
  - NEUMOCONIOSIS SIMPLE
  - NEUMOCONIOSIS COMPLICADA

Tabla IV

PATOLOGIA A ESTUDIAR EN EL SEGUNDO ESCALON

- SERVICIO DE NEUMOLOGIA DEL INSTITUTO NACIONAL DE SILICOSIS
  - CARCINOMA PULMONAR
  - EFUSION PLEURAL
  - ARTRITIS REUMATOIDE
  - ESCLERODEMIA
  - TUBERCULOSIS PULMONAR

Tabla V

PATOLOGIA A ESTUDIAR EN EL SEGUNDO ESCALON

- SERVICIO DE CARDIOLOGIA DEL INSTITUTO NACIONAL DE SILICOSIS
  - COR PULMONALE
  - CARDIOPATIA ISQUEMICA

Tabla VI

PATOLOGIA A ESTUDIAR EN EL SEGUNDO ESCALON

- SERVICIO DE FISIOLOGIA RESPIRATORIA DEL INSTITUTO NACIONAL DE SILICOSIS
  - OBSTRUCCION CRONICA AL FLUJO
  - SINDROME RESTRICTIVO

En los Laboratorios de la mina se realizan las pruebas analíticas pertientes para confirmar el diagnóstico de diabetes mellitus, intolerancia a la glucosa o hiperlipidemias (Tabla VII).

Las placas radiográficas son leidas por tres lectores según los criterios de la ILO del 80.

El seguimiento previsto para el colectivo estudiado pretende que, a lo largo del proyecto, no se "pierda" más del 5% de los componentes de partida.

En cuanto al segundo escalón, al tratarse aquí de estudios específicos que se realizan en el Instituto Nacional de Silicosis, se cuenta para ello con toda la estructura médico-técnica de éste Centro de Investigación.

DESCRICCION DE LA PARTE TECNICA

La parte técnica es controlada y supervisada por el Departamento Técnico de Instituto Nacional de Silicosis.

El control del polvo se realiza de la siguiente manera: En cada pozo se muestrean mensualmente los puestos de trabajo donde prestan sus servicios los trabajadores del colectivo estudiado. Este control de polvo es realizado por los Servicios de toma de muestra existentes en los pozos, de acuerdo

con las normas establecidas por el Departamento Técnico del Instituto Nacional de Silicosis.

Los aparatos utilizados para el control pulvígeno son los gravimétricos de larga duración que seleccionan el polvo de acuerdo con la curva definida de Johannesburgo y cuyo resultado se especifica en miligramos de polvo respirable por metro cúbico de aire, en cuanto a la sílice libre la toma de muestra se realiza utilizando el inyector de aire comprimido de uso habitual. (Tabla VIII).

Tabla VII

PATOLOGIA A ESTUDIAR EN EL SEGUNDO ESCALON

- LABORATORIO DE HUMOSA
- DIABETES MELLITUS
- INTOLERANCIA A LA GLUCOSA
- HIPERLIPEMIAS

Table VIII

DESCRICCION DE LA PARTE TECNICA

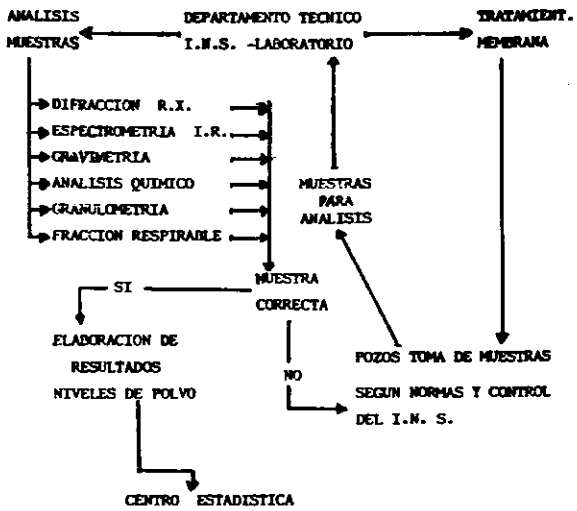


Tabla IX

ANALISIS DE MUESTRAS

El análisis de muestras en realizado en los laboratorios del Departamento Técnico del Instituto Nacional de Silicosis, donde se realiza la preparación previa de las membranas antes deenviarlas a la mina, asi como todo el tratamiento posterior a la toma de muestras.

El análisis de sílice libre y de todos los componentes minerales, se realiza utilizando "preferentemente" los métodos de difracción de rayos X y espectrometría de infrarrojos.

SERVICIO DE ESTADISTICA

Al Servicio de Estadística, adscrito al Departamento Técnico del Instituto Nacional de Silicosis, afluyen todos los datos médicos y técnicos, siendo analizados y tratados estadísticamente.

ESTADO ACTUAL DEL PROYECTO

Hasta la fecha se han realizado dos ciclos de reconocimientos médicos (el inicial, al ingreso en la mina, y el primero de los periódicos que se les va a efectuar, del que se llevan reconocidos hasta la fecha unos 2.400 trabajadores del total de los 3.000), asi como la valoración contínua de las características mineralógicas y de los niveles de polvo (mg/m^3 y % de SiO_2) existente en los distintos puestos de trabajo, pudiendo decir que, prácticamente, se siguen controlando el total de los componentes del colectivo inicialmente selecionado.

BENEFICIOS SOCIALES DEL PROYECTO

El cumplimentar los objetivos que persigue el proyecto va a imponer conocer la peligrosidad real del polvo que se produce en neustras minas, pudiendo entonces planificar una prevención del mismo acorde con el riesgo que dicho polvo conlleva y que, indudablemente, va a suponer una disminución de la Neumoconiosis de los Mineros del Carbón, la cual, además de las graves consecuencias que supone para los mineros que la padecen, desde el punto de vista exclusivamente de las indemnizaciones económicas y refirien donos a la región de Asturias donde se realiza el proyecto presentado, alcanza un coste de unos 10.000 millones de pesetas anuales.

Por otra parte, el segundo objetivo referente al conocimiento del estado de salud de los mineros va a suponer, sin duda, la necesidad de realizar ciertos cambios de los hábitos en el comportamiento del colectivo estudiado que repercutirán muy favorablemente en la calidad de vida de los mineros del carbón.

DUST EXPOSURE AND COALMINERS' RESPIRATORY HEALTH

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During the last 20 years my colleagues and I have been publishing a series of reports describing the relationships between dust exposure and coalminers' respiratory health. Those reports were from the British Coal Board's Pneumoconiosis Field Research—probably the most comprehensive long-term epidemiological study of an industrial population ever undertaken. It began 35 years ago in the late 1960's. It provided interim estimates of risks of coalworkers' simple pneumoconiosis for different levels of dust exposure, and this information was used by the British authorities, and by our colleagues here in the USA as basis for fixing dust exposure limits in coal mines. Soon afterwards, the same data were used to show that exposure to coal mine dust also increased risks of having symptoms of chronic bronchitis and of suffering some reduction in breathing capacity, as measured by the forced expiratory volume.

Many other studies were completed subsequently, as the field research continued at 10 of the original 24 mines that had been selected originally, in 1953. They refined, elaborated, and eventually verified the reliability of the CWSP risk estimates that were first produced in the late 60's and early 70's; explored the effects of exposure to dust on coal miners' mortality; described how exposure to respirable dust increased miners' chances of having pathological determined emphysema, and more recently, showed how exposure to respirable dust was related quantitatively to risks of developing not only coal workers' simple pneumoconiosis, but also the more serious disabling, and often fatal condition, PMF—progressive massive fibrosis of the lung.

This afternoon I will describe results from some further analyses of some of the accumulated material which were aimed at expressing the long-term working-life risks of pneumoconiosis, and of other effects of dust exposure on respiratory health, on a common baseline: the different mean concentrations of respirable dust to which a miner might be exposed during his working life under different scenarios of exposure limits and his responses to them.

First, however, I need to remind you of the essence of the strategy used in the research which generated the information in the medical data; radiographic signs of pneumoconiosis, respiratory symptoms and lung function levels, were obtained at medical surveys at each of the 24 mines, representing, in each case, an approximate 10-year period of observation during the calendar years 1953 through 1968. Two further medical surveys, generating a further decade of observations were completed during 1978 at 10 of the mines that were still open.

The exposures to dust for each individual miner who worked at the pits during the 25-year period, were calculated by keeping careful records throughout about precisely where each man was working during each of the tens of thousands of shifts that he attended. The average concentrations for such "occupational groups" were multiplied by the number of shifts each worked in them; and those products of concentrations (n mg/m^3) and shifts (converted into hours) were to give estimates of each individual's exposure to dust. Exposures experienced before the research measurements began were estimated, from data acquired by interviews with each man about where, how long, and what kind of work he had been doing and the results from the dust sampling. Thus, each man's cumulative exposures to respirable dust, for the whole of his preceding working life was calculated, the units being products of concentrations of dust and time. The various disease risk estimates were therefore expressed as functions of exposures measured in those units.

If we assume that a miner starts exposure at 20 years of age, and continues working underground for 35 years, with 1630 working hours per year, then those exposures can be expressed as mean of concentrations of dusts. So we may ask from the data: What risks of disease may be expected at age (20 + 35) = 55 for different mean concentrations of respirable dust?

The pneumoconiosis risk estimates were calculated from the most comprehensive set of data, describing more than 5,000 to approximately 5-year man intervals of exposure during the whole 25-year period. This study involved more than 30,000 miners from all 24 mines.

The results from a study were first described briefly here in Pittsburgh 5 years ago. Risks of pneumoconiosis were higher, for any given level of exposure at pits with greater carbon content in the coal. This is illustrated for category 1, simple pneumoconiosis, for higher categories, 2 or 3, and also for PMF.

Don't be misled by the apparently widening gap between the two lines in this series of graphs—this is due to the changing scale on the vertical axes of the graphs. The effect of the higher (91b) carbon content is about 2 to 3 additional percentage concentration, and about 5 additional percentage probability units at 7 mg/m^3.

Note, however, that the PMF risk, at the end of a 35-year exposure period increases steadily and smoothly with the mean concentration of dust experienced. This is a reflection of two important factors:

First, a small, but statistically highly significant increase in PMF risks among man with *no* simple pneumoconiosis (i.e., category 0);

Second, a very much more substantial increase in risks for that small minority of miners who develop even category 1 simple pneumoconiosis—and increase very clearly with increasing exposure.

The very dramatic increase in PMF risks after they develop simple pneumoconiosis is illustrated, which shows what happens if a man develops category 1, or even category 2, during the first 10 years of his 35-year exposure. At low (2 mg/m^3) concentrations, there is an approximate ten-fold increase in the risk if a man has category 1 already at the age of 35, and a 20-fold increase if he progresses during those first ten years to category 2. These results demonstrate dramatically reduction in developing PMF by reducing dust levels. This will effectively eliminate, or at least reduce, the higher risks associated with the early presence of simple pneumoconiosis, and will also protect the majority of miners, with no pneumoconiosis, from the small but finite, PMF risks at higher concentrations.

Risks of ending the 35-year exposure periods with respiratory symptoms are taken from a study of a sample of miners from 10 of the mines, who all attended the first four of the medical surveys. The sample was selected to provide an approximate uniform distribution of exposures to dust and to maximize the statistical precision of estimates of exposure-response relationships.

At hypothetical zero dust levels, cigarette smokers in this population stood a more than 3-fold higher chance than lifelong non-smokers of reporting chronic cough and sputum production. The just over 7% probability at zero exposure for non-smokers reflects the effects of all other causes of chronic bronchitis. Nevertheless, the risk more than doubles, at about 18%, for non-smokers who are consistently exposed to high (i.e., 7 mg/m^3) concentrations of dust.

A similar picture is found when considering breathlessness, that is men who acknowledge that they are breathless when they walk at their own pace on level ground: an approximate three-fold increase for cigarette smokers (as compared with non-smokers) at low dust concentrations, and also an approximate three-fold increase in the risk for non-smokers who are exposed to concentrations of dust as high as 7 mg/m^3.

Do these dust-related increases in bronchitic symptom risks imply corresponding increases in lung function impairments? A recent re-analysis of data first published in 1973, shows that they do.

If the dust-associated decrements in FEV_1, small or average, are expressed as risks of having an FEV_1 less than 80% of that expected in non-smoking miners with no exposure to dust, then the risk of having this deficiency increases steadily with increasing exposure, both among cigarette smokers and non-smokers; and what is more, at approximately the same rates. Note again, that the risk for a non-smoker who has been exposed to high (7 mg/m^3) concentrations of dust, is comparable to that attributable to cigarette smoking in the absence of dust exposure.

FEV_1 65% of that predicted, also shows the relationship with exposure; and again, the effect attributable to smoking, at zero exposures, is similar in magnitude to that associated with a high, 7 mg/m^3, exposure over 35 years in non-smokers.

Slides not provided.

CORRELATIONS BETWEEN RADIOLOGY, RESPIRATORY SYMPTOMS AND SPIROMETRY IN ACTIVE UNDERGROUND COAL MINERS IN BRAZIL[a]

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INTRODUCTION

In Santa Catarina's coal district, with around 200,000 inhabitants, there are about 2,000 cases of pneumoconiosis, most of which are from underground coal mining.

It is suspected that the coal mining industry, the main local economic activity, is responsible not only for pneumoconiosis but also for airway chronic irritation-resulting pathologies. Pneumoconiosis is caused directly by occupational dust exposure and the other related pathologies are caused by a number of factors, especially dust exposure,[12] cigarette smoking and occupational and environmental exposure to SO_2,[14] which is high due to the existence of underground diesel exhaust machines and of large open coal depots and rejects. Brazilian coal is rich in sulphur.

Some previous papers related to coalworkers pneumoconiosis (CWP) in Brazil have already been published. They focus on clinical and radiological aspects of the cases[15] and the occurrence of progressive massive fibrosis.[16] We lack information, i.e., epidemiological data which address questions about the occurrence, not only of pneumoconiosis, but also about the prevalence of respiratory symptoms and functional impairment of the exposed population.

Dust exposure conditions in Brazilian coal mining are different from those where classical works on CWP were performed. The Brazilian coal has plenty of ashes, i.e.; just 60% of mined material is coal. Many environmental measurements show high quartz concentrations, often above 10%[17] which makes us suppose that the CWP in Brazilian mines has a distinct clinical and evolutive behavior from the classical CWP. Probably the same happens in relation to respiratory symptoms and lung function impairment.

This is the first prospective epidemiological study about the respiratory compromise in active Brazilian underground coalworkers.

METHODS

During 1984, six underground mines in Santa Catarina's coal district were investigated. They employed 2,134 miners, which corresponded to a third of the underground miners in the region. One of the mines was manual, 3 were semimechanized and 2 were mechanized. A random sample of 50% of the miners (within each job description) was selected from the 6 mines' records. A summary of the sample is presented in Table I. Sickness absence, vacation and refusal were the reasons for the absence of workers. In these cases there was no replacement.

The 956 miners were submitted to a questionnaire on respiratory symptoms adapted from a questionnaire on Chronic Bronchitis (MRC, UK, 1976) by 6 trained professionals, and a spirometry with a dry-wedge spirometer (Vitalograph, Vitalograph Limited, Buckingham, UK).

A minimum of 3 curves were obtained for each miner. For analysis, only spirometries having a maximum difference of 100 ml for the FEV_1 between the 2 best curves were accepted.[1] FEV_1, FVC and the ratio of FEV_1/FVC were calculated. The values were transformed to BTPS.

The companies were responsible for the radiographs, which were considered valid until 1 year before the interview. Each radiograph was read independently by 3 experienced readers, according to the 1980 ILO International Classification.[7] The profusion of small opacities was given by the median of the 3 readings.

The exposure index used was the number of years spent underground (number of years of exposure, NYE) in one or more jobs described individually. Approximately one third of the miners referred having had more than one job. The smoking habits were calculated in pack-years (PY), and the nutritional status by the formula weight/height^2 (Quetelet Index).

The correlations between two variables were analysed through contingency tables. The correlations between NYE, PY and functional respiratory parameters were obtained through loglinear[3] and multiple linear regression models. The correlation of multiple variables and the occurrence of pneumoconiosis was initially analysed through a multiple linear regression model, where the relative importance of the independent variables was deduced. Due to the existence of dichotomous variables a probit regression analysis was also performed[4] to predict the probability of occurrence of the dependent variable (in this case, pneumoconiosis). Throughout this study "p" values were considered significant below the 5% level.

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RESULTS

The mean age of the 956 miners was 30.7 ± 5.7 (21–50). The mean number of years of exposure (NYE) was 5.8 ± 4.5 (0–26).

Only 816 radiographs were obtained from which 108 were considered inappropriate for reading (quality 4). The prevalence of pneumoconiosis was 5.6% (40 cases with profusion 1/0 or above). The NYE of miners with pneumoconiosis was 8.4 ± 4.7. Eighty cases (11.3%) were read as profusion 0/1 and the remaining 588, 0/0.

The presence of respiratory symptoms is presented in Table II. Cough and/or phlegm were only considered positive if they were present for at least 3 months. Breathlessness was considered positive if it occurred at heavy efforts.

Table III shows the lung function tests mean values for 768 miners. The remaining 188 (20%) had their spirometries invalidated because of technical defects. Both groups had a similar mean age and mean height but miners with accepted spirometries, had the mean NYE significantly lower ($p < 0.01$).

The distribution of the observed/predicted FVC and FEV_1 values was similar: 41.3% of the miners presented FEV_1 lower than 80% and 39.8% FVC lower than 80%, while 8.7% presented FEV_1 lower than 60% and 7.5% FVC lower than 60%. Only 9.8% of the miners presented the ratio FEV_1/FVC lower than 70%.

Out of the 956 miners, 580 (60.7%) were smokers, 128 (13.4%) ex-smokers and 248 (25.9%) non-smokers. The

Table I
Sampling of Underground Miners

MINE	METHOD*	NO OF MINERS	SIZE OF THE SAMPLE	NO OF MINERS ATTENDING	% ATTENDING
1	SM	191	93	73	78
2	Me	250	128	122	95
3	Me	595	306	260	85
4	SM	598	299	274	92
5	SM	267	135	130	96
6	Ma	233	102	97	95
TOTAL		2134	1063	956	90

* SM = Semi Mechanized
Me = Mechanized
Ma = Manual

Table II
Cough, Phlegm and Breathlessness in Underground Miners

	COUGH (%)	PHLEGM (%)	BREATHLESSNESS (%)
Yes	331 (34,7)	337 (39,5)	291 (30,4)
No	625 (65,3)	619 (60,5)	665 (69,6)
TOTAL	956 (100)	956 (100)	956 (100)

smokers' pack-years mean (PY) was 10.1 ± 8.4 and the ex-smokers' 11.2 ± 9.9.

Table III
Mean Values of Lung Function Tests in 768 Miners

TEST	MEAN ± SD
FEV_1 (l)	3.73 ± 0.64
FVC (l)	4.59 ± 0.73
FEV_1/FVC (%)	81.2 ± 9.00
FEV_1 O/P (%)	95.5 ± 30.30
FVC O/P (%)	102.0 ± 35.00

Table IV shows the isolated correlations between NYE, PY, lung function tests and respiratory symptoms. Both NYE and PY presented a significant correlation with the presence of cough, phlegm and breathlessness. Regarding lung function tests, only a significant negative correlation was found between NYE and FEV_1/FVC.

The influence of smoking and the number of years of exposure were studied in relation to lung function tests in loglinear and multiple linear regression models, the latter with FEV_1, FVC and FEV_1/FVC as dependent variables. The results are presented in Tables V and VI. (The results of the loglinear model which comprises FEV_1, PY, and NYE were omitted for being similar to the results obtained through the model with FVC, PY and NYE).

Loglinear models indicated that in the analysis between NYE, PY and FVC, and NYE, PY and FEV_1, the structure that better explains both relationships contains a significant association between NYE and PY. The iterations between NYE, PY and FEV_1/FVC had low "p" values, thus were not analysed. The multiple linear regression analysis showed that the effect of NYE was more relevant in relation to FEV_1 and FVC but PY is more relevant in relation to FEV_1/FVC.

Finally, the behavior of respiratory symptoms, functional parameters and NYE and PY were analysed in relation to the presence of pneumoconiosis. In the first analysis a multiple linear regression model was fitted with profusion of small opacities as the dependent variable. The results are shown in Table VII. NYE and breathlessness were significantly associated with the presence of pneumoconiosis. FVC was not considered as an independent variable in the above-mentioned table. PY was neglected due to its minimum contribution in the equation.

The multiple linear regression model is not the most suitable for analyzing variables with dichotomous values such as cough, phlegm and breathlessness. For a better understanding of the relationships we applied the probit regression technique, assuming for the dependent variable (profusion) a dichotomous value (0 = category 0, 1 = category 1 or above). The respiratory symptoms such as cough, phlegm and breathlessness assumed the values 0 = absent and 1 = present). The FVC and FEV_1 are expressed in centiliters. The results are presented in Tables VIII to X.

The probit regression analysis confirms the significance of NYE and breathlessness in relation to the prediction of pneumoconiosis and in addition it shows a significant correlation with FEV_1/FVC (positive) and FEV_1 (negative). The distribution of the predicted values among the subjects shows that there is a good chance of classifying an individual correctly given known variables.

DISCUSSION

The radiological evaluation was affected since the industries were in charge of the examinations. Consequently 140 radiographs were not sent and 108/816 were considered inadequate for classification. The prevalence of 5.6% of pneumoconiosis is not high. However, the mean NYE of cases is very low. The CWP prevalence in underground United States miners in the late 70's was just below 5%, but the mean exposure time was much higher than the 8.4 years here observed.[13]

The quartz concentrations exceeded 10% in more than one third of the samples of respirable dust in the investigated mines. In three fourths of the samples the TLV of quartz was exceeded.[17] These quartz concentrations are likely to affect the estimates of pneumoconiosis prevalence in underground coal mining when compared to countries where there are lower quartz concentrations.[8]

Approximately 1/3 of the miners complained of cough, phlegm and breathlessness. This figure seems to be excessive, nevertheless, there are not comparative data available from a control population. The environmental levels of SO_2 are high in the region due to the existence of large open coal depots.

A third of the miners, having valid lung function tests, presented the FEV_1 and the FVC below 80%. Miners with rejected lung function tests for analysis (20% of the sample) have shown a NYE mean significantly higher than the miners with valid tests. This may probably have underestimated the functional effects resulting from dust exposure. Both NYE and PY correlated significantly with the presence of cough, phlegm and breathlessness.

The analysis of the NYE and PY influence over the functional parameters showed that only NYE associated significantly with the drop in FEV_1/FVC. When the effects of these two factors were analysed in a multiple linear regression model, NYE proved to be more important in relation to the decline in FEV_1 and FVC, while PY proved to be more important in relation to the decline in FEV_1/FVC. This latter is, comparatively, a better isolated test for bron-

Table IV

X^2 Values for Contingency Tables. Number of Years of Exposure (NYE) or Pack Years (PY) and Lung Function Tests of Respiratory Symptoms

	NYE (DF)	PY (DF)
FEV_1	6.02 (4)	2.2 (4)
FVC	1.7 (4)	3.3 (4)
FEV_1/FVC	9.5* (4)	5.5 (4)
COUGH	21.2*** (2)	20.2***(2)
PHLEGM	11.6** (2)	6.15* (2)
BRETHLESSNESS	50.8*** (2)	13.9***(2)

* $p \leq 0.05$
** $p \leq 0.01$
*** $p \leq 0.001$
DF = Degrees of Freedom

Table V

Observed Adjusted Values for the Log Linear Model PY.FVC, PY.NYE (Probability = 0.6876)*

FVC	NYE	PY NS	PY 10	PY 10	PY ES	TOTAL
	0 - 5	9(7.3)	8(11.9)	2(2.5)	0(0.5)	19
< 0.60	5 - 15	2(4.1)	8(4.8)	3(2.3)	1(0.5)	14
	15 -	1(0.5)	1(0.3)	0(0.2)	0(0.0)	1
	0 - 5	42(42.2)	62(61.5)	33(28.7)	1(1.0)	138
0.60 - 0.60	5 - 15	24(23.8)	25(25.1)	23(26.7)	1(1.0)	73
	15 -	3(3.0)	1(1.5)	2(2.6)	0(0.0)	6
	0 - 5	136(76.5)	136(132.7)	54(57.9)	5(4.5)	270
> 0.80	5 - 15	45(43.1)	51(54.1)	57(53.9)	4(4.5)	157
	15 -	5(5.5)	3(3.2)	6(5.2)	0(0.0)	14
T O T A L		206	285	180	12	693

* λ and t values were significant only to 2 levels of FVC and to all levels of the table PY x NYE.

Table VI

Coefficients, Standard Error (SE) and F Value of the Multiple Linear Regressions

DEPENDENT VARIABLE	INDEPENDENT VARIABLES	COEFFICIENT	SE	F
	CONSTANT	368.6514		
FEV_1	NYE	-2.0007	0.5122	15.25*
	PY	-0.4581	0.2671	2.94
	CONSTANT	445.9138		
FVC	NYE	-1.9781	0.5903	11.23*
	PY	-0.2002	0.3078	0.42
	CONSTANT	82.6080		
FEV_1/FVC	PY	-0.1457	0.0399	13.31*
	NYE	-0.0898	0.0766	1.37

*p< 0.005

Table VII

Coefficients, Standard Error (SE) and F Value of the Multiple Linear Regression, Dependent Variable: Profusion

	COEFFICIENT	SE	F
Constant	0.2664		
NYE	0.1396	0.0385	13.13*
BREATHLESSNESS	0.1957	0.0723	7.32*
COUGH	0.0807	0.0749	1.16
FEV_1	-0.0003	0.0003	1.10
QUETELET INDEX	0.0640	0.0764	0.70
PHLEGM	0.0417	0.0712	0.34
FEV_1/FVC	0.0013	0.0032	0.16

*p < 0.005

Table VIII
Probit Regression Coefficients. Dependent Variable: Profusion (0 or 1)

	COEFFICIENT	SE	T	P
CONSTANT	-9.4601	4.9535	-1.9098	0.0562
NYE	0.0582	0.0183	3.1835	0.0015*
BREATHLESSNESS	0.5627	0.1809	3.1109	0.0019*
FEV_1/FVC	0.1235	0.0595	2.0762	0.0379*
FEV_1	-0.0265	0.0129	-2.0532	0.0401*
FVC	0.0192	0.0105	1.8247	0.0680
QUETELET INDEX	-0.0492	0.0301	-1.6348	0.1021
COUGH	-0.1141	0.1965	-0.5809	0.5614
PHLEGM	0.0374	0.1915	0.1953	0.8452
PY	-0.0007	0.100	-0.0074	0.9407

chial obstruction. The loglinear model showed that the interaction cigarette smoking-years of exposure was significant for the structure of the relationships with FEV_1 and FVC.

Table IX
Change in Probability Evaluated at P = 0.056

	P = 0.056
NYE	0.0066
BREATHLESSNESS	0.0639
FEV_1/FVC	0.0140
FEV_1	-0.0030
FVC	0.0022
QUETELET INDEX	-0.0056
COUGH	-0.0130
PHLEGM	0.0042
PY	-0.0001

The contribution of dust exposure on lung function was at first minimized in the literature, due to the complexity of the analysis of all respiratory hazard factors related to coal mining.[11] Recent and reliable data clarified these points, showing the relationship between dust exposure in coal mines and respiratory symptoms.[5,9] Data analysis on the relationship between dust exposure and cigarette smoking was addressed by Elmes.[2] In British coal industry, cigarette smoking is today the main cause for determining miners' functional deterioration, although both factors have their contribution. A more recent paper on these relationships in British coal workers showed that the combined effect of dust exposure and cigarette smoking appears to be additive, and there are no definite proofs, that smoking is more important than dust exposure.[10]

Although there are no routine dust sampling in Brazilian coal mines that permit us to derive cumulative indices of exposure, it can be supposed that dust exposure hazards in Brazilian coal mines are not comparable to British, American and German findings due to qualitative differences in respirable quartz. In fact, the loglinear analysis indicates an important effect of the association between cigarette smoking and dust exposure on the determination either of FEV_1 or FVC. Since miners with rejected lung function tests presented a mean NYE significantly higher than the analyzed group, the effect of dust exposure on the lung function parameters is likely to be underestimated. We believe that only the longitudinal follow-up of these miners will clear up the confused correlations of these variables.

Table X
Predicted Probabilities (in Intervals of 0.1) by Observed Value (0 or 1)

	PREDICTED									
	0-.09	.1-.19	.2-.29	.3-.39	.4-.49	.5-.59	.6-.69	.7-.79	.8-.89	.9-1.0
OBSERVED										
0	568	78	19	3	0	0	0	0	0	0
1	21	14	2	3	0	0	0	0	0	0

The multiple linear regression model showed that NYE followed by breathlessness are the most significant factors related to pneumoconiosis. Multiple linear regression models are not suitable in the presence of dichotomous variables due to its difficulties in estimating probabilities restricted to the interval 0.1. In addition, the multiple linear regression assumes that the effect of the independent variables is constant along the whole variation of the predicted dependent variable. The probit regression analysis seems to be more appropriate in these circumstances and yields estimated coefficients which are asymptotically unbiased, efficient and consistent.[4]

The results of the probit analysis were similar to those of the multiple regression analysis including the FEV_1/FVC and FEV_1 as significant variables. This analysis demonstrates that for each year of exposure a 0.6% effect is added to the observed probability of pneumoconiosis (5.6%). Cough, phlegm and smoking had no relation with the presence of pneumoconiosis. In British coal miners, smoking does not affect the risk of developing CWP.

These data indicate a probable excess of respiratory symptoms in Brazilian coal miners. Cough, phlegm and breathlessness were significantly related to both dust exposure and smoking. The association of dust exposure and smoking showed a significant effect in relation to the FEV_1 and FVC. Although the dust exposure effect was underestimated, we are not able to conclude which one of these variables was more responsible for lung function deterioration. The most determinant factor, as far as pneumoconiosis is concerned was the dust exposure; individuals with pneumoconiosis tended to have breathlessness and a low FEV_1. This group of miners will be followed up in 1989.

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15 YEAR LONGITUDINAL STUDIES OF FEV_1 LOSS AND MUCUS HYPERSECRETION DEVELOPMENT IN COAL WORKERS IN NEW SOUTH WALES, AUSTRALIA

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Recent longitudinal studies from the United Kingdom[9] and the United States[1] have shown that coal mine workers suffer a decline in FEV_1 which is a function of age, height, smoking habit and respirable dust exposure. Although each of these studies has been criticized for bias due to the restriction of the study to current workers who had been examined and re-examined after an 11 year interval[10] it has been shown that those workers who leave the coal mining industry do not differ greatly in their response to dust exposure, thus suggesting that any such bias is small.[11]

Previous cross-sectional studies in New South Wales have shown clear positive associations between chronic mucus hypersecretion and age, smoking, relative dust exposure and alcohol consumption and similar, but less clear, associations between airways obstruction (loss of FEV_1) and the above factors.[8] Comparison of multiple regression analyses of the entire workforce examined in 1971–74 and 1977–80 showed that the negative regression relationship of FEV_1 with relative dust exposure (years worked at face) was statistically significant at the 5% level only in the earlier study, which would have included more men who had worked in a period of poorer dust control (i.e., before about 1955).[7] To confirm these findings and to enable more direct inferences as to the relative aetiological significance of dust exposure, smoking and alcohol on chronic mucus hypersecretion and airways obstruction, two complementary longitudinal studies based on the entire NSW workforce were carried out. In the first study, methodology was deliberately chosen to be comparable with the U.K. and U.S. studies mentioned above. In the second study a somewhat different methodology was used to provide further information about the actual time course of changes in both airway obstruction and chronic mucus hypersecretion, as a function of age, smoking, relative dust exposure and alcohol consumption.

STUDY 1

Methods

In New South Wales, all mineworkers are examined in regional medical bureaus, by occupational physicians, every 2–3 years. At each examination, a full smoking and alcohol consumption history are obtained. Standing height without shoes and FEV_1 (better of two satisfactory efforts, Vitalograph Spirometer ATPS 20°C) are measured. Data are recorded in a standardized fashion and maintained in a computer-based records system.[5]

All workers who had been examined in the period 30 June 1970–30 June 1973 and in the period 30 June 1983–30 June 1986 *and* at least once in the intervening period were included in the study. From the computer-based records system, the following data were extracted:

1. Age at latest examination (years).
2. Height at latest examination (cm).
3. Tobacco smoked per week (gm/wk)
   3.1. at initial examination (previous smoking amount)
   3.2. mean of all examinations, including initial examination (concurrent smoking amount).
4. Alcohol consumed per week (gm/wk) (mean of all examinations).
5. Dust exposure index at initial examination (6 × years worked underground at face + 1 × years worked underground not at face prior to initial examination). The ratio 6:1 corresponds to the ratio of mean full shift gravimetric exposures in the two sites.
6. Dust exposure index between examinations (6 × years worked underground at face + 1 × years worked underground not at face between examinations). (Concurrent dust exposure).
7. Standardized change in FEV_1, (ΔFEV_1, L)

$$\frac{(FEV_1\ (1970\text{–}73) - FEV_1\ (1983\text{–}86)) \times 15}{\text{(actual years between)}}$$

The sample comprised 2,807 men. This represented 24.5% of the men who were examined between 1970–73 and had complete data for all variables.

Results

Means and standard deviations of all variables are shown in Table I. The multiple regression of ΔFEV_1 on variables 1–6 was calculated. The results are shown in Table I.

It can be seen from Table I that ΔFEV_1 has significant ($P<0.05$) positive regression coefficients on age, previous dust exposure, previous smoking amount and alcohol consumption but not on height, concurrent smoking amount or concurrent dust exposure.

Table II shows some significant correlations among the independent variables, but with the exception of age/previous exposure ($r = 0.38$), they are low (<0.19). A high age/exposure correlation is a consistent feature of all epidemio-

Table I
Means and Regression Coefficients

	b	P	Mean (SD)
y variable			
ΔFEV_1 = ($\frac{FEV_1\ 1970\text{-}73 - FEV_1\ 1983\text{-}86}{\text{actual years between}}$) X 15 (litres)			0.81(0.81)
x variables			
Age at last examination (year)	0.75×10^{-2}	<0.001	45.5(8.9)
Height at last examination (centimetres)	0.72×10^{-3}	NS	173(19)
Dust exposure index (concurrent)	-0.24×10^{-4}	NS	43.9(39.5)
Dust Exposure index (previous)	0.14×10^{-2}	<0.001	21.3(35.8)
Tobacco gm/wk (concurrent)	0.83×10^{-4}	NS	49.4(106)
*Tobacco gm/wk (previous)	0.33×10^{-3}	<0.01	57.2(130)
Alcohol gm/wk	0.18×10^{-3}	<0.05	171(168)
Constant			0.24

R = 0.14
n = 2807

* Included in a separate analysis. Other regression coefficients remained stable to 2 decimal places.

logical studies in a relatively stable workforce. The two variables, however, were retained in the multiple regression as separate variables of independent patho physiological interest. Mean loss of FEV_1 in 15 years was 0.81L (SD 0.81L). Mean FEV_1 in 1970–73 was 3.77L; mean FEV_1 in 1983–86 was 2.96L. It is interesting to note that the cross-sectional regression coefficient for age was −0.038 L/yr giving an estimated loss in 15 years of 0.6L.[7]

Discussion

The mean loss of FEV_1 of 0.81L in 15 years is in good agreement with the U.K. and the U.S. studies[9,1] which found mean FEV_1 losses in 11 years of 0.5L, 0.48L respectively. Mean FEV_1 loss in a "normal" population is about 0.3L in 11 years.[2]

The cohort in the present study was slightly younger than in the U.K. and U.S. studies (mean age at final examination 45 compared to 50 (U.K.) and 49 (U.S.)).

Loss of FEV_1, was related to previous dust exposure and previous smoking amount. Mean smoking amount reduced significantly in the 15 year period (57.2 gm/wk in 1970–73; 49.4 gm/wk (average of all examinations including 1970–73). The proportion of smokers in 1970–73 was 55% while in 1983–87 it was 43%.

Table II
Correlation Coefficients

	Age	Height	Dust (Concurrent)	Dust (Previous)	Smoking§	Alcohol
Age	1.00					
Height	-0.07	1.00				
Dust (concurrent)	0.10*	-0.02	1.00			
Dust (previous)	0.38*	-0.03	0.19*	1.00		
Smoking§	-0.02 0.02	0.02 0.00	0.00 0.00	0.02 0.03	1.00 1.00	
Alcohol	0.11*	0.03	0.03	0.10*	0.12*	1.00

* P<0.0001

§ upper figure is smoking (concurrent)
lower figure is smoking (previous)

The lack of relationship of loss of FEV_1 to concurrent smoking is thus not as surprising as it would seem at first glance. Men already affected by obstructive lung disease continued to lose FEV_1, even though their smoking habit was reduced.

The lack of relationship of loss of FEV_1 to concurrent dust exposure is also not surprising. Most of the obstructive lung disease due to dust would have developed in the men exposed to the higher dust concentrations obtained prior to 1955. These men would have continued to deteriorate whilst those exposed to concurrent dust concentration would not be so severely affected.

This finding is consistent with previous cross sectional studies on the New South Wales workforce[7] and with the U.K. longitudinal study.[9] The finding of a lack of association of loss of FEV_1 with height is difficult to explain. Both the U.K. and U.S. studies showed a strong positive relationship between FEV_1loss and height, which would be expected if smoking and dust exposure caused a proportional detriment in lung function in men of different heights. As Morgan notes, there is nothing to suggest that height itself renders an individual more or less likely to emphysema or chronic bronchitis.[10]

A possible explanation of the finding in the present study is the inclusion in the study group of taller men who work in open cut mines. Underground and face workers tend to be self selected for smaller stature because of low roof conditions in some mines. These are the workers exposed to the highest dust levels. This effect would oppose the normal proportional loss effect and thus lead to a non-significant regression coefficient. Neither the U.K. nor U.S. study included open-cut workers.

It is possible to make rough estimates of the relative effects of previous smoking and previous dust exposure on FEV_1 loss. The respective regression coefficients are 0.33×10^{-3} L. $gm.^{-1}$ wk, and 0.14×10^{-2} L. unit of dust exposure $index^{-1}$ Thus the effect of having smoked 140 gm/wk (20

cigarettes/day) prior to 1970 is a loss of 46.2 mL in 15 years whereas the effect of having worked continuously at the face for 10 years prior to 1970 (assuming the average man aged 30 in 1970 would have started work at 20) would be a loss of 84 mL. This analysis is a little misleading as it does not take into account either the variance of the dependent and independent variables or the correlation of previous dust exposure with age. An alternative examination of the relative effects can be made by comparing the standardized regression coefficients for previous smoking (0.056) and previous dust exposure (0.062), suggesting a roughly equal effect.

STUDY 2

Methods

The study cohort comprised all workers who had been examined and had complete data at each of the successive 5 year intervals from 1970. The examination nearest in time to 30 June 1970, 1975, 1980, 1985 was taken as the reference examination for each interval. This study cohort comprised 847 men. At each examination, FEV_1, smoking and alcohol data were obtained as above. In addition, the presence or absence of chronic mucus hypersecretion was ascertained by a modified MRC respiratory symptom questionnaire.[8] The cohort was subclassified into four age cohorts (aged 16–25(1) (130 men), 26–35(2) (214 men), 36–45(3) (269 men), 46–55(4) (234 men) in 1970. In each 5 year interval these cohorts were further subclassified by relative dust exposure, smoking amount and alcohol consumption as follows:

Relative Dust Exposure

High: Majority of 5 year period working underground at face.
Medium: Majority of 5 year period working underground not at face.
Low: Majority of 5 year period working in surface.

Smoking Amount

Non-Smoker
Ex-Smoker
1–84 gm/wk tobacco (Low)
>84 gm/wk tobacco (High)

Alcohol Consumption

High: >300 gm/wk (High)
Low: <300 gm/wk (Low)

The dependent variables were chronic mucus hypersecretion (% affected) and mean FEV_1/ht^2.[3]

Results

Figures 1–6 show the development of chronic mucus hypersecretion and airways obstruction with time for each age subcohort, as a function of relative dust exposure, smoking amount and alcohol consumption.

There is a clear relationship between chronic mucus hypersecretion and both dust exposure and smoking amount in all age subcohorts. In cohorts 1, 3, 4 the same relationship is apparent for alcohol consumption. There is a progressive increase of chronic mucus hypersecretion with time.

Airway obstruction also shows a progressive increase with time in all subcohorts. There is a strong relationship with smoking amount and a weaker relationship with dust exposure and alcohol consumption. It should be noted that the "sub-subcohorts" at any time may include different individuals, as smoking habit, drinking habit and work site may change between examinations. For this reason we were uncertain as to how best to statistically analyse the data. As statistical analysis of longitudinal data of this type is still in a developmental phase we decided to merely present for visual inspection the time course of means and proportions by sub-subcohort.

However, the results of studies 1 and 2, taken together, clearly show that concurrent dust exposure, concurrent smoking and alcohol consumption are associated with increased mucus hypersecretion and that dust exposure and smoking before 1970 are associated with the development of airways obstruction.

These findings and also consistent with pathological studies demonstrating dust induced bronchitis[4] and emphysema[6] in coal workers. Alcohol consumption has been shown to reduce mucociliary clearance[12] and the adverse effects of smoking are universally accepted. There thus exists a clear patho physiological basis for the findings.

Conclusion

Longitudinal studies of the entire New South Wales working coal industry workforce show a clear association between past dust exposure, smoking and alcohol consumption and the development of chronic mucus hypersecretion and airways obstruction.

We have not followed up exworkers but evidence from other studies suggests that this does not cause significant bias.

Any such bias is likely to be in the direction of a "healthy worker effect" whereby the least affected remain at work. Hence these studies are likely to have underestimated the effects of dust exposure on lung function in coal workers.

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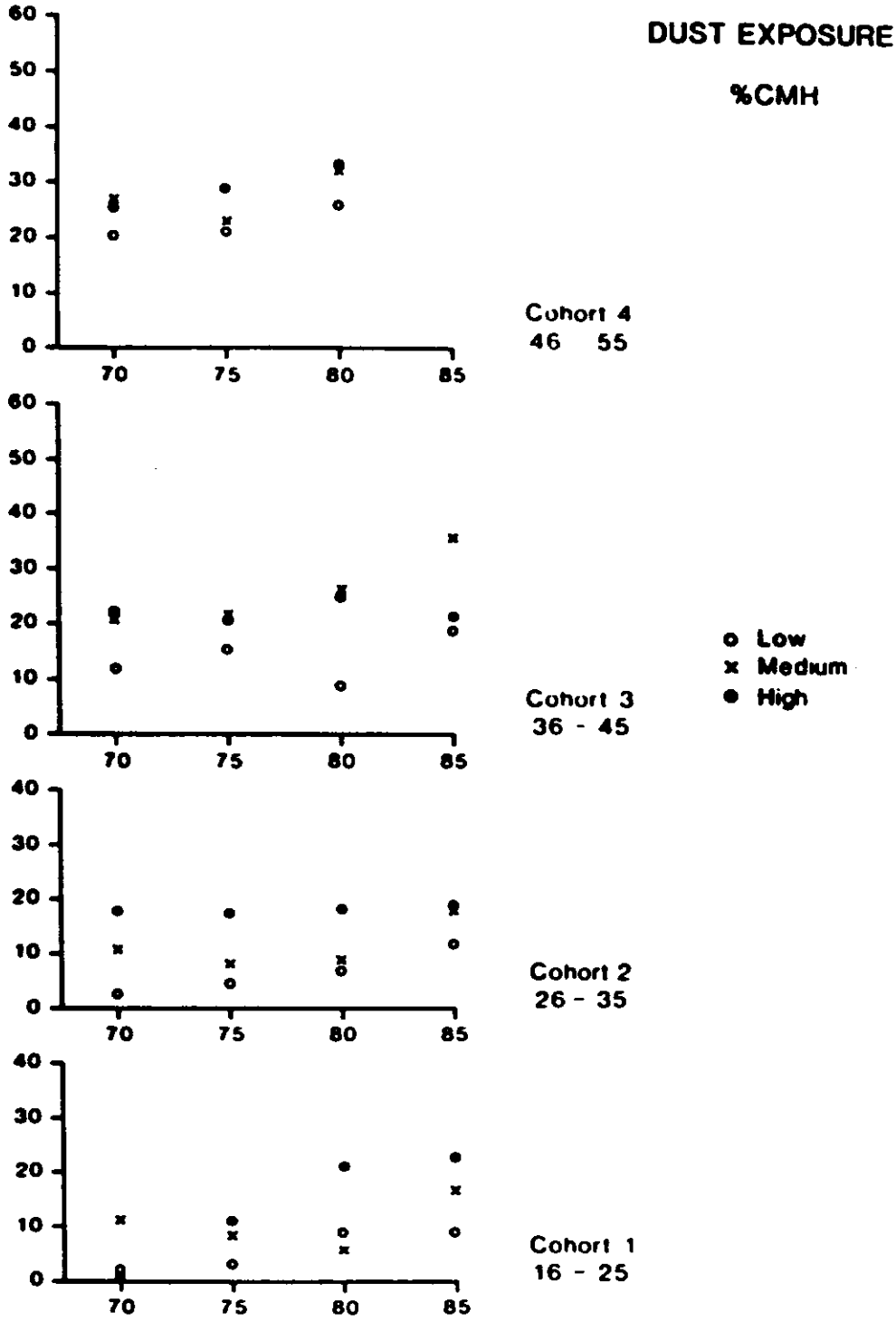

Figure 1. Development of chronic mucus hypersecretion by age and time related to relative dust exposure.

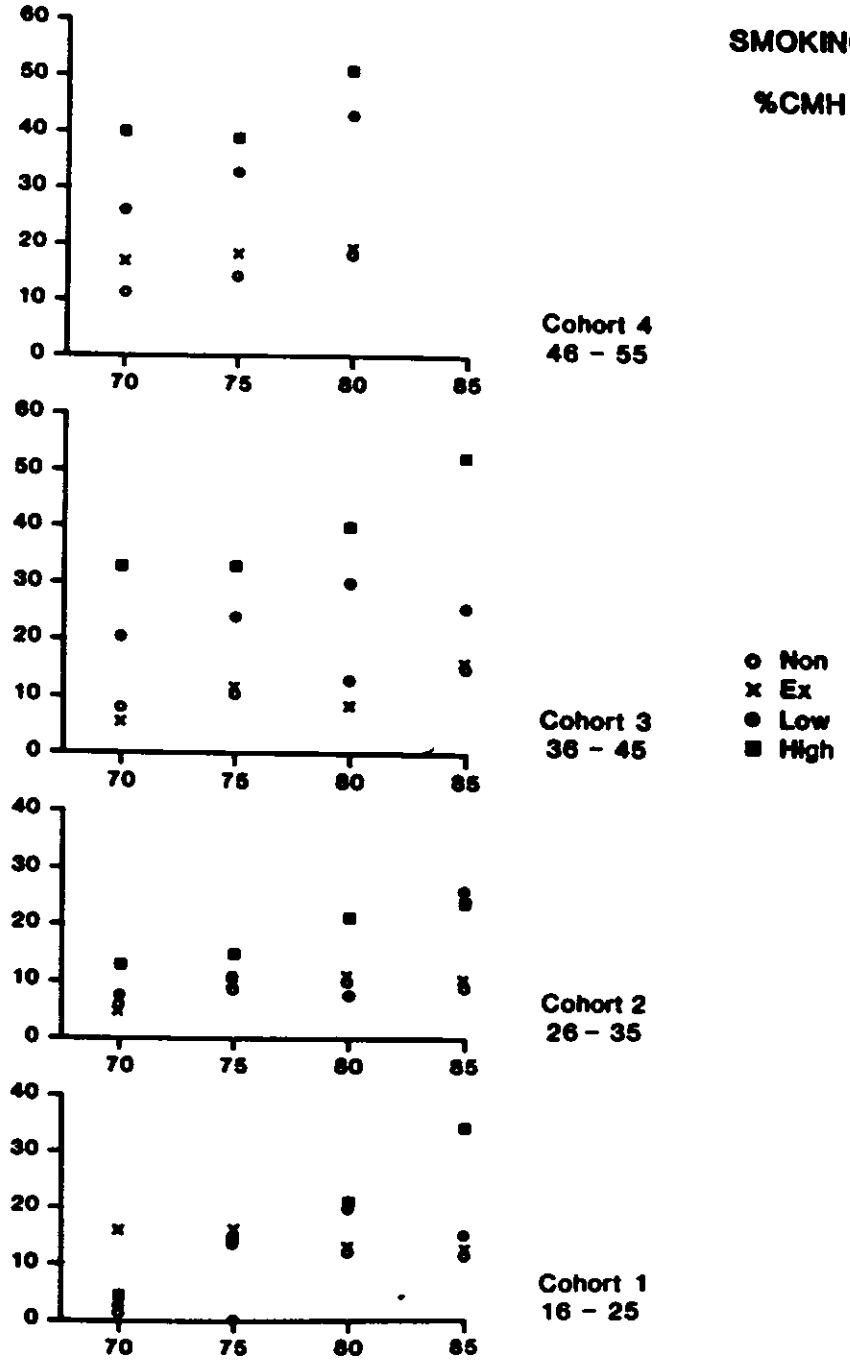

Figure 2. Development of chronic mucus hypersecretion by age and time related to smoking history.

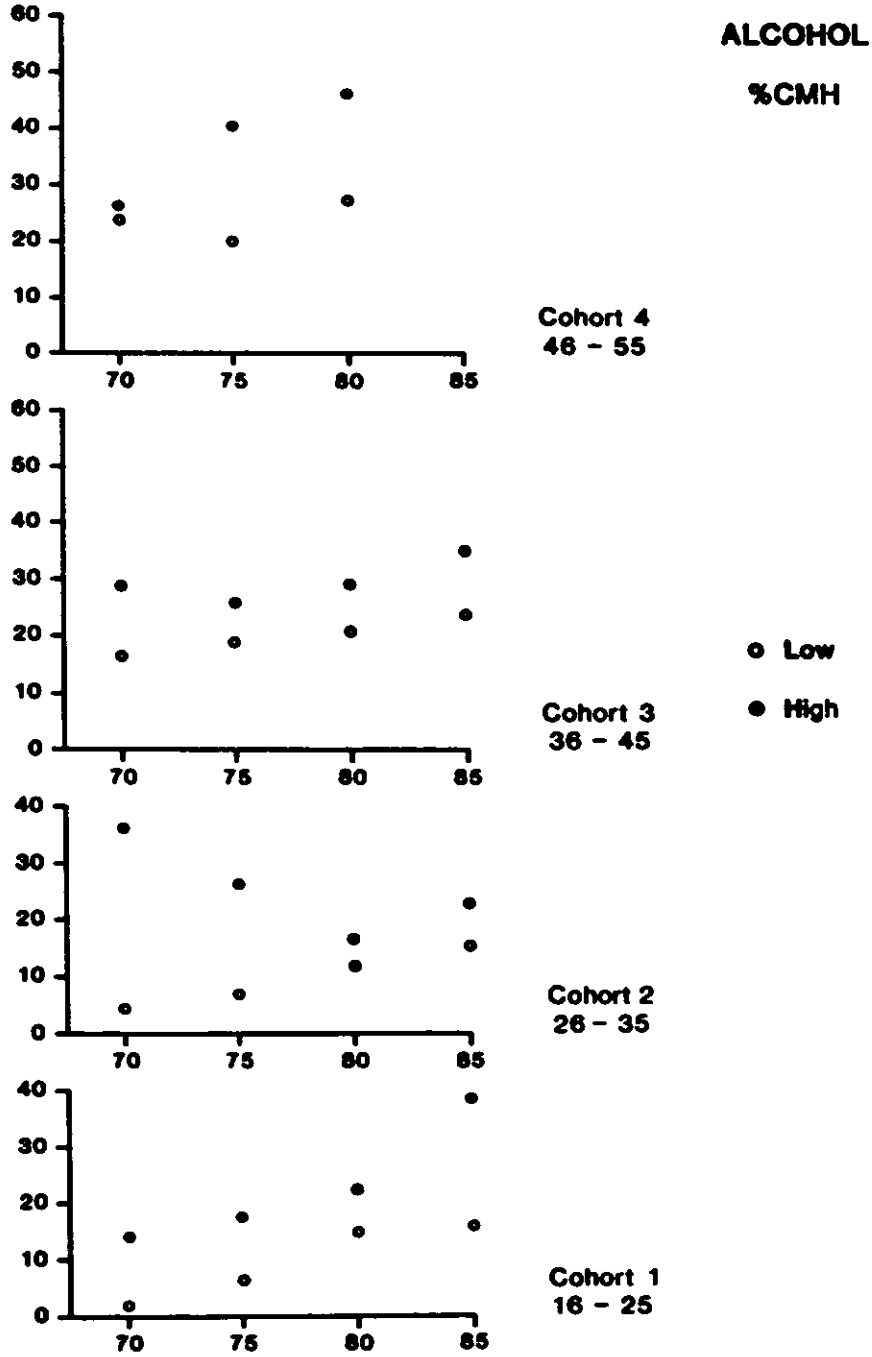

Figure 3. Development of chronic mucus hypersecretion by age and time related to alcohol history.

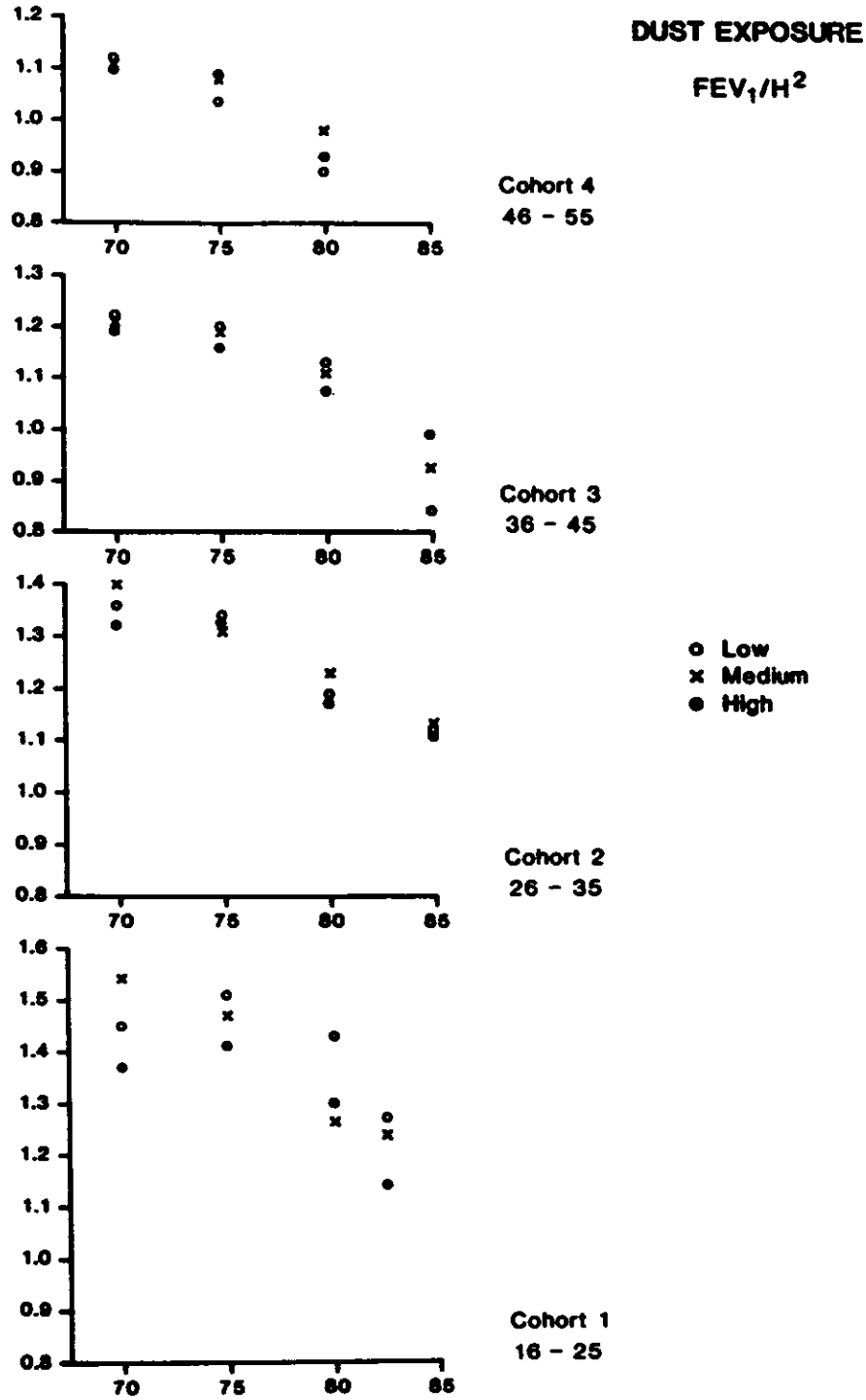

Figure 4. Development of airway obstruction by age and time related to relative dust exposure.

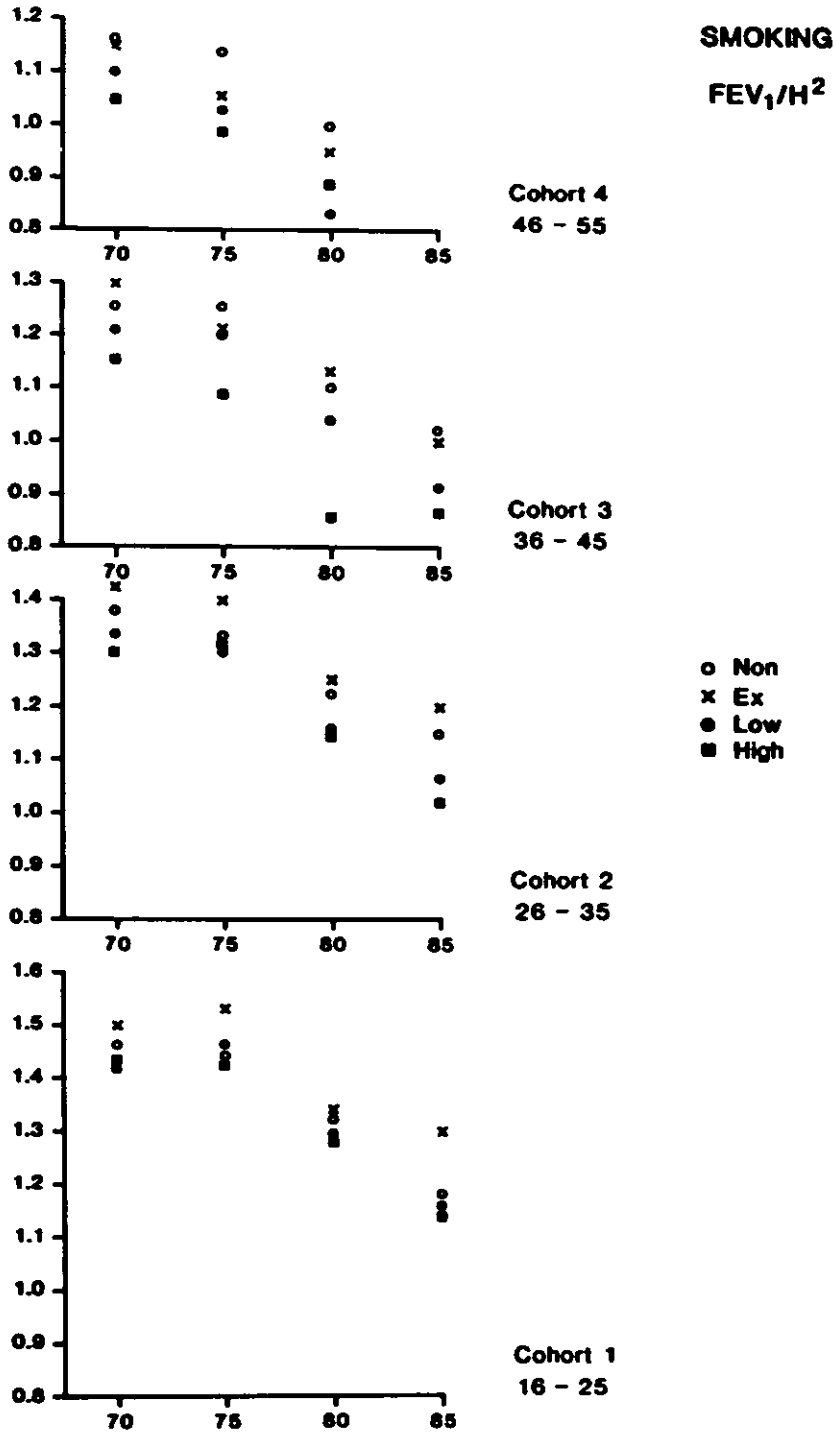

Figure 5. Development of airway obstruction by age and time related to smoking history.

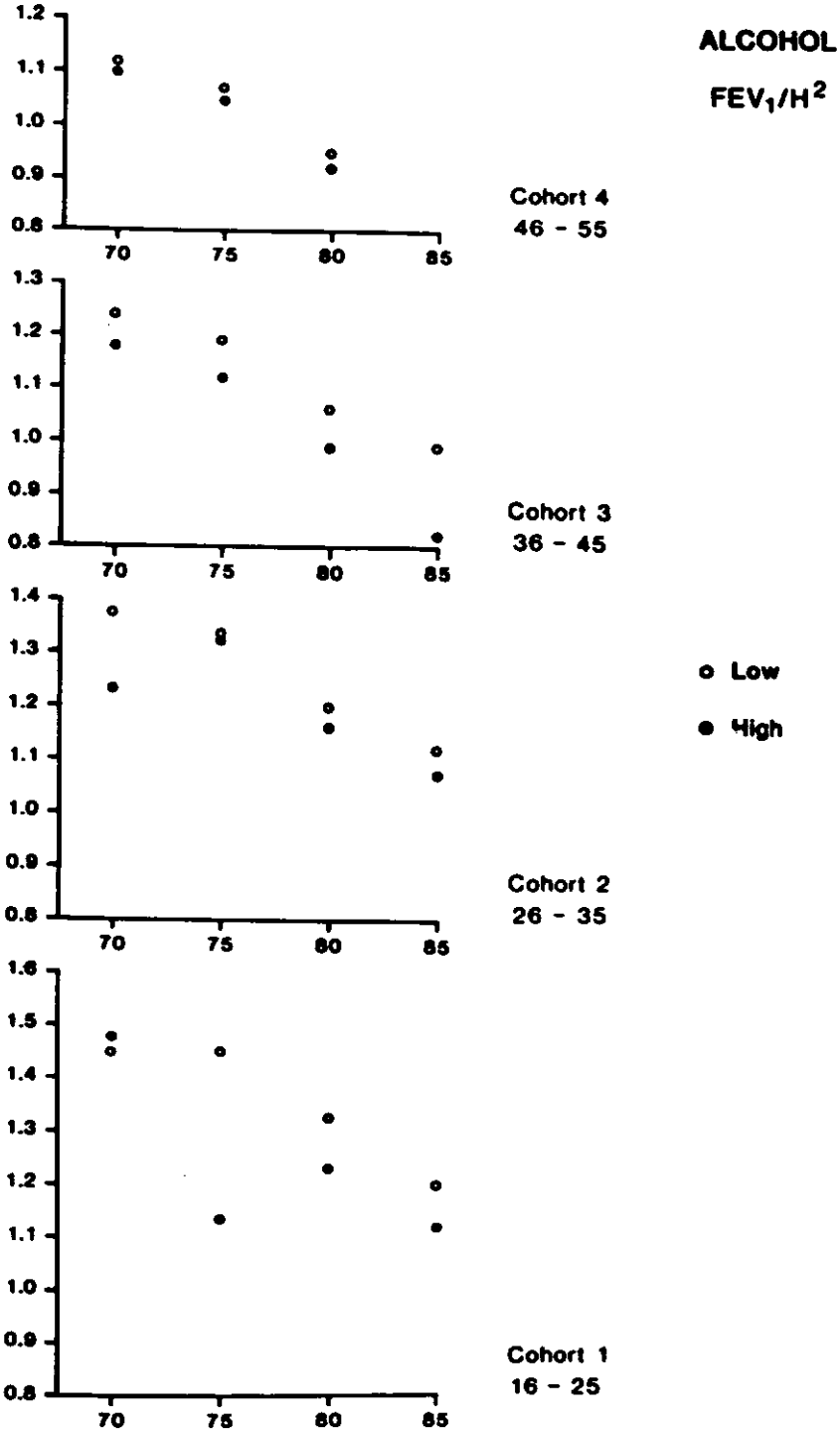

Figure 6. Development of airway obstruction by age and time related to alcohol history.

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PROGRESSIVE MASSIVE FIBROSIS DEVELOPING ON A BACKGROUND OF MINIMAL SIMPLE COAL WORKERS' PNEUMOCONIOSIS

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ABSTRACT

Recent British data suggest that the majority of progressive massive fibrosis (PMF) cases in coal miners develop on a background of category 0 or 1 simple pneumoconiosis. To evaluate this phenomenon in American coal miners, data from the NIOSH National Coal Study (NSCWP) and Coal Workers' X-ray Surveillance Program (CWXSP) were examined. All available 5-year film pairs on individual miners which showed PMF on the later, but not on the earlier film were studied (n=136 pairs). Readings were either the median of 3 "B" readers (NSCWP) or a single "B" reader (CWXSP). All films on each miner were reviewed in a side-by-side format with dates known by an unblinded "B" reader. Only 69 of the 136 cases were thought to be true incident cases of PMF. Of the 67 excluded cases, 26 were thought to have PMF on all films, and 11 were considered to be borderline but negative cases. Eighteen others were given other diagnoses for mass-like lesions on the chest x-ray. In the 69 confirmed cases, the prevalence of category 0, 1, 2, and 3 simple CWP on the earlier films was 14%, 43%, 33%, and 9%, respectively. These values for the PMF films were 1%, 43%, 38%, and 17%. The primary simple CWP opacity on the PMF films was: p-9%, q-20%, and r-65%. The high prevalence of "r" opacities and the rapid disease progression observed in some cases suggest that free silica over-exposure may have played an important role in PMF in this population. The results also seem to corroborate recent British data. Although further evaluation is needed, these data re-emphasize the importance of strict dust control.

INTRODUCTION

Recent British data suggest that the majority of progressive massive fibrosis (PMF) cases in coal miners develop in miners whose chest x-ray approximately 5 years previously showed category 0 or 1 simple (presumedly coal workers') pneumoconiosis.[1,2] This frequent development of PMF on a background of minimal simple coal workers' pneumoconiosis (CWP) is surprising since previous research indicates that the attack rate of PMF is near zero in those with minimal pneumoconiosis, rising rapidly in miners with the higher stages of simple CWP.[3,4] This newly described phenomenon is presumedly related at least in part to the very high prevalence of miners with minimal simple CWP in the lower dust-exposed present-day workforce. Thus the low attack rates in miners with minimal simple CWP multiplied by the very large number of miners at risk yield a substantial fraction of the total new PMF cases. However, Hurley and Jacobsen[5] have suggested from more recent data that the attack rate of PMF in working coal miners with category 1 simple pneumoconiosis may be 3 to 4 times higher than previously reported.

The existence of this phenomenon has not been clearly documented in the North American literature. Furthermore, some have questioned the reliability of the radiographic diagnosis of PMF in the absence of a background of category 2 or 3 simple pneumoconiosis and especially in miners with category 0 simple CWP.[6] This issue is obviously an important one, relating to the pathogenesis of PMF and to the effectiveness of medical surveillance as a method of prevention of PMF.

In order to evaluate this phenomenon in American coal miners, data from the National Institute for Occupational Safety and Health (NIOSH) National Study of Coal Workers' Pneumoconiosis (NSCWP), and Coal Workers' X-Ray Surveillance Program (CWXSP) were evaluated.

METHODS

Selected posterior-anterior (PA) chest x-rays from the NSCWP and CWXSP were examined. The NSCWP is a research program involving selected coal mines and miners across the country. The CWXSP is a surveillance program covering all U.S. underground coal miners. Both data bases have had four "rounds" or groupings of x-rays of U.S. coal miners taken at approximately 5-year intervals. The overall time interval ranged from 1969 to 1988. From these two files, all available film pairs in adjacent rounds on individual miners which were interpreted as showing PMF on the later, but not on the earlier film were studied (n=136 pairs). Although the NSCWP and CWXSP files contain films of over 1300 miners with PMF, the great majority of these cases have only one x-ray on file, or PMF on all available x-rays. These two programs to date have a total of 194 cases of PMF at-

tacks. Excluded from the present study were 58 cases: 37 had PMF attacks over 3 or 4 rounds (i.e., not over adjacent rounds); 6 had PMF attacks documented by 1 x-ray in each program; 2 represented disagreement between programs; and 13 had films which were involved with other studies or not located during the time of the re-readings. These x-ray readings were based on the ILO classification current at the time of the x-ray. They were the original interpretations done at the time, and were based on either the median of 3 NIOSH "B" readings (NSCWP) or a single "B" reader reading (CWXSP).[7] One additional stipulation for the NSCWP cases was that the earlier film could not be read as showing PMF by *any* reader.

All 136 x-ray pairs, along with any additional x-rays available on the 136 miners, were then reviewed in a side-by-side format with dates known by a single "B" reader. This reader (the first author) knew the purpose of the study, the fact that the x-ray sets were thought to represent incident cases of PMF, and the source of the films. However he was unaware of prior actual ILO readings, and miner tenure and job title. The 1980 ILO classification[8] and standard films were utilized in these readings. In addition to the usually recorded ILO classification data, the location, number, and calcification of PMF lesions were noted.

RESULTS

One hundred fifteen of the 136 cases came from the CWXSP, and the remaining 21 came from the NSCWP. For 54 miners (40%), PA films were available from either 3 or 4 rounds. In review, only 69 of the 136 cases were thought to be true incident cases of PMF. The reviewer's interpretation of the 67 non-incident cases of PMF is summarized in Table I. Twenty-six of the cases were thought to have PMF on both films, and 11 were considered to be borderline (showing "ax"—coalescence of small opacities) but negative cases. Eighteen others were given other diagnoses for mass-like lesions on the chest x-ray. Most were considered granulomata, either multiple or calcified solitary nodules. In 10 of these 18 cases, the abnormality was in fact present on both films. It should be noted that in 6 cases, the program readings reported a regression in PMF in a later film. As the data in Table I suggests, there seemed to be better agreement between the reviewer and the NSCWP compared to the CWXSP.

In 69 film pairs, the later film was thought to show a new abnormality consistent with PMF. These decisions were made regardless of the background of simple CWP. The new lesions regarded as PMF (Table II) were unilateral in 35

Table I
Reviewer Interpretation of Non-Incident Cases of PMF*

Review Interpretation	NSCWP++	CWXSP+	TOTAL	
A. PMF on both films	2	24	26	(39%)
B. Not PMF				
1. Ax	3	8	11	(16%)
2. No apparent PMF lesions	0	12	12	(18%)
3. Other diagnosis likely				
a. Granuloma	0	12	12	(18%)
b. Other	1	5	6	(9%)
Total	6	61	67	(100%)
Total cases in Study	21	115	136	

* Values are numbers of films (%)
++ NSCWP = National Study of Coal Workers' Pneumoconiosis
\+ CWXSP = Coal Workers' X-Ray Surveillance Program

Table II
Descriptive Aspects of Incident PMF Cases
(n = 69)

Detail	Numbers of Cases	(%)
Category A	61	(88%)
Unilateral	35	(51%)
Mid or Lower Lung Zones	6	(9%)
Calcified	0	(0%)

cases, category A in 61 cases, and calcified in no case. Subsequent films were available in 13 cases, and of these 8 showed progression to a higher PMF stage, and 6 showed progression of simple pneumoconiosis.

The prevalence of category 0, 1, 2, and 3 simple pneumoconiosis in the earlier (non-PMF) films in the 69 cases was 14%, 43%, 33%, and 9%, respectively (Table III). Three of the category 0 films were classified as negative (category 0/0) and seven were classified 0/1. The distribution in category 1 was: 1/0—8 films; 1/1—12 films, and 1/2—10 films. The prevalence of category 0, 1, 2, and 3 simple pneumoconiosis for the PMF films was 1%, 43%, 38%, and 17%, respectively. The one category 1 film was classified as 0/1.

In 9 cases, there was a progression of simple pneumoconiosis between the non-PMF and PMF films of 3 to 6 minor profusion categories. In 6 of these, "r" type small opacities predominated.

In the 67 reviewed cases which were not thought to demonstrate attacks of PMF, there was a higher prevalence of category 0 simple pneumoconiosis. The prevalence of category 0, 1, 2, and 3 simple pneumoconiosis in the earlier films was 42%, 36%, 18%, and 4%, respectively. These values for the later films were 34%, 39%, 24%, and 3%.

The type (size and shape) of small opacity in the incident PMF cases is shown in Table IV. Rounded opacities predominated, and of those, the "r" lesions were most common, occurring as the primary opacity in 69% of the PMF films.

DISCUSSION

This study has reviewed a small group of presumed incident cases of PMF in coal miners, primarily to determine the background of simple CWP present on the PMF x-ray and on a film taken approximately 5 years earlier. With the aid of side-by-side reading and using a single reader, almost half of the cases were not thought to be true PMF incident cases. There are several possible explanations for these rather surprising results. Obviously the review interpretations could be incorrect, and because of the largely unblinded nature of the reading trial, this may indeed explain at least part of the discrepancy. However, the side-by-side technique should reduce reading errors caused by variable film technique and quality.[9] It seems likely therefore, that the results can also be explained in part by the variability in detecting PMF on single films among different readers at different times. Although intuitively one might consider the accurate detection of large opacities (PMF) to be easily achieved, other research indicates this is not the case.[6,10,11] In addition, in at least some cases the disagreement was not in detecting the (often obvious) large opacity *per se*, but rather in interpreting the large opacity as being "consistent with pneumoconiosis."[8] These findings have several practical implications regarding x-ray reading format that are being further evaluated.

The high prevalence of category 0 and 1 simple CWP on the 69 incident PMF x-rays, and on films taken approximately 5 years earlier (Table III), seems to corroborate recent British reports.[1,2] However, one must hasten to point out that none of the PMF cases have been confirmed pathologically. Thus other diagnoses including tumor and tuberculosis are possible. Especially in cases with no background of simple CWP, many would argue that ascribing a large opacity to PMF is going beyond the ILO General Instructions to record appearances that *might* be due to pneumoconiosis.[8] The NIOSH Study Syllabus, prepared by the American College of Radiology, for example, illustrates a lung mass as a carcinoma, stating, "Do not confuse this with a large opacity of pneumoconiosis. There is not a background of small opacities."[12] In 13 cases, the availability of subsequent films made the former alternative somewhat less likely however. On the other hand, the presence of a background of simple pneumoconiosis does not guarantee that a large lesion is PMF. Unfortunately,

Table III
Major Profusion Category of Simple Pneumoconiosis in Incident PMF Cases* (n = 69)

Major Profusion Category of Simple Pneumoconiosis	Earlier (non-PMF) Film	PMF Film
0	10 (14%)	1 (1%)
1	30 (43%)	30 (43%)
2	23 (33%)	26 (38%)
3	6 (9%)	12 (17%)
Total	69 (100%)	69 (100%)

* Values are numbers of films (%)

Table IV
Type (Size and Shape) of Small Opacities in Incident PMF Cases* (n = 69)

Type of Small Opacity	Earlier (non-PMF) film+ Predominant Opacity	Earlier (non-PMF) film+ Secondary Opacity	PMF Film Predominant Opacity	PMF Film Secondary Opacity
p	9 (14%)	3 (5%)	6 (9%)	5 (7%)
q	19 (29%)	24 (36%)	18 (20%)	25 (36%)
r	37 (56%)	36 (55%)	45 (65%)	35 (51%)
s		3 (5%)		1 (1%)
t	1 (1%)			3 (4%)
u				
Total	66 (100%)	66 (100%)	69 (100%)	69 (100%)

* Values are number of films (%).
\+ Three films were category 0/0.

especially when unilateral as occurred in 50% of cases in this study (Table II), the lesions of PMF are not very characteristic; Parkes has noted the variability of the presentation of PMF.[13]

To confirm a diagnosis of PMF with greater certainty, one would need clinical information including longitudinal radiological follow-up, and in many cases pathological specimens. However, the British data[1,5] is strengthened by the finding of increased attack rates of PMF with increasing simple pneumoconiosis category, starting with category 0. One would not expect mass lesions of other etiologies to follow such a pattern. Unfortunately, the data in this present study is too limited for such an analysis.

Another assumption that needs to be considered is that the small opacities on the chest x-ray represent pneumoconiosis, and specifically CWP. The rapid progression of these lesions in several cases, as well as the high prevalence of "r" opacities suggest that free silica may be the important etiological agent in at least a part of this population. Further evaluation to determine job titles and dust exposure data in this cohort in continuing. It seems safe to conclude however, based on the more "classic" cases of PMF developing on a background of category 2 or 3 simple pneumoconiosis, that strict dust control remains an important issue.

It must be emphasized, however, that this is a very restricted study population. The design also excluded 37 new PMF cases which occurred over non-consecutive rounds of the NSCWP or CWXSP. In addition, it is possible that miners who knew they already had the higher categories of simple pneumoconiosis may have acted differently than miners who knew they had either no or minimal disease. More of the former group, for example may have left the industry, or refused further x-rays for various reasons. Thus the cohort selection was biased towards rapidly developing PMF cases, and perhaps towards PMF cases in those with minimal pneumoconiosis 5 years previously. Furthermore, the prevalences of simple pneumoconiosis found here should not be considered representative of all miners developing PMF, because of the selection factors and study design features discussed above.

While interesting observations on film reading technique, medical surveillance, PMF in coal miners, and dust control can be made from this small study, one must emphasize the preliminary nature of the findings. Further research is clearly needed before conclusive answers will be available.

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EXPOSURE ESTIMATES FOR THE NATIONAL COAL STUDY: THE USE OF MSHA COMPLIANCE DATA FOR EPIDEMIOLOGIC RESEARCH

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INTRODUCTION

Quantitative estimates of exposure in epidemiology greatly improve a study's ability to detect low level effects, distinguish between competing effects of etiological agents and perhaps most importantly, establish exposure-response relationships that can serve as the basis for public health intervention. However, the usefulness of exposure estimates depends on their accuracy and precision. Systematic bias in exposure measures will result in biased estimates of the exposure response relationship while random errors in measurement or misclassification will bias the observed association toward the null.[1]

The usefulness of accurate exposure data has been exemplified by research on the health effects of respirable coal mine dust by the British Pneumoconiosis Field Research (PFR) started in 1952.[2] The PFR studies get much of their strength from the concurrent measurement of health status and coal dust exposure over many years. The studies have been able to define the separate effects of dust exposure and confounding exposures[3] and to quantitatively define exposure-response relationships.[4,5,6]

Until recently, detailed exposure-response studies have not been possible in the United States. With the advent of the Federal Coal Mine Health and Safety Act of 1969, the National Study of Coal Workers Pneumoconiosis (NSCWP) was initiated. The study was set up as a series of rounds of health data collection. Miners for the first round of the study were selected from a group of 31 mines. In the second and third rounds, miners from additional mines were added to the group. The cohort for the fourth round of the study, concluded this year, includes a subset of younger miners who participated in the first two rounds.

The usefulness of the NSCWP studies for defining the exposure response relationship has been limited. Dust exposure estimates for the NSCWP were originally intended to be made using measurements taken on each individual miner by the Mine Safety and Health Administration (MSHA) compliance program.[7] However, the first two rounds were unable to use this data because only a few years of exposure data had been collected at the time. Instead, these analyses relied on years worked or years underground as a surrogate for exposure.[8,9] The third round of the NSCWP made limited use of exposure data in the analysis of pulmonary function changes.[10]

The exposure data collected for the MSHA compliance monitoring program have produced one of the largest exposure data sets in existence. It now contains about 18 years worth of personal exposure monitoring from all U.S. underground coal mines. Used appropriately, these data may provide a very substantial basis for precise exposure estimates for the NSCWP.

The overall purpose of our study is to combine measurements of miners' lung function with existing historical measurements of exposure in order to develop a quantitative exposure-response relationship. The current report is limited to analysis of the exposure data. Descriptive analyses of the data will first be undertaken and potential sources of bias explored. An exposure matrix will be designed with mine, occupation and year as the three dimensions. The final estimates of the mean exposure level in each cell of the mine, occupation and year matrix will be made with a regression model. The mean exposures will then be merged with the work histories of the miners in the study cohort in order to estimate cumulative exposure for each participant. These cumulative exposures will then be used to estimate the exposure-response relationships for pulmonary function and radiographic indices.

COLLECTION OF EXPOSURE DATA

The exposure data comes from the MSHA coal mine health compliance program. The law enacted in 1969 requires coal mine operators to maintain respirable dust levels below specified levels. To ensure compliance with the standard, operators are required to periodically conduct air sampling and MSHA compliance inspectors visit each coal mine several times each year and collect additional samples.[11]

The protocols for air monitoring have changed over time. Operators were originally required to sample miners in highly exposed occupations, termed High Risk, or Designated Occupations, repeatedly and all other miners from two to four

times each year. In 1980 these requirements were altered to reduce the operators' sampling burden. Occupations with low expected exposures were dropped from the personal monitoring requirement and area samples were employed instead.

MSHA inspector sampling follows a similar pattern although the number of samples is much lower. Inspectors sample each of the Designated Occupations although they exercise discretion in deciding which other occupations or miners to sample.

All samples used here are full shift personal samples collected with a 10 mm nylon cyclone-filter assembly. Results are determined gravimetrically by MSHA. The specified sampling flow rate is 2 liters per minute and a correction factor is applied to the result to make it comparable to the British MRE sampler upon which the federal exposure standard is based. The data provide an internally consistent measure of respirable coal mine dust and are therefore appropriate for investigation of chronic respiratory effects.

DATA SET DESCRIPTION

The exposure data used for this study was collected by MSHA and files containing the data were obtained from two sources. NIOSH provided data tapes which contain all exposure data for underground coal mines from 1970–1979. There is a total of 3,226,602 samples contained in the NIOSH data set.

The data covering 1979–1987 was obtained from the Bureau of Mines (BOM). The BOM supplied data tapes of all underground coal mine samples for the years 1979–1987, totalling 1,519,892. A breakdown by year and sample source is given in Table I. Note that the number of operator generated samples is significantly reduced after 1980 when the revised sampling protocols were adopted.

The information contained in both data sets include (a) date of sample, (b) MSHA mine number, (c) occupation code (d) concentration, and (e) social security number, along with various information about the type of sample, type of mine, sampling time, etc.

POTENTIAL LIMITATIONS OF THE EXPOSURE DATA

Several potential problems with the use of the data for epidemiologic analysis may be identified. Although the overall number of samples is very large, about 4.7 million, they are not equally distributed between mines, occupations and years. Most samples are taken in the High Risk, or Designated Occupations. Thus, in many cells of the mine, year and occupation matrix, there is no data at all.

The fact that the exposure data is based on a regulatory compliance program suggests that the way in which the samples are taken may lead to bias. MSHA compliance sampling continues for up to five days, depending on the results of the earlier samples. These sampling rules may lead to more sampling of jobs with higher exposures. In addition, it has been suggested[12] that adjustments in the work process or engineering controls could be made which would reduce exposures on subsequent days of a compliance inspection. Thus, use of an average of all inspector data, without respect to the day it was taken, might lead to a biased estimate of exposure.

Table I

Number of Underground Coal Mine Dust Samples in Bureau of Mines Data Set 1979–1987

YEAR	OPERATOR	INSPECTOR	(%)	TOTAL
1979	417,912	23,546	(5.3)	441,458
1980	269,092	19,642	(6.8)	288,734
1981	56,862	29,845	(34.4)	86,707
1982	39,755	27,342	(40.8)	67,097
1983	118,692	26,523	(18.3)	145,215
1984	109,929	26,686	(19.5)	136,615
1985	98,927	26,882	(21.4)	125,809
1986	93,479	24,767	(21.0)	118,246
1987	85,886	24,125	(21.9)	110,011
Total	1,290,534	229,358	(15.1)	1,519,892

For non-Designated Occupations, both inspector and operator sampling may concentrate on particular jobs with a history of high exposure. Thus, the data is likely to be weighted toward high exposures.

It has also been suggested[13,14] that operator data deviates from the lognormal distribution which one would generally expect in exposure data. They show that operator data has a large number of low exposure samples, yielding lower mean exposure levels than inspector data.

METHODOLOGY

The overall analytic strategy is to (a) choose a sample of mines, (b) conduct descriptive analyses, (c) assess bias, (d) reduce the number of categories for analysis, (e) specify the best model for prediction of mean exposures and (f) calculate estimates of exposure.

First, a sample of mines will be chosen. All members of the round four cohort originally worked in one of 36 mines but most have also worked in other mines. Since the 36 mines constitute a substantial proportion of the total time spent in mining, it is reasonable to use these mines as a sample with which initial exploratory analyses and development of our final analytic strategy will be done. Using this model, the actual exposure estimation will then be done for all mines in the cohort members' occupational histories.

Second, descriptive analyses will include distributions of the number of data points and means within each mine, year and occupation category. The degree to which the data conforms to the expected lognormal distribution will then be assessed. In order to avoid analyzing the distribution as a combination of heterogeneous distributions, the data will first be log-transformed and then standardized (subtract mean, divide by standard deviation) within each three-way matrix cell. The data will then be analyzed as a single distribution, or stratified on pertinent categories such as occupation. The log-transformed data will be examined for skewness and kurtosis and histograms will be generated to visually assess normality.

Third, we will examine the issues of potential bias to determine the best use of the data. Since we do not have any standard by which to measure bias in different parts of the data, we must analyze the data internally, and use the information we have to select the most reliable data and estimate the magnitude of the potential bias.

Potential sources of bias will be examined to see if they make a substantial difference in the exposure estimates. For instance, the means of inspector versus operator samples will be compared and samples from the first day of a compliance inspection will be compared to subsequent days. If substantial differences are observed, we will consider adjusting the data to account for the bias. If adjustments are not possible, we will use the data which most closely reflect representative exposure conditions. The magnitude of the potential bias will be estimated and reported with the final results.

Fourth, we will explore reducing the number of cells in the mine, year, occupation matrix by examining the differences between mines and by attempting to collapse the number of occupational categories. These reductions will help both in simplifying the final analytic model adopted and by grouping data across similar categories in which data may be very sparse.

The difference between mines will be assessed first. If no substantial difference can be observed, we will remove the mine effect from the dimensions of the matrix. If differences do exist, the effect of individual mines or mine groups will necessarily be included in subsequent analyses.

Second, we will reduce the number of occupations from the 197 MSHA codes to a smaller number of homogeneous exposure categories. Means for each occupation will be calculated and rank ordered. Grouping of occupations will then be done to identify occupations with mean exposures within, for example, 0.2 mg/m^3. Analysis of variance will then be conducted within each group, controlling for mine and year, to assess the validity and effectiveness of the grouping.

Finally, after the potential biases are examined, the final most valid data is selected and the categories for analysis are defined, a regression model will be developed to estimate means and variances of exposure in a mine, exposure category and year matrix. This part of the analysis will be conducted on a larger data set incorporating all mines which appear in the work histories of the NSCWP cohort.

The analysis will be done in a two stage process. First the effect of year for each occupation group and mine will be estimated. Then these "offsets" can be used in the regression model to estimate the exposure category and mine effects. The model will generally be of the form:

$$C_i = a + \sum^{m} \beta_m k_{m\,i} + \sum^{x} \beta_x k_{x\,i} + Y_i + e_i$$

where C_i is the sample result, β_x and β_m are the estimated regression coefficients for each exposure category and mine, respectively, k_x and k_m are the dummy variable indicators for exposure category and mine respectively and Y_i are the offsets calculated for each year within individual mine and exposure categories. The parameter estimates will then be used to calculate the mean and standard deviation of exposure in each category of the matrix.

PRELIMINARY ANALYSIS OF TWO SAMPLE MINES

Two of the original NSCWP study mines were chosen for this preliminary analysis. Table II shows the number of samples in each of the two mines by source of collection. Only a small percentage of the overall data is collected by inspectors.

Table II

Number of Underground Coal Mine Dust Samples in Bureau of Mines Data Set 1979–1987

	INSPECTOR	(%)	OPERATOR	(%)	TOTAL
Mine 1	285	(2.1)	13,018	(97.9)	13,303
Mine 2	913	(4.1)	21,269	(95.9)	22,182
Total	1198	(3.5)	24,287	(96.5)	35,501

Figure 1 shows the number of samples collected in each mine by year. It is evident that the overall number of personal samples was greatly reduced after 1980.

Only some of the occupations have had substantial monitoring of exposure. Out of the 197 possible occupation codes, samples were actually taken in only 76 and 108 of the categories in the two mines, respectively. Thus, many of the occupation codes had no data in them at all although some of these occupations may not exist in these two mines.

Figure 2A and B shows an example of the exposure data distribution, in this case for all years in one mine and a single, highly monitored occupation, continuous miner operator. The untransformed data (Figure 2A) is highly skewed, while the log-transformed values (Figure 2B) are much closer to normal, with a skewness coefficient of −0.43. There appears to be an over representation of sample values of 0.1 mg/m^3. These low values occur mainly in the operator collected data and may represent some bias.

Finally, Figure 3 shows the arithmetic mean concentration of respirable dust based on both operator and inspector data for continuous miner operator in the two mines. Although there is a visually observed downward trend, the year to year variability in the means is also apparent.

CONCLUSION

The data collected by the MSHA coal mine compliance program forms a very substantial basis for relatively precise exposure estimates for the fourth and subsequent rounds of the NIOSH National Study of Coal Workers Pneumoconiosis. These estimates should greatly enhance the power of the NSCWP to detect any possible effects of the relatively low dust exposure levels present after enactment of the MSHA law. The estimates will also help establish the exposure-

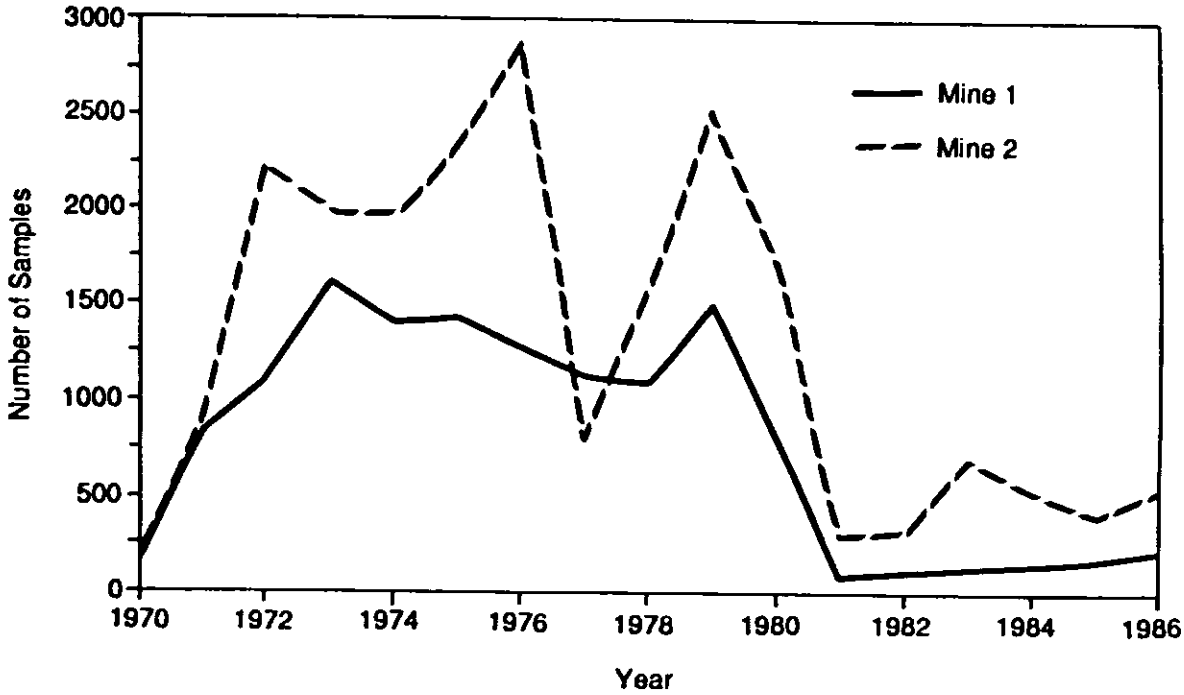

Figure 1. Number of samples by year for two selected mines.

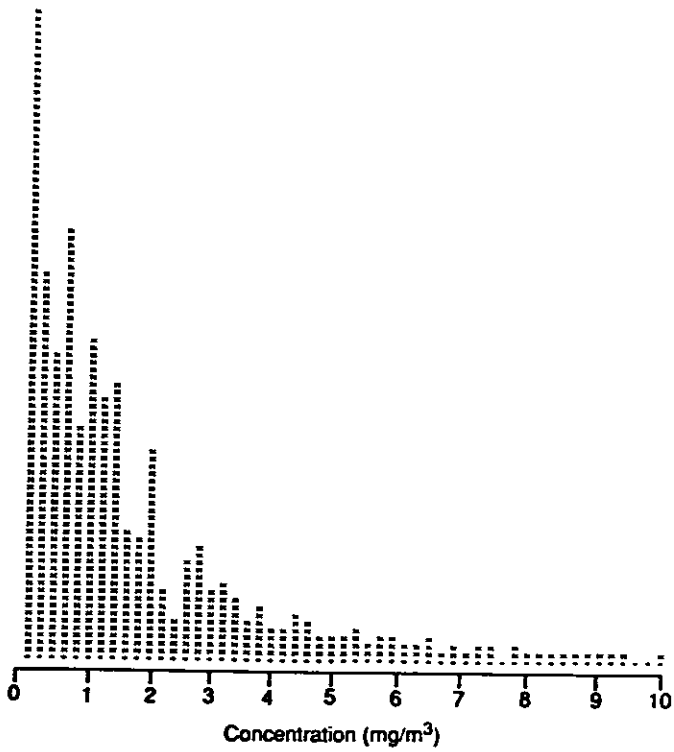

Figure 2A. Histogram of untransformed sample values for continuous miner operator, 1970–1986. (Arithmetic mean = 1.6 mg/m³, skewness = 1.8, kurtosis = 3.8.)

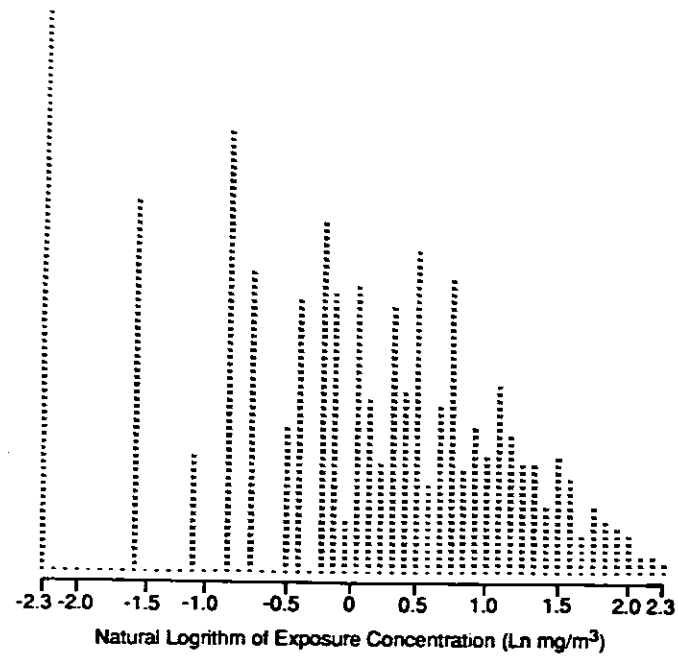

Figure 2B. Histogram of log transformed values for continuous miner operator, 1970–1986. (Geometric mean = 0.95, geometric standard deviation = 3.1, skewness = −0.43, kurtosis = −0.48.)

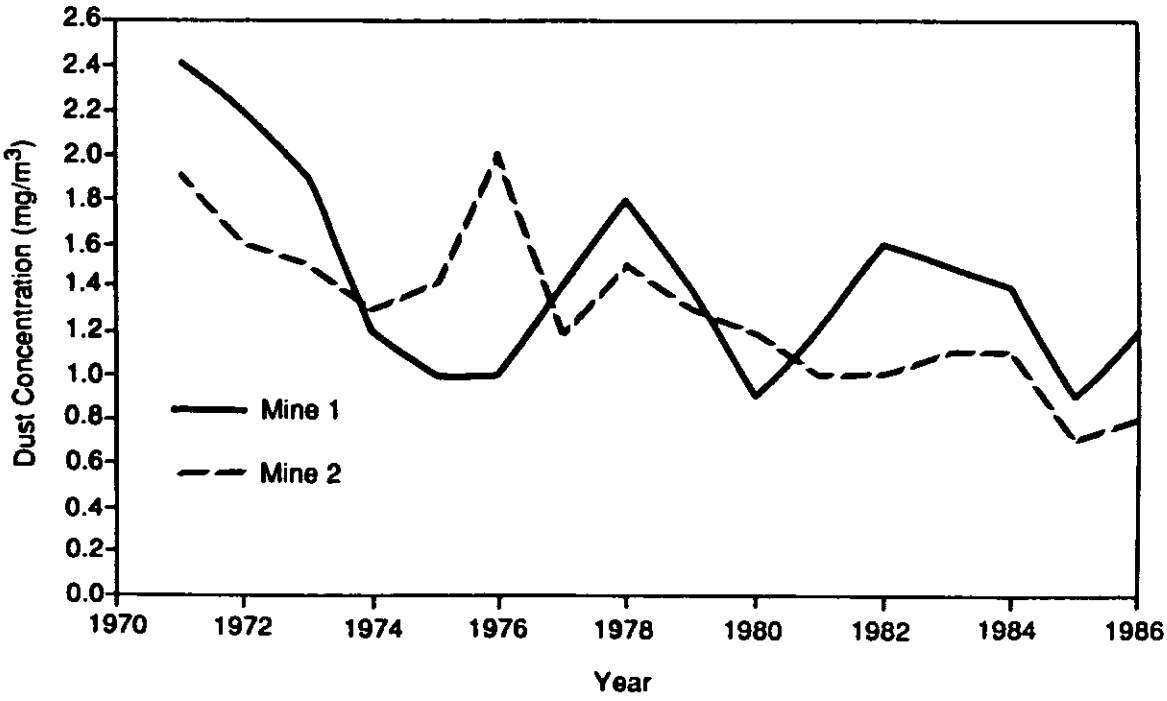

Figure 3. Arithmetic mean exposures by year for continuous miner operator in two selected mines.

response relationship and separate the effect of dust from other confounding exposures.

By grouping similar occupations into exposure categories, and by using regression modelling techniques, the problem of data sparseness will be substantially limited. Although there may be some bias in the data, the magnitude of the error is unlikely to greatly affect the observed exposure-response relationship.

In addition to enhancing the analysis of the current NSCWP studies, development of quantitative exposure estimates across the mining industry will also substantially help future research into various parameters of coal mine dust induced disease.

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PREVALENCES, INCIDENCE DENSITIES AND CUMULATIVE INCIDENCES OF PNEUMOCONIOTIC CHANGES FOR TWO GROUPS OF MINERS OF A MINE IN WESTERN GERMAN COAL MINING

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INTRODUCTION

There is a discussion in the Federal Republic of Germany that the average level of respirable dust in the underground coal mine atmosphere has to be reduced for minimizing the risk of coalworkers' pneumoconioses (CWP). Now it was offered a level of 2 mg/m^3, a value having been in force in the U.S. since December 1972.[1] To determine an adequate level, extensive studies according to the problem of CWP caused by respirable coal mine dust in dependence on various stratigraphic horizons have been started. This relation between coal rank and frequency of CWP—sometimes described as a geographical or "mine effect"—was often mentioned in the last twenty years.[11,14,18,19,20,21,22] In German research on pneumoconioses cytotoxicity of dust and the outcome of dust exposure on animals was extensively studied. The development of pneumoconiotic abnormalities in chest radiographs of miners has not been investigated to the same extent. Therefore it seems to be expedient to study the data collected by the physicians carrying out regular medical surveys of all miners in Germany to estimate the risk of developing pneumoconiotic abnormalities in chest radiographs in relation to time underground.

MATERIAL

The totality of miners who left the mine as workers in 1980 (group 1) or 1985 (group 2) took part in this longitudinal study. Group 1 and group 2 were pooled to form a third study group (group 3). The study avoids further selection bias since all miners who turned off were included in the investigation. Table I gives information on the study groups. The number of the retired gives workers in the whole study group (group 3) amounts to 952 persons. 548 miners left in 1980, 404 turned off in 1985.

Table I

Information on Study Groups: — group 1: all miners who retired as workers in 1980; group 2: all miners who retired as workers in 1985; group 3: group 1 and group 2 pooled

		Number of persons	Cumulative observation time / yr	Mean time of observation per person / yr	Number of chest radiographs	Mean number of chest radiographs per person
group 1	a	548	2767	5.1	2214	4.0
(1980)	b	115	2456	21.4	1092	9.5
group 2	a	404	4789	11.9	3047	7.5
(1985)	b	174	4561	26.2	2095	12.0
group 3	a	952	7556	7.9	5261	5.5
(1980;1985)	b	289	7017	24.3	3187	11.0

a: all miners
b: subset of miners who worked at least five years underground

The miners enter the study with the beginning of their time underground. Time of investigation ends with the last medical survey. In Table I cumulative observation time and mean time of observation per person by study group are presented. Observation time includes time underground and subsequent time on surface. In the whole study group (group 3) 41 miners were examined in medical surveys after they finished work underground. They contribute 403 years of observation time during their subsequent time on surface to the total cumulative observation time of 7556 years. 663 miners turned off with an individual time underground less than five years. Their contribution to total cumulative observation time of the whole study group amounts to 539 years. Therefore the average observation time per person who turned off with an individual time underground less than five years was just 0.81 years. The subgroup of miners who worked at least five years underground (group 3b) comprises 289 persons and covers 92.9% of the total cumulative observation time (group 3a). On average every miner of this subgroup is observed for 24.3 years.

As a whole 5261 full size posterior anterior chest radiographs comprising 5.5 radiographs on average per person are taken into account. 3187 radiographs are concerned with those working at least 5 years underground at an average value of 11.0 radiographs per person (Table I). First valuation of the radiographs took place during medical survey, a further one by a second physician ('side-by-side method'[1]) at sole knowledge of underground time, both according to ILO-classification of 1980,[10] supplemented by the 'supplying set of standard films to ILO 80 of Hauptverband der gewerblichen Berufgenossenschaften e.V.' Final valuation was determined by joint examination, partly with a third physician in case of disagreement. For seven cases the first radiograph was valued >0/0. These persons were kept in the study and the grading linearly interpolated. The results on hand show neither jumps nor regressions.

According to the stress-strain-model both parameters must be defined as precisely as possible. The strain part is exactly determined by a great number of double-examined radiographs with respect to categorization. Stress is partly described rather precisely in the references with information about dust quantity, concentration, influence and retention time. Further on exposure periods are referred to.[2,8,9,11] The data of this study do not give exact information on dust quantities (respirable dust concentration) and actual number of shifts. In the information of underground years these variables are implied, if not precisely defined.

The study was designed as a cohort study. In a classical design of a prospective study the study groups are defined as cohorts fixed in respect to calendar time or age.[6] This design was not practicable with regard to our data basis. The forming of a fixed cohort requires a survey of all employees of one or two years between 1950 and 1955 in order to answer the questions about the development of pneumoconioses. Complete data from this period were not available. Therefore the study groups were formed as dynamic cohorts in respect to calendar time and age.[12] Admissibility criterion was retirement in a fixed calendar year (1980 or 1985). No further selection was made. All retiring workers have had no symptoms and preliminary stress at the beginning of the study.

The two turning-off groups (1980/1985) are showing differences in regard to calendar time and age. Figure 1 informs about time at risk in dependence on age. Time is classified into intervals of two years according to the mean interval of medical survey. The curves do not only distinguish in the maximum but also in the distribution. The curves reflect the dynamic of the cohort in respect to age. In Figure 2 the time at risk is also displayed but in dependence on calendar time. The 'three elephants' show a break at the same time in 1973, the period of the 'oil crises' (additional employment). Here as well, the curves show the effect of the dynamic cohort in respect to calendar time. The differences between group 1 and group 2 are not examined in this study further on.

The study groups are transformed into cohorts fixed in respect to observation time.[12] The miners enter with the beginning of their work underground. In the main study terminus is the last medical survey until they finished mining underground.

Prevalences and incidence densities[15] of all categories of CWP are computed for each study group and for each two-year interval of time underground. Intervals are closed on the left side and open on the right. Confidence intervals for the prevalence proportions (binomial distribution) are determined.[5] The median (with upper 95% confidence limit[23]) and the 95th centile of coalworkers' simple pneumoconiotic (CWSP) are computed in relation to time underground. Calculation of cumulative observation time, candidate time,[15] and rates are done by PERSON-YEARS 1.2, a FORTRAN program for cohort study analysis.[4] For estimation of risk associated with varying time underground cumulative incidences are computed using the density method.[12] In most figures time underground is limited to a period of 0 to 32 years to present reliable data only.

RESULTS

Prevalence of CWSP

Figure 3 shows the relation between prevalence proportions of category 0/1 or more, 1/0 or more and 1/1 or more CWSP and time underground for the whole study group (group 3). In the interval of 28 to 30 years underground the prevalence of CWSP $\geq$ 1/1 is 15.5%. The 95% confidence interval for this value spans from 9.7% to 22.7% and is based on the data of 129 persons. The curves are ranked systematically with abnormality level and increase progressively with time underground ignoring smaller fluctuations.

Figure 4 shows the median with its upper 95% confidence limit and the 95th centile of CWSP (prevalent cases) for the whole group (study group 3) in relation to time underground. The median is 0/0 for the whole time period presented and never statistically different from 0/0 on the 5% level during the total time of observation. The upper confidence limit of the median is 0/0 for the period from 0 to 30 years underground. In the last presented interval from 30 to 32 years underground the upper confidence limit reaches 0/1. The 95th centile of CWSP is 0/0 in the period from 0 to 14 years underground and changes profusion category after that point every 3.5 years on the average. The .95 fractile reaches profusion category 2/1 in the interval from 28 to 30 years underground.

Incidence of CWSP

Cumulative observation time and candidate time for profusion categories of CWSP in relation to time underground are presented in Figure 5. The curves refer to all miners in the whole group (study group 3) who worked underground for at least 5 years. Therefore the curves are censored at the left. The ommitted values are: 1020 years (673 years) of cumulative observation time in the interval from 0 to 2 years (2 to 4 years) underground. The top curve shows the decline of cumulative observation time due to loss of cases in respect to time underground. The lower curves (top down) represent candidate time for profusion category 1/1, 1/0 and 0/1 of CWSP respectively. The curves rank inverse with abnormality level. The top curve showing cumulative observation time is equivalent to the curve of candidate time for profusion category 3/+ because no incidence of 3/+ happened during time underground. Candidate time as proportion of cumulative observation time decreases monotonously for the three presented categories of CWSP in the interval from 0 to 32 years underground. Moreover the decline of relative candidate time is ranked with category of CWSP.

Figure 6 presents the incidence density (number of incident cases per 100,000 years of candidate time) of CWSP category 0/1, 1/0, 1/1 and 2/2 respectively related to time underground. The data concern the whole group (study group 3). Although there is a lot of fluctuation increasing trends of incidence densities of CWSP are shown generally. The rate of profusion category 2/2 amounts to 500/(100,000 years) after about 30 years mining underground.

For assessment of risk cumulative incidences are given in Figure 7 for the whole group (study group 3). The risk of developing category 0/1, 1/0, 1/1, or 2/2 (starting category 0/0) increases with time underground. Moreover the incline of the curves is increasing with time underground in general. The curves rank clearly with CWSP category. The risk of developing category 2/2 after 28 to 30 years working underground amounts to 2.7%. The cumulative incidence of CWSP category 1/1 is 16.6% for the interval from 28 to 30 years underground. The prevalence proportion of category $\geq$ 1/1 for the same interval of time underground was found to be 15.5% (95% confidence interval spans from 9.6% to 22.7%). Similar relations between cumulative incidences and corresponding prevalences were determined for other categories of CWSP. Therefore the estimation of risk given by the cumulative incidences seem to be reliable.

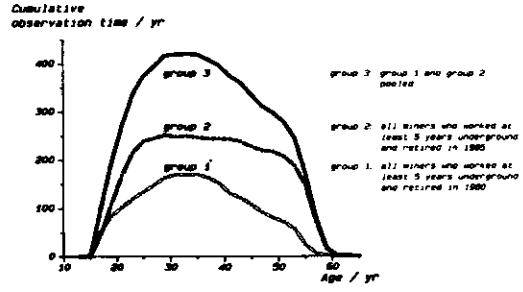

Figure 1. Cumulative observation time by two-year intervals of age.

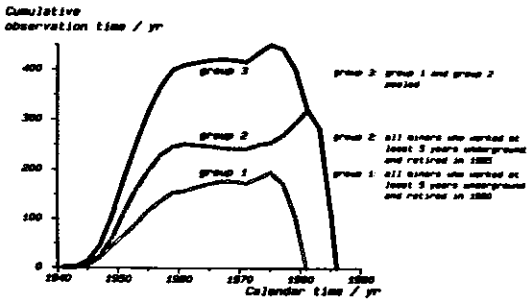

Figure 2. Cumulative observation time by two-year intervals of calendar time.

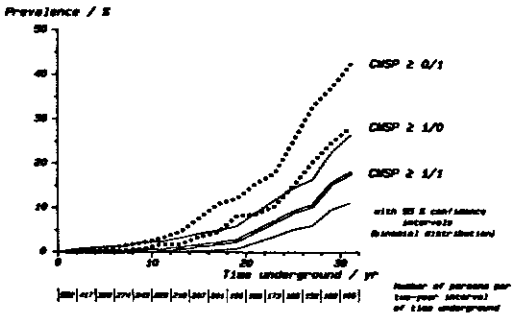

Figure 3. Prevalence proportion of CWSP (profusion) in two pooled groups of miners (all miners who retired as workers in 1980 or 1985) by two-year intervals of time underground.

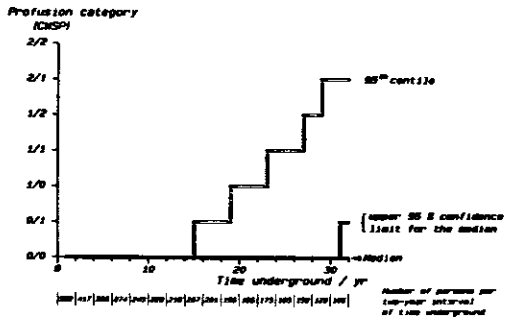

Figure 4. Median with upper 95% confidence limit and 95th centile of CWSP (profusion) in two pooled groups of miners (all miners who left the mine as workers in 1980 or 1985) by two-year intervals of time underground.

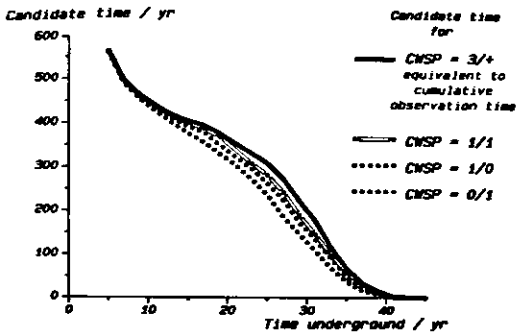

Figure 5. Cumulative observation time and candidate time for CWSP (profusion) in two pooled groups of miners (all miners who retired as workers in 1980 or 1985) by two-year intervals of time underground.

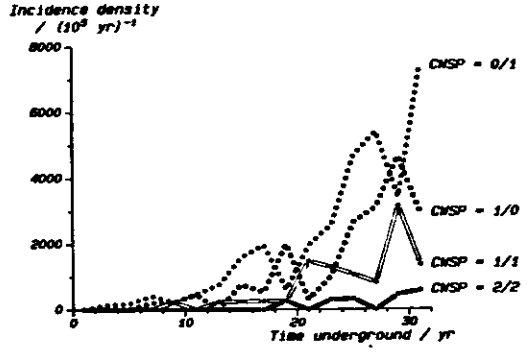

Figure 6. Incidence density of CWSP (profusion) in two pooled groups of miners (all miners who retired as workers in 1980 or 1985) by two-year intervals of time underground.

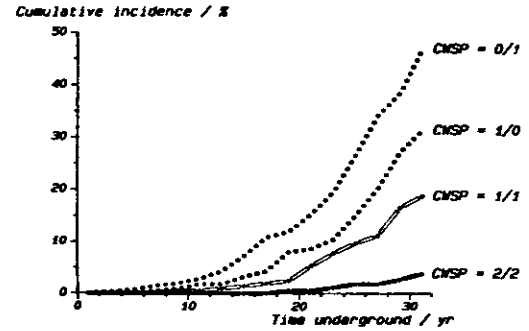

Figure 7. Cumulative incidence of CWSP (profusion) in two pooled groups of miners (all miners who left the mine as workers in 1980 or 1985) by two-year intervals of time underground.

DISCUSSION

Prevalence of CWSP

The prevalence proportions found in our study agree with results given in reports of British and American studies in general. Hurley et al.[9] found a prevalence for category ≥ 2/1 CWSP of 1.2% (1.3% respectively) in an investigation of 465 (456) British miners who worked 25 (30) years underground. From the study's data corresponding prevalences of 1.8% (5.4%) are yielded. For a comparison of the results it is necessary to take into account that the selection procedure used in sampling the British study group "may have led to a preferential inclusion of healthier man."[9] Attfield et al.[1] determined a prevalence proportion of 3.0% (1.4%) for category CWSP ≥ 1/1 (CWSP ≥ 2/1 respectively) after about 20 years underground in an investigation of a not systematically sampled group of 1252 U.S. miners.

Recent German studies on prevalence of CWP performed by Ulmer et al.[7,24,25,26,27,30] presented results not corresponding to those of this study. Ulmer et al. described the development of CWP in terms of "averaged categories" in relation to age taken as an indirect measure of time underground. They reported an "averaged category" of 1/2 or 2/1 CWSP after about 30 years mining underground. The median of CWSP in this study is 0/0 after 30 years underground and is significantly less than 0/1. Whether these differences may be due to selection bias or e.g., "mine effects" is still under discussion. Ophoff[17] in a study based on 218 selected German miners re-

ported an "averaged category" of about 0/1 after 20 years underground. Reisner et al.[18,19,21] also performed several studies more than ten years ago. The authors[18] presented a prevalence of about 9% for CWSP ≥ 2/1 after 20 years underground. It is, however, very difficult to compare these results with the findings of this study, because the chest radiographs were not classified according to the ILO-standard, while Reisner et al. tried to overcome this problem by a translation from the former classification into ILO-standards, a procedure which leaves a lot of uncertainty.

Incidence of CWP

The risk of British coal miners to develop CWSP was described by Jacobsen et al.[9,11,28] The given estimates of risk vary substantially due to a "mine effect." For a mean dust concentration between 2.5 and 4.5 mg/m^3 the average risk of developing CWSP ≥ 0/1 in ten years working underground was found to be in the range of 2 to 10%. Attfield et al.[1] studied U.S. coal miners. An estimate of risk of developing category 0/1 or more in about ten years of 1.9% was found here. The mean dust concentration was reported as 2.5 mg/m^3 or less. Our assessment of risk by cumulative incidences agree with the findings in this study. For the whole study group (group 3) a cumulative incidence for developing category 0/1 after 10 years underground of 1.9% was computed.

Reisner et al.[18] calculated estimates of risk of developing CWSP ≥ 1/0 ("translated" category, cf. 3.1) in 35 years underground of 5 to 50%. The variation is due to a "mine effect." The corresponding cumulative incidence found in our study is 27% (group 3).

In our study we observed just one case of progressive massive fibrosis (PMF): one miner developed a large opacity of type A during time underground. Large opacities of type B or C did not occur. The one incident case corresponds to an incidence density of 14/(100,000 a). Hurley et al.[8] described a mean rate of PMF in British miners of 180/(100,000 a). The rate was 0 in one mine.

Implications

This study shows that the study design chosen produced valid results comparable to those of other authors. The portion of miners working more than 30 years underground is too small to estimate exact risk of development of CWP yet. Therefore a study is planned about all miners having worked more than 20 years underground selected from the totality of miners who turned off in 1973, 1974, 1975, 1976, 1977, 1980, and 1985. Moreover, calendar time will be taken into account as a covariable. In the future, analysis will be extended to the development of shape-size. Later the aspect of stress shall be determined more precisely to estimate the risk in relation to the respirable dust concentration in order to attribute to the discussion on dust level. We hope to estimate the risk of CWP by using this method more adequately and by this help to minimize that risk in the future.

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THE PREVALENCE OF COAL WORKERS' PNEUMOCONIOSIS IN A NEW COAL FIELD IN LUBLIN/POLAND

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ABSTRACT

In cooperation between Lublin/Poland and Bochum/FRG, 1130 coal miners were examined by X-rays and a complete lung function investigation including challenge test. The prevalences of X-ray changes and of lung function disturbances are in the same order in both centres. Smoking habits of miners have a clear influence on lung function. X-ray changes show in Lublin, too, a linear relationship between ILO-classification and exposure time.

No Paper provided.

AN ANALYSIS OF THE EFFECTS OF SMOKING AND OCCUPATIONAL EXPOSURE ON SPIROMETRY AND ARTERIAL BLOOD GASES IN BITUMINOUS COAL MINERS IN SOUTHERN WEST VIRGINIA

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INTRODUCTION

In evaluating the presence of pulmonary disability in coal miners, the Federal Black Lung Program utilizes primarily spirometry and arterial blood gas analysis for objective assessment of the degree of pulmonary insufficiency in a given individual. Emphasis is placed upon the measurement of the forced expiratory volume in one second (FEV_1) to assess the degree of bronchial obstruction and the arterial oxygen tension at rest and during exercise to assess the efficiency of alveolar gas exchange. Presently utilized disability standards for the FEV_1 and the arterial oxygen tension in the Federal Black Lung Program were established and promulgated in 1980.[1]

The effects of the inhalation of coal mine dust on lung function, particularly the oxygenating function, have been controversial. In fact, the need for arterial blood gas measurements in determining the presence of pulmonary disability in the coal mining population has been questioned in a recent study.[2] Because our experience with the results of pulmonary function tests and arterial blood gas studies performed both at rest and during exercise indicated the importance of arterial blood gas measurements in the disability evaluation of coal miners, a formal analysis of data we had collected over the past few years was undertaken. The results of that analysis constitute the basis of this report.

METHODS

Both spirometry and arterial blood gas studies were obtained on a cohort of 2725 active miners or ex-miners who were evaluated for disability. With few exceptions the men studied were or had been actively employed as miners in the bituminous coal mines in southern West Virginia. Data collected on each applicant included age, height, weight, smoking history and the number of years employed in mining. For the purpose of this analysis, only the years spent in underground mining were utilized. A minimum of three forced vital capacity tracings were obtained on each subject utilizing a Stead-Wells spirometer. The FEV_1 measurements were obtained from the forced vital capacity tracings. At least two of the FEV_1 values had to agree within 5% for the study to be acceptable. The largest FEV_1 was reported. For the arterial blood gas study an arterial catheter was inserted usually in the radial artery, occasionally in the brachial artery. Following insertion of the arterial line the subject was permitted to rest in the sitting position for 15 to 20 minutes before a sample of arterial blood was drawn and analyzed immediately for oxygen tension, carbon dioxide tension and pH. Each subject was then exercised on a treadmill for a period of 6 minutes to ensure the achievement of a steady state. The intensity of exercise was increased in incremental steps until the subject was either too fatigued to continue or an oxygen consumption of about 25cc/Kg/minute was achieved which is the oxygen consumption observed in men undergoing moderately heavy manual labor. Subjects were provided rest periods of approximately 30 minutes between incremental increases in exercise. Expired gas was collected to permit the calculation of oxygen consumption and arterial blood samples were obtained during the sixth minute of exercise and analyzed immediately. In the earliest studies the arterial blood samples were analyzed in one blood gas analyzer. In subsequent studies which represented the majority, each arterial sample was analyzed simultaneously in either two or three different blood gas analyzers. All of the blood gas analyzers were calibrated immediately before and after each sample was analyzed. Agreement within 3 mm Hg was required for arterial oxygen tension values and within 2 mm Hg for arterial carbon dioxide tension values for the measurements to be acceptable. The average values for the blood gas tensions so measured was reported. The disability standard for the FEV_1 was 60% of the age, sex and height corrected predicted normal value. For the arterial oxygen tension the disability standard was 60 mm Hg at normal carbon dioxide tension or the oxygen tension adjusted for decreasing carbon dioxide tension.

RESULTS

Table I indicates that 732 or about 27% of the cohort of 2725 met the presently utilized disability standards of the Federal Black Lung Program. Slightly less than 5% were disabled by the FEV_1 standard alone while almost 18% were disabled by the arterial blood gas standard. Mean age, mean number of pack years of cigarette smoking and mean number of years of underground mining were similar in the four groups analyzed.

All of the subjects disabled by arterial blood gas criteria alone had FEV_1 values above 60% of the predicted normal. Considering any FEV_1 value equal to or above 80% of predicted normal to be in the normal range, values in the 60–79% range then indicate mild bronchial obstruction. Table II indicates that two-thirds of those disabled by the arterial blood gas standard alone had FEV_1 values within the normal range, indicating the absence of physiologically significant bronchial obstruction.

Table III indicates that about 14% of the subjects who had never smoked met disability standards. The majority of those who met disability standards were disabled as the result of arterial blood gas abnormality. Almost 26% of ex-smokers met disability/standards, the majority on the basis of arterial blood gases alone. Approximately 34% of the subjects who were smokers at the time of the study met disability standards. As in the case of the never smokers and ex-smokers, the majority of smokers met disability standards as the result of arterial blood gas abnormality.

If we combine ex-smokers and smokers into a single group of those who were actively exposed to cigarette smoke, the percentage of those disabled is about 30%. This figure is approximately twice the percentage of disabled who had never smoked.

Table IV indicates a direct relationship between the percentage of those disabled by arterial blood gas alone and the number of years spent underground. On the other hand note

Table I

Frequency of Disability by Mean Age, Mean Years Underground, Mean Years of Smoking and Type of Pulmonary Insufficiency

	Disabled			Non-Disabled
	Spirometry Only	ABG Only	Both	
Number of Subjects	128 (4.7%)	486 (17.8%)	118 (4.3%)	1993 (73.1%)
Mean Age	53.4	54.4	55.1	52.2
Mean Years Underground	23.4	27.2	24.5	23.8
Mean Pack Years	21.4	23.5	25.2	19.3

Table II

FEV_1 in Those Disabled by ABG Criteria Only

Percentage of Observed FEV_1 to Predicted	Disabled	Non-Disbled
60-79%	160 (32.9%)	399 (20.0%)
≥ 80%	326 (67.1%)	1594 (80.0%)
Total	486	1993

Table III

Frequency of Disability by Smoking Status and Type of Pulmonary Insufficiency

	Disabled			Non-Disabled	Total
	Spirometry Only	ABG Only	Both		
Never Smokers	21	66	7	564	658
Ex-Smokers	41	141	38	627	847
Smokers	66	279	73	802	1220
Total	128	486	118	1993	2725

Table IV

Frequency of Disability by Duration of Underground Mining and Type of Pulmonary Insufficiency

	Disabled			Non-Disabled	Total
Years Underground	Spirometry Only	ABG Only	Both		
1-9	18 (7.3%)	28 (11.3%)	15 (6.1%)	186 (75.3%)	247
10-19	32 (4.6%)	89 (12.7%)	20 (2.8%)	557 (79.8%)	698
20-30	37 (4%)	168 (18%)	43 (5%)	665 (73%)	913
31+	41 (5%)	201 (23%)	40 (5%)	585 (67%)	867
Total	128 (4.7%)	486 (17.8%)	118 (4.3%)	1993 (73.1%)	2725

the relative constancy of the percentage of those disabled by spirometry alone despite the increasing number of years spent underground.

Using the height-weight ratio as an indicator of the presence of obesity, the data did not reveal an increase in prevalance of obese subjects meeting disability standards by arterial blood gas criteria. In fact the data suggest that those individuals with disabling arterial blood gas values tended to be leaner than those without disabling values. Also of interest is the fact that slightly more than one-fourth of the 604 subjects who met arterial blood gas disability standards did so at rest only. The remainder of the 604 subjects met arterial blood gas disability standards at rest and exercise or during exercise only. These two latter observations will be presented and discussed in a subsequent publication.

DISCUSSION

There is general agreement that the inhalation of coal mine dust in susceptible individuals produces a disease process which has its origins in the small airways[3] and produces the characteristic pathologic lesion known as the coal macule.[4] In a relatively small percentage of those afflicted the disease process goes on to progressive massive fibrosis which may distort the lung airways. Since the 80–90% of the total airway resistance in man resides in the large airways and since the FEV_1 is determined primarily by an increase in airflow resistance in the large airways, it is not surprising that a disease process affecting primarily the small airways will not usually produce a significant decrease in the FEV_1 in the majority of those affected. Thus the fact that about 3% of those subjects who never smoked were disabled by spirometry alone is not an unexpected finding. It is also interesting to note that only slightly in excess of 5% of those who smoked were disabled by spirometry alone. Published studies document separate effects of cigarette smoking and the inhalation of coal mine dust on decrements in FEV_1.[5,6,7]

On the other hand recent studies have demonstrated the fact that in coal miners abnormalities of alveolar gas exchange consisting of an increased alveolar-arterial gradient for oxygen as well as decreases in arterial oxygen tension occur both at rest as well as during exercise without significant decrement in the pulmonary diffusing capacity.[8] Using radioactive isotopes and sophisticated computer technology Susskind and his group have demonstrated the presence of regional uneven distribution of alveolar ventilation to pulmonary capillary blood flow in nonsmoking bituminous coal miners sufficient to explain an observed increase in alveolar-arterial oxygen gradient and decrease in oxygen tension. In that study 19 of the 20 coal miners studied had impaired gas exchange for oxygen while only 4 of the cohort had minimal airway obstruction.[9] Thus the explanation for impaired gas exchange appears to reside primarily in the presence of uneven alveolar ventilation-pulmonary capillary blood flow relationships which is the most common cause of arterial desaturation in diseases diffusely affecting the small airways.

It must be noted that our data were obtained on miners and ex-miners who were applying for disability and thus represent a cohort of subjects of poor pulmonary health. Our data are not representative of the universe of coal miners. Yet it is instructive to note the similarity of findings in Schiffman's analysis of anthracite miners in Pennsylvania who had applied for disability benefits.[10] Furthermore, studies in asymptomatic coal miners have demonstrated impairment in alveolar gas exchange for oxygen, both at rest and during exercise, though quantitatively less marked than those noted in our study.[8,11,12]

CONCLUSIONS

1. The inhalation of coal mine dust produces significant effects on lung function and arterial blood gases in the absence of cigarette smoking.
2. The major functional pulmonary problem produced by the inhalation of coal mine dust appears to be impairment of the oxygenating function of the lung. Published studies suggest that this problem is caused by an increase in regional inhomogeneity of the alveolar ventilation pulmonary capillary blood flow relationships with resultant increase in the size of the physiologic shunt which causes a decrease in arterial oxygen tension.
3. Of lesser frequency, but nonetheless present, was a significant increase in the airway resistance as measured by a decrease in the FEV_1 as the result of the inhalation of coal mine dust.
4. The use of arterial blood gas studies is a justified and important component of disability evaluation among many of those applying for benefits under the Federal Black Lung Program.

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THE FOURTH ROUND OF THE NATIONAL STUDY OF COALWORKERS' PNEUMOCONIOSIS: A PRELIMINARY ANALYSIS

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INTRODUCTION

The year 1969 was a landmark time for underground coal miners in the United States, for it was in that year that the Federal Coal Mine Health and Safety Act was passed.[1] This enacted three provisions of benefit to miners: a low dust exposure limit; an x-ray surveillance and job transfer program; and a requirement that research be carried out on the health of coal miners, on dust reduction techniques, and on safety in mines.

Of these three provisions, that involving research activities into the health of miners was satisfied through the creation of a research project known as 'The National Coal Study' (now known as the National Study of Coalworkers' Pneumoconiosis (NSCWP)), currently administered by the National Institute for Occupational Safety and Health.

This project was begun in August 1969 with medical surveys at 31 nationally distributed mines. The mines were chosen to represent different coal seams and mining methods. Other criteria for selection were a working force of at least 100 miners, expected continued coal production for at least another 10 years, and preferably some earlier dust measurements. Of the 31 mines, 17 had been environmentally sampled in a study by the Bureau of Mines.[2,3]

The medical surveys were undertaken through use of mobile examination units which went from mine to mine. At each mine the complete workforce was examined by being given a postero-anterior and lateral chest x-ray, by undertaking spirometry, and by answering questions on chest symptoms using a slightly modified version of the British Medical Research Council's symptoms questionnaire.[4] In addition, working and smoking histories were ascertained, and demographic information and height and weight determined. The participation rate at this initial round of surveys (Round 1) was excellent, at 91%.

Two further rounds of surveys were completed subsequent to Round 1. The second round began about three years after Round 1, the methods being virtually the same. Owing to the closure of mines in the period between these rounds, and in order to improve representation, nine additional mines were brought into the study for this round. Round 3 began in 1977, the procedures being again virtually identical to those of the previous two rounds.

Figure 1 shows some information graphically on the timing of the surveys. It also shows the permitted exposure limits in force during this time, and the general trend in dust levels based on the survey reported by Jacobson,[3] and from data collected by the Mine Safety and Health Administration.[5]

The data collected in the three completed rounds have led to the publication of many findings and results on lung disease in U.S. coal miners. It has been shown that CWP prevalence follows a trend with the rank of coal, with tenure in mining, and with job.[6] In addition, indices of lung function and chest symptoms have been shown to be correlated with job and with tenure underground.[7,8] More recently results have been published on longitudinal change in ventilatory function,[9] and on incidence and progression of CWP.[10] Many other reports have been published.

The remainder of this paper is concerned with the rationale for the fourth round, and a description of its design and methods. This is followed by a description of the status of the selected cohort and an examination of selection bias.

NEED FOR A FOURTH ROUND

A further round of examinations in the NSCWP was deemed necessary for the following reasons:

1. The period of follow-up between rounds 1 and 3 was too short for proper evaluation of the effectiveness of the dust control limit set by the 1969 Act.
2. Participation in Rounds 2 and 3 at 75% and 52% was much lower than the 91% attained at Round 1, leading to uncertainty in the later findings.
3. Rounds 1–3 were concerned only with miners employed at time of examination. The omission of ex-miners may have led to bias in the reported results.

STRATEGY FOR THE FOURTH ROUND

Continuation of the NSCWP along the lines of the previous three rounds was thought inadvisable for these reasons:

a. Mine based surveys were starting to prove inadequate as a mechanism for follow-up of miners. The closure of mines and the movement of miners between mines and to other jobs meant that members of the study examined in the early rounds were no longer at the same mines, and therefore being lost to the study.

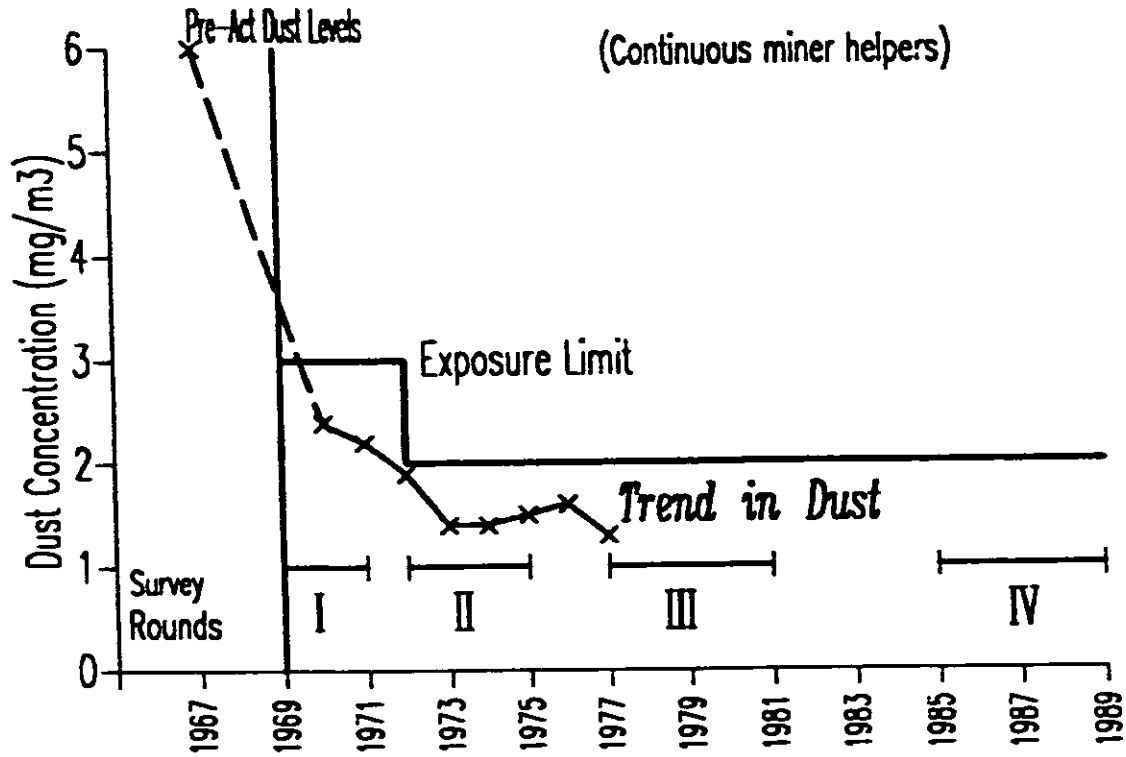

Figure 1. Dust limits, dust exposure trends, and NSCWP surveys, 1967–89.

b. Mine based surveys were inappropriate for examination of ex-miners.
c. Experience during the third round had shown that the lack of interest in the study by miners was exacerbated by mine based medical surveys.
d. Most importantly, the aims of the NSCWP had evolved from research into the relationship between dust characteristics and indices of respiratory health into an evaluation of the effectiveness of the 2 mg/m^3 dust standard. This change in emphasis called for a change in the nature of the design of the study.

For the above reasons it was decided that the fourth round would not be based on mine visits but would rather center around the location and examination of a cohort defined by initial attendance at either Round 1 or Round 2. The intent of this exercise was to measure changes in health over the intervening period. These changes could then be compared to those expected to occur under 2 mg/m^3 based on current knowledge on dust exposure and disease.

FOURTH ROUND PLANNING

The fourth round follow-up cohort was formed from two subsets of miners who attended either Round 1 or Round 2 initially. The selection criterion that miners had to be young enough at these rounds for them to have been able to work a further 15 or so years up to the fourth Round was imposed. This led to 3719 miners remaining out of the 9081 Round 1 miners and 3677 out of the 9343 Round 2 miners, making a total of 7396 miners for follow-up.

Without the age criterion the cohort would have consisted of mainly older coal miners, most of whom would have retired before the 4th round. As this investigation was intended to be a study of those potentially able to work the inter-survey period between the first two rounds and round 4. those older than 45 at Round 1, and 48 at Round 2 were excluded from the cohort.

Figure 2 shows the geographical distribution of the cohort of interest. This, of course, follows the distribution of mines originally selected for the study, which itself reflected the general pattern of employment in the various coal fields.

Table I shows some basic statistics on the cohort by round (see Appendix for brief details of the data and methods). The miners of Round 2 were slightly younger and less experienced because many of them had just started work as a result of the hiring boom that took place in coal mining in the early 1970s. In other respects the groups were very similar.

DATA COLLECTION METHODS

Two methods of data collection were used. In cases where it was established that a sufficiently large cluster of the cohort miners were working at a particular mine, a survey was held at that mine. Three such mine surveys were held, the number being few because most of the study mines had been shut down or were inactive during the data collection period.

In order to improve participation NIOSH staff spent extensive amounts of time talking to the miners at those mines.

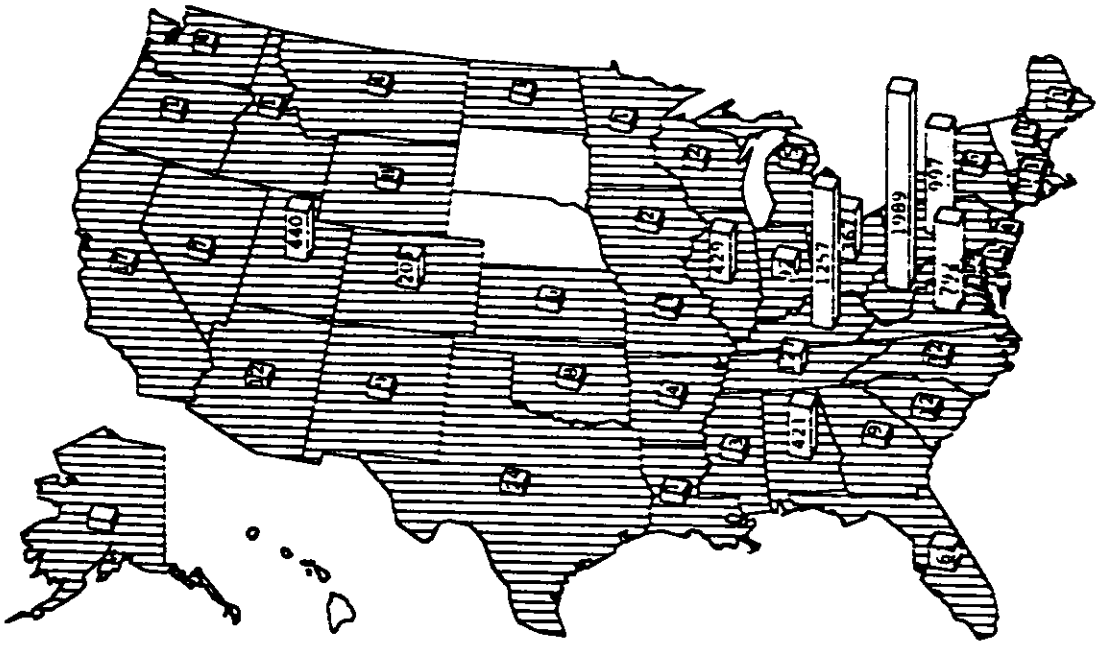

Figure 2. Geographic location of miners.

Table I
Details of Selected Cohort: Information from Round 1 and 2

	Round 1	Round 2
Number	3719	3677
Age (yr)	33	30
Tenure UG (yr)	7	5
% Smokers	61	59
% Obstructed	20	19
% CWP Cat 1+	5	2
% CWP Cat 2+	1	0
% Cough	22	19
% Dyspnea	9	13

Notes: all percentages rounded for simplicity of presentation. Zero percentages may actually be less than 0.5%.

In addition, participation was encouraged by the presentation of special stickers, ball hats, and belt buckles.

The remainder of the data collection was undertaken using so-called 'community surveys.' In these, suitable geographical clusters of the cohort were identified and examined, the mobile testing unit being set up at a convenient location, often a hospital, clinic, union building or shopping mall.

Twenty community surveys have been completed to date. The procedure at each was similar and was as follows. Current information on addresses was obtained from the Internal Revenue Service. These addresses were then examined and suitable clusters identified. Such clusters had to include a reasonable number of miners (150–350) yet not be too extensive (a radius of about 30 miles or less).

Once an area was identified and defined, a suitable location for the mobile examination unit was found. Attention then turned to locating a person who would make telephone contact with the miners and arrange appointments. Meetings were also held with local union officials and others to inform them of the study and to enlist their support.

After a suitable location was established notification letters were sent to all miners. These included a letter of support from the head office of the United Mine Workers of America

(UMWA) and usually another from the local UMWA District President. Once the letters had been sent the telephone person began calling the miners and setting up appointments.

Contact with miners was difficult in many cases owing to unlisted telephone numbers and lack of telephones. Letters were sent where telephone contact proved impossible although the reply rate was low. Whenever possible personal contact was made by visits to the house by the telephone person or by members of the examination team at the time of survey.

Out of the 7396 cohort members, 4712 were selected for examination in the three mine and twenty community surveys held to date. Additional community surveys are planned in order to complete data collection, although it is not expected that all of the cohort will be selected for examination as many are located too remotely or too sparsely to justify a survey in their area. The completed surveys have been held throughout all but one of the states in which the original mines were located, and as a result the 4712 selected miners are distributed by state in roughly the same proportion to the cohort state distribution (Figure 3).

STATUS OF SELECTED SAMPLE

Figure 4 shows the breakdown of the 4712 selected cohort members according to status at time of examination (final status). The groups are denoted as follows: 1. Examined; 2. No contact; 3. Moved; 4. Refused; 5. No-shows (had appointments but did not attend); 6. Deceased; 7. Valid reasons for non-attendance; and 8. Probable excuse.

The no contact group consisted of those with whom telephone contact was not made, and who did not return letters. In many cases the person could not be reached when a personal visit was made also. Such people may have left the area, become reclusive, been out of the area or worked away from home, or may have died; certainly, exact determination of the reason was impossible. The crude participation rate was 60%, while if those who had died, moved or had valid reasons for non-attendance were excluded, the rate rose to 68%. If the no contacts are also excluded the rate was 74%.

STUDY OF PARTICIPATION BIAS USING EARLIER DATA

Since there is the potential for bias, in that the healthy may choose to be tested while the unfit be unable to or refuse (perhaps through fear of loss of health benefits), an examination of bias was made. This was done in two ways. Firstly, bias was measured indirectly by tabulating data from the initial rounds of the study according to status at round 4 (see Appendix for brief details of the data). The second approach is described in the next section of this report.

Table II shows data from the Round 1 part of the cohort tabulated according to the first five of the final status groups described earlier (the valid reasons and excuses groups, being small, were omitted, while the deceased group is not relevant to discussions of bias). The table shows that age differed little between the five groups, while smokers were more frequent in all of the non-examined groups. The refusal group was noteworthy for having the most reports and findings of ill health as well as having the longest tenure. The movers

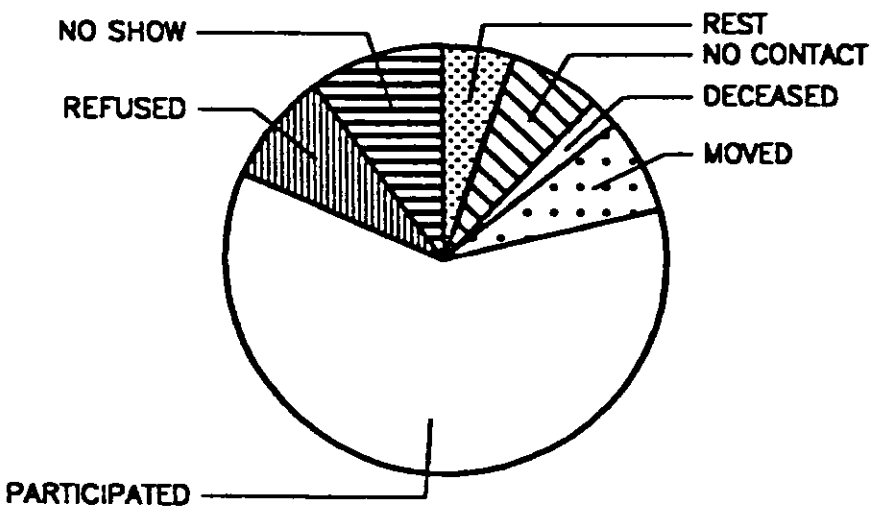

Figure 3. Distribution of complete cohort, and of those selected for examination to date, by state.

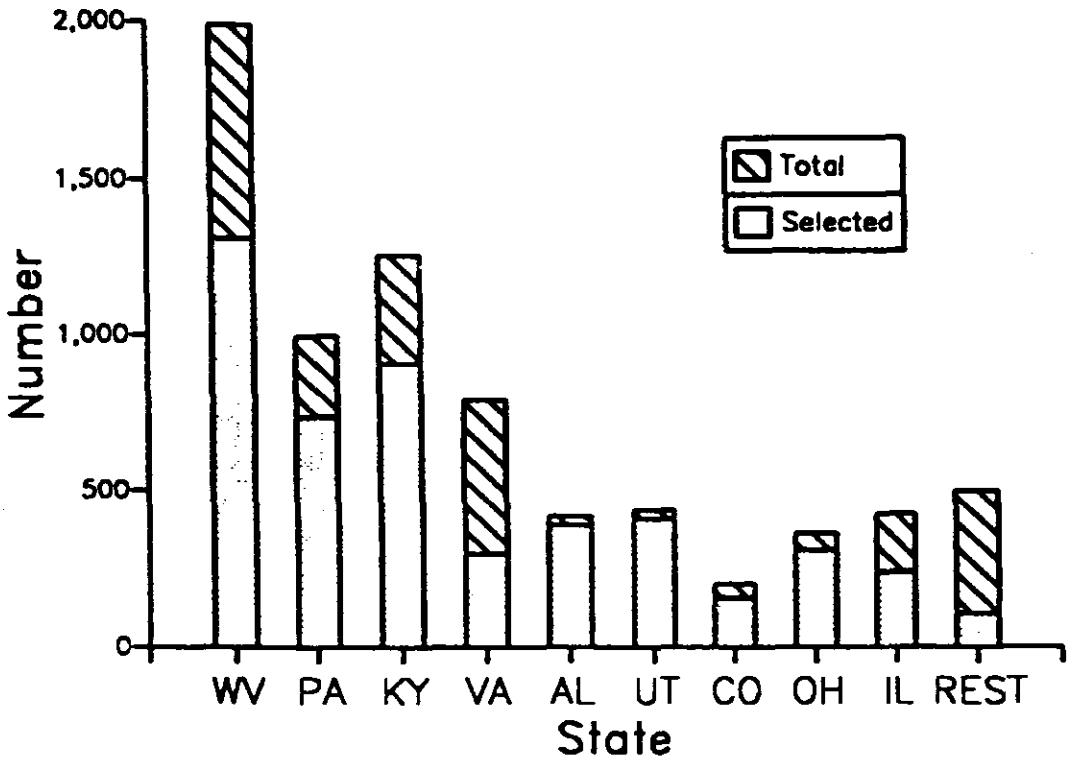

Figure 4. Distribution of final status of selected group.

Table II
Medical Information at Round 1 by Final Status at Round 4

	Examined	No contact	Moved	Refused	No show
Number	1549	125	166	206	186
Age (yr)	33	32	30	33	31
Tenure UG (yr)	7	8	5	9	7
% Smokers	58	62	71	66	67
% Obstructed	20	17	18	24	20
% CWP Cat 1+	5	3	2	8	6
% CWP Cat 2+	1	1	1	1	1
% Cough	20	23	20	26	21
% Dyspnea	7	10	8	9	9

Note: all percentages rounded for simplicity of presentation. Zero percentages may actually be less than 0.5%. Deceased, unknown status, and two other small non-participating groups omitted (n=173).

group had the most smokers but generally had the fewest signs of health problems.

Table III shows the data for the Round 2 part of the cohort. In general the results parallel those seen in Table II. Again the age range between the groups is small, and the examined group had the fewest smokers. The refusal group had the longest tenure, greatest percentage obstructed, most CWP and high levels of symptoms, as they did in Table II. Similarly, movers were younger, had large numbers of smokers, yet tended to have fewest signs of lung disease. There was

more evidence of lung problems in the no contacts in this Round 2 part of the cohort.

Overall, the results from both portions of the cohort indicate the following. The refusals appeared to have had more exposure to coal dust, smoked more, and had more disease. This excess of disease is balanced in part by the deficit seen in the movers. No-shows in general had about as much abnormality as those examined, while the findings were mixed for the no contacts.

In general, there is evidence of bias, but it does not appear severe. This observation is confirmed by the results of Table IV, which shows the data by round for the examined group compared to that for those not examined, and for all of the cohort excepting deceased miners. It shows that only minor

Table III

Medical Information at Round 2 by Final Status at Round 4

	Examined	No contact	Moved	Refused	No show
Number	1357	197	170	203	288
Age (yr)	30	31	28	33	29
Tenure UG (yr)	5	7	4	8	5
% Smokers	56	69	69	60	59
% Obstructed	18	21	18	23	15
% CWP Cat 1+	2	5	2	5	2
% CWP Cat 2+	0	0	0	1	0
% Cough	16	25	16	23	21
% Dyspnea	11	19	13	16	13

Note: all percentages rounded for simplicity of presentation. Zero percentages may actually be less than 0.5%. Deceased, unknown status, and two other small non-participating groups omitted (n=185)

Table IV

Examination of Bias for Round 1 and Round 2 Cohorts

	Round 1 cohort Examined			Round 2 cohort Examined		
	Yes	No	All	Yes	No	All
Number	1549	801	2350	1357	990	2347
Age (yr)	33	32	33	30	30	30
Tenure UG (yr)	7	7	7	5	6	5
% Smokers	58	66	61	56	63	59
% Obstructed	20	20	20	18	18	18
% CWP Cat 1+	5	5	5	2	1	2
% CWP Cat 2+	1	1	1	0	0	0
% Cough	20	23	21	16	21	18
% Dyspnea	7	9	8	11	15	12

Notes: all percentages rounded for simplicity of presentation. Zero percentages may actually be less than 0.5%. The not examined and total groups exclude deceased miners.

differences existed between those tested and those not tested, the biggest discrepancies occurring for smoking (7–8% difference) and for cough (3–5% difference) and dyspnea (2–4% difference). When the data for the examined group are compared to those for all living miners the differences are trivial, indicating that the examined group may be reasonably representative of the whole.

ANALYSIS OF BIAS USING COMPENSATION DATA

The above approach is not particularly satisfactory, since there was a 10–15 year inter-round period during which lung disease could develop. The second approach used more current data from the U.S. Department of Labor (DOL) on Black Lung compensation. To do this, a file of information on name, Social Security number and final status was sent to the DOL. This was matched with the DOL records and a table created showing the percentage in each final status category that had been granted benefits. (While a more powerful analysis would have used DOL medical data in an approach similar to that used in Tables II and III, no formal agreement existed at the time this was written that would have permitted the necessary exchange of data.)

The history of DOL compensation is complicated and much too lengthy for description here in detail. However, two broad periods of time between 1970 and 1988 can be identified during which the regulations were less and more restrictive respectively, viz. pre- and post-1980. Award of compensation was contingent on either ventilation tests or x-ray results during each period, but the criteria were made much more strict after 1980. In addition the rebuttable presumption that lung disease was the result of coal mining was repealed at that time. The result of this tightening was to reduce the approval rate from a high of 46% to 5% (section 435 claims under the 1977 amendments compared to section 718 claims, post 1981 amendment—figures from DOL staff). Since the criteria for these two time periods are so distinctly different the results have been subdivided accordingly.

Table V shows the percentages of miners in each of the final status groups (both rounds combined) who were awarded benefits based on the less and more restrictive criteria respectively, and overall. They show that those examined had the lowest percentage in receipt of benefits, while refusals had the most, followed by the no-contacts, movers and no-shows. This pattern is evident both in those awarded benefits under the less and under the more restrictive criteria, although the differences under the latter criteria are much less pronounced. The overall percentage of miners awarded benefits was 4.9% (excluding deceased miners), compared to the 2.9% seen in those examined, indicating the possibility of bias. Based on the more restrictive criteria, these percentages are 0.9% overall, and 0.8% in the examined group, suggesting the absence of severe bias.

CONCLUSIONS

Data collection is continuing in order to fill some of the major gaps in miner selection noted earlier and to increase the number of examined cases in the round 4 cohort. At this point in time about 65% of the combined round 1 and 2 cohorts have been selected for examination. Of those 4805 miners, 60% have been examined. On the basis of earlier data, the examined group appears to be in slightly better health than those alive at time of survey who did not attend. Certain subgroups of the nonparticipants, specifically those who refused, tended to have, and to report, distinctly more signs of ill health. This excess is balanced to some extent by the apparent better health of those who moved. The data from

Table V

Percentage of Miners Receiving DOL Black Lung Benefits Awarded Under Different Regulations by Final Status at Round 4

	Examined	No contact	Moved	Refused	No show
Number	2906	322	336	409	474
Benefits approved under less restrictive regulations	1.9	8.4	5.7	9.3	3.6
Benefits approved under more restrictive regulations	0.8	0.6	0.3	1.5	1.1
total approved benefits	2.6	9.0	6.0	10.8	4.6

the DOL on black lung benefits confirm that bias may be present, but its actual extent is hard to judge in the absence of medical information.

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APPENDIX ON DATA AND METHODS

Symptoms

The questions used were identical for both rounds 1 and 2. Presence of cough was indicated by positive replies to questions 1 or 2, plus a positive reply to question 3, where the three questions are:

1. Do you usually cough first thing in the morning (on getting up*) in the winter?
2. Do you usually cough during the day (or at night*) in the winter?
3. Do you cough like this on most days (or nights*) for as much as three months each year?

*For those who work at night.

Dyspnea was defined on the basis of positive answers to the following two questions:

4. Are you troubled by shortness of breath when hurrying on level ground or walking up a slight hill?
5. Do you get short of breath walking with other people of your own age on level ground?

Spirometry

The FEV_1 and FVC data for round 1 were based on the maximum of three blows after two practice blows. In round 2 the maximum was taken from at least five blows after two preliminary blows. In both rounds the same type of rolling seal spirometer was used and the methods were similar. A person was classified as obstructed if his FEV_1/FVC ratio was less than 0.7 at all three rounds.

Radiology

CWP was defined in both rounds using small combined opacities. In round 1 the profusion of combined opacities was derived from the maximum of the small rounded and small irregular profusions. In round 2 the recorded profusion of small combined opacities was used, if available; if not, the maximum of the rounded and irregular scores was used, as for round 1. The classification used for these two rounds was the ILO 1971 version.[11]

While the readings quoted for round 2 were derived from the median of three readings, those from round 1 was taken from the reader who noted the least amount of abnormality of three readers, since it has been shown subsequently that his interpretations were much more compatible with abnormality levels reported by others before, during and after round 1.

PROGRESSION OF COAL WORKERS PNEUMOCONIOSIS (CWP) IN A COAL MINE

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ABSTRACT

The paper relates to the chest X-ray examinations of 125 underground coal mine workers. It was a new mine. The miners were freshly recruited from village areas. They were chest X-rayed at entry level and then after 6 years and again after 10 years of working. The first two surveys used MMR 70mm×70mm, 200 mA at 100 kV and the third used 300mm×380mm, 15mA at 85kV. The average respirable airborne dust concentrations at working places as measured by gravimetric dust sampler and label personal sampler were 23.9 and 34.9 mg/m^3 respectively. 1959 ILO Pneumoconiosis Classification was used.

The X-ray results indicated that all the workers were free from CWP at entry level. After 6 years of work, the attack rate of CWP for Z, P and Q categories were 38, 1 and 1 respectively. After another 10 years of work, 15 workers developed CWP of category P-1 and above (12%), P being 10, Q-4, R-1 and Z-1. Thus, the CWP rate of attack in 16 years of underground work were: P—(8%), Q—(3.2%), and R—(0.8%) and the ratio of P:Q:R in 16 years were: 10:4:1. Boom type Road Header cutter-loader coal cutting machines were used at the coal faces.

No Paper provided.

A RATIONALE FOR ASSESSING EXPOSURE-DOSE-RESPONSE RELATIONSHIPS FOR OCCUPATIONAL DUST-RELATED LUNG DISEASE

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INTRODUCTION

The complex chain of processes linking occupational exposure to airborne particles with the occurrence of related lung disease is summarized in Figure 1. Epidemiology is usually concerned with relating the two ends since it is the disease on the one hand which is the 'problem' and exposure at the other which can be monitored and controlled. However, it has long been held that, by a proper understanding of the intermediate processes and its incorporation into the epidemiological framework, substantial further advances will be made possible in epidemiology and risk assessment. From multidisciplinary studies carried out worldwide into (a) the physical nature of the aerodynamic transport of airborne particles in the respiratory tract and their deposition in the lung, (b) the kinetics of their redistribution, clearance and storage, (c) the cellular and pathological responses to the presence of particles in the lung, and (d) epidemiology itself, such understanding is now available. The task now is to bring together and apply the knowledge which has been acquired.

This paper reviews the factors to be considered, including not only the level of initial challenge (i.e., involving considerations of the intensity of exposure, rate of deposition in the lung) but also the time-dependent history of exposure (involving considerations of sampling strategy), chemical composition and indices of biological response. The ultimate objective is a dosimetric approach to the problem. What is presented here is a hypothesis upon which such an approach can be built.

THE CONCEPT OF 'DOSE'

The concept of 'dose' is a fundamental issue. In the first instance, it involves the mass rate of deposition in the respiratory tract. The usual approach to this is to assume a conventionalized deposition fraction of the airborne particulate and to measure exposure in terms of that fraction. For the alveolar fraction, a number of quantitative definitions have been widely used, notably that recommended by the British Medical Research Council.[1] In risk assessment, however, it is worth noting that such an approach does not allow for possible differences in deposition for workers engaged in different levels of physical activity (where breathing parameters might vary). Some of our estimates for underground mineworkers in different occupational groups (based on previous measurements of breathing patterns for similar groups of workers and on published lung deposition data) suggest that such effects could lead to differences in alveolar deposition by as much as x2, as compared with exposure measured according to a conventionalized deposition fraction. This suggests in turn that, at least in some epidemiological research, a more flexible approach to dust sampling may be desirable using instruments capable of providing a wider range of information (including particle size distribution and composition). Instruments suitable for this purpose, including dust 'spectrometers', are now available. Some have been the subjects of recent comparative studies carried out in several European laboratories, as reported elsewhere at this Conference by Vincent.

As far as 'dose' is concerned, however, the relationship between exposure and the rate of mass deposition in the lung is just the first stage in the process. The next step is to consider what happens after material has been deposited. In order to express dose in the context of potentially-hazardous inhaled particulate material, a useful starting point is the approach which is widely used for dealing with the dosimetry of inhaled radioactive particles.[2] Thus the hazard-related dose received by lung tissue is equivalent to the integral over time of the amount of particulate material present combined with some modifying 'harmfulness' (or 'damage') function. The latter describes the rate at which the intrinsic property associated with the hazard is transmitted from the material to the tissue and how it changes with the time during which the material is in contact.

In setting out to construct a quantitative dosimetric model, consider first the exposure history. This may be expressed as E_n, reflecting the mass deposited in the lung during the N^{th} day since exposure began. From this, cumulative exposure (C) at the n^{th} day is

$$C(N) = \sum_{n=1}^{N} E_n \qquad (1)$$

which is the form widely employed in epidemiological studies (where E_n is usually obtained in terms of the measured concentration of an appropriate dust fraction, time weighted over the working shift).

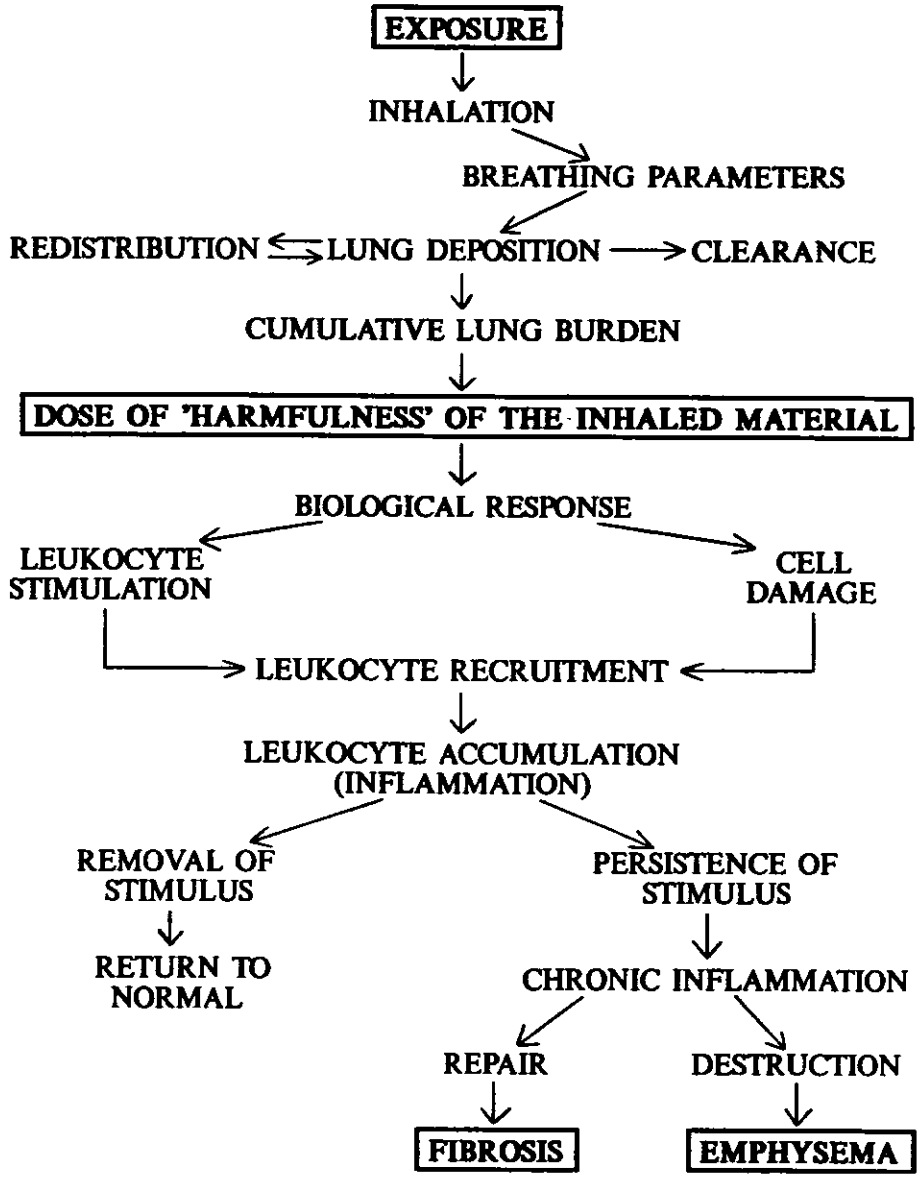

Figure 1. Processes linking exposure, dose and response associated with health effects due to mineral dusts in the deep lung.

Next consider the time-dependent retention of particulate material in the lung. The function R_m describes the proportion remaining of a particular 'packet' of material at the m^{th} day after it has been deposited. The distinction is drawn between n (which refers to the overall time elapsed since exposure began) and m (which refers to the time elapsed since a particular packet of material has been deposited in the lung). The value of R_m (between 0 and 1) is determined by the kinetics of redistribution, clearance and storage of the deposited particles. By combining E_n and R_m, the accumulated mass (M) after N days have elapsed may be shown to be

$$M(N) = \sum_{n=1}^{N} E_n R_{N-n+1} \qquad (2)$$

We now introduce the damage function G_m, which defines the rate per unit mass at which harmfulness is being transmitted to the tissue at the m^{th} day after is has been deposited. It may thus be regarded as a hazard-related 'fingerprint' for the material in question. The transferred property which is responsible for initiating the cell damage may be physical, mineralogical or biochemical.

We now have the three essential elements for constructing a dosimetric model. Hypothetical examples are given in Figure 2. These may be combined as follows:

Day	Dose received
1	$E_1R_1G_1$
2	$E_1R_2G_2 + E_2R_1G_1$
3	$E_1R_3G_3 + E_2R_2G_2 + E_3R_1G_1$

and so on. The cumulative dose of harmfulness is equivalent to the sum of all the contributions indicated. Thus at the N^{th} day, we have

$$H(N) = \sum_{n=1}^{N} E_n \left\{ \sum_{m=1}^{N-n+1} R_m G_m \right\} \qquad (3)$$

In relation to the epidemiology of dust-related lung disease, it is suggested that Equation (3) should replace Equation (1) and other simplistic forms of dose assessment.

PRACTICAL CONSIDERATIONS

Practical implementation of the proposed rationale involves quantitative description of the three key elements; E, R and G.

The first of these is derived from measurements of dust concentration in a way such that the life-time dust exposures of individual workers may be described. This is a complex task. In the first place, it involves choosing a sampling instrument that provides a measurement of the airborne concentration of a dust fraction relevant to the disease in question. In the case of pneumoconiosis, this is the respirable fraction (although there may still be some debate about the particular quantitative criterion by which this should be defined). In turn, there are many instruments available which can provide the required information. In choosing the instrument, considerations of how best to make the measurement relevant to the true exposure of the individual worker raises questions of personal versus static (fixed point) sampling which have been discussed elsewhere.[3] Both types provide the time-weighted shift average of the exposure concentration. The frequency of sampling and its relevance to the assessment of long-term exposure are a matter of sampling strategy, involving considerations of the 'smoothing' that takes place in the body after particles have been deposited (which, in turn, is dependent on R).[4] Furthermore, since the exposure history, if it is to be useful, must reflect the life-time experience of the individual worker, and since he (or she) may move around the workplace from time to time, a record of time worked in particular occupations is an important ingredient towards construction of exposure history. Finally, since it is likely that epidemiology will be desirable for workers for whom exposure records in the early years are either non-existent or imperfect, it may be necessary in many cases to retrospectively estimate exposure histories on the basis of intelligent extrapolations backwards, taking into account more recent measurements and engineering histories of the industries in question.[5,6]

As far as R is concerned, substantial progress in understanding has been made in recent years, mostly based on inhalation studies with animals.[7,8,9] Therefore we now have pharmacokinetic models which are applicable to various toxic and non-toxic, fibrous and non-fibrous materials over wide ranges of exposure level. It is, however, important to note, that such models are relevant strictly only to the animals in question, and need to be validated with respect to humans. Data obtained during epidemiological research in the British coal industry, in particular information from autopsy studies on the lung burdens of mineworkers for whom exposure histories are known, are at present being examined in order to explore the feasibility of establishing such a link.

Although the third quantity, G, is just as important in relation to dose, it is still more difficult to quantify. In the case of radioactive particulate matter (the starting point for the dosimetric hypothesis), the harmful property which is transferred between the particulate matter and the lung tissue is relatively easy to identify (e.g., ionizing radiation of a well-defined type). For mineral dusts, however, like those encountered in many industrial workplaces, the nature of the property is not known. Quartz is one example where, although there are well-known health hazards associated with inhaling respirable particles, somewhat inconsistent epidemiological findings have emerged, especially when other materials are present. As a result, attempts to determine the basic nature of the harmfulness of quartz have not

yet provided definitive answers. European research, involving several laboratories, is presently in progress to address this question, as described elsewhere at this Conference by Robock.

In setting out to quantify G, mineralogical assessment alone does not provide all that is required. Neither (necessarily) does toxicity evaluation based on in vitro cell viability tests. In our own Institute, we are at present exploring how progress might be achieved by direct reference to the cellular response in the lung itself.[10] Bronchoalveolar lavage studies in rats exposed to dusts known to produce contrasting health effects (relatively-innocuous titanium dioxide and highly toxic quartz, for example) have been carried out. These have involved measurements of responses reflecting lung injury (e.g., leukocyte recruitment). Some of the results are particularly relevant in the present context—although the conclusions are preliminary at this stage. Some examples are shown in Figure 3, where the dusts were delivered into the lungs of the rats by inhalation and the leukocyte recruitment assessed subsequently (in terms of neutrophil counts). For the titanium dioxide, the results suggest a biological response is provoked which falls after the cessation of exposure. This in turn suggests that the intrinsic 'harmfulness' of the ma-

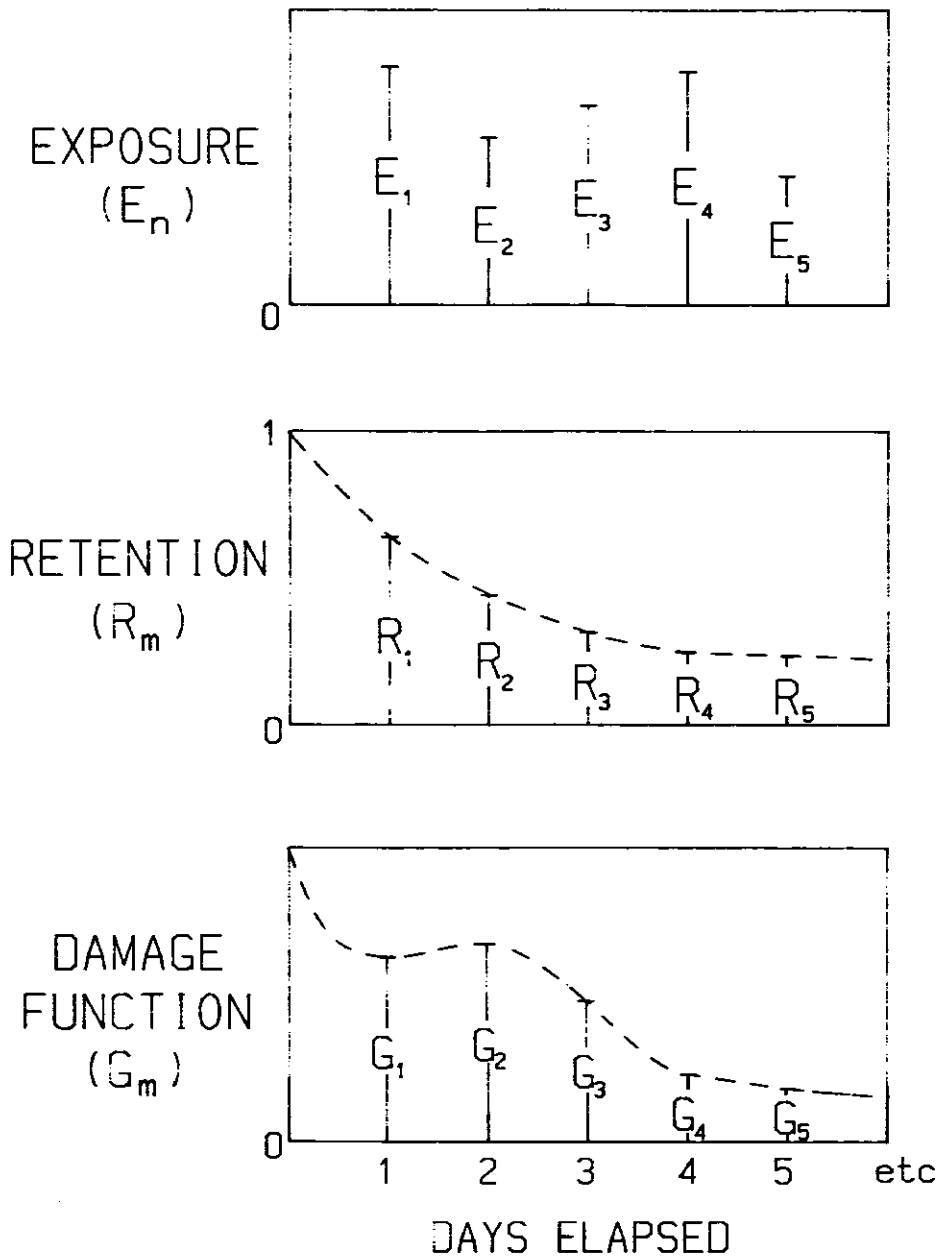

Figure 2. Hypothetical examples to illustrate the quantitative nature of exposure (E), retention (R) and damage function (G).

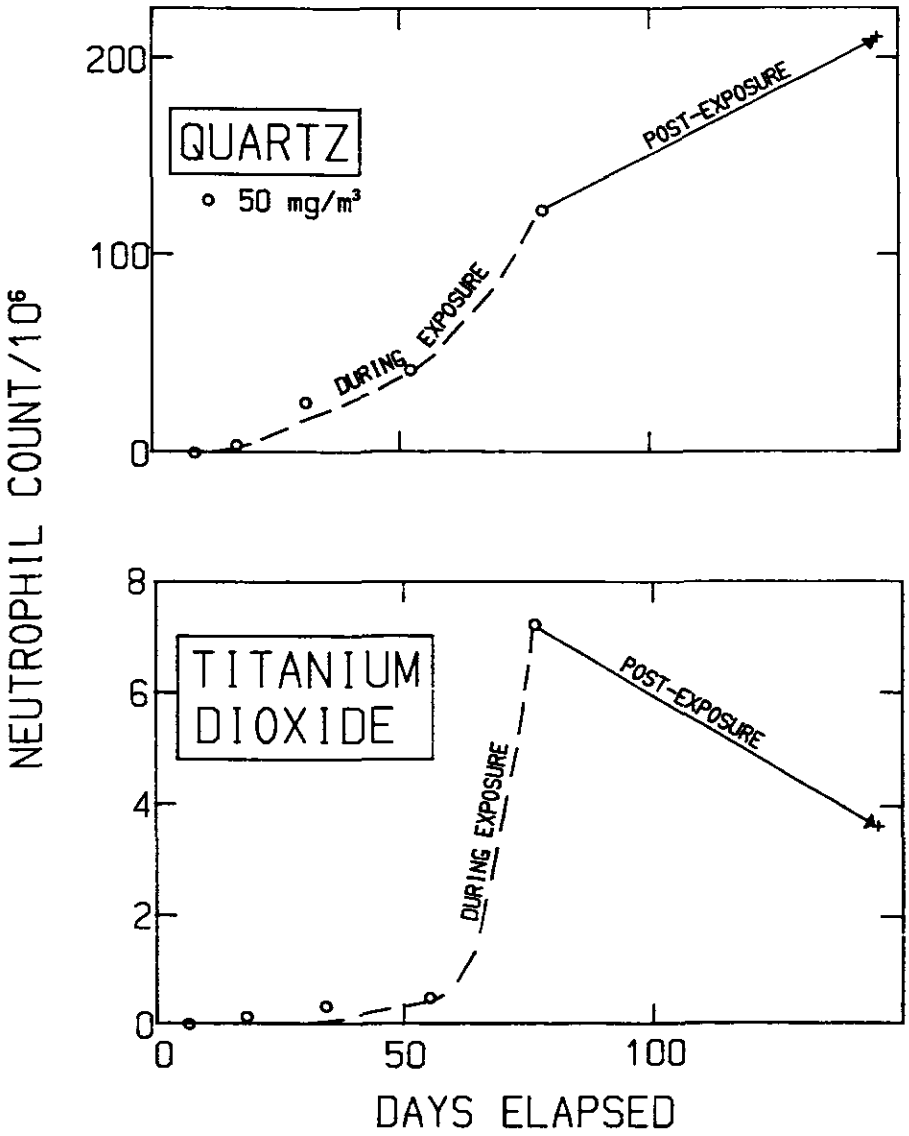

Figure 3. Typical results of cell-lavage study, showing neutrophil response during exposure- and post-exposure for quartz and titanium dioxide inhaled by rats at 50 mg/m³ (respirable). The results shown are means for four rats.

terial is not persistent but rather the damage function, G, decays with time. Throughout, its magnitude is relatively small. In contrast, the biological response to the inhaled quartz is much greater in magnitude and is much more persistent. That is, G is high upon arrival in the lung, and—unlike titanium dioxide—does not decline, even post-exposure. From these findings, the dosimetric implications are clearly consistent with what is known about the contrasting hazards associated with inhaling each of these two materials. Further work is now needed to place such ideas on a more quantitative footing, and to extend them to other, more-realistic mineral dusts.

CONCLUDING REMARKS

In the preceding, we have discussed the main ingredients of a dosimetric model for assessing the risk associated with inhaling airborne particles. The rationale for its development is summarised in Figure 4. At this stage, it is no more than an initial hypothesis. Before it can be proposed as a working model, it is necessary, (a) to establish the validity of pharmacokinetic models, derived originally from the results of animal inhalation studies, for describing retention in humans, and (b) to establish the validity of (and extend) the biological assays aimed at quantifying G for dusts relevant to work-

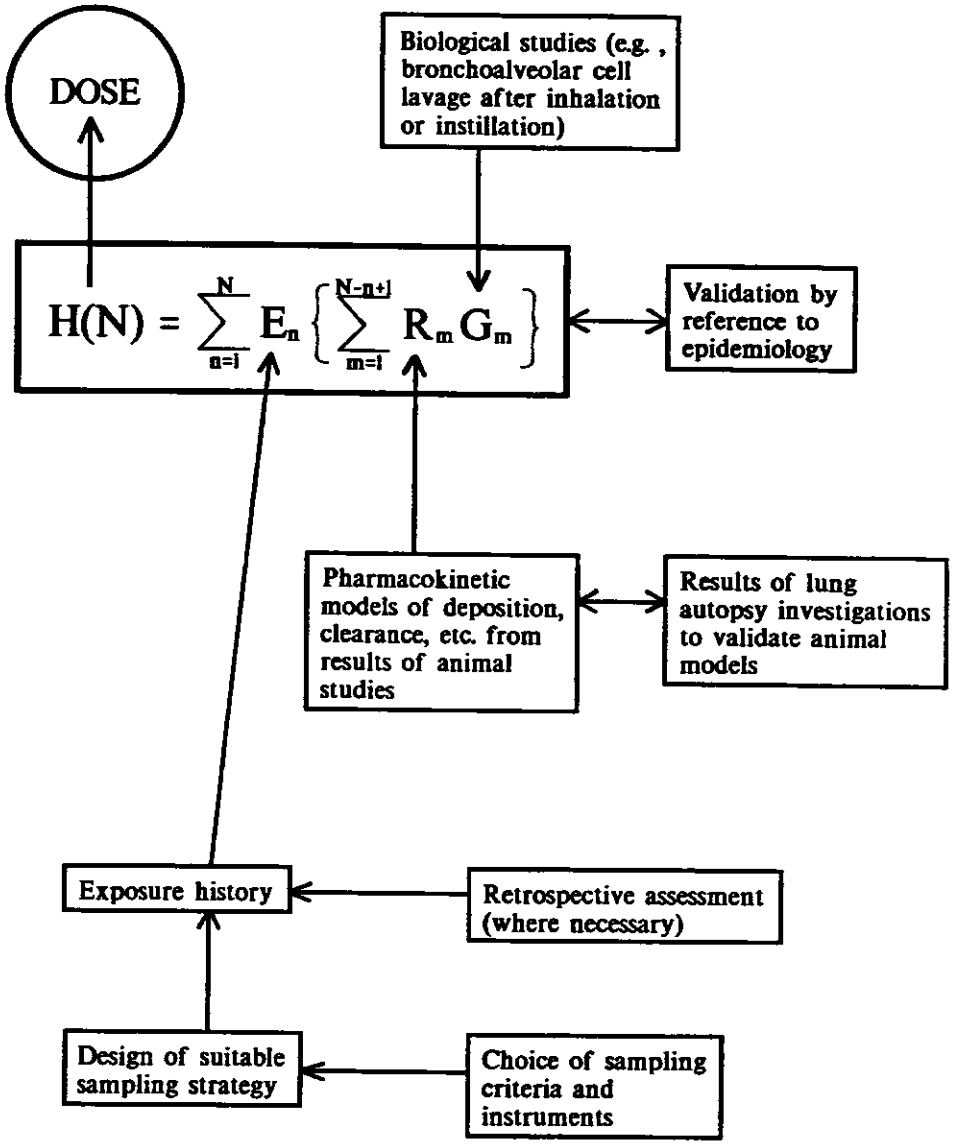

Figure 4. Summary of the rationale for the development of a dosimetric model.

place exposures. Some such studies are in progress. Having once established the working hypothesis, the next step is to validate it with respect to epidemiology for working populations whose exposure and occupational histories are sufficiently well-known. From this scenario, it may therefore be assumed that the emergence of an actual working dosimetric model is still some years away.

The broad benefits of the dosimetric approach to epidemiology have already been mentioned. Notably, as far as epidemiology is concerned, it is anticipated that improved sensitivity (and specificity) and reduced variability in explaining the relationships between the environment and health will be achieved. In turn, improved standards setting, more representative dust sampling strategies, and more effective control procedures (through appropriate worker deployment strategies, technical measures, etc.) will be made possible.

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SIGNIFICANCE OF THE FIBRE SIZE OF ERIONITE

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ABSTRACT

At the VIth International Conference at Bochum we demonstrated that by treating rats with erionite from Oregon, we were able to produce 100% mesotheliomas by both pleural implantation and by inhalation; the only fibre to produce these results under experimental conditions. In contrast to this we failed to produce any tumours with a non fibrous synthetic form of this material. Our colleagues who had studied the Oregon material, in 'in vitro' tests to detect genotoxicity, stated that it was the only dust which they had examined which gives reproducible positive results. We were able to produce two samples from the Oregon erionite of fibrous dusts; one of which contains fibres all of which were less than 5.0 microns in length and, the other containing fibres greater than 5.0 microns to test whether specific sized erionite fibres would produce tumours. Following intrapleural inoculation of the large fibres mesotheliomas occurred in 94% of the rats in contrast to none in those receiving the shorter fibre. In the inhalation study 60% of the animals exposed to longer fibres developed tumours but none of those exposed to the shorter material. A detailed study including the size of the two original preparations and of the fibres recovered from animals receiving both treatments has been undertaken. The significance of these studies will be discussed and the relevance to the biological findings contrasted.

See Table of Contents, Part II, for Paper.

EXPERIMENTAL STUDIES IN RATS ON THE EFFECTS OF ASBESTOS INHALATION COUPLED WITH THE INHALATION OF TITANIUM DIOXIDE

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INTRODUCTION

Many inhalation studies in experimental animals have been undertaken to examine the pathogenicity of mineral fibres.[7,2,5] So far, however, work has concentrated on the effects of pure dust clouds in spite of the fact that, in the industrial environment, fibres are inhaled at the same time as isometric dust particles of many types. To examine the effects of other dusts inhaled with mineral fibres, we commenced a study in which amosite (a long fibre preparation) and chrysotile (UICC 'A') asbestos were administered to rats over the same time period as titanium dioxide, an innocuous particulate dust, or quartz, a highly toxic material.

MATERIAL AND METHODS

Groups of 48 rats of the AF/HAN strain were treated with one of the asbestos varieties at a dose level of 10 mg/m^3 of respirable dust with either titanium dioxide at 10 mg/m^3 or quartz at 2 mg/m^3. The inhalation period was one year and subsequently most of the animals were allowed to live out their full life span. Groups of four rats were killed at the end of the dusting period and similar groups six months later. From these animals the left lung was ashed to determine the content of retained dust, while the right was processed for histology. All lung tissue was serially sectioned with sections examined at multiple levels throughout the organ. Sections were also examined routinely from all major organs and all areas of pathological change detected macroscopically at autopsy. Sections were stained with haematoxylin and eosin, Van Gieson's method for collagen or Gordon and Sweet's method for reticulin. The area of lung tissue occupied by pulmonary interstitial fibrosis was measured using an automatic image analyser (Graphic Information Systems Ltd., GDS1). For the determination of retained asbestos, half of the left lung was ashed at low temperature in nascent oxygen and infrared analysis undertaken of a potassium bromide disc containing the dust residue. For titanium dioxide the rest of the lung tissue was analysed by atomic absorption following muffle ashing. Comparisons of levels of interstitial fibrosis and the retained asbestos content of lung tissue were undertaken using conventional analysis of variance techniques. Differences in the number of pulmonary tumours found in the experimental groups were examined using the Pearson chisquare statistic. The studies involving titanium dioxide and asbestos and quartz and asbestos were not undertaken synchronously. At present only the data from studies with titanium dioxide are complete and these are presented in this paper.

RESULTS

At the end of the dusting period, histological examination of lung tissue revealed large amounts of both asbestos and titanium dioxide intermingled within pulmonary macrophages and in deposits of fibrosing granulation tissue in the region of the terminal and respiratory bronchioles which are the characteristic early signs of lung pathology in rats exposed to asbestos (Figure 1). These lesions consisted mainly of macrophages, giant cells and fibroblasts with reticulin and collagen fibres found in increasing density as the study progressed. Giant cells were particularly noticeable in animals treated with asbestos and titanium dioxide with the phagocytosed titanium dioxide particles packed in the peripheral regions of cytoplasm along with the multiple nuclei. Short asbestos fibres were also found in this peripheral area but longer fibres transfixed the clear central regions of cytoplasm. As the rats aged, pulmonary fibrosis extended in some lung areas to involve the alveolar walls in the parenchyma between the terminal bronchioles. The first sign of this alveolar interstitial fibrosis is a rounding up of Type II epithelial cells which then progressively increase in number as the interstitial space is thickened with fibrous deposits until the airspaces may become lined completely by cuboidal epithelium. In some areas the fibrotic thickening of septa predominates but, in others, epithelial change is more pronounced leading to a pattern of adenomatosis. In the most advanced stages of this condition, some remodeling of the lung architecture occurs with thick walled airspaces no longer corresponding to the original alveoli. The process is probably equivalent to the development of honeycombing in human lungs. The area of lung tissue involved in this type of advanced 'fibrosis' in those animals surviving to within two months of the end of the study (age 34 months or more) is illustrated in Table I with comparable figures from recent studies using the same chrysotile or amosite samples on their own.[2,4] The inhalation of titanium dioxide as well as asbestos did not increase the amount of fibrosis produced.

With the production of pulmonary tumours, however, a marked difference was found between those animals inhaling asbestos only and those inhaling asbestos and titanium dioxide (Table II). For this comparison, two studies using UICC chrysotile 'A' were available.[2,4] In the two studies with UICC chrysotile alone, the number of pulmonary

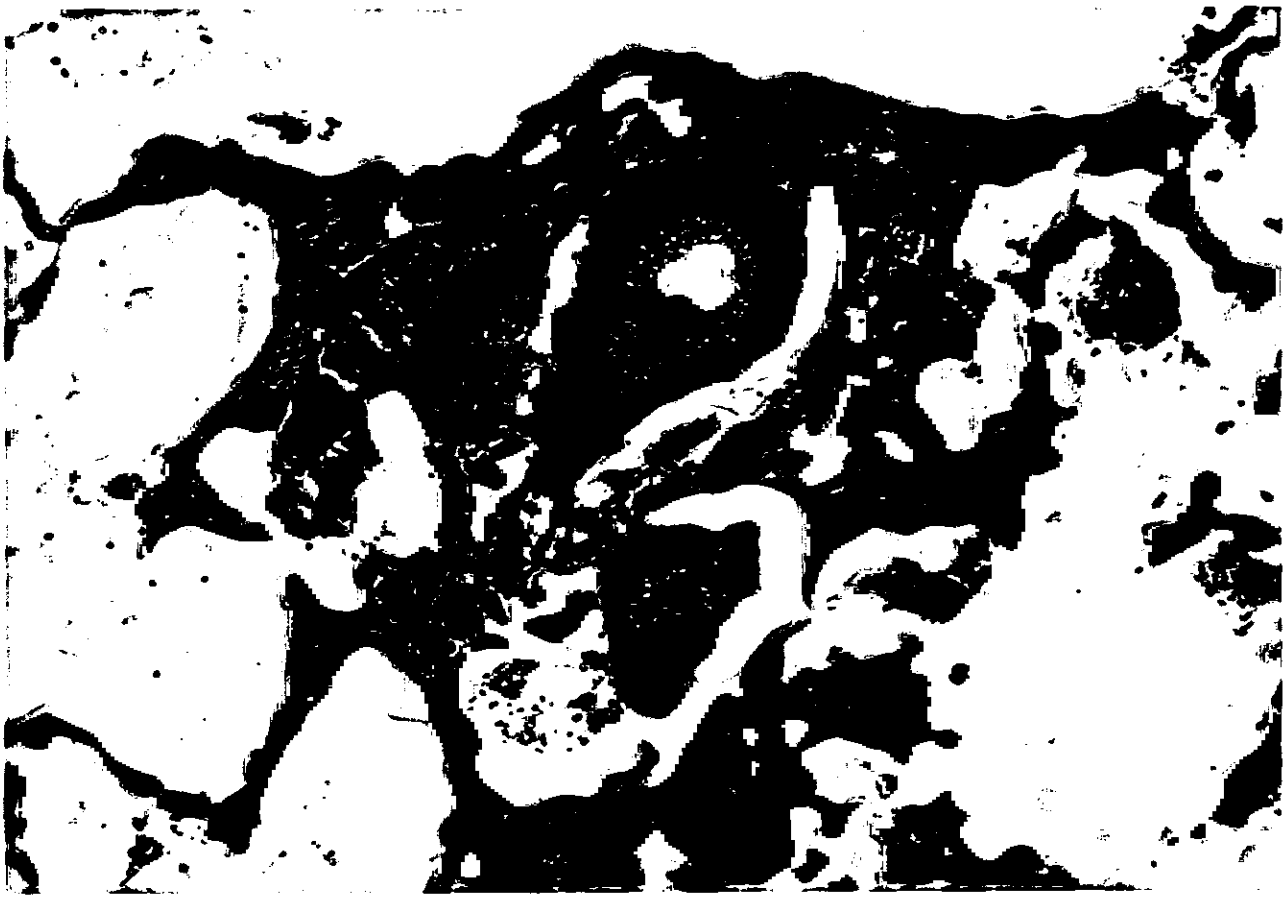

Figure 1. An area of fibrosing granulation time formed in the walls of respiratory bronchioles in a rat after 12 months inhalation of amosite and titanium dioxide. Fibres and particles of titanium dioxide (which appear black) are mingled together in phagocytic cells both free in the alveolar spaces and in the solid tissue of the lesion. Two foreign body giant cells are present with dust packed in the peripheral regions of the cytoplasm but with relatively clear centres. Magnification x 400.

Table I

The Percentage of Lung Parenchyma Occupied by Pulmonary Interstitial Fibrosis

CHRYSOTILE	CHRYSOTILE PLUS TITANIUM DIOXIDE	AMOSITE	AMOSITE PLUS TITANIUM DIOXIDE
12.2% (1.5-24.3)	12.9% (3.8-26.1)	11.0% (0.4-34.6)	9.5% (0.7-20.7)

Figures are means of all animals surviving until within two months of the end of the study. Group sizes varied from 12 - 18 months.

Table II
Pulmonary Tumours

TUMOUR TYPE	CHRYSOTILE		CHRYSOTILE PLUS TITANIUM DIOXIDE	AMOSITE	AMOSITE PLUS TITANIUM DIOXIDE
	1	2			
Adenoma	7	6	4	3	1
Adenocarcinoma	6	4	12	3	8
Squamous carcinoma	2	4	3	4	3
Mixed/ undifferentiated			5	1	5
Pleural mesothelioma			2	2	2
Peritoneal mesothelioma				1	
TOTAL	15	14	26	14	19
No. of animals	40	37	41	40	40

tumours produced was almost identical, indicating a good degree of reproducability in the animal model. The inhalation of titanium dioxide as well as chrysotile resulted in approximately twice the number of pulmonary tumours. With amosite and titanium dioxide, tumour production was approximately 50% higher than with amosite alone. For the experiments with chrysotile asbestos, the figures for all pulmonary tumours were significantly different ($P < 0.02$) and even more significant if only malignant tumours were considered ($P < 0.004$). For amosite the difference did not reach statistical significance with the group sizes used ($P > 0.10$).

Figures for the lung dust content of animals six months after the end of the dusting are illustrated in Table III. The presence of titanium dioxide, a particulate dust normally considered to be innocuous is associated with double the amount of chrysotile as normally retained at the same timepoint following this asbestos dose on its own. For animals treated with amosite and titanium dioxide, the retained amosite dose was 60% more than with amosite alone. Even with very small groups of only four rats, the differences in chrysotile retention were significant ($P < 0.05$). With the amosite experiments once again the differences were not large enough to reach significance ($P > 0.10$).

DISCUSSION

The results of studies with titanium dioxide and asbestos indicate that the inhalation of a particulate dust normally considered to be innocuous may increase the carcinogenicity of both amosite and chrysotile. Lung dust analysis suggests that this may result from increased retention of asbestos with the increase in pulmonary tumours very closely matching the increase in lung dust content. Whether or not this finding indicates an increased hazard for asbestos workers exposed to mixed dusts in the industrial environment needs careful consideration. Studies examining the buildup of amosite and titanium dioxide in the lungs of rats over a one year exposure period followed by a short clearance period of 38 days have been reported.[6] In this study no reduction of amosite clearance was found compared to similar studies with amosite alone. However, dose levels were different from those in the present study (2.5 mg/m^3 for amosite and 15 mg/m^3 of titanium dioxide) and the clearance period was short covering time when much dust is known to be in macrophages free in the alveoli. The six month period covered by the present paper is a time when dust is being incorporated into solid lesions in the lung parenchyma. The increased retention reported for amosite (as well as chrysotile) may reflect an increase in this process.

Table III

Lung Asbestos Burdens Six Months After the End of Dust Exposure

CHRYSOTILE	CHRYSOTILE PLUS TITANIUM DIOXIDE	AMOSITE	AMOSITE PLUS TITANIUM DIOXIDE
315 (49)	710 (71)	3080 (370)	4980 (499)

Figures are in microgrammes and are the means of groups of four animals. Standard deviations in brackets.

A continuing debate about asbestos-related pulmonary carcinomas concerns the question of whether or not these tumours occur in the absence of pulmonary fibrosis.[1] In the present study, levels of fibrosis were found not to increase with an increase in lung tumours when asbestos was administered with titanium dioxide. However, the principal does appear to apply since all the animals developing pulmonary tumours did have quite large amounts of pulmonary fibrosis as well. It may be that while fibrosis is an essential precursor of tumour development, the area of fibrosis is not the most important factor. The amount of dust retained in any area of fibrosis and the cellularity of the lesions may be much more important. In addition, the method of measuring advanced interstitial fibrosis that we have adopted involves ignoring, in animals with tumours, those areas of lung occupied by the tumour itself and estimating fibrosis as a percentage of the remainder. Thus a tumour may arise in a large area of fibrosis but overgrow this and eliminate it. The percentage of fibrosis in the remaining lung tissue may be relatively small.

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THE ROLE OF FIBER LENGTH IN CROCIDOLITE ASBESTOS TOXICITY *IN VITRO* AND *IN VIVO*

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INTRODUCTION

Inhalation of asbestos fibers during occupational exposures is associated with the development of pleural plaques and effusions, diffuse interstitial fibrosis, and an increased incidence of cancer including bronchogenic carcinoma and malignant mesothelioma. The geometry and dimensions of asbestos fibers are important factors in the pathogenesis of these diseases. Short fibers or spherical mineral particles which reach the alveoli are rapidly cleared from the lungs. Long, straight fibers characteristic of amphibole asbestos are translocated to the pleural and peritoneal linings. In contrast, curly serpentine fibers are trapped in the upper respiratory tract or at tracheobronchial bifurcations. Serpentine fibers also fragment and are gradually cleared, while unmodified amphiboles persist in the lungs.[1,2]

These differences in deposition, translocation, and clearance may account for the different pathogenicity of short and long asbestos fibers after inhalation. Alternatively, long fibers may have intrinsically different effects on potential target cells in the lung than short fibers. Support for this alternate mechanism is based on numerous *in vitro* models of asbestos toxicity and transformation. In many of these *in vitro* models, long fibers are more biologically active than short fibers or spherical particles as monitored by acute cell lysis, disruption of the cytoskeleton, inhibition of cell proliferation, stimulation of various enzyme activities, and transformation *in vitro*.[3-9]

We have re-examined the importance of fiber length using two models of crocidolite asbestos toxicity *in vitro* and *in vivo*. Acute toxicity of long or short fibers was demonstrated in primary cultures of thioglycollate-elicited mouse peritoneal macrophages *in vitro*. In contrast, after direct intraperitoneal injection of crocidolite asbestos fibers, long fibers were more toxic than short fibers. This differential toxicity *in vivo* is due to more effective lymphatic clearance of short fibers from the peritoneal lining. However, if lymphatic clearance was prevented, short fibers were toxic, as well as carcinogenic, in this *in vivo* model.

MATERIALS AND METHODS

Preparation and Characterization of Asbestos Fibers

Crocidolite asbestos which was prepared and characterized according to the Union Internationale Contre Le Cancer (UICC) was used to prepare samples enriched in short and long fibers as described previously.[10]

In Vitro Toxicity Protocol and Assay for H_2O_2 Release

Thioglycollate-elicited mouse peritoneal macrophages were plated onto 12-mm glass coverslips ($2.5–5 \times 10^4$ cells per coverslip) and exposed to various doses of short or long crocidolite fibers for up to 24 hours. Viability was determined using fluorescein diacetate (FDA). Superoxide dismutase (SOD) and catalase were prepared as reported; final concentrations are given in the table legends. Deferoxamine-coated fibers were prepared as described.[11] For assay of H_2O_2 release, elicited macrophages (10^6 cells per 35-mm well) were exposed to various doses of short or long crocidolite fibers for up to 6 hours. H_2O_2-mediated oxidation of phenol red was assayed as previously described.[11]

In Vivo Injury

Male C57B1/6 mice were injected intraperitoneally with mixed crocidolite (200 μg), short crocidolite (120 μg), or phosphate buffered saline (PBS) using the procedure of Moalli et al.[10] These doses of short and mixed crocidolite contained an equal number of fibers. Mice were sacrificed after 3 days. Peritoneal lavage fluid was used to measure lactate dehydrogenase (LDH) activity. The diaphragm was dissected and stained with trypan blue as described previously.[10] In some experiments, mice were injected intraperitoneally with agarose blue A spherical beads. Two days later, 120 μg of short crocidolite fibers were injected intraperitoneally. Mice were sacrificed 3 days later.

NBT Reduction *In Vivo*

Mice were injected with 1.5 ml thioglycollate (4% w/v), 200 μg of titanium dioxide, 200 μg of crocidolite asbestos alone, or 200 μg of crocidolite asbestos which had been presoaked in 10 mM deferoxamine and then rinsed as described above. Mice were sacrificed 3 days later following a 15 minute exposure to 0.3 mg/ml nitroblue tetrazolium (NBT). Fixed diaphragms were dissected and viewed under a dissecting stereomicroscope (2–80 x). Reduced NBT formed a blue precipitate (formazan).

Induction of Mesotheliomas

Male C57B1/6 mice were injected intraperitoneally with crocidolite asbestos. Two series of experiments were conducted: in Series A, 20 mice were injected weekly with either 200 μg/ml of long crocidolite or 200 μg/ml of mixed crocidolite fibers (40 mice total). In Series B, 15 mice were injected weekly with either 120 μg/ml of short crocidolite

or 480 μg/ml of long crocidolite fibers (30 mice total). The doses of long and short crocidolite used in Series B contained the same number of fibers as 200 μg/ml of mixed crocidolite. At the intervals indicated, complete autopsies were performed on all mice.

RESULTS

Preparation and Characterization of Long and Short Fibers

Native UICC crocidolite asbestos was used for separation of long fibers and short fibers by repeated centrifugations. The number of fibers per mg of each fiber sample was determined by transmission electron microscopy and is shown in Table I. Greater than 60% of the long fiber preparation is longer than 2.0 μm, while 90% of the short fiber preparation is shorter than 2.0 μm. The doses used in these *in vitro* and *in vivo* experiments were adjusted to contain an equal number of native, long, or short fibers. The doses listed in Table I correspond to 2.8–5.6 × 10^9 fibers/10^6 cells in the *in vitro* experiments and approximately 5.7 × 10^8 fibers/10^6 resident peritoneal macrophages in the *in vivo* experiments. For the *in vitro* experiments, the dose was kept constant with respect to cell number and surface area of the culture dish. The LD_{50} corresponds to approximately 25 μg of native crocidolite asbestos fibers/cm; 2 complete time and dose response curves were published previously.[11] In the *in vivo* experiments to produce mesotheliomas, approximately 40 weekly injections of 200 μg of native crocidolite asbestos fibers were used. The total dose delivered to each mouse over this time period is approximately 2 × 10^{10} fibers. This dose is comparable to human occupational exposures to asbestos fibers estimated at 10^{10}—10^{11} fibers during a lifetime.[12] In contrast, previously reported models to induce mesotheliomas in rodents use a single dose of fibers ranging from 10–25 mg injected intrapleurally or intraperitoneally.[1,13-17]

In Vitro Toxicity of Long and Short Fibers

Long or short fiber preparations of crocidolite asbestos caused a dose-dependent decrease in viability of thioglycollate-elicited mouse peritoneal macrophages. As shown in Table II, equal numbers of long and short fibers killed 20–30% of the cells after six hours. After 24 hours, only 7.0 ± 0.2% of the cells exposed to short fibers were viable, while 6.4 ± 1.5% of the cells exposed to long fibers remained viable. At earlier time points, there is a lag in short fiber toxicity most likely due to the delayed time in settling onto the cultured cells.

Toxicity of Long and Short Fibers Depends on Release of Reactive Oxygen Metabolites

Previous studies have shown that acute asbestos toxicity in a variety of *in vitro* models is mediated by reactive oxygen metabolites.[11,18,19] While phagocytosis of any particle triggers the release of superoxide anion and H_2O_2, the toxicity of asbestos fibers is postulated to depend on the iron-catalyzed generation of the hydroxyl radical. We tested whether a similar oxidant-dependent mechanism is responsible for acute toxicity of long and short crocidolite asbestos fibers in our *in vitro* model system.

We tested whether long and short fiber preparations stimulated the release of H_2O_2 from elicited mouse peritoneal macrophages in vitro. As shown in Table II, equal numbers of long and short fibers produced similar release of H_2O_2 after six hours of exposure. Both long and short fiber preparations also stimulated the production of superoxide anion as shown by the reduction of NBT.

Acute toxicity of native crocidolite asbestos fibers to macrophages is prevented by exogenous superoxide dismutase and catalase which detoxify superoxide anion and H_2O_2, respectively, or by coating fibers with deferoxamine

Table I

Characteristics of Crocidolite Asbestos Fiber Preparations

Sample	# of Fibers per mg x 10^9	% of Fibers ≥ 2.0 μm long	*In Vitro* Dose (μg)	*In Vivo* Dose (μg)
Mixed (native) fibers	2.93	23.6	50	200
Long fibers	1.22	60.3	120	480
Short fibers	4.64	9.4	30	120

Short and long asbestos fibers were separated from native crocidolite asbestos by differential centrifugation as described in Materials and Methods.

Table II

Viability and Release of H_2O_2 by Elicited Mouse Peritoneal Macrophages Exposed to Short or Long Crocidolite Asbestos Fibers for Six Hours *In Vitro*

Sample	Viability	nmoles $H_2O_2/10^6$ cells
Control (untreated)	100 ± 3.2[a]	0
Long fibers	19.0 ± 7.5	25.7 ± 9.8
Short fibers	31.3 ± 5.8	23.6 ± 4.8

[a] Mean ± SD.

Thioglycollate-elicited mouse peritoneal macrophages (2.5-5.0 x 10^4 cells per 12-mm glass coverslip) were exposed to equal numbers of short (30 µg) or long (120 µg) crocidolite asbestos fibers. After six hours, viability was determined by the ability to hydrolyze and retain fluorescein diacetate as described in Materials and Methods. For determination of H_2O_2 release; 10^6 cells per 35-mm multiwell were exposed to equal numbers of short (180 µg) or long (720 µg) crocidolite asbestos fibers. After six hours, release of H_2O_2 was measured as described in Materials and Methods. No H_2O_2 was detected when 0.5 mg/ml catalase was included in the reaction mixture.

which prevents the iron-catalyzed formation of the hydroxyl radical.[11] As shown in Table III, exogenous superoxide dismutase or catalase decreased the toxicity of long or short fibers. Deferoxamine-coated long or short fibers were also less toxic in this *in vitro* model.

In Vivo Toxicity of Crocidolite Asbestos Fibers

We have previously characterized the acute mesothelial reactions to a single intraperitoneal injection of 200 µg of crocidolite asbestos fibers in mice. The morphological reactions to asbestos fibers were studied by scanning electron microscopy of the diaphragm. Between 1-3 days after injection of asbestos fibers, mesothelial cells become swollen, develop blebs, and detach from the surface of the diaphragm.[10] Macrophages phagocytizing asbestos fibers also show morphologic evidence of injury. Three days after injection of native crocidolite asbestos fibers, there was increased trypan blue staining of the diaphragm and increased LDH activity recovered in the peritoneal lavage fluid (Table IV). A single intraperitoneal injection of PBS, thioglycollate broth, or titanium dioxide or silica particles did not injure the peritoneal lining.

Reactive Oxygen Metabolites are Released from Macrophages Exposed to Asbestos Fibers *In Vivo*

A single injection of crocidolite asbestos fibers has been shown to stimulate an inflammatory response characterized by accumulation of macrophages on the mesothelial surface.[10] Nitroblue tetrazolium (NBT) was used to detect production of reactive oxygen metabolites *in situ*. Three days after injection of native crocidolite asbestos fibers, mice were injected intraperitoneally with NBT and sacrificed 15 minutes later. Blue formazan precipitates were found at sites of asbestos fiber deposition on the surface of the diaphragm. This localized staining was completely inhibited by SOD. A nondegradable particle, titanium dioxide, or a soluble inflammatory agent, thioglycollate broth, did not cause reduction of NBT at the mesothelial lining. Peritoneal macrophages collected by lavage three days after a single injection of 200 µg of native crocidolite asbestos fibers showed spontaneous release of H_2O_2 when assayed *in vitro* (39.2 ± 2.8 nmoles $H_2O_2/10^6$ cells/hour). Neither macrophages collected three days after injection of PBS or thioglycollate broth nor resident peritoneal macrophages released any detectable H_2O_2 when assayed *in vitro*.

Exogenous Scavenging Enzymes or Deferoxamine Reduces Crocidolite-Induced Injury *In Vivo*

We next investigated whether the enzymes SOD and catalase decreased crocidolite-induced injury *in vivo*. SOD and catalase conjugated to polyethylene glycol (PEG) were used to prolong their stability *in vivo*. Both PEG-catalase and PEG-SOD significantly decreased the number of trypan blue-positive cells on diaphragms exposed to crocidolite (Table IV). Treatment of crocidolite-injected mice with PEG-SOD or PEG-catalase also reduced LDH activity compared to crocidolite alone (Table IV). It is unlikely that the protection

afforded by PEG-SOD and PEG-catalase was due to the nonspecific adsorption of proteins onto crocidolite fibers. Inactivated PEG-catalase did not prevent crocidolite-induced injury and PEG-conjugated bovine serum albumin did not protect cells from crocidolite-induced damage.

We tested whether the iron chelator, deferoxamine, could decrease crocidolite-induced injury *in vivo*. Mice were injected intraperitoneally with deferoxamine-coated crocidolite and then sacrificed after 3 days. Deferoxamine significantly decreased the number of trypan blue stained cells on the diaphragm compared to crocidolite alone (Table IV) and produced a dose-dependent decrease in recovered LDH activity.

In Vivo Toxicity of Long and Short Fibers

We next compared the acute toxicity of short, long, and mixed crocidolite *in vivo*. In contrast to mixed or long crocidolite fibers, a single intraperitoneal injection of 200 μg of short crocidolite fibers results in only a mild inflammatory response and little cellular injury. Longer fibers, on the other hand, are trapped on the surface of the diaphragm at the lymphatic stomata. We tested whether short crocidolite would be acutely cytotoxic *in vivo* if fibers were not cleared from the peritoneal cavity. To obstruct stomata, mice were injected intraperitoneally with Amicon agarose blue A beads (50–150 μm in diameter) and 2 days later injected with 120 μg of short crocidolite fibers. Recovered LDH activity was the same when mice were injected with short crocidolite fibers plus agarose beads or when mice were injected with mixed crocidolite fibers (Table V). Agarose beads alone did not increase recovered LDH activity. Similarly, trypan blue staining on the surface of the diaphragm was similar after injection of mixed crocidolite alone or short crocidolite fibers plus agarose beads.

Carcinogenicity of Long and Short Fibers

Crocidolite asbestos fibers are not only toxic to mesothelial cells *in vitro* and *in vivo*, but are also carcinogenic. On the basis of our previous observation that short fibers can injure the mesothelial lining if lymphatic clearance is obstructed, we tested whether repeated exposures to short fibers would obstruct lymphatic clearance and produce mesotheliomas. Mice were injected weekly with equal numbers of native, long, or short crocidolite asbestos fiber

Table III

Protection Against Toxicity Caused by Long or Short Crocidolite Asbestos Fibers by Superoxide Dismutase or Catalase

Sample	Viability	
Control (untreated)	100 ± 9.8	[a]
Long fibers	3.3 ± 0.5	
Long fibers + catalase	61.6 ± 14.2	[b]
Long fibers + SOD	74.2 ± 3.5	[c]
Short fibers	38.8 ± 8.1	
Short fibers + catalase	97.6 ± 9.1	[d]
Short fibers + SOD	94.2 ± 4.9	[b]

[a] Mean ± SD.
[b] P< 0.01 as compared to long or short fibers alone.
[c] P< 0.001 as compared to long fibers alone.
[d] P<0.002 as compared to short fibers alone.

Thioglycollate-elicited mouse peritoneal macrophages were exposed to equal numbers of long (120 μg) or short (30 μg) crocidolite asbestos fibers for six hours. Where indicated, superoxide dismutase (SOD; 420 μg/ml) or catalase (50 μg/ml) was added. Viability was determined as described in Materials and Methods. Cultures treated with SOD or catalase alone showed no loss of viability.

Table IV

Trypan Blue Staining and LDH Activity in Peritoneal Lavage Fluid Three Days after Intraperitoneal Injection of Native Crocidolite Asbestos Fibers Alone or with Exogenous Scavengers

Treatment	Number of Trypan Blue Stained cells per 0.5 cm^2	LDH activity (Units/ml)
Control (PBS)	73 ± 24 [a]	44.0 ± 13.0 [a]
Crocidolite asbestos	798 ± 105 [b]	154.0 ± 13.0 [b]
Crocidolite + PEG-SOD	247 ± 49 [c]	90.3 ± 7.5 [c]
Crocidolite + PEG-catalase	349 ± 46 [d]	66.7 ± 6.5 [c]
Crocidolite + deferoxamine	381 ± 14 [d]	83.0 ± 6.0 [c]

[a] Mean ± SEM of triplicate mice.
[b] P< 0.001 compared to control (PBS).
[c] P< 0.002 compared to crocidolite alone.
[d] P< 0.02 compared to crocidolite alone.

Mice were injected with 1.0 ml of PBS or 200 µg of native crocidolite asbestos fibers. Where indicated, mice also received an injection of 500 units of PEG-SOD or daily injections of 500 units of PEG-catalase as described in Materials and Methods. Finally, mice were injected with 200 µg of crocidolite asbestos fibers which had been presoaked in 10 mM deferoxamine, then rinsed as described in Materials and Methods. Peritoneal lavage fluid was collected three days later and assayed for lactate dehydrogenase (LDH) activity. The dissected diaphragms were stained with trypan blue and counted as described in Materials and Methods. Three mice were used in each treatment group. Injection of PEG-SOD or PEG-catalase did not significantly increase the extent of trypan blue staining as compared to controls.

preparations. After 22–60 weekly injections, animals were sacrificed as they developed ascites or evidence of intestinal obstruction. After injection of native crocidolite asbestos fibers, 37.5% of the mice developed mesotheliomas. In comparison, 23.5% of mice injected with long fibers and 50.0% of mice injected with short fibers had mesotheliomas.

DISCUSSION

In this report, we present evidence that both long and short crocidolite asbestos fibers are toxic to thioglycollate-elicited mouse peritoneal macrophages *in vitro*. Both fiber preparations stimulated release of H_2O_2 from these cells. As shown in previous investigations, reactive oxygen metabolites mediate acute asbestos toxicity.[11,18,19] Long and short fiber preparations of crocidolite asbestos also killed macrophages via a similar, oxidant-dependent mechanism. As with native crocidolite asbestos fibers, catalase, superoxide dismutase, or deferoxamine decreased the toxicity of long or short fibers.

Numerous *in vitro* studies have reported that long asbestos fibers are more biologically active than short asbestos fibers.[3-9] The differences between these previously published studies and the data reported here reflect different experimental protocols and different definitions of acute toxicity. In these experiments, we exposed primary cultures of elicited mouse peritoneal macrophages to equal numbers of fibers in the absence of serum. Toxicity, as defined by hydrolysis and retention of fluorscein diacetate, was monitored up to 24 hours. Similar results were obtained using erythrosin B staining or trypan blue uptake. Under these conditions, similar to peritoneal macrophages *in vivo*, these cells do not proliferate. Finally, we obtained our short fiber preparation by centrifugation, not by milling which alters the surface properties of asbestos fibers.[20]

Table V

In Vivo Injury Caused by Intraperitoneal Injection of Mixed or Short Crocidolite Asbestos Fibers Alone or with Argarose Beads

Treatment	Extent of Trypan Blue Staining	LDH Activity (units/ml)
Control (PBS)	−	44.0 ± 13.0 [a]
Control (beads)	−	59.0 ± 4.9
Short fibers	+	93.5 ± 18.8 [b]
Short fibers + beads	+++	168.0 ± 30.0 [c]
Mixed fibers	+++	164.0 ± 32.0 [c]

[a] Mean ± SEM of triplicate mice.
[b] P< 0.02 compared to control (PBS).
[c] P< 0.05 compared to short fibers alone.

Mice were injected intraperitoneally with 1.0 ml of PBS, 120 µg of short crocidolite asbestos fibers, or 200 µg of mixed (native) crocidolite asbestos fibers. Where indicated, two days before injection of short crocidolite asbestos fibers, mice were injected intraperitoneally with agarose beads as described in Materials and Methods. After 3 days, the mice were sacrificed. Peritoneal lavage fluid was collected and assayed for LDH activity and the diaphragms stained with trypan blue as described in Materials and Methods.

Fiber dimensions are also an important factor in the chronic reactions to asbestos fibers. In animal models, long fibers are more inflammatory and fibrogenic than short fibers.[1] More effective clearance of short fibers from the lungs may be responsible for these different reactions to long and short fibers. However, even with direct implantation of fibers into the pleural or peritoneal cavity, long fibers induce mesotheliomas more effectively than short fibers or spherical mineral particles.[13,14] In previous studies, we confirmed that direct intraperitoneal injection of long fibers produced more mesothelial cell injury *in vivo* than injection of short fibers or spherical mineral particles. Long fibers are not as readily cleared through lymphatic stomata at the peritoneal lining, while short fibers and spherical mineral particles accumulate in regional lymph nodes.[10] In this report, we present evidence that short fibers are also cytotoxic *in vivo* and carcinogenic if lymphatic clearance is obstructed or saturated. It is not known whether occupational exposure to massive doses of short rated. It is not known whether occupational exposure to massive doses of short fibers or other particulates may also saturate pulmonary lymphatic clearance mechanisms and increase the risk of developing mesotheliomas.

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DOSE-RESPONSE RELATIONSHIPS IN PNEUMOCONIOSIS

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ABSTRACT

In pneumoconiosis epidemiology, dose-response relationships (DR) are determined to quantify the dose leading to a certain effect. Current standards are based on DR that do not consider dust elimination or dust residence time. This is a serious deficiency, especially for chronic diseases with long latent periods where significant exposures are those occurring early in work history. DR should 1) consider the fact that tissue reaction progresses after termination of exposure, 2) give more weight to the contribution of dust inhaled during early exposure than that inhaled later, 3) differentiate heavy exposure over a short time from a longer but less intense exposure, and 4) account for pulmonary clearance. A rat model of silicosis was utilized to relate exposure to the disease process. Rats were exposed, in 3 groups, to a total dose of 24 mg/m^3 • months. The 1st was exposed to 4 mg/m^3 for 6 mo., the 2nd to 2 mg/m^3 for 12 mo., and the 3rd to 5 mg/m^3 for 3 mo. followed by 1 mg/m^3 for 9 mo. Rats were sacrificed 3, 6, 12 and 24 mo. from the onset of exposure. Response parameters used in the model were dry and wet lung weights, hydroxyproline and histology. Without exception, all response parameters showed better correlation with models that take into consideration residence time and pulmonary clearance. The conventional model of calculating DR resulted in poor correlations.

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THE EFFECT OF SINGLE AND MULTIPLE DOSES OF COAL DUST ON THE BRONCHO-ALVEOLAR FREE CELLS AND ALVEOLAR FLUID PROTEASE INHIBITORS

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ABSTRACT

It is well known that a period of many years of continuous coal dust exposure is required before the pulmonary lesions of coal workers pneumoconiosis appear. The purpose of this study is to compare the population of free cells and anti-proteases in the alveolar space following single and multiple intratracheal instillations of coal dusts. Bituminous coal dust processed to concentrate particles 20 μ or less in diameter were instilled intratracheally into hamsters. Broncho-alveolar lavage was performed 3 and 90 days following the introduction of the coal. After a single dose of 4 mg of coal dust an increase in both alveolar macrophages and neutrophils was observed. The elastolytic activity of the culture fluid in which the macrophages were sustained was increased. The total concentration of the anti proteases in the alveolar fluid, both α1 protease inhibitor (α1Pl) and α2 Macroglobulin (α2M) were not significantly different from control values. Multiple coal dust instillations were performed at 5–7 day intervals over 4–5 weeks. At 3 and 90 days after the 5th instillation the alveolar fluid neutrophils and macrophages were increased as compared with controls. The total elastolytic activity of the leukocytes was greater at day 3 than day 90. However the α1Pl and α2M concentrations in the alveolar fluid were also increased as compared to controls at both 3 and 90 days following the last dust instillation. These data indicate a simultaneous increase in the elastolytic burden and in the protease inhibitor activity of the alveolar fluid. Emphysema is not present by histologic study suggesting that no significant imbalance between proteolytic and anti-proteolytic forces occurred as a result of the coal dust treatments. These studies demonstrate that both the number of alveolar free cells and the anti-proteases in the alveolar environment may be modulated by the coal dust burden and by time. Supported by NIOSH Grant #OH01717.

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MINERAL FIBRE IN THE LUNGS OF WORKERS FROM A BRITISH ASBESTOS TEXTILE PLANT

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INTRODUCTION

The material examined in this study consisted of random specimens of lung parenchyma which had originally been collected at autopsy for histopathological examination. The specimens of fixed tissue were embedded in paraffin wax blocks and represented samples obtained from individuals previously employed at a British asbestos textile plant who died between the years 1964 and 1975.

The asbestos textile plant where the various individuals had been employed had used chrysotile as its principal raw material, this being imported from Canada and Africa. Crocidolite was used between 1932 and 1969 and over this period represented approximately 5% of the total amount of asbestos processed.[1] No amosite was apparently used at any time for production purposes.

When these tissue samples were originally collected the assay of the specimens for their fibrous mineral content had not been considered. They represented a unique collection of biological material from individuals who for various lengths of time were employed in a plant which has been extensively studied for more than 30 years.

The plant has been the focus of several publications concerned with relating the effects of exposure to asbestos on health.[1-7] However, these studies have not been able to assess the effects of exposure to the various asbestos minerals processed. The British Occupational Hygiene Society used data from this factory in determining its hygiene standard[10] for chrysotile and the mesotheliomas occurring in this factory have been attributed to chrysotile exposure.[11] Information on the mortality of the workers at this plant has been shown to be very different from that of an American textile plant where crocidolite was not extensively used.[8,9] Mesothelioma, lung cancer and asbestosis have been causes of death of the workers in the British plant but not in the American operation where lung cancer and asbestosis cases have been more prevalent.

An examination of the limited working histories of the cases revealed that three had originally been employed in an asbestos fibre store some distance from the textile plant and for a further six, no information regarding period of employment was available. Results from these eight cases are therefore not reported here. The available information regarding the causes of death of the remaining 98 individuals showed that 20 were due to a mesothelioma, 24 to asbestosis and/or lung cancer and 54 were due to other causes.

The specimens have been examined to estimate fibre loadings, the relative concentrations of the various fibre types retained in the tissue and their physical characteristics. These results are reported here and compared with similar data obtained from 46 cases of exposure from an American asbestos plant.

A fibrosis category for the 98 British textile plant cases was also estimated from histopathological sections which had been previously cut from the paraffin wax blocks examined in this study. This information was used to compare fibrous grading with asbestos fibre lung burdens.

METHODS

In each case the tissue specimen was first extracted from its wax block in warm Xylene solution. When separated from the Xylene each specimen was immediately washed in ethanol to remove the wax-rich Xylene solution and dried at 80°C to evaporate the ethanol. The weight of the dry tissue specimen was then recorded. Tests with wet lung tissue specimens which had been prepared in wax and then subsequently extracted in the manner outlined have shown that the dry weight of the tissue recovered was on average 15% of the wet tissue weight. This value of dry tissue weight as a percentage of wet weight corresponds closely to figures obtained from wet lung tissue specimens dried to a constant weight at 80°C.[18]

The tissue specimens were placed in glass centrifuge tubes and digested with 5 mls of 5N KOH solution at a temperature of 80°C in a heated block. The KOH digests were then diluted with distilled water and centrifuged to the bottom of their respective tubes and the diluted KOH solution decanted. The residue was resuspended in distilled water and centrifuged again to remove residual KOH. The washed pellet was then dried in the centrifuge tube and the remaining organic material removed by oxidation at 300°C in an oxygen atmosphere. The ashed pellet was finally resuspended in distilled water whose pH had previously been adjusted to a value of 1.5 and filtered almost immediately onto 0.2 μm pore size polycarbonate (Nuclepore) filters to produce an even deposit. If the suspension was judged to be too concentrated aliquots of 50%–20% were taken. In this particular study this problem was only encountered in a few instances

because of the small quantity of dried tissue available from each wax block which varied from 1.3 mg to 85.7 mg.

The filtered tissue extract was prepared for examination in a Philips EM 400T analytical electron microscope by the direct transference technique.[19] A layer of carbon was deposited onto the dust deposit on the filter and portions cut to the approximate size of gold specimen support grids. The carbon-coated filter portions were deposited carbon upon the grids and the filter material removed using a bath of chloroform.

The mineral fibres in the preparations were examined at a magnification of 20,000X, random areas being scanned to determine their concentration per unit area of the filter preparation. Each fibre when encountered was identified using an energy dispersive X-ray analysis sytem attached to the microscope. The quantity, length, diameter and identity of all fibres (i.e., particles observed in random areas of the grid with a 3:1 axial ratio) in the preparations were therefore recorded. The preparation, counting techniques and identification procedure adopted have been described in detail elsewhere.[12,13,14,15,16] The extent of fibrosis in the various cases was estimated from microscopic examination of histological sections and were graded on a scale of 0–4, 0 being normal, 1 minimal, 2 slight, 3 moderate and 4 severe. This grading has been described in more detail in a similar study of asbestos-related deaths in the United Kingdom in 1977.[16]

RESULTS

The average results for the concentrations of asbestos and other fibre types observed in the 98 cases examined are given in Table I from which it can be seen that all the asbestos mineral types were detected. The geometric mean values for the cases are presented together with arithmetic means because of the very wide range of fibre concentrations determined. Geometric mean values have also been employed as a means of presentation of other data in this paper. Chrysotile fibres were the most numerous of the asbestos particles observed but appreciable quantities of both crocidolite and tremolite were present together with minor concentrations of amosite and anthophyillite.

The combined size distributions of the major asbestos fibre types extracted from the samples are given in Table II. It can be seen from this table that the majority of the chrysotile fibres observed were less than 5 microns in length and finer than 0.25 microns in diameter. More crocidolite and tremolite fibres were longer than 5 microns when compared with chrysotile and a larger proportion of these fibres were greater than 0.25 microns in diameter with tremolite on average the larger of the fibre types. Some consideration must be given to the size of fibres detected in tissue specimens when the quantities of the various asbestos minerals are being assessed as the number of concentrations of the individual fibrous minerals do not equate directly to their mass concentrations because of size distribution differences. It is likely

Table I

Mean Concentrations of Number and Mass of Various Fibre Types Determined in 98 Cases from a British Asbestos Textile Plant

Mineral Fibre Type	Fibre Concentrations 10^6 gram dry lung tissue			
	10^6 fibres/ gram A.M.	10^6 fibres/ gram G.M.	Range of concs.detected 10^6 fibres/gram	Fibre Mass ug/gram A.M.
Chrysotile	175.4	89.4	1.5 - 1389.6	6.0
Crocidolite	79.8	10.1	ND - 2056.9	8.4
Amosite	4.9	0.2	ND - 153.3	4.2
Tremolite	21.8	2.4	ND - 203.7	8.5
Anthophyllite	0.5	0.02	ND - 15.2	0.2
Mullite	31.8	11.3	ND - 246.8	-
Rutile	6.2	0.2	ND - 411.3	-
Iron	4.1	0.7	ND - 25.2	-
Others	3.8	-	ND - 29.7	-
Total	328.3	190.0	11.1 - 2508.4	-

ND - Not Detected
A.M. - Arithmetic Mean
G.M. - Geometric Mean

that the techniques used in the preparation of lung tissue specimens do enhance the number concentration of chrysotile fibres to a greater extent than amphibole fibres. This can be related directly to the fibrilar structure of chrysotile and is supported by the scarcity of fibre bundles observed in lung preparations.

In Table III the fibre concentration data collected has been presented on the basis of cause of death. This shows that on average larger concentrations of amphibole asbestos were detected in lung tissue where the cause of death was due to asbestosis and/or lung cancer than either mesothelioma or other causes of death. Crocidolite levels can be seen to be similar for mesothelioma cases, asbestosis and lung cancer cases, these levels being higher than the average for other causes of death. Table IV presents the average lung fibre burdens of chrysotile, amphibole and total asbestos on the basis of fibrosis grading together with average years of service for cases falling within each category. The chrysotile levels were found to increase in step with the fibrosis grading but the amphibole levels did not. It was also observed that the fibrosis grading did not increase directly with the average years of service. The average lung fibre burdens for the significant asbestos minerals are compared on the basis of years of service in Table V which show that the amphibole mineral fibres tend to accumulate with years of service but chrysotile levels are relatively static.

The average results for the concentration of fibres detected in the lung tissue of 46 cases from an America textile plant are presented in Table VI. When compared with the British results in Table I, it can be seen that chrysotile and amphibole levels are lower. The marked reduction in the amount of amphibole fibre in the American cases is due mainly to the difference in the higher concentration of crocidolite observed in the tissues from the British cases. The tremolite levels in both groups of cases are similar. A greater range of all fibre concentrations were also detected in the British cases when compared with the American group.

The results from the British and American cases are compared further in Table VII where size distribution data has been used to calculate the average concentration of fibres longer than 5 microns for each asbestos type. In Table VIII this analysis has been extended further to compare the averages of fibres longer than 5 microns and finer than 0.25 microns. From both tables the most significant difference between the fibre concentrations is the greater proportion of long and thin amphibole fibres in the British cases. The major contributor to this difference being the significant amount of crocidolite occurring in the British cases.

DISCUSSION

In this study the asbestos mineral fibre detected in the lungs from 98 individuals previously employed in a British asbestos

Table II

Combined Size Distributions of Major Asbestos Fibre Types Observed in the Lungs of British Textile Plant Cases (%)

Length Ranges Microns	Diameter Ranges Microns						
	Chrysotile	Crocidolite			Tremolite/Actinolite		
	0-0.25	0-0.25	0.25-0.5	> 0.5	0-0.25	0.25-0.5	> 0.5
< 5	91.8	88.0	1.5	-	73.6	12.0	3.1
5-10	4.9	8.3	0.7	0.2	5.5	1.8	1.1
10-20	2.3	0.9	0.3	-	1.0	0.5	0.6
> 20	1.0	0.1	-	-	0.6	-	-

Table III

Geometric Mean Concentrations of Asbestos Fibres Detected in Lung Tissue and Expressed on the Basis of Cause of Death

Number of Cases	Cause of Death	Fibre Concentrations 10^6/gram of Dry Tissue				
		Chrysotile	Crocidolite	Amosite	Tremolite	Total Amphibole
20	Mesothelioma	64.5	13.0	0.4	2.0	24.8
24	Asbestosis & Lung Cancer	100.4	14.3	0.1	8.9	47.5
54	Other Causes	99.1	8.4	0.2	1.5	19.4

Table IV

Geometric Mean Asbestos Lung Fibre Burdens of Chrysotile, Amphibole and Total Asbestos Fibre Counts with Years of Service Compared on the Basis of Fibrosis Grading

Number of Cases	Years of Service	Fibrosis Grading	Mean Fibre Levels 10^6/gram of Dried Lung Tissue		
			Chrysotile	Total Amphibole	Total Asbestos
16	20.6	0	59.7	12.5	83.7
12	7.1	1	84.4	9.6	130.3
54	16.6	2	95.1	24.4	153.2
16	20	3	103.9	107.2	240.4

Table V

Geometric Mean Lung Fibre Burdens of the Significant Asbestos Minerals Compared on the Basis of Years of Service

Number of Cases	Years of Service Range	Mean Fibre Levels 10^6/gram of Dried Lung Tissue				
		Chrysotile	Crocidolite	Amosite	Tremolite	Total Amphibole
23	0-10	67.3	2.5	0.2	0.5	7.3
29	10-20	102.0	7.3	0.2	2.9	21.6
23	20.30	115.6	26.7	0.2	2.5	37.9
23	30-50	78.6	29.5	1.0	13.6	64.4

Table VI

Mean Concentrations of Number and Mass of Various Fibre Types Determined in 46 Cases from an American Asbestos Textile Plant

Mineral Fibre Type	Fibre Concentrations 10^6/gram Dried Lung Tissue			
	10^6 fibres/ gram A.M.	10^6 fibres/ gram G.M.	Range of concs. detected 10^6 fibres/gram	Fibre Mass ug/gram A.M.
Chrysotile	58.1	29.3	1.6 - 319.7	1.9
Crocidolite	2.3	0.1	ND - 67.2	2.7
Amosite	1.8	0.1	ND - 16.8	3.8
Tremolite	15.8	2.2	ND - 95.8	17.1
Anthophyllite	0.2	0.03	ND - 2.7	0.01
Mullite	5.6	1.3	ND 43.6	-
Rutile	1.0	0.2	ND - 8.1	-
Iron	1.6	0.2	ND - 5.3	-
Others	0.3	0.02	-	-
Total	86.7	47.4	2.1 - 319.7	-

ND - Not Detected
A.M. - Arithmetic Mean
G.M. - Geometric Mean

textile plant who died between the years 1964–75 was found to consist of chrysotile in association with appreciable quantities of amphibole fibre. On average the most prominent amphibole mineral detected was crocidolite with a lower concentration of tremolite and only minor quantities of other amphibole fibre types. The quantity of asbestos was found to accumulate an average with years of service, this accumulation being more pronounced for the amphibole minerals than chrysotile. This provides further proof of the selective retention of amphibole fibre which has been demonstrated in many investigations of mixed fibre occupational exposures. There was no clear relationship between years of exposure and fibrosis grading indicating that exposures within a particular industrial operation have varied significantly for various individuals. An increase of amphibole asbestos mineral concentrations in tissue with fibrosis grading is more pronounced than corresponding chrysotile fibre levels. This would lend further support to the hypothesis that the major cause of asbestosis in Great Britain has been the result of the inhalation and retention of amphibole asbestos mineral.[16] The average levels of amphibole fibre in tissue were found to be larger in those cases where the cause of death was due to asbestosis and/or lung cancer when compared with either mesothelioma cases or other causes of death. Chrysotile levels did not, however, vary significantly with cause of death; these observations are similar to those reported elsewhere.[20]

Comparing fibre lung burdens of British textile plant workers with those of an American plant have revealed that there are some similiarities in the mineralogy of the asbestos dust retained. Tremolite levels are similar although chrysotile contents are on average higher in the British cases. The most significant difference between the two groups is the high level of crocidolite fibre in the British cases. If these mineralogical

Table VII

Comparison of the Geometric Mean Concentration of Asbestos Fiber Types and Proportion Greater Than 5 Microns in Length Detected in the Lungs of Cases from British and American Textile Plants

Fibre Type	Number Concentrations 10^6/gram of Dry Tissue			
	British Cases		American Cases	
	Total	> 5um in length	Total	> 5um in length
Chrysotile	89.4	7.5	29.3	3.2
Crocidolite	10.1	1.1	0.1	0.058
Amosite	0.2	0.05	0.1	0.049
Tremolite/Actinolite	2.4	0.3	2.2	0.34
Total Amphibole	24.7	2.8	3.5	0.6

Table VIII

Comparison of the Geometric Mean Concentration of Asbestos Fibre Types and Proportion Greater Than 5 Microns in Length and Less Than 0.25 Microns in Diameter Detected in the Lungs of Cases from British and American Textile Plants

Fibre Type	Number Concetnrations 10^6/gram of Dry Tissue			
	British Cases		American Cases	
	Total	> 5um in length < 0.25um diameter	Total	> 5um in length < 0.25um diameter
Chrysotile	89.4	7.5	29.3	3.2
Crocidolite	10.1	0.97	0.1	0.048
Amosite	0.2	0.02	0.1	0.023
Tremolite/Actinolite	2.4	0.2	2.2	0.1
Total Amphibole	24.7	2.1	3.5	0.2

differences are compared with the information on mortality of workers from both plants, it would appear that the mesothelioma cases occurring in the British factory can only be related to the more extensive use of crocidolite in their manufacturing operations. This conclusion could only have been obtained by a comparison of the mineralogy of the lung contents of workers from the two textile plants.

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PATHOLOGICAL STUDIES OF ASBESTOTIC PLEURAL PLAQUES —PRELIMINARY EXPLORATIONS OF HISTOGENESIS

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Pleural plaques were present in 33 of 55 autopsy cases of asbestos workers. Their exposure periods to asbestos were 5–23 years (mean 18.1 years). Twelve of them employed as miners, 21 millers. They were mainly exposed to chrysotile.

Pleural plaque is local patchy thickening with sharp borders from the surrounding normal pleura, yellow-white, harder texture. The surface may be smooth, nodular or navel. No adhesion between visceral and parietal pleura is a conspicuous feature. Pleural plaques are often found on the parietal pleura, particularly on bilateral, posterior and diaphragm pleura. In a few cases they can be seen on visceral pleura or parietal pericardium. Pleural plaques are not encountered at the apex or the costophrenic angles. Plaques are wide variety of shapes and sizes. In order to grade severity of plaques, the total area of pleural plaques is surveyed and expressed as cm^2. The total area has been graded into 3 degrees according to less than 100 cm^2; and 100–300 cm^2; and more than 300 cm^2. The degree 1, 2, and 3 were recognized in 11, 10, and 12 cases, respectively. To determine whether degrees of plaques related to exposure periods to asbestos we divided 33 cases into groups according to the interval of 10 years. There appears to be no significance to correlation between the degrees of plaques and exposure periods to asbestos. A man with degree 1 or less had been exposed to asbestos for more than 20 years. Conversely, degree 3 plaques can be seen in a case of less than 10 year standing. The maximum area of plaques was 916 cm^2 in the present reported cases. Degrees of pleural plaques were not related to standings; it could be conceivable that individual differences, especially, the differences in the sensitivity to asbestos stimulation on pleura play a role in the occurrence of the plaque.

We analyzed previously 15 lung tissues with plaques by the bleach digestion technique and carried out asbestos body counts, SEM-EDXA for core fibre elemental component of the fibre. The results of asbestos body counts are given in Table I. These results showed that the extent of the degree of plaque was not also related to asbestos body counts in the lung tissues.

Typical pleural plaques are made up of bundles of collagen fibres. They are arranged in basket-weave, or concentric circle, avascular and having few cellular elements. Sometimes, a mesothelial cell lining can be seen on the plaque surface (Figure 1). Fibrocytic nuclei were found in collagenous fibre bundle. The structure of thinner plaques was different from this. They consist of the mesothelial lining on surface and beneath loose connective tissue, fibroblasts and monocytes; these changes can be also found on some portions of typical plaques. We refer to the changes as an earlier stage of plaques. On the other hand, a massive chronic inflammation cellular infiltration of lymphocytes and plasma cells and vascularity were often found in deeper portions or periphery of plaque (Figures 2,3). There are many polarizing particles

Table I
Results of Asbestos Body Counts in 15 Cases with Various Degrees of Pleural Plaques

Grades of plaque	Case number	No. of Bodies per gram of dried tissie	G	SD_{lg}	SE_{lg}	T test Compare with grade0–I	T test Compare with grade I
I	5	3.3×10^3–95×10^3	21.253	0.568	0.254	T=1.602 P>0.05	
II	7	0–218×10^3	1.626	2.270	0.858	T=0.411 P>0.05	T=0.961 P>0.05
III	3	6.7×10^3–114×10^3	3.228	0.674	0.389		

in intercollagenous fibres, the deepest and beneath mesothelial lining in polarized light microscopy. Most of them are needle-like, free, a few in dust-cells. A few fibres can be found in deposits digested plaques and on sections of plaques *in situ* in SEM. Their elemental compositions are mainly Si, Mg and a few Fe, similar to that of chrysotile, while other fibre compositions are mainly Si and Ca. To classify these fibres is difficult only according to EDXA. On the basis of above-mentioned results, we regard initial formation portion of plaque was beneath the mesothelial lin-

Figure 1. Mesothelial lining on the surface, lower earlier plaque changes. H.E. x 200.

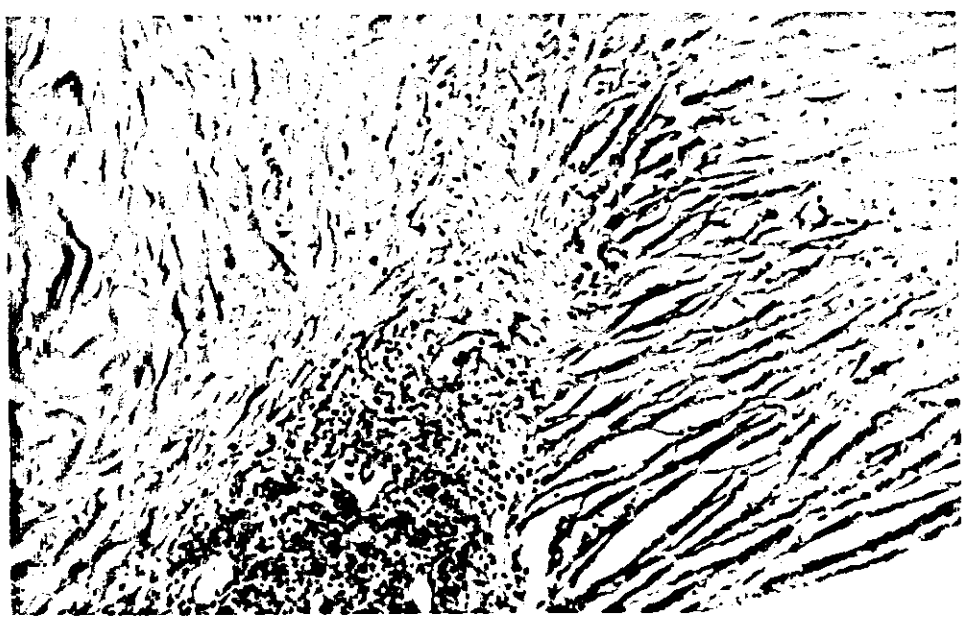

Figure 2. A massive infiltration of chronic inflammation cells on periphery of the plaque. H.E. x 100.

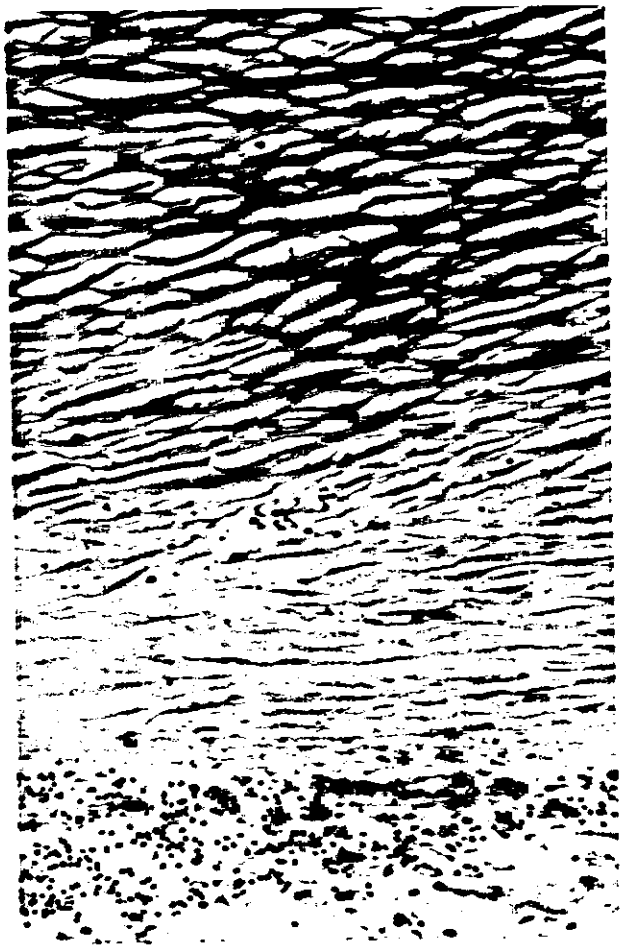

Figure 3. The plaque was clearly divided into 3 zones from base to top: lymph-like cells and vascularity, fresher connective tissue, and hyalinized collagen fibres. The picture showed that development of the plaque was from base of it. H.E. x 100.

ing. Earlier stage changes were dust-fibrous reaction then typical plaque pictures occurred owing to increasing and hyalinization of collagenous fibres. An important point to note is similarity in histopathological pictures of pleural plaques and chronic pleurisy (suppulative or tuberculous). It is not easy to distinguish among them even in light microscopy. But, there is a mesothelial cell lining on surface of plaque; only for this reason, pleural plaques surface was smooth. On the contrary, initial changes of chronic pleurisy occurred in pleural cavity, mesothelial cells desqamate firstly, then adhesion of parietal and visceral pleura

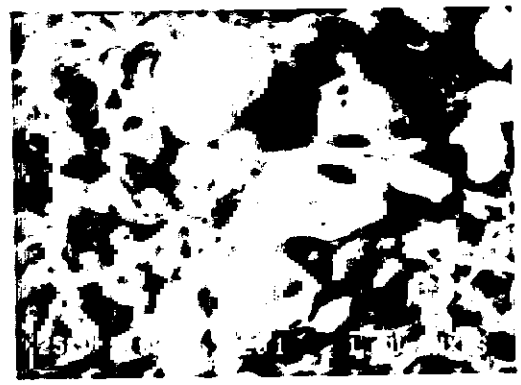

Figure 4. Asbestos fibre and its energy dispersive X-ray spectra, elemental composition. The fibre seems to be chrysotile.

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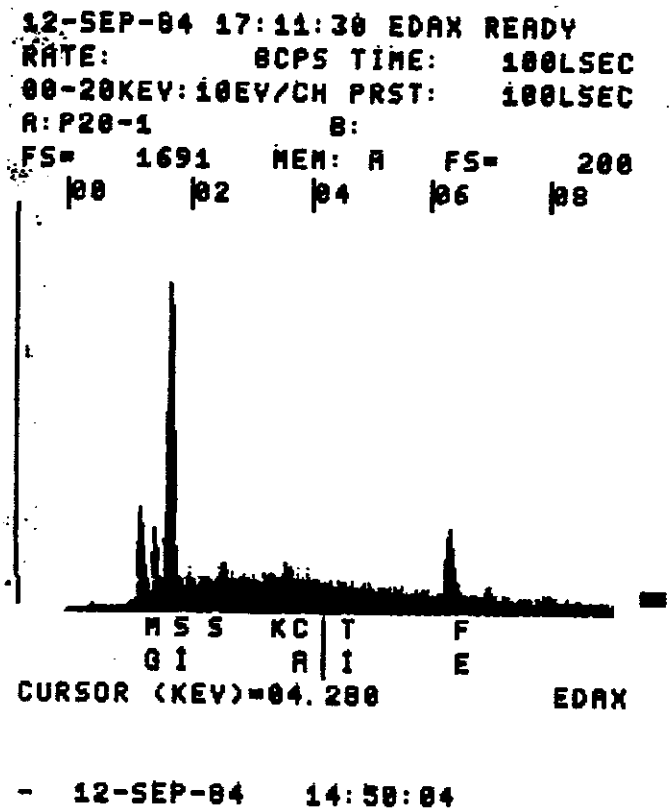
  100.001  LIVE SECONDS
KV= 25.    TILT= 0.    TKOFF=28.

            ZAF CORRECTION

ELEM    K       Z       A       F

MG  K  0.189  1.022  0.406  1.008
SI  K  0.440  1.022  0.460  1.002
P   K  0.014  0.988  0.304  1.002
S   K  0.014  1.014  0.405  1.002
K   K  0.021  0.974  0.704  1.009
CA  K  0.037  0.997  0.767  1.009
TI  K  0.020  0.913  0.861  1.019
FE  K  0.264  0.914  0.966  1.000
```

ELEM	CPS	WT % ELEM
MG K	39.790	25.315
SI K	147.999	44.455
P K	4.800	2.964
S K	4.730	2.187
K K	6.470	1.953
CA K	10.420	2.989
TI K	4.680	1.572
FE K	43.020	18.565



developed, and resulted in the cavity disappearing. It is true, for Thomson noted the mesothelial cells play no part in plaque formation,[1] but, because the mesothelial cell lining had still remained it is possible to explain the peculiarity of plaques; i.e., no adhesion, smooth. In addition, infiltration of chronic inflammation cells in basic or peripheral portions of plaques might play a role in development of plaques, because there are general changes seen in chronic inflammation fibrosis. Yet fibrocytic nuclei were most in base of the plaque, and the fewer, the more surface. Therefore, portion of plaque formation is beneath mesothelial cell lining, origin of growth is the base of plaques. Of course, reformation of plaque can also occur beneath mesothelial lining of typical plaque. We have found that infiltration of chronic inflammation cell was sandwiched between collagenous fibres, and earlier changes were beneath mesothelial lining of typical plaque.

The exact route by which the inhaled fibres reach the parietal pleura is yet unknown. Three possible routes have been drawn by Bignon.[2] 1) Asbestos fibres penetrated directly into pleural cavity, 2) by lymph vessels, 3) by blood system. Our cases have mainly been exposed to chrysotile, but the fibres extracted from lung tissues belong to amphibole according to EDXA results. These fibres were long and straight. The penetration of amphibole is stronger than chrysotile because the latter is curved. It is suggested the first hypothesis seems impossible. It seems possible that inhaled chrysotile fibres broke into thinner and shorter fibres in lung tissue, then they were transported to pleura by lymph vessels, and induced formation of pleural plaque. In view of these reasons, we may understand the presence of chrysotile fibres in pleural plaques (le Bouffan).[3] That is the reason, why chrysotile was hardly found, and amphibole easier seen in our deposits of digested lung tissues.

SUMMARY

In order to assess the severity of pleural plaques the degree of the plaques has been reported. It is adaptable for asbestos workers that pleural plaques were graded into 3 degrees by the area interval of 100 cm^2 and 300 cm^2. Because the degree of plaques have no relation with asbestos standing, individual differences might play a role in occurrence of plaque. It has been observed that initial portion was beneath mesothelial cell, and origin of growth was the base of plaques. Some aspects, such as absence adhesion, smooth surface, asbestos body counts in lung tissues were not concerned with degrees of plaques and can be explained by the findings. Studies seem to suggest that inhaled asbestos fibres can be transferred from lung tissue to parietal pleura, but exact routes have yet to be demonstrated.

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SIMILARITIES IN THE FIBROGENICITY OF ASBESTOS FIBRES AND OTHER MINERAL PARTICLES RETAINED IN HUMAN LUNGS

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INTRODUCTION

Many new types of fibrous materials are being developed for application in advanced technology and industry. A mathematical model constructed for predicting the fibrosis-inducing potential of airborne particles of such materials has two parts. Data on fibre inhalation required by the first part, which computes from the size distribution of the particles the fraction that would achieve long-term pulmonary retention, were obtained from a uniquely suitable environment in the asbestos mining industry.[1] The asbestos mining industry has also been the source of an index of fibrogenicity for use in the second part of the model which estimates the severity of fibrosis produced by the retained particles.[2]

Asbestosis, the interstitial pulmonary fibrosis induced by inhaled asbestos dust, has long been recognized as a dose-related disease. Epidemiologists and industrial hygienists have mainly used fibre counting methods for estimating exposures. Fibre counting has also been the method used in inhalation studies. In inoculation and 'in vitro' experiments with materials such as the UICC standard reference samples, doses have been measured by gravimetric means. Many authors have suggested that fibrosis is a particle surface effect but no study appears to have been based on the measurement of exposure in terms of particle surface area. Since results of animal experiments are often at variance with epidemiological findings, mainly because the methods for dose evaluation differ, any data that are obtained require epidemiological verification. Three recent studies have therefore been based on human pulmonary material.

FIRST STUDY

Identification of the fibrosis-related fibre parameter proved particularly elusive until use was made of a South African report[3] that in the period 1959 to 1964 prevalence of 'slight asbestosis' and 'total asbestosis' in asbestos miners had been the same in North Western Cape Province, which produces a small-diameter crocidolite, and in the Transvaal which mines crocidolite and a closely related amosite, both of large diameter. The first part of the mathematical model was applied to data on the size and concentration of airborne fibres in South African asbestos mines[4] in order to determine which concentration parameter of retained fibres (number, surface area or volume) would show equal asbestos dose in the two regions with equality in asbestosis response. The relevant parameter turned out to be the total surface area of retained fibres per unit weight of tissue and fibrogenicity was independent of amphibole type. Analogous evidence on the Finnish anthophyllite mine at Paakkila supported these findings.

SECOND STUDY

For this study to determine relationships between retained amphibole fibres and fibrosis, tissue specimens were obtained from post-mortem lungs of workers who had been employed at one of four mining locations: Paakkila, NW Cape, Transvaal and the Australian crocidolite mine at Wittenoom. A sample, about 1.5 ml in volume, taken from each lung specimen was sliced into three portions. The middle portion was used to prepare a paraffin section, stained either by haematoxylin and eosin or by a trichrome method. Figure 1 shows the continuous numerical scale of fibrosis[5] one of us (TA) employed in a blind assessment of the severity of interstital fibrosis by scanning the paraffin section in a microscope fitted with a x10 objective. Each successive field was allotted a score between 0 and 8. The mean score for about 50 fields examined was taken as the fibrosis for the sample.

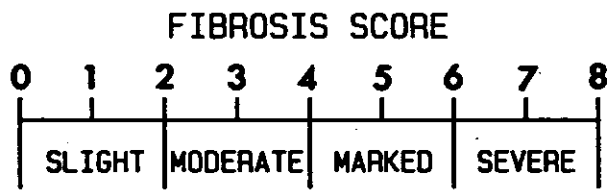

Figure 1. Fibrosis Scale.

The other two portions of the sample were treated together with potassium hydroxide for the extraction of mineral dust. Evaluation of the dust by a method combining magnetic alignment of fibres with subsequent examination by light scattering[6] gave fibre concentration in terms of fibre volume

per microgramme of dry tissue; data on fibre diameters and lengths were used to calculate the concentration in terms of fibre number and fibre surface area.

When surface area was used as the parameter of fibre quantity, the fibre concentrations in specimens showing a given degree of fibrosis were approximately equal:

Wittenoom = NW Cape = Transvaal = Paakkila.

This relationship confirmed the findings of the first study that the severity of fibrosis was related to aggregated fibre surface area and was independent of amphibole type.

When volume was used as the parameter, the fibre concentration in specimens showing a given degree of fibrosis increased progressively:

Wittenoom NW Cape Transvaal Paakkila.

Table I shows the large differences in fibre size in the four mining areas that account for this relationship. For instance, the average ratio of surface area to volume (which is inversely proportional to fibre diameter) for Wittenoom fibres is about 20 times that for Paakkila fibres; consequently, a given degree of fibrosis was induced by a smaller volume of Wittenoom fibres than Paakkila fibres. When number was used as the parameter, the fibre concentrations in specimens showing a given degree of fibrosis decreased progressively:

Wittenoom NW Cape Transvaal Paakkila.

Differences in fibre size also account for this relationship. The surface area of the average Paakkila fibre is about 25 times that of the average Wittenoom fibre; consequently, a given degree of fibrosis was induced by far fewer Paakkila fibres than Wittenoom fibres.

THIRD STUDY

The second study gave an intimation that chrysotile and quartz had fibrogenicity similar to that of amphiboles. The third study was designed to pursue this interesting lead and attempt to quantify the fibrogenicity of asbestos and other minerals. As tissue specimens with preponderance of a specified mineral are difficult to find, the study examined the feasibility of a method that would treat specimens as sources of relationships somewhat akin to simultaneous equations and make multiple-mineral specimens an advantage. Far more specimens were required than the number of equations needed in the algebraic analogy, to compensate for the expected wide intra- and inter-subject variations in severity of fibrosis such as had been observed in the second study. Specimens ranging widely in particle concentration and mineral type were obtained from asbestos mines and factories, gold mines, a platinum mine, shipyards and other workplaces. The compositional data presented in Figure 2 show that often the predominant mineral type in a specimen was not the nominal work material.

Dust was extracted from specimens by removal of tissue by either the potassium hydroxide method or low temperature ashing. Scanning transmission electron microscopy was used for identification and size analysis of individual mineral particles. Fibres were modelled as cylinders, the width of the image seen in the electronmicrograph being taken as the fibre diameter. Talc, kaolinite, chlorite, mica, clay and other flaky particles were modelled as elliptical discs lying flat, 0.2 times the length of the minor axis of a disc being recorded as its thickness. Quartz particles were modelled as spheres, the observed projected area diameter of a particle being taken

Table I
Fibre Size Characteristics

	PAAKKILA anthophyllite	TRANSVAAL amosite crocidolite	NW CAPE crocidolite	WITTENOOM crocidolite
MEDIAN DIAMETER (μm)	0.6	0.2	0.06	0.04
RELATIVE VOLUME	500	50	4	1
RELATIVE SURFACE AREA	25	10	2	1
RELATIVE SURFACE AREA / VOLUME	1	4	10	20

as the diameter of the sphere. Because no measurement could be made on the vertical projected area of particles, which for assessing the surface area of quartz particles is as important as the horizontal projected area, the size data for quartz are less accurate than for most other minerals.

The results obtained from the third study provided further confirmation of the findings regarding amphibole fibres, and discussion will therefore be directed to ascertaining what they say about the fibrogenicity of mineral particles in general.

Figure 3a shows the results of plotting the fibrosis score for each tissue sample against the corresponding concentration for all particles expressed in terms of surface area. In this Figure, and more so in Figures 4 and 5, some of the data points lie on or are close to an axis, and in order to avoid

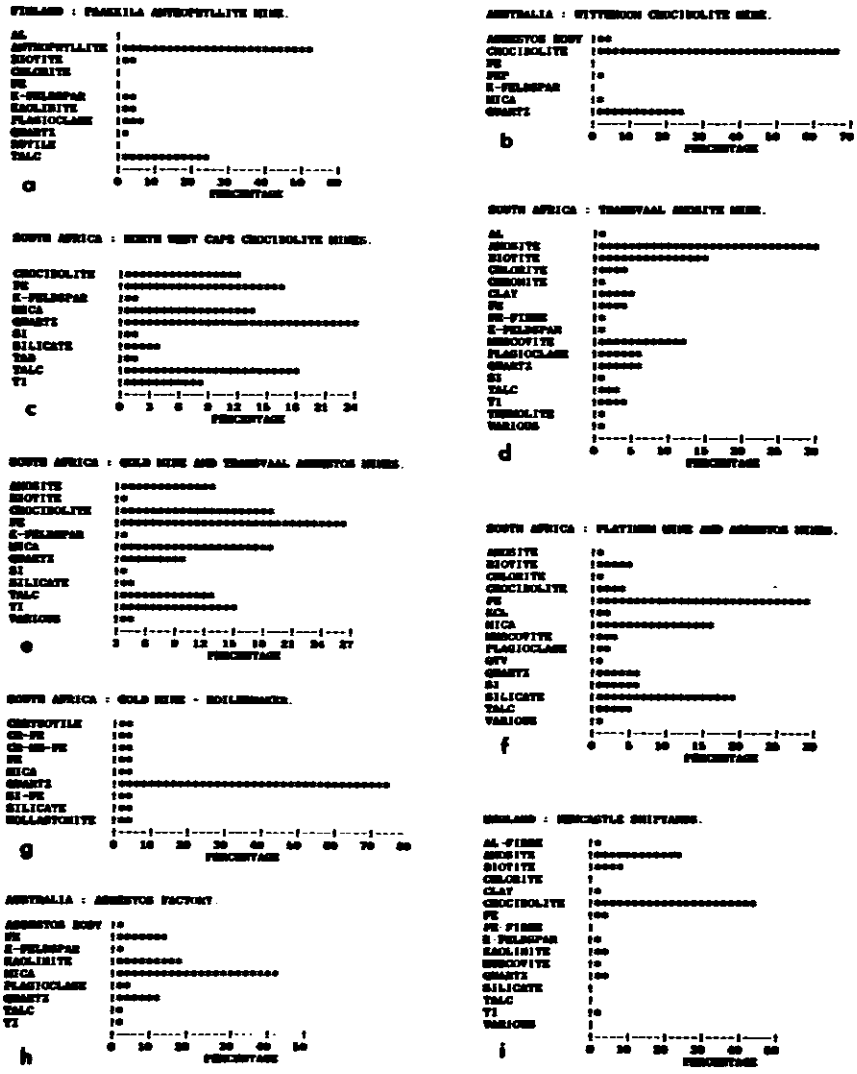

Figure 1. Country of origin of lung tissue specimen; industry; percentage frequency of retained mineral particles.

their obscuration by the scales each scale has been displaced transversely. The regression line is also omitted as it too would otherwise obscure some interesting data points, but may be visualized using the open circles K and E that mark the ends. The point K gives the value of the constant in the regression equation that represents the degree of fibrosis at zero particle concentration. The value of the constant is shown above the graph, together with the correlation and the coefficient (the slope of the regression line) that represents the fibrogenicity for 'all particles.'

Figures 3b-e show the results of plotting the fibrosis score against concentration of various particle fractions ('asbestos + quartz', 'asbestos', 'quartz', 'all-asbestos-quartz'), again with the concentration expressed in terms of aggregated particle surface area. Figures 4 and 5 show data of the type given in Figure 3, and refer to concentrations now expressed in terms of aggregated particle volume and particle number respectively. The statistical data given in the Figures 3-5, are collated in Tables II–IV. Comparison in rows is invalid in Table IV since the fibrogenicity units differ.

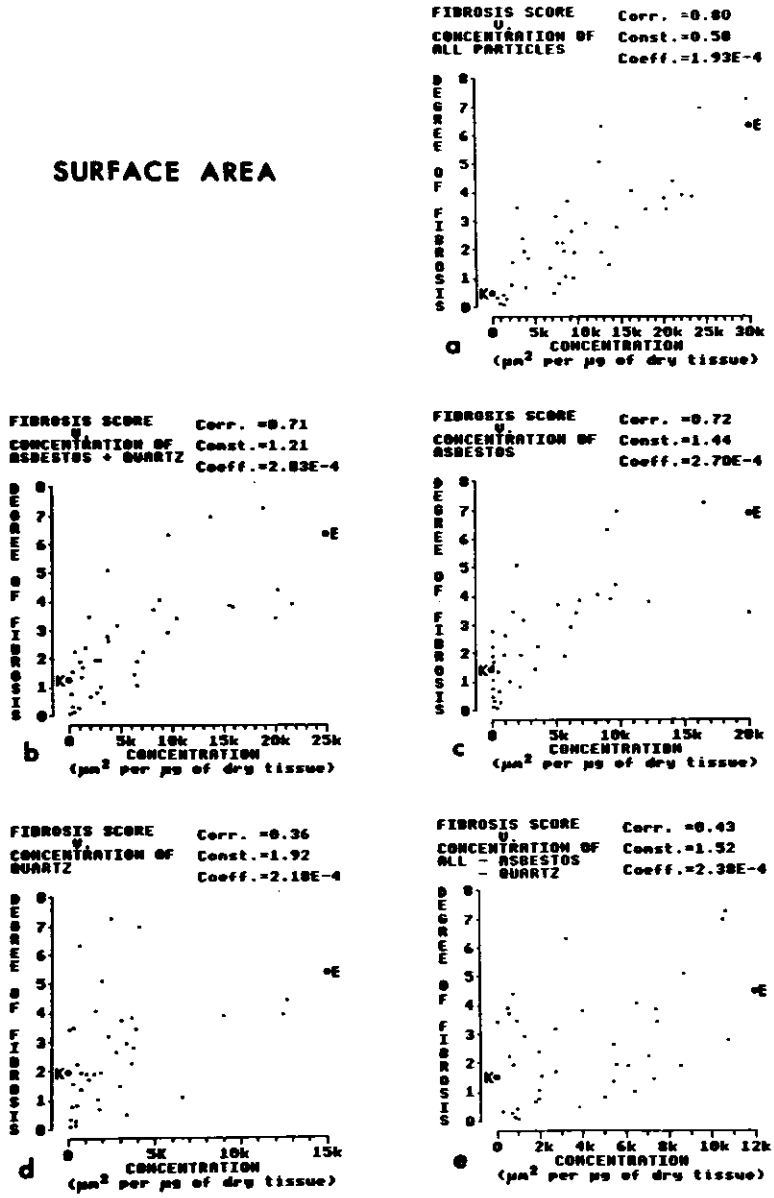

Figure 3. Relationship between severity of fibrosis and particle surface area (μm^2) per unit weight (μg) of dry tissue for various fractions of the retained dust.

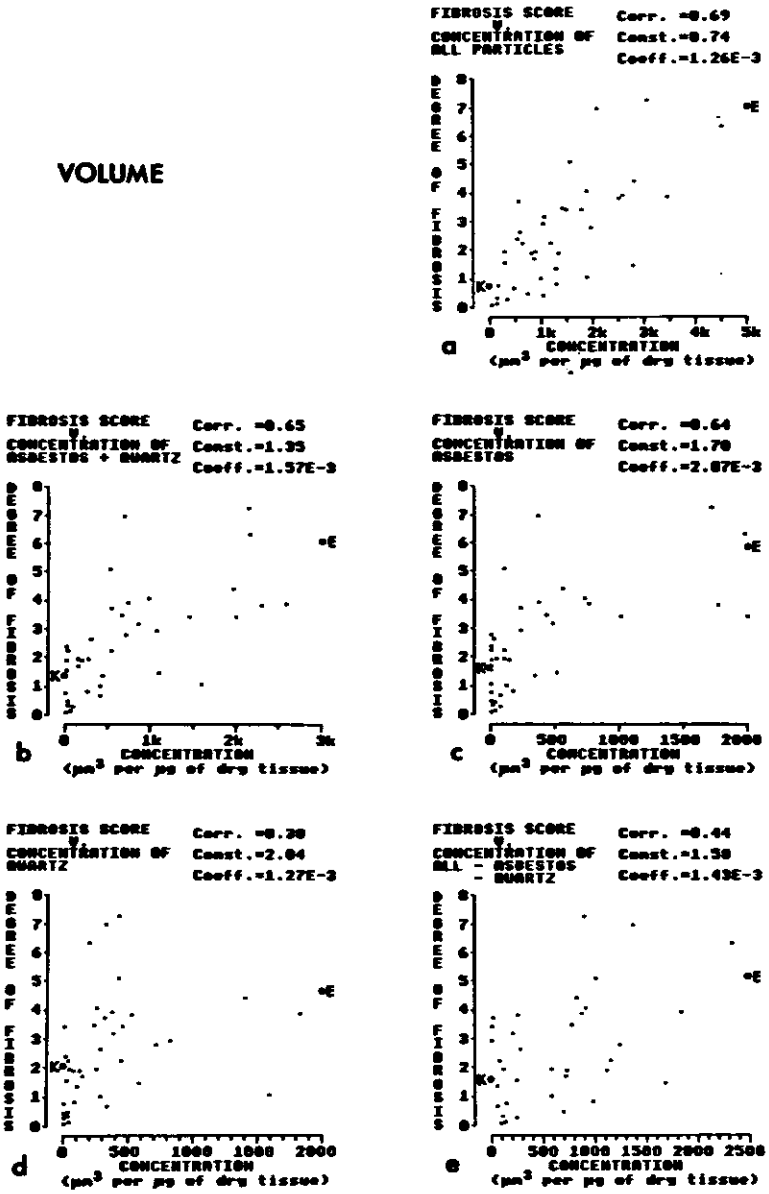

Figure 4. Relationship between severity of fibrosis and particle volume (μm^3) per unit weight (μg) of dry tissue for various fractions of the retained dust.

The substantial scatter of the data points in Figure 3a reflects the wide inter- and intra- subject variations in the degree of fibrosis which are associated with a given particle concentration and stem from differences in the cellular composition of samples taken from different parts of the lung. These are random variations however, and the correlation of 0.80 is the highest seen in Figures 3–5. The data points near the origin suggest that the value of 0.5 for the constant overestimates the fibrosis that is associated with zero particle exposure. The fibrogenicity is 1.93E-4 units (significance level 0.0001); or rounding the reciprocal, 5000 million μm of particle surface area per gramme of dry tissue induce one degree of fibrosis.

The greater scatter of the data points in Figure 3b for 'asbestos + quartz' than that in Figure 3a for 'all particles', the decrease of correlation from 0.80 to 0.71, and the increase in the constant from 0.50 to 1.21, all testify to the presence in the tissue specimens of fibrogenic particles that are not asbestos or quartz. The fibrogenicity of 2.38E-4 units shown in Figure 3e for these other particles which constitute the'all-asbestos-quartz' fraction is, in the present biological context, equal to that for 'all particles'. This fraction, as may be seen in Figure 2, contains a wide assortment of minerals including talc, kaolinite and iron particles. The suggestion that these data indicate similar fibrogenicity of most of the

Table II
Correlation of Fibrosis Score with Particle Concentration

	SURFACE AREA	VOLUME	NUMBER
ALL PARTICLES	0.80	0.69	0.50
ASBESTOS + QUARTZ	0.71	0.65	0.49
ASBESTOS	0.72	0.64	0.49
QUARTZ	0.36	0.30	0.37
ALL - ASBESTOS - QUARTZ	0.43	0.44	0.33

Table III
Constant in Regression Equation

	SURFACE AREA	VOLUME	NUMBER
ALL PARTICLES	0.50	0.74	1.55
ASBESTOS + QUARTZ	1.21	1.35	1.82
ASBESTOS	1.44	1.70	1.90
QUARTZ	1.92	2.04	1.83
ALL - ASBESTOS - QUARTZ	1.52	1.58	1.78

of the minerals is more acceptable than that some are not fibrogenic while others are more fibrogenic than asbestos and quartz.

The relatively low correlation of 0.36 shown in Figure 2d for the 'quartz' fraction may be attributed to the inaccuracy, mentioned earlier, in the measurement of the surface area of quartz particles compared with other particles. However, the value of 2.18E-4 units for the fibrogenicity is comparable to those for the other fractions and for 'all particles'.

Examination of Table II shows that evaluating 'all particles' and expressing their concentration in terms of aggregated surface area provides the best correlation between particle concentration and fibrosis. This indicates that an index of fibrogenicity needs to be closely related to surface area, which is dependent on both particle size and shape and may be a major factor in the disease mechanism. The lower correlation values which occur when concentration is expressed in terms of volume instead of surface area are not unexpected; while volume is a function of particle size it is not a function of shape and cannot therefore be a complete substitute for surface area in the quantification of concentration, or in turn, of fibrogenicity. Table IV shows that, for similar reasons, if the index of fibrogenicity is based on particle volume instead of surface area then this changes the ranking of the fractions in order of increasing fibrogenicity. Tables II and IV also show that when concentration is expressed in terms of particle number, the correlation values fall even lower, the fractions differ more in fibrogenicity and the ranking order alters yet again. These marked changes stem from the fact that particle number is not a function of either particle size or shape and consequently, even more than volume, cannot be a complete substitute for surface area. Quartz illustrates the marked influence particle shape and size have on the value obtained for a mineral's fibrogenicity when assessment of concentration is based on particle number. Figure 5d for quartz shows the most complicated of all the relationships represented in Figures 3–5. Notable is the marked difference in Table IV between the fibrogenicity of 6.09E-4 units for quartz and the more equal values for the other fractions. The sources of this difference are the

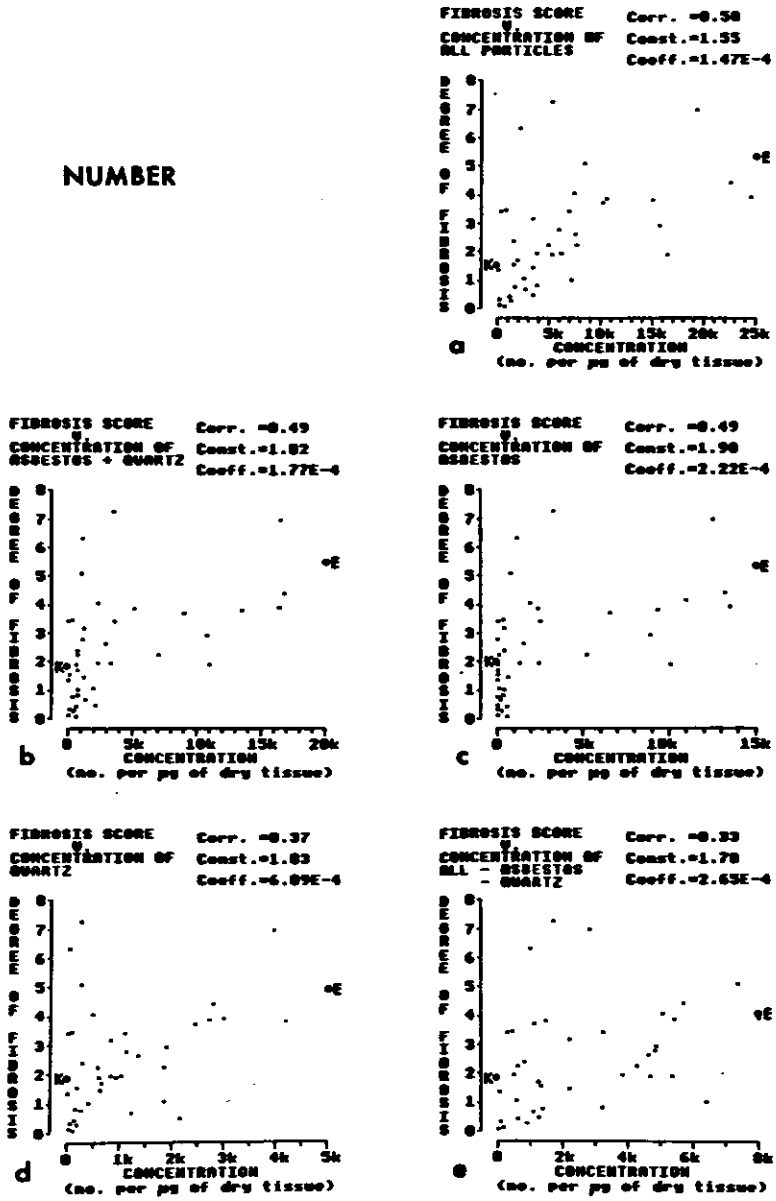

Figure 5. Relationship between severity of fibrosis and particle number per unit weight (µg) of dry tissue for various fractions of the retained dust.

dissimilarities between quartz and the majority of the other minerals in particle shape and size, factors that particle number cannot represent.

Thus the third study showed that evaluating the aggregated surface area of a retained dust provided the best index of its fibrogenicity. Evaluation of aggregated particle volume provided a reasonable index. The index based on particle number was unrealistic, especially when evaluation did not include all particles.

IMPLICATIONS

Many tissue specimens used in the third study showed mineral contents markedly different from those implied by the type of industry from which they came. Figure 2h shows the recorded contents, which include an asbestos body but no asbestos particle, of a specimen from the lungs of a man who had worked in an asbestos factory. The specimen gave a fibrosis score of 6.96, the penultimate score obtained in the second and third studies. Results of the third study indicate that, at a concentration of 5000 particles per micro-

Table IV
Fibrogenicity by Particle Surface Area, Volume or Number

	SURFACE AREA (degree of fibrosis /μm^2 /µg dry tissue)	VOLUME (degree of fibrosis /μm^3 /µg dry tissue)	NUMBER (degree of fibrosis /no. /µg dry tissue)
ALL PARTICLES	1.93E-4	1.26E-3	1.47E-4
ASBESTOS + QUARTZ	2.03E-4	1.57E-3	1.77E-4
ASBESTOS	2.70E-4	2.07E-3	2.22E-4
QUARTZ	2.18E-4	1.27E-3	6.09E-4
ALL - ASBESTOS - QUARTZ	2.38E-4	1.43E-3	2.65E-4

gramme of dry tissue, the contents, which are typical of asbestos-associated minerals, could have made a substantial contribution to the fibrosis observed. This specimen, together with others which show similar features, suggests that even in the asbestos industry evaluation of air samples should include all mineral types and, preferably, should assess the aggregated surface area of the particles which would achieve long-term pulmonary retention.

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PATHOLOGY OF MALIGNANT MESOTHELIOMA AMONG ASBESTOS INSULATION WORKERS

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ABSTRACT

An epidemiological investigation of a cohort of 17,800 asbestos workers has revealed a high incidence of malignant mesothelioma among these workers during the period covered by this study (1975–1986). 278 consecutive cases of definite (234) and probable (44) mesothelioma in the cohort group were pathologically characterized. Data was derived from; 113 (40.7%) autopsies, 153 (55.0%) biopsies, and in 12 (4.3%) cases, there was a combination of autopsy and biopsy. The site of the tumor was 160 (57.5%) peritoneal, 97 (34.9%) pleural, 18 (6.5%) pleural and peritoneal, 1 (0.4%) pleural and pericardial and 2 (0.7%) pleural, peritoneal and pericardial. Cell type was 178 (64.0%) epithelial, 25 (9.0%) fibrous and 75 (27.0%) biphasic. The presence or absence of both diffuse interstitial fibrosis and asbestos bodies in the lung sections were ascertained in 137 of the 278 cases. Fibrosis was seen in all but 6 (95.6%). All but 6 cases were positive for the presence of asbestos bodies (95.6%). There were no deaths at age 39 or younger; between 40 and 49, 28 (10.1%); between 50 and 59, 99 (35.6%); between 60 and 69, 89 (32.0%); between 70 and 79, 50 (18.0%) and $\geq$ 80 years, 12 (4.3%). It was possible to calculate years from first exposure to death in 273 of the 278: none among 9 years or shorter; 1 between 10 and 19 (0.4%); 50 (18.3%) cases between 20 and 29; 129 (47.3%) between 30 and 39; 58 (21.2%) between 40 and 49, and 35 (12.8%) were 50 years and longer.

INTRODUCTION

Since January 1, 1967, we have been conducting an extensive prospective mortality study of a cohort of 17,800 asbestos insulation workers in the U.S.A. and Canada. The study continues; however, significant initial important data have been obtained, and have been published.[1] Data 1967-1976 revealed that in 2,221 consecutive deaths, approximately 20% of the insulation workers died from lung cancer, approximately 7% died from malignant mesothelioma: other cancers such as esophagus, colon, rectum, larynx, kidney and stomach were also higher in incidence among these workers in comparison with the general population.[1] Further experience (1967-1984) has shown that malignant mesothelioma in approximately 10% of the insulators (356/3,500) have died from malignant mesothelioma and the incidence of the tumor has increased with extension of years after first exposure to asbestos.[2]

Since 1975, one of us (YS) has evaluated all pathological materials of the study. 278 cases of the malignant mesothelioma were reviewed. It was found that these could be categorized as definite (234) and probable (44) (1975-1986). Here, our objective is to clarify the pathological characteristics of these 278 cases of malignant mesothelioma, and to study relationships of the tumor to other factors, such as the severity of pulmonary fibrosis (revealed by histopathological study), age at death, years after first asbestos exposure to death, and to cigarette smoking.

MATERIALS AND METHODS

278 consecutive cases of malignant mesothelioma in which pathological diagnosis was established (YS) between 1975 and 1986, were used as materials.

Pathology slides (histopathology) from various hospitals, additional slides systematically stained at our laboratory, autopsy and surgical pathology reports, and operative reports were thoroughly reviewed: type of specimens, primary site, cell type and the presence of pulmonary asbestosis were investigated.

Levels of diagnostic certainty of malignant mesothelioma has been classified into 5 categories, definite, probable, possible, unlikely and definitely not.[3] Classification of diagnostic certainty was decided by comprehensive pathological analysis of the tumor[4] consisting of gross appearance (from atuopsy or surgical pathology reports or the operative report), histology, histochemistry, immunocytochemistry and electron microscopy. Gross appearance and histology were used as the essential components in the comprehensive analysis in all cases, and both histochemistry (PAS with and without diastase, colloidal iron with and without hyaluronidase) and immunoperoxidase for CEA and cytokeratin were used in the large majority of the cases. Electron microscopy of the tumor was also available for the diagnosis in a small number cases.

Pulmonary asbestos was evaluated by histopathology of non-

neoplastic lung parenchymal sections. The presence of diffuse interstitial fibrosis has been accepted as the histopathological criterion of pulmonary asbestosis, particularly if associated with ferruginous bodies, when adequate material is available for study of the latter. The severity of asbestosis was classified as none/minimal, mild, moderate and severe, as reported previously.[5]

Age at death, years after first exposure to death, and smoking history were investigated in each of the cases.

RESULTS

Based on the foregoing diagnostic criteria, the 278 cases were classified as 234 definite mesothelioma (84.2%) and 44 probable (15.8%). Although 30 additional cases were "possible" mesothelioma, these 30 cases were excluded for the present study. Derivation of the pathology specimens consisted of 153 (55.0%) surgical, 113 (40.7%) autopsy and 12 (4.3%) both autopsy and surgical. The primary site of the tumor was 160 (57.5%) peritoneal, 97 (34.9%) pleural and 21 (7.6%) other (Table I). The primary site of the 21 "other" cases could not be ascertained since the tumor was spread along two or three body cavities (pleura and peritoneal or pleura and pericardium or pleura, peritoneal and percardium) at autopsy. The ratio of the incidence between the pleural and peritoneal mesotheliomas was 4 to 6. Cell types were classified as 178 epithelial (64%), 75 biphasic (27%) and 25 (9%) fibrous (Table II). The ratio of the 3 cell types was quite similar between the pleural and peritoneal mesotheliomas. Age at death was; none in 39 years and younger, 28 between 40 and 49 years old (10.1%), 99 between 50 and 59 (35.6%) and 151 in 60 years old and older group (54.3%). Years from first exposure to death was; none in 9 years or shorter, 1 between 10 and 19 years (0.4%), 50 between 20 and 29 years (18.3%), 129 between 30 and 39 (47.3%), 58 between 40 and 49 (21.2%) and 35 in 50 years and longer (12.8%). Such long latency is similar to lung cancer among insulators.[5]

Histological evaluation of pulmonary asbestosis was done in 137 of the 278 cases (in which pulmonary parenchyma slides or paraffin blocks were submitted). Diffuse interstitial fibrosis and ferruginous bodies were seen in 131 of the 137. The degree of diffuse interstitial fibrosis was 6 (4.4%) none, 31 (22.6%) mild, 39 (28.5%) moderate and 61 (44.5%) severe. Ferruginous bodies were 6 none (4.4%), 41 small in number (29.9%), 36 moderate (26.3%) and 54 large (39.4%). It is to be noted that, in general, it may be difficult or impossible to detect ferruginous bodies in standard 5 μ sections. Indeed, we were rather surprised to see them as frequently as we did. Pulmonary asbestosis (diffuse inter-

Table I

Malignant Mesothelioma Insulation Workers—Primary Site

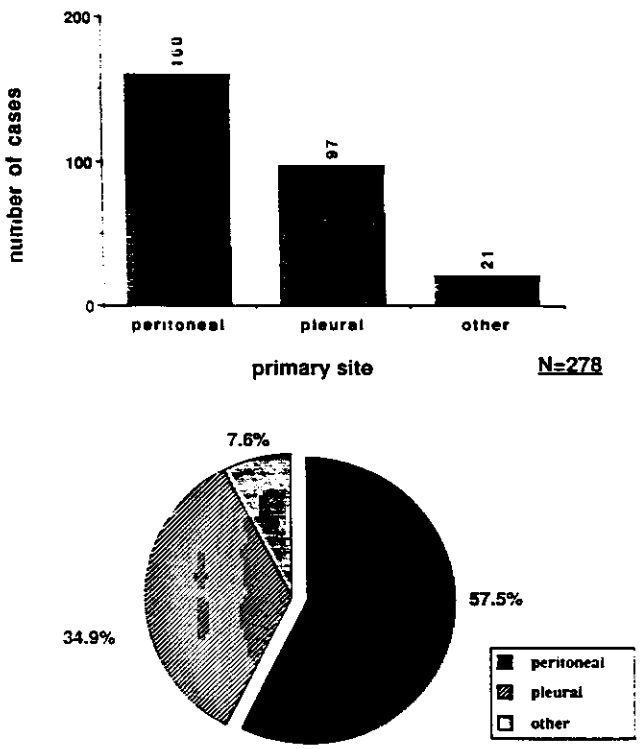
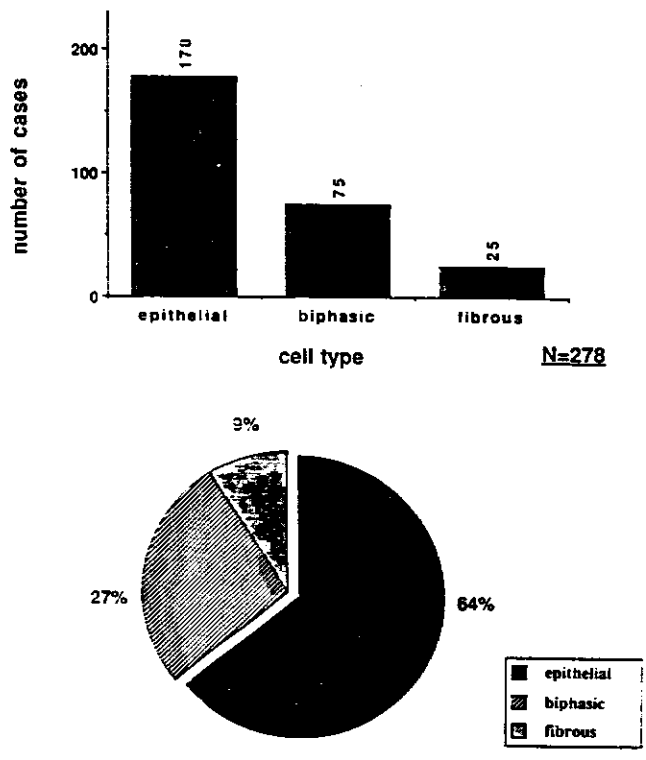


Table II

Malignant Mesothelioma Insulation Workers—Cell Type



stitial fribrosis with ferruginous bodies) was present in 95.6% of the 137 mesothelioma cases. The severity of asbestosis (represented by the degree of diffuse interstitial fibrosis) was compared between the pleural and peritoneal mesotheliomas; proportionally, severe interstitial fibrosis was higher in incidence in pleural mesothelioma (48.2% to 36.5%). The degree of asbestosis was compared between the 137 malignant mesothelioma and the insulators' lung cancer (415 consecutive cases; unpublished data). The severity of asbestosis was proportionally milder in the mesothelioma cases (44.5% vs. 56.0% in severe, 28.5% vs. 36.3% in moderate, 22.6% vs. 6.5% in mild, and 4.4% vs. 1.2% in none/minimal. (Table III).

Smoking history was available in 185 of the 278 mesothelioma cases. There were 144 present and ex-cigarette smokers (77.8%), 17 pipe and/or cigar smokers and tobacco chewers (9.2%) and 24 who had never smoked (13%). This smoking history data were compared with that of the insulators' lung cancer cases (532 in which smoking history was known): present or ex-cigarette smokers were smaller in proportion (77.8% vs. 91.6%) in the mesothelioma group, and the non-smokers were larger in proportion in the mesothelioma group (13% vs. 1.3%). (Table IV).

COMMENTS

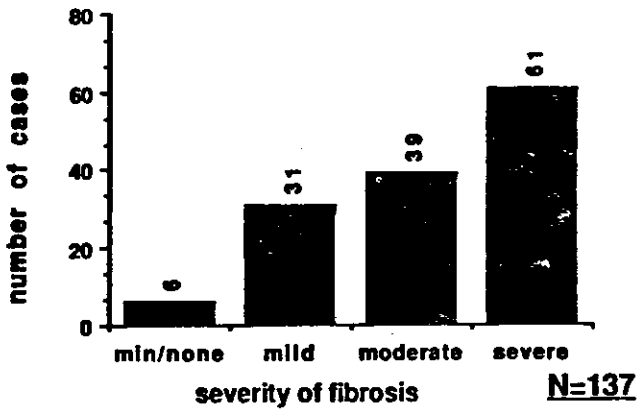
To the present, no specific single method has been available to establish a definitive diagnosis of malignant mesothelioma. Consequently, comprehensive pathological analysis of the tumor is still the best approach to establish such a definite diagnosis.[4]

It has been reported that the incidence of peritoneal mesothelioma was higher than that of pleural mesothelioma among insulation workers.[1,2] The present study has confirmed these initial reports. Presently, no clear explanation has been available as to why the incidence of the malignant peritoneal mesothelioma is so high among insulators.

The comparative proportion of cell types (epithelial, biphasic and fibrous) of the insulators' mesothelioma is similar to that of mesothelioma in general. Pulmonary asabestosis was almost always present (95.6%) in the insulators mesothelioma cases. It is known however, that pulmonary asbestosis is occasionally absent in the lung sections of malignant mesothelioma patients who had been mildly exposed to asbestos by environmental asbestos exposure or family contact to asbestos. It was interesting, when the severity of pulmonary asbestosis between malignant mesothelioma and

Table III

Malignant Mesothelioma Insulation Workers
—Interstitial Fibrosis



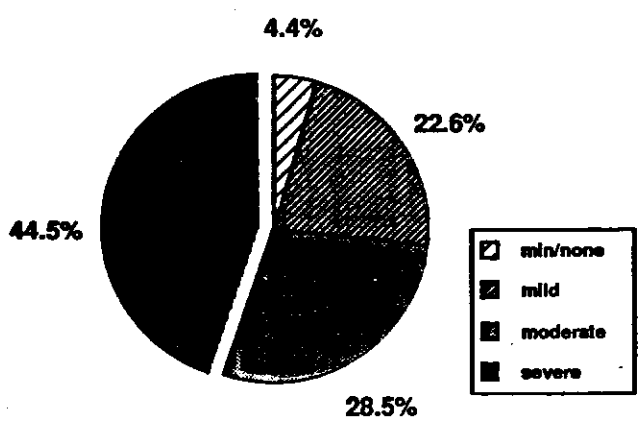
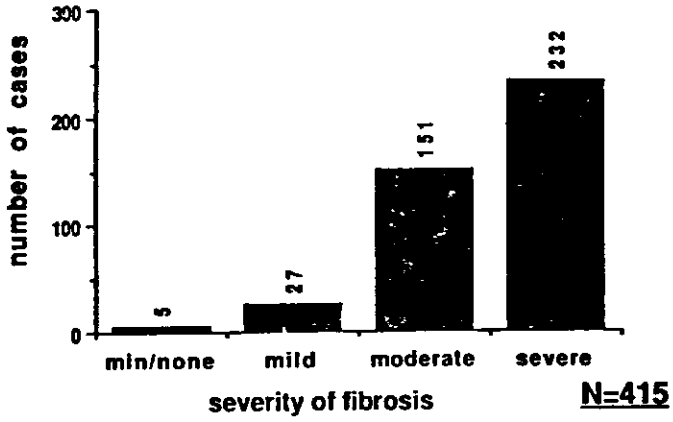


Table III

Lung Cancer-Insulation Workers
Interstitial Fibrosis



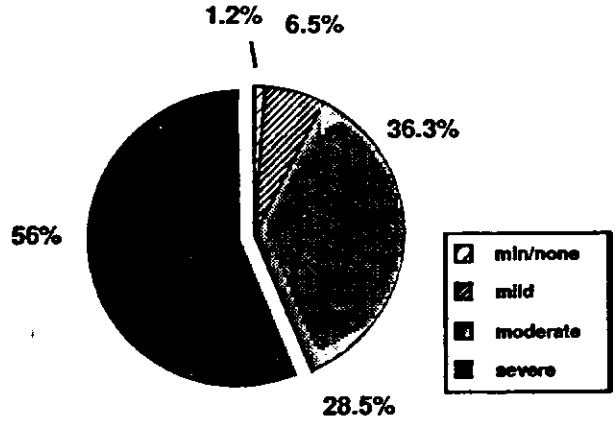
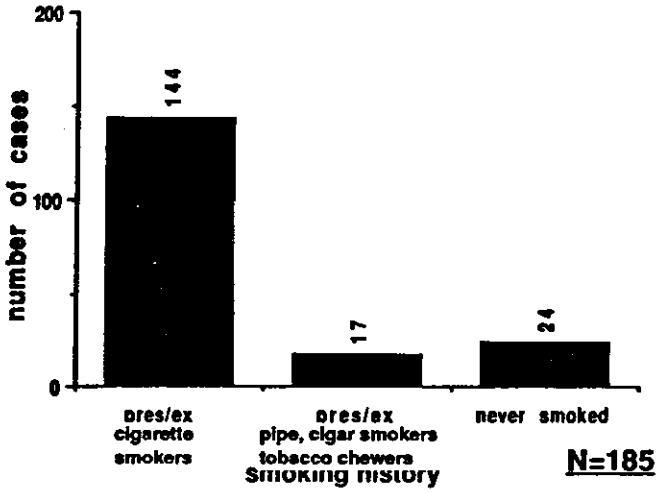


Table IV
Malignant Mesothelioma-Insulation Workers
Smoking History



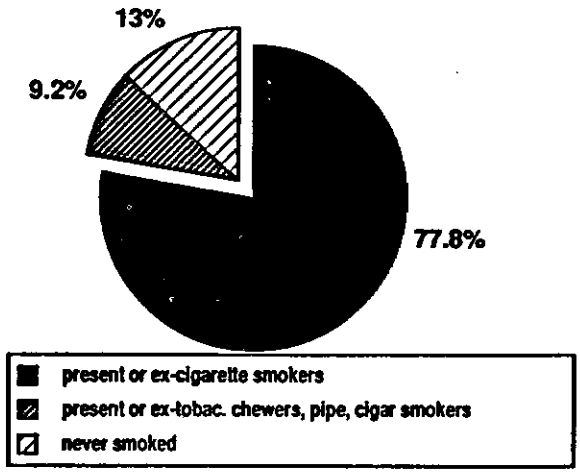
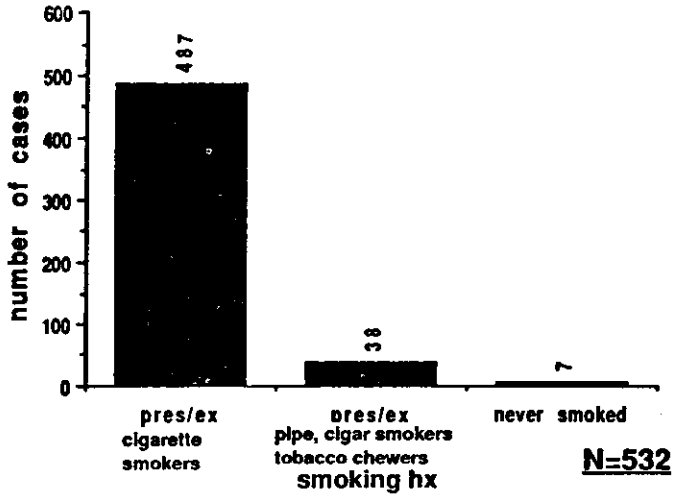
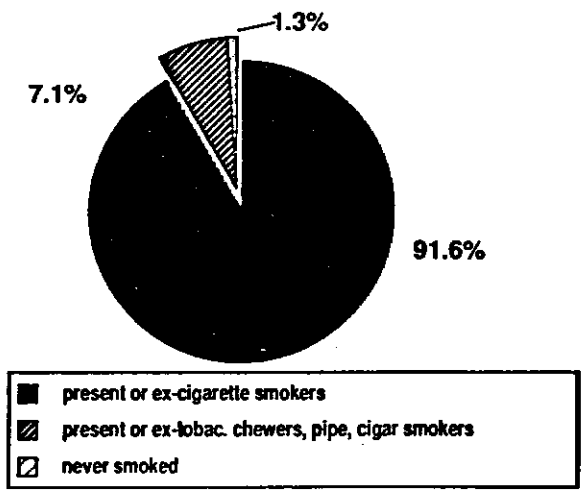


Table IV
Lung Cancer-Insulation Workers
Smoking History





lung cancer among asbestos insulation workers was compared, the former was comparatively milder in the severity.

It has been suggested that malignant mesothelioma may be induced with smaller doses of asbestos, in comparison to asbestos related lung cancer.

Age at death and years from first exposure to death were similar to that seen in other studies, including our preliminary ones of the same cohort.[1,2]

It has been reported that, unlike lung cancer, cigarette smoking does not exert a causal influence in malignant mesothelioma.[6,7] The present study has revealed that the current and ex-cigarette smokers were smaller in proportion in the mesothelioma cases, compared with those in the lung cancer cases among the asbestos insulation workers and that non-smokers were proportionally much higher in the mesothelioma cases (13% vs. 1.3%).

SUMMARY

The pathology and epidemiological features of 278 cases of malignant mesothelioma (234 definite and 44 probable) among asbestos insulators were investigated. These cases were those personally studied since 1975.

1. The primary site was 160 (57.5%) peritoneal, 97 (34.9%) pleural and 21 other (7.6%; 18 pleural and peritoneal, 2 pleural, peritoneal and pericardial, and 1 pleural and pericardial).

2. Cell types were 178 (64.0%) epithelial, 75 (27.0%) biphasic and 25 (9.0%) fibrous. These proportions were quite similar in pleural and peritoneal mesothelioma.

3. Histopathologically, pulmonary asbestosis was found in 95.6% (131/137) of the mesothelioma cases; 44.5% were severe, 28.5% moderate, 22.6% mild, and 4.4% were minimal or none.

4. 89.9% (250/278) were 50 and older at death. None were 39 or younger. Years after 1st exposure to death were 20 years and longer in 99.6% (272/273). None were found in less than 9 years. A single case was seen between 10 and 19 years.

5. There were present and ex-cigarette smokers in 144/185 (77.8%), 9.2% cigar, pipe and chewing tobacco, and 13% (24/185) were non-smokers. Non-smokers were proportionally much higher in comparison with the insulators' lung cancer cases.

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PLEURAL PLAQUES IN A U.S. NAVY ASBESTOS SURVEILLANCE POPULATION: PREDOMINANT LEFT-SIDED LOCATION OF UNILATERAL PLAQUES

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ABSTRACT

The radiographic distribution of pleural plaque was studied in a U.S. Navy Asbestos Medical Surveillance population of 105,064 workers. Chest radiographs were interpreted to show "possible" (1.8%), probable (2.5%), or "definite" (1.8%) plaque. Plaques were more likely to be bilateral as interpreter certainty increased, but 19% of "certain" pleural plaques were still unilateral. Of these unilateral plaques there was a marked left-sided predominance, which increased with increasing certainty of interpretation. Further research is needed to determine whether this consistent left sided predominance of unilateral plaque represents: lateralizing interpreter bias, greater visability of plaques when they are on the left, or some physiologically greater susceptibility of the left side.

No paper provided.

PUBLIC HEALTH IMPLICATIONS OF THE VARIABILITY IN THE INTERPRETATION OF "B" READINGS

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BACKGROUND

Despite the care that has been given to interpretation, competent observers have repeatedly encountered difficulties in the consistent classification of radiographs. Researchers have been aware of the variability present in the interpretation of chest radiographs for many decades. As early as 1947, Birkelo published a paper evaluating the prevalence of tuberculosis observed in chest radiographs.[1]

Shortly after this study was conducted, Garland published a classic study on the scientific evaluation of diagnostic procedures. In this paper, Garland states that "though useful when, as occasionally happens, the chest radiograph is used as the sole examination, its reliability may be evanescent." He goes on to say in "nearly every activity that can be tested, it has been repeatedly demonstrated that humans, even experts in a given field, exhibit enormous variations in their ability to be consistent with themselves and others equally competent in applying to mass-survey work. ... Consequently, every day persons throughout the country are being informed that their chests are free from disease when, in point of fact, they probably are not (and visa versa). This results in false security on the one hand and needless alarm on the other hand."[2]

The purpose of this paper is to discuss the public health implications of the reliability of the "B" reading program, that is, the ability of different "B" readers to accurately and consistently reproduce findings during repeated examination of radiographs of people with disease of known or unknown status. For example, when a problem with pneumoconiosis is suspected, films may be submitted to one or several readers for interpretation. If multiple readers agree, then it is likely that their interpretation is correct. It is possible that readers may agree and still be incorrect in their interpretation. If agreement is low, then the usefulness of the interpretation is suspect.

METHODS

The issues on which this paper is based arose from a call received by the Minnesota Department of Health (MDH) in January, 1985, from a "B" reader and radiologist (Reader 1) in northern Minnesota. This is an area that has historically had many problems related to asbestos in mine tailings. The radiologist stated he had found diffuse and/or circumscribed pleural thickening in approximately 30% of 500 sequential chest radiographs taken during the preceding two months in his clinic practice. Subsequent review of the films by MDH staff led to consultation with the National Institute for Occupational Safety and Health (NIOSH).

At the request of the MDH, a "B" reader (Reader 2) from NIOSH came to Minnesota to review these findings. Reader 2 reviewed 259 films interpreted by Reader 1 and 310 films from other regional clinics. Reader 2 confirmed the apparent increase in pleural changes seen by Reader 1 and noted similar increases in other regional clinics. Because of the confirmed increase, two additional radiographic evaluations were arranged.

Five hundred and sixty-six films were transported to Reader 3, a pulmonary physician and experienced "B" reader in New York City. Following this third reading, the films were shipped to NIOSH in Morgantown, West Virginia. At NIOSH, the films were randomly allocated in equal numbers among ten blocks. Negative and positive control films were added so there were 100 films per block. Positive control films were selected for the presence of pleural changes. Films were then interpreted independently by three readers who had been selected from a panel of five readers. The trial was a randomized incomplete block design with each of five readers being assigned six blocks and each film read a total of three times. Films were read in Morgantown, and readers were unaware of the origin of the films. Except for Reader 1, all readers interpreted the films according to the 1980 International Labor Office (ILO) classification system. Reader 1 interpreted films only for pleural changes.

ANALYSIS AND RESULTS

A kappa statistic was used to measure concordance between Readers 1 through 3. Concordance was not measured in this way between members of the NIOSH panel because of the large number of possible combinations. This statistic measures agreement between readers and simultaneously accounts for agreement due to chance. A kappa statistic is continuous and ranges between -1 and $+1$. A statistic of 0 or less represents poor agreement and a statistic of $+1$ reflects complete agreement.[3]

As seen in Table I, concordance between Readers 1 and 2 was moderate (kappa = 0.58) for the presence of any pleural thickening. Readers 2 (NIOSH consultant) and 3 (New York reader) agreed on 70 films being positive for pleural changes and the kappa statistic was 0.39, once again indicating a moderate degree of concordance (Table II). However, when

Table I

Presence of Pleural Thickening: Concordance Between Readers 1 and 2

Pleural Thickening (First Reader)	Pleural Thickening (Second Reader) Absent	Present	Total
Absent	97 (37.4)*	23 (8.9)	120 (46.3)
Present	32 (12.4)	107 (41.3)	139 (53.7)
Total	129 (49.8)	130 (50.2)	259 (100.0)

*Percent
KAPPA = 0.58

Table II

Presence of Any Pleural Changes: Concordance Between Readers 2 and 3

Pleural Thickening (Second Reader)	Pleural Thickening (Third Reader) Absent	Present	Total
Absent	363.5)*	13 (2.3)	364(65.8)
Present	119(21.5)	70(12.7)	189(34.2)
Total	470(85.0)	83 (15.0)	553**

* Percent
** Excludes 13 films rated as not readable.
KAPPA = 0.39

pleural plaquing and diffuse pleural thickening were examined by side (Tables III and IV), concordance was poor, with a kappa statistic of 0.26 and 0.20 respectively. Thus under more stringent criteria, agreement appeared to diminish considerably.

According to Readers 1 and 2, approximately 70% of males and 25% of females from Reader 1's clinic had pleural abnormalities. The proportion of males and females read as positive varied considerably between Readers 2 and 3. Overall, Reader 2 noted 54% of males and 15% of females had pleural abnormalities. Reader 3 found 25% of males and 5% of females had pleural abnormalities. The NIOSH readers found 8% of males and less than 1% of females positive for pleural changes. These differences between readers were statistically significant using McNemar's test.[3]

Table V shows the number of Minnesota films read as positive by zero, one, two, or three of the NIOSH (Morgantown) readers. A total of 24 (4.2%) of the Minnesota films were read as positive by at least two readers. In addition, the number of positive control films (n=34) read as positive (i.e., sensitivity) was approximately 55% but varied slightly from reader to reader. The number of negative control films (n=400) read as negative (i.e., specificity) was 98% or more for all readers.

Data from the control films were used to estimate the conditional probability of a film being positive given zero, one, two, or three positive readings (Table VI). The value for "Π" represents the approximate probability of a film being positive if it was drawn at random from the batch of all Minnesota films. The value for "p1" represents sensitivity and the value for "p2" represents specificity. For this trial, we see that the conditional probability of a film being positive for any pleural changes given zero, one, two, or three positive readings (under the conditions of this trial) was

Table III

Pleural Plaquing*: Concordance Between Reader 2 and Reader 3 Bilaterally

Pleural Plaquing (Second Reader)	Pleural Plaquing (Third Reader) None	Unilateral Left	Unilateral Right	Bilateral	Total
None	393	1	6	1	401
Unilateral Left	17	3	0	0	20
Unilateral Right	17	1	4	1	23
Bilateral	77	8	10	14	109
Total	504	13	20	16	553

* Only includes plaques noted on the chest wall
KAPPA = 0.26

Table IV

Diffuse Pleural Thickening: Concordance Between Reader 2 and Reader 3 Bilaterally

Diffuse Thickening (Second Reader)	Diffuse Thickening (Third Reader) None	Unilateral Left	Unilateral Right	Bilateral	Total
None	503	4	1	1	509
Unilateral Left	10	4	0	0	14
Unilateral Right	7	0	1	1	9
Bilateral	19	1	1	0	21
Total	539	9	3	2	553

KAPPA = 0.20

Table V

Number of Films with Zero, One, Two, or Three Positive Readings for Pleural Changes*

	Category of Film Reading			
	Zero	One	Two	Three
Number	436	44	14	10

*NIOSH readers only.
Sixty two unread films are not counted.
(N = 566, including unread films.)

Table VI

Probability of a Film Being Positive Given Zero, One, Two, or Three Positive Readings for Pleural Changes*

	Number of Positive Readings			
	0	1	2	3
$\Pi = 0.09$				
$P_1 = 0.55$	0.01	0.36	0.97	~1.0
$P_2 = 0.98$				

NIOSH readers only.

0.01, 0.36, 0.97, and approximately 1.0 respectively. It should be noted that values for Π, sensitivity, and specificity are dependent upon the mix of positive and negative radiograph readings.

In order to further evaluate the reasons for the variability observed in the NIOSH trial, logistic regression procedures were used with the absence and presence of pleural changes coded 0 and 1 respectively. Independent variables used in the prediction equation were age (<60, ≥60), sex, parenchymal opacity profusion (two levels, ≤0/1 and ≥1/0), and the presence of other pulmonary abnormalities (two levels: none, any). The regression model fit well and there were no significant interaction terms. Assumptions required for logistic regression were satisfied. The summary odds ratios and 95% confidence intervals for each of five NIOSH readers are presented in Table VII. For example, Reader 1 was 5.5 times more likely to find evidence of pleural changes if the film being interpreted had evidence of parenchymal opacities of 1/0 or greater compared to films with opacities rated 0/1 or less. As seen in this table, age and sex did not influence radiograph interpretation for pleural changes. However, for some readers, profusion and/or the presence of other diseases

Table VII

Odds Ratio and 95% Confidence Intervals for Four Factors Used in Predicting the Presence or Absence of a Positive Reading for Pleural Disease

	Factor			
Reader	Age	Sex	Profusion	Other Abnormalities
1	NS*	NS	5.5 (1.6, 18.6)	4.6 (1.5, 13.9)
2	NS	NS	NS	NS
3	NS	NS	NS	3.4 (1.2, 10.0)
4	NS	NS	26.1 (7.7, 88.3)	NS
5	NS	NS	NS	4.7 (1.2, 18.2)

* Not significant.

appeared to exert a moderate to strong influence on the interpretation of films for the presence of pleural abnormalities.

DISCUSSION

Many studies have been published evaluating factors that affect the interpretation of radiographs. These factors include: film quality, subject age and weight, presence of disease, and reader.[4-10]

Liddell found that film quality tended to be higher for radiographs of men with no evidence of coal worker's pneumoconiosis and to decrease with increasing chest wall thickness. The subject's age was not found to substantially affect film quality.[5] Pearson et al. found that the proportion of unsatisfactory films increased with increasing values of the ratio of weight to sitting height.[8] These findings are of interest because it has been demonstrated that technical faults are, in general, randomly distributed and attributable to errors in taking and processing films rather than in differences between subjects even though there may be a slight tendency for the proportion of unsatisfactory films to increase with increasing weight.[8]

Further, Liddell found film quality introduced only slight biases into the reading of pneumoconioses although readers tended to find more parenchymal abnormalities in overexposed films and fewer parenchymal abnormalities in underexposed films when compared to good films.[5] Other investigations, however, have found that readers tend to read more abnormalities in underexposed films and less abnormality in overexposed films.[6,7] In Minnesota, film quality was adequate for all but a handful of radiographs. For this reason, it seems unlikely that film quality affected the results of the Minnesota study.

Reader experience also plays a role in the evaluation of radiographs. Different readers appear to compensate differently for changes in film quality. Reger et al. found that

experienced readers were better able to compensate for changes in film quality. In addition, certain readers either consistently find more abnormalities or less abnormalities on films compared with their colleagues.[9] Felson et al. found that readers with minimal training tended to find more cases of coal workers with pneumoconiosis than experienced readers. Felson attributed the differences between readers found in his study to several factors: 1) inherent interobserver disagreement; 2) lack of experience with the classification system in use; and 3) lack of familiarity with the radiographic manifestations of coal workers' pneumoconiosis.[10]

The problems encountered during the MDH investigation were in many ways similar to those described above. The percentage of films interpreted as abnormal varies among readers. These readers appeared to have been influenced by factors such as the presence of disease, and anecdotally, reader experience may have played a major role. The original readers were both newly certified "B" readers and were not experienced in interpreting films with asbestos-related disorders. These were also the readers who found the highest percent of individuals with pleural changes.

Two years after the original investigation was completed, eight radiographs that the investigators thought were "definitely positive" were sent to a pulmonary physician for review. After reviewing the medical records and films, this physician felt that the pleural and/or parenchymal abnormalities in six of the cases (75%) could be best explained by the presence of diseases unrelated to the pneumoconioses.

This finding, in part, led the MDH to once again evaluate the original data and develop the logistic regression model described above. This model confirms that the reading of radiographs for the presence of pleural abnormalities is at times strongly influenced by the presence of parenchymal opacities and/or diseases; however, it was not possible to define the nature of this relationship.

The magnitude of inter-reader agreement has undergone considerable scrutiny. Early studies on this problem were conducted by Birkelo, Garland, Fletcher, and Yerushalmy.[1,2,10,11] In 1970, Reger and Morgan had 2,337 radiographs evaluated by 4 readers. The percent of films interpreted as having complicated coal workers' pneumoconiosis ranged from 8.0% to 22.5%.[9] In only slightly more than one half (56.7%) of these films was there agreement between readers. Felson et al. evaluated inter-reader agreement for 3 readers. For films read as normal, pairs of readers agreed with each other between 10.1% and 68.9% of the time. For abnormal films, agreement ranged between 5.5% and 10.2%.[10]

Several studies have examined the variability in the radiographic assessment of pleural changes. In a review of 674 radiographs of naval dockyard workers, Sheers et al. found the prevalence of pleural changes to range between 14% and 30%.[12] Reger et al. evaluated inter-reader variability in the radiographic detection of pleural changes in 555 radiographs.[13] Radiographs were evaluated twice for each worker—first using a posterior-anterior (PA) film and then using PA plug oblique films. The prevalence of pleural abnormalities in this study ranged between 40% and 81% and a higher detection rate was found with the use of additional radiographs. Using PA films only, the kappa statistic for inter-reader agreement for the presence of pleural plaques averaged 0.33 and for diffuse pleural thickening 0.43. The addition of oblique films caused a decrement of the kappa statistic to 0.23 and 0.25 for pleural plaques and pleural thickening respectively.[13]

A higher detection rate of pleural abnormalities using three radiographs (left anterior, oblique, right anterior oblique and PA) compared with PA only was also shown by Baker and Green.[14] The high detection rate, however, appears to be at the expense of sensitivity, specificity and reliability.[13] The number of positive control films read as positive (i.e., sensitivity) was only 55% in the MDH study. It seems that any further decrement in sensitivity resulting from the use of oblique films would, in most instances, be unwarranted.

Green et al. examined the effect of using a broad (any pleural thickening) versus a strict criterion (pleural thickening of 2 mm or greater) on the prevalence of pleural changes in high risk (asbestos exposed) and low risk (no or little asbestos exposure) groups. Using a broad criterion, prevalence ranged from 45.1% (low risk) to 40.9% (high risk), and, using a strict criterion, prevalence ranged from 2.6% (low risk) to 9.4% (high risk).

Depending upon the number of positive readings and the readers selected, the percent of Minnesota films positive for pleural changes varied between 2% and 38% (Table VIII). Thus, we were faced with a problem where "case definition" was highly dependent upon the judgement of the investigators and it was not clear which was the best set of interpretations to use. We do not feel the results of the MDH study support the use of a specific (e.g., 2 mm) threshold criteria. However, we concur with the conclusion of Green et al. that there is a "great need for specific criteria and uniform methodology" in the interpretation of pleural findings.

The low sensitivity and high inter-reader variability present in the evaluation of films for asbestos-related pleural or parenchymal changes could significantly influence the results of an epidemiologic study. Readers 1 and 2 found a large

Table VIII

Number of Positive Pleural Readings by Sex
(N = 2755 Readings)*

Number of Positive Readings	Sex		Percent Of Total	Total
	Male	Female		
0	122	231	62	353
1	82	38	21	120
2	38	8	8	46
3	23	5	5	28
4	10	0	2	10
5	8	1	2	9
Total	283	283		566

* Five B Readers per film (10 not read by reader 2, 3 not interpreted by reader 3, and 62 not interpreted by members of the NIOSH panel.

number of abnormalities in both men and women indicating what appeared to be a generalized environmental exposure to asbestos. Subsequent investigation revealed widespread steam tunnels to many regional homes. These tunnels, as well as the pipes within homes, appeared to be asbestos-lined. Another possible source of exposure was piles of taconite mine tailings near or within town limits. Because of concern about environmental exposures, the third and subsequent readings were done. In later readings, when substantially fewer abnormalities were found in women, it was thought that the problem was probably occupational rather than environmental in origin.

It is felt that the low sensitivity of the interpretation of radiographic changes of the pleural should be more widely recognized among those involved in occupational disease surveillance. The impact of this variability in radiographic readings on public health decisions was illustrated in Minnesota and, to date, the significance of these apparent abnormalities is still difficult to evaluate.

Based on these findings and a review of the epidemiologic literature, we feel further consideration should be given to resolving the issues presented here. We would like to make the following recommendations to optimize the use of information found on the chest radiograph:

1. A threshold for determining the presence or absence of pleural changes should be developed. In part, the problem encountered by the MDH arose because of the ambiguity in defining pleural changes. Dr. E. Nicholas Sargent (personal communication) recommends the use of a scoring system similar to that used for parenchymal changes (e.g., 0/0, 0/1, 1/0, 1/1) with 0/0 indicating a high degree of certainty that a particular shadow does not represent a pleural abnormality (e.g., muscle, fat) and 1/1 indicating a high degree of certainty that a shadow does represent a pleural abnormality (e.g., plaque);

2. Experiments should be conducted in which the "B" reader is asked to interpret films with and without an abbreviated medical history. At the end of each reading, the interpreter should be asked to conclude if, given the patient's (worker's) medical history, any changes seen are most likely due to a pneumoconiosis, other disease, both, or if such a determination cannot be made;

3. It appears that the interpretation of pleural changes may be too complex. This complexity makes the interpretation of inter-reader agreement difficult. If possible, the reading of pleural changes should be simplified;

4. One third of the "B" reading form is devoted to interpreting changes of the pleura. However, there are very few films in the set of ILO standard films devoted to these changes. These films should be enhanced to reflect the degree and nature of changes that are presented on the ILO-NIOSH "B" reading form; and

5. "B" readers, in the course of their training, should be cautioned about the implications and utility of "B" reading. Knowledge of the problems involved in the epidemiologic use of radiographs should be a routine part of the "B" reader examination and/or course of study.

Inter-reader variability in the interpretation of radiographs has been evaluated in the past. This is the first instance known to the authors where this problem has had a direct impact on public health. When initially presented with this problem, the authors (DP and AB) consulted national experts on asbestos-related disorders; all agreed that we might have a major public health problem related to environmental asbestos exposure. As our investigation evolved, it appeared that this was not really an environmental problem at all, but was due to inter-reader variability in the interpretation of radiographs, thus substantiating previous studies on the problem of inter-reader variability.

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THE CANADIAN PNEUMOCONIOSIS READING PANEL STUDY

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ABSTRACT

The Canadian Pneumoconiosis Reading Panel was organized to determine the reading levels of volunteer Canadian physicians on the 1980 pneumoconiosis classification, and to develop a feedback method for influencing a uniform level of readings. 999 chest X-rays were selected from three groups:[1] 40–70 year old males with no fibrogenic dust exposure and whose X-rays were taken because of a statutory requirement. No films from this group were rejected because of symptoms or radiologic abnormality.[2] Workers in silica or asbestos exposure with normal initial films who later developed silicosis or asbestosis.[3] Additional films represented several other industrial lung diseases. 30 randomized films were read every 2 weeks in rotation by 26 readers. Feedback analysis indicated whether a reading was within 1 minor category of the group average for a given film on small opacities or was over or under that criterion. It is hypothesized that with continuing experience most readers will eventually read near the group mean and outliers may be identified. Subsequent group readings are proposed on an annual or bi-annual basis. At the present stage all films have not been read by every member and no overall group mean categorization of each film is available. Feedback has, therefore, been provided in relation to readings by a single reader from the National Coal Board who has evaluated all films. Results of the first returns show that 31% of films were overread by panel members in comparison with this reader, 4% were underread and 65% were in agreement, as defined above. Subsequent feedback results are under analysis. Advantages and disadvantages associated with the method will be discussed.

The ILO Classification was developed to help in the coding of X-ray appearances of the Pneumoconioses for epidemiologic purposes. This should allow comparison between readings done under different jurisdictions.

Since its introduction in 1958, the ILO system has undergone several changes, until the (1980) protocol confirmed that reference films and the not definitions should take precedence in cases of doubt.[1] The absence of such proviso prior to 1980 has led to quite marked differences of opinions between expert readers in different areas. The 1980 modification of the ILO Classification was introduced for routine use by the Chest Clinics run by the Government of the Province of Ontario in 1983, once the MESU (Medical Surveillance) computer data entry facilities became available.

With routine use of the ILO Classification arose a need to ensure that all readers interpret the code uniformly. While various attempts to meet this problem have been made elsewhere, there existed no system of quality control of ILO readers in Canada. A national network of readers was required in order to assure that consistency and reliability of readings are maintained. The Canadian Pneumoconiosis Reading Panel[2] was formed to meet two essential requirements: 1) to determine the current reading levels of physicians in all Canadian provinces who employ the ILO 1980 radiographic pneumoconiosis classification, and 2) to develop a method of feedback which would influence those physicians to approach a uniform standard level of reading.

The initiative to form the panel came from physicians at the Ministry of Labour (Ontario) and from the McMaster University. The two best known models of quality control of ILO readers, the British and the American were reviewed.

In the United Kingdom the program is run entirely by the National Coal Board which decides who shall sit on the panel of readers. Panel members are regularly tested and their reading patterns evaluated. Incorrigible outliners are eliminated.

As run by the National Coal Board, the British system is very efficient. It is however, designed for and operating in a small, densely populated country.

In the United States, a different system is used. Regulations under the Federal Mine Safety and Health Act[3] give statutory recognition to official users of the ILO system who are known as "A" and "B" readers. The status of an A or B reader is obtained after successfully passing appropriate examinations set up by NIOSH. The recent proposals for requalification every three years rather than four indicates that some doubt arose about qualified readers being able to sustain an even quality of readings between examinations and in maintaining uniformity of readings in International com-

parisons. Some 40 Canadian physicians known to be reading pneumoconiosis films were contacted and agreed to become members of an all-provinces germinal body of the reading panel.

METHODOLOGY

More than 10,000 films were gathered by the Ministry of Labour and from that quantum a test collection of 1,000 plates was made. The final selection of films was made by three readers from the Ministry of Labour and one from the University of McMaster (Table I).

The 309 "normal" films were from government employees whose X-rays were taken because of a statutory requirement of the day, and who according to records had never worked in fibrogenic dust exposure; they were males between the ages of 40 and 70; and no films were rejected because of symptoms or observed abnormality.

Table I

Sources for Film Selection

Civil servants, obligatory films	309
Asbestos (insulators)	104
Asbestos (Quebec miners)	49
Asbestos + silica	4
Silica (foundry)	57
Silica (Ontario hard rock miners)	339
Coal workers (British)	100
Nepheline syenite	15
Hard metal (tungsten c. - cobalt)	8
Talc	6
Beryllium	4
Bauxite (hydrous aluminum oxide)	5
TOTAL	1,000

Three hundred and thirty-nine films were selected from known Ontario hard rock miners in silica exposure who had normal initial films and who by consensus reading eventually developed silicosis.

A large proportion of films from that series were selected from the stage where half of the selection panel readers read 1/0 and the other half 1/1 for small regular opacities.

Analogous selection methods were used for choosing 104 films from Ontario Asbestos Workers. Additional films were received from the British National Coal Board and from Quebec Asbestos Mine Survey.

The selected films were completely randomized, their labels of origin blackened out and then divided into lots of 30 films which were sent every two weeks in rotation to each of 26 readers, who remained available of the original 40.

Readers record their findings and return reports to a central depository. At quarterly intervals, feedback is provided with indication of whether a reader is within 1 minor category of the group average for a given film or is over or under the criterion. For this presentation, complete records are available on only 16 readers. Ten dropped out because of inability to maintain a regular flow of 30 films every 2 weeks and held up the distribution process.

It is hypothesized that with continuing feedback most serious readers will eventually read near the group mean and the outliners will be identified.

After an initial development period, group readings with all available members are proposed on an annual or bi-annual basis.

At the present stage all films have not been read by each member of the panel and no overall group mean categorization of each film is available. Feedback has therefore been provided in relation to readings by a single reader from the British National Coal Board who has evaluated all films.

DISCUSSION

Looking at the available data (Table II, Figures: 1, 2, 3, 4 and 5) it appears that our hypothesis is supported by subsequent facts. During the time of the study, 14 out of the 16 readers agree more with the standard while 2 of them agree less. Also there is less over as well as under reading. However, one has to be very much aware of the shortcomings

Table II

88-07-19 ILO Panel Comparisons

Analyzed Data Presented as a Percentage of Valid Readings

PHYS	OVER-READING			AGREEMENT			UNDER-READING		
	1ST	2ND	3RD	1ST	2ND	3RD	1ST	2ND	3RD
01	23	15	17	74	75	77	3	10	6
02	27	30	32	68	64	61	5	7	6
03	35	35	25	62	61	70	3	4	5
04	21	11	7	73	82	89	7	7	4
05	17	11	9	74	81	84	9	8	7
06	40	35	40	57	61	56	3	3	4
07	29	24	21	69	70	74	2	5	5
08	20	12	7	74	82	93	6	5	0
09	50	42	25	49	57	75	2	2	0
10	27	25	15	68	74	85	0	0	0
11	6	9	5	86	81	88	8	9	7
12	28	22	13	71	72	82	2	6	5
13	35	29	21	63	70	75	3	1	3
14	18	13	11	76	81	88	5	6	7
15	30	—	18	66	—	78	4	-	4
16	38	19	23	61	80	74	1	1	3

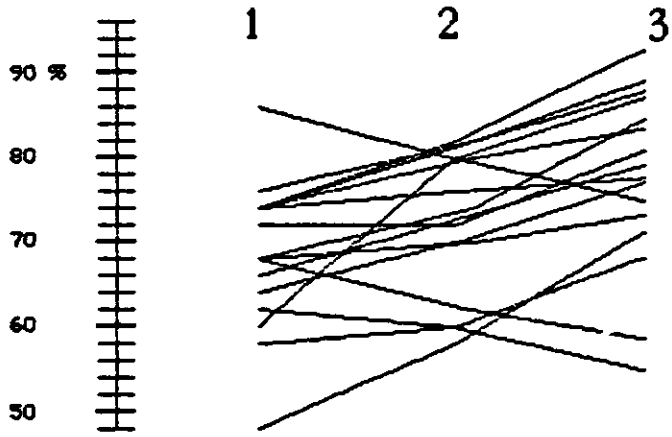

Figure 1. Agreement with provisional standard.

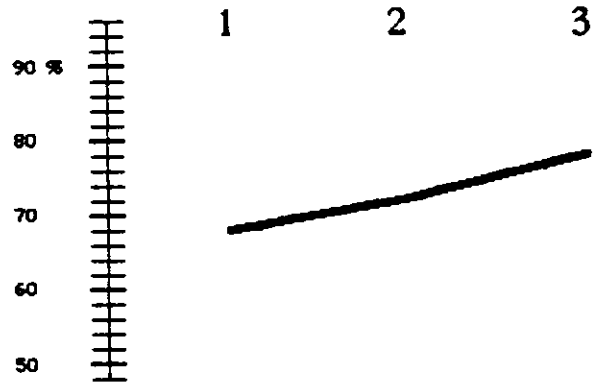

Figure 2. Average agreement with standard.

	Agree	Over-read	Under-read
More	14	1	8
No change	0	1	3
Less	2	14	5

Figure 3. Change in agreement with standard.

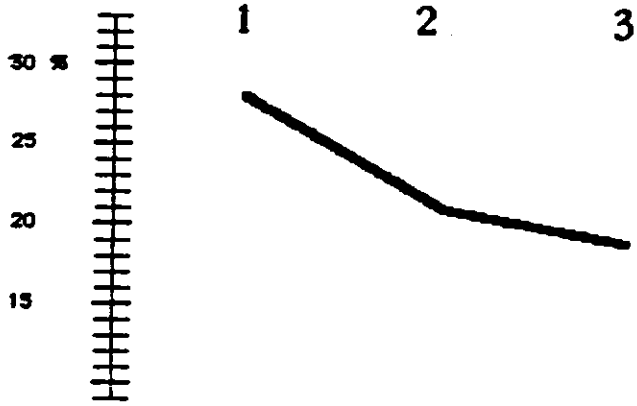

Figure 4. Over-reading of small opacities.

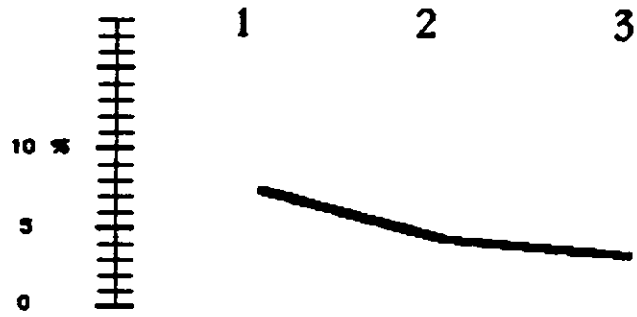

Figure 5. Under-reading of small opacities.

of this study which is no more than a preliminary communication on an ongoing project.

The number of readers was small as is the number of films reported in the third reading, (due to a slow distribution system that had to be revised). In this context, it should be noted however, that the apparent trend is the product of roughly 8,000 individual reports, as each of the 16 readers has read around 500 of the test films currently available.

No comparison with other countries other than Great Britain. Last, but not least, there were no controls. Bluntly put, one does not know to what extent the apparent trend is the result of the feedback information offered, and what would happen if members of the panel were left to their own devices.

Future efforts therefore, should include 1) setting up a control group of readers who will receive less or no feedback; 2) current standard may need to be revised using a larger number of films.

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CHEST IMAGING: A NEW LOOK AT AN OLD PROBLEM

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The chest is one of the most complex segments of the body to examine radiographically. Comparison radiographs of the chest are challenging to an interpreter. Since radiographic technique can affect the management of the patient, it is extremely important to document the technical factors used for a chest examination. Follow-up studies must be technically consistent.

The use of a short exposure time (10 ms or less) helps stop motion. Minute vascular patterns or calcification must not be "blurred out." If one were to purchase a state-of-the art chest radiographic room, at the present time a typical recommendation would be a three phase generator with 150 kVp output combined with a 10:1 or 12:1 ratio grid. Techniques required for pneumoconiosis utilize lower kilovoltage values (approx. 110 kVp) with high ratio grids. Although the air gap technique has been popularized in Canada by Wilkinson and Fraser, this technique is not in common use in the United States.

The enactment of Public Law, 91-173, stating that every underground coal miner shall have an opportunity to have a chest X-ray examination for the purpose of establishing health and safety standards for the nations coal miners, generated new interest in chest radiographic technique.

CONTROL OF SCATTER RADIATION

Scatter radiation can segmentally damage a radiographic image. A chest radiograph can appear to be properly exposed, but portions of that image can be damaged by scatter. In a non-grid chest image, up to 65% of the radiation reaching the screen/film can be scatter. Non-grid chest radiographs are usually made at approximately 85 kVp, often with a single phase generator with a timer of questionable accuracy. Modern chest studies utilize high ratio grids with high kilovoltage values.

Common problems encountered with grid radiography of the chest include:

1. Improper processing conditions, particularly with hand processing. The use of an automatic processor does not guarantee quality radiographs unless a Quality Assurance program is utilized.
2. Grid focus. Often an improperly focused grid is used for chest radiography. If a medium focus grid (40" FFD) instead of a long focus grid (72" FFD) is used for chest radiography, a bilateral grid cutoff (approximately 2" of each side of the chest radiograph) occurs. Both costophrenic angles seem underexposed. This bilateral artifact can be interpreted as poor screen contact. Incidentally, poor centering to a grid can produce unilateral cutoff of an image. The use of a laser positioning device helps center the central ray to the grid as well as the patient to the film holder.
3. A low to moderate kilovoltage value with a high ratio grid, can be disastrous with a high contrast radiographic film. As kilovoltage is raised, for example to 140 kVp, a high ratio grid (12:1) must be used. As kilovoltage is lowered, for example to 90 kVp, a 6:1 low ratio grid is required.

   There is a difference in radiographic techniques when using either single phase or three phase equipment. Three phase radiation is virtually ripple free as opposed to single phase X-ray (100% ripple). Dramatic technical adjustments in kilovoltage must be considered, for example, a single phase 125 kVp technique requires approximately 108 kVp when using a three phase generator. Since three phase current is virtually ripple free, higher ratio grids are often required.
4. Poor inspiration. This problem is compounded when using an automatic exposure control such as a photo timer or an ionization chamber. If a patient is exposed at maximal expiration, even though the diaphragms are elevated and the cardiac silhouette is widened, an adequate density is often produced by an automatic exposure control. Proper density (blackening) cannot overcome cardiac distortion or compacting of the lungs due to expiration.

MEDIASTINAL INFORMATION

Information gained regarding the mediastinum is often at the expense of proper exposure of the lung fields. The use of a compensatory filter to "see through" the mediastinum is a substitute for a film with appropriate sensitometric characteristics. Latitude or extended latitude films are re-

quired for mediastinal information. A compensatory filter has a fixed opening for mediastinal penetration; "one size does not fit all."

THREE PHASE

If the same kilovoltage value, for example, 110 kVp is used with single phase and three phase generators, the three phase image will produce scatter similar to a single phase 125 kVp exposure. Unless, mAs values are lowered either manually or by an automatic exposure control, the three phase image will be approximately 2X overexposed. Even when an appropriate mAs adjustment is made, there is a difference in contrast with the three phase study. A higher ratio grid may be required for three phase imaging techniques. Three phase exposures are shorter than single phase exposures and help to stop motion.

AUTOMATIC EXPOSURE CONTROL

An Automatic Exposure Control (AEC) helps insure that exposures are of consistent density. The radiographer initiates the exposure but the AEC determines its length. Positioning skills are essential. Relationship of a patient to the AEC sensor must be a constant concern. In the lateral projection, if the patient moves slightly backward, a large portion of the cassette will be exposed to the primary ray. This "primary beam leak" produces considerable scatter that can strike the lateral sensor, shortening the exposure time.

When using an AEC, concern for the minimal response (minimal reaction) time of the unit is essential. The minimal response time is defined as the shortest possible automatic exposure achievable by your AEC. The use of faster screen/film combination produces more film blackening per unit of exposure, and can accentuate your minimal response time difficulties particularly with older equipment. Often, a small to medium patient will require less radiation for proper exposure of their chest radiograph, than an AEC is capable of delivering at a predetermined kilovoltage and milliampere setting. If a high kilovoltage three phase technique is used, the MRT may produce technical difficulties with more than half of your images. If a proper kilovoltage has been selected with an appropriate grid, and if your minimum response time (often 100th/sec) cannot be changed, then the milliampere setting must be lowered to match patient size. For example, a frail, approximately 100 lb. patient could require 50 mA, while a muscular adult might require 300–400 mA.

CAUTION: Never reduce kilovoltage to compensate for an MRT difficulty. A reduction in kilovoltage produces short scale contrast with blackened lungs and chalk-like osseous and mediastinal structures.

COLLIMATOR DIFFICULTIES

On occasion, an image "cutoff" can occur on a radiograph if one of the internal shutters of the collimator is out of alignment. The shutters within the collimater closest to the X-ray tube can be misaligned. If a shutter slips into the primary beam, there is a radiation cutoff. Unfortunately, the light beam pattern on the patient formed by the collimator is created by the exit shutters. A simple test to determine if this difficulty is occurring with your unit will be demonstrated during this presentation as well as during the poster-board demonstration.

A COMPARISON OF THE PROFUSION AND TYPE OF SMALL OPACITIES REPORTED WITH THE 1980 AND 1971 ILO CLASSIFICATIONS USING READINGS FROM THE COALWORKERS' X-RAY SURVEILLANCE PROGRAM

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INTRODUCTION

The 1980 ILO classification differs markedly from its predecessor in the way small opacities are handled (see Appendix). The 1971 system required the separate assessment of the profusion of rounded and of irregular opacities. Based on these, a combined score had then to be determined. Under the latest classification the profusion of both types of opacity is assessed simultaneously in one score. The interpreter has then to make a qualitative judgment on the relative contributions of each type of opacity to the overall profusion by stating which is primary and which is secondary.

This change, which seems fairly trivial, has certain possibly serious implications. First, it makes for difficulty in the comparison of information on rounded or irregular opacities with past data. For instance. since the new combined score for small opacities cannot be quantitatively apportioned into separate scores for rounded and irregular opacities, prevalences of specific categories of rounded, and of irregular opacities cannot be derived for comparison with figures obtained under the 1971 revision. Instead, only the comparison of prevalences based on combined opacities from the 1971 classification with those using the small opacities score from the 1980 revision is possible.

More importantly, perhaps, is the possibility that the mere change in the method of reporting has made a profound change in the manner in which small opacities are now perceived and reported. It may be, now that readers can forego the difficult task of separate assessment of the profusion of rounded and irregular opacities while still having to record the different types of opacity present, that mixtures of opacities will be reported more often.

In order to explore this and other related questions, information on profusion and type of small opacity was extracted from records of the Coalworkers' X-ray Surveillance Program (CWXSP).[1] This is a nationwide program which enables all underground coal miners to receive free periodic X-rays. Miners with signs of coalworkers' pneumoconiosis (CWP) are notified, and may at their discretion work in low dust areas of the mine. The program has been in operation since 1970. Up until 1981 it used the 1971 ILO classification.[2] At that time a change was made to the current system.[3]

METHODS

The analyses were undertaken on data for all readable films from both sets. No special account was taken of film quality. Information on tenure underground, supplied by the miners at examination, was grouped into ranges and used for stratification in the analysis.

All of the X-rays were read by interpreters who had passed the NIOSH B-reader test,[4] and all X-rays were taken at facilities that had to conform to certain NIOSH requirements for quality.[5] Each interpretation used in this analysis was that of one B reader. Sixteen B readers were utilized in the CWXSP during 1981, 15 of these being employed throughout the year.

This analysis concentrates on the profusion of small opacities, and on the primary and secondary type of small opacities reported. The zones of involvement were not considered, nor were any other abnormalities.

During 1981 the CWXSP changed from using the 1971 to using the 1980 classification. In that year 7338 X-rays were read using the former classification, and 7438 using the latter. The data for this one year therefore provide a useful base for the comparison of the two classifications. Accordingly these data were used in the following comparison.

Since the two classification systems were different, the readings from one had to be converted into the format of the other in order to be comparable. Since the 1980 data cannot be quantitatively broken down into separate assessments of round and irregular opacities, while the 1971 revision scores are capable of being combined into pseudo-1980 determinations, the earlier data were converted for comparison with the later. The following is a description of the operations performed to do this.

1971 Classification

The 1971 classifications were converted to pseudo-1980 readings using the following algorithm.

1. The 1971 combined small opacity profusion was taken as the 1980 small opacity profusion.

2. Primary Type

   Acting on the assumption that the 1980 primary type is synonymous with the greatest profusion of rounded or of irregular opacities seen under the 1971 revision, the algorithm compared the two 1971 profusions. If the rounded opacities were reported as most profuse the primary type was defined as rounded. On the other hand, if the profusion of irregular opacities was greater than that for rounded the primary type was set equal to irregular. If the two profusions were equal, the type was assigned randomly.

3. Secondary type

   If both rounded and irregular opacities had been recorded, the secondary type was set equal to the type for whichever profusion was the less. If the profusions were equal, the secondary type was whichever of the two that was not allocated to the primary type. If only rounded, or only irregular opacities were reported in the 1971 scheme, the secondary type was put equal to the primary type.

   Note that the above procedure, while simulating the process a reader might go through under the 1980 scheme in assessing an X-ray, cannot fully duplicate all patterns of possible responses. While mixtures of rounded and irregular types can be obtained as primary and secondary entities, mixtures of types within the rounded range (p, q, r), or within the irregular range (s, t, u), are impossible as the information is just not available in the 1971 classification. As a result such combinations as p/q or s/u are absent from these pseudo-1980 scores, with a consequential problem in comparison with the actual scores from the 1980 classification.

1980 Classification

The readings from the 1980 classification were analyzed as reported, using the actual scores. In the few cases where small opacities were reported but the secondary type was left blank it was put equal to the primary type.

RESULTS

The numbers of readings were 7,338 and 7.438 for the 1971 and 1980 classifications respectively. The mean tenure underground was 5.3 years for the first group, and 4.8 years for the second.

Profusion

Overall, the percentage of films read as showing small opacities was the same under both classifications, at 6.1%. Table I shows these percentages plus those for other profusions obtained using each classification. Figure 1 shows these data plotted against various tenure ranges.

Primary Opacity Type

The proportions of positive X-rays (category 0/1 or greater) tabulated according to opacity type by each classification are

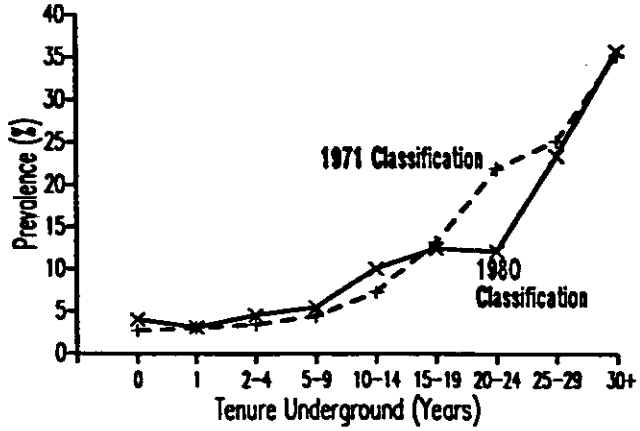

Figure 1. Percentage of films noted as showing category 0/1 or greater small opacities by tenure underground and classification used.

shown in Table II. No major change was seen in the general reporting of rounded and irregular opacities, 56% of all opacities being reported as rounded using the 1971 classification and 52% using the 1980 revision. Moreover, within the rounded opacity group, the percentages of opacities reported as being p, q and r remained about the same after the introduction of the 1980 scheme. However, there was a major change in the way small irregular opacities were interpreted, with type s being reported twice as frequently as before ($X^2 = 38$, 5 d.f., $p < .001$), mainly at the expense of type t.

Figure 2 explores this topic in more detail by breaking the data down by profusion of small opacities (0/1, 1/0 and 1/1+). It shows that the readings for categories 0/1 and 1/0 are similar to those overall, with type s opacities being recorded more often than type t under the 1980 classification. However, for the small number of films classified as 1/1 or greater the findings are different, and indicate a movement from recording type p opacities to noting those of type s. While the proportions of films classified as rounded under the two classifications are quite similar for the 0/1 and 1/0 categories, the greater willingness to note type s opacities results in more irregular opacities being reported for 1/1 or greater films when read using the 1980 scheme.

Miners with longer tenure were also found to be more likely to be classified as having rounded opacities under the 1971 system (Figure 3). This was probably another manifestation of the phenomenon seen in the data of Figure 2 and associated with the higher categories of small opacities.

Secondary Types

As noted earlier, the restrictions in the way data on secondary type was derived from the 1971 classification, and the presence of missing values in the 1980 classification data complicates the interpretation of this information.

Table III gives the percentages of positive films classified by secondary type in a manner analogous to Table II.

Table I

Percentage of Films Showing Small Opacities of Various Profusions by Classification Used

Classification	Percentage of films showing 0/1+	1+	2+	Number of Films
1971	6.1	2.7	.2	7338
1980	6.1	3.1	.2	7438

Table II

Percentage of Films with Small Opacities by Reported Type of Primary Opacity

Classification	Percentage classified as type: p	q	r	s	t	u	Number of Positive Films
1971	16	39	1	15	29	0	443
1980	13	38	1	31	18	0	454

Table III

Percentage of Films with Small Opacities by Reported Type of Secondary Opacity

Classification	Percentage classified as type: p	q	r	s	t	u	Number of Positive Films
1971	16	38	1	17	29	0	443
1980	15	34	1	26	25	0	454

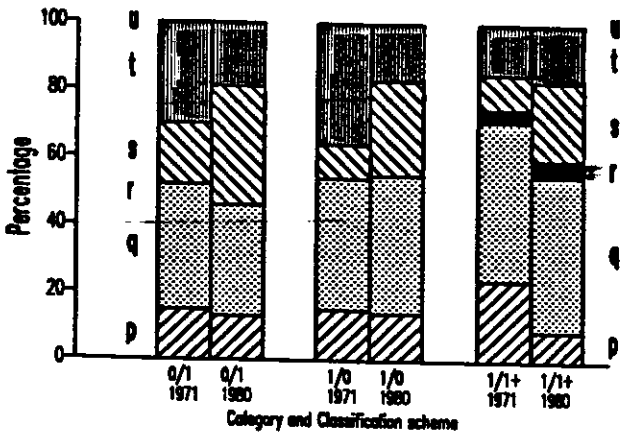

Figure 2. Rounded opacities as a percentage of all small opacities by profusion category and classification used.

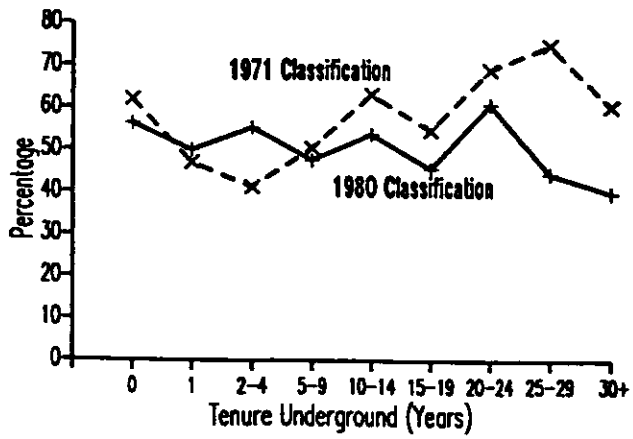

Figure 3. Rounded opacities as a percentage of all small opacities by tenure underground and classification used.

The data show similar trends to those seen for the primary type. In particular the 1971 secondary type distribution is almost identical to the primary type distribution given in Table II. While the 1980 secondary type distribution follows that for the primary type, fewer type s and more type t opacities were reported, although the division between rounded and irregular is not affected.

The relationships with secondary type and profusion, and with tenure were similar to those for the primary type for each classification scheme.

Primary and Secondary Type Together

This analysis looks at the pairs of scores for primary and secondary type among all films noted as showing small opacities (Table IV).

The main observation from this table is that the percentage of films where both primary and secondary types were reported as rounded is diminished under the 1980 scheme, the balance going to cells where mixtures of rounded and irregular opacities were reported ($X^2 = 7.1$, 1 d.f., $p < .01$). On the other hand, the percentage of films where irregular opacities were reported as primary and secondary remained the same.

Larger Temporal Changes

The above analysis has concentrated on readings obtained during the one year both classifications were in effect. Before concluding this analysis it seemed sensible to place these changes in the wider perspective of larger temporal changes. In this way the transitoriness of any effects brought about by the introduction of the 1980 classification could be assessed.

Figure 4 gives some data from 1978 to 1986 on the prevalence of various categories of rounded opacities seen in the CWXSP (Note: these must not be taken as estimates of prevalence in working miners as the CWXSP records are not representative of this group). The data show a trend towards lower prevalence with time, a trend that was not disturbed by the change to the new classification. (The apparent cyclical trend is an artifact arising from the procedures under which the CWXSP operates.)

The percentage of positive films recorded as having primarily rounded opacities in each year is shown in Figure 5. There is a clear indication of a trend towards more frequent re-

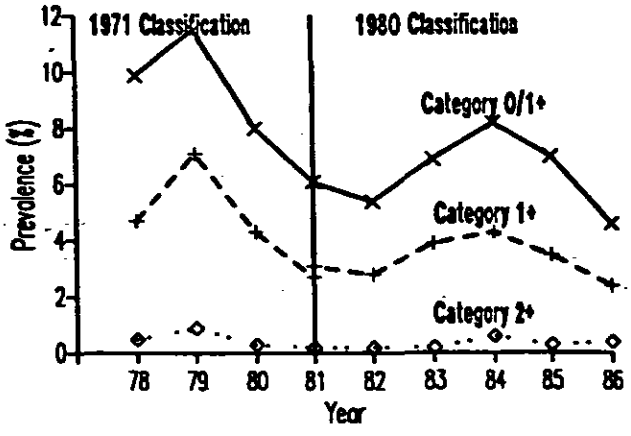

Figure 4. Percentage of films noted as showing various categories of rounded opacities by year of examination and classification used.

Table IV

Percentage of X-rays Classified by Both Primary and Secondary Type and by Classification Scheme

		1971 Secondary			1980 Secondary		
		Rounded	Irregular	Total	Rounded	Irregular	Total
PRIMARY	Rounded	215 (48.5)	33 (7.4)	248 (55.9)	187 (41.2)	47 (10.4)	234 (51.6)
	Irregular	22 (5.0)	173 (39.1)	195 (44.1)	37 (8.1)	183 (40.3)	220 (48.4)
	Total	237 (53.5)	206 (46.5)	443 (100.0)	224 (49.3)	230 (50.7)	454 (100.0)

Note: percentages of total for each classification are in parentheses.

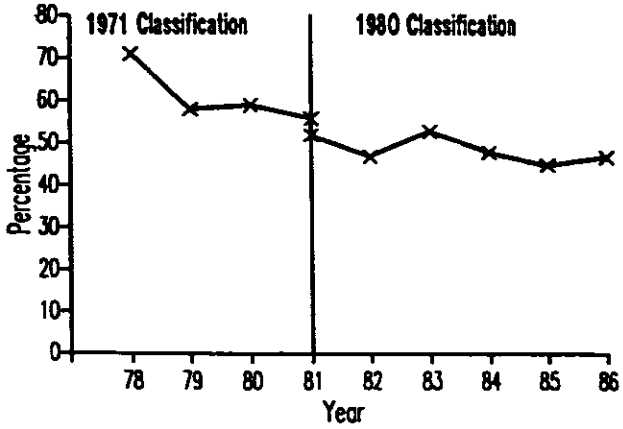

Figure 5. Small rounded opacities as a percentage of all small opacities by year of examination and classification used.

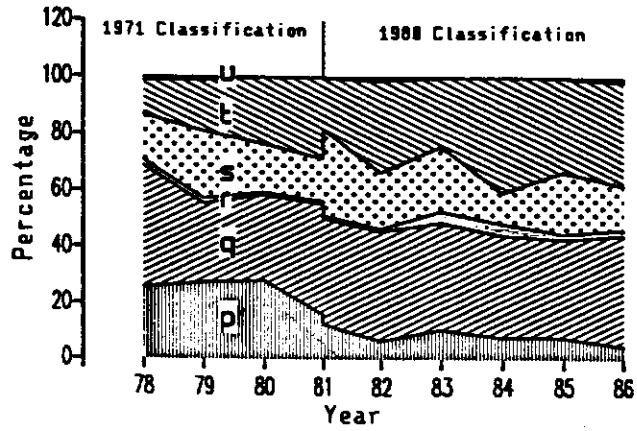

Figure 6. Small rounded opacities as a percentage of all small opacities by year of examination and classification used.

porting of irregular opacities, this being unaffected by the classification change. Figure 6 shows that this trend occurred at the expense of type p opacities, and again, the new classification is not implicated in this. Interestingly, the switch between the recording of type s and type t opacities in 1981 noted earlier is seen to be largely transient; by 1983 readers were again reporting type t opacities more frequently. Throughout the whole period r and u type opacities were infrequently reported, and no obvious trend is apparent.

DISCUSSION AND CONCLUSIONS

The data presented here indicate that the introduction of the 1980 classification had little lasting effect on the reporting of small opacities. In 1981 no marked increase or decrease in the percentage of positive film was seen, and the general temporal variation in prevalence in the program continued quite smoothly through the classification changeover.

Furthermore, although there was a switch to more frequent reporting of type s opacities at the expense of type t in 1981, this appeared to be transient, and the new classification did not interrupt a trend towards an apparent greater willingness to report irregular opacities, both as primary and secondary types. Researchers should be aware of these trends; further work is underway on this topic. In particular, the temporal trend seen in Figure 6 is being examined to see if it is reader artifact, or whether it reflects a change in the exposure and tenure of the miners x-rayed over that period.

It should also be noted that there are other differences between the 1971 and 1980 classifications which may have directly or indirectly influenced X-ray interpretation. For example, in the 1980 scheme, the standard radiographic illustrations of the small opacities take precedence over their written definitions. Many different standard X-rays were also used in the 1980 scheme. Based on the findings in this report, these changes also seemed to have had little lasting effect on the trends of reading small opacities.

It is important to note that these findings may not be applicable to readings obtained on other occupational groups. The films read in this study were all of coal miners, or coal miners to be, and the general level of abnormality reported was slight. Findings for other groups, such as those for workers exposed to fibers, and for films showing greater abnormality may well be different. Of course, it is also true that readers other than those considered in this study may not have exhibited the trends reported on here.

In summary, the conclusions are as follows. Adoption of the 1980 classification in the CWXSP did not lead to any change in the amount of small opacities reported. There was, however, a short lived switch to the greater reporting of type s opacities at the expense of those of type t. There was also an indication that fewer type p opacities were reported for X-rays with profusions of 1/1 or greater. These effects were found to be small, however, when compared with temporal trends seen over the last 10 years. These indicate that there has been a gradual but continuous movement from the reporting of rounded opacities towards irregular opacities.

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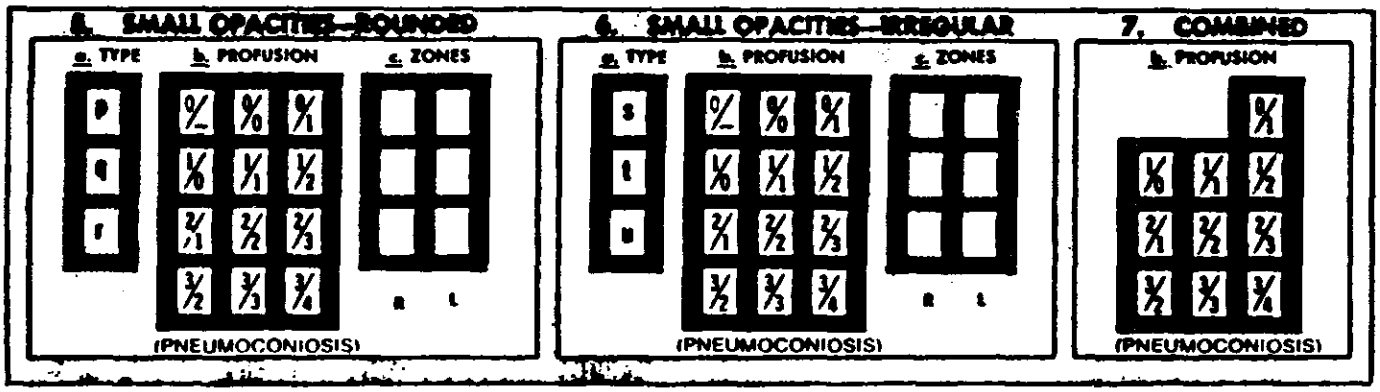
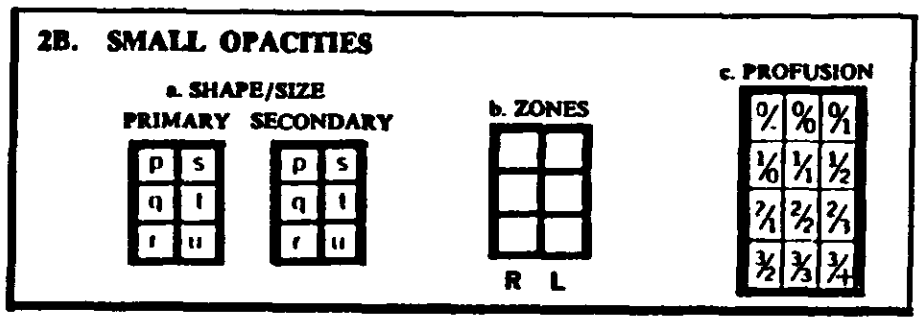
APPENDIX



1971 Classification of small opacities



EDUCATIONAL STANDARDS-SETTING PROGRAMS OF THE ACR TASK FORCE ON PNEUMOCONIOSIS IN SUPPORT OF NIOSH

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The Task Force on Pneumoconiosis of the American College of Radiology is in its eighteenth year of providing advice, counsel and educational programs in support of activities of the National Institute for Occupational Safety and Health. This is a remarkable length of service for a partnership between a public health agency and a national medical specialty society. The task force was created to solve problems stemming from the 1969 enactment of the Coal Mine Health and Safety Act. This established in the United States a national surveillance program for active coal miners and a compensation program for former miners and their survivors. The key bit of medical evidence specified in the law was a chest radiograph of good quality, interpreted by a qualified physician using a standardized descriptive system.

Unlike many countries which created earlier miner surveillance programs, the American law did not allow NIOSH to establish an expanded public health agency to undertake the entire program. Instead, NIOSH turned to the private sector of medicine for help.

In 1969, only a few American physicians were familiar with coal workers' pneumoconiosis, despite the prevalence of mining in this country. Even fewer understood the International Labor Office Classification of Chest Radiographs, which the new law specified for use. The miners were suspicious of the intentions of the mine operators and their plans for providing the needed chest X-ray examinations. In short, everything needed doing immediately.

Under a series of contracts, the task force developed programs in three areas.

1. Setting standards for physicians and facilities to participate in the surveillance programs established under the law.
2. Developing new and innovative teaching methods to acquaint radiologists and other physicians with the radiologic manifestations of CWP and the use of the ILO classification system.
3. Developing a climate of cooperation between NIOSH and other federal agencies and interested physician groups in several appropriate disciplines.

The task force was built upon the five radiologists who made up the Public Health Service panel. They were Drs. Eugene P. Pendergrass, George Jacobson, Russell H. Morgan, Benjamin Felson and Leonard Bristol. Drs. Felson and Bristol remain active. To this core, the ACR added other radiologists, chest physicians, physicists, pathologists, radiographers and epidemiologists to provide expertise and liaison. Dr. Edgar L. Dessen became the chairman and remains so. Several other members of the task force have served during the entire span of its existence. They include Drs. Jerome Wiot, E. Nicholas Sargent, and Jerome Kleinerman who are active in this conference.

STANDARD SETTING

The task force served as a panel of experts to advise NIOSH on the development of criteria for physicians and for facilities.

The A and B reader system was devised to assure that physician participants are skilled in chest radiographic interpretation. Physicians from several disciplines routinely interpret chest radiographs in this country. Thus, NIOSH could not rely entirely upon a single specialty certification.

The A reader qualification is necessary to supervise an approved facility and to make primary interpretations for the program. It is attained by most physicians through attendance at one of the seminars offered for NIOSH by the task force.

The B reader status is achieved by sitting and passing a six hour examination involving 125 chest radiographs. The radiographs must be scored correctly using the current version of the ILO system. More than 500 American physicians and perhaps 50 from other countries have become B readers. This provides a reservoir of talent for federal programs, for industrial programs and, increasingly, for litigation of disability claims. The B reader test was devised by Dr. Russell Morgan and validated by the task force.

The task force also advised NIOSH about technical standards for facilities. The difficult task of detecting early signs of CWP is made almost impossible by poor quality radiography. Standards for film, equipment and personnel were recommended and adopted. The task force developed measuring programs, designed phantoms, tested film-screen combinations and processing systems and devised training sessions for radiographers and physicists. These efforts involved other public health agencies, state radiation programs and leading manufacturers of film and equipment.

The criteria for radiographic quality which originated with these efforts have become a standard part of the education of radiologists and radiographers and a basic element in the marketing of X-ray imaging systems.

PHYSICIAN EDUCATION

At the beginning of the program, NIOSH had an obligation to interest private physicians in becoming part of a demanding radiologic process so that the mandated examinations would be available to miners in the many communities throughout some 20 of our 50 states. The task force organized a series of teaching programs.

The most innovative of these was the viewbox seminar which will be demonstrated at the end of this conference and offered for the 29th time this weekend. The method involves a test-teach-test sequence in which each participant works with his own set of radiographs and is required to make decisions on each case, using the ILO system to record his conclusions.

For several years, the task force presented seminars at the American Medical Association conferences on occupational health. It conducted one seminar specifically for academic radiologists, pulmonologists and radiographers and provided each attendee with a set of teaching materials devised by the task force.

In addition, the task force has offered seminars for radiographers, for industrial and union physicians, for administrative law judges who decide most compensation claims, for attorneys who contest such claims and for other public health groups. Two syllabi on radiographic technique remain in general usage.

When asbestos related disease emerged as a significant public health problem, the task force worked with NIOSH and the National Cancer Institute to develop a teaching module and monograph on asbestos related disease. The package contained radiographs, micrographs, clinical and statistical data and a historic summary of the problem. The modules were placed in the audio-visual centers of every American medical and osteopathic school. Hundreds of copies of the monograph were sold to individual physicians.

Articles in the scientific literature have described the task force's efforts and results.

LIAISON

From its beginning, a major effort of the task force was to involve other medical disciplines, allied health scientists, public health agencies and the manufacturing and supplier community in coordinated efforts to support NIOSH and other federal programs.

With the approval of NIOSH, the task force has provided advice and monitoring to the coal miner compensation programs of the Social Security Administration and the Department of Labor. It has advised the Navy Department, the State Department and the Food and Drug Administration. It built working relationships with the American College of Chest Physicians, the American Occupational Medical Association, the American Medical Association, the American Osteopathic College of Radiology, the American Society of Radiologic Technologists, the College of American Pathologists and other groups.

When interest was expressed in revising the ILO system, the task force, supported by NIOSH, organized the international committees and efforts which led to the 1980 version which is in world-wide use today. The ACR Institute is the designated supplier of standard radiograph sets to ILO.

The U.S. Congress amended the Coal Mine Health and Safety Act in 1972 and again in 1977 to broaden benefits and ease qualification requirements. On both occasions, the task force provided expert testimony about medical and technical aspects of the proposed legislation.

When the U.S. was suggested as a possible site for this seventh International Conference on the Pneumoconioses, the task force supported NIOSH by developing the feasibility study and a general plan for the meeting. Members of the task force have served on the committees for the meeting. The seminar demonstration on Friday and the full seminar were planned for the convenience of conference attendees.

SUMMARY

For nearly two decades, the task force has provided a broad base of support to NIOSH and through its good graces to other public and professional channels dealing with the radiologic definition of dust retention diseases. From a situation in 1969, in which Americans were far behind other nations dealing with CWP, task force efforts have been crucial to the development of national programs for miner and other worker surveillance, to physician education, to quality assurance efforts and for liaison between public sector agencies and professional medical and allied health societies. The task force is currently in the first year of its fifth contract with NIOSH.

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EFFECT OF THERMAL TREATMENT ON THE SURFACE CHARACTERISTICS AND HEMOLYTIC ACTIVITY OF RESPIRABLE SIZE SILICA PARTICLES

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ABSTRACT

Thermal and chemical treatment of respirable size silica dusts samples is shown to induce marked changes in their hemolytic activity. The cytotoxicity of crystalline α-quartz (Min-U-Sil), and fumed silica (Cab-O-Sil) particles, as measured by a hemolytic activity protocol, is decreased by calcination and can be related to the dehydroxylation of the surface. The hemolytic activity of β-cristobalite particles of respirable dust size was also determined and found to be lower than that of α-quartz. The change in the surface structure resulting from thermal treatment is detectable by photo-acoustic infrared spectroscopy and zeta-potential measurements. The absorption band in the 3200–4000 cm^{-1} frequency region of both Cab-O-Sil and Min-U-Sil disappears upon heat treatment while a sharp band, identified with single silanol groups, at 3750 cm^{-1} increases in intensity. The zeta potential-pH profile, in the pH range of 4.0–7.0, of the calcined, siloxane surfaced particles is more negative than that of material with a silanol surface.

The cytotoxicity of the crystalline and fumed silica dusts was also found to be strongly dependent on particle size. Fumed silica of large surface area (small particle size) exhibits an initial increase in hemolytic activity upon calcination. This result confirms other experimental observations pointing to a particle size of maximum toxicity.

INTRODUCTION

The toxicity of silica and other mineral particles, as manifested by their role in inducing pneumoconiosis, fibrosis, silicosis and other pulmonary disorders is largely traceable to the characteristics of particle surfaces and to particle morphology. The great wealth of data on the physical and chemical properties of silica is still insufficient for a comprehensive understanding of the specific parameters to be associated with fibrogenic activity and, correspondingly, with the optimum means for characterizing and quantifying the toxicity of dusts, and the design of possible preventive or therapeutic methods.

The great diversity of parameters that have been proposed and tested for correlation with cytotoxicity suggest that more than one mechanism may be involved in the fibrotic activity of silica particles. The crystalline structure of the material (more active tridymite versus less active crisobalite and passive stishovite), freshly formed surfaces and free radicals associated therewith, silicic acid adsorbed onto silica surfaces, the concentration of hydroxyl groups at silica surfaces, particle size and morphology, among other properties, have been investigated and found to correlate in tests of cytotoxicity.

The main thrust of research presented here is to seek more definitive correlations of silica particle properties with cytotoxic activity to identify the mechanism or mechanisms leading to cytotoxic activity and the most suitable instrumental methods for identifying the material properties associated with silicosis and other pathogenic properties of respirable dusts. In the present paper are presented results on the effect of dehydration and dehydroxylation of crystalline and amorphous silica particles on their cytotoxicity as measured by hemolytic activity. One of the prevalent theories on the mechanism of silicosis presumes that such activity is induced by "clean surfaces of crystalline silica, usually quartz,"[1] hence it is deemed of interest to assess the cytotoxic potential of the most common structures of such surfaces.

The main feature of normal, clean quartz surfaces is the degree of surface hydration. The normal, anhydrous surface terminates in -Si-O-Si- (siloxane) groups. Equilibration with water will first result in the formation of —Si—O—H (silanol) groups and, eventually, the physisorption of water onto the silanol groups.[1] Particularly well formed and clean surfaces of quartz may adsorb more than four molecular layers of water.[2] Another type of "clean" quartz surface, but not included in the present study, is that resulting from the fresh cleavage of quartz crystals. Such surface may present broken bonds in the form of free radicals which may exhibit particularly high chemical reactivity.[3] In the present study we compare the cytotoxic activities of quartz and amorphous silica dusts dehydroxylated at different temperatures and re-equilibrated with the atmosphere over prolonged time periods, thus comparing the relative cytotoxicities of surfaces of crystalline and amorphous silica particles covered by adsorbed water, silanol, and/or siloxane groups.

EXPERIMENTAL METHOD

Materials: The materials used in this study were Min-U-Sil crystalline silica dust from two different batches obtained from U.S. Silica Inc. of Pittsburgh, PA, Cab-O-Sil, a fumed silica dust provided by the CABOT Corporation, and respirable size β-cristobalite dust, a standard reference material of National Bureau of Standards. X-ray diffraction analysis showed Min-U-Sil to be essentially pure α-quartz, while the Cab-O-Sil dust exhibited no detectable crystallinity. The Min-U-Sil particle size ranged from 0.4 to 10.0 microns with 98.2% of the particles below 4.7 μm and 85.2% below 1.1 μm; its BET specific surface area was determined as 5.2 m^2/g. The β-cristobalite particle size was in the 2–5 μm range with a specific surface area of 2.5 m^2/g. The Cab-O-Sil material consists of 2 to 40 μm diameter aggregates formed by primary particles of 0.1 to 0.2 μm diameter. The BET specific surface of the M-5 grade Cab-O-Sil used in most of the experiments reported was measured to be 195.4 m^2/g. Other grades of Cab-O-Sil tested had specific surface areas of 100, 255, and 380 m^2/g. The thermal treatment of the materials were conducted in air at temperatures ranging between 100 C and 1095 C for time periods of 48 and 72 hours.

Hemolysis assay: The test protocol developed by Harington et al.[4] was used, with slight modifications (Wallace et al. (4a)), for the present investigation. Dusts were made up to a stock concentration of 2 mg dust per ml of calcium- and magnesium-free Dulbecco's phosphate buffered saline (PBS) obtained from Sigma Corp of St. Louis, MO. The dust-saline mixture was stirred in a sonicator bath until the dust was fully dispersed and suspended in the liquid phase. The stock suspension was then diluted to make sample preparations, in duplicate, of 0.04–2.0 mg dust/ml PBS. Sheep blood erythrocytes, supplied by Scott Laboratories of Fiskeville, RI, were washed twice with PBS, centrifuged at 990g and diluted to a 2% by volume suspension in PBS. Equal volumes of dust suspension and the 2% erythrocyte suspension were then mixed to obtain mixed suspensions of 1% by volume of erythrocyte cells and dust concentrations in the range of 0.02 to 1.0 mg dust/ml. These suspensions were subsequently incubated for 30 minutes at room temperature with agitation every 10 minutes and then centrifuged at 990g. The amount of hemoglobin released was determined colorimetrically on a Bausch and Lomb Spectrometer (Spec 20) at a wavelength of 540 nm. Negative controls consisted of 1% suspensions of erythrocyte cells in PBS and positive controls of an equal volume mixture of water and 2% by volume suspension of erythrocytes in PBS.

EXPERIMENTAL RESULTS

The hemolytic activity of untreated Min-U-Sil, β-cristobalite, and Cab-O-Sil, as function of dust concentration, are compared in Figure 1. These results show that on a per unit weight basis the Cab-O-Sil material is about an order of magnitude more active than the crystalline Min-U-Sil. On a surface area basis, however, Min-U-Sil is more toxic than the amorphous material by, approximately a factor of 3 to 4, since the specific surface area of Cab-O-Sil was found to be over 30 times larger than that of Min-U-Sil. The hemolytic activities of Cab-O-Sil and β-cristobalite are, on the other hand, comparable on a unit area basis. This is in general agreement with other findings on the relative biological activity of various allotropic forms of silica.[1,5,6] However, a test of hemolytic activity conducted on Cab-O-Sil material of different specific surface areas (Figure 2) shows a decrease in activity with increasing specific surface area (or decreasing primary particle size) suggesting that a different mechanism may underlie the toxicity of the fumed silica particles. This latter finding is in qualitative agreement with the particle size dependence of colloidal silica reported by Harley and Margolis.[7]

The effect of calcination on the hemolytic activity of Min-U-Sil and Cab-O-Sil and the change in the specific surface area of the materials on calcination is illustrated in Figures 3 and 4. It is evident from these results that the percent decrease in hemolytic activity exceeds the percent decrease in surface area by sintering, indicating a net decrease in activity on a per unit of surface basis. This decrease in activity coincides with the dehydroxylation of the silica surface reported for various types of silica.[1] The dehydration/dehydroxylation process was followed by photo-acoustic spectra of surface modes of the calcined materials and is illustrated in Figure 5. The untreated sample exhibits a broad absorption band in the 3000–3700 cm^{-1} range which is associated with hydrogen bonded silanol groups and adsorbed water molecules, and the sharp 3747 cm^{-1} band characteristic of free silanol groups. Calcination leads first to the disappearance of the broad band and an increase in the intensity of the free silanol group concentration at temperatures below 800°C and, subsequently, to the disappearance of this band at temperatures above 800°C. It has been found by previous investigators of the dehydroxylation of silica surfaces that at temperatures below approximately 400–450°C less than half of the hydroxyl groups have been removed and thus there is an appreciable concentration of adjacent hydroxyl groups which facilitate rapid rehydroxylation of the surface. As the calcination temperature is increased beyond this range the dehydroxylation process becomes more irreversible until, at around 1100°C, a fully dehydrated, hydrophobic siloxane surface is attained.[8,9] This process appears remarkably well reflected in the observed hemolytic activity of calcined silica particles shown in Figures 3 and 4, which leads to the conclusion that the hemolytic activity of the siloxane surface is much lower than that of the normal, hydroxylated surface, regardless of the type of crystal structure (α-quartz or amorphous) under consideration. It was also observed that the calcined materials, maintained under normal desiccator conditions, recovered their cytotoxicity with time. For fumed dusts calcined at 800–950°C this recovery occurs over a period of 10 to 20 days, as is illustrated in Figure 6. For crystalline materials and calcination temperatures where a fully siloxinated surface is generated, these times were found to be considerably longer. For example, a sample of Min-U-Sil calcined at 1100°C recovered only about 30% of its precalcination activity after a period of 180 days. This observation is in general agreement with hydroxylation rates reported by other researchers.[1,9] The recovery of cytotoxicity by the calcined dusts is accompanied by the reappearance of the I.R. absorption bands characteristic of the hydroxylated surface.

Another method for monitoring the surface structure changes of the silica particles is by the measurement of the electrophoretic mobility or "zeta-potential." This potential measures, if other variables are held constant, the magnitude of the electric charge of the surface double-layer of the particles. It is thus a convenient method for detecting changes in the surface structure of particles. Figures 7a and 7b compare zeta-potential-pH profiles for untreated and calcined Min-U-Sil, and for β-cristobalite and α-quartz (Min-U-Sil), respectively. For the calcined samples it is observed that the zeta potential decreases for calcination temperatures up to 500°C which may be associated with desorption of water from the particle surface and a corresponding increase in the double-layer potential. Further dehydroxylation to form surface silane bonds results in a reduced electrical double-layer potential and, consequently, a more negative zeta potential. Cristobalite particles have a lower zeta-potential than quartz particles and a lower hemolytic activity as well.

The effect of degree of surface hydroxylation was also tested by treating Min-U-Sil samples with alkaline and acidic solutions. It has been reported that the rehydroxylation of partly dehydroxylated silica surfaces is catalyzed by alkali.[10] Min-U-Sil samples calcined for 48 hours at 800°C and which had lost 50% of their hemolytic activity by this treatment, recovered their full hemolytic potential after immersion in a stirred 5% solution of NaOH in water. Similar treatment of non-calcined Min-U-Sil dust resulted in a slight increase in hemolytic activity while exposure to acid solutions (10% HCl) had no significant effect on hemolytic activity, as is shown in Figure 8a. However, the enhancement of hemolytic activity resulting from the alkaline solution treatment was found not to be permanent and the particles so treated were observed to return to the initial cytotoxic levels over a period of 40–80 days (Figure 8b).

CONCLUSIONS

A test of the effect of dehydration and dehydroxylation on the cytotoxicity of respirable silica dust particles, as measured by their hemolytic activity, suggests that such activity can be correlated with the total concentration of surface silanol groups in the sample. Although this may not be the only mechanism for cytotoxicity of silica, the finding confirms the results of Nash et al. of some years ago.[11] This correlation appears, however, to be independent of the structure of the underlying silica (crystalline or amorphous), contrary to other findings on this issue. The concentration of OH groups on hydroxylated silica surfaces is not a readily definable parameter and may vary with particle size, porosity, degree and type of crystallinity, thermal history, etc.[12,13] which may explain the great variability in cytotoxicity resulting from various surface treatments of the material. In the study reported here, the elimination of hydroxyl groups at calcination temperatures above 500°C coincides well with the observed decrease in cytotoxicity.

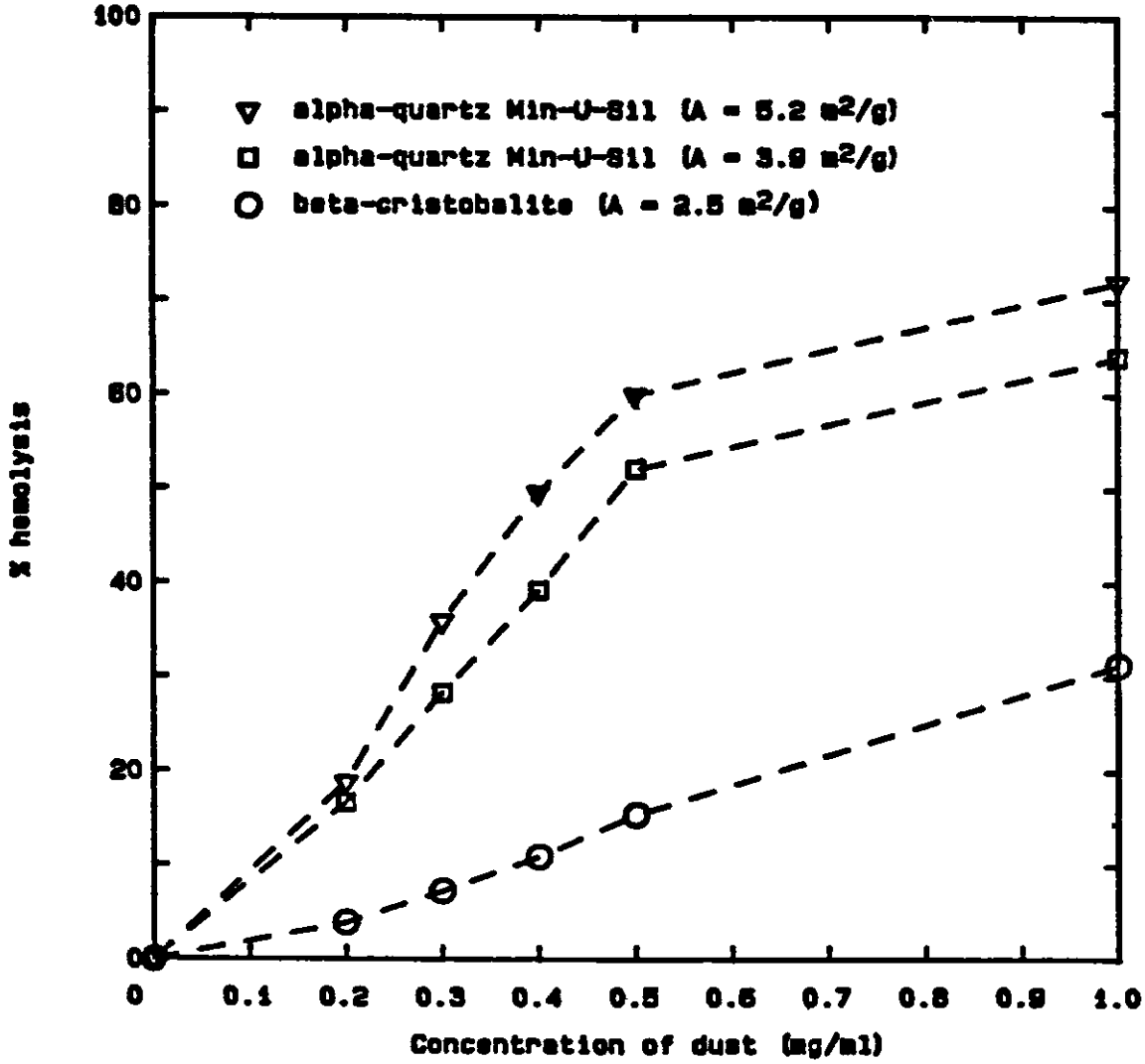

Figure 1a. Cytotoxicity as function of dust concentration for quartz and cristobalite.

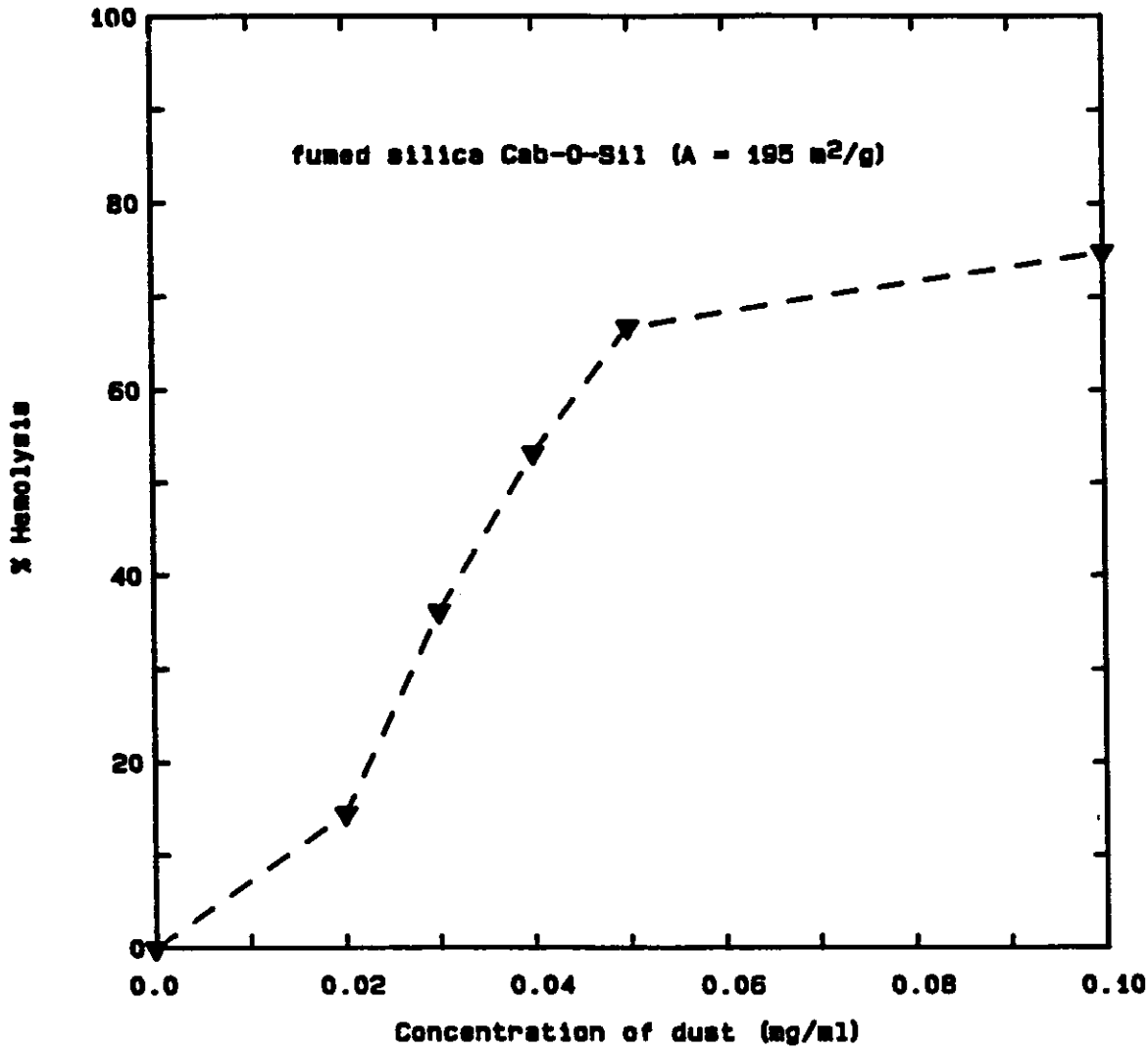

Figure 1b. Cytotoxicity as function of dust concentration for fumed silica (Cab-O-Sil).

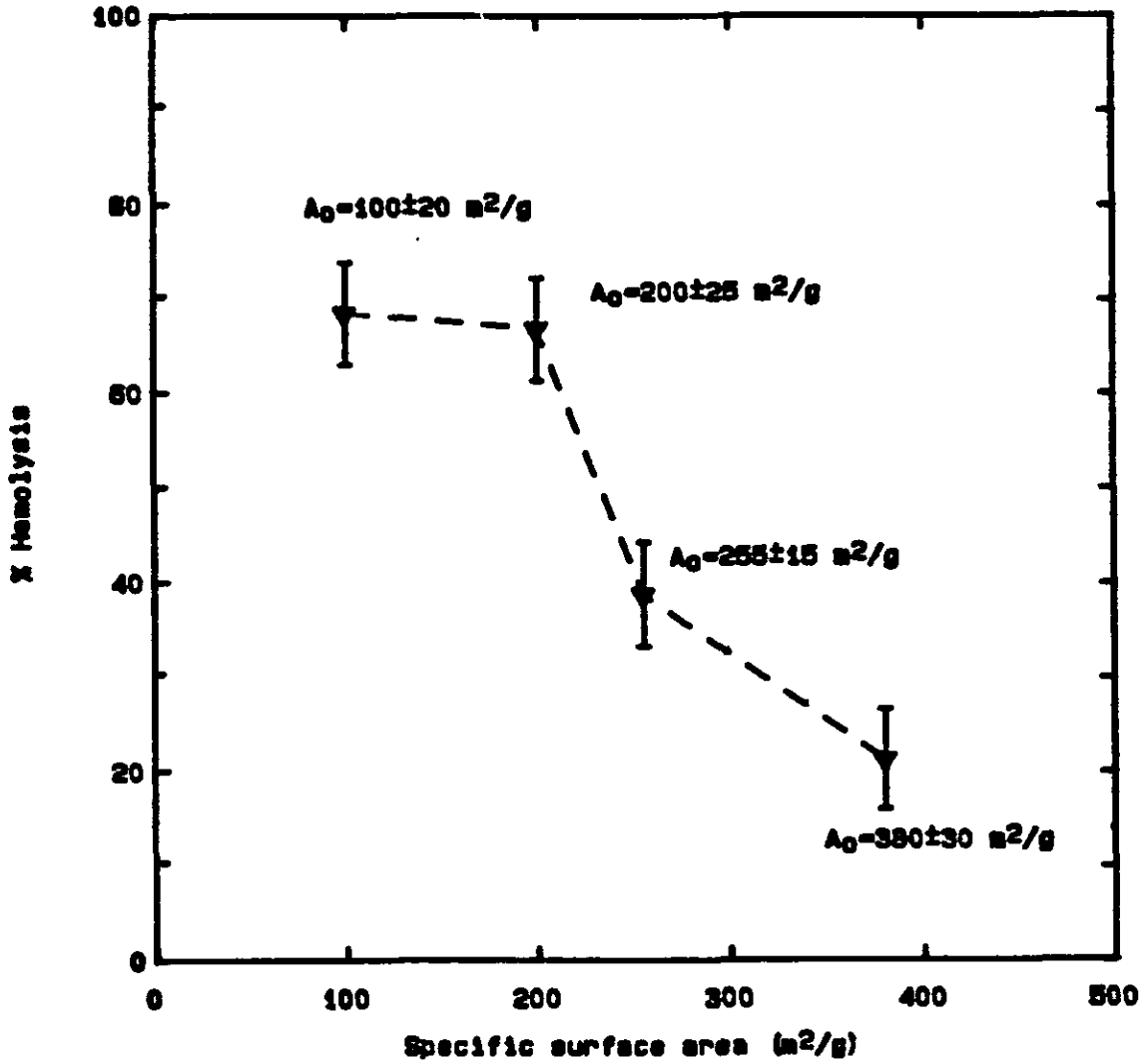

Figure 2. Hemolysis by fumed silicas of different surface areas (tested at dust concentration of 0.05 mg/ml).

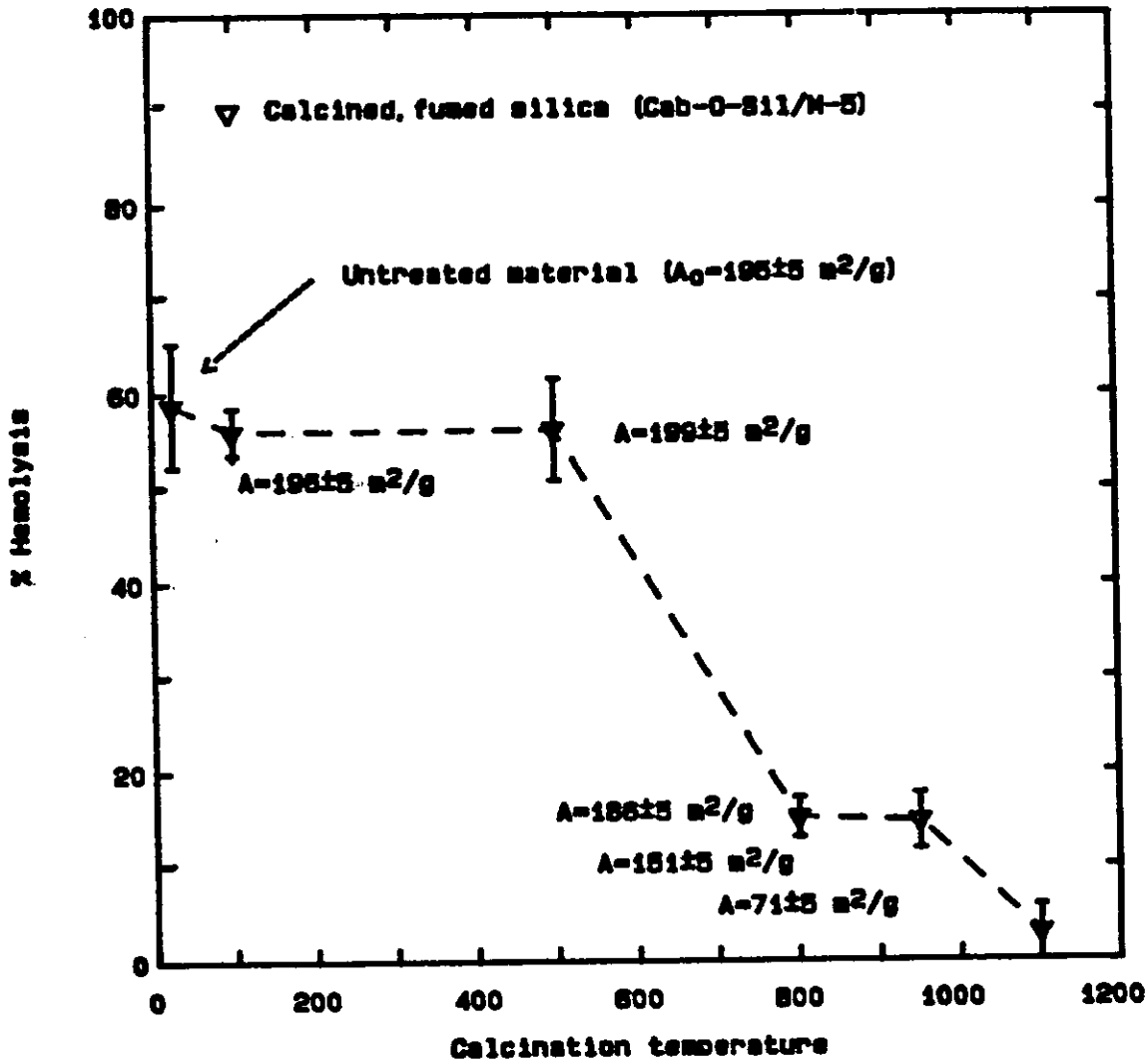

Figure 3. Hemolysis by calcined Cab-O-Sil (tested at dust concentration of 0.05 mg/ml).

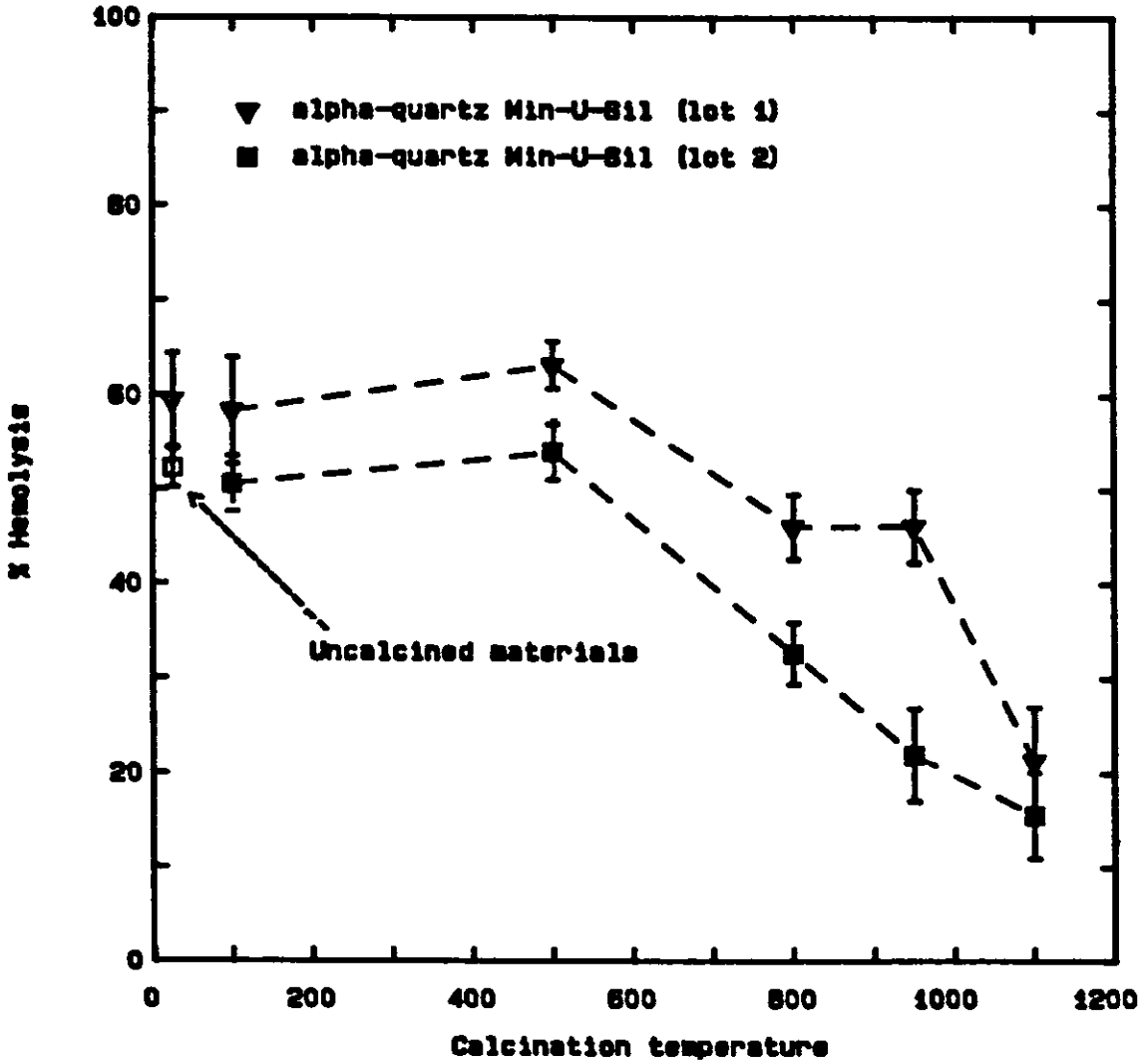

Figure 4. Hemolysis by calcined Mun-U-Sil (tested at dust concentration of 0.5 mg/ml).

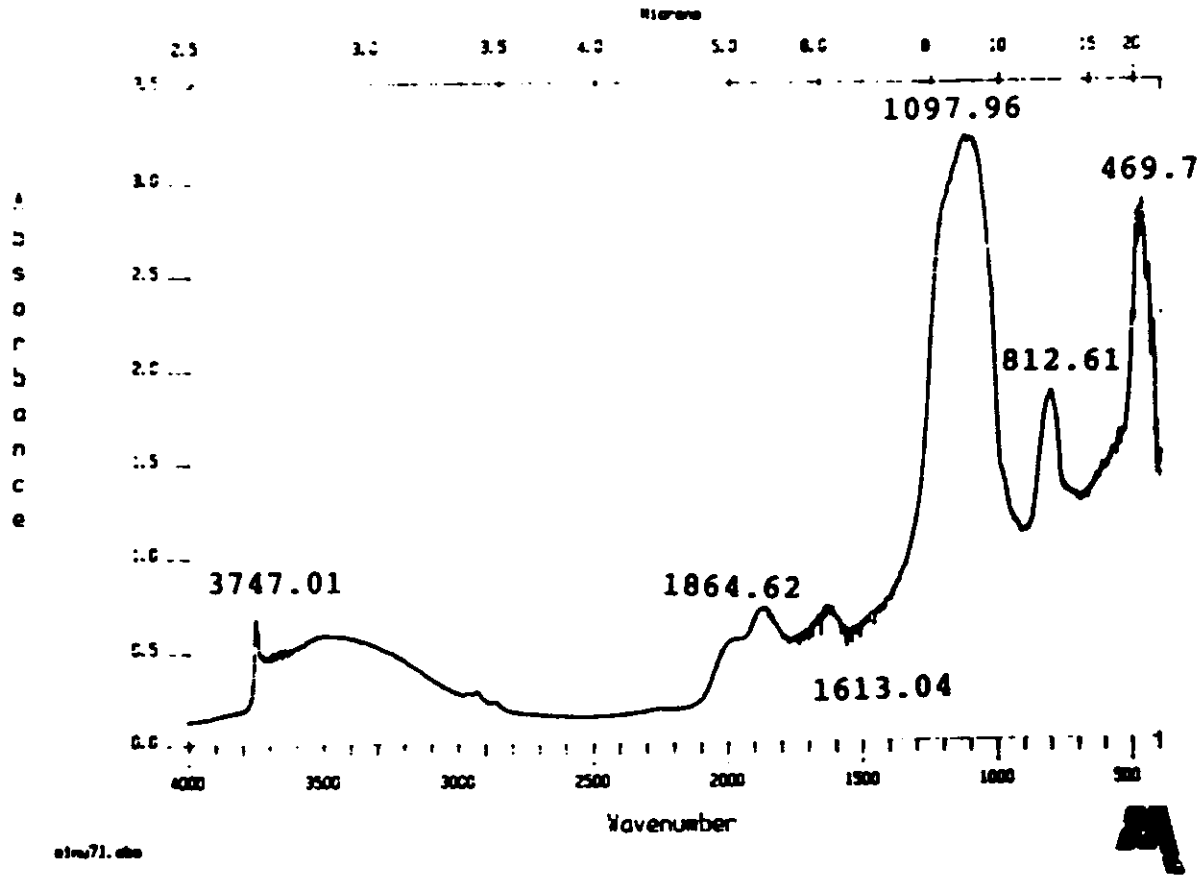

Figure 5a. Untreated CAB-O-SIL.

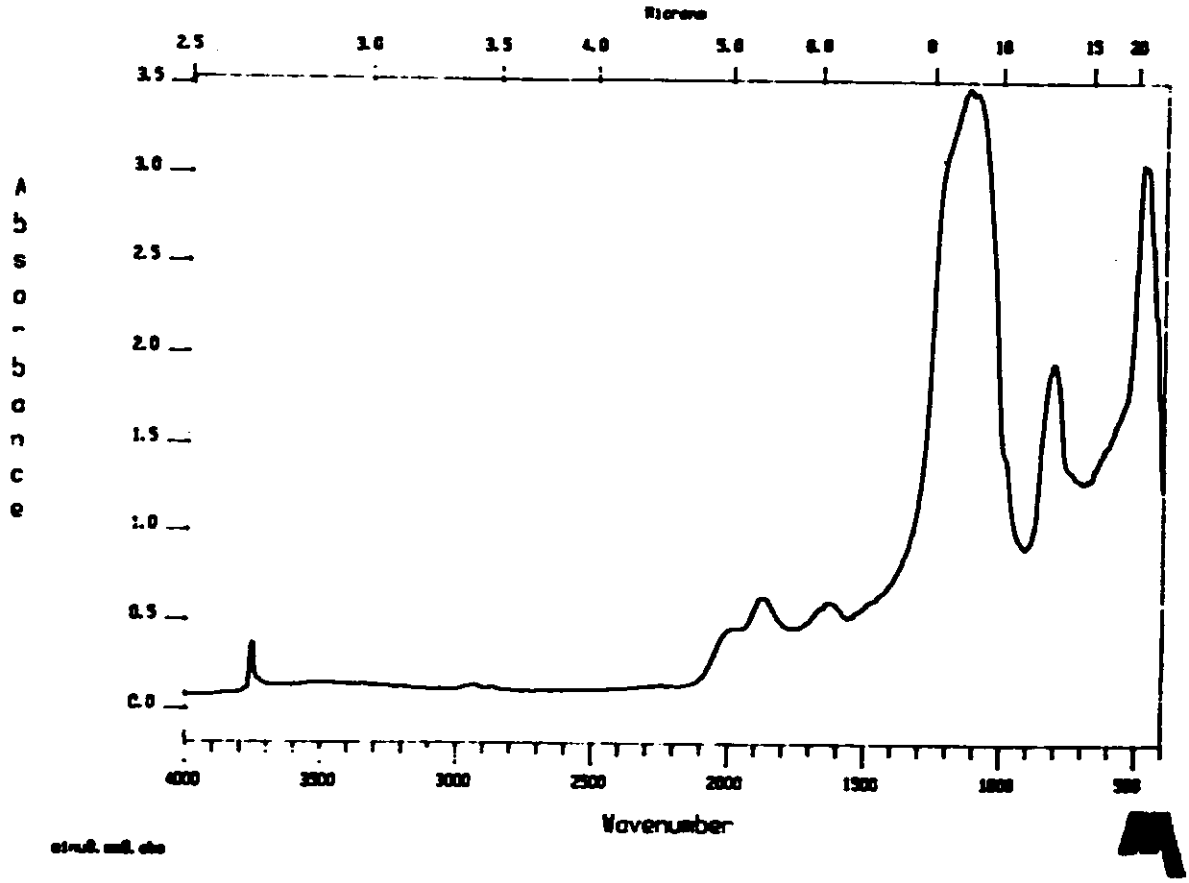

Figure 5b. CAB-O-SIL calcined 800°C.

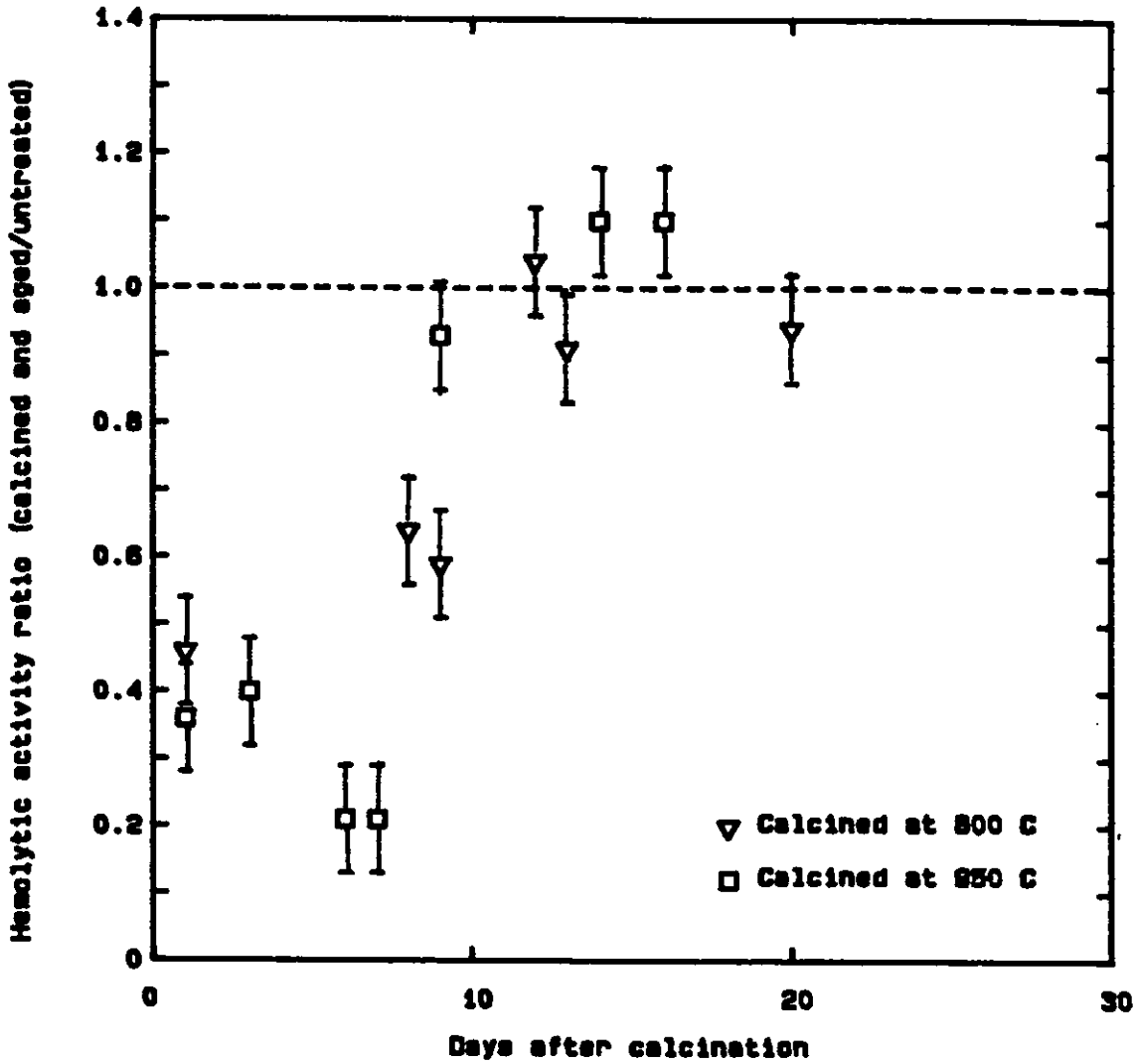

Figure 6. Hemolytic activity recovery of calcined Cab-O-Sil by aging (tested at dust concentration of 0.05 mg/ml).

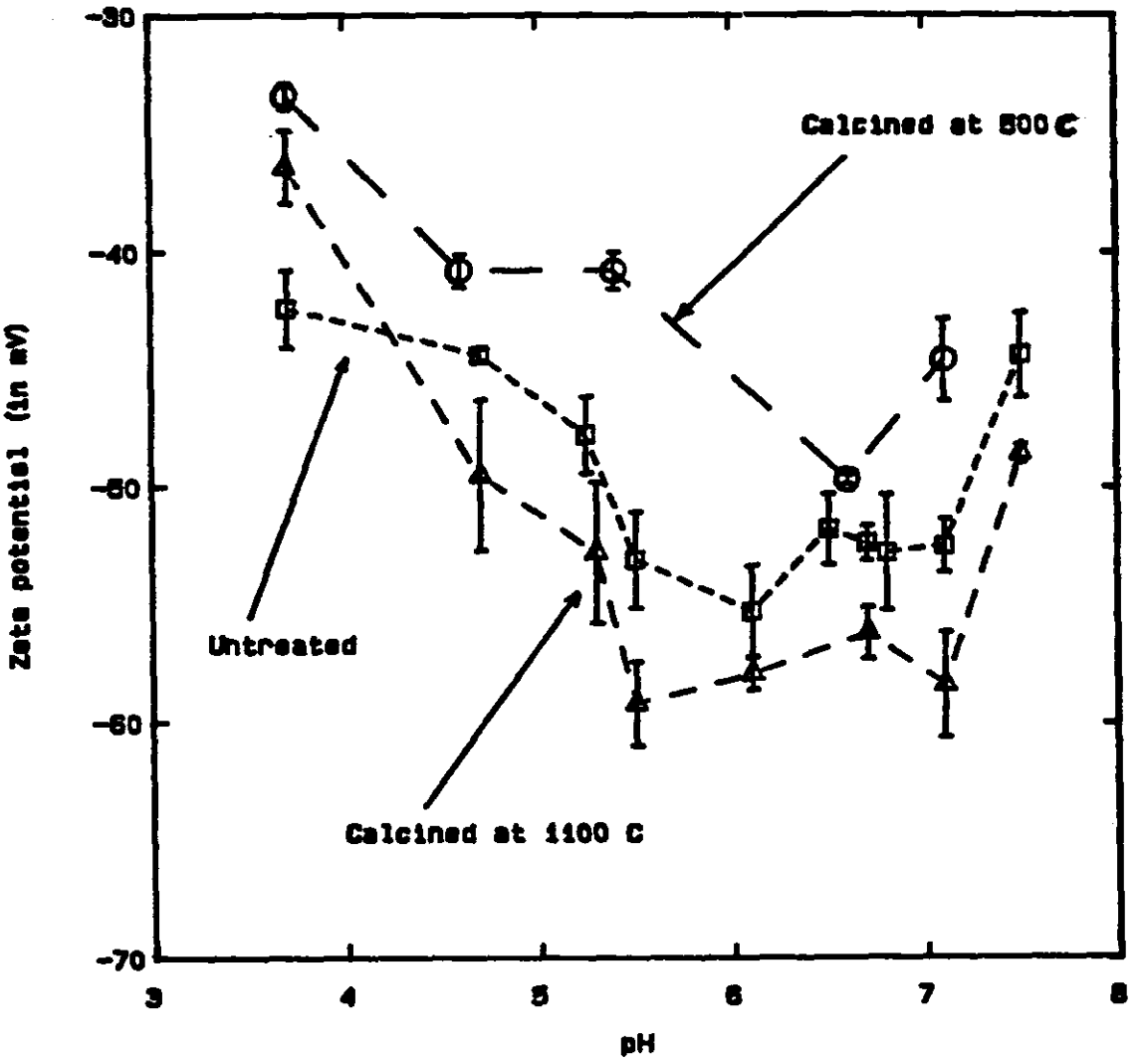

Figure 7a. Effect of calcination on zeta-potential of alpha-quartz (Min-U-Sil) dust in 0.1M KCl.

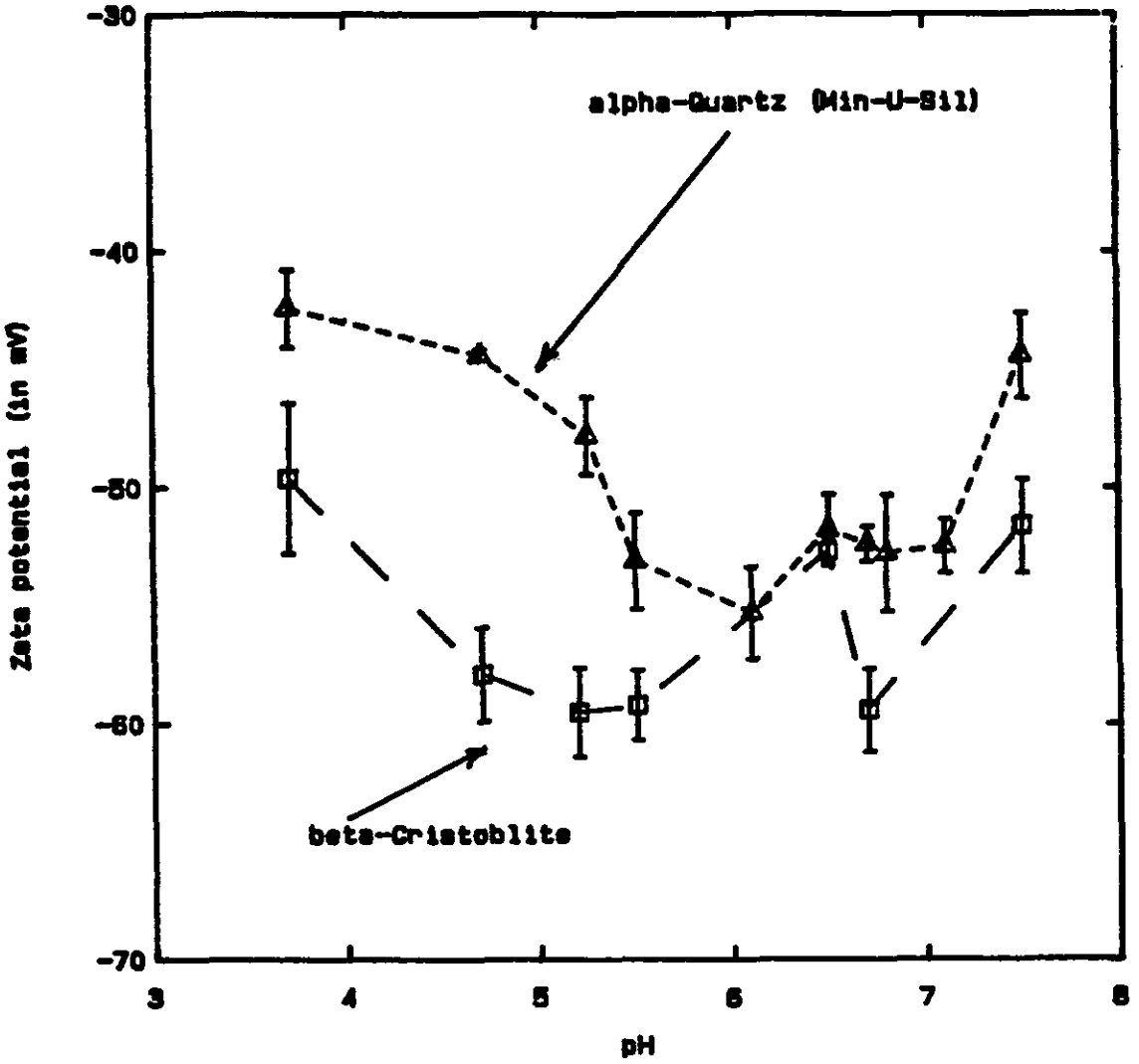

Figure 7b. Effect of crystalline structure on zeta-potential alpha-quartz (Min-U-Sil) and beta-cristobalite (in 0.1M KCl).

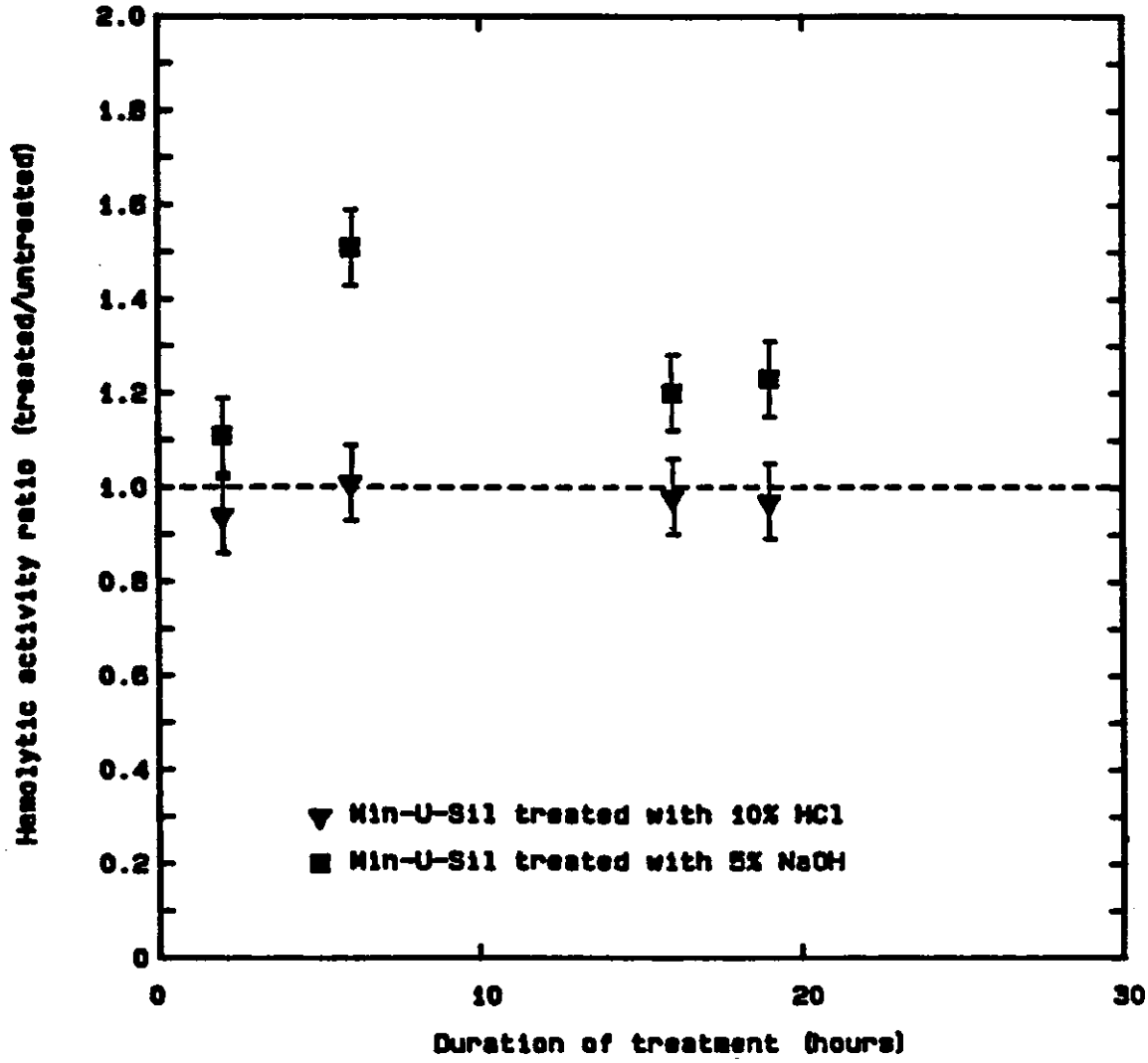

Figure 8a. Min-U-Sil treated with 5% NaOH or 10% HCl (tested at dust concentration of 0.5 mg/ml).

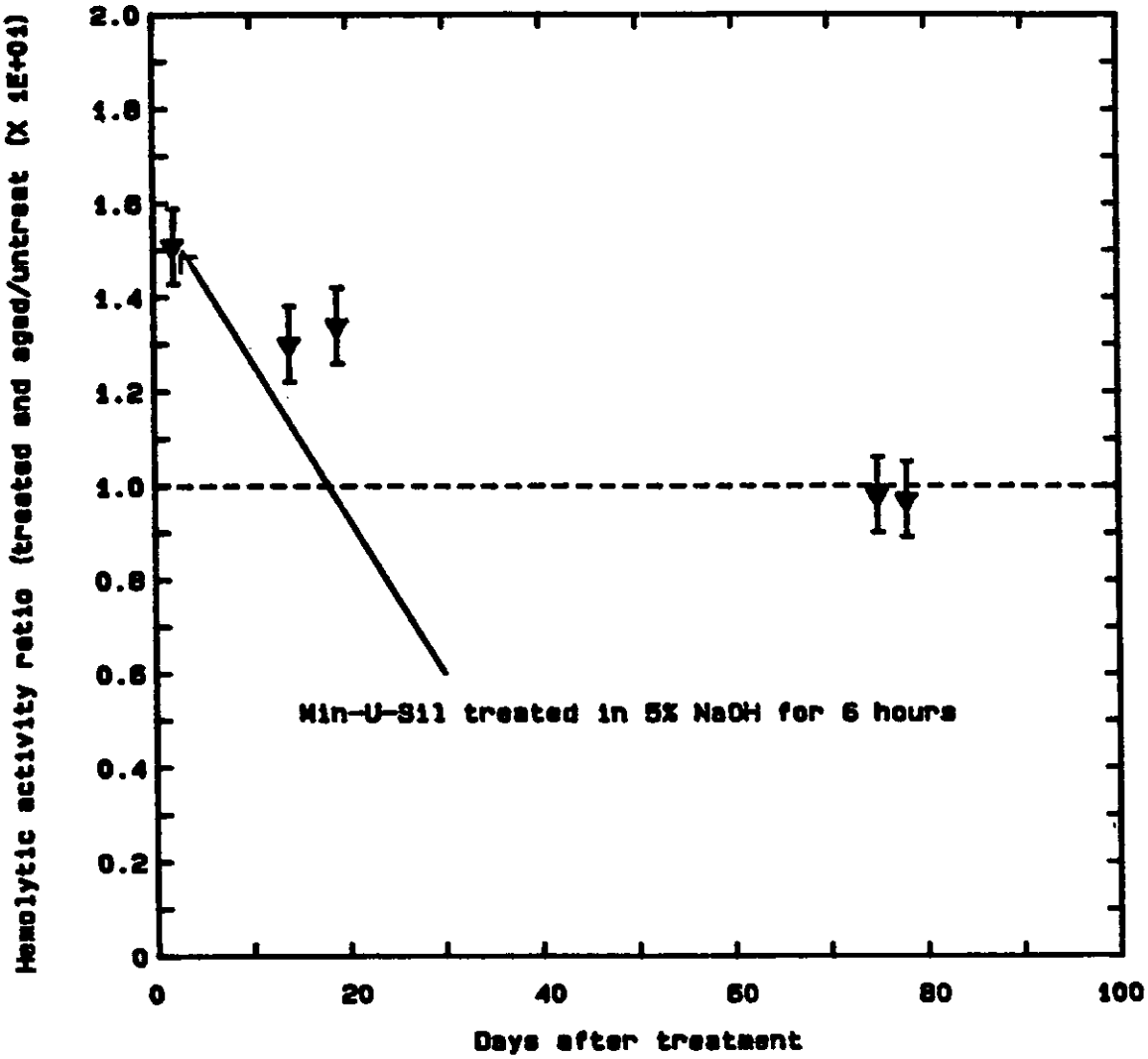

Figure 8b. Hemolytic activity recovery of treated Min-U-Sil by aging (tested at dust concentration of 0.5 mg/ml).

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RESPIRABLE PARTICULATE INTERACTIONS WITH THE LECITHIN COMPONENT OF PULMONARY SURFACTANT

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ABSTRACT

Dipalmitoyl glycerophosphorylcholine (lecithin) dispersed in physiologic saline, a model of the primary component of pulmonary surfactant, is adsorbed by respirable quartz and aluminosilicate dusts. Dust cytotoxicity as measured by erythrocyte hemolysis and pulmonary macrophage enzyme release is suppressed by this adsorption. The degree of suppression of hemolytic potential versus specific adsorption of lecithin from dispersion in saline by respirable quartz and kaolin dusts are compared with dusts' BET specific surface areas to interpret the prophylactic effect of lecithin adsorption. Dust hemolytic potential versus medium pH is presented. Fourier transform infrared spectroscopy and photo-acoustic spectroscopy of lecithin on quartz and of lecithin on kaolin are presented and reviewed with results of studies of the time course of removal of lecithin adsorbed on mineral surfaces by digestion by phospholipase enzyme. Results are discussed in terms of a model of prompt neutralization of respired mineral dusts by pulmonary surfactant, and a gradual re-toxification by digestive processes acting on the adsorbed prophylactic surfactant coating following phagocytosis.

INTRODUCTION

Quartz dust of respirable size is well known to cause fibrotic lung disease, but numerous questions persist in the understanding of the initiation and progression of this disease. Our approach concentrates on physical and chemical aspects of mineral dusts early-on in their interactions with living organisms, and we have chosen simplified models to investigate that interaction.

In the alveolar spaces of the lung, tissue is coated with a surface-active material (pulmonary surfactant), which, among other functions, mechanically stabilizes the lung from collapse by reducing the surface tension of water in the alveolar sacs.[1] This surfactant is also the material that is first contacted by a mineral particle that is transported to an alveolus and is impacted there. This surfactant material has been studied extensively. The primary components are known to be proteins (about 11% in dog lavage fluid), and phospholipids (about 88%).[2] Phosphatidyl cholines constitute roughly 80% of the phospholipid fraction; about 70% of the phosphatidyl choline fraction is dipalmitoyl lecithin (DPL).[2] Respirable aluminosilicate particles are capable of adsorbing dipalmitoyl lecithin from dispersion in physiologic saline, a model for a possible initial event occurring upon deposition of a particle in a pulmonary alveolus.[3]

As may be seen from Figure 1, the DPL molecule has several fixed charges at neutral pH; a positive charge on the trimethylamine (choline) moiety, and a negative charge on the phosphate group. Also evident are the two fatty acid residues of palmitic acid, which are bonded through ester likages to the glycerol segment of the molecule. The fatty acid moieties of phosphatidyl choline make the molecule insoluble in aqueous solutions under normal conditions, but a colloidal unit of aggregated molecules called a micelle is usually formed spontaneously above a certain minimum concentration. Small micellar vesicles are generally formed in the laboratory by using ultrasonic agitation or by solvent evaporation methods.

Our simplified system uses dispersions of DPL in physiological saline as a surrogate pulmonary surfactant, and we have used quartz, a crystalline, fibrogenic dust, and kaolin, an aluminosilicate clay that is not generally considered fibrogenic.[4-10] The approach has been to use *in vitro* cytotoxicity assays (sheep erythrocyte hemolysis and lysosomal enzyme release from pulmonary macrophages) to examine the effects of the surrogate surfactant on mineral dust cytotoxicity.[11]

The first results of the *in vitro* system were that DPL above a certain concentration virtually eliminates cytotoxicity of both dusts;[11] curves of cytotoxicity vs. DPL to dust ratios are shown in Figures 2 and 3. The effect has also been demonstrated with other materials, such as serum proteins and alveolar washings.[12,13] The effect was seen in both cytotoxicity assays, and a dose-response pattern is observed for both dusts.[11] The two untreated dusts are about comparable in cytotoxicity on a BET specific surface basis; the

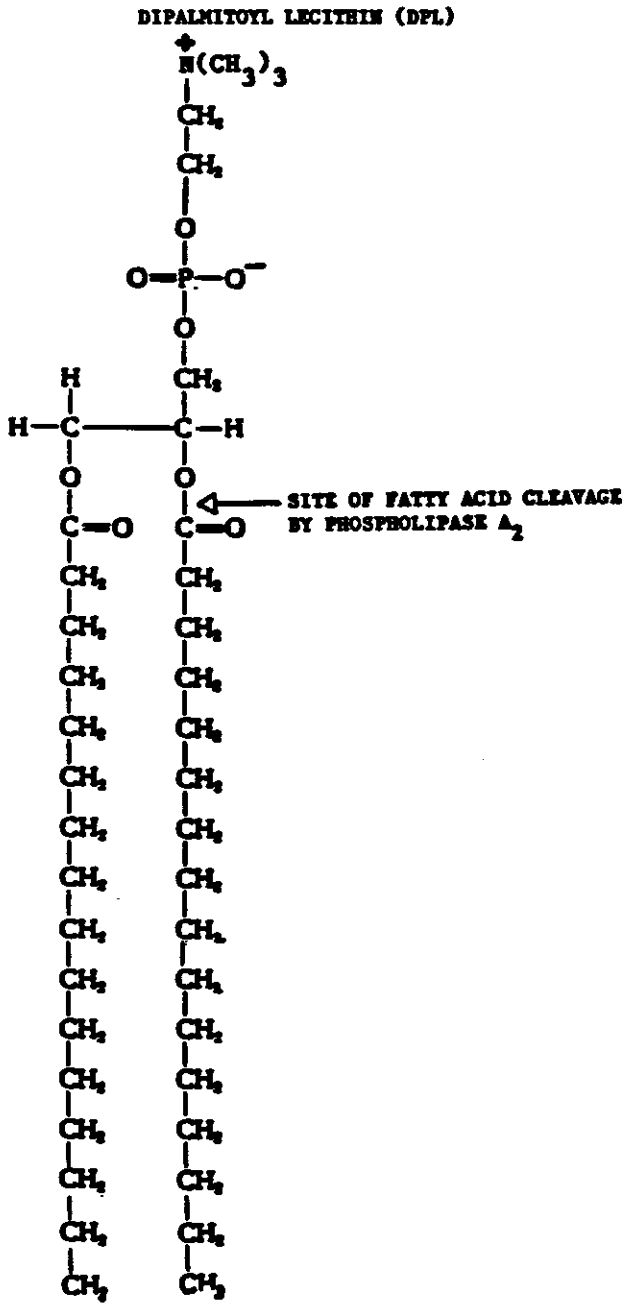

Figure 1. Structural formula of phosphatidyl choline molecule.

quartz is about 4 m^2/g for the less than 5 micron size, and the kaolin is about 13 m^2/g for the same size fraction.[11]

While this finding is significant, it is surely not the *in vivo* situation. Quartz is certainly fibrogenic in normal individuals, at least after extended periods. Some of the prevailing theories on silicosis have been recently reviewed;[14] our next approach was to reexamine the current hypotheses on the initiation of fibrosis, and modify them if necessary. Our working hypothesis is shown in Figure 4.

Our principal efforts were directed toward item 5, the degradation of surfactant coating on dusts by pulmonary macrophages. We have been using a cell-free *in vitro* model to characterize enzymatic digestion of dipalmitoyl lecithin adsorbed on mineral dusts, while developing cellular *in vitro* methods to measure digestion of labelled dipalmitoyl lecithin from phagocytized respirable dusts. In particular, we sought to determine if such adsorption could occur, and if there are mineral specific differences in the rate of such digestion. Our artificial "lysosome" contained the enzyme phospholipase A_2, derived from porcine pancreas, to simulate the phospholipase enzymes found *in vivo*.[15] These enzymes have been identified in many cells, and we have isolated and concentrated phospholipase A activity from rat liver cell lysosomes, but not at sufficient activity levels to allow large scale laboratory use.[15] The use of commercially prepared enzyme of known activity, rather than a cell culture or *in vivo* system, allows the elimination of numerous uncontrollable variables, so that attention can be focussed on differences between dusts.[16-18] Our laboratory protocol is shown in Figure 5.

RESULTS AND DISCUSSION

When the coated dusts are treated with the phospholipase A_2, several things are evident (Figures 6 and 7). For both dusts, for a short period of time, toxicity in the hemolysis assay may exceed that of the untreated dusts. The Figures indicate that this is invariably the case at the 2 hour point. Subsequent assay of lipids indicate that the hydrolysis product lysophosphatidyl choline (lysolecithin) is retained on the dusts. This product results when the fatty acid ester linked to the center carbon of the glycerol chain is hydrolyzed to a free fatty acid, leaving an hydroxyl group; this substance is also highly lytic to cell plasma membranes, thus explaining the exaggerated cytotoxicity. As time progresses, less lysolecithin is found to be associated with the dusts, as seen in Figures 8 and 9.

The most significant finding is that the quartz toxicity returns to essentially its untreated value, even with fairly low enzyme levels relative to the kaolin. Analysis of the retained lipids confirms that the dust is almost free of adsorbed DPL or other lipids, as seen in Figure 10.

The situation for kaolin is quite different; toxicity is not restored except at quite high activity levels, and lipids are retained on the surface to a much greater extent, as seen in figure 11.

The results up to this point raise an important question: what is the basis for a difference in re-toxification of quartz and kaolin dusts? We have looked at several methods to try to clarify this difference, although the case is by no means closed.

In general, enzymatic digestion of substrate molecules is quite dependent on molecular conformation. Because quartz and kaolin surface structure and functional groups differ significantly, we are investigating the possibility that conformational differences between lecithin adsorbed to quartz and to kaolin surfaces might provide differing degrees of steric hindrance to digestive removal, with resultant differences in rates of restoration of surface cytotoxic potential.

To examine this hypothesis, we used Fourier Transform Infrared Spectrophotometry at the West Virginia University Physics Department to look at the spectra of DPL on both quartz and kaolin, and compared the spectral features to the pure DPL spectrum. The DPL-coated quartz and DPL spectra are shown in Figure 12. Samples were prepared as wet films of DPL or coated dusts on a KBr pellet substrate. In the DPL treated quartz, the 3024 cm^{-1} trimethylamine band disappears, but the 3400 cm^{-1} band associated with P—O—HOH is not suppressed. For the kaolin, shown in Figure 13, the 3400 cm^{-1} group has virtually disappeared, and the trimethylamine band is suppressed and shifted. The evidence here is strongly suggestive of a quartz-trimethyl amine association, and a kaolin-phosphate association. There also exists the possibility of a kaolin-trimethylamine association, but the evidence is not as strong. The use of dry or moist samples for IR spectroscopy limits extrapolation of these results to dusts immersed in aqueous media. But the data suggest an association of the phosphate moiety of lecithin with basic aluminol groups on the alumina octahedra portions of the kaolin surface, and a consequent hindrance of enzymatic hydrolysis of the nearby glycerol-to-fatty acid ester.

To consider quartz and kaolin surface functions involved in direct lysis of erythrocyte membrane, in the absence of surfactant coating, we also performed some limited experiments to determine whether pH significantly affected dust cytotoxicity in the hemolysis assay. Quartz would be expected to show only acidic characteristics, due to surface silanol groups, while kaolin may have acidic silanol surface groups, as well as weakly acidic and weakly basic aluminol surface groups. An experimental problem arises here, however: the red blood cells are subject to hemolysis when a hydrogen ion, or other ion, gradient is present across the membrane. We tried to see whether the external osmolarity could be increased to offset this gradient, and the results are shown in Figure 14. The method seemed reasonable down to pH 5, so all blood suspensions were adjusted to 400 mOsm for the pH dependence experiments.

Figure 15 shows the dependence of hemolysis on pH. For both quartz and kaolin, the slope is positive between pH 5 and 7, suggesting that a charge dependent mechanism is involved with hemolysis for both dusts. The acidic character of both dusts suggests an acid-base interaction of the minerals with the trimethylamine group of membrane lecithin. Inter-

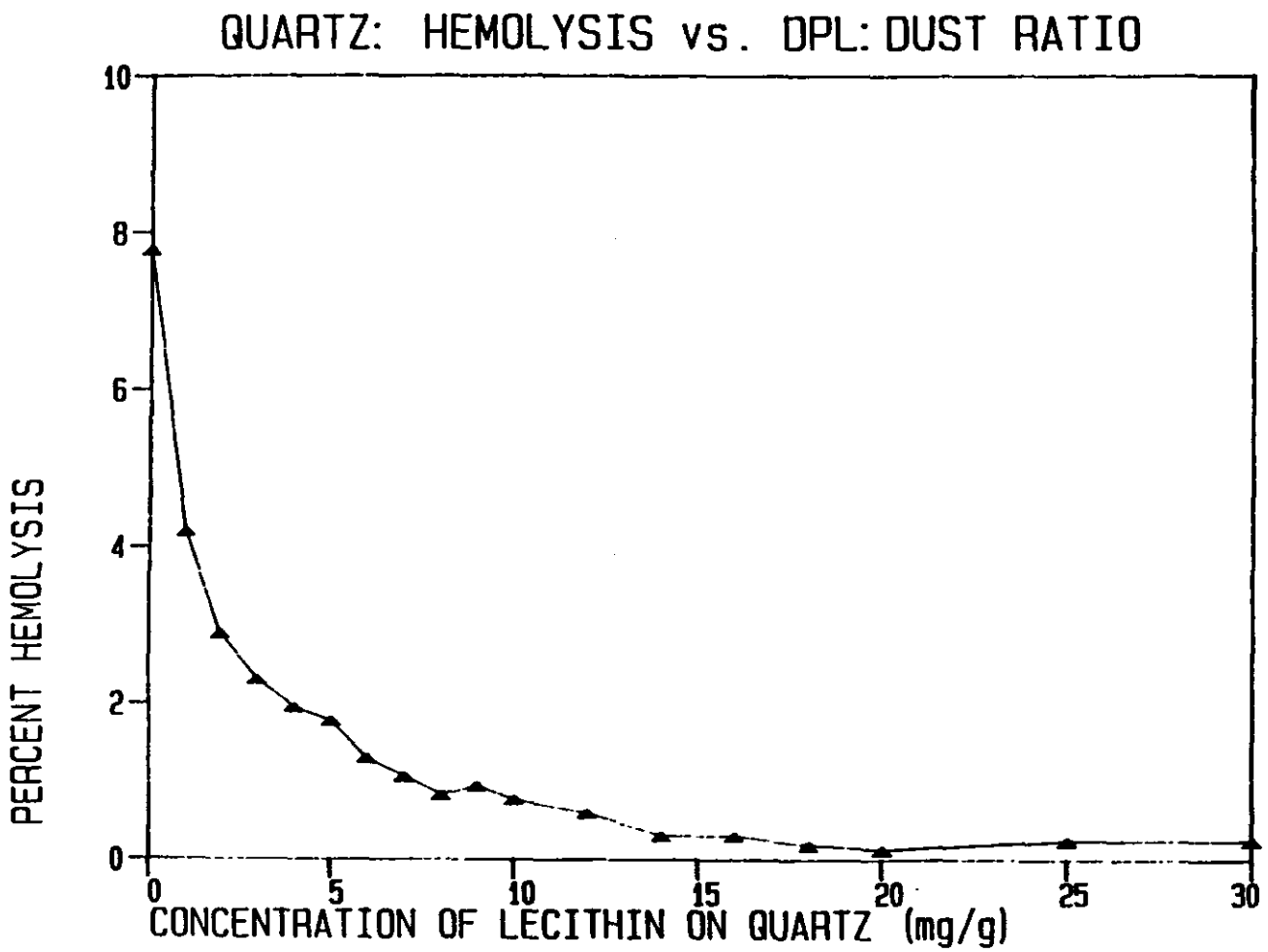

Figure 2. Percent hemolysis vs. DPL: quartz ratio.

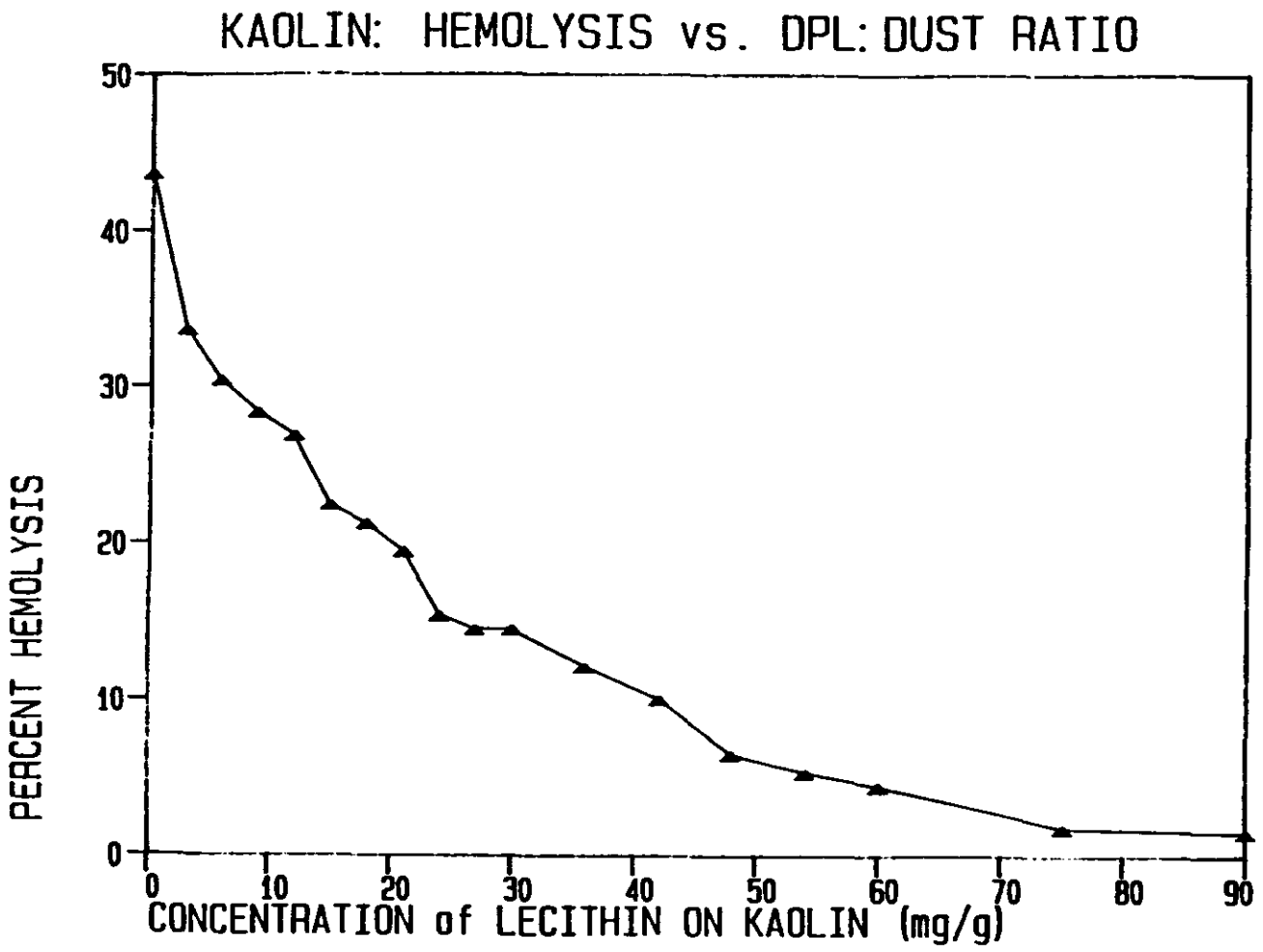

Figure 3. Percent hemolysis vs. DPL: kaolin ratio.

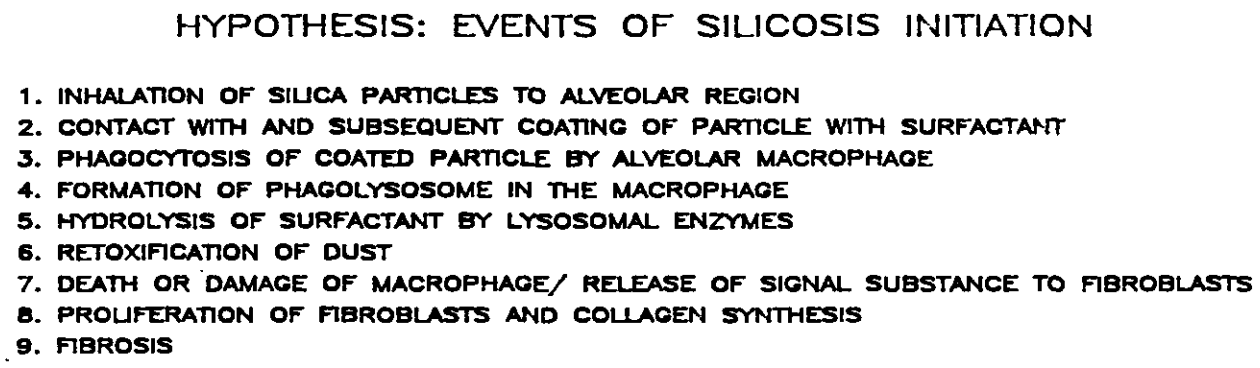

Figure 4. Working hypothesis for silicosis initiation.

LABORATORY PROTOCOL

1. PREPARE DPL DISPERSION IN SALINE WITH ULTRASONIC AGITATION
2. DUST COATED WITH DPL FOR 1 HOUR AT 37 DEGREES C
3. EXCESS DPL RINSED FROM DUST
4. INCUBATE DUST WITH PHOSPHOLIPASE A2 FOR 2 TO 72 HOURS
5. DUST RINSED WITH EDTA BUFFER TO INACTIVATE ENZYME (TWICE)
6. DUST RESUSPENDED IN BUFFER/CYTOTOXICITY ASSAY
7. LIPIDS EXTRACTED FROM REST OF DUST WITH SOLVENT
8. LIPIDS SEPARATED BY THIN LAYER CHROMATOGRAPHY
9. LIPIDS RECOVERED AND QUANTIFIED BY PHOSPHORUS ASSAY

Figure 5. Laboratory protocol for *in vitro* cell free system.

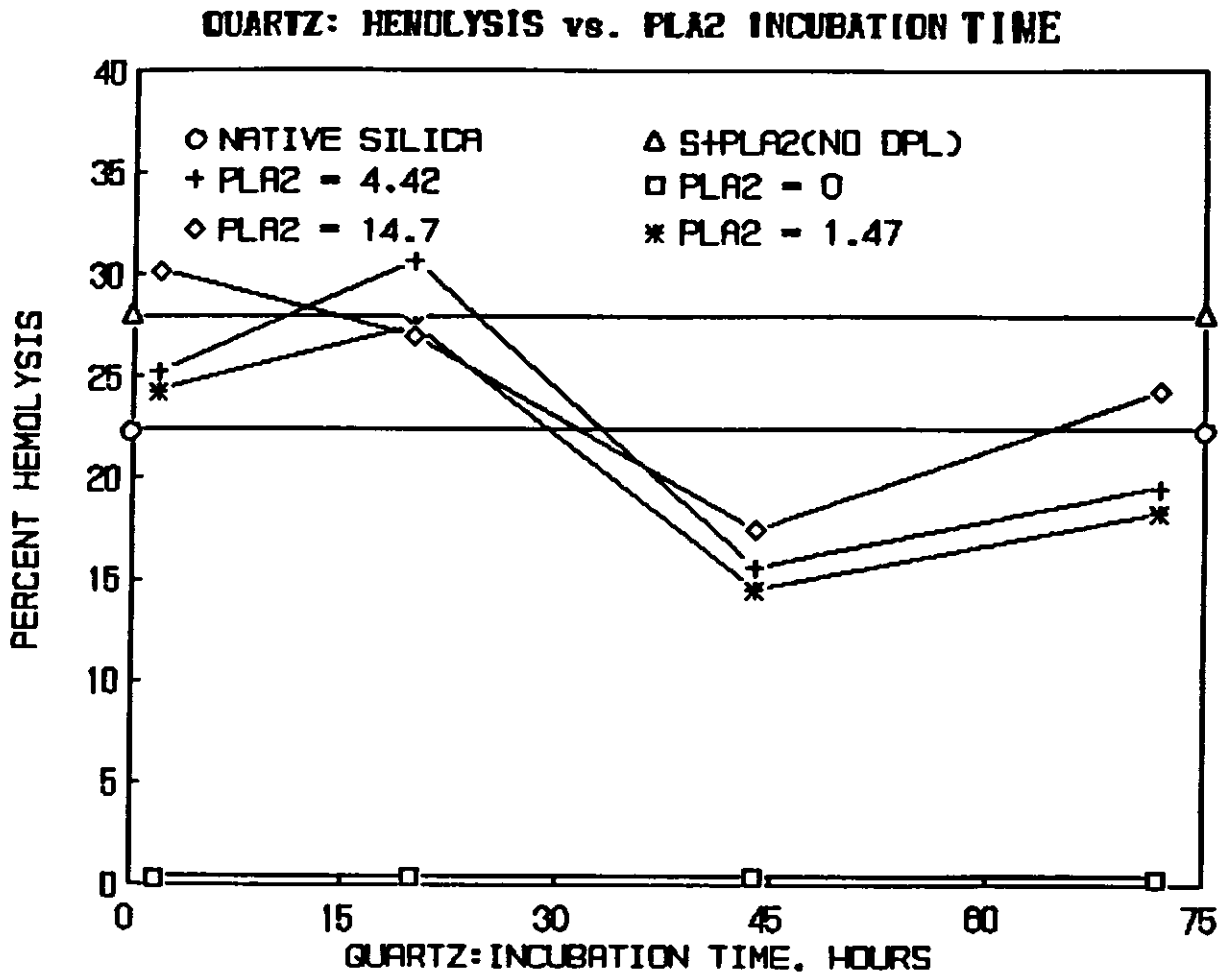

Figure 6. Hemolysis vs. time for DPL-coated quartz treated with phospholipase A_2.

pretation of these results on the pH dependence of the lytic potential of uncoated dusts are compromised by questions of the effect of pH on the lytic fragility of the membrane itself.

An overall research hypothesis which presents itself is that native quartz and aluminosilicate dusts can damage cellular membrane by direct interaction with dissociated mineral surface acidic silanol groups; that adsorption of the lecithin portion of pulmonary surfactant masks and thereby passivates these mineral surfaces; that phospholipase enzymatic digestion of lecithin coated dusts following their phagocytosis can remove the protective surfactant coating and restore cytotoxic potential of dusts within the phagocytic cell; and that the rate of this restoration may be affected by conformational differences between lecithin adsorbed to acidic silanol groups on quartz and to acidic silanol and basic aluminol groups on kaolin.

CONCLUSIONS

The surface toxicity both of quartz and kaolin dusts is eliminated in short-term cytotoxicity assays by coating the dusts with DPL.

Lecithin treated quartz is readily re-toxified by phospholipase A_2 in a cell-free *in vitro* system, and is relatively free of retained phospholipids.

DPL treated kaolin is not readily re-toxified at comparable enzyme levels, and retains both DPL and phospholipid degradation products.

The pH dependence suggests that both quartz and kaolin have acidic surface groups that are involved in hemolysis, and also may associate with the positively charged trimethylamine group of DPL.

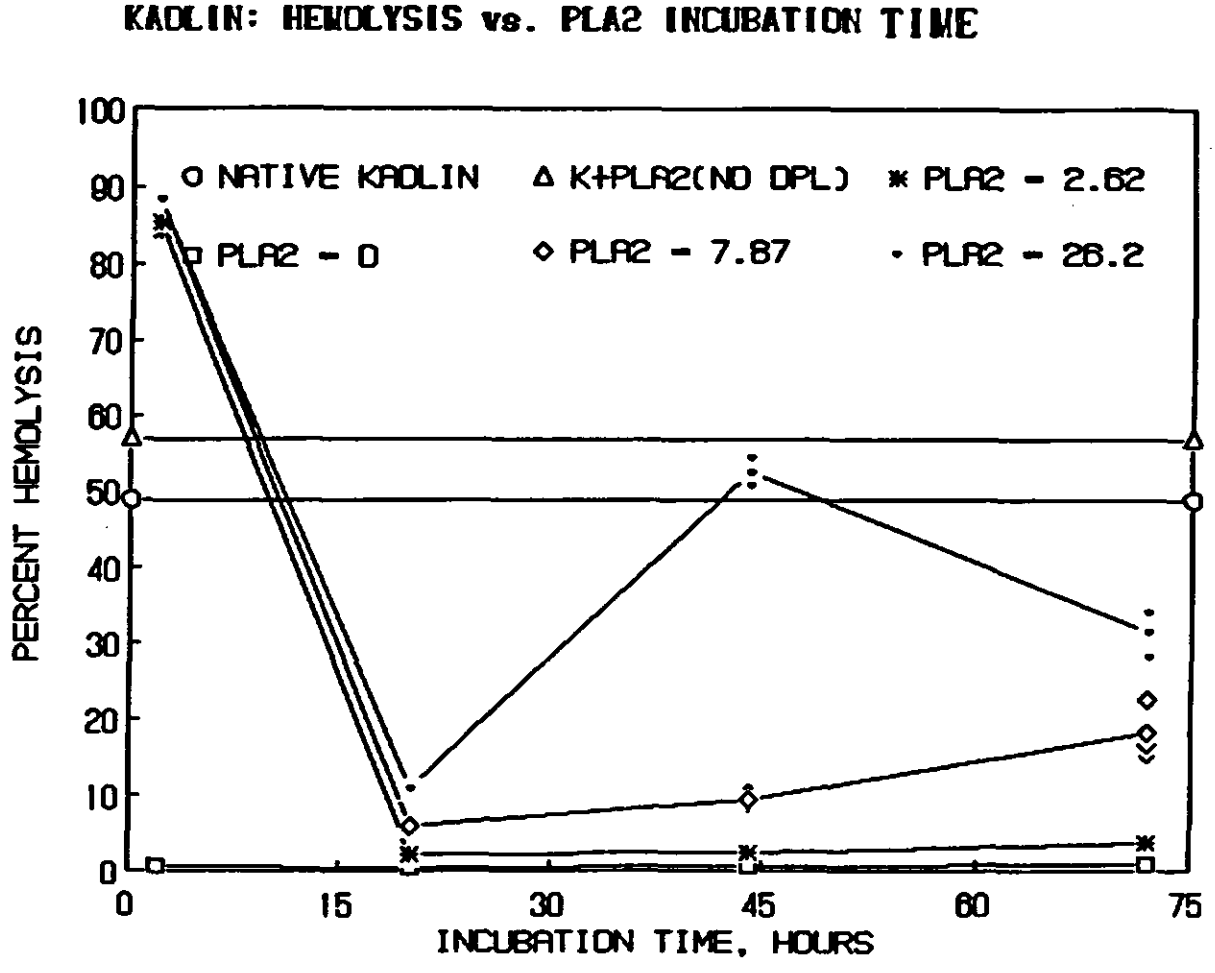

Figure 7. Hemolysis vs. time for DPL-coated kaolin treated with phospholipase A_2.

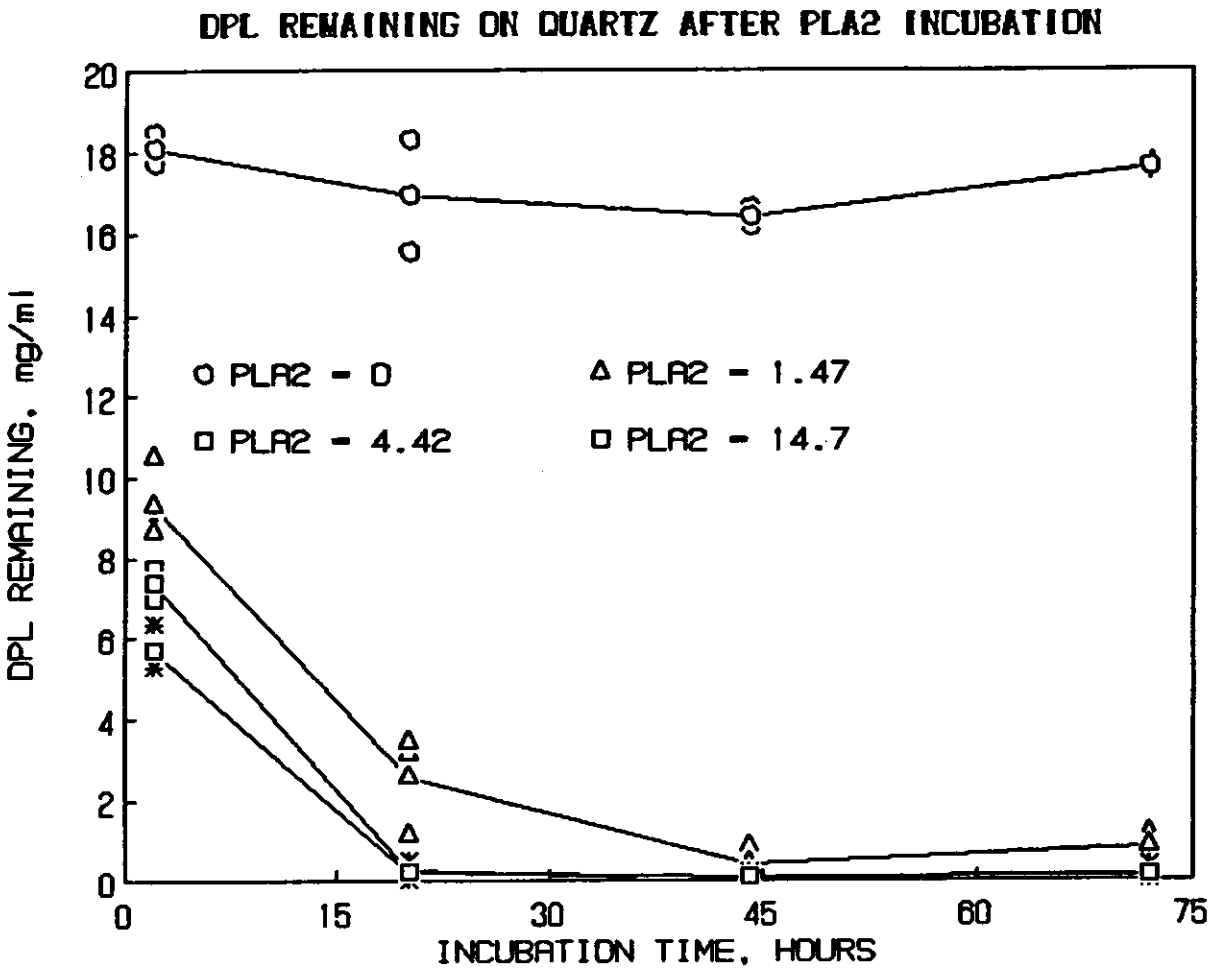

Figure 8. Lysolecithin retained on quartz after PLA_2 incubation vs. time.

FTIR spectra suggest that kaolin probably interacts with the phosphate group of DPL, and both quartz and kaolin probably interact with the trimethylamine group. Thus, there may be a surface chemistry effect in the differing rates of hydrolysis by phospholipase A_2.

ACKNOWLEDGMENT: This research has been supported by the Department of the Interior's Mineral Institute Program administered by the Bureau of Mines through the Generic Mineral Technology Center for Respirable Dust under Grant number G1135142.

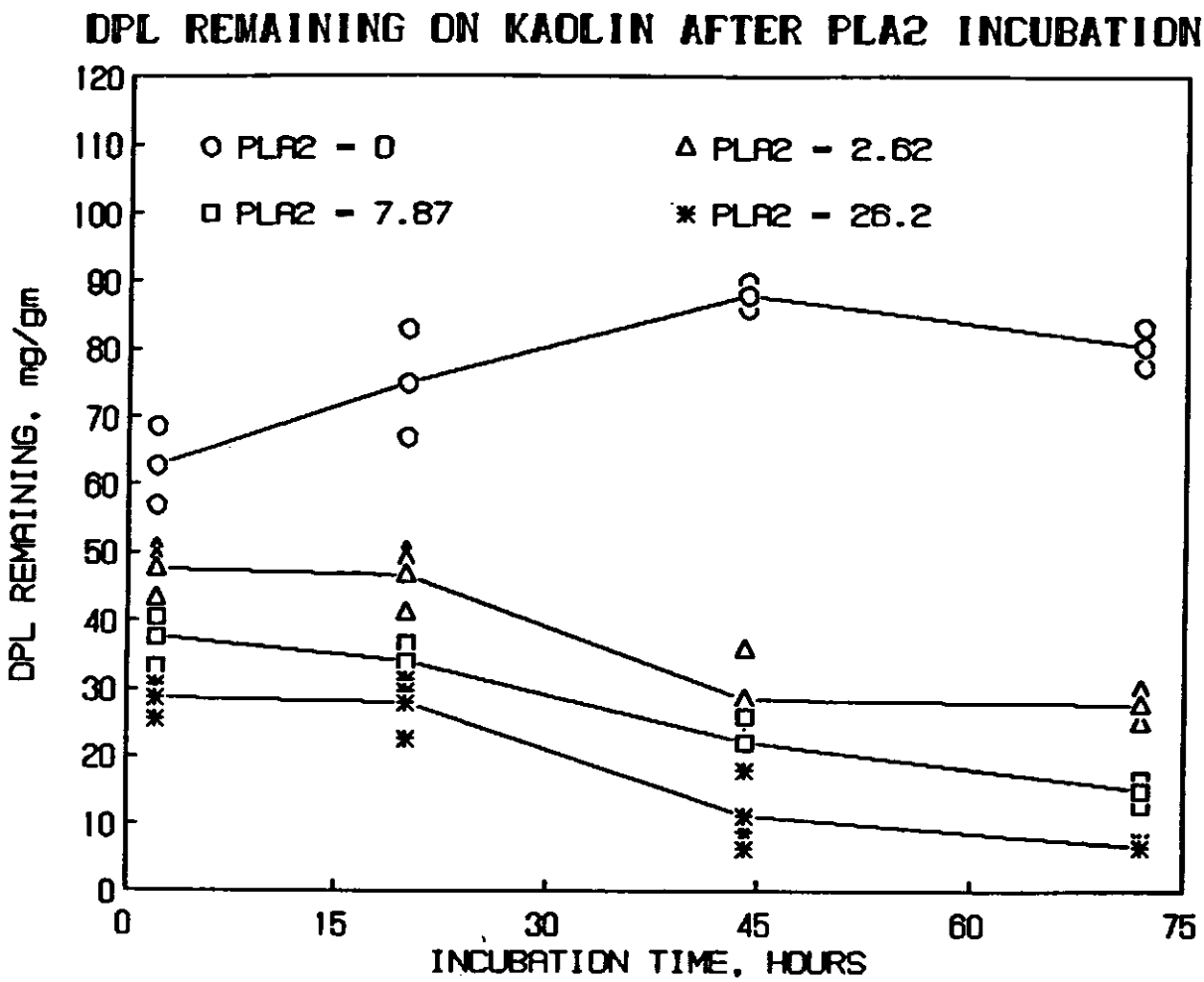

Figure 9. Lysolecithin retained on kaolin after PLA_2 incubation vs. time.

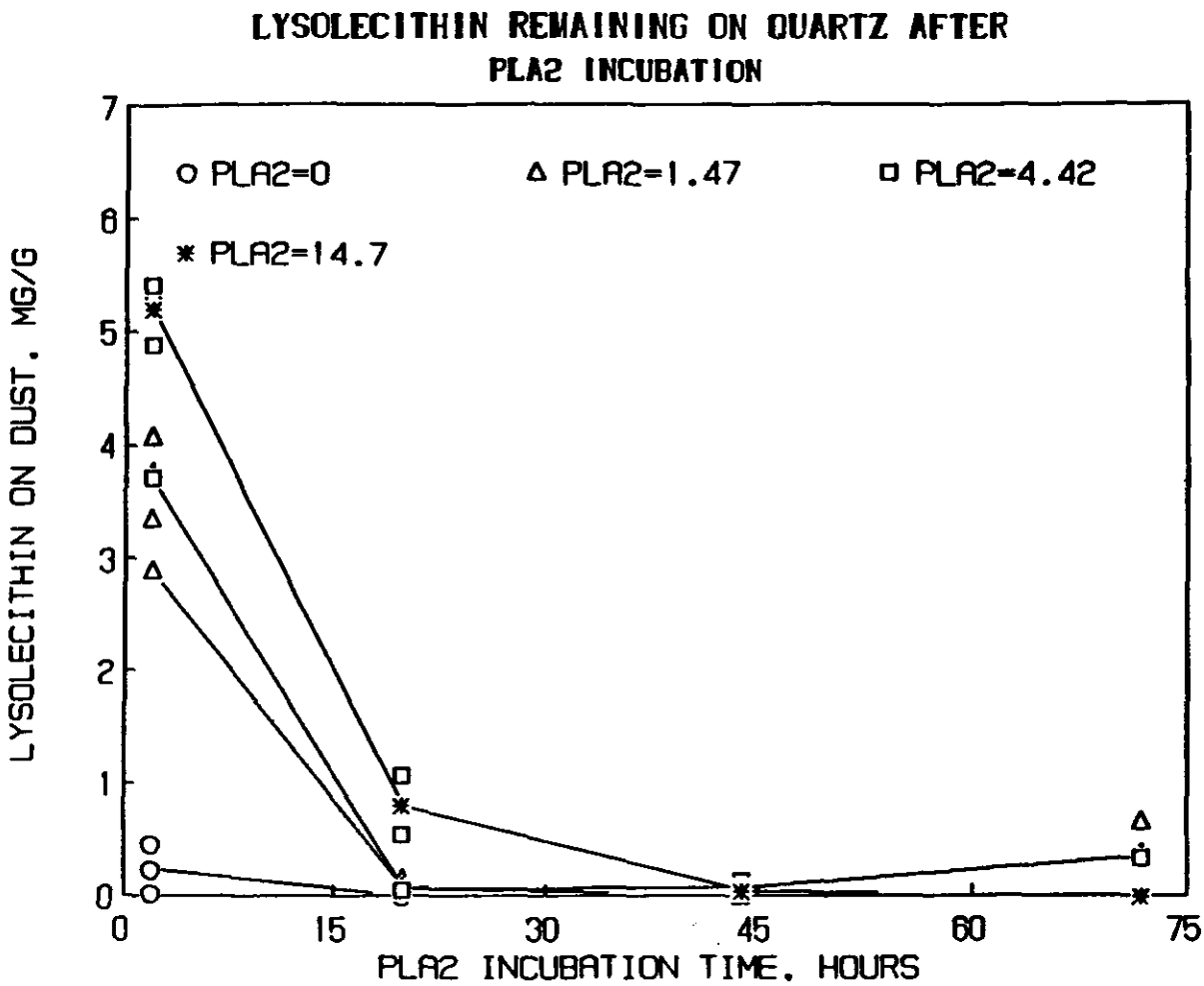

Figure 10. DPL retained on quartz after PLA_2 incubation vs. time.

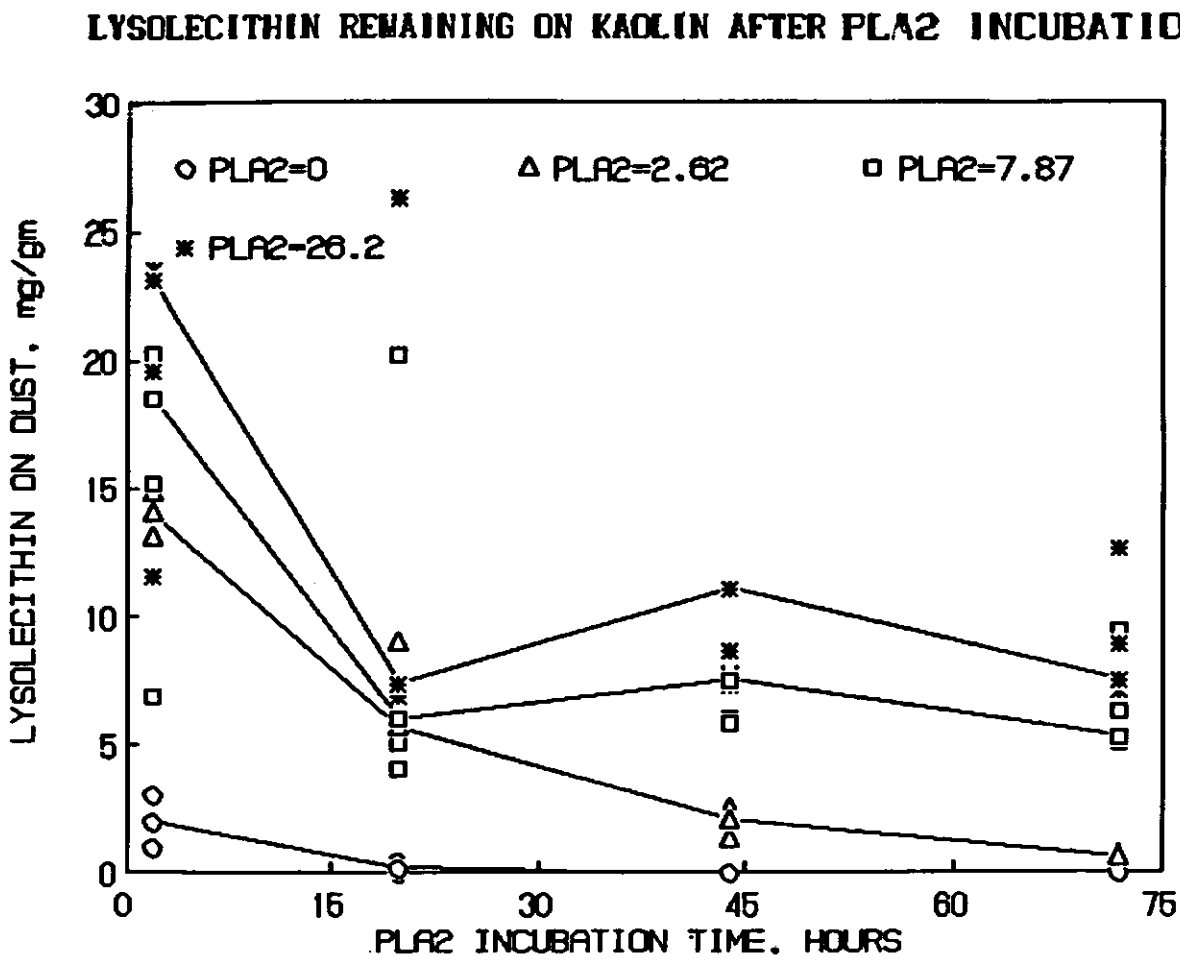

Figure 11. DPL retained on kaolin after PLA_2 incubation vs. time.

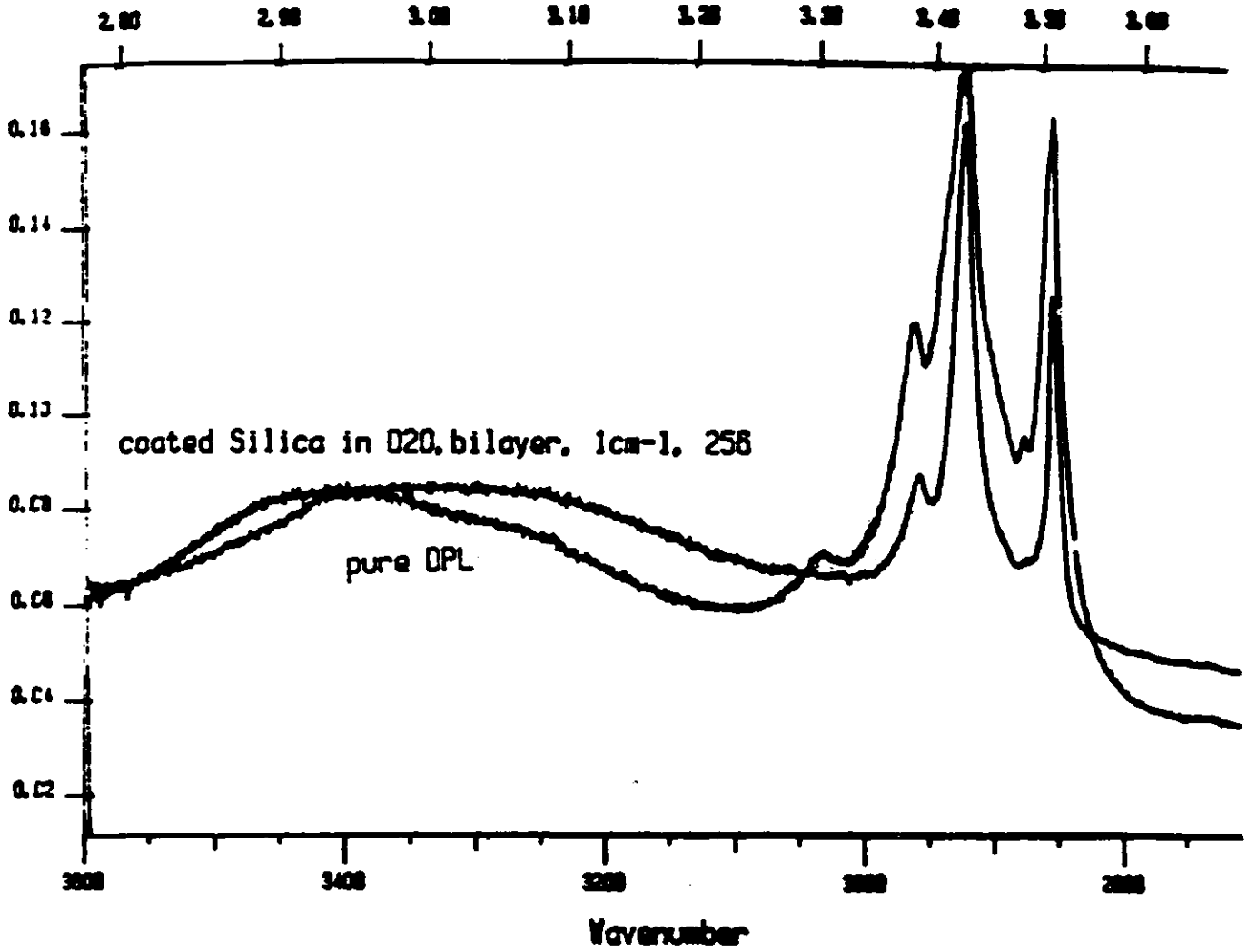

Figure 12. FTIR spectra of DPL-coated quartz and DPL only, 2750–3600 cm^{-1}.

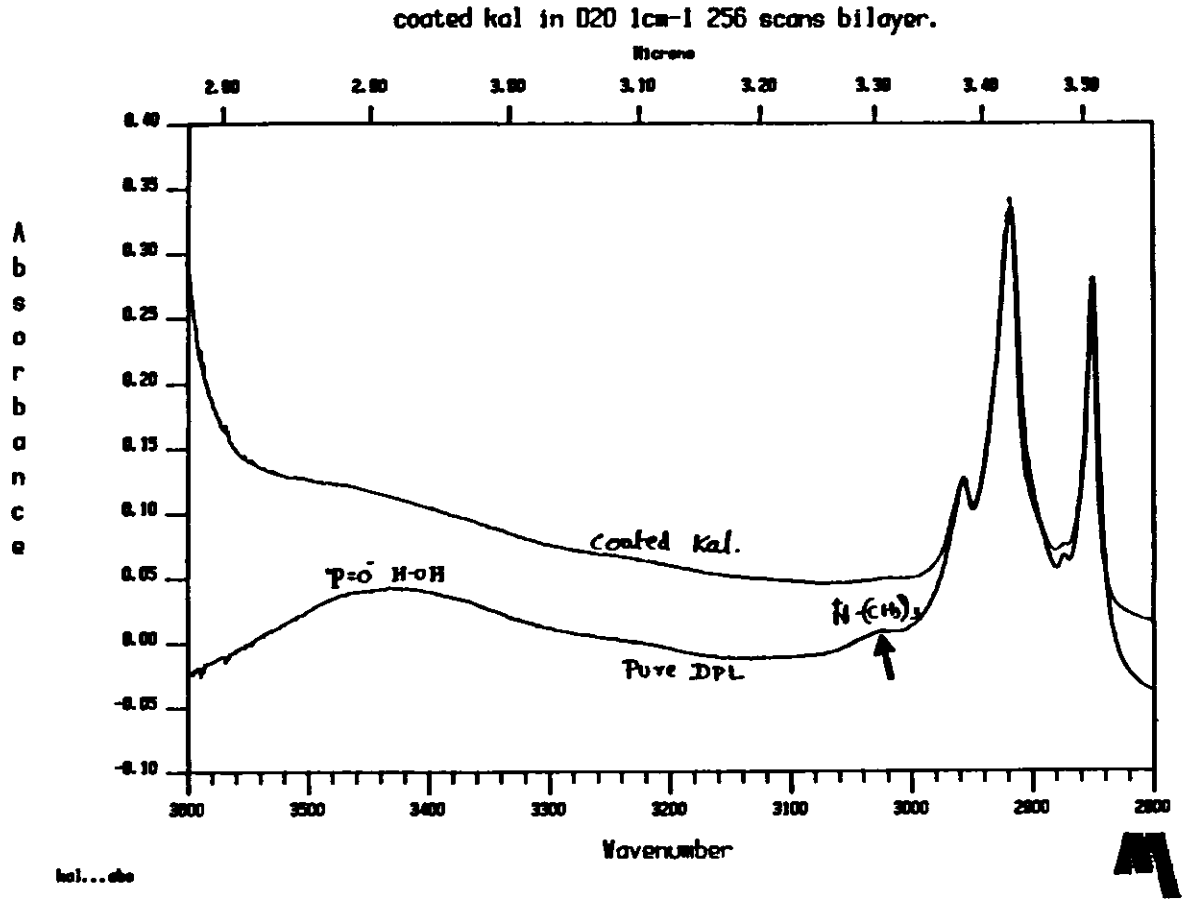

Figure 13. FTIR spectra of DPL-coated kaolin and DPL only, 2800–3600 cm^{-1}.

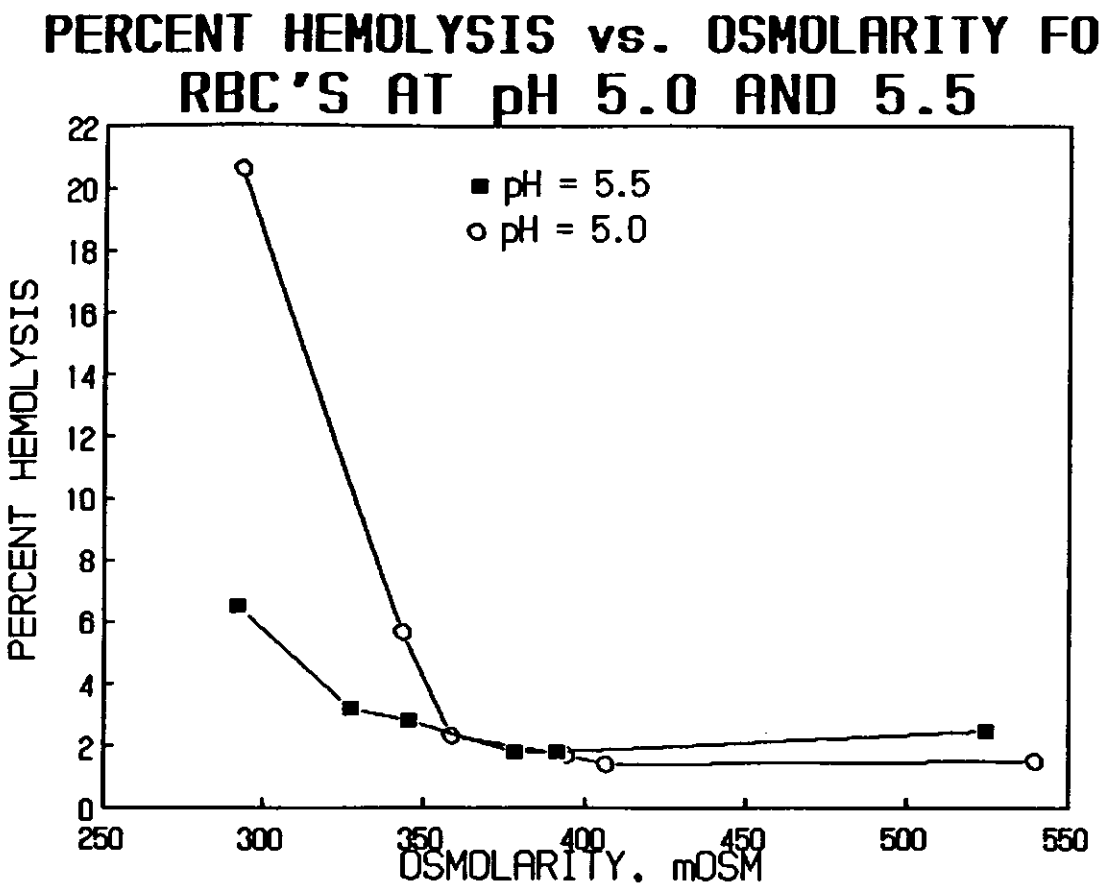

Figure 14. Percent hemolysis vs. osmolarity at pH 5 and pH 5.5.

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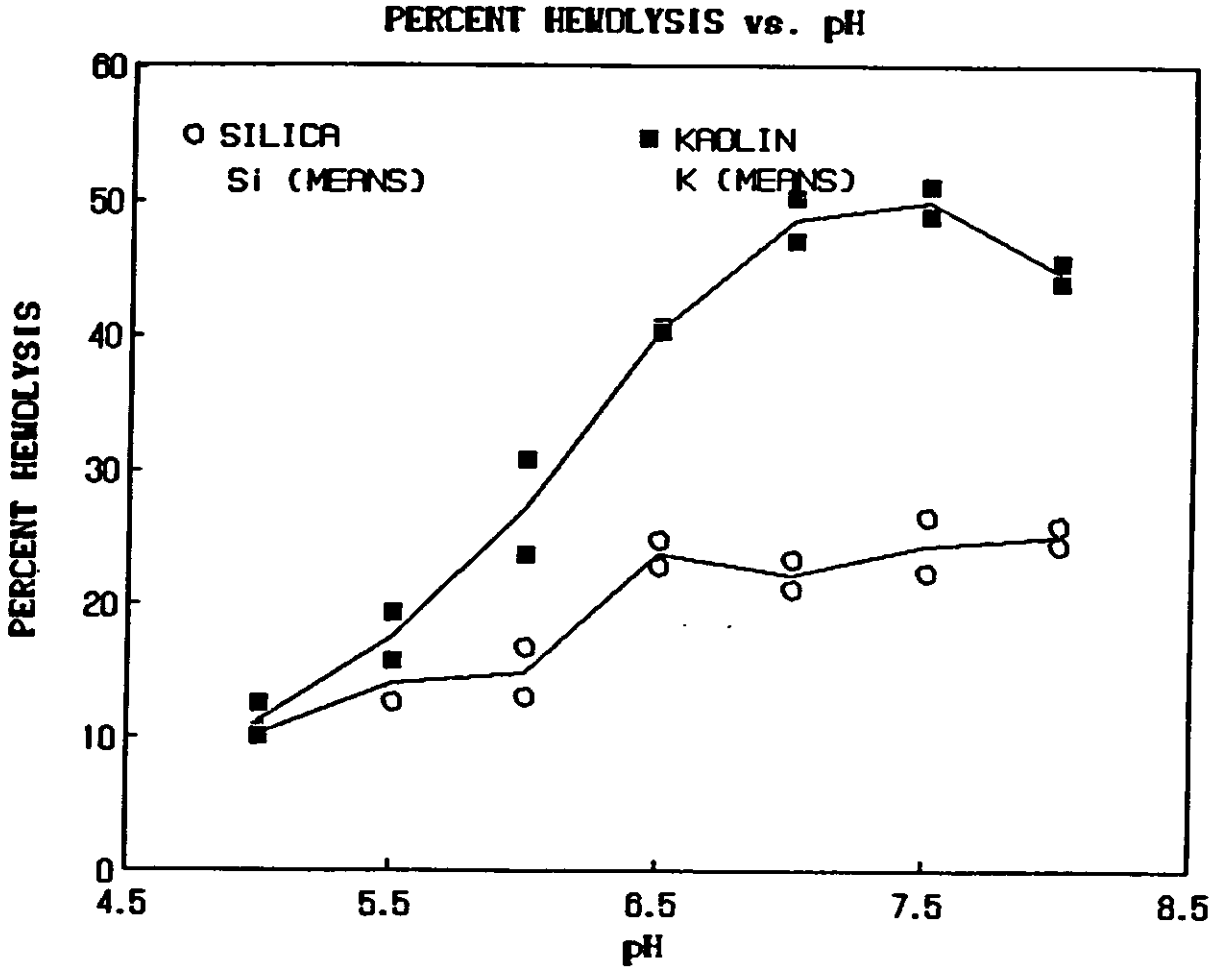

Figure 15. Percent hemolysis vs. pH for silica and kaolin @ 400 mOsm.

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DUSTS CAUSING PNEUMOCONIOSIS GENERATE ·OH RADICALS AND RED CELL HEMOLYSIS BY ACTING AS FENTON REAGENTS

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ABSTRACT

We hypothesized that dusts can produce toxic hydroxyl radicals (·OH) from lung H_2O_2. Amosite asbestos, silica (Minusil) and kaolin generated substantial ·OH, measured by conversion of 13 mM DMSO to methane with 1 mM H_2O_2 as substrate and 1 mM ascorbate (A) as reductant. Methane generation measured by gas chromatography was prevented by the ·OH scavenger dimethylthiourea (DMTU), or dust preincubation with the iron chelator transferrin (TRAN, 2 mg/ml).

	Methane ppm (mean±SEM)			
	−A	+A	A+DMTU	A+TRAN
Amosite 1 mg/ml	4±.1	1,008±53	4±.2	3±0
Minusil 1 mg/ml	3±2	1,032±46	0±0	1±0
Kaolin 1 mg/ml	3±.2	925±55	4±.3	23±3

Human red cell hemolysis was significantly antagonized by the anion channel blocker 4,4'-diisothiocyano-2,2'-stilbene disulfonic acid (DIDS, 1 mM), the hydroxyl radical scavenger n-propyl gallate (PG, 6 mM), the H_2O_2 scavenger catalase (CAT, 100 U/ml), or preincubation of dust with transferrin (TRAN, 2 mg/ml).

*p<.001 compared to untreated	%Hemolysis (mean±SEM)				
	Untreated	DIDS	PG	CAT	TRAN
Amosite 1 mg/ml	77±2	30±3.3*	29±.4*	32±1*	2±0*
Minusil 1 mg/ml	62±1	10±.5*	38±.5*	40±.6*	2±0*
Kaolin 1 mg/ml	50±.6	12±.1*	22±.2*	21±.3*	2±0*

Thus, hemolysis is caused by a dust-mediated Fenton reaction with superoxide anions (O_2-) and H_2O_2 from hemoglobin autooxidation as reducing agent and substrate.

No Paper provided.

EFFECT OF METAL ELEMENTS IN COAL DUSTS ON THE CYTOTOXICITY AND COAL WORKERS' PNEUMOCONIOSIS

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INTRODUCTION

It has been proved that many factors could influence the occurrence and progress of coal workers' pneumoconiosis (CWP). Among them, the composition of coal dust is regarded as an important factor contributed to the difference of CWP Prevalence in different coal mine areas. Therefore, the effects of metal elements in coal dust Were concerned gradually. Sorensen et al., stated that the concentration of some metals such as Fe, Pb, Cu, and Ni in the coal from a PA mine having a high incidence of CWP was higher than a sample of coal from a UT mine with low disease incidence.[13] Different contents of some trace metals in the lungs of coal miners from different collieries were also reported.[1] Furthermore. Christian et al. found that the effects of nickel (Ni) and Zinc (Zn) were very important to the pathogenicity of coal dust.

Coal is the principal energy resource in our country and millions of coal workers are being exposed to various kinds of coal dust. In some mines, the concentration of coal dust was tens, even hundreds times higher than the healthy standard (10 mg/m^3. It was also found that the incidence of CWP did not keep balance among different collieries.

In order to explore the factors which contributed to this difference, especially the effects of metal elements, we selected six coal dusts from six coal mines which were typical in our country. The research plan consisted of two parts, in the first one, both epidemiological investigation and laboratory experiments were designed, and in the second part, both *in vitro* and *in vivo* test were included.

MATERIALS AND METHODS

Part One

Animals: healthy, male Wistar rats (200 to 220g wt.) were supplied by the animals centre of our university, and were divided randomly into each group.

Coal dusts: six coal dusts were prepared by the grinding of coal samples which were collected from six coal mines in China. They were numbered 1, 2, 3, 4, 5, and 6, respectively. More than 90% of particles were less than 5 μm in diameter. The content of free silica (SiO_2) in coal dust was measured with the pyrophosphoric acid weight method, and the contents of Zn and Ni in coal dust were determined by the method of Proton Induced X-ray Emission (PIXE).

Cytotoxicity test in vitro: the rat pulmonary alveolar macrophages (PAM) were collected with the method of Myrvik's.[11] The lungs were lavaged with D-Hanks' solution and the lavages fluid was centrifuged (1,500 rpm × 10 min). The concentration the cell suspension prepared with 1640 medium was 1×10^6 cells/ml. Each aliquot (2.0 ml) of this suspension was transferred to a culture vassel. The exposure concentration of coal dust was 100 μg/ml in the medium. After exposing to coal dust and heat-killed yeasts for 2.5 hours at 37.0°C, the phagocytic rate and phagocytic index of PAM were measured using a modification of the technique of Graham et al.[8] At 24 hours after exposure, the viability of PAM was determined by the trypan blue exclusion technique, and the necrotic rate of PAM was observed under the light microscope after stained with Giemsa dye. The surface morphology of PAM at 24 hours after exposure was observed with the scanning electronic microscope (SEM) and following three types of changes were described: (1) intense response: the morphology of cell surface changed apparently, the pseudopodia occurred actively, the vaculose in cell membrane and the indistinct cell border were also seen; (2) faint response: cells were round and the microvillion the cell surface were densy and well-distributed; (3) modiate response: lay between above two states.

Epidemiological investigation: according to the occupational history, coal workers (mainly blasting coal workers) were selected in six coal mines. CWP was diagnosed on the basis of the diagnostic standard published in 1983 in China, and the detection rate (numbers of CWP/100 examined coal workers × 100%) was used to indicate the prevalence condition of CWP in each coal mine.

Part Two

In this part, coal dust 2 which contained the highest content of Ni (called nickel-coal dust) was chosen to carry out following tests to explore the antagonistic effect of Zn further.

In vitro test: rat PAM were isolated and collected as described in the first part. Five groups were designed, as showed in Table II. The exposure concentration of nickel-coal dust in the medium was 100 μg/ml. After exposing to the nickel-

coal dust and different dose of zinc chloride ($ZnCl_2$) for 24 hours at 37.0°C, the ATP levels in PAM were determined with a fluorescence fluorescase enzyme system.

In vivo test: 1.0 ml suspension which contained 50 mg nickel-coal dust and different dose of $ZnCl_2$ were intratracheally installated into rat lungs (see Table III). At fifteen days after installation, lungs were lavaged with D-Hanks' solution and PAM were isolated by centrifugation. The contents of Zn and k ions in the PAM were measured by the method of atom absorption spectrophotometer (AAS).

Statistical Treatment

The statistical significance of differences between each two groups was evaluated by *t* test $P<0.05$ was accepted as the level of significance.

RESULTS AND DISCUSSION

The results of the first part of this study were showed in Table I.

1. The results of the cytotoxicity test *in vitro* showed that coal dust 2 was the most cytotoxic, and coal dust 3 was the least one. The sequence of the cytotoxicity was coal dust 2>6>5>4>1>3. That was consistent with the results of epidemiological investigation of CWP in six coal mines.
2. The contents of SiO_2 in six coal dusts were less than 5% except coal dust 2, and it was found that they were not correlative to the cytotoxicity of coal dust and the detection rate of CWP in six coal mines. In recent years, many results from both experimental study and epidemiological investigation proposed that if SiO_2 content in coal dust was less than 5% or 10%, no evidence could be found about its influence on the cytotoxicity and the prevalence of CWP.[9,12,14] The effect of SiO_2 in coal dust is influenced by many interfering factors, and it was regarded that some metal elements may play an important role in this process.[10]
3. Coal dust 2 had the most cytotoxic effect on PAM with the highest content of Ni, while coal dust 3 contained the highest content of Zn and correspondingly, its cytotoxicity was the least and the detection rate of CWP in coal dust 3 was the lowest. So it was concluded that the contents of Zn and Ni in coal dust correlated closely with the cytotoxicity and the detection rate of CWP. Christian et al. found that the leachates from PA coal sample had more cytotoxic effect *in vitro* than that from UT coal sample, and the PA leachates contained more Ni and less Zn than the UT one.[2,3] It is widely known that Zn is one of the essential trace metals and is very important to maintain the structures and functions of living cells.[4] Ni has been proved to be cytotoxic both *in vitro* and *vivo*.[8,16] Therefore, further studies on the

Table I

Results of the Analyses and the Cytotoxicity Test of Coal Dusts and the Epidemiological Investigation in 6 Coal Mines

Source of Coal Dusts	Composition			Cytotoxicity						Investigation
	SiO_2 (%)	N_i (ppm)	Z_n (ppm)	Viability (%)	Phagocytic Rate(%)	Index	Necrotic Rate(%)	Surface Response	Harmful Sequence	Detection Rate of CWP
2	5.45	155.5	87.8	75.7	30.2	0.44	23.8	intense	5.4	23.60
6	2.23	72.3	82.5	73.8	42.2	0.68	20.0	intense	4.6	4.68
5	1.55	39.4	78.8	75.2	47.7	0.83	20.3	mediate	4.2	2.83
4	1.55	38.6	73.6	73.6	46.2	0.63	18.2	mediate	3.6	2.60
1	2.80	108.5	75.4	76.0	48.7	0.72	16.6	mediate	1.8	1.87
3	3.65	129.4	342.3	80.0	58.2	0.86	17.3	faint	1.4	0.90

Table II
ATP Levels in Rat PAM After Exposing to the Nickel-Coal Dust and Zn for 24 Hours *in vitro*

Groups	ATP levels ($x10^3$umol/$4x10^6$PAM)	P Value
1. nickel-coal dust(100ug/ml) $ZnCl_2$(0.2ug/ml)	3.883±1.270 (n=11)	(1 and 3)*
		(2 and 3)*
2. nickel-coal dust(100ug/ml) $ZnCl_2$(0.4ug/ml)	3.239±1.654 (n=9)	(3 and 4)*
		(1 and 5)*
3. nickel-coal dust(100ug/ml)	0.756±0.331 (n=9)	(2 and5)*
4. $ZnCl_2$(0.2ug/ml)	3.194±0.921	(3 and 5)*
5. physiological saline (control)	1.575±0.525 (n=12)	(4 amd5)*

*P<0.05

Table III
The Content of K and Zn Ions in Rat BAM in 15 Days After Intratracheal Instillation of Nickel-Coal Dust and $ZnCl_2$

Groups	K(Mg/10^{10}PAM) $\bar{x} \pm s$	P value	Zn(mg/10^{10}PAM) $\bar{x} \pm s$	P value
1. nickel-coal dust (50mg/ml) $ZnCl_2$(0.1mg/ml)	26.35±9.77 (n=5)	(1 and 3)* (1 and 5)*	1.12±0.57 (n=5)	(1 and 3)* (1 and 5)*
2. nickel-coal dust(50mg/ml) $ZnCl_2$(0.2mg/ml	23.41±6.04 (n=7)	(2 and 5)* (5 and 6)*	0.93±0.28 (n=7)	(2 and 4)* (2 and 5)*
3. $ZnCl_2$(0.1mg/ml)	17.42±5.07 (n=5)		0.52±0.30 (n=5)	
4. $ZnCl_2$(0.2mg/ml)	18.87±6.60 (n=6)		1.64±0.77 (n=6)	
5. nickel-coal dust(50mg/ml)	11.76±1.53 (n=7)		0.38±0.06 (n=4)	
6. physiological saline (control)	29.64±14.09 (n=7)		0.62±0.33 (n=6)	

*P<0.05

effects of Zn and Ni on the cytotoxicity of coal dust and on the etiology of CWP are needed.

4. Fisher et al. reported that Zn was antagonistic to the cytotoxicity of Ni *in vitro*.[5] Waalkes et al. also suggested that the pre-treatment with zinc acetate could increase the resistance of rat to the toxicity of nickel acetate.[15] In this results, coal dust 3 contained the highest content of Zn and high content of Ni, but its cytotoxicity was the least. Therefore, it is possible that Zn is antagonistic to the cytotoxicity of Ni in coal dust.

In order to explore the antagonistic effect of Zn toward the cytotoxicity of Ni further, we carried out the second part of this study.

1. The effects of $ZnCl_2$ and nickel-coal dust on ATP levels in PAM *in vitro* (Table II). The ATP levels in nickel-coal dust group were significantly lower than that of control group ($p<0.05$). However, in the nickel-coal dust and $ZnCl_2$ mixed group the ATP levels increased remarkably comparing with that of nickel-coal dust group ($p<0.05$). It is already proved that ATP is the direct energy resource for cell activities and the reducing of ATP levels in cell is the sensitive index for reflecting the damage of cell structure and function.[6] In this test $ZnCl_2$ increasing the ATP levels in PAM after exposing to nickel-coal dust *in vitro* indicated that appropriate dose of $ZnCl_2$ could antagonize the cytotoxicity of nickel-coal dust.

2. The effects of $ZnCl_2$ and nickel-coal dust on the contents of K ions in PAM *in vivo* (Table III). At fifteen days after instillation of nickel-coal dust, the content of K in PAM in rat BAL was significantly lower than that of control group ($p<0.05$). However, when certain dose of $ZnCl_2$ was instillated with nickel-coal dust, the K content in PAM increased notedly ($P<0.05$). The results in Table III also revealed that the content of Zn in PAM in nickel-coal dust and $ZnCl_2$ mixed group was significantly higher than that of nickel-coal dust group. The contents of ions in cell are correlated closely with the permeability of cell membrane which changed significantly in the early stage of cell damage.[7] So the results in this test proved that $ZnCl_2$ could reduce the toxicity of nickel-coal dust to cell membrane *in vivo*.

The prevalence of CWP changed significantly in different coal mine areas in China. The understanding of the relationship between the Zn and Ni content and the pathogenecity of coal dusts will provide a new basis for the explanation of this difference and for getting deeper understanding of the etiology of CWP, and further, for paying more attention to the prevention of CWP in high prevalence coal mines.

In summary, the results of this study proposed that the cytotoxicity of coal dust and the detection rate of CWP did not correlate with the content of SiO_2 (<5%), but correlated closely with the contents of metal elements in coal dust. The cytotoxicity and the detection rate of CWP were higher in coal dust with high content of Ni; on contrast, the cytotoxicity and the detection rate of CWP were lower in coal dust which contained high content of Zn. It was found further that appropriate dose of $ZnCl_2$ was antagonistic to the cytotoxicity of nickel-coal dust both *in vitro* and in vivo.

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DETECTION OF HYDROXYL RADICALS IN AQUEOUS SUSPENSIONS OF FRESH SILICA DUST AND ITS IMPLICATION TO LIPID PEROXIDATION IN SILICOSIS

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INTRODUCTION

Despite considerable effort over the years, the mechanism by which the quartz particles exert their toxic action on cells and the processes by which these actions progress to fibrosis are still not fully understood.[1,2] It is generally thought, nevertheless, that the interaction of the quartz particles with the cell membranes is the starting point of the silicotic process.[3] We felt that the mechanism of the membrane damage by quartz might involve oxygenated free radicals because (a) a suspension of quartz particles in contact with alveolar macrophages has been reported[4,5] to initiate an enhancement of lipid peroxidation, defined broadly as the oxidative deterioration of polyunsaturated components of lipids, and (b) hydroxyl (•OH) radicals are known to be capable of peroxidation by abstracting hydrogen atoms from cell-membrame Lipids[6] and initiating lipid peroxidation in lysosomal membranes.[7] Moreover it is known that exposure of cell membranes, fatty acids and unsaturated food oils to ionizing radiation, which generates •OH radicals, causes rapid peroxidation.[6] Earlier studies of the aqueous chemistry of quartz suspensions have reported detection of H_2O_2,[8] implicating the formation of •OH radicals as transient species, but, we are not aware of any report of the detection of •OH radicals in quartz suspensions and this provided the motivation for the present undertaking. Since it is known that, because of their high reactivity (hence short life time) in aqueous media, the •OH radicals cannot be detected via electron spin resonance (ESR) directly,[9,10] we have used ESR combined with the spin-trap methodology[9] for studying the •OH formation.

MATERIALS AND METHODOLOGY

Crystalline silica with particle sizes of 0.2 to 2.5 mm was obtained from the Generic Respirable Dust Technology Center, Pennsylvania State University, University Park, Pennsylvania. Particles in the range of smaller than 25 microns were produced by hand grinding in air, using an agate mortar and pestle because of the structural similarity of agate to that of quartz. Also a rather mixed particle size, rather than a specific range, was employed, with a view to roughly approximate the random particle-size distribution in the mining atmosphere. ESR spectra were obtained at X-band (~9.7 GHz) using a Bruker ER 200D ESR spectrometer. For accurate measurements of the g-values and hyperfine splittings, the magnetic field was calibrated with a self-tracking NMR gaussmeter (Bruker, model ER035M) and the microwave frequency was measured with a frequency counter (Hewlett-Packard, Model 5340A). 5,5-dimethyl-1-pyrroline-1-oxide (DMPO) was purchased from Aldrich and used without further purification, since very weak or no ESR signals were obtained from the purchased sample when used by itself. If necessary the background signals were subtracted from those related to quartz by using an Aspect 2000 microcomputer.

RESULTS

Some typical results of the ESR spin-trapping studies are shown in Figure 1. We found that a 0.1 M aqueous solution of the spin-trap DMPO alone, with unground particles or with TiO_2 powder did not give a detectable ESR spectrum. TiO_2 was used as a control because it is known not to be fibrogenic[11] and has a structure resembling quartz (SiO_2). However, when quartz was ground in a 0.1 M DMPO (aqueous) solution or when ground quartz particles were mixed with 0.1 M DMPO (aqueous) solution, an ESR spectrum (g = 2.0059), consisting of a 1:2:2:1 quartet pattern with a splitting of 14.9 G, was observed (Figure 1a). Based on earlier work,[9,12,13] this spectrum was considered to be due to the DMPO-OH adduct.

Two further tests were made to identify the spectrum. First, the Fenton reaction ($Fe^{2+} + H_2O_2 \rightarrow Fe^{3+} + •OH + OH^-$),[14] known to produce •OH radicals, was used as a standard. The ESR spin-adduct spectrum obtained by mixing 0.085 M H_2O_2, 0.0165 M $FeSO_4$ and 0.1 M DMPO was the same as that of Figure 1a (obtained with ground quartz), thus attesting to the formation of the •OH radical in the quartz suspension.

As a second, confirmatory, test of the •OH radical. formation, spin-trap ESR experiments were performed in which ethanol was added as a secondary trap. It has been shown[10,15] that in the presence of ethanol, the intensity of the DMPO-OH signal decreases, because ethanol scavenges some of the •OH radicals to form the ethanolyl radicals[12] which react with DMPO to give the spin-adduct DMPO-

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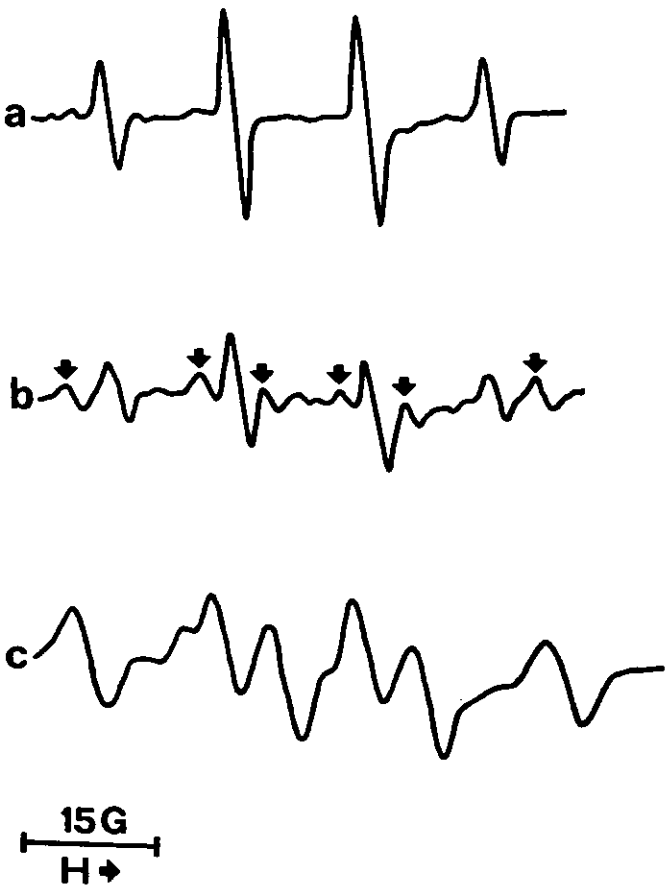

Figure 1. ESR spectra recorded 2 minutes after mixing 100 mM DMPO aqueous solution with (a) freshly ground quartz particles; (b) same as (a) but with 30% ethanol added; (c) same as (a) but with excess ethanol. Receiver gain, 5×10^5; modulation amplitude, 2 G; scan time, 100 seconds; field, 3460 ± 75 G.

$CHOHCH_3$. The ESR spectrum of the spin-adduct DMPO-$CHOHCH_3$ was indeed observed as indicated by arrows in Figure 1b (for 30% ethanol) and more clearly in Figure 1c, obtained in the presence of excess ethanol, thus confirming the •OH radical formation in the quartz suspension.

The intensity of the •OH radical adduct signal increases with the amount of grinding (Table I), thus showing that the •OH radical generation is related to some surface property of the freshly made dust, most likely the silicon-oxygen radical sites known to form on grinding.[16-21] Additional spin-trap measurements as a function of the time of "aging" of the dust after grinding showed that freshly generated quartz dust produces more •OH radicals than that which had been stored in air after grinding (Table II). In order to characterize the kinetics of the dust's aging on its ability to generate •OH radicals, attempts were made to determine whether the reaction was of the first order (a straight line plot for log (con.) vs. time) or second order (straight line plot for $(con.)^{-1}$ vs. time). The analysis indicated the kinetics to be neither first nor second order but of a more complex nature. Thus while it was not possible to define a unique half-life for the decrease in the •OH radical producing potential of the quartz dust on storage after grinding, we note that, on the average, freshly ground quartz dust loses its •OH-generating capacity to about 50% in approximately 1 day.

DISCUSSION

It is clear that the breakage of quartz crystals implies the homolysis of Si-O-Si bonds and the generation of silicon-based radicals ($\equiv Si\bullet$, $\equiv SiO\bullet$, $\equiv SiOO\bullet$)[8,16-21] We have indeed verified that Si • and SiO •-type of radicals are produced by grinding in air, and that the radicals decay as a function of time when the dust is stored in air after grinding,[17] with a half-life of about one and a half day. Earlier workers[16] have reported that the crushing of quartz under vacuum produces SiO •-type radicals whose concentration decreases drastically on exposure to atmosphere with a half-life of about 30 hours.

Table I

Dependence of the ESR Intensity of the DMPO-OH Adduct (i.e., •OH production) on Size (grinding times) of Quartz Particles

Grinding times (minutes)	Relative ESR intensity
0.0	0.0
0.5	0.3 ± 0.3
1.0	1.1 ± 0.6
2.0	2.3 ± 0.7
4.0	3.4 ± 0.8
10.0	5.1 ± 1.2

Table II

Dependence of the ESR Intensity of the DMPO-OH Adduct (i.e., •OH production) on the "Aging" of Quartz Dust

Time after grinding	Relative ESR intensity
5 minutes	5.2 ± 0.8
1 day	3.2 ± 0.8
2 days	1.9 ± 0.7
3 days	1.7 ± 0.8
4 days	1.3 ± 0.7

Following Kalbanev et al.,[8] we suggest that the •OH radical production might involve the following steps:[8]

$$\equiv SiO\bullet + H_2O \rightarrow \equiv SiOH + \bullet OH \quad (a)$$
$$\equiv SiO\bullet + \bullet OH \rightarrow \equiv SiOOH \quad (b)$$

Kalbanev et al. have also suggested[8] that the hydrolysis of SiOOH could produce H_2O_2, according to reaction (c):

$$\equiv SiOOH + H_2O \rightarrow \equiv SiO\bullet + H_2O_2 \quad (c)$$

The yield of H_2O_2, depending on the pH and the temperature of hydrolysis, was reported to be as high as 10^{18} molecules/g quartz particles,[8] enough to be measured by the standard method of wet analytical chemistry, the MnO_4^- reduction:

$$2MnO_4^- + 5H_2O_2 + 4H^+ \rightarrow 5O_2 + 2Mn^{2+} + 8H_2O \quad (d)$$
(pink) (colorless)

We verified the reducing activity of our quartz particle suspension with respect to KM_nO_4, although the H_2O_2 yield was measured to be about an order of magnitude smaller for our samples than those of Kalbanev et al.[8] Thus experiments were carried out to examine whether the •OH radical formation was through the Fenton reaction,[14] the Fe^{2+} possibly being a trace impurity. The experiments consisted of spin-trap measurements in which diethylenetriaminepenta-acetic acid (DETAPAC) (0.03 – 3.0 mM) was used as a strong metal-ion chelate. it is known that the iron-DETAPAC complex formation stops the •OH generation from H_2O_2.[9] On adding DETAPAC the •OH radical-related ESR signals showed no variation in either the g value or the observed splitting pattern but only a small (20 %) decrease in intensity even at the high DETAPAC (3 mM) levels. This result, together with the dependence of the •OH radical concentration on time and surface freshness, suggests that the Fenton-type mechanism is not a major contributor to the •OH radical generation in our quartz suspensions.

After this work was essentially complete,[17-20] two significant reports have appeared. In the first, Fubini et al.,[21] have report the formation of Si •, SiO •, and SiO_2 • radicals on quartz particles ground in air, without contact with water. They suggest a possible role of these radicals (or some other surface property) in the mechanism of quartz-induced fibrosis. Our ESR results on the silicon-based radicals,[18,19] agree with Fubini's.[21] We further show that the concentration of the Silicon-based radicals is time dependent[17] and that their reaction with aqueous media generates (perhaps) an even more potent species,[18-20] the •OH radicals. The second paper, by Gulumian and Van Wyk,[22] reported the detection of •OH formation in aqueous suspension of glass and quartz fibres *in the presence* of H_2O_2, and the scavenging of the generated •OH radicals by the prophylactic agent (polymer) polyvinylpyridine N-oxide (PVPNO). They suggest that the therapeutic efficacy of PVPNO in silicosis might be related to its scavenging effects on •OH radicals. Our work shows that the grinding process itself causes the quartz surface to be a source of •OH radicals in aqueous media and that this activity decreases with the aging of the dusts.[19,20] This higher toxicity of fresh dust must be taken into consideration in the future *in vitro* or *in vivo* laboratory (e.g., animal exposure) studies of quartz and related mineral dusts.

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COBALT SENSITIVITY IN HARD METAL ASTHMA —HARMFUL EFFECTS OF COBALT ON HUMAN LUNGS

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ABSTRACT

Twelve workers diagnosed as suffering from hard metal asthma on the basis of peak flow diaries and positive bronchoprovocation with cobalt chloride ($CoCl_2$) were studied for sensitization to cobalt using specific RAST (radioallergosorbent test with Co-HSA (cobalt conjugated human serum albumin) and Co-resin (cobalt conjugated exchange resin), saturated ammonium sulfate precipitation test with radioactive cobalt (Co-SASPT), skin test with $CoCl_2$ by intradermal Co-IDST) and patch (Co-PT) techniques, and lymphocyte stimulation test with $CoCl_2$ (Co-LST).

Eleven of 12 subjects sera which selectively bound ^{57}Co were divided into two groups. Seven sera showed evidence of specific IgE antibodies to Co-HSA and/or Co-resin on the basis of comparison with 60 control sera from asthmatic patients without a history of hard metal exposure, while four sera had no reactivity to these solid matrices. Further support for Co reactivity comes from blocking experiments where non-labelled Co^{2+} (1mM) inhibited specific antigen-antibody association. There was a strong relationship between RAST values and wheal diameters with 1% $CoCl_2$ ($r = 0.82$) in the subjects. The results in Co-PT does not agree with those in Co-LST, while correlation was seen in the patients with contact dermatitis. These findings suggest the development of hard metal asthma from cobalt sensitivity, although the involvement of type IV allergic reaction remains unknown.

No Paper provided.

EVALUATION OF PULMONARY REACTIONS IN HARD METAL WORKERS

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INTRODUCTION

The production of hard metal components of equipments for different technological uses is presently actively expanding in several countries.[9,10] Consequently, the number of workers exposed to risk of inhaling hard metal particles is increasing.

Lung disorders from exposure to hard metals have been known since almost 50 years, and recently cobalt has been recognized as the major responsible agent.[3,8,9] Both asthma and more severe deep lung involvement can occur, with possible evolution in fibrosis.[2,8,9]

In the last two years we had the opportunity to thoroughly investigate two groups of workers exposed to inhalation of hard metals in completely different occupational settings and to evaluate their pulmonary reactions by bronchoalveolar lavage (BAL). The main findings are reported in this paper.

MATERIALS AND METHODS

Subjects

Group A consisted of 26 workers, 25 males and one female, 18 smokers and 8 non-smokers, aged from 21 to 64 years (mean 32.9 years), engaged in the production of hard metal tools for 2 to 49 years (mean 10.4 years), and therefore exposed to tungsten carbide, titanium, tantalum and cobalt.

Group B consisted of 5 male workers, aged from 21 to 26 years, all but one non-smokers, engaged only in grinding hard metal tool edges by means of high-speed diamond-cobalt wheels with oily coolants for 1 to 9 years (mean 5 years) in a small workshop, with no proper protective equipments.

Two workers of group A, one non-smoker and one smoker, both 30 years of age, exposed for 7 and 13 years respectively, complained of work-related asthma, but were in remission at the time of study. Two workers of group B, non-smokers, aged 21 and 26, suffered from severe exertional dyspnea and complained of weight loss; they had been exposed for 6 and 5 years respectively, and were no longer exposed since 6 months when first studied.

Methods

The 31 workers were hospitalized and were investigated by the following protocol: personal and occupational history; routine clinical and laboratory checkup; chest X-rays; lung function tests; patch tests for cobalt and tungsten, and skin tests for common inhalant allergens; bronchoalveolar lavage (BAL); elemental determination by neutron activation analysis in BAL, blood, urine, toenails and pubic hair.

BAL was performed according to the method currently used in our institute, and cytologically examined as described elsewhere.[4] Lymphocyte typing in BAL was performed on cytocentrifuge preparations by monoclonal antibodies in an immunoperoxidase assay, as described in detail elsewhere.[5]

Elemental determination in biological specimens was carried out by neutron activation analysis, as described elsewhere.[7]

RESULTS AND DISCUSSIONS

In group A, no significant alterations were observed at chest X-rays. Lung function tests showed no significant impairment of the ventilatory function, whereas one subject with asthma and 4 additional workers presented a slight impairment of the pulmonary diffusion of gas.

On the contrary, BAL cytology showed a marked increase of total cells with a high percentage of lymphocytes in the non-smoker asthmatic subject (Table I). Increased percentage of lymphocytes (17%) with total cells somewhat above the highest normal value for smokers was detected also in one of the asymptomatic workers.

A moderate relative or absolute increase of lymphocytes was present in 8 additional workers, one with asthma (Table II). The increase of BAL lymphocytes was mainly due to an increase of suppressor (OKT8+) cells, with consequent inversion or marked reduction of the OKT4/OKT8 ratio, independent from the smoking habits.

Among the 5 young workers of group B, exposed to the fine aerosol spray originating from high-speed wet-grinding of hard metal edges, the two with severe dyspnea showed quite similar clinical features, consisting in diffuse irregular opacities at chest X-rays, associated with a significant restrictive impairment of the ventilatory function.

The cytology of BAL (Table III) showed in both cases an alveolitis of high intensity, characterized by an enormous increase of total cells, with numerous bizarre giant cells, marked eosinophilia, increased absolute number of lym-

Table I

Bronchoalveolar Lavage Cytology in the 26 Hard Metal Workers of Group A (mean values and ranges)

Cases	No.	Total cells /ml x 10^{-3}	% Macrophages	% Lymphocytes	% Neutrophils	% Eosinophils
Asthma	1 NS	1800	61	36	0	3
	1 S	640	91	7	2	0
No symptoms	7 NS	173 (95-235)	76 (51-91)	15 (7-27)	3 (<1-6)	<1 (0-2)
	17 S	700 (235-1530)	91 (80-99)	6 (<1-17)	3 (<1-5)	<1 (0-1)

NS, non-smoker S, smoker

Table II

Bronchoalveolar Lavage Lymphocyte Behavior in Hard Metal Workers of Group A

No. of cases		BAL lymphocyte number	Ratio OKT4/OKT8
2	1 asthma	markedly increased	0.15
	1 no symptoms	increased	0.2
8	1 asthma	slightly increased	0.35
	7 no symptoms		0.2-0.8
16	no symptoms	normal	0.9 (1 case)

Table III

Bronchoalveolar Lavage Cytology in the 5 Hard Metal Workers of Group B (individual values)

Cases	No.		Total cells /ml x 10^{-3}	Macrophages %	Lymphocytes %	Neutrophils %	Eosinophils %
Interstitial lung disease	2	NS	3000	78	3	1	18
		NS*	2475	62	32**	3	3**
No symptoms	2	NS	120-210	68-72	23-27	4-5	0-<1
	1	S	375	87	10	2	<1

NS, non smoker S, smoker

* under steroid treatment since two months

** BAL pre-treatment at another institution: Lymphocytes 5%, Eosinophils 60%

phocytes with inverted OKT4/OKT8 ratio (0.52 and 0.58 respectively). The lymphocyte subpopulations in blood were normal.

The BAL findings correlated strictly with the histological features observed at open lung biopsy, performed in one case. In fact, histology showed alveolar filling by large mononuclear cells with occasional giant cells, involvement of the alveolar wall (edema, infiltration by lymphocytes and eosinophils) and hyperplastic alveolar lining, and was therefore typical for a desquamative interstitial pneumonitis.

Patch tests for cobalt were positive only in one case.

The 3 asymptomatic workers of group B showed only a slight increase of lymphocytes at BAL, with decreased OKT4/OKT8 ratios (Table III).

As far as concerns the concentrations of cobalt, tungsten and tantalum in biological specimens, evaluated by neutron activation analysis and presently available only for 11 subjects (including the two with asthma of group A and one of group B with the severe subacute lung disorder), no relation was observed between the presence of disease and the amount of any of the metals. The concentrations of cobalt and tungsten were in most instances one to three orders of magnitude compared to normal mean values (data not shown).

The highest values of all three means were observed, independently from signs and symptoms, in the workers with exposure of longer duration, and this was particularly true for concentrations at sites of deposit such as hair and nails. The behavior of the metals in the various specimens was constantly different and indicative of a relatively high mobility of inhaled cobalt. In fact, cobalt concentrations were the lowest in BAL and the highest in nails, hair and blood, whereas tungsten levels were the highest in BAL and the lowest in blood (median values for cobalt in BAL 4.6 ng/ml, in nails 8000 ng/g, in hair 5550 ng/g and in blood 6.2 ng/ml; median values for tungsten in BAL 348 ng/ml, in nails 5540 ng/g, in hair 875 ng/g and in blood 0.3 ng/ml).

Our findings support the hypothesis that immunological mechanisms play a fundamental role in the pathogenesis of respiratory disorders from exposure to hard metals. The occurrence of asthmatic or interstitial alterations, in fact, seems based on individual hypersusceptibility and not on the degree of occupational exposure.

The relatively low prevalance of respiratory symptoms in group A (2 among 26 workers with severe and often prolonged exposure) also points to individual factors in the pathogenesis of overt disease, and is in agreement with data from the literature.[8]

A lymphocytic alveolitis at BAL with reduced OKT4/OKT8 ratio has been occasionally reported in subjects with hard metal disease or cobalt lung.[1,3,6] However, our finding of a tendency to an increase of lymphocytes of deep lung, with an imbalance of T-lymphocyte subpopulations, in several asymptomatic workers does not seem to have been reported so far, and suggests a more frequent effect of the exposure on the local immune system, whose pathogenetic significance cannot at present be stated.

In group B, the lung pathological changes were more severe and more frequent (2 out of 5 workers). These observations are in agreement with data of the literature, which indicate a higher risk in operations on hard metals involving the use of coolant fluids and producing fine aerosol sprays.[9] In this

group too, however, individual hypersusceptibility seems important, but the type of lung changes suggests different pathogenetic mechanisms. In fact, in agreement with the observations of Davison et al.,[2] the histological and cytological features are not those typical for hypersensitivity pneumonitis.

Even though immunological hypersusceptibility seems to be the most probable pathogenetic factor, the specific immune reactions directly involved in the induction of the different disorders are still poorly understood. Therefore, it is impossible at present to propose sensitive and specific tests for the early identification of hypersusceptible individuals.

In the medical surveillance of exposed workers, the aim should be to detect early respiratory alterations. Lung function tests and BAL in selected cases should be considered at the present time the methods of choice.

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PULMONARY AND CARDIAC FINDINGS AMONG HARD METAL WORKERS

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ABSTRACT

Excessive exposure to dust in the cemented tungsten carbide industry has been associated with the development of hard metal disease primarily manifested by asthma, pneumonitis or interstitial pulmonary fibrosis.

We have examined a group of 41 former hard metal workers with a history of mean duration of employment of 10.5 years (SD±5.3). In addition to a high prevalence of respiratory symptoms, abnormal chest radiographs were found in 13 workers, 8 of whom were classified as 1/1 according to the ILO International Classification of Radiographs of Pneumoconioses, 1980. There was an association between roentgenologic findings and right ventricular function as evaluated by radionuclide ventriculography.

These findings suggest that effects of excessive exposure in hard metal processing occur with appreciable prevalence and that it may be feasible to correlate roentgenologic findings according to the ILO Classification with cardiac function in this occupational lung disease.

No Paper provided.

THE PROTEAN MANIFESTATION OF HARD METAL DISEASE

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ABSTRACT

Seven subjects with hard metal disease have recently been investigated. The subjects included both those involved in the production of hard metal and also users of the finished product. Several underwent bronchoalveolar lavage and the lavage fluid showed the presence of characteristic giant cells that have previously been described in histological sections. Four subjects presented with interstitial fibrosis of uncertain etiology and only subsequently did the diagnosis of hard metal disease become evident. In the other three subjects the condition presented as a hypersensitivity pneumonitis with the chest radiograph showing rounded opacities of varying size. These subjects all had bouts of low grade fever, shortness of breath and fleeting radiographic abnormalities. All of these had restrictive pulmonary impairment and abnormal gas transfer, but following cessation of exposure, there was radiographic clearing and improvement in lung function. In two subjects, however, substantial restrictive impairment and a reduced diffusing capacity persisted, in conjunction with a clear chest radiograph. In both instances, the chest film showed persistent small lung volumes. Although hard metal disease is an uncommon condition, early recognition is important if permanent irreversible damage is to be avoided.

No Paper provided.

INTERACTION OF PARTICULATES WITH OXIDATION PRODUCTS IN WELDING FUMES

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ABSTRACT

The sudden onset of a generalized pattern of pulmonary fibrosis in a welder using methylene chloride aerosol (antispatter compound) while using an electric arc apparatus, has suggested a mechanism of injury involving highly reactive chlorine species adsorbed on metal particulates.

The simulation of arc welding under laboratory conditions in the presence of methylene chloride aerosol has verified the presence of phosgene ($COCl_2$) in concentration proportional to the quantitative presence of the aerosol. Heated metal surfaces of different ferrous alloys indeed produce phosgene gas in proportion to the amount of methylene chloride. Concentrations of phosgene range from 0.3 to 8.0 ppm., depending on the duration (2–12 min.) of the actual welding procedure and the amount of methylene chloride used (10, 50, 100 ppm).

The histological characteristics of the pulmonary fibrosis studied in biopsy samples obtained from the affected worker are quite consistent with a mechanism involving the reactive chlorine species absorbed on the surface of respirable particulates.

The implication of these observations for the health of welders appears obvious, demanding renewed attention for the safety of this trade.

No Paper Provided.

AIRWAY OBSTRUCTION AND REDUCED DIFFUSION CAPACITY IN SWEDISH ALUMINUM POTROOM WORKERS

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Aluminum is produced by electrolytic extraction from alumina (Al_2O_3) in the presence of fluoride. The aluminum potroom workers are exposed to various airborne contaminants such as aluminum-oxide, particulate and gaseous fluorides, sulphur dioxide and organic particles. Several investigators using dynamic spirometry have reported of obstructive lung function impairment in aluminum potroom workers[1,2,6,7] even without signs of atopy.[4] It has also been shown that exposure to alumina can cause pulmonary fibrosis in laboratory animals.[3] This study was undertaken in order to study the degree and nature of the affection of the lung function using more extensive lung function tests.

MATERIAL AND METHODS

Subjects

The exposed group consists of 38 male aluminum potroom workers (mean age 39 years, range 21–63 years) who had been employed for at least one year (mean 14 years, range 1–32 years). Twenty office workers (mean age 48 years, range 24–65 years) from the same factory served as controls. Only individuals without signs of atopy were included in the study. All participants were nonsmokers at the time of the investigation. In the exposed group 14 were ex-smokers and in the control group 8 were ex-smokers.

Exposure

During the last decade the local industrial health organization has performed frequent measurements of fluoride and total dust exposure. In 1987, when this investigation was performed, the participating potroom workers had a mean exposure of 0.4 mg/m^3 fluorides and 1.7 mg/m^3 total dust. The exposure is below the Swedish TLV values (fluorides 2 mg/m^3, total dust 10 mg/m^3).

Lung Function Measurements

The lung function tests were performed upright in the sitting position. The tests were performed twice or more, and the best value was chosen. Signals from the dry, rolling seal spirometer, the N_2-meter with a pneumotachograph, the CO-meter, and the body box of the hybrid type were computerized, and the calculation of different variables was guided by the cursor for interactive control of critical points in some curves. Following variables were calculated: vital capacity, total lung capacity, residual volume, forced expiratory volume in one second (FEV_1), maximal expiratory flow at 50% of the forced vital capacity (MEF_{50}), mean transit time, closing volume, slope of the alveolar plateau, and single breath pulmonary diffusion capacity (TL_{COSB}).

Bronchial Challenge Test

Bronchial provocations were performed by inhalations in a De Vilbiss Nebulizer of methacholine in increasing concentrations from 0.5 mg/ml, each incremental of dose representing a four-fold increase of the methacholine concentration. Peak expiratory flow was measured three minutes after starting the inhalation. The provocation was ceased when PEF decreased 20% or more of the pre-challenge values or after inhalation of the highest concentration (32 mg/ml). Calculations of the concentrations of methacholine that yields a decrease in PEF of 20 and 10% from the pre-challenge values was performed.

Statistics

Values of the lung function measurements were calculated as percent of reference values used at the laboratory. Values from the bronchial reactivity test were transformed to logarithms before analysis. Statistical analyses were performed by two-tailed Student's t-test for independent observations.

RESULTS

The individuals in the control group were older than in the exposed group. There were no significant differences in the previous smoking habits between the groups. One individual in each group had a mild bronchial asthma, but none of the participating subjects had considerable symptoms from the airways.

The controls had normal lung function values compared to the reference values. In the exposed group there was significantly decreased FEV_1 ($p<0.005$), MEF_{50} ($p<0.01$), and TL_{COSB} ($p<0.05$), whereas RV was significantly increased ($p<0.05$) compared to the control group. No other differences were significantly different between the ex-

posed and control groups. Nor were there any differences in bronchial reactivity.

DISCUSSION

This investigation has shown an obstructive lung function impairment but no bronchial hyperreactivity in aluminum potroom workers. Further they had a reduced diffusion capacity compared to the control group. The control group was chosen from the same aluminum reduction plant as the potroom workers. Since the number of current non-smokers was limited it was not possible to match the groups for age, and the comparison of lung function tests between the groups was performed after that the values were expressed as percent of predicted values in order to abolish the confounding effect of age.

The results with obstructive lung function impairment is in accordance with several other studies,[1,2,4,6,7] but these studies have often shown a more pronounced reduction in lung function. Neither did we find any affection on the bronchial reactivity, which has earlier been reported.[5] These discrepancies from earlier studies can be explained in several ways. Only men without known lung or atopic diseases have been employed in the present industry. Further the exposure to dust and fluorides is low compared to many other aluminum reduction plants, and the use of respiratory protection equipment has been frequent.

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BLOOD PROLIFERATION TO BERYLLIUM: ANALYSIS BY RECEIVER OPERATING CHARACTERISTICS

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ABSTRACT

Chronic beryllium disease is a cell mediated granulomatous lung disease. Since testing of beryllium proliferation of bronchoalveolar lavage cells appears to be diagnostic of this entity, we re-evaluated the proliferative response of blood cells to beryllium to see if it could have utility for screening. Twenty-seven patients with chronic beryllium disease, documented by histology and a positive lung proliferative response to beryllium, were compared to 30 controls. Beryllium proliferative response (stimulation index or SI) was tested with 4 different concentrations (0.1–100 μM) of BeF_2 and $BeSO_4$ on day 3, 5 and 7 of *in vitro* culture (24 tests). A greater variance of the SI of the control cells by beryllium was noted with increased time in culture and decreased concentrations of beryllium. A significant difference was observed between beryllium patients and controls only with 100 or 10 μM beryllium salts. To evaluate the optimum stimulation index, receiver operating characteristic (ROC) curves (true positive vs. false positive) were generated. With a predicted maximum prevalence of 3%, a slope of 33 on the ROC curve would equate the gain of finding a case with the costs of misdiagnosis. Maximum sensitivity (31%) was observed by testing with 100 μM BeF_2 or $BeSO_4$ on day 3 and 5 using a SI of >3. This suggests that blood proliferation to beryllium may be useful in screening for chronic beryllium disease. Application of medical decision theory and the receiver operating characteristic curve should be useful for evaluating screening tests for occupational lung disease.

No Paper provided.

PATHOLOGIC AND IMMUNOLOGIC ALTERATIONS IN BERYLLIUM DISEASE IDENTIFIED AT EARLY STAGES BY FIBEROPTIC BRONCHOSCOPY AND BERYLLIUM-SPECIFIC LYMPHOCYTE ASSAY

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ABSTRACT

Beryllium lung disease is a chronic granulomatous disorder in which a beryllium-specific immune response plays a central role. Prior research has demonstrated that lymphocyte activation by beryllium salts, an *in vitro* measure of the cellular immune response, has high specificity and sensitivity for chronic beryllium disease. In the present study 20 beryllium-exposed workers underwent complete clinical evaluation, including chest radiograph, pulmonary physiology, exercise physiology, bronchoalveolar lavage (BAL), lung biopsy, and lymphocyte transformation tests (LTT) of blood and BAL lymphocytes. We identified 12 cases of beryllium disease each of whom had pathologic changes on biopsy, lymphocytic alveolitis on BAL, and positive LTTs. This group of patients was remarkable for its paucity of clinical findings. Five had minimal or no respiratory symptoms, four had normal physical examinations. Five had no increase in interstitial markings on chest radiograph. In nine cases, pulmonary function tests were normal or showed mild airflow limitation, normal diffusing capacity for carbon monoxide and normal oxygen exchange during exercise. Eight beryllium-exposed workers were found to have non-beryllium lung diseases; two of these eight demonstrated beryllium sensitization. We conclude that by using fiberoptic bronchoscopy with transbronchial biopsy and BAL to obtain lumphocytes for testing beryllium sensitization, it is possible to identify beryllium workers who have histopathologic and immunologic alterations consistent with chronic beryllium disease. These findings may precede frank clinical illness and physiologic impairment, having important implications for our understanding of the natural history of beryllium disease.

No Paper provided.

EVALUATION OF LUNG BURDEN IN STEEL FOUNDRY WORKERS

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INTRODUCTION

Pneumoconiosis, which has been regarded as silicosis is the best known occupational lung disorder of foundry workers. The main hygienic attention has been focused on silica. However, metal fumes and dusts are generated by several foundry activities. Inorganic material emitted from the furnace, ladles, and castings in iron foundries consists of compounds of iron, manganese, calcium, magnesium, aluminum and silica. Fumes and dusts generated from alloyed steel melting and cast cleaning contain in addition chromium and nickel compounds. Chromium and nickel compounds may cause a large variation of different reactions in the respiratory tract.

The quantity of magnetic material retained in the lungs can be estimated by measuring the remanent magnetic field of the chest area. Because the worker's exposure has often been heterogenous, an MPG instrument with a pulse coercive force unit was used to detect the magnetically dominating particle population in the lungs. The MPG instrument that senses dust quality has been described earlier by Kalliomäki and coworkers.[1,2] Urinary chromium and nickel excretions have been recently applied as a biological monitoring method in workers exposed to some chromium and nickel compounds.

The aim of the study was to estimate the levels of magnetic material retained in the lungs in steel foundry workers representing typical occupations. The MPG results are compared with urinary chromium and nickel values among a group of the studied subjects.

MATERIAL

Subjects

We studied 61 workers representing various typical occupations in one steel foundry (Table I). Of the subjects studied, 32 persons worked in the foundry hall and 29 in the fettling shop. The lung functions (VC=vital capacity; $FEV_{1.0}$ =forced expiratory volume in Is; MMEF were within the normal limits).

Working Environment

This steel foundry produces a wide selection of acid resistant and stainless steel parts for the cellulose and chemical industry. The foundry also produces iron casting. The industry hall and the fettling shop are located in separate buildings. In the foundry studied, the working conditions have received considerable attention. The total dust levels, silica and metal concentrations decreased essentially due to the improvements in ventilation and working methods. In this foundry the average total dust levels in personal samples and general airborne samples were about 3–4 mg/m^3 during 1976–1980.

The steel cast cleaning is performed by flame cutting, carbon arc gouging and grinding. Manual metal arc (MMA) welding is also done. Dust concentrations measured by personal sampling in the fettling shop at different times varied from 2 to 20 mg/m^3 and the metal concentrations ranged from 1 to 7 mg/m^3 for iron, from 60 to 790 µg/m^3 for chromium, and from 50 to 1100 µg/m^3 for nickel. Chromium and nickel concentrations were determined in urine spot samples collected after working hours several times among the workers in the fettling shop during 1982 and 1984. The average urinary chromium and nickel levels expressed as umol/1 were 0.60 and 0.32 for welders, 0.66 and 0.37 for flame cutters and carbon arc cutters and 0.08 and 0.08 for grinders.

Dust Samples

Preliminary magnetic measurements have been made for some dust samples collected from the foundry and fettling shops (Table IV). The samples were collected on millipore filters.

METHODS

The *in vivo* MPG measurements were performed with a magnetopneumograph instrumentation with dust quality sensing.[1,2]

Measurement of the coercive force of dust retained in the lungs is complicated: the object to be measured is substantial, the dust is quite low and the orientation of particles (relaxation) due to the static demagnetizing field creates errors.

The application of the static demagnetizing field can be avoided if a pulse coercive force (H_{cp}) is measured instead of the coercive force. The pulse coercive force is the amplitude of a short demagnetizing pulse, which demagnetizes a previously magnetized sample. Measurements of dust samples show that the pulse coercive force depends on the process generating the dust, in the same way as the coer-

Table I
Occupation, Number and Exposure Time and Lung Functions of the Studied Steel Foundry Workers

Group	N	Exposure time (a)		VC		$FEV_{1.0}$		MMEF	
		mean	SD	mean	SD	mean	SD	mean	SD
In the foundry hall									
1. Molders, core makers	9	24	7	97	17	97	19	91	41
2. Smelters, furnace men	6	13	6	95	10	99	6	91	26
3. Workers shaking out castings	4	21	7	90	6	98	9	100	18
4. Foremen, cleaners	13	8	5	98	13	101	13	101	14
In the fettling shop									
5. Flame cutters, carbon arc cutters	11	12	6	106	15	107	16	96	30
6. Fettlers (grinders)	13	18	8	100	16	102	21	94	28
7. Manual metal arc	5	16	9	101	14	107	15	107	18

cive force. As the duration of the demagnetizing pulse can be short (less than ls) the orientation error is minimized.

The pulse coercive force of the dust in the lungs is the first parameter to be measured. First the chest area of a subject is magnetized with a short pulse (50 mT, 0.5 s), and the remanent flux density of the lungs (B_{r1}) is measured several times. One minute after the magnetization, a fixed demagnetization pulse (15 mT, 0.5 s) is applied, and the remaining flux density (B_{r2}) is measured as earlier. The ratio B_{r2}/B_{r1} is the measure of the coercitivity or magnetic hardness of the dust. This ratio varies from 0.00 to 0.40 depending on the quality of the dust.

The measurements of the magnetic properties of dust samples were made by a microcomputer-controlled magnetometer.[3]

RESULTS

In the foundry shops the average magnetic field and pulse coercive force measured in different occupational groups did not differ essentially in the various group (Table II). These results indicate that the metal particles originate from the same source and that not only smelters, casters and furnace, men but also molders and core makers have lung retention of metallic dust. The figure of magnetic hardness indicated that dusts and fumes are magnetically "soft" material. In the fettling shop the highest remanent magnetic moment was observed among flame cutters and carbon arc cutters (Table II). The figure for magnetic hardness measured in different groups also varied. The figure for magnetic hardness differed significantly from that found in fumes from the melting and casting process.

The results for the magnetic properties of dust samples collected from the same working processes in the foundry and fettling shops are presented in the Table IV. The preliminary results indicated that the magnetic properties of the dust samples from the different working processes in the foundry varied remarkably. A systematic study for characterization of dust and fumes from different working activities would therefore be needed to find suitable calibration factors between the remanent magnetic field and the amount of dust, retained in the lungs.

Table II

The Results of the Magnetopneumograph (MPG) with Dust Quality Sensing of the Studied Steel Foundry Workers

Group	N	Number of smokers	Average magnetic field (B/nT)		Appr. amount of dust	Figure of magnetic hardness (B_{r2}/B_{r1})	
			mean	g	g	mean	SD
In the foundry hall							
1. Molders, core makers	9		0.5	2.0	0.1	0.09	0.05
2. Smelters, furnace men	6		0.5	1.8	0.1	0.07	0.12
3. Workers shaking out castings	4		0.4		0.1	0.07	
4. Foremen, cleaners	13		0.3	1.3	0.05	0.05	0.05
In the fettling shop							
5. Flame cutters, carbon arc cutters	11		5	4.4	0.2	0.27	0.09
6. Fettlers (grinders)	13		0.5	3.0	0.1	0.37	0.19
7. Manual metal arc (MMA) welders	5		3	2	1.0	0.28	0.14

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Table III

Individual Exposure Parameters: Average Magnetic Field (B), Urinary Chromium (U-Cr) and Nickel (U-Ni) Determined for Some Subjects in the Fettling Shop

Subject	Occupation	exposure time (a)	U-Cr (umol/l)	U-Ni (umol/l)	B lungeo (nT)
1.	welder/MMA	10	0.55	0.22	3
2.	1. flame cutter 2. welder/MMA	9 3	0.85	0.43	5
3.	flame cutter and carbon arc cutter	9	1.07	0.74	2
4.	flame cutter and carbon arc cutter	12	0.51	0.69	7
5.	1. flame cutter 2. grinder	8 9	0.08	0.08	2
6.	flame cutter and carbon arc cutter	5	0.85	0.41	6
7.	flame cutter and carbon arc cutter	4	0.33	0.24	2
8.	1. grinder 2. flame cutter	6 3	0.12	0.12	1
9.	flame cutter and carbon arc cutter	10	0.09	0.13	0.2
10.	flame cutter and carbon arc cutter	13	0.33	0.33	15
11.	1. grinder 2. flame cutter	10 3	0.26	0.36	0.7
12.	flame cutter and carbon arc cutter	14	1.24	0.42	4
13.	grinder	11	0.2	0.19	0.2

U-Cr < 0.05 umol/l, unexposed subjects
U-Ni < 0.10 umol/l, -"-

Table IV

Specific Remanent Magnetic Moment M_{rs} (Am^2/kg) and Pulse Coercive Force H_{cp} (kA/m) for the Dust Samples Collected from Some Working Processes in the Steel Foundry and Fettling Shops

Sample	N	M_{rs} (Am^2/kg)		H_{cp} (kA/m)	
		mean	SD	mean	SD
Sample collected from working area near direct arc furnace	4	0.23	0.11	24.9	11.4
Sample collected from breathing zone of carbon arc cutters of acid resistant steel casting	6	2.9	0.5	30.5	0.3
Sample collected from breathing zone of grinders of acid resistant steel casting	4	1.7	0.05	12.5	0.1
Manual metal arc (MMA) welding of acid resistant steel casting	5	0.6	0.06	20.5	0.9
Ambient air sample collected from the fettling shop		1.8	0.1	24.5	1.2

SCREENING LUNG FUNCTION USING SINGLE BREATH CARBON MONOXIDE DIFFUSION CAPACITY

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Routine pulmonary function testing as an industrial screening and diagnostic tool has been used for over 40 years within the beryllium industry. By today's standards, the first tests were crude measures of forced vital capacity (FVC) using instruments designed to follow post surgical patients. However, the relative inaccuracies of the methods and equipment were offset by a weekly frequency of testing. Using this crude data interpretation between individual tests was difficult, but utilizing mean changes or sliding means improved the sensitivity and proved a useful means of identifying or following employees with significant respiratory disease. Cases of acute beryllium disease were always associated with significant changes in the vital capacity, but those changes accompanied or followed the onset of significant symptoms or chest radiographic changes. However, this early experience proved that frequent testing is much more valuable than annual or even semi-annual determinations. Early pulmonary function findings in chronic beryllium disease (CBD) are frequently subtle and often not appreciated until symptoms or radiographic changes have already appeared.

Early reports by Gaensler et al.[1] indicated the functional changes in CBD are restrictive in type and the most marked changes were seen in the carbon monoxide diffusion capacity during both the steady state test and exercise. Ferris[2] also noted an increased alveolar-arterial oxygen difference. This finding was also noted by Gaensler.[1] In 1969 Andrews, Kazemi, and Hardy[3] reporting on 41 cases of CBD followed over several years observed that 39% showed an obstructive spirometric pattern while only 20% were of the restrictive type and only 36% showed an interstitial picture. Our own experience in over 60 cases of CBD covering over 40 years is similar to the findings of Rossman et al.[4] where gas transfer and/or increased oxygen alveolar-arterial gradient were the most marked and consistent functional defects.

In our series the major functional spirometric changes were of the restrictive type. When obstructive changes were noted they appeared either late in the course of the disease or when cigarette smoking was present as a confounding factor. In some cases the spirometric changes were minimal while in others there was a significant decline in both the FVC and the one second timed vital capacity (FEV_1). Our experience has not included a case where the FEV_1 declined more rapidly than the FVC. In selected cases the FVC declined more rapidly than the FEV_1, but the excess rate was not significant.

In view of the fact that the first pulmonary function changes frequently affect gas transfer before any appreciable changes are seen in spirometry values and overcome the shortcomings of spirometry alone single breath carbon monoxide diffusion (DLCO) studies were introduced as a routine screening measure in 1975. An arbitrary, routine frequency of twice a year was initially selected which, for our purposes, this has proven to be both an effective and workable frequency.

Despite the much greater technical difficulties associated with measuring DLCO accurately, this additional parameter has not only been technically feasible in the industrial settings but also very valuable as a screening tool for the early identification of interstitial pulmonary changes. As our previous experience with vital capacity determinations had shown, the frequency of measurement is paramount to provide the sensitivity to identify the early interstitial changes. The DLCO has shown a significant change in some cases before while the FVC, FEV_1, and flow rates have remained constant. Figure 1 shows the DLCO and FVC of a 30 year old male who eventually became symptomatic and had CBD confirmed by beryllium, lung lymphocyte proliferation studies and transbronchial biopsy. It is readily seen that his DLCO declined significantly while his FVC actually increased or remained constant for over a year before it commenced to fall.

Only one of our cases (Figure 2) which have been diagnosed since the initiation of DLCO measurement, has not shown a noticeable change in the DLCO. This case was initially identified by very subtler radiographic changes which in retrospect seem to have first appeared concomitantly with the introduction of DLCO determinations. This case has been asymptomatic and by older diagnostic procedures would probably still be only a suspected or questionable case; however, his pulmonary lymphocytes show an enhanced T-4/T-8 ratio, they proliferate upon stimulation with both beryllium sulfate and beryllium fluoride, and he has typical granulomas in his transbronchial biopsy. Both his spirometry and diffusion values have remained around 100% of his predicted values and declined at a predicted rate. (Figure 3)

Figure 4 represents a male who first became symptomatic in 1984 with bronchitis-like symptoms of cough and mid chest discomfort. It can be seen his spirometry values were not remarkable; however, over the next 1-1½ years he

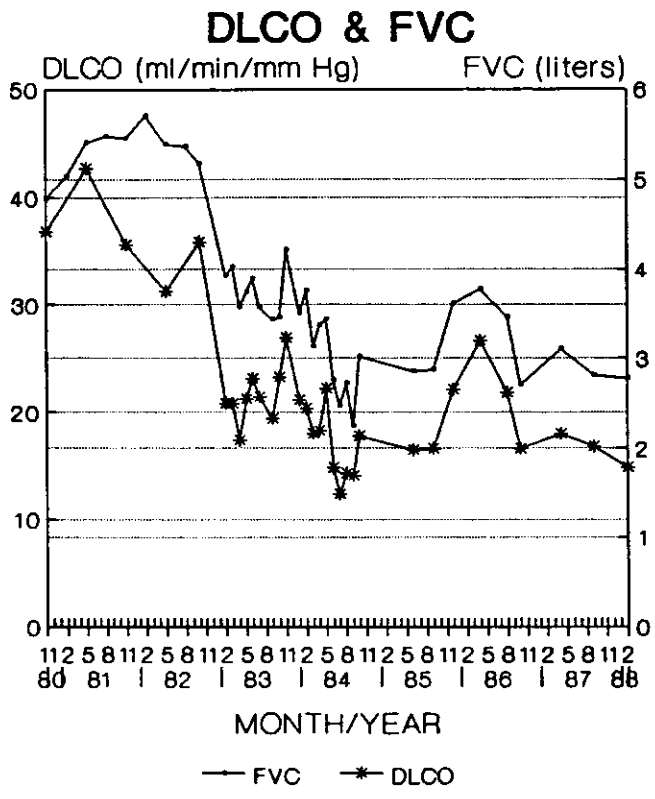

Figure 1

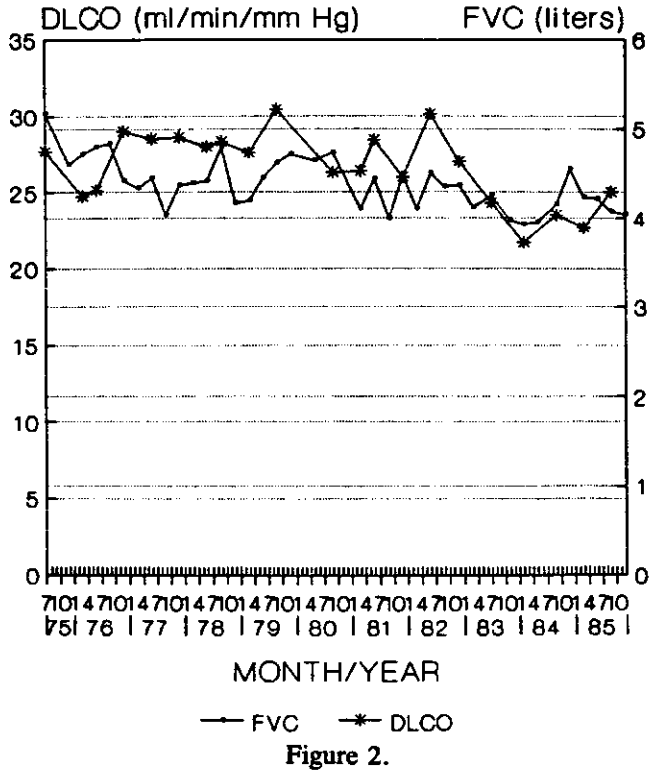

Figure 2.

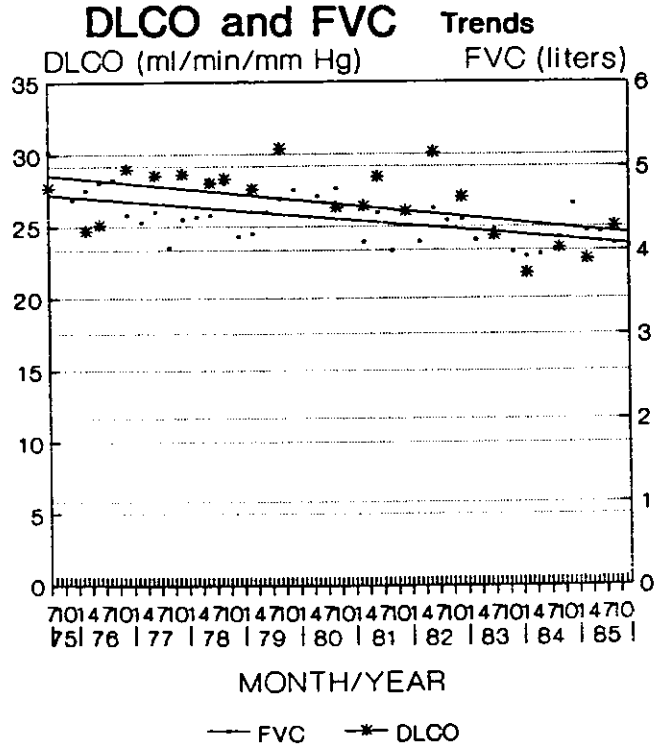

Figure 3

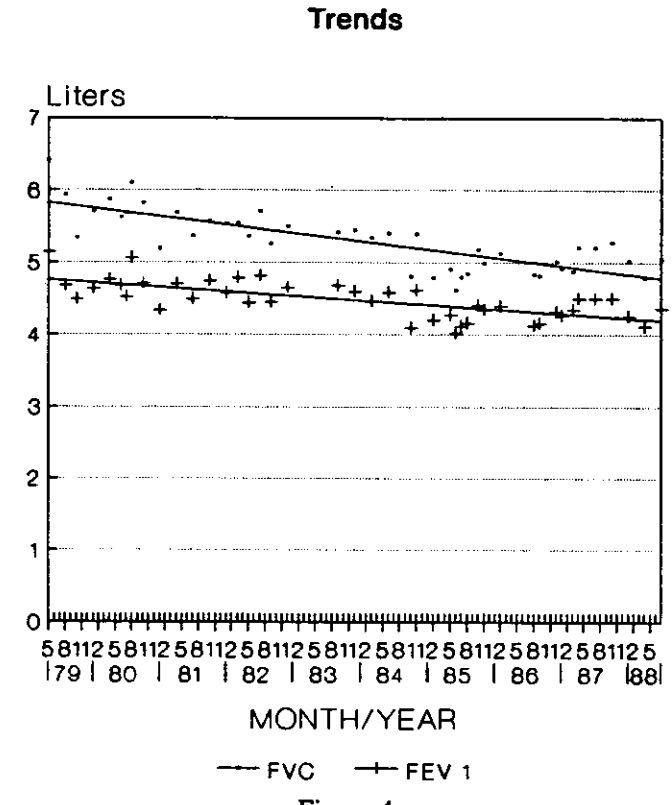

Figure 4

showed a steady but not drastic decline in DLCO. (Figure 5) The patient has continued to have some vague chest discomfort, but his DLCO and spirometry values have remained greater than 100% of predicted. Nonetheless, he underwent bronchoalveolar lavage and a transbronchial biopsy which confirmed his pulmonary cells were sensitive to beryllium stimulation and he had granuloma in the biopsy. At the present time his most significant physiological finding is an arterial blood oxygen of 79% saturation.

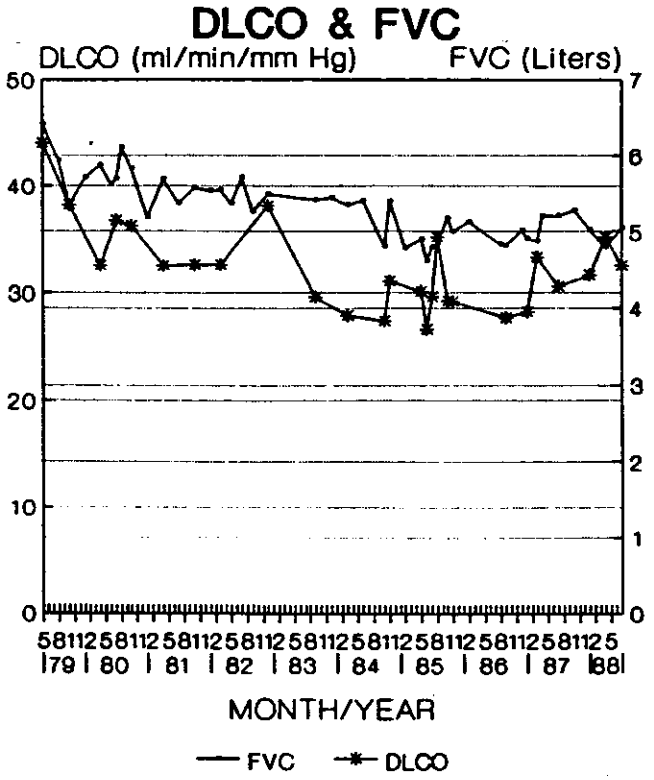

Figure 5.

Figure 8 is a 55 year old male who became symptomatic several years before DLCO testing was introduced to his plant site. Despite repeated diagnostic studies which did not include lung biopsy a firm diagnostic conclusion could not be made. His FVC was declining at an excessive rate, and the scattered DLCO studies which were available further indicated pathology existed. In 1985 he underwent bronchoalveolar lavage with beryllium proliferation studies and transbronchial biopsy confirming the working impression of

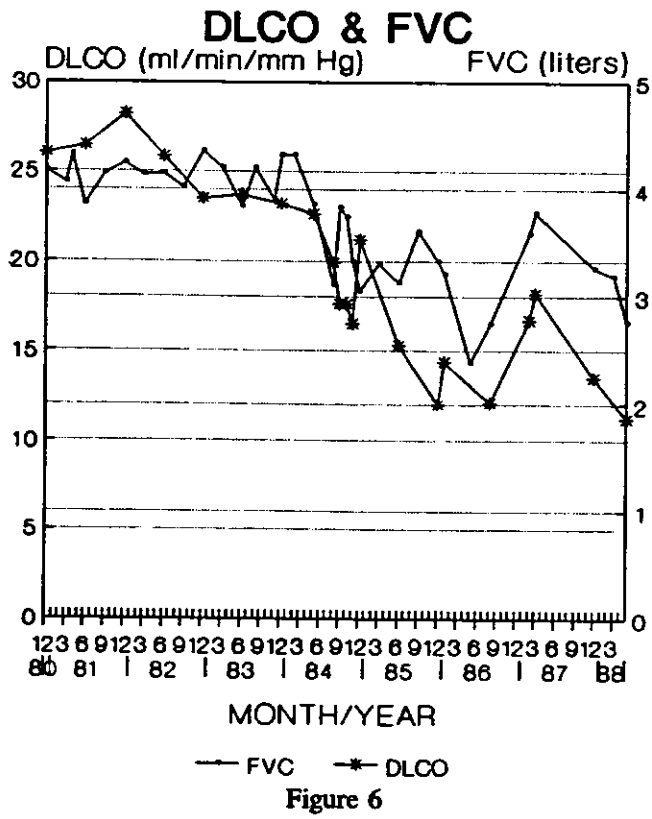

Figure 6

The next case (Figure 6) is a 42 year old female who presented in August 1984 with persistent respiratory symptoms and a significant initial drop in both FVC and DLCO. Her physical examination and chest radiograph were clear. We elected to follow her for a few months before proceeding with further diagnostic testing. When she first became symptomatic, we had not had any experience with pulmonary lymphocyte proliferation studies and still had to rely upon chest X-ray to indicate significant changes were occurring. For the next year her FVC fluctuated but seemed to stabilize; however, the DLCO continued to decline. Early in 1986 in view of the significant decline in both FVC and DLCO, further studies including bronchoscopy and biopsy were being planned. At the same time her annual chest X-ray showed bilateral interstitial infiltrates. The proliferation studies and biopsy confirmed a diagnosis of CBD which had been suspected earlier based upon the DLCO screening studies. This case is unusual in that the rate of decline in DLCO has been greater than the decline in spirometry. (Figure 7) In nearly all of our other cases the regression curves for both these values are parallel over time.

CBD. Steroid therapy was introduced and he has stabilized with a moderate amount of pulmonary impairment.

The last case (Figure 9) is a 30 year old male who worked in the beryllium reduction process where beryllium hydroxide is reduced to beryllium metal. An intermediary step in the process involves the melting of beryllium fluoride. Over a period of several days there were episodic releases of BeF_2. A few months later he developed marked pulmonary symptoms and a profound drop in both spirometry and DLCO. (Figure 10) However, the DLCO changes were the earliest and most dramatic. He was immediately removed from the beryllium reduction process and showed a rapid, significant improvement in his pulmonary function values. In view of a normal chest X-ray and the dramatic recovery, there remained a serious question concerning a beryllium etiology to his physiological changes; therefore, he returned to work in the original work area. Almost immediately, he again demonstrated a drop in spirometry and DLCO, and he was immediately removed from all further exposure to beryllium. Again his pulmonary functions significantly im-

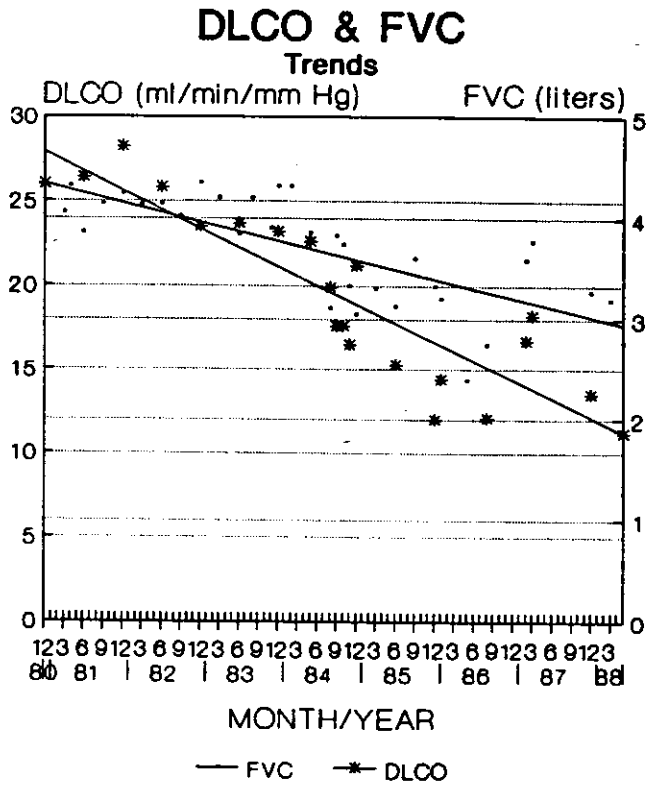

Figure 7

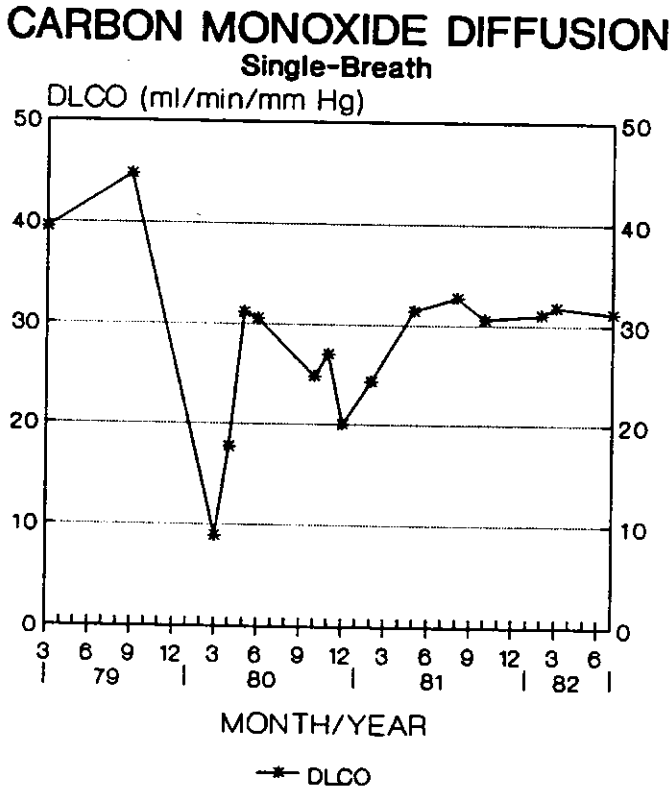

Figure 9

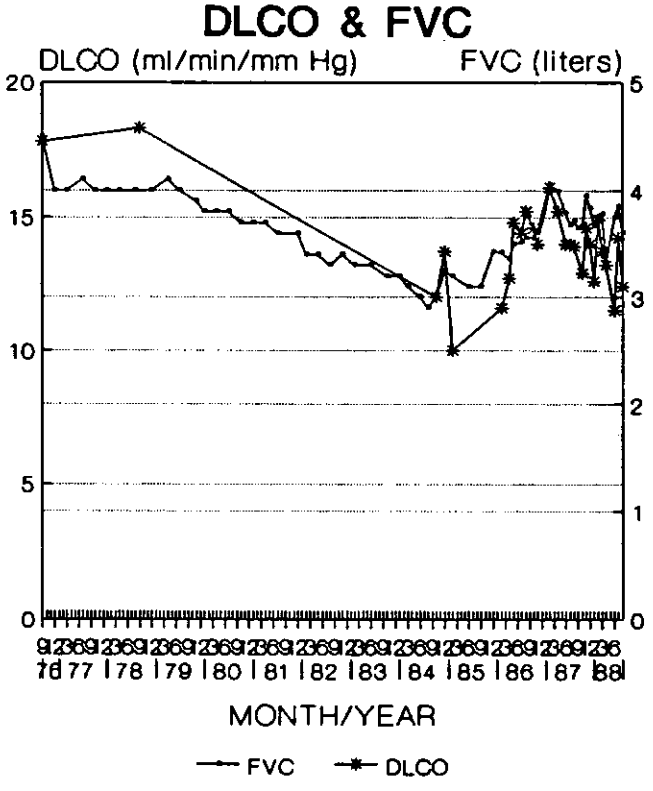

Figure 8

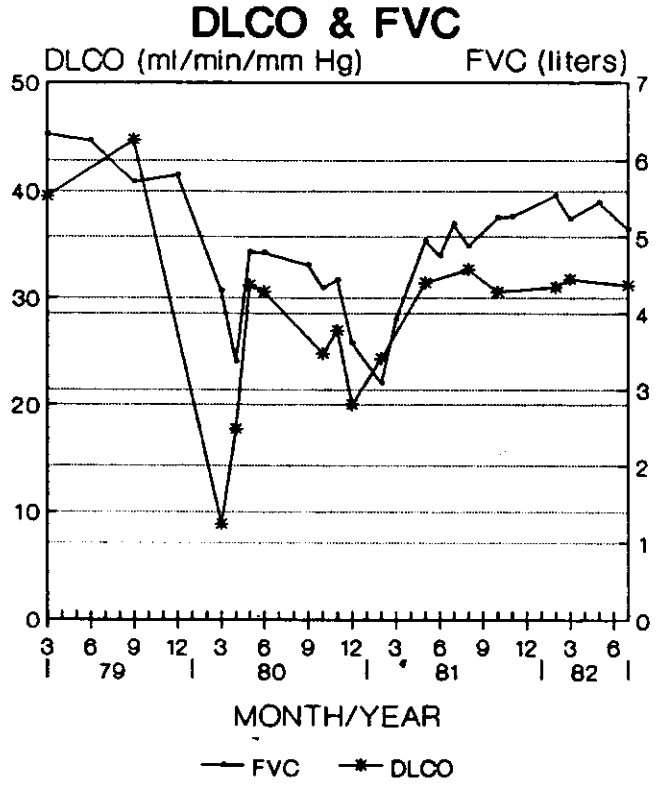

Figure 10

proved. Subsequent proliferation studies and biopsy have shown his pulmonary lymphocytes are sensitized to beryllium and his biopsy shows granulomas. He remains asymptomatic and works in an area away from potential exposure to beryllium.

In conclusion our experience over the past thirteen years has indicated that routine, single-breath, carbon monoxide diffusion studies are possible and feasible in an industrial clinic. In cases of interstitial disease the DLCO generally is the first parameter to change and, over a long term, closely parallels spirometric changes. The DLCO may be abnormal before either the chest radiograph or spirometry is affected. Furthermore, when abnormal in CBD cases, the spirometric pattern has been restrictive with obstructive changes have only observed where there has been a heavy concomitant use of tobacco. Also, frequent use of in-house diffusion measurements is a simple and convenient means of following a response to therapy.

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HEALTH EFFECTS OF HIGH DUST EXPOSURE AMONG WORKERS FROM MILLING PROCESS PULVERIZATION IN FOUNDRY GOLD-BARS ENTERPRISE

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ABSTRACT

All were men aged from 19 yrs to 72 yrs, of which 68% were from 20 yrs to 49 yrs and 30% were 50 years or more. ***Radiographic examination:*** Resumes X-ray findings according to the ILO standard. The 60.5% of the whole group had less than 10 years of exposure. This group showed 62% of NORMAL X-ray and 38% were abnormal by adding 27.5% of suspicious findings and 10.3 of positive findings. The second group had 10 to 35 years of exposure. This group showed 15.7% of NORMAL X-ray films and 82.3% of abnormal films of which 42.1% were suspicious and 42.3 positive. It is evident that the positive X-ray is closely related to the longer exposure time. ***Spirometric study:*** Table III, shown in the group of less than 10 years of exposure 28.5% of NORMAL FILMS and 71.5% of abnormal films composed by 32.1% of pure obstructive syndrome, 17.8% of pure restrictive syndrome and 21.4% as mixed syndrome. In other words, the syndrome of respiratory obstruction in total reached to 53.5% and the restrictive reached 39.2%. The group of workers with 10 to 35 years of exposure was 39.2% of the whole group from which only 11.1% were normal and 78.3% abnormal: 44.4% were pure obstructive syndrome, 16.6% of pure restrictive syndrome and 27.7% of mixed lung function. ***According to the smoking habit:*** X-ray findings. The group of NOT Smoking showed 51.4% of normal telefilms and 48.6% of abnormal films adding 34.3 of suspicious and 14.3% of positive X-ray findings. The group of smokers showed only 23% of NORMAL X-rays and 77% of abnormal test-films. We compare the same relationship, moving from the X-ray examination to the lung function tests, the latter being the major power of diagnosis. Unfortunately the lung function test has no specificity and only the X-ray finding together with the occupational history of work is of diagnostic value.

In order to complete the evaluation of the area of inorganic dust exposure, the National Pneumoconiosis Program scheduled the study of the workers population exposed to hard rocks' dust of golden miners at the south of the country.

Our study involved more than five groups of workers from both upper and underground jobs as from oldest to modern extraction-industrial processes.

Particularly we focused on one group of 48 workers exposed to high levels of breathable dust particles about five times above the permissible level from the primary trituration to the final pulverization workplaces.

They were all men aged from 10 years to 72 yrs, (Table I), 68% of them from 20 yrs to 49 yrs and 30% from 50 years or more.

During the time of exposure they were grouped in two main categories—those with less than 10 years (Group I = 60.5%) and those with 10 years up to 35 years (Group II = 39.5%). The number of smokers is written below that of the non-smokers, although this table is made in order to compare the effect of the time of exposure on the X-ray, spirometry and alveolar diffusion test.

Table I
Groups of Ages

AGE YEARS	NUMBER	%
< 20	1	2
20 - 29	13	16,5
30 - 39	7	15
40 - 49	13	26,5
50 - 59	7	15
60 y M.	7	15
TOTAL	48	100

"A/hh.-

In order to see the effect of the smoking habit in this high dust exposed group of workers we reorganized them according to the NOT Smoking (NS) and smoking (S) for the effect on the X-ray, spirometric and diffusion test results.

RESULTS

Radiographic Examination

Table II, resumes X-ray findings according to the ILO standard. The 60.5% of the whole group had less than 10 years of exposure. This group showed 62% of NORMAL X-ray and 38% were abnormal by adding 27.5% of suspicious findings and 10.3 of positive findings.

The second group had 10 to 35 years of exposure—This group showed 15.7% of NORMAL X-ray films and 82.3% of abnormal films of which 42.1% were suspicious and 42.3 positive. It is evident that the positive X-ray is closely related to the longer exposure time.

Spirometric Study

The Lung function tests performed were VC, FEV_1, MEF 25, MEF 50, MEF 75, PF, MVV, TC, RV, RV/TLC and alveolo-diffusion test. This test allows us to classify the main function disturbances such as the syndrome of restrictive and ventilatory obstruction and the lung diffusion capacity diminution.

Table III—Showed in the group of less than 10 years of exposure 28.5% of NORMAL FILMS and 71.5% of abnormal films composed by 32.1% of pure obstructive syndrome, 17.8% of pure restrictive syndrome and 21.4% as mixed syndrome. In other words the syndrome of respiratory obstruction in total reached 53.5% and the restrictive reached 39.2%.

The group of workers with 10 to 35 years of exposure added 39.2% of the whole group, from which only 11.1% were normal and 78.3% abnormal: 44.4% were pure obstructive syndrome, 16.6% of pure restrictive syndrome and 27.7% of mixed Lung function syndrome.

Table IV—Shows the results of the application of the alveolo-diffusion test exploration (DLCO).

Only 14.8% of decrease DLCO was found in the group of less than 10 years of exposition.

The second group of 10 to 35 years of exposure showed 17.8% of DLCO decreases.

In order to make it easier for the reader to see the differences between the main groups we performed the following three Tables, V, VI and VII.

It is evident to see in Tables V, VI and VII that the increase of the risk has direct relationship with the time of

Table II
X-ray (Telefilm 14" × 17") Results

EXP. YEAR	NORMAL	%	SUSPICIOUS	%	POSITIVE	%	ABNORM	%	TOTAL	%
< 10 YRS.	NS 15 S 3 — 18	62	NS 7 S 1 — 8	27.5	NS 2 S 1 — 3	10.3	38		NS 24 S 5 — 29	60.5
> 10 to 35 yrs.	NS 3 S 0 — 3	15.8	NS 5 S 3 — 8	42.1	NS 3 S 5 — 8	42.1	84.2		NS 24 S 8 — 19	39.5
TOTAL	21	43.7	16	33.3	11	22.9			48	100

Table III
Spirometry Results

EXPOSURE TIME	NORMAL	%	OBSTRUCTION	%	RESTRICTION	%	MIXED	%	T.. ABN.	TOTAL	
< 10 yrs.	NS 7 S 1 — 8	28.5	NS 7 S 2 — 9	32.1	NS 4 S 1 — 5	17.8	NS 6 S 0 — 6	21.4	71.5	28	60.8
10 to 35 yrs.	NS 1 S 1 — 2	11.1	NS 7 S 2 — 8	44.4	NS 4 S 1 — 3	16.6	NS 2 S 3 — 5	27.7	88.8	18	39.2
TOTAL	10	21.7	17	37	8	17.3	11	24.1		46	100

Table IV
Alveolar-Diffusion Test

EXPOSURE TIME	NORMAL	%	DICREASE	%	TOTAL	%
< 10 yrs	NS 19 S 4	23 85.1	NS 4 S 0	4 14.8	27	60
10 to 35 Years.	NS 9 S 5	14 77.8	NS 2 S 2	4 22.2	18	40
TOTAL		37 82.2		8 17.8	45	100

MA/bb.-

Table V
Radiology

EXPOSURE YRS.	% NORMAL	% ABNORMAL	TOTAL
< 10	62	38.0	100
>10 to 35	15.7	84.3	100

X^2 = 8.87 > 3.84 P= 0.005
Z = 2.9 > 1.95
Relative Risk = 2.2.

Table VI
Espirometry

EXP. TIME	% NORMAL	% ABNORMAL	TOTAL
< 10YRS	28.5	71.5	100
10 to 35	11.1	88.9	100

X^2 = 2 < 3.84 P < 0.005
Z = 1.41 < 1.95
Relative Risk= 1.2

exposure and also to prove the importance of the diagnostic value of the chest X-ray.

According to the Smoking Habit

Table VIII: The group of NOT smoking workers was 73%, but only 27% for the smoking group, from slight to heavy smokers.

X-ray Findings

The group of NOT smoking showed 51.4% of normal telefilms and 48.6% of abnormal films was 34.3 of suspicious and 14.3% of positive X-ray findings. The group of smoking people showed only 23% of NORMAL X-ray and 77% of abnormal test-films.

Table VII
Diffusion

EXP. TIME	% NORMAL	% DLCO - DIMINUTION	
< 10 YEARS	85.1	14.9	100
10 to 35	77.8	22.2	100

X^2 = 0.762 < 3.81 P-0.005
Z = 0.872 < 1.95
Relative Risk = 1.5

Table IX: Spirometric Findings

The group of not smoking workers was 76%.

The percentage of NORMAL telefilms was 22.9 and the abnormal was 77%, composed of obstruction 37.1, restriction 14.2% and mixed syndrome 25.7%.

The group of smoking workers was 18.1% and the percentages of abnormal telefilms was 81.6 composed of obstruction 36.3%, restriction 27.2% and mixed syndrome 18.1%.

The total percentage for obstructive syndrome was 62.8 for the not smoking group and 81.6 for the smoking group.

The total percentages of restrictive syndrome was 39.9 for the not smoking group and 45.3 for the smoking group.

Table X: The alveolo-diffusion test showed 17.6% of diminution in the not smoking group and 18.2% for the smoking group.

In order to make it easy for the reader to view the results, we made Tables X, XI, and XII, which resume the percentages of NORMAL VERSUS ABNORMAL. The close relationship between the abnormal findings on X-ray and lung function tests for the smokers and the longest time of exposure is evident.

We compare the same relationship, moving from the X-ray examination to the lung function tests, the latter being the major power of diagnosis. Unfortunately the lung function test has no specificity and only the X-ray findings, together with the occupational history of work, is of diagnostic value.

Table VIII
According to the Smoking Habit

X-RAY - (TELEFILM 14"x17") RESULTS

	NORMAL	%	SUSPICIOUS	%	POSITIVE	%	TOTAL
NO SMOKING	<10-15 >10-3 18	51.4	< 10-7 > 10-5 12	34.3	< 10-2 > 10-3 5	14.3	35 73
SMOKING	< 10-3 >10-0 3	23	< 10-1 > 10-3 4	30.8	< 10-1 >10-5 6	46.2	13 27
TOTAL	21	43.7	16	33.3	11	23	48 100

Table IX
According to the Smoking Habit

	NORMAL	%	OBSTRUCTION	%	RESTRICTION	%	MIXED	%	TOTAL
NO SMOKING	<10-7 >10-1 8	22.9	<10-7 >10-5 13	37.1	< 10-4 > 10-1 5	14.2	10-9 9	25.7	35 76
SMOKING	<10-1 >10-1 2	18.1	<10-2 >10-2 4	36.3	< 10-1 > 10-2 3	27.2	< 10-0 > 10-3 2	18.1	11 24
TOTAL	>10-8 <10-2 10	21.7	>10-9 <10-8 17	37	> 10-5 < 10-11 8	17.3	< 10-6 > 10-5 11	24	46

Table X
According to the Smoking Habit

DIFFUSION

	NORMAL	%	DIMINUTION	%	TOTAL	%
NO SMOKING	<10-8 > 9 9 28	82.4	<10-4 >10-2 6	17.6	>10-23 <10-11 34	75.6
SMOKING	<10-4 >10-5 9	81.8	<10-0 >10-2 2	18.2	<10-4 >10-7 11	24.4
TOTAL	37	82.2	8	17.8	45	100

Table XI
According to the Smoking Habit

RADIOLOGY

GROUPS	% NORMAL	% ABNORMAL	TOTAL
NS	51.4	48.6	100
S	23	77.0	100

X^2 = 3;84 - 3,84 $P < 0.005$

Z = 1.95

Relative Risk= 2.8

Table XII
According to the Smoking Habit

SPIROMETRY

GROUPS	% NORMAL	% ABNORMAL	TOTAL
NS	22.9	77.1	100
S	18.1	81.9	100

X^2= 0.63 < 3,84 $P < 0.005$

Z = 0.79 < 1.95

Relative Risk= 1.06

Table XIII
According to the Smoking Habit

DIFUSSION

GROUPS	% NORMAL	% ABNORMAL	TOTAL
NS	82.4	17.6	100
S	81.8	18.2	100

X^2 = 0 < 3.84 $P < 0.005$

Z = 0 < 1.95

Relative Risk= 1.02

INVESTIGATIONS INTO THE SPECIFIC FIBROGENICITY OF MINE DUSTS IN HARDCOAL MINES OF COUNTRIES IN THE EUROPEAN COMMUNITY

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Results of investigations in the field of pneumoconiosis research in the last 30 years indicate that the mine dusts in the various deposits of European and American hardcoal mines have a different fibrogenicity.[1-4] Although epidemiological research into coal workers' pneumoconiosis in British coal mines (Figure 1) has revealed a clear relationship between the occurrence of radiological lung changes (ILO category 2 and higher) and the mass concentration of respirable dust in one and the same colliery, a significant difference is to be observed in the frequency of the occurrence of pneumoconiosis between collieries where either high rank coal (colliery T) or low rank coal (colliery Q) is mined with comparable dust exposure. In colliery T with high rank coal, the response is several times greater than that in colliery Q with low rank coal. At the same time, the curve of the occurrence of pneumoconiosis as a function of the dust concentration is far steeper for colliery T than for colliery Q. Similar relationships have been observed in Germany, France and the USA.

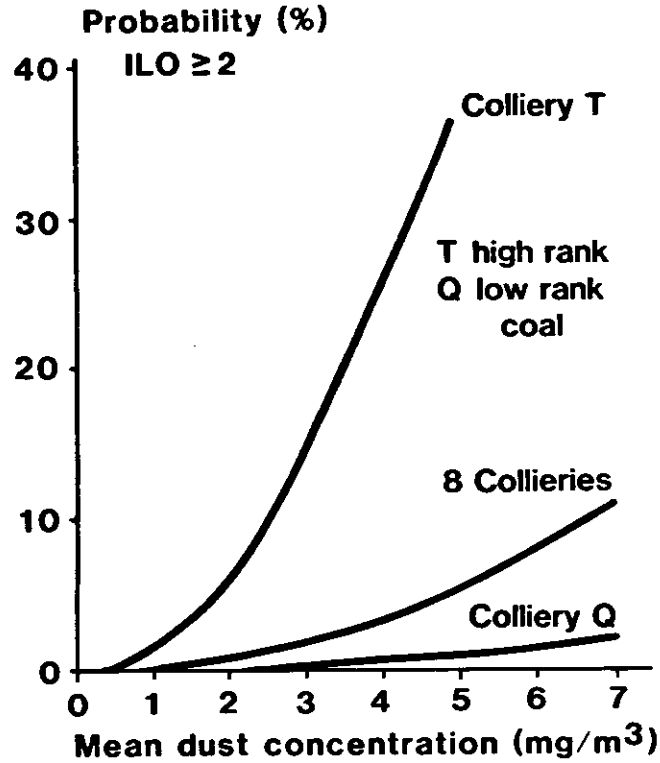


Figure 1. Estimated (percent) probabilities of category 2 or higher simple pneumoconioses, in relation to mean dust concentration.[3]

Even today, these differences cannot be explained by reference to the dust composition, even with the quartz contents determined by X-ray diffraction or infrared spectrography. As can be seen from the following table (Figure 2) of results from British investigations,[3] the frequency of the occurrence of pneumoconiosis (ILO category greater than 2/1) in the high rank coal seams (colliery W) is roughly 10 times higher than in the low rank coal seams (colliery Q), although the quartz content of the dust from colliery W is only one quarter of the value for the dust from colliery Q. The mineral content (ash content) of the dust from colliery W is also correspondingly lower than that of the dust from colliery Q. Similar results were obtained in earlier investigations[5,6] and also from a more recent investigation[7] in Germany as can be seen in the following table (Figure 3). Here again, as with the results of the British investigations, a ratio of 1:10 is to be observed in the prevalence of radiological changes (ILO category 2/1 and higher)—with an exposure time of 22 to 30 years—as a function of the rank of the coal and, at the same time, a lower cumulative quartz dust dose with higher prevalence.

The occurrence of the pneumoconiosis does not therefore correlate generally with the quartz content of the dusts. A more obvious correlation appears to exist with the specific petrographic characteristics of the stratigraphic horizons, which have a modifying effect on the fibrogenicity potential of the mine dusts. The rank of the coal could therefore be taken as an initial indicator for this potential.

Cell experimental investigations (Figure 4) with mine dusts taken from various stratigraphic horizons of German hardcoal mines,[1,2] allow the following conclusions to be drawn, which also correspond to the results of the epidemiological investigations.

- The cytotoxicity (decrease in TTC reduction activity means an increase in cytotoxicity) of dust samples from one and the same stratigraphic horizon increases with increasing ash (mineral) and quartz content.

Colliery	Prevalence 2/1+ Observed / Predicted x 100	Dust composition (%) Quartz	Ash
Q (low rank)	18	5,4	70,6
Y	67	3,6	32,7
V Seam 1	78	3,4	41,9
V Seam 2	78	2,0	26,2
W (high rank)	182	1,4	17,4

Figure 2. Prevalences of ILO categories 2/1+ in various British collieries with low resp. high rank coal and different composition of dust.[3]

	Cohort size	Dust dosis (22/30 years) c	c_q	Prevalence >1/1 ILO %	≥2/1 ILO %
Group 1 (low rank seams)	109	3700	3200	9,2	1,8
Group 2 (high rank seams)	109	5500	1800	31,2	18,8

Figure 3. Prevalences of ILO categories 1/1 and higher in German low rank coal resp. high rank coal seams in relation to mean total respirable dust doses c and respirable quartz dust doses c_q.[7]

- The same cytotoxicity of approx. 35% (65% TTC-RA) is observed for dusts from the later stratigraphic horizons with low rank coal (horst strata), however, only at roughly three times the ash (mineral) or quartz content of dusts from earlier horizons with high rank coal (lower Essen strata), as shown in Figure 5.

The petrographic characteristics of the stratigraphic horizons or deposits which could be responsible for the differences in specific cytotoxicity and fibrogenicity are:

- The quartzes from the various horizons have a different effect. Either the quartz from the earlier horizons with high rank coal has a far greater fibrogenicity, or the quartz from the later horizons with low rank coal has only a very low fibrogenicity. It was possible to show that structural impurities (Al ions in Si lattice positions among others) introduced into the lattice during the genesis of the quartzes or introduced subsequently into the surface by associated minerals led to a reduction in the cytotoxicity (Figure 6) and also, during *in vivo* experiments on animals, to a reduction in the fibrogenicity.[8,9] The less disturbed, i.e., the purer, the SiO_4 tetrahedra of a quartz are, the greater its specific fibrogenicity potential.
- X-ray diffractive, amorphous silica present in differing contents in mine dusts has an amplifying effect on the cytotoxicity[9] and fibrogenicity (Figure 7) compared with standard quartz DQ 12, as shown by the lymph node test in the animal experiment.[10]
- The other associated minerals occurring along with the quartzes in the mine dusts have an amplifying, i.e., additionally fibrogenous, effect in horizons with high rank coal (e.g. kaolinite) but an inhibiting effect in horizons with low rank coal.
- The individual particles of the respirable dust in the various horizons have either a differing heterogeneity (intergrowths) or are more homogeneous (with free active surfaces).

However, the relationships between the cytotoxicity of the dusts, their fibrogenicity and the results of the epidemiological investigations must be examined more closely.

On 1st October 1987, the first 2-year phase of a joint European research programme sponsored by the EEC was started to corroborate these non-contradictory and exemplary investigation results and to discover measurable properties of the mine dusts which allow the specific fibrogenicity potential to be definitively characterized. This programme is entitled "Characterization of Mine Dusts with Respect to their Specific Fibrogenicity." The research institutes involved in this programme are the Instituut voor Reddingswezen, Ergonomie en Arbeidshygiene (IREA), Hasselt/Belgium, the Centre d'Etudes et Recherches de Charbonnages de France (CERCHAR), Verneuil-en-Halatte/France, the Steinkohlenbergbauverein, Essen/W. Germany, the Silikose-Forschungsinstitut, Bochum/W. Germany and the Institute for Occupational Medicine, Edinburgh/UK.

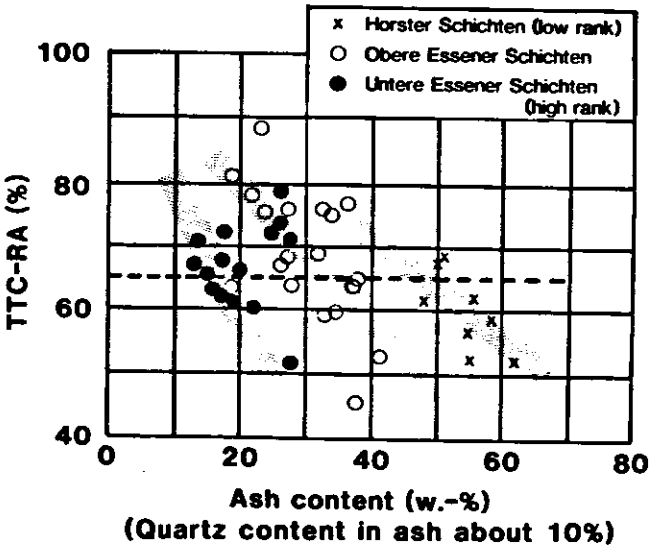


Figure 4. Cytotoxic effects (100-TTC-RA%) of German mine dusts from different stratographic horizons in relation to ash (mineral)-content.[2]

The sample material used in this programme is quartzes of various genesis and purity, mine dusts from earlier programmes (1960's and 1970's) and current mine dusts. The mine dust samples are or were taken using BAT-II samplers (CPM-3 samplers in France) from various strata over a number of weeks in such a way that at least 3 samples from each seam with different mineral (quartz) content can be examined in order to enable the trend of a dose/response relationship to be determined in a biological experiment. Dust samples from a total of 11 seams in the Ruhr coalfield and 4 seams in the Saar coalfield in Germany, 2 seams in Belgium, 3 seams in France and 4 seams in the UK were used.

The investigations incorporate:

- An extensive mineralogical, physical and chemical analysis, in particular of the individual particles, using electron microscopy (STEM) and laser-induced mass spectrometry (LAMMA),
- Luminescence measurements of their electron structure,
- The adsorption and desorption behaviour,
- Cytological, histological and biochemical *in vitro* reactions,

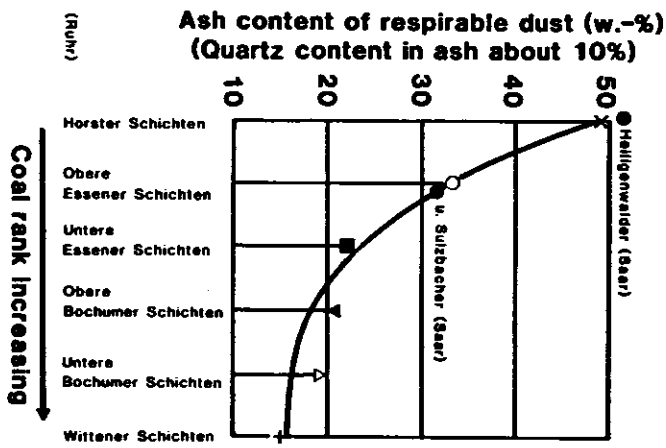


Figure 5. Ash (mineral)-content in German mine dusts from different stratographic horizons with same cytotoxic effect (35% depression of TTC-RA 120/Figure 4).[2]

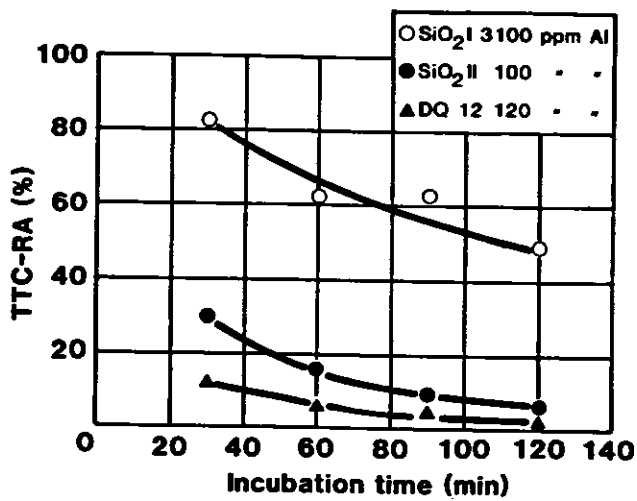
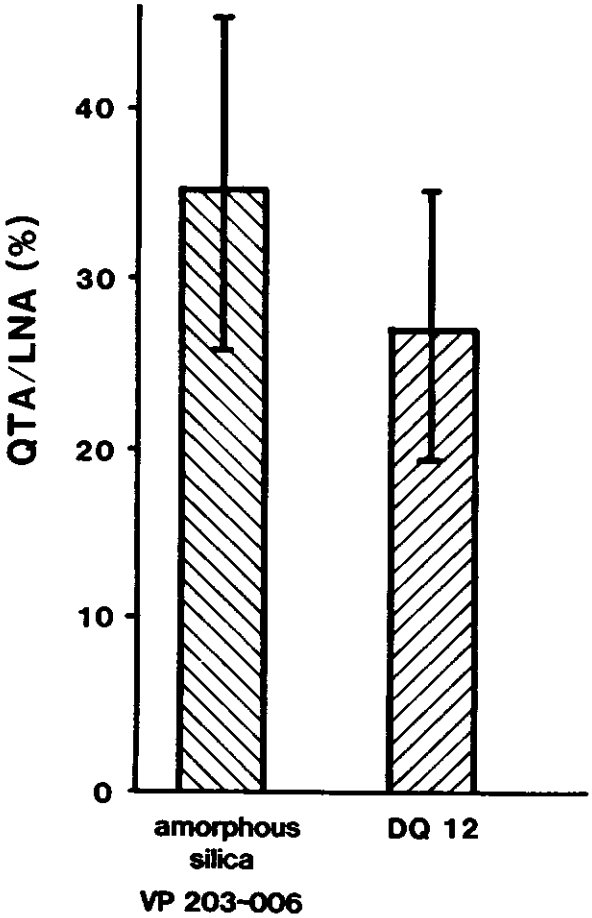


Figure 6. Cytotoxic effects (100-TCC-RA%) of 3 quartzes with different Al-content.[8]



Ffigure 7. Fibrogenic effects in lymph nodes of rats by amorphous silica (VP 203–006) and standard quartz DQ 12.[10]

- *In vivo* experiments, however only in a 2nd phase after positive completion of this lst phase, and
- Epidemiological examinations on selected groups of miners who, at least during the first 5 years of their employment, were exposed to dust in only one stratographic horizon.

The aim of these investigations is to be able to characterize the specific fibrogenicity of a quartz dust or any other mineral dust using a measurable parameter k. In addition to the quartz concentration c_q used alone to date to determine the fibrogenous risk potential R_F of a dust

$$RF = f(c_q, t, I) \quad (1)$$

(in addition to the exposure time t and individual susceptibility I), it would then be possible to introduce specific factors k, k_1 and k_2 for the fibrogenicity potential into this risk equation:

$$R = f(c, k_1 \cdot c_q, t, I) \quad (2)$$

$$R = f(k_2 \cdot c, k_1 \cdot c_q\, t, I) \quad (3)$$

or simply

$$R = f(k \cdot c, t, I) \quad (3)$$

where c is the concentration of the total respirable dust and c_q the concentration of the respirable quartz dust.

Based on this type of analysis, it would then be possible to obtain scientifically corroborated limit values which can be different for the individual stratigraphic horizons or deposits. Furthermore, this method could then be applied to all other sectors of industry in which fibrogenous dusts occur.

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SEEKING THE "RANK FACTOR" IN CWP INCIDENCE: ROLE OF RESPIRABLE DUST PARTICLE PURITY

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INTRODUCTION

The search for the cause(s) of coal workers' Pneunoconiosis continues despite the vast amount of research that has been undertaken over the past forty to fifty years. Good correlation between the mass of dust inhaled over workers' lifetimes and the incidence of the disease has led to the development of effective environmental standards and implementation of good procedures for the control of dust generation and dispersion in the working place. Research has only begun, however, to uncover the biochemical mechanisms involved in initiating the disease.

Correlation between the rank of the coal seam in which miners worked and disease incidence and severity is acknowledged worldwide, but the agents in the higher rank coal seams which cause CWP are still not defined. The basic components of the coal seams, i.e., the elements and minerals, are generally known, but the way in which they interact with human pulmonary cells is largely still a mystery.

The process of disease development is a biochemical one which depends on the characteristics of the pulmonary cells within their immediate biochemical environment and the characteristics of invading respirable coal mine dust particles, probably both chemical and physical ones. The cell-particle relationship, therefore, must be defined, and both cells and particles must be characterized according to properties which potentially are involved in the disease process.

Following such characterization, specific respirable dusts from different coal seams, which appear to have different effects on coal workers, must be obtained or constructed and then used in experiments designed to determine dust toxicity or the response of animals exposed to the dusts.

The results presented here focus on characterizing properties of respirable coal mine dust particles collected from operating longwalls in West Virginia and Virginia. Longwall panels were selected for analysis because the respirable dust in the coal face areas is largely uncontaminated by rock dust and analysis of the dust yields results unconfounded by rock dust.

The major emphasis has been placed on the characterization of mineral particles, although the analysis is presently being extended to include coal particles as well. This approach was selected because bulk analyses of dusts do not give the level of detail needed to unlock the key elemental and mineralogical roles in the disease process and because the role of minerals in disease development is contradictory at present. Another reason for this emphasis hinges on the known toxicity of quartz and the possible interaction of clay minerals with quartz in reducing overall dust toxicity.

This research has been supported by the Department of Interior's Mineral Institutes program administered by the Bureau of Mines through the Generic Mineral Technology Center for Respirable Dust under allotment grant number G1135142.

THE ROLE OF QUARTZ AND OTHER MINERALS

Although a majority of the studies on the role of quartz in CWP suggest a relationship does exist, some researchers have found contradictory evidence.[1] Interaction of quartz with other minerals may be a factor in reducing the influence of quartz in the disease process. Martin et al.[2] showed that mineral matter in coal inhibited the fibrogenic effect of quartz on experimental rats. They suggested that the surface characteristics of quartz particles were modified, thereby reducing their fibrogenic response.

Leiteritz et al.[3] found that the incidence of CWP in West German mines was related to the concentration of quartz in the dust and to the fine dust concentration whenever similar mines were compared. Interestingly they found a lower amount of quartz in higher rank coals. Davis et al.[4] found that noncoal minerals, including quartz and clay minerals, increased in concentration as the severity of CWP increased. They concluded that quartz is not the only cause of disease progression. Reisner and Robock,[5] studying the cytotoxicity of respirable coal dusts in the German Federal Republic, found that cell damage was positively correlated with the mineral content of dust and with coal rank and age as the mineral content was controlled.

These results clearly indicate an interaction between quartz and other minerals, most probably the clay minerals, in the disease process. It is evident that the mix of the minerals in respirable dusts, the intimacy of the mixing (i.e., whether clay mineral particles are bonded to quartz particles, and where, or merely lying adjacent to them), and the size frac-

tional relationship among the minerals may all be important aspects for continuing research. Further, a special relationship, which is yet to be defined, exists between these factors and the rank of the coal seam.

Toxicity tests on quartz, clay minerals, and specific mixes of the two, similar to the research presently being conducted by Wallace et al.,[6] and exposure-response experiments on animals using specific, representative mixes of minerals in dusts may be crucial to understanding and defining the mechanisms involved in CWP. The types of dusts which should be used in these experiments remain to be defined. They certainly need to be representative of the respirable dusts existing in working mines, and a number of different dusts, some from apparently harmless environments and others from toxic ones, need to be used and results compared. A methodology for characterizing and describing such representative dusts will be presented next.

METHODOLOGY

In order to study the characteristics of respirable-sized dust particles, dust samples were collected from longwall faces in accordance with 30 CFR 70.2 precollector. Samples were taken at seven to nine different locations on panels depending on the manpower configuration and the distribution of ventilating air. In an effort to ensure the representativeness of the dust particles from a coal seam, full-shift sampling was done over three different shifts, resulting in twenty-one to twenty-seven samples being obtained from each panel (three at each location sampled).

Scanning electron microscopy interfaced with energy dispersive x-ray analysis (EDXA) was selected as the procedure best able to study dust particles in the detail required. Due to the limitations of the in-house scanning electron microscope (SEM), which had to be operated manually, a strategy of identifying and characterizing 100 mineral particles per sample was adopted during particle analysis. An image analysis system was not available, thus particle sizing and shape analysis had to be done manually.

Dust samples from two different longwall panels operating in coal seams of significantly different rank were analyzed under the SEM. The Beckley seam is of higher rank (14,670 Btu, 18.8% volatile matter) than the Pittsburgh seam (13,660 Btu, 39.7% volatile matter). An elemental spectrum had to be obtained under EDXA for anywhere from 800 to 1200 particles in order to determine their mineralogy before 100 minerals could be identified. After a mineral particle was identified, it was sized according to its breadth (Feret's diameter) and ordinally ranked for its general shape and angularity of its periphery.

Analysis of 2684 particles was made from the Pittsburgh seam samples, while 700 particles were analyzed from the Beckley seam before obstacles to further progress were encountered. The data was then analyzed for variations in mineralogy by location on each longwall panel, for variations in mineralogy by coal seam, for mineral particle size variation by location on each longwall panel, for mineral particle size variation by coal seam, for differences in shape and angularity, for size-fractional mineralogy, and for the purity of mineral particles with respect to normal stoichiometric elements. Descriptive statistics and analysis-of-variance (ANOVA) techniques were used to pinpoint differences in the various parameters.

PRIMARY FINDINGS

Five major minerals were found to exist in the two coal seams: calcite, illite, kaolinite, quartz, and pyrite. The Beckley seam samples contained a substantially higher percentage of calcite particles (32.7% versus 20.7%) and kaolinite particles (10.3% versus 2.0%) than the Pittsburgh seam, while the relationship with illite particles (35.6% versus 55.8%) and pyrite particles (1.3% versus 6.0%) was reversed. The percentage of quartz particles (8.5% versus 8.7%) was virtually the same for each seam.

Although the percentage of quartz particles was the same for each seam, the purity of the quartz particles was very different. Only 28% of the quartz particles analyzed for the Pittsburgh seam were uncontaminated by non-stoichiometric elements, whereas 64% of those analyzed for the higher rank Beckley seam were uncontaminated. This information could potentially explain the contradictions on the role of quartz in CWP incidence since stoichiometric quartz is known to be cytotoxic. Contaminated, and hence toxically turned off, quartz particles may also be the key factor in defining the protective role that clay minerals have appeared to play in some studies.

In general, twice as many mineral particles are pure in the Beckley seam samples compared to those analyzed from the Pittsburgh seam. This finding is consistent for each mineral. This may be the rank factor alluded to in much of the literature concerning CWP, and this rank factor may indicate the geologic processes occurring during the time the minerals were formed. Hence, quartz occurring in the Beckley coal seam and in the overlying sandstone stratum may have been formed without major interaction with alumino-silicate clays, which were found to be the chief contaminants in the Pittsburgh seam quartz particles analyzed.

The mineralogy of respirable-sized particles was found to vary significantly by location on a longwall panel. For example, in the Pittsburgh seam the percentage of illite particles increased quadratically at a decreasing rate along the coal face from the fresh air point at the headgate (13%) to the farthest point along the face at the tailgate (77%). The percentage of quartz particles, on the other hand, remained nearly constant at each location. The amount of contamination of mineral particles by nonstoichiometric elements also remained nearly constant along the panel.

A major conclusion is that mineral particles comprising strata formed by sedimentary processes are as heterogeneous as coal particles. There is no such thing as standard quartz, illite, kaolinite, pyrite and calcite particles. This is especially true in the lower rank coal seams in West Virginia as compared to the higher rank coal seams. Therefore a trend exists toward relative mineral particle purity according to the rank of the coal seam.

Mineral particles identified from the Beckley seam were smaller, in general, than those from the Pittsburgh seam (1.36 versus 1.58 micrometers), although the size of quartz par-

ticles in the Beckley seam were larger than those in the Pittsburgh seam. Mineral particle size was also found to be significantly smaller at the tailgate location than at any other location on a longwall panel (1.17 versus 1.58 micrometers for the Pittsburgh seam). Particle mineralogy by size fraction was found to vary significantly, although differently for each coal seam studied.

CONTINUING RESEARCH

Research priority for this project is now focusing on determining the percentage of all respirable dust particles that are single phase or multi-phase minerals versus single phase organic or multi-phase organic-inorganic complexes. This effort is being accomplished using a semi-automated procedure involving particle imaging followed by EDXA. Both coal and noncoal particles are being analyzed, and size fractional variations are being pursued. The mineral purity factor will be developed further, but additional emphasis will be focused on determining the extent of inorganic inclusions in organic particles. Initial results are just being obtained from this procedure, which will analyze 2000 particles per sample. Important size distributions for both coal and mineral particles will result from this research.

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THE INFLUENCE OF SHAPE, SIZE AND COMPOSITION OF INDIVIDUAL DUST PARTICLES ON THE HARMFULNESS OF COALMINE DUSTS: DEVELOPMENT OF METHODS OF ANALYSIS

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INTRODUCTION

The relationship between dust exposure and the probability of developing simple pneumoconiosis in UK coalmines was established in the field research programme over a period of more than 25 years (Figure 1). However, as demonstrated by Hurley et al. (1982) and Walton et al. (1977) the data for certain collieries do not fit the model developed for the main group. Some high rank collieries have higher probability of developing pneumoconiosis than predicted by the model from dust exposure data while other low rank collieries have much lower probabilities. Similar patterns are found for the same collieries in the development of progressive massive fibrosis.

Table I shows details from two of these anomalous collieries. Colliery Q is a low rank coalmine with moderate dust and quartz exposure but low prevalence of pneumoconiosis and observed:expected ratio of about 18% in the Hurley (1982) model. In the Walton (1977) model when other factors are involved including the mineralogy and interactions between minerals the observed:expected ratio is close to 100%. In contrast, with Colliery W, a high rank mine, the dust exposure is moderate and the quartz exposure is low but the prevalences are high and the observed:expected ratios from both models are around 200%. Thus while the dust composition data may be used to explain the lower prevalence in some low rank mines there is still no satisfactory explana-

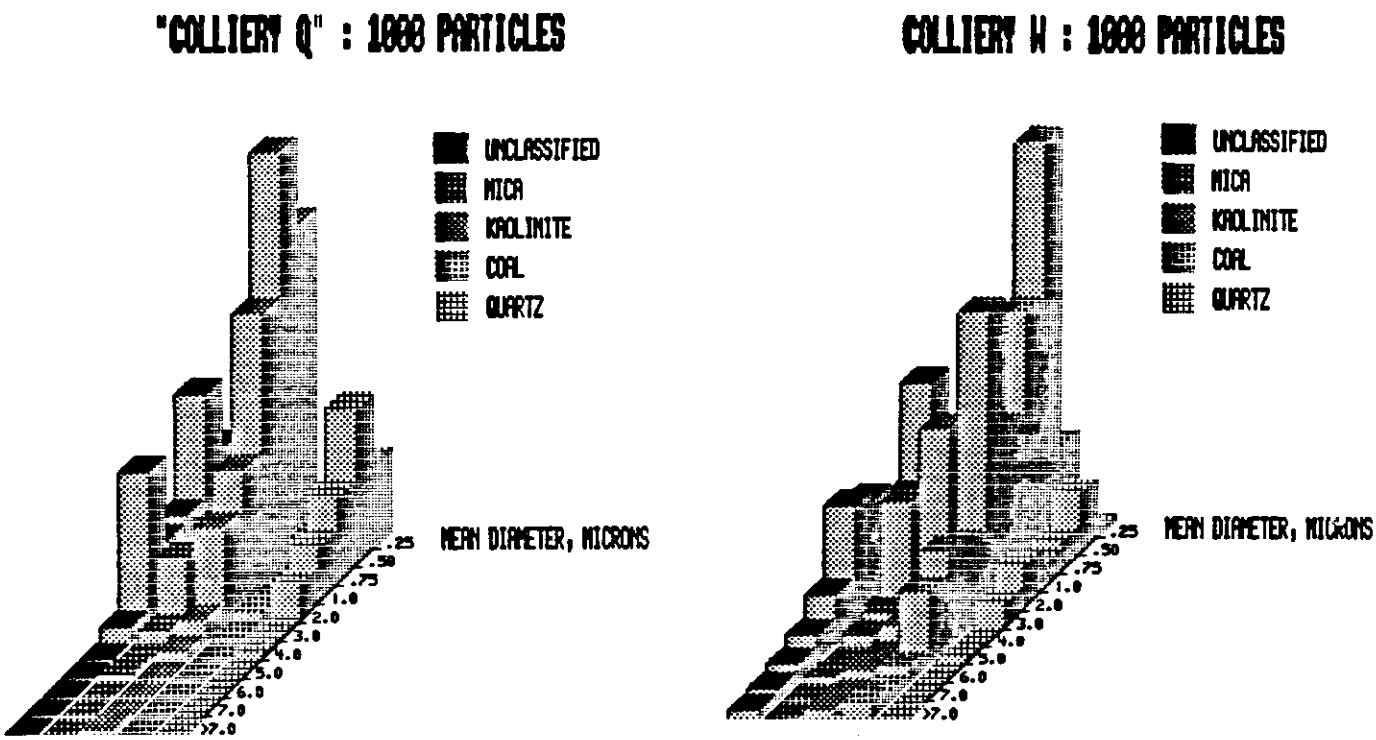

Figure 1a and b. Typical particle size and composition data derived for a low rank coalmine Colliery Q and a high rank coalmine Colliery W showing clear differences in the coal quartz and kaolinite particle sizes and proportions.

Table I

Epidemiological Data from a High Rank and a Low Rank Colliery
Showing the Differences in Fit to their Statistical Models
Devised by Walton (1977) and Hurley (1982)

	Colliery W High Rank	Colliery Q Low Rank	
Dust Concentration (mg m^{-3})	5.0	5.9	) Mean of
% Quartz	1.4	5.4	) 11 years
% Ash	17.4	70.6	)
Observed/Expected 2/1+	182	18	
Observed/Expected 0/1+	214	99	
Prevalence 0/1+	18.3	3.3	
Prevalence 2/1+	6.0	0.8	

tion for the higher prevalence of simple pneumoconiosis and PMF in the high rank mines.

In the early stages of PFR programme it was observed that many of the coal particles on thermal precipitator slides from high rank collieries appeared to be very much larger than expected. These observations were also reflected in the ratios between particle number and respirable dust mass concentrations established in the programme (Jones 1974). Similarly, particles with large projected areas have now been seen in a range of respirable mine dust samples and in dust samples recovered from the lungs of coalminers suggesting that these large particles in fact have small aerodynamic diameters. It seems likely that these particles from high rank collieries are plate-like. If so then like long fibres they may also be difficult for lung clearance. This factor has not yet been considered in epidemiological studies.

In the current project, supported by the European Coal and Steel Community, we are setting up a method to measure, rapidly and automatically, the shape, size and composition of individual particles in the dusts and to find out if the differences suggested by these earlier observations are real.

METHODS

The method is based upon a Cambridge Instruments Scanning Electron Microscope with a Link Analytical LZ-5 light element X-ray detector, both controlled by a Link AN 10,000 multi-channel analyser and image processor.

The method has been applied to airborne dust samples loaded on polycarbonate membrane filters examined using a secondary or back-scattered electron image in the first instance.

The EM image signal is acquired by the AN 10,000 and digitised. The signal intensity at each point is measured and features are detected by searching for intensities above a given threshold level. The positions and sizes of all features larger than a given minimum are recorded to a results file and the computer then directs the electron beam to each one in turn. The X-rays generated are collected and analysed and the chemical composition is recorded with the other data in the file. This is repeated over many fields of view, building up data on more than 1000 particles in each sample.

The results file is then compared with a set of chemical classes based upon the compositions of the expected minerals. Each particle is classified and size distributions are prepared for each class. The time taken for each set of 1000 particles is about 2 hours.

A large number of factors are defined by the user for feature detection, feature analysis and data evaluation.

FEATURE DETECTION

For feature detection, only the setting of the threshold signal levels caused any real difficulties. Initial work with the secondary electron images showed insufficient contrast between the smaller particles and the background making particle detection very unreliable. We avoided this and other problems by adopting the techniques of Scanning Transmission Electron Microscopy to the SEM. Routine sample preparation methods identical to those used for airborne asbestos dusts were used.

The advantages of this change include low image noise and very low sensitivity of the thresholding routines to gross signal level changes. In addition, there is a very much lower level of background noise in the X-ray counting routines. The disadvantages are in the additional sample preparation necessary although there are possibilities for direct impaction of samples on to pre-coated TEM grids.

X-RAY ACQUISITION

Only small sections of the full 10 KeV X-ray spectrum are necessary for particle identification. The minerals of interest in these samples are Coal, Quartz, Kaolinite and Mica, and the elements required to identify them are carbon, oxygen, aluminum, silica and potassium. Suitable X-ray energy

ranges or windows are set up to count only the X-ray's characteristic of these elements and to provide suitable background counts for subtraction from the element counts.

X-ray counts of any duration can be made up to hundreds of seconds but counts for 1500 milliseconds have been found to be sufficient for classification and suitably fast.

DATA PROCESSING

Mineral composition limits must be described for all of the elements in the X-ray window file for each mineral of interest in order that the particles may be classified. The ranges of compositions, established as a standards file, are shown in Table II and illustrate some important features. The ranges do not represent precise compositions for a number of reasons. Firstly, the classes need to be broad to accommodate the statistical variation found with low X-ray counts resulting from short analysis times. Secondly, the breadth allows for a degree of cross-contamination of X-ray spectra by adjacent particles or by fine particles on the surfaces of larger ones. At the same time, however, a wide range of compound particles will remain unclassified as will such minerals as $CaCO_3$ and FeS_2.

SIZE DISTRIBUTION

The only remaining task for the data processing is the size distribution calculation. This may be undertaken for any of a range of parameters, including maximum, minimum or mean Feret diameters, projected area, circumference etc., or any ratio of these. Any range of sizes in any number of size classes may be established for the calculations for each of the mineral categories. In the development work carried out to date mean projected diameter has been used to describe particle size.

RESULTS

Typical results are shown in Figures 1a and 1b for the high rank and low rank coalmine dusts. The low rank coalmine dusts from Colliery Q show a low proportion of coal particles, high kaolinite and moderate mica and quartz. Almost all of the particles are less than 2 μm mean projected diameter. In contrast the high rank dust from Colliery W contains a much higher proportion of coal particles, very low amounts of quartz and moderate-low amounts of kaolinite and mica. While most of the mineral particles are less than μm in projected diameter a large number of the coal particles are considerably larger and would constitute an even higher proportion of the mass. The actual mineral compositions of both dusts as determined by normal analytical methods are reasonably consistent with the proportions in the mineral categories shown.

The two respirable dusts illustrated here should contain similar aerodynamic size ranges since they were collected in the same way using the same sampling instruments. The proposed explanation for the larger particles in the anthracite dust is that they are flat and plate-like and therefore aerodynamically small. Confirmation of this from three dimensional image analysis is also in progress.

DISCUSSION AND CONCLUSIONS

There is no single unifying physico-chemical theory of toxicology for all coal mine dusts. For example, the proportion of quartz in the dust, the nature of its surface, the mitigating effects of the clay minerals and the nature of the coal particle surface (oxygen free radicals) have all been used to explain observed differences in toxicity. If large plate-like particles, like long thin fibres, are difficult for lung clearance mechanisms to handle then the shape and size of the coal particles may also be important factors. This may then be the simplest hypothesis to explain the prevalence of coalworkers simple pneumoconiosis and progressive massive fibrosis in South Wales.

The preliminary conclusions from the study so far are two:

1. The method as established using STEM can be used to provide rapid automatic shape, size and composition information on a large number of individual particles.

Table II

Composition Ranges of "Standard" Minerals Used for Discrimination of Minerals from X-ray Counts

	Coal	Quartz	Kaolin	Mica
C	20 - 100	<20	<30	<30
O	<35	15 - 80	15 - 70	15 - 70
Al	<20	<15	15 - 70	15 - 70
Si	<20	15 - 80	15 - 70	15 - 70
K	<5	<5	<5	5 - 30

Ranges are broad and do not reflect precise compositions
Allows for low X-ray counts (short analysis times)
Allows for some compound particles, adjacent particles, sub-μm particles on surfaces of larger ones
Still wide range of 'unclassified' compositions [e.g. $CaCO_3$, TiO_2]

2. There appear to be real differences in the shapes and sizes of the coal minerals in dusts from coalmines of different rank.

Once it has been fully developed we believe that this method of dust analysis will have a useful role to play in epidemiological studies of coalworkers' pneumoconiosis.

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HARDGROVE GRINDABILITY INDEX OF COAL AND ITS RELATIONSHIP WITH COAL WORKERS' PNEUMOCONIOSIS

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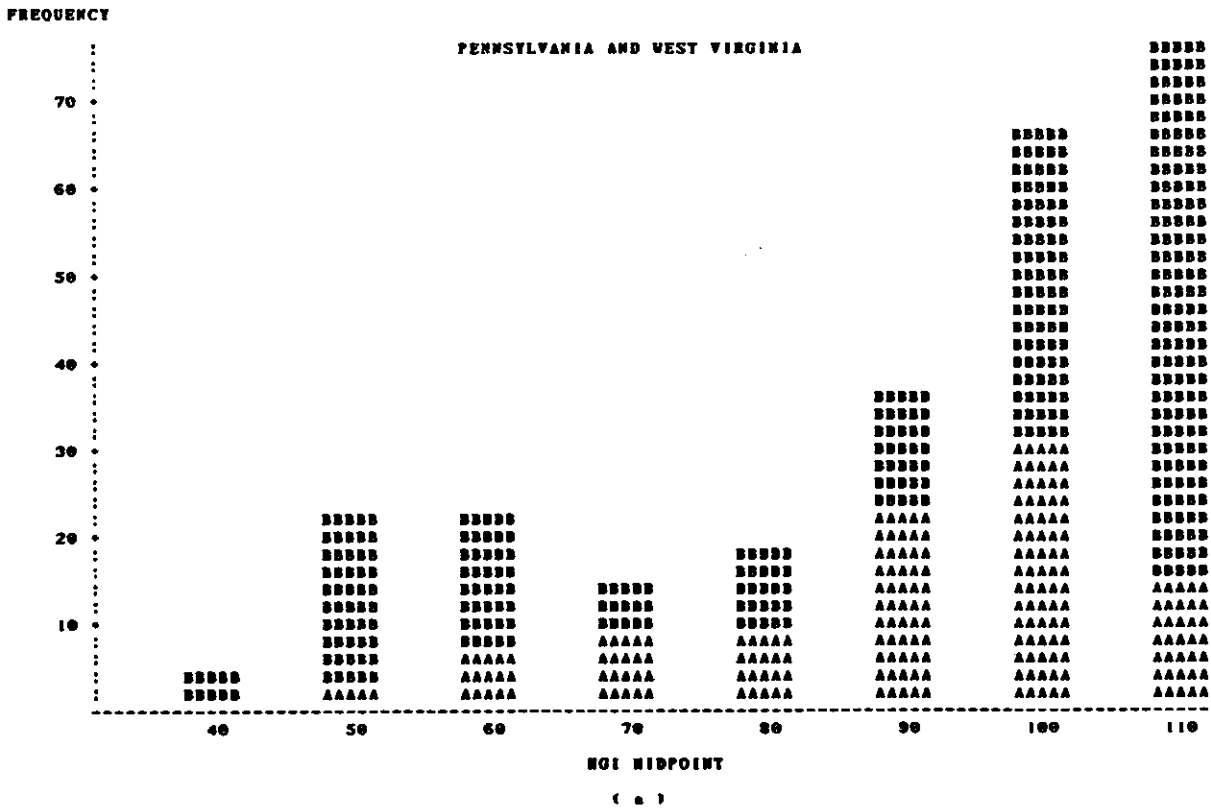
The prevalence of coal workers' pneumoconiosis (CWP) is generally considered to be directly related to the rank of coal, (1) mass of respirable dust, (2) free silica in coal, (3) and a few other factors such as trace elements (4) and diesel fuel emission.

The present study emphasizes on the mass of dust and dust generation potential using indirect measuring technique. Hardgrove Grindability Index (HGI) of coal is a measurement of the resistance to abrasion and crushing and therefore an indirect measurement of generation potential of fine particles and dust upon crushing. HGI is used in this study because of two reasons: (1) there is a large published data bank available, and (2) there seems to be a better correlation between HGI and coal dust level than any other factors. Rank of coal has long been recognized to have positive correlation with coal workers' pneumoconiosis (CWP). HGI values of coal is not only controlled by rank but also by mineral (ash) content and maceral composition and the size of vitrain bands.[5] Dull coals (durain rich coals) tend to be hard and exhibit lower HGI than bright coals (vitrain rich coals) of the same rank. Mineral matter, particularly dispersed, fine grained mineral matter, acting similar to other inertinite macerals, tend to cause a decrease of the HGI of the coal. More than 2000 entries of HGI of United States coals were published by the U.S. Bureau of Mines and about half of them came from the states of Pennsylvania and West Virginia.[6] There are sufficient data points from these two states to make an acceptable 2 evaluation of any relationship between HGI and CWP, also based on published data.[7]

Results of evaluation of available Pennsylvania and West Virginia data indicate that there is a very good correlation between Hardgrove Grindability Indexes of coals (Figure 2) and the prevalence of CWP (Figure 3). Both plots are presented here on a county basis for easy comparison because the CWP result was published on a county basis. High HGI values come from high rank bituminous coals (low volaltile bituminous) occurring in those counties along the Allegheny front immediately west of the Appalachian folding belt that coincide well with the rank distribution of the coals. No petrographic data are available for detailed studies of the effect of maceral composition and HGI. Lower Kittanning coal is generally known in this region as a dull coal and rich in durain. On the other hand the Lower Freeport coal is a bright coal. Figure 1a is a plot of the frequency distribution of HGI of all available Lower Kittanning and Lower Freeport coals in Pennsylvania and West Virginia. There seems to be more Lower Kittanning coals exhibiting low HGI number than Lower Freeport coals, suggesting potential effect of the differences in petrographic composition. To further refine the technique and to remove the strong influence of rank differences, data from a single county (Clearfield County, Pennsylvania) were plotted (Figure 1a) and exhibit similar result. Petrographic effect is minimized in very high rank (also with high HGI, for example low volatile bituminous) coals because of the convergence of macerals in which individual macerals are progressively indistinguishable. Comparison between Lower Kittanning coal and Upper Freeport coal (also a bright coal) shows a similar result.

In summary, Hardgrove Grindability Index can be a good indicator of prevalence of coal workers' pneumoconiosis because it encompasses many of the dust generating factors such as rank, ash content, petrographic composition, and other factors yet to be isolated. If all other factors are the same the coal that tends to generate the most dust could also cause more CWP.



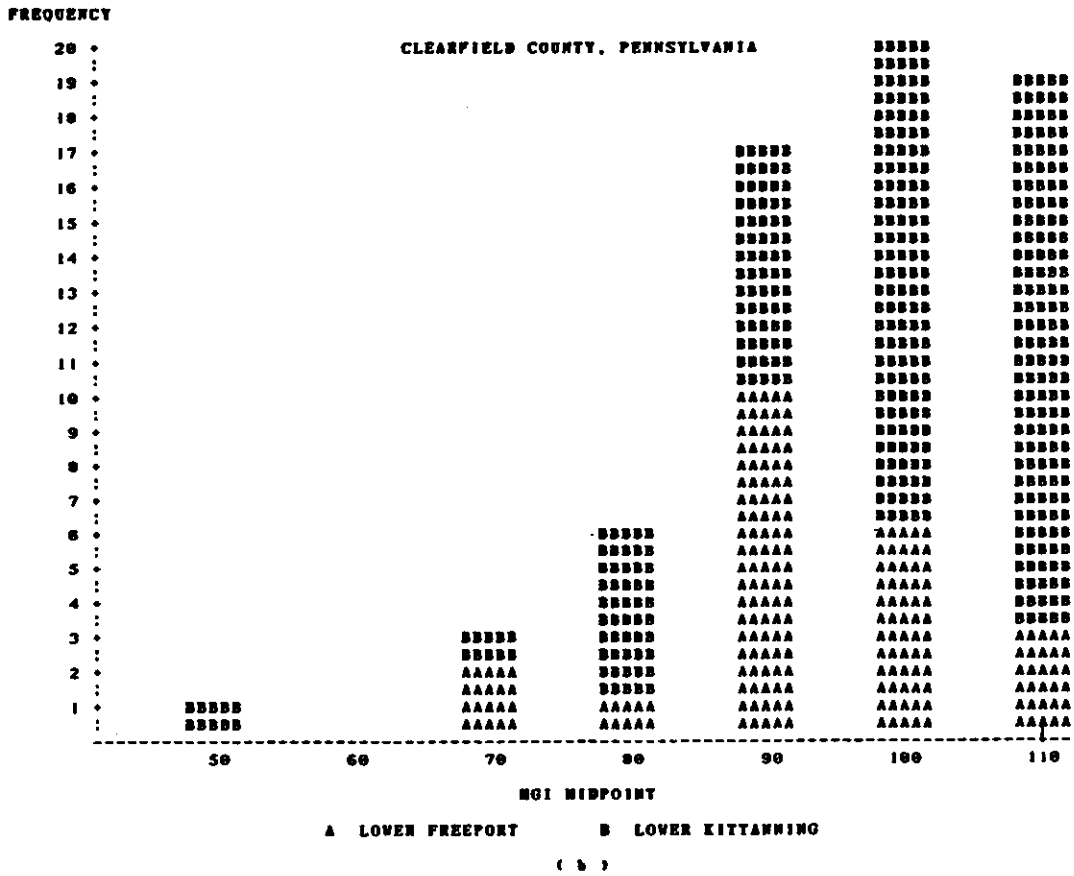


Figure 1. HGI frequency distribution of Lower Freeport and Lower Kittanning coals.

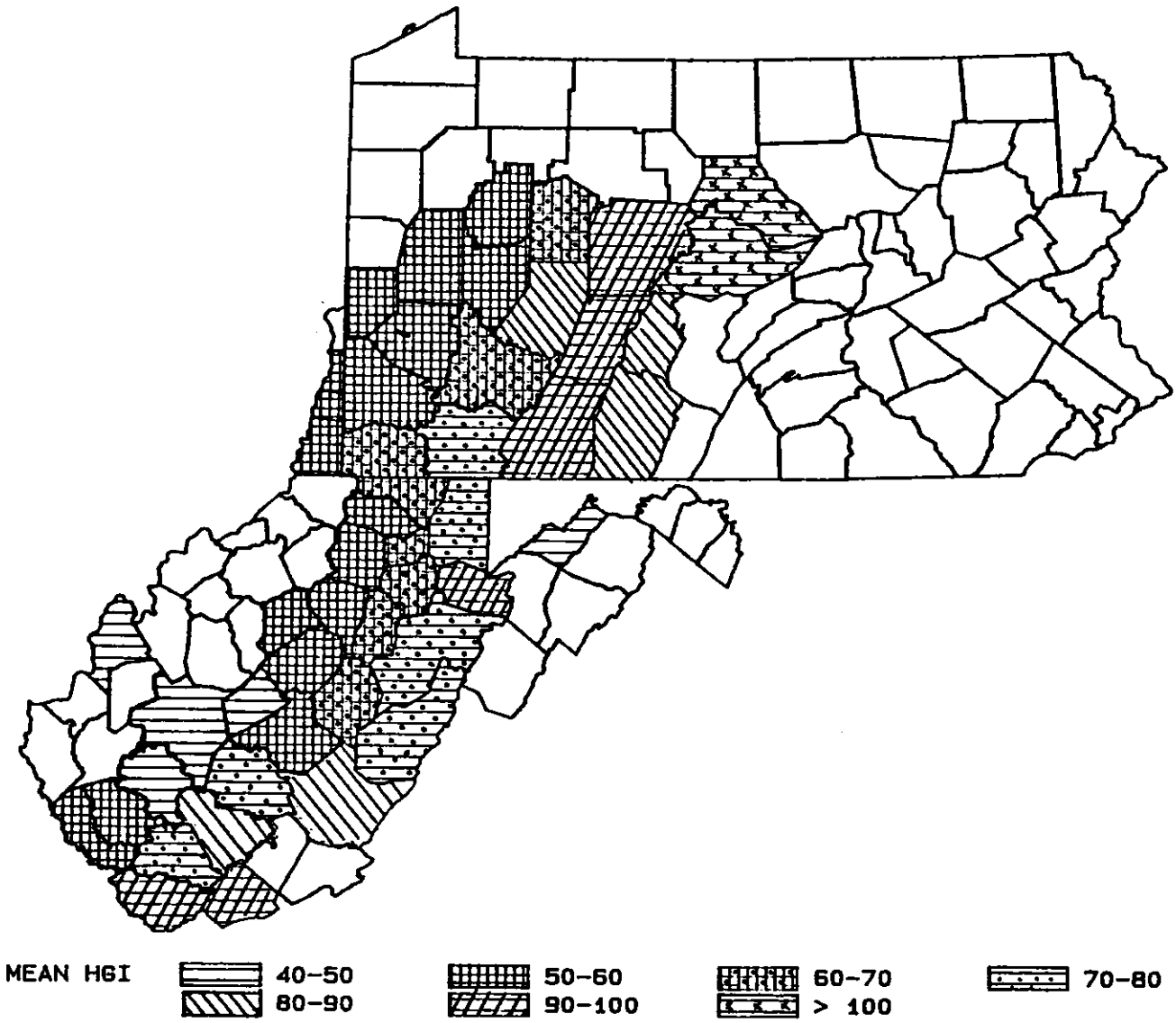


Figure 2. HGI averages for WV and PA.

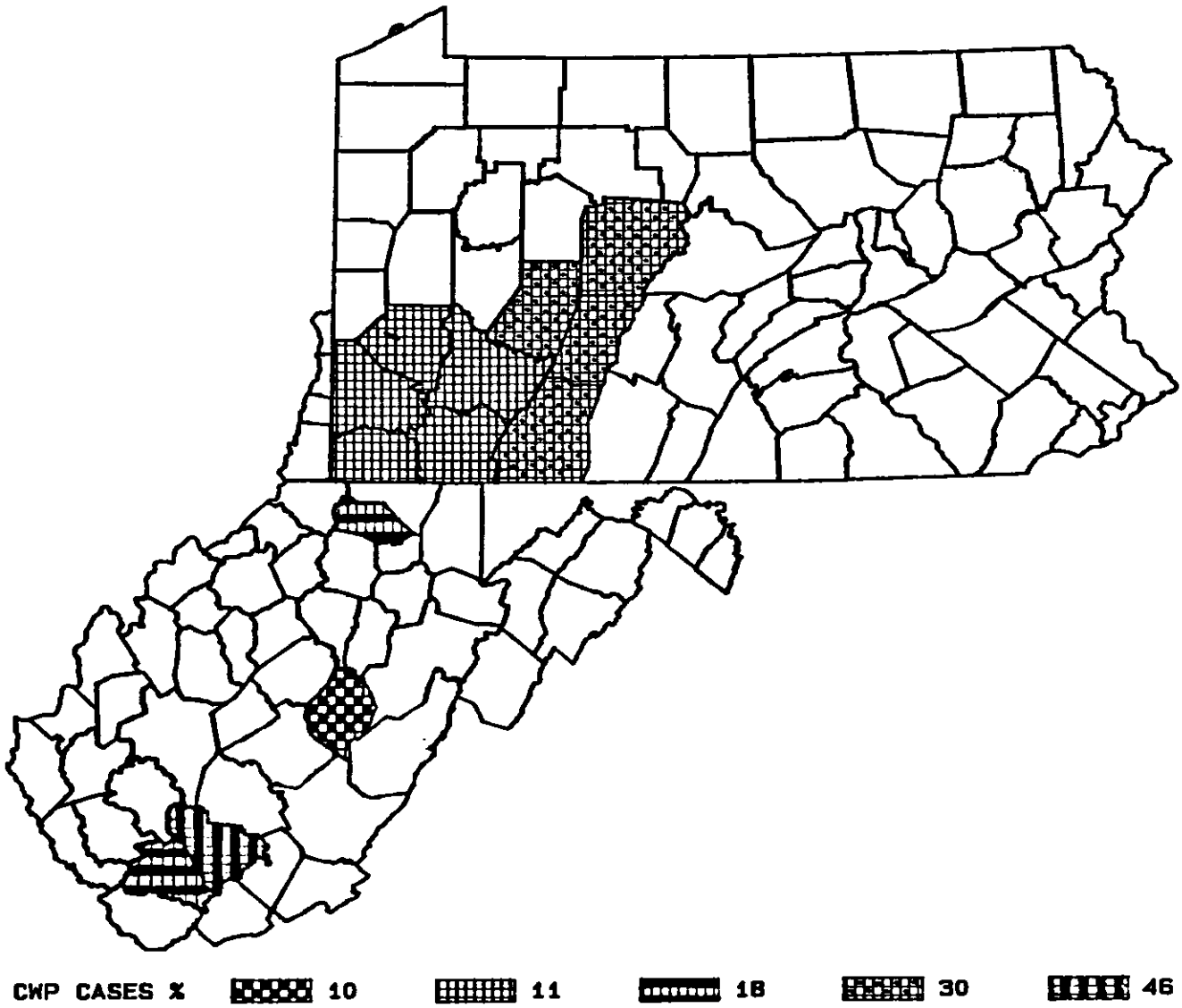


Figure 3. CWP cases for WV and PA.

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MINERAL CONTENT VARIABILITY OF COAL MINE DUST BY COAL SEAM, SAMPLING LOCATION, AND PARTICLE SIZE

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ABSTRACT

Size-selective airborne dust samples were collected using 4-stage cassette impactors at 9 different locations in each of five coal seams in order to determine the mineral content and its variability as a function of coal seam, sampling location, and particle size. Coal seams investigated were the Upper Freeport, Pittsburgh, Kittaning, Coalburg, and Pocahontas. Mineralogical analyses were done by an X-ray powder diffraction photographic technique.

Common minerals found in coal mine dust were illite, calcite, kaolinite, quartz, siderite, dolomite, gypsum, anhydrite, and pyrite. Among these minerals, illite and calcite were the two dominating minerals followed by kaolinite and quartz. It was found that mineral content was significantly affected by coal seam and particle size. In contrast, no statistical significance was found between samples collected at different locations within a section and sections within a mine. The variability of the mineral content was found to be quite high, with the mineral specific CV being .5 or greater.

INTRODUCTION

In spite of its long history of incidence, and the large amount of research conducted on it, coal workers' pneumoconiosis (CWP) is still prevalent among coal miners and needs further research to develop effective preventive and remedial measures. Although the dose-response relationship between simple CWP and coal mine dust has been established,[1] the causal agent(s) and the mechanism(s) involved in the progression of simple to complicated CWP are not yet defined. Many plausible hypotheses have been made to explain the mechanisms involved in the disease progression, however, none of them is satisfactory. In addition, the source of variation in occurrence of CWP among miners in different geographic areas,[2] rank of coal seam,[3,4] and job[5] remain unsolved.

As a result, more epidemiological and medical efforts have been directed toward identifying the causal agent(s) by investigating the physical and chemical properties of coal mine dust. Among the many factors investigated, the mineralogical composition has received attention because past epidemiological and post-mortem lung tissue studies have shown some correlation with the prevalence and severity of CWP and the quantity and type of minerals found in the coal mine dust.[6-8] Such findings have inspired many toxicological studies designed to assess toxicity of coal minerals *in vivo* and *in vitro*. These investigations have reported toxicity of coal minerals although contradictory toxicological results on the toxicity of each mineral by itself and in combination have been reported.[9-12]

Although these studies have provided us useful medical and toxicological information of coal minerals, some of them should be interpreted cautiously because the experimental settings used may not be comparable to actual mine situations. Furthermore, the studies provided little or no information about the "dust" used (i.e., dust size, mineral content, etc.). A recent review of one hundred toxicological studies and experiments designed to assess the health effects of exposure to coal and coal related minerals[13] revealed that, in many cases (43%), the geographic location where the test substance was obtained was not reported. Rarely was a specific seam or mine identified. The review also disclosed that many studies (67%) did not list how the test substance was obtained or created. Among those preparation methods reported, grinding or crushing of bulk coal samples was the main preparation technique used (22%). It was followed by collecting airborne mine dust at the coal face or in the return airway. Compounding the interpretation problem is the fact that the mineral composition of the dust was not incorporated for assessing dust toxicity in the majority of studies. In addition, most studies concentrated on evaluating the toxicity of a limited number of minerals and were not designed to assess the interaction of those minerals found in coal mine dust.

It is clear that toxicological studies designed to evaluate the effect of coal mine dust with different mineral combinations and concentrations are currently lacking because the mineral content as well as variability of coal mine dust has not been defined. Therefore, the purpose of this research was to identify the mineral matter contained in coal mine dust, to

establish the variability of each mineral, and to find those factors that affect mineral content changes so that the results can be used as the basis of dust selection in toxicological research.

EXPERIMENTAL PROCEDURE

Sampling Location

Details of the sampling methodology have been reported previously.[14,15] Thus, only a brief summary is provided here. Six working sections from five mines, one section from each of four mines and two sections in one mine, located in the Appalachian bituminous coal field were investigated. In each mine, dust samples were collected at nine different locations on a continuous mining section. These locations include: the intake airway, the dinner hole, immediately before and after the continuous miner, immediately before and after the roofbolter, the feeder, the haulageway, and the return airway. These locations were selected such that the researchers could monitor the contribution of mining activities to the changes observed in the mineral content of the dust in the mine air as it moves from the intake side of the face to the return side. These locations are illustrated in Figure 1.

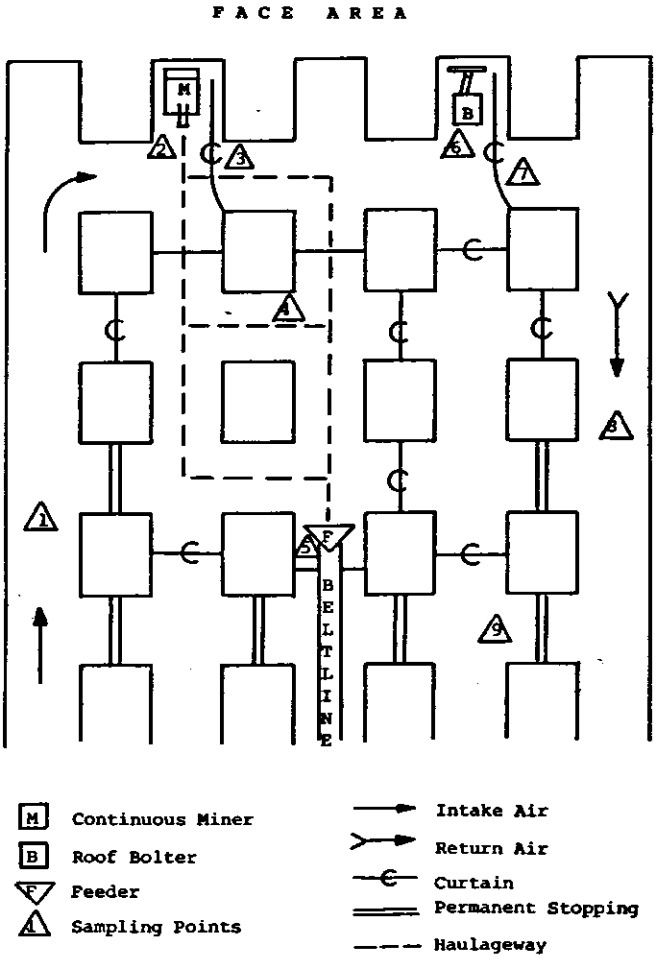


Figure 1. A typical continuous mining section layout and the sampling locations selected for study.

Sampling Equipment

Dust samples were collected using 4-stage cassette impactors. They were designed and constructed using a modification of an original design described by Jones et al.[16] Figure 2 shows the exploded view of the cassette impactor. Aluminum foil was used as the collection substrate for stages 1 to 4 and a standard 37 mm, 5 μm pore size, polyvinyl chloride (PVC) membrane filter was used for the last stage. The aluminum substrates were brush coated with a mixture of Apiezon L grease and toluene to reduce particle bounce. Sampling was done at a flow rate of 5 liters per minute (LPM) to improve dust collection efficiency by increasing the Reynolds number (Re). The flow rate was maintained with three MSA Model G air sampling pumps connected with tubing and Y-connectors to a pre-calibrated precision rotameter. Figure 2 also shows the in-mine dust sampling equipment arrangement.

Analysis

The analytical method used for the characterization of the mineral content of the dust samples was X-ray diffraction powder photography. The X-ray machine used was a Norelco X-ray generator type 12045/3 manufactured by North American Philips Electronic Instruments. The camera used was a Debye-Scherrer geometry camera of 114.6 mm diameter. The diffraction pattern was recorded on Kodak diagnostic, direct exposure DEF 329, GBX-2 film. Dust samples were mounted onto a thin glass spline mounted in wax on a copper stud. The sample to be X-rayed was placed into the camera which was then mounted on the X-ray generator. The aligned, rotating sample was exposed to copper Ka radiation monochromated with an Ni filter for 5 hours. The X-ray unit was operated at a voltage of 35 kilo-volts at 20 milliamperes. Each mineral was identified from the location of its diffraction line by comparing the film spectrum with the spectral data reported in the American Society of Testing Materials (ASTM) Powder Data File. Semi-quantitative estimation of the minerals present in the dust sample was accomplished by measuring the intensity of the diffraction lines and using weighting factors to compensate for the differences in the diffraction intensity of individual minerals. In this procedure, the intensity of each mineral was measured from the developed X-ray films using a microphotodensitometer. The height of each peak was measured after the estimated background which occurs primarily because of the grease and the organic coal dust matrix was subtracted. The raw intensities were then multiplied by weighting factors determined by Renton.[17] Mineral percentages were then calculated using the sum of weighted intensities as the denominator.

RESULTS AND DISCUSSION

Mineral matter here is defined as the inorganic and discrete mineral grains. In this study, only those minerals commonly found with relatively high abundance (>0.1%) were analyzed.

The minerals identified in the airborne coal mine dust samples were calcite, illite, kaolinite, quartz, siderite, dolomite, gypsum, anhydrite, and pyrite. The term illite describes an illite

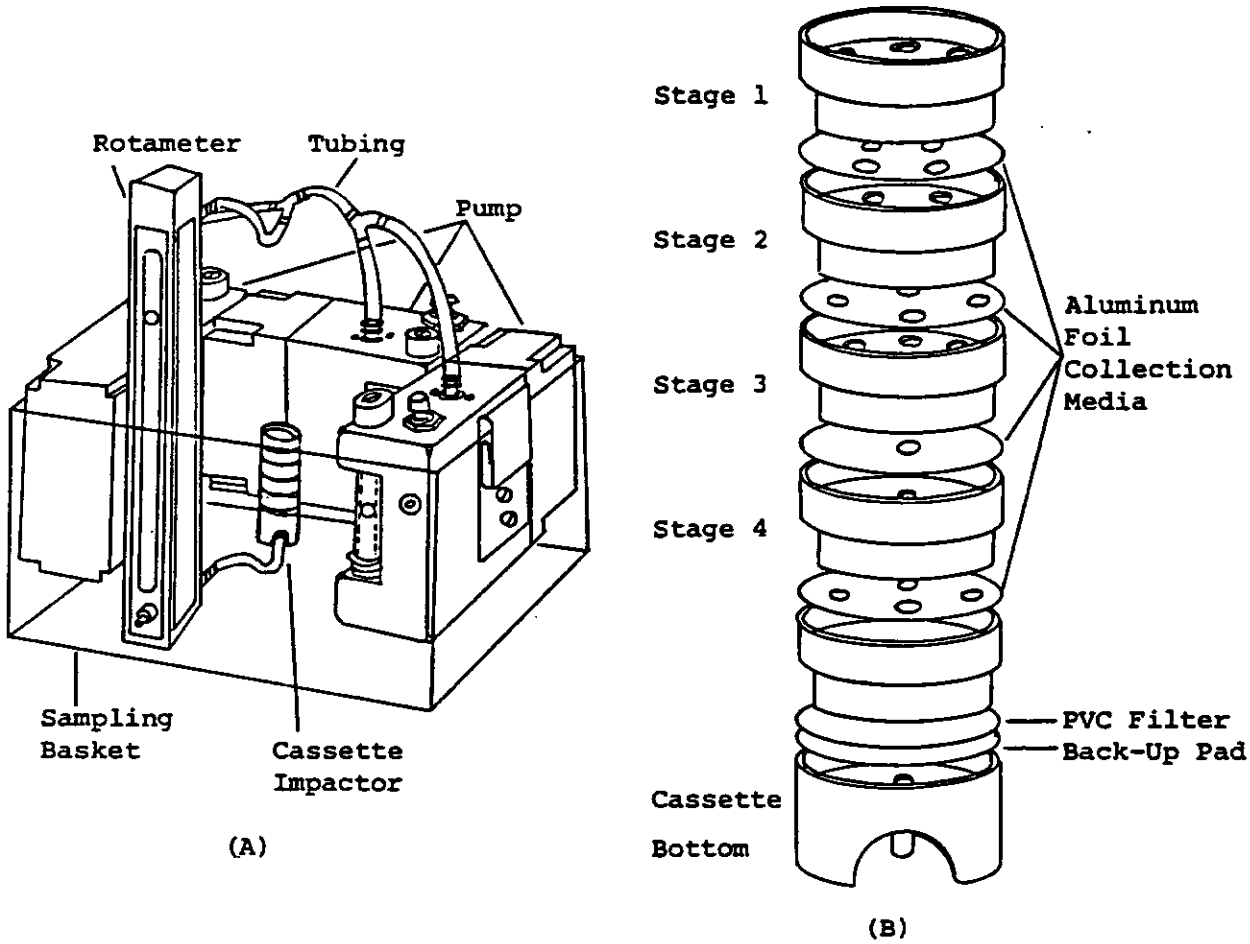


Figure 2. (A) Assembled in-mine sampling arrangement showing the pumps, tubing, and impactor. (B) Exploded view of the cassette impactor.

dominated mixed layered clay. The distribution of each mineral is depicted in Figure 3. Among these minerals, illite was the most dominant consisting of 43% +/− 22% of the mineral matter found in the samples collected. The other major mineral was calcite which amounted to 28% +/− 24% of the sample material. Similarly, kaolinite accounted for 9% +/− 8% of the sampled material, while quartz accounted for 4% +/− 4%. For these four minerals, the coefficient of variation (CV) ranged from 0.5 to 1.0. This is indicative of the very high variability found in the mineral content of coal mine dust. Other minor minerals, with concentrations ranging from 1 to 10%, included dolomite, siderite, and gypsum. The CVs for these minerals ranged from .68 to 1.47. Trace minerals with less than 1% concentration were anhydrite and pyrite.

In order to find factors affecting mineral content changes, the data were analyzed by a two-level nested-crossed analysis of variance (ANOVA). Subsequently, differences in mean values were evaluated using the Duncan's Multiple range Test. The ANOVA revealed that the coal seam factor was the cause of significant changes in mineral content for almost all minerals in the coal mine dust sampled in the region. Two exceptions were gypsum and siderite. A statistically significant high percentage of illite was found in the Coalburg seam while the lowest concentration was found in the Pittsburgh seam. Distribution patterns similar to that of illite were also observed for kaolinite and quartz. The distribution pattern for calcite, however, was almost opposite the patterns observed for the silicate minerals. Calcite content was the highest in the Pittsburgh seam while the lowest concentration was found in the Pocahontas and the Coalburg seams. In the case of such minerals as dolomite, anhydrite, and pyrite, they were more coal seam specific. The Pocahontas seam contained a significantly high (about 4 to 7 times) percentage of dolomite while more anhydrite was found in the Coalburg seam. Reportable amounts of pyrite were found only in the Upper-Freeport and the Pocahontas seams. The distribution of mineral content by coal seam is provided in Figure 4.

The working sections within a mine did not cause significant mineral content changes. No statistically significant changes in mineral content were observed between two working sections within a mine located in the Pittsburgh seam for all minerals except calcite. Similarly, the overall effect of

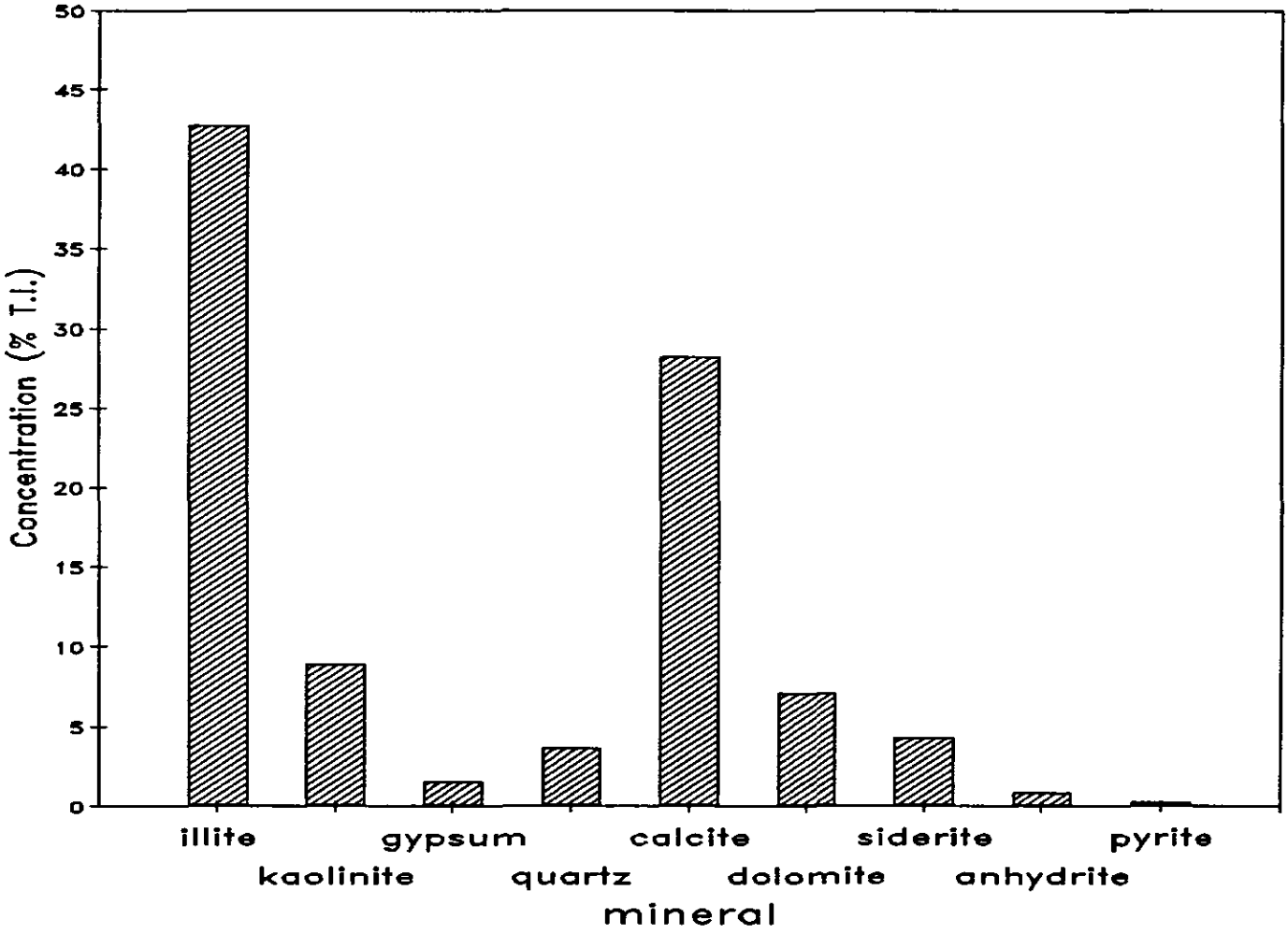


Figure 3.Overall mineral content distribution of the Appalachian bituminous coal field.

sampling location on mineral content was not statistically significant. Although no statistically significant difference was found, some trends were observed. The distribution of mineral content by sampling location is illustrated in Figure 5. High percentages of illite, kaolinite, and quartz in the samples collected near the continuous miner were observed while their concentrations were low in the samples collected in the return airway. Illite and kaolinite percentages were also relatively high in the feeder area. These results suggest that coal cutting and dumping liberates those minerals contained in coal. Their concentration then decreases as they gradually mix with other minerals as the mine air travels to the return airway. Quartz and siderite were relatively rich in the intake air samples while dolomite was found in the samples from near the roofbolter. Calcite content was the lowest in the coal producing area and the highest in the samples from the return air followed by the samples from the dinner hole. No particular patterns were observed for gypsum, anhydrite, and pyrite.

The distribution of mineral content by particle size is provided in Figure 6. The results of the ANOVA showed significant size effects on the mineral content for all minerals except kaolinite and pyrite. Subsequent analysis showed that the illite concentration was the highest in the size range of 1 to 3.5 μm followed by the size range of 6.6 to 10 um. The pattern for gypsum was similar to that of illite. For calcite, the trend was exactly opposite of the illite pattern. The highest concentration was found at the top stage (over 10 μm) followed by the third stage (3.5 to 6.6 μm). The pattern for quartz was similar to that of calcite although the highest concentration was observed on the third stage. Dolomite content was the highest on the top stage while no statistically significant difference in mineral content was found among the rest of the stages. The trend for siderite was exactly opposite of that of dolomite. Although some patterns of mineral content change as a function of particle size were observed, no general relationship was established.

CONCLUSIONS

This research identified nine common minerals associated with coal mine dust in samples collected on continuous mining section in the Appalachian Bituminous coal field. Among these minerals, illite and calcite followed by kaolinite and

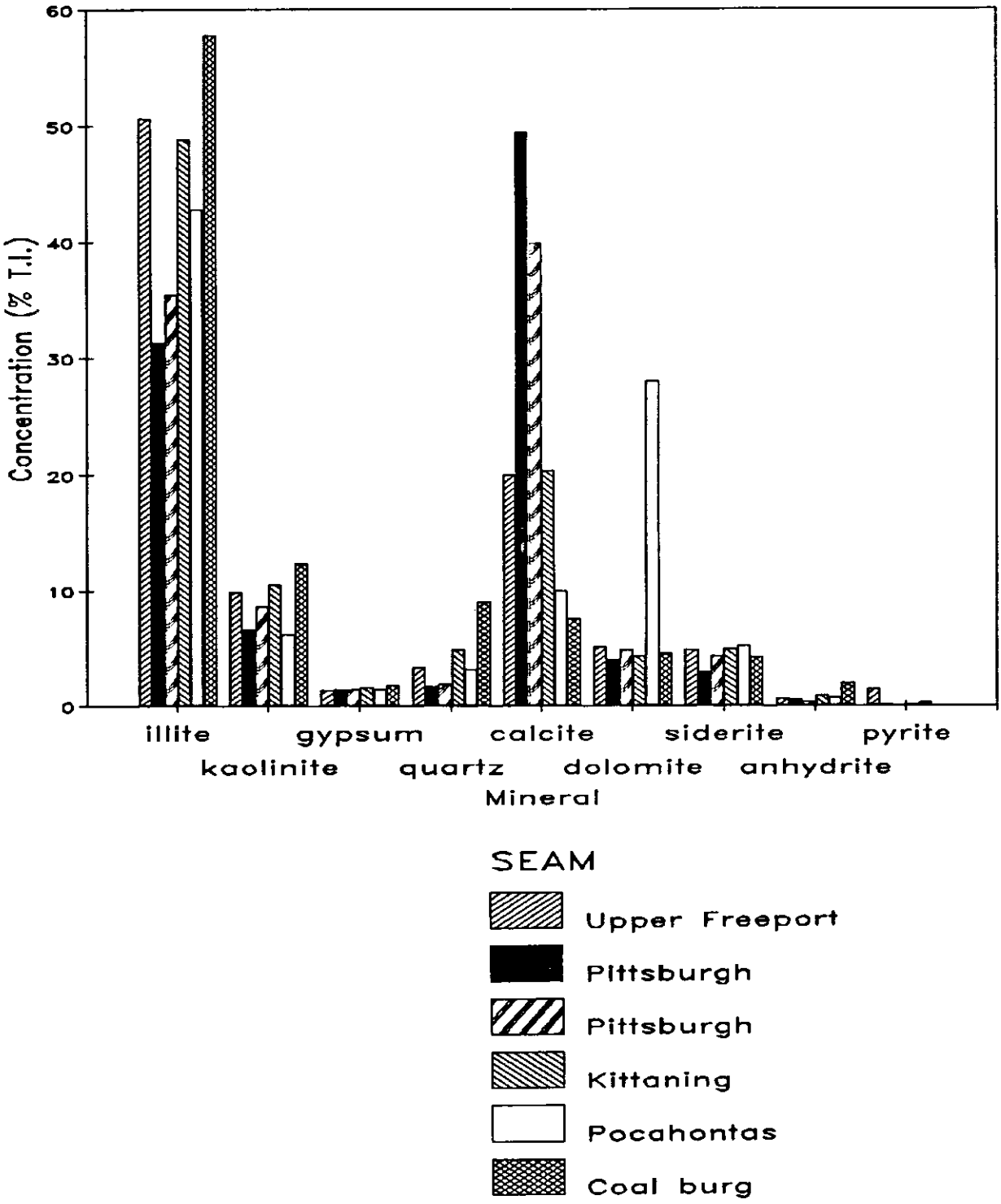
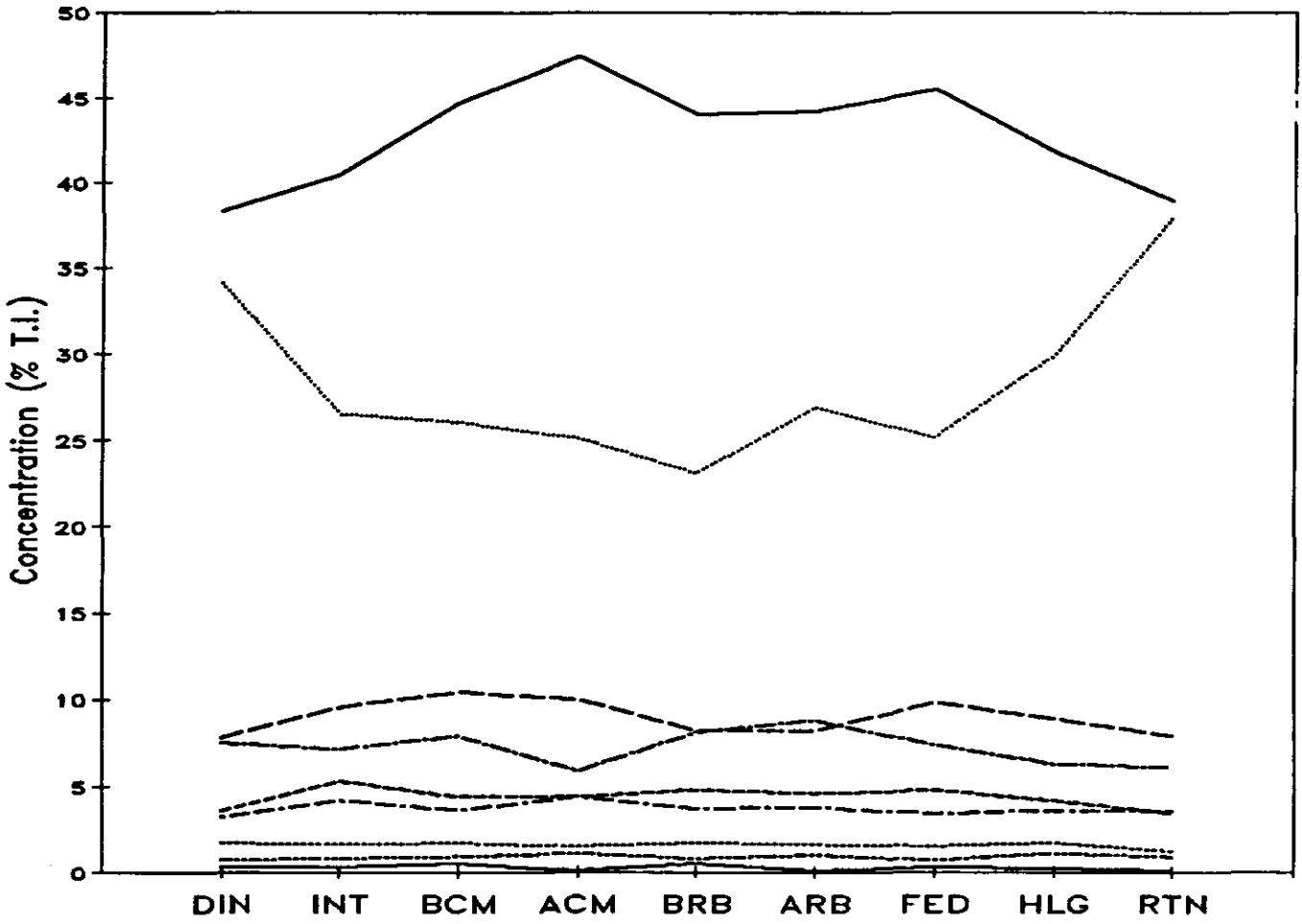


Figure 4. Mineral content distribution by coal seam.



LEGEND

illite
kaolinite
gypsum
quartz
calcite
dolomite
siderite
anhydrite
pyrite

LEGEND

DIN - Dinner Hole
INT - Intake Airway
BCM - Before Continuous Miner
ACM - After Continuous Miner
BRB - Before Roof Bolter
ARB - After Roof Bolter
FED - Feeder
HLG - Haulageway
RTN - Return Airway

Figure 5. Mineral content distribution by sampling location.

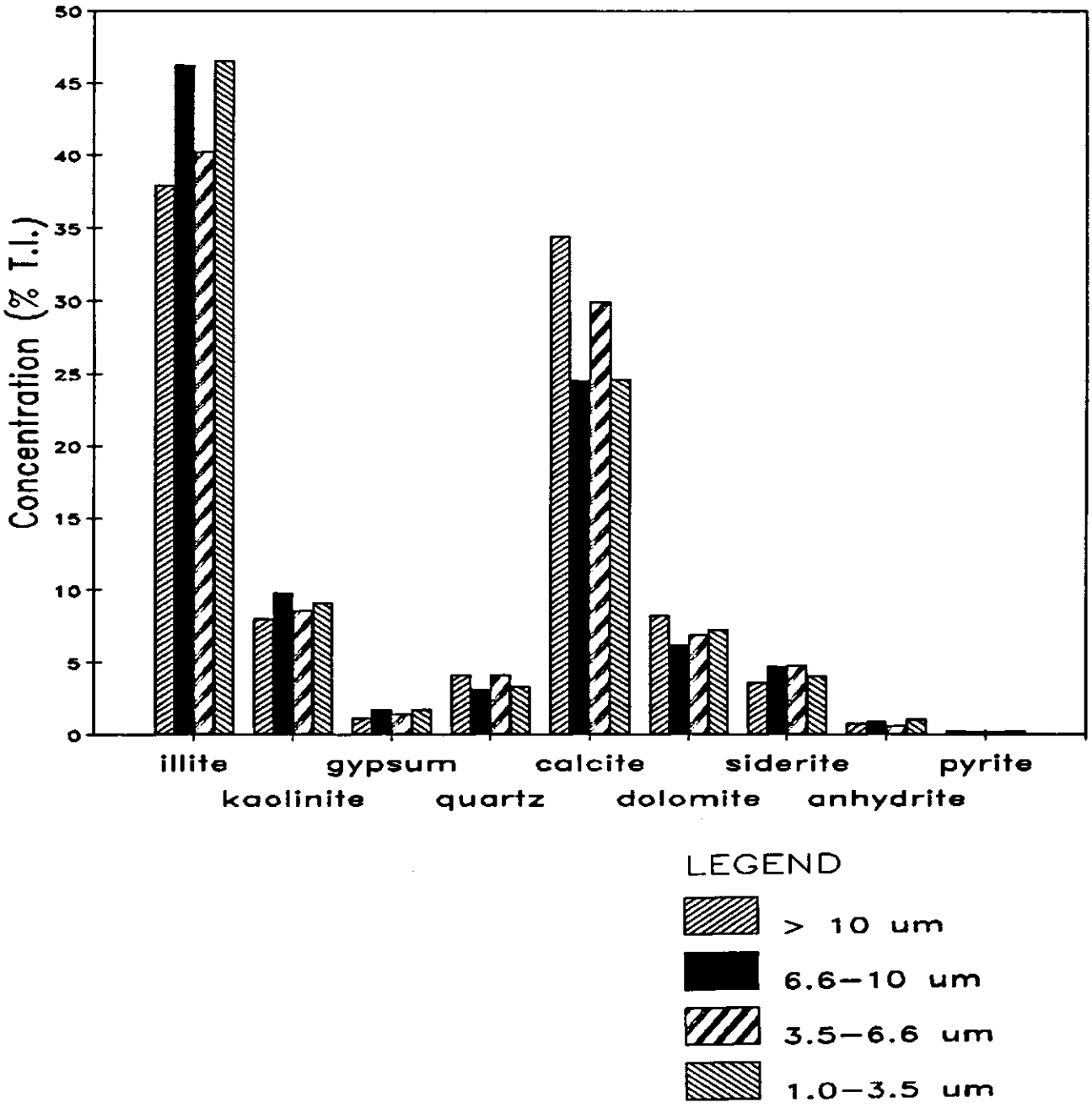


Figure 6. Mineral content distribution by particle size.

quartz are the dominant minerals. The relative abundance of all minerals except siderite and gypsum, however, is coal seam specific. This indicates the existence of coal seam variability. Also, mineral content was affected by particle size although no general relationship was established. The influence of sampling location upon changes in mineral content proved to be minimal. Likewise, no statistically significant difference was found between two working sections within a mine. However, significant variations in particle size distribution and respirable dust concentration were observed between sampling locations.

The results of this research clearly indicate that mineral content is highly variable and dependent upon coal seam and particle size. Therefore, it is clear that much of the previous medical and toxicological research on coal mine dust and CWP, which failed to consider, evaluate, and report the size specific mineral content of the administered dust can supply only limited information about the causal relationship between CWP and coal mine dust. This has left significant gaps in our knowledge of CWP causation and is at least to some degree, responsible for the conflicting results obtained by some of the past research. Thus, it is imperative that future

research of this kind should carefully consider the physical and chemical nature of the "dust" used, and report in detail on the "dust" source, preparation method, and nature. This will allow appropriate interpretations to be drawn from the results, and subsequent research can be based upon it.

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A COMPARATIVE ANALYSIS OF THE ELEMENTAL COMPOSITION OF MINING-GENERATED AND LABORATORY-GENERATED COAL MINE DUST

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ABSTRACT

The occurrence of Coal Worker's Pneumoconiosis (CWP) has been potentially linked with several characteristics of coal such as rank, volatility, percent content of ash and non-coal components, quartz content, and the presence of several trace elements. According to the National Research Council, numerous epidemiological studies indicate that the incidence of CWP varies significantly with the composition and/or the concentration of the coal mine dust.[4]

Although advances in dust-suppression techniques have markedly reduced respirable-dust levels in underground coal mines, the National Research Council has concluded that chemical characteristics of respirable dust from different coal seams should be studied. With this objective in mind, research has been conducted in underground coal mines located in the eastern and midwestern United States, and in the laboratory to characterize the elemental composition of mining-generated airborne dust and laboratory-generated dust derived from samples taken from these mines. The goal of the research is to determine if a relationship exists between mining-generated and laboratory-generated dust from the same mine.

INTRODUCTION

The Federal Coal Mine Health and Safety Act of 1969 was enacted to ensure healthier and safer working conditions for miners. In 1970, it provided for an underground respirable dust standard of 3.0 mg/m^3 in active coal mine workings and was subsequently lowered, in 1972, to 2.0 mg/m^3 as long as the mine dust contained less than five percent quartz. Despite the current respirable-dust standard, coal miners are continually being diagnosed as developing CWP. The amounts of black-lung compensation payments continue to rise and are approaching two billion dollars annually. The compensation payments are partially funded by an excise tax on coal. Currently, the tax amounts to $1.10 per ton for coal mined underground and $0.55 per ton for surface-mined coal.

Coal extraction by a continuous mining machine (CMM) is the most common underground method in the U.S. industry today and accounts for slightly more than two-thirds of the nation's deep-mining production (Figure 1).[1] Even if longwall mining should become more commonplace, it can proceed only after ventilation and access entries have been driven by CMMs.

The Mine Safety and Health Administration (MSHA) is required to inspect all underground coal mines four times each year and collect dust samples twice each year. MSHA inspectors also sample specific occupations in a mining operation that are typically exposed to the highest respirable-dust concentrations and which create potential hazards to the individuals assigned to these worksites. Such occupations are referred to as designated occupations (DO). Examples of DO would include the continuous-miner operator and the continuous-miner-operator helper. Additionally, the MSHA inspectors sample other underground occupations suspected to have high dust exposures such as roof bolters. These are referred to as nondesignated occupations (NDO).[8]

Thus, since a CMM operator and helper have DO, and other personnel such as the section foreman and the shuttle-car operators may be exposed to dust generated by the CMM as well, the purpose of this paper will be to discuss the relationship between the elemental composition of mining-generated airborne dust sampled from the immediate ventilation return of a CMM and laboratory-generated dust derived from channel samples taken from the mines. The elemental composition of the dust in the immediate ventilation return was chosen to be compared to the laboratory-generated respirable dust because it is close to the dust generating source, which is the CMM, and samples can be safely taken from this area.

The potential contributions of this research to the coal mining industry are: 1) after more fundamental knowledge of the cause(s) of CWP is learned, in particular certain trace elements, the laboratory-generated respirable dust could be used to identify a potentially hazardous coal seam. Also, this research could possibly aid in understanding the fundamental causes of CWP by producing mining-simulated samples of coal dust which could be used in epidemiological studies,

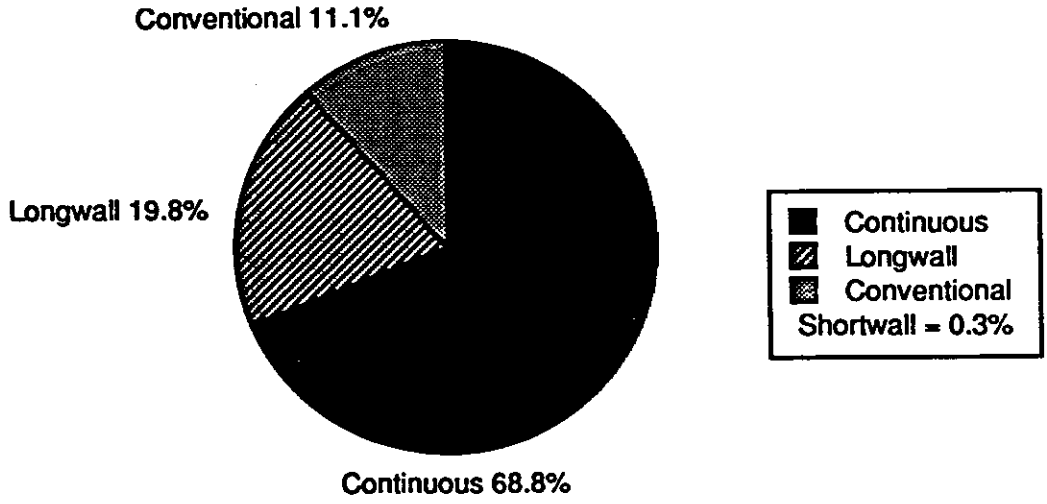

Figure 1. Underground coal production by type of mining for 1983.

and 2) assuming there is no difference in the elemental composition of a drill-core sample and a channel sample from the same location, a mining company could predict a new mine's respirable dust elemental composition in the immediate ventilation return by using exploratory drill-core samples of the roof, coal, and floor rock to prepare the laboratory dust. Ventilation engineers could then use engineering design and control measures during pre-mine planning to reduce the incidence and severity of CWP by better ventilating the potentially hazardous coal seam. If this proper planning prevented any future changes to the ventilation equipment and mine design, much time and money could be saved.

SCOPE OF WORK

To investigate the variability of the chemical characteristics of respirable dust, airborne dust samples from eight underground coal mines located in the eastern and midwestern United States were collected with eight-stage Sierra Model 298 Marple cascade impactors marketed by Andersen Samplers, Inc. as well as twenty-five channel samples of mined material. Each channel sample was removed from the middle of the coal face before mining occurred. Sampling of the mining-generated dust was conducted by Lee.[3] He sampled the entire working sections, primarily for characterization purposes, to obtain information on the locational variability of dust characteristics. Research performed for this study used the elemental analyses of the mining-generated dusts he sampled in the immediate ventilation returns of CMMs.

The procedure that was used to produce the laboratory-generated respirable dust was based on the Hardgrove grindability test, a test which reflects the pulverizing characteristics of coal. This test was chosen for several reasons. First, it is repeatable and reproducible; a consistent amount of input energy is used as well as a specified size range of feed material to be crushed (the channel samples). Secondly, it is thought to generate secondary dust in a way similar to that of the crushing and grinding of the coal and rock as they pass through the arc-shaped cutting path of the CMM's cutter head. The potential effect on dust generation by this secondary grinding mechanism may be at least as much as that produced by primary fragmentation, which is dust produced by the cutting action of the bit against the coal or rock.[5] Finally, the Hardgrove grindability test is well known and is used in the coal industry to guide mineral-processing engineers in estimating the capacity of mills used to grind coal.

One hypothesis of dust researchers in the Generic Technology Center for Respirable Dust is that the elemental as well as the physical characteristics of coal-mine dust will make a difference in the incidence and severity of the Black-Lung disease. Coal-mine dust is generated not only from coal, but also from any rock partings contained within the seam or any roof or floor material mined with the coal. Thus, coal-mine dust may not have the same elemental characteristics as the coal being mined.

Given that hypothesis, mixtures proportional to each thickness mined of roof, coal, and floor rock derived from the channel samples of the face areas from which the respirable dusts were generated by the CMMs were used to produce the feed material which was pulverized in the Hardgrove machine. The minus 400-mesh fraction (<37 μm) (U.S. series standard test sieve) that was collected after pulverization was placed in a fluidized-bed aerosol generator manufactured by TSI, Incorporated and dispersed in an aerosol test chamber manufactured by Elpram Systems, Inc. While the minus 400-mesh fraction was being dispersed in the aerosol test chamber, it was also being sampled with the eight-stage cascade impactors in the same manner as the dust in the immediate ventilation return of the CMM was sampled.

The elemental composition of the mining-generated dust and the laboratory-generated dust were determined from stages 3, 5, and 7 (10 μm, 3.5 μm, and 1.0 μm aerodynamic diameter, respectively) of a cascade impactor by the Proton induced X-Ray Emission (PIXE) method by the Element Analysis Corporation of Tallahassee, Florida. To perform

a PIXE analysis, a beam of protons is used to excite the atoms in the dust mass of a particular impactor stage. The X-rays emitted as a result of this excitation are analyzed to determine the elements that originated the various wave lengths. The number of X-rays that are emitted in a particular range are counted and the amount of each element in the dust can be calculated with an error that can be determined statistically for each element.

The PIXE method quantifies the mass of all elements simultaneously but had one limitation: the commercially available analysis is set up to determine only those elements that have an atomic number greater than or equal to sodium. The PIXE analysis is also a nondestructive method; therefore, any elements contained in the volatile material of the dust samples are not lost by an ashing procedure and dust samples can be archived for future use. The PIXE method easily gives a multi-element analysis from small dust masses which ranged from 5 to 120 μg.

DESCRIPTION OF THE ANALYSIS

After receiving the elemental analyses from the outside company, the data were grouped by mine, channel-sample location, and stage according to their identification as a laboratory-generated dust or a mining-generated dust. Since each element's weight fraction of the total dust mass had an associated error plus or minus its weight fraction, a range of values occurred for an element's weight fraction. For example, if iron's weight fraction of a dust mass was 2.50E-3 (0.00250) with a ±10 percent error, then the range of iron in the dust mass was from 2.25E-3 to 2.75E-3. For a few elements in quantities near the PIXE analysis' detection limits, an error of more than 100 percent occurred. This presented no problem when adding more than 100 percent of the original weight fraction to itself, but when subtracting it, the weight fraction of the particular element was entered as zero, since a negative quantity of an element does not physically exist.

After a range of values for a particular element was calculated, all weight-fraction ranges of the mining-generated and the laboratory-generated dust from the same mine and particular impactor stage were sorted for a minimum and a maximum weight fraction value. Once these two values were identified, their average value could be calculated and column graphs drawn. The height of the column represented the average value, and the difference between the maximum value and the average value represented the error bar value. See Figures 2 through 5 for examples of some of the elemental values.

In those cases where the weight fraction of the laboratory-generated dust fell short of or exceeded the range of the mining-generated dust, or did not appear at all as in the cases for Na, Sb, and Ba, they were considered unsuccessful predictors. Thus, for the 32 elements, the laboratory-generated dust was considered a successful predictor 73% of the time for stage 3, 65% of the time for stage 5, and 57% of the time for stage 7. This resulted in an overall predictability of 65% (see Table I).

CONCLUSIONS AND RECOMMENDATIONS

1. By observing Figure 2, the carbon or the organic fraction in the coal dust appears to increase with decreasing dust size.

2. Although different researchers have differing opinions on the elements which they believe have an impact in contracting CWP, evidence indicates that elements such as Pb, Ni, and Zn are contained in greater amounts in bituminous-coal-miner's lungs than normal concentrations of these elements.[6,7] As such, the standard procedure developed to produce a laboratory-generated dust appears to predict well the concentrations of Pb, Ni, and Zn (with 100%, 85%, and 81% accuracy, respectively) in the immediate ventilation return of a CMM (see Figures 3, 4, and 5). Thus, potential problem mines or coal seams may be identified during planning stages.

3. Ba, Sb, Cd, and Na were the most difficult elements for the laboratory-generated dust to produce in detectible amounts. They were detected in the mining-generated dust in mines where roof and floor rock were mined with the coal seam. Poor detection of these elements in the laboratory-generated dust may be due to inadequate grinding of the rock component during sample pulverization. It is recommended that a refined procedure of the one used in this research be developed to better predict the mining-generated dust when rock is concurrently mined with the coal seam.

An important contribution of this research was that it developed and described a standard procedure, or a tool, which has shown promise for measuring the variability of the elemental composition of coal mine dust in the immediate ventilation return of a CMM through the use of a laboratory-based process.[2]

To make the successful technology transfer in which a coal mining company is able to predict a proposed mine's airborne dust elemental characteristics in the immediate ventilation return of a CMM by using the standard procedure presented in this paper, it is recommended that core samples of a coal property be used to prepare the laboratory-generated dust which would be compared to the mining-generated dust sampled as close as possible to the core location after mine development. This would allow verification of the assumption that a core sample could successfully be used in place of a channel sample to produce laboratory-generated dust that has elemental characteristics similar to those of dust sampled in the immediate ventilation return of a CMM.

Finally, it is recommended that researchers investigating the significance of elements and chemical variations on cell cultures and live animals use a laboratory-generated dust which is similar in composition to actual mine dust to perform their studies. This would better represent the dust that miners actually breathe.

As medical investigations continue to find the cause(s) of CWP, and if a portion of the cause(s) is found to be certain elements or particular concentrations of those elements in the mine dust, then the successful application of this research will contribute to the reduction in incidence and severity of CWP and reduce the cost of attaining that goal.

Table I

Lab Dust in the Same Concentration Range as Mine Dust

Element	Stage 3	Stage 5	Stage 7	Totals
C	hypothetical	hypothetical	hypothetical	-
O	hypotthetical	hypothetical	hypothetical	-
Na	0/3 = 0%	0/2 = 0%	0/1 = 0%	0/6 = 0%
Mg	6/8 = 75%	5/9 = 56%	1/8 = 13%	12/25 = 48%
Al	5/9 = 56%	5/9 = 56%	5/9 = 56%	15/27 = 56%
Si	6/9 = 67%	4/9 = 44%	3/9 = 33%	13/27 = 48%
P	9/9 = 100%	8/9 = 89%	7/9 = 78%	24/27 = 89%
S	6/9 = 67%	7/9 = 78%	6/9 = 67%	19/27 = 70%
Cl	8/9 = 89%	5/9 = 56%	7/9 = 78%	20/27 = 74%
K	4/9 = 44%	3/9 = 33%	1/9 = 11%	8/27 = 30%
Ca	4/9 = 44%	3/9 = 33%	0/9 = 0%	7/27 = 26%
Ti	6/9 = 67%	5/9 = 56%	6/9 = 67%	17/27 = 63%
V	4/6 = 67%	4/7 = 57%	0/6 = 0%	8/19 = 42%
Cr	2/7 = 29%	5/8 = 63%	1/8 = 13%	8/23 = 35%
Mn	6/9 = 67%	5/9 = 56%	4/9 = 44%	15/27 = 56%
Fe	5/9 = 56%	3/9 = 33%	3/9 = 33%	11/27 = 41%
Ni	7/9 = 78%	7/9 = 78%	9/9 = 100%	23/27 = 85%
Cu	data suspect	data suspect	data suspect	-
Zn	8/9 = 89%	8/9 = 89%	6/9 = 67%	22/27 = 81%
Ga	9/9 = 100%	9/9 = 100%	8/8 = 100%	26/26 = 100%
Ge	7/7 = 100%	6/6 = 100%	5/6 = 83%	18/19 = 95%
As	6/6 = 100%	4/4 = 100%	5/5 = 100%	15/15 = 100%
Se	6/6 = 100%	4/5 = 80%	5/6 = 83%	15/17 = 88%
Br	6/9 = 67%	5/9 = 56%	8/9 = 89%	19/27 = 70%
Rb	8/9 = 89%	5/8 = 63%	6/9 = 67%	19/26 = 73%
Sr	9/9 = 100%	7/9 = 78%	6/9 = 67%	22/27 = 81%
Zr	9/9 = 100%	7/8 = 88%	7/8 = 88%	23/25 = 92%
Mo	7/7 = 100%	7/8 = 88%	3/6 = 50%	17/21 = 81%
Cd	1/6 = 17%	0/2 = 0%	0/1 = 0%	1/9 = 11%
Sb	0/3 = 0%	0/3 = 0%	0/3 = 0%	0/9 = 0%
Ba	0/1 = 0%	0/1 = 0%	0/1 = 0%	0/3 = 0%
Pb	9/9 = 100%	9/9 = 100%	9/9 = 100%	27/27 = 100%
Totals	163/222 = 73%	140/215 = 65%	121/211 = 57%	424/648 = 65%

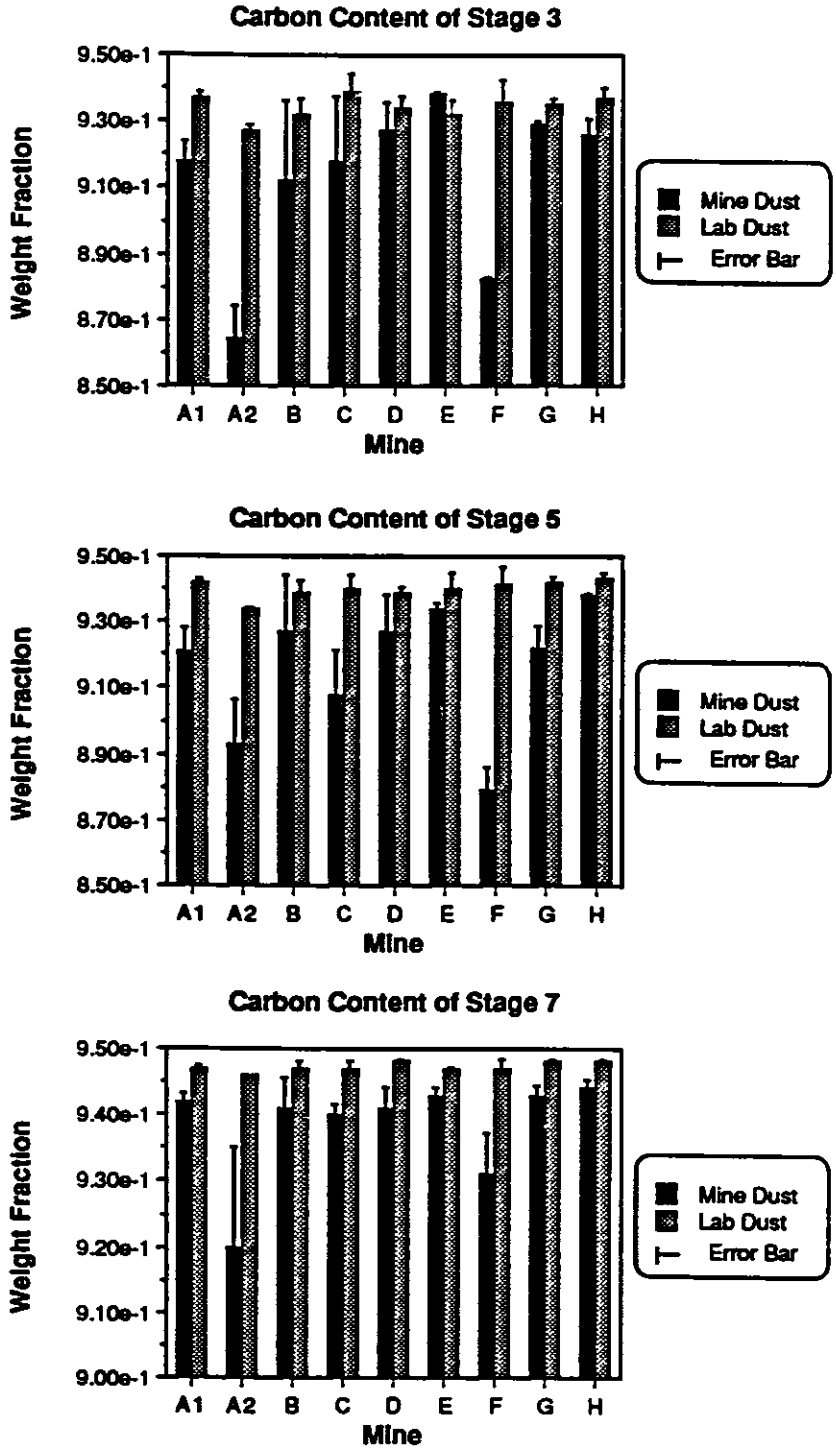

Figure 2. Carbon content by stage and mine.

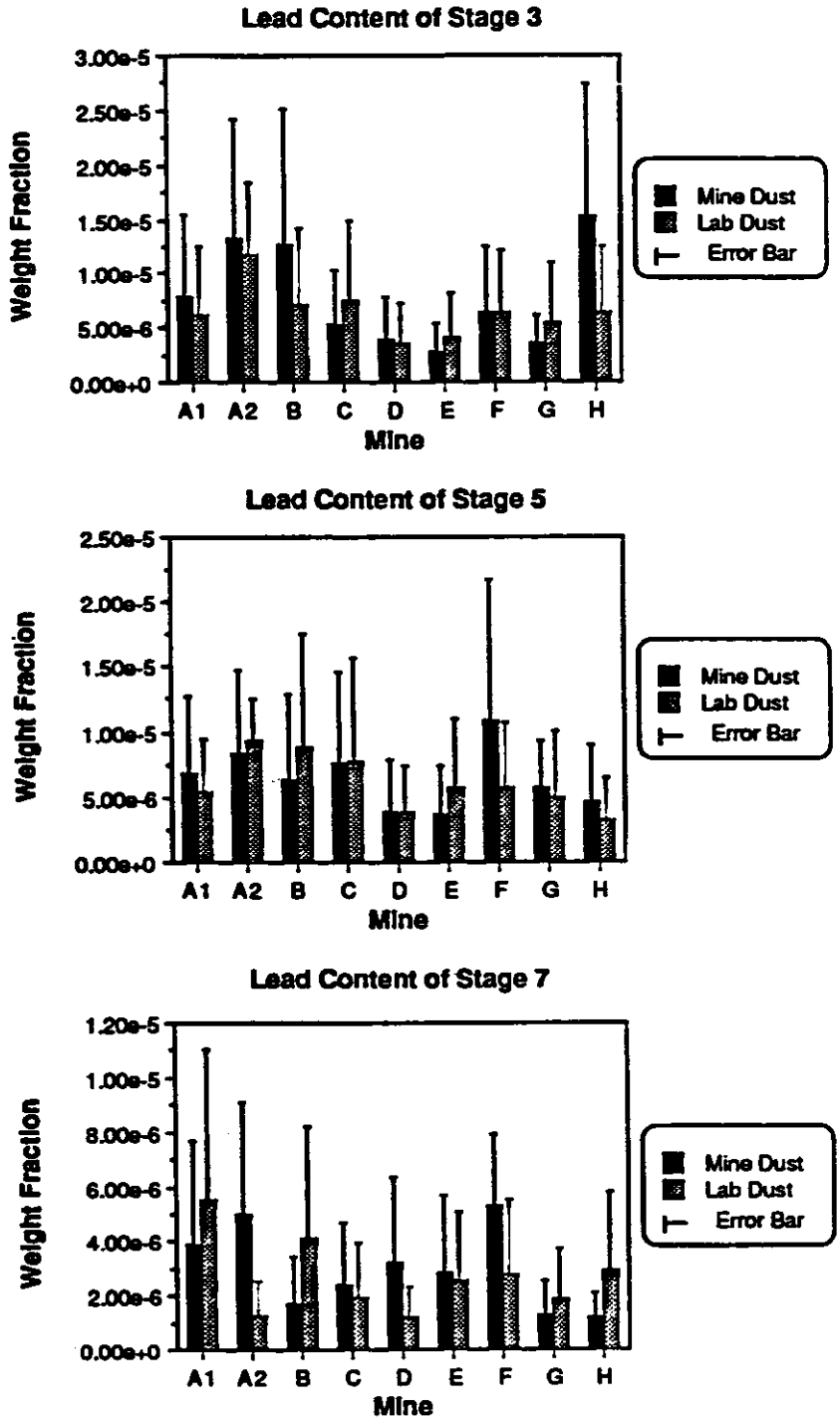

Figure 3. Lead content by stage and mine.

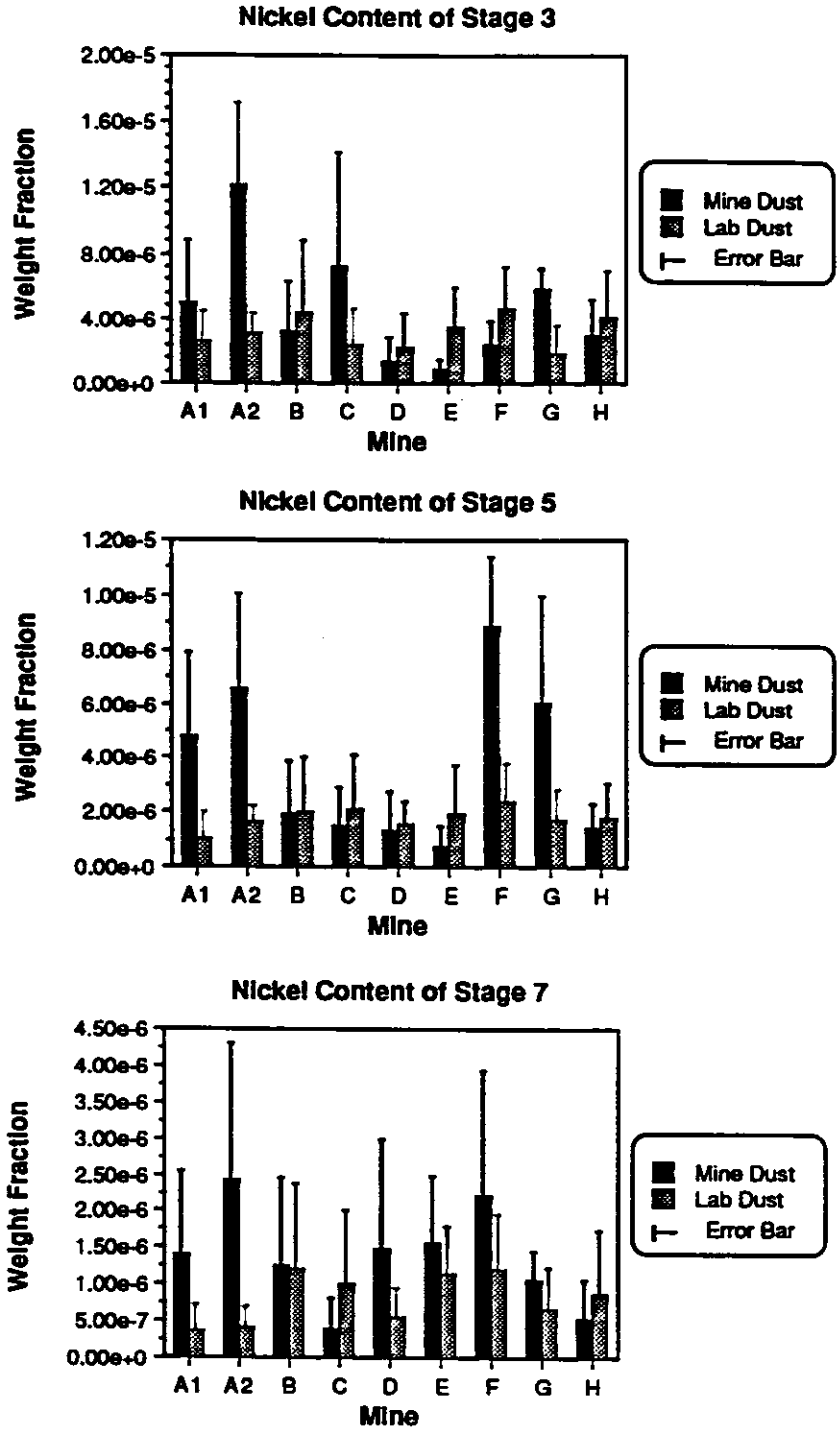

Figure 4. Nickel content by stage and mine.

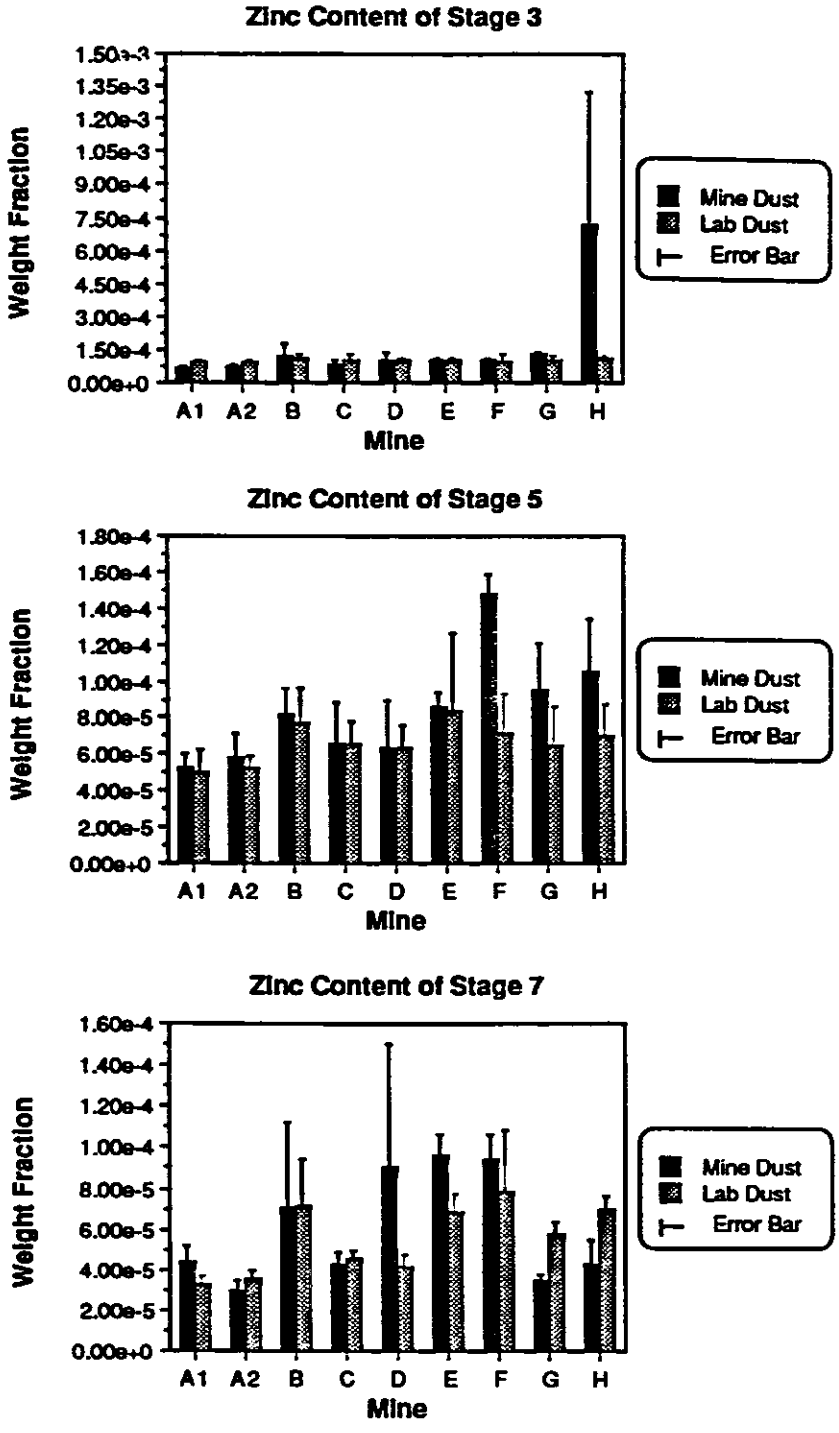

Figure 5. Zinc content by stage and mine.

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DISCLAIMER: Reference to the manufacturer as used in the text are for identification purposes only and do not imply endorsement by the authors. The opinions and conclusions expressed in this paper are those of the authors and do not represent the opinions of The Pennsylvania State University, the Generic Mineral Technology Center for Respirable Dust, or the U.S. Bureau of Mines.

ACOUSTIC IMPEDANCE METHOD FOR DETECTING LUNG DYSFUNCTION

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ABSTRACT

The acoustic impedances of seven rat lungs were measured at frequencies between 100 and 6400 Hz. Rats were divided into two groups: a silica exposed group (N=3) and a control group (N=4). The silica exposed group was injected intratracheally with silica solution. Three of the control group were intratracheally injected with saline. Between four and six weeks after the injections, all lungs were excised and degassed. Lungs were suspended in a pressure chamber, with the trachea canula attached to the end of a tapered impedance tube. The lungs were subjected to transpulmonary pressures between −30 cm H_2O and 6 cm H_2O to simulate deflation and inflation. With transpulmonary pressure being held constant, the impedance tube was excited with random noise. A dual channel analyzer calculated $H_{12}(f)$, the transfer function between the two microphones. This function was used to calculate the lung's impedance at that pressure. The impedance magnitude spectra of both groups typically had peaks at 2000, 3500, and 5500 Hz. Statistically significant differences (90% confidence level or greater) between the two groups occur at the 3500 Hz peak at transpulmonary pressures of 20, 8, 6, 4, and 2 cm of H_2O. This fact seems to confirm that this method can detect lung disease. Further research will indicate whether this method will be able to detect the onset of coal worker's pneumoconiosis.

INTRODUCTION

One of the first studies of impedance of the human lung were conducted by DuBois et al.[2] using the forced oscillation technique. This technique, however, was limited to frequencies below 30 Hz. Further studies by Van Den Berg[6] revealed that the lung reflected higher frequency sounds (100–10,000 Hz), instead of behaving as an anechoic termination. This discovery has lead to several studies of the acoustical properties of both human and animal lungs at high frequencies.[3,4,5]

Ishizaka et al.[4] measured the input impedances of laryngectomized human subjects using a two microphone technique. This study reported peaks in the impedance magnitude at 640, 1400, and 2100 Hz. Fredberg et al.[3] used a transient forced oscillation technique to measure the input impedance of excised canine lungs for frequencies up to 10,000 Hz. Jayaraman and Frazer[5] used a two microphone technique in combination with transmission matrix theory to study changes in the acoustic impedance of excised rat lungs during deflation and inflation.

This study's focus is to determine the differences in the acoustic impedance of excised silicotic and healthy rat lungs. Seven Long Evans Hooded rats, weighing between 200 and 250 g, were divided into two groups. The silica-exposed group (N=3) were intratracheally injected with a silica-saline solution to induce silicosis. Three rats of the control group (N=4) were given a sham exposure of saline. During a period four to six weeks after injection, all lungs were excised and degassed.

METHODS

Figure 1 displays a block diagram of the impedance tube facility used in this study. An excised lung is attached to the end of a tapered tube within a plexiglass pressure chamber. Random noise, produced by a Bruel and Kjaer 2032 dual channel analyzer, is amplified and introduced into the tube via a side-mounted speaker driver (University, type ID-30C-8). The standing waves thus formed in the impedance tube are measured by two Bruel and Kjaer 4136 pressure microphones mounted 2.3 cm apart in a plexiglass cylinder. The signals of these microphones are the inputs to the dual channel analyzer, which calculates the transfer function between the two microphones, H_{12}, and its inverse Fourier transform , h(t). Following Jayaraman and Frazer's example,[5] exponential weighting is applied to h(t) and transmission matrix theory applied to the resulting transfer function to yield the input impedance of the excised lung.

The plexiglass chamber's pressure is controlled by a variable speed pump to produce transpulmonary pressures between 30 and −6 cm of H_2O. The difference between chamber pressure and atmospheric pressure is monitored by a water manometer. A lung is first inflated to 30 cm of H_2O, then deflated to −6 cm of H_2O, pausing at several pressures for impedance measurements. Once fully deflated, the lung is inflated to 30 cm of H_2O, again stopping at various pressures for measurements.

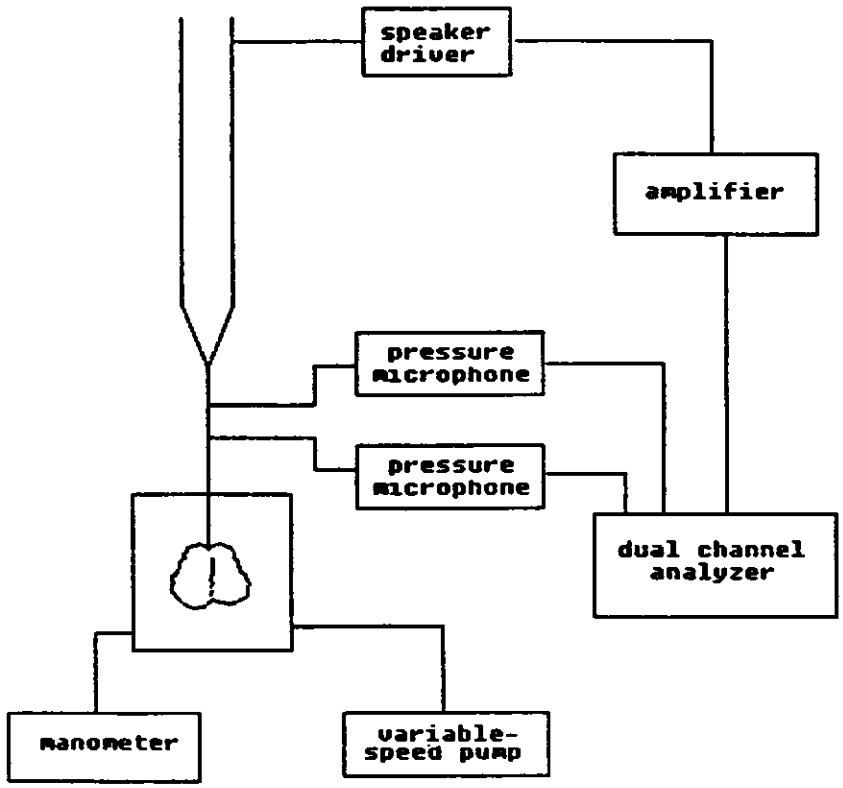

Figure 1. Block diagram of impedance measurement facility.

RESULTS

The average magnitude spectra of the silica and control groups are presented in Figures 2, 3, and 4 for transpulmonary pressures of 30, 8, and 2 cm of H_2O, respectively.

DISCUSSION

The impedance magnitude spectra of all rats have been computed for transpulmonary pressures of 30, 20, 10, 8, 6, 4, 2, 0, and −2 cm of H_2O. Typical rats in both groups had

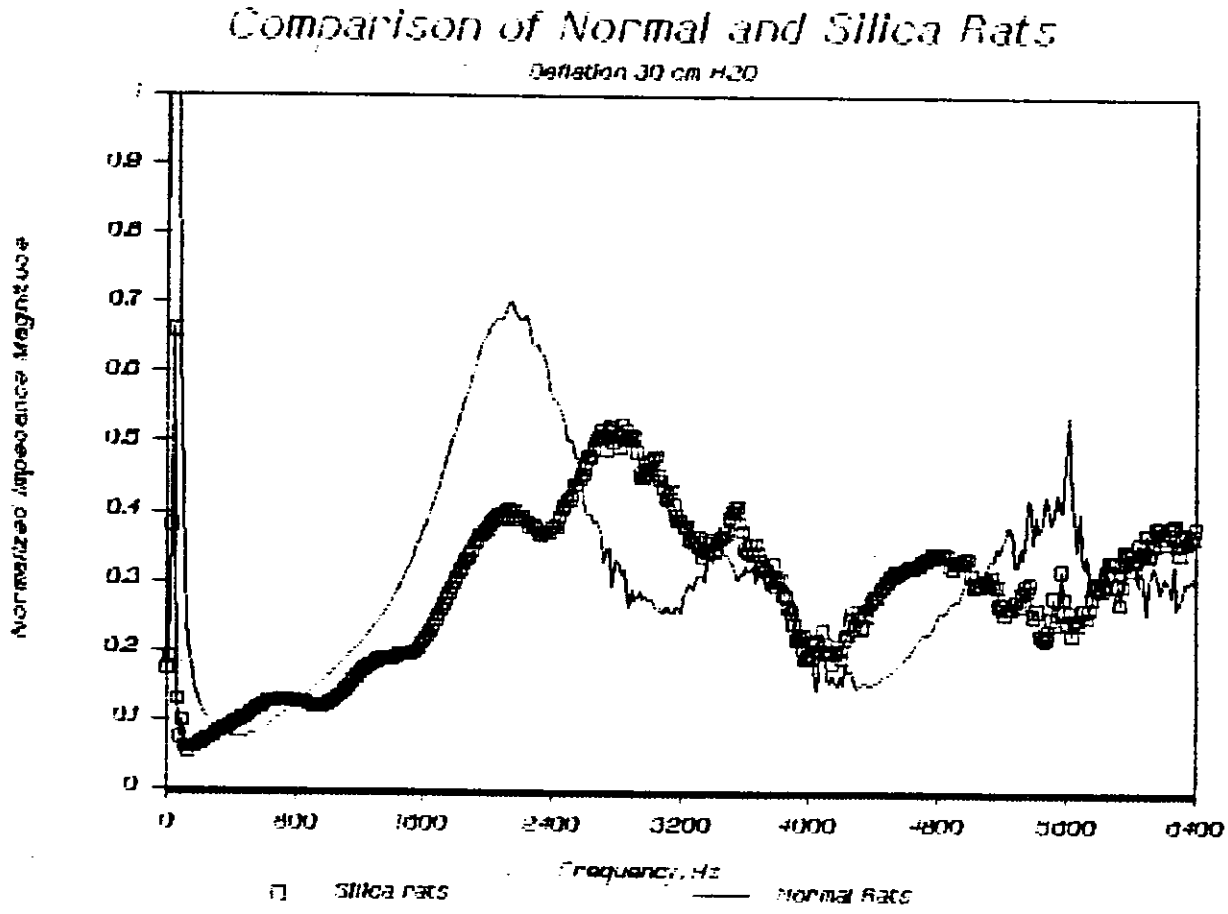

Figure 2. Comparison of average impedance spectra of silica and control groups. Deflation 30 cm H_2O.

peaks at 2000, 3500, and 5500 Hz. The placement of these peaks compare favorably with the study of Jayaraman and Frazer,[5] with the exception that in this study, no peak occurred at 600 Hz.

Significant differences between the silica and control groups occurred at the peak at 3500 Hz. T-tests performed on the peak magnitudes at this frequency showed that the silica group had significantly higher impedance (90% confidence

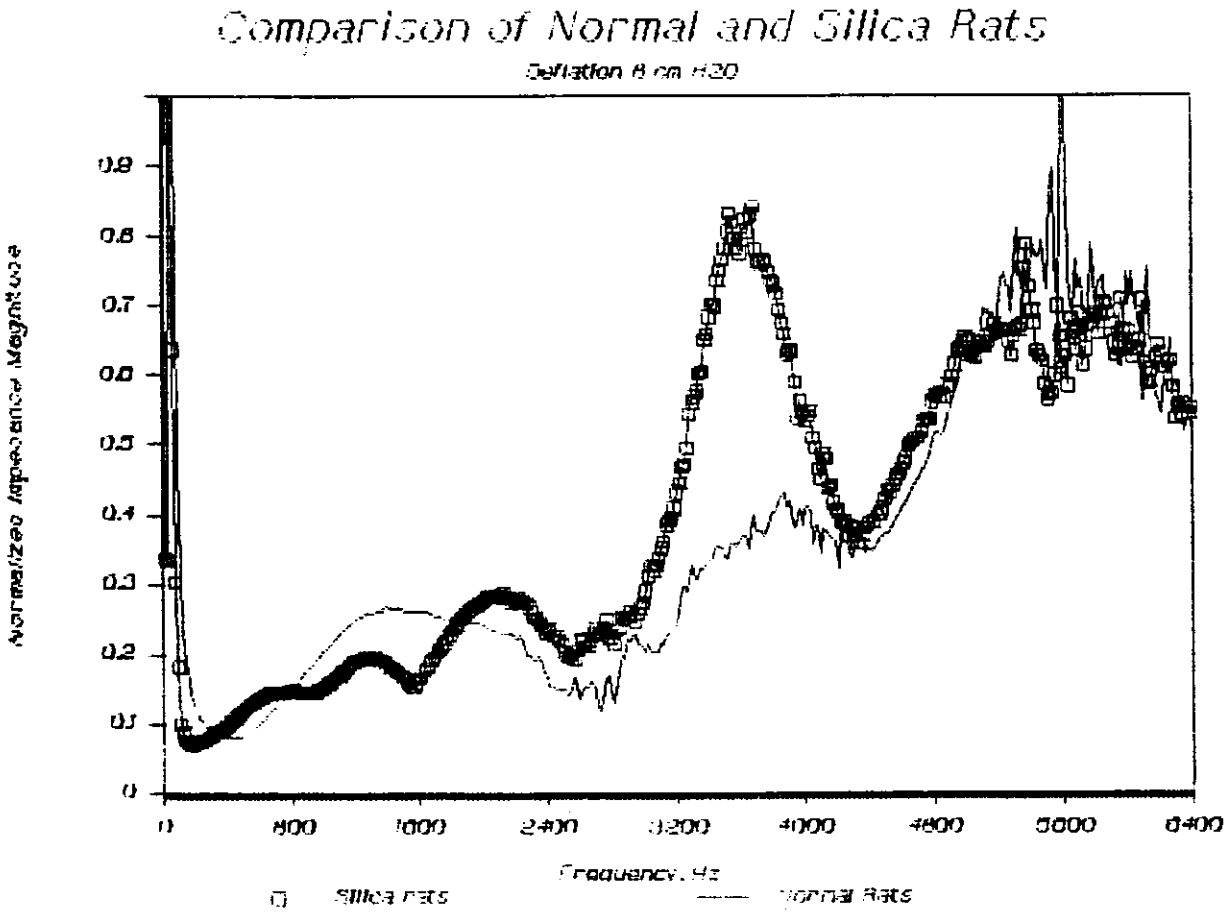

Figure 3. Comparison of average impedance spectra of silica and control groups. Deflation 8 cm H_2O.

level) at transpulmonary pressures of 20 and 8 cm of H_2O during deflation. The silica group also had significantly higher impedance (98% confidence level) at 3500 Hz at pressures of 6 and 4 cm of H_2O during deflation. These findings show that changes in the mechanical properties of lung tissue and the closure of airways occurred at higher pressures in the silica group than with the control group. This finding agrees with the work of Chvalova et al.[1] which found that the pressure-volume curve of silicotic rats was shifted to higher pressures compared to normal rat lungs.

CONCLUSIONS

The above findings indicate that silicosis in rat lungs can be detected by measuring the lung input impedance. The key indicator thus far is the impedance magnitude of the peak at about 3500 Hz. Further studies will determine the effectiveness of the method in detecting the development of lung diseases and if the measurement of acoustic impedance can be an effective clinical tool for the treatment of lung diseases.

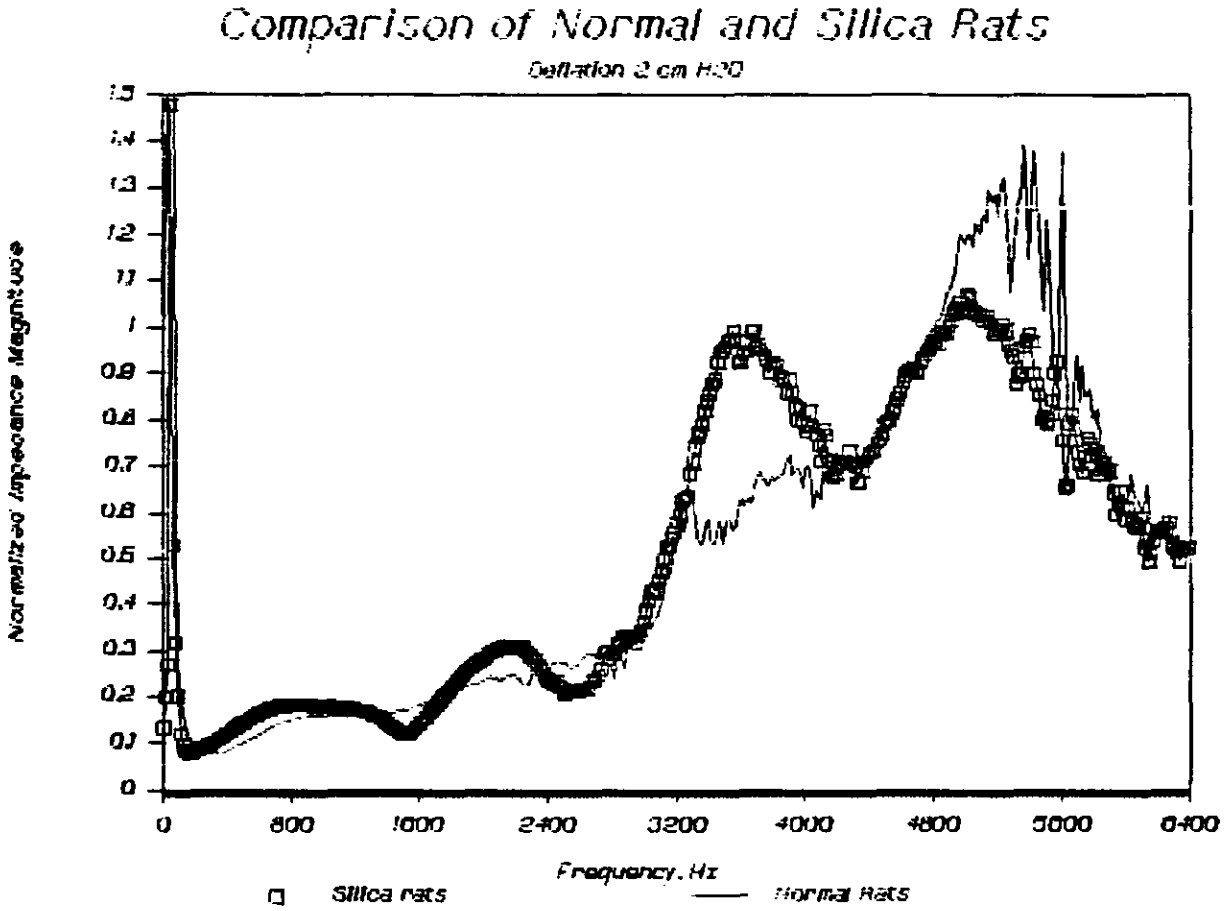

Figure 4. Comparison of average impedance spectra of silica and control groups. Deflation 2 cm H_2O.

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ACKNOWLEDGMENTS: The authors wish to thank the Division of Respiratory Disease Studies, NIOSH, Morgantown, WV for the use of their facilities during this study. This research has been supported by the Department of the Interior's Mineral Institute Program administered by the Bureau of Mines through the Generic Mineral Technology Center for Respirable Dust under grant number G1135142.

CONNECTIVE TISSUE COMPONENTS AS STRUCTURAL BASIS IN LUNG RESEARCH

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ABSTRACT

The connective tissue of the lung is a complex structure influencing its functional properties in health and disease. Under normal circumstances, the connective tissue helps to evenly distribute mechanical forces over the entire surface of the lung, contributes to the overall elastic properties of the parenchyma and mediates intercellular communications as well as cell-matrix-interactions. Components of the connective tissue are collagen molecules, proteoglycans, glycoproteins and elastin. In lung fibrosis an accelerated accumulation of interstitial matrix molecules, predominantly collagen, has been reported. To achieve a morphological analysis of the composition of the lung connective tissue, collagen types I, III, IV and V, the glycoproteins fibronectin and laminin, and proteodermatan-sulfate were isolated. Polyclonal antibodies directed against these antigens were used in indirect immunofluorescence studies of the lung tissue. The results revealed that under normal conditions the matrix molecules participated in the development of specific structural properties of the lung. However, irritation of the lung resulted in a disorder of connective tissue components. The present results indicate that the morphological analysis of matrix molecules may be able to explain functional properties of the lung.

INTRODUCTION

A fundamental prerequisite for understanding convulsive procedures at the alveolar wall is the knowledge about its structural composition in correlation to its functions. The functional structures of the alveolar-capillary region of the lung are the epithelial cells of the alveolar space, the surfactant, the alveolar macrophages, the components of the interstitial connective tissue and the endothelial cells of the capillaries.

The distortion of the genetically defined functional structure by exogeneous or endogeneous noxes obviously induces a metabolic disorder of lung collagens and other components of the extracellular matrix. The changes to matrix components may result in an enhanced accumulation of collagen and fibrous material like elastin leading to lung fibrosis.[1] Since collagen (60–70%), elastin (25–30%), proteoglycans (1%) and fibronectin (0.5%) are major components of the interstitial structure, their inappropriate distribution is of important interest. Moreover, the development of basement membranes, which can be studied by the distribution of laminin, might be a key feature of fibrotic lung disorders.[1] The distribution of different collagen types has been made with immuno-histochemical markers.[2,3] However, these studies showed different results concerning the ratio of collagen type I and type III. In our study we focused on the distribution of these collagen types and of fibronectin and laminin.

MATERIAL AND METHODS

Tissue samples of human lungs were obtained after autopsy and stored immediately at −70°C.

IMMUNOLOGICAL REAGENTS

Antibodies directed against collagen types, fibronectin or laminin were of the same origin as previously described.[4] Antibodies against the core protein of proteodermatan sulfate were kindly provided by Dr. H. Kresse, Physiologisch-Chemisches Institut of the University of Münster/FRG. The specificity of these antibodies was shown in an earlier publication.[5]

IMMUNOFLUORESCENCE

Tissue section 6–8 µm were cut with a SLEE (Mainz,FRG) cryomicrotome, mounted on glass slides, and fixed by air-drying for up to 12 hrs. The fixed tissue sections underwent two different staining procedures: for collagen types, fibronectin and laminin they were stained directly with the first antibody, for proteoglycan they were pre-incubated with chondroitin ABC lyase (Sigma). For pre-incubation, sections were treated with 5 mU chondroitin ABC lyase for 5 minutes at room temperature. The enzyme was inactivated by washing with distilled water for 1 minute. Pre-incubated and untreated tissue sections were allowed to react with antibodies either

directed against the core protein of proteodermatan sulfate or against collagen type I, type III, fibronectin or laminin for 30 minutes of room temperature. Excess antibody was removed by washing five times with phosphate buffered saline, pH 7.5. Bound antibodies were labelled for visualization in a fluorescence microscope (Orthoplan, Leitz, FRG) with anti-rabbit IgG conjugated with fluorescin-isothiocyanate or anti-goat IgG in case of collagen types, also isolated with FITC (Behringwerke, Marburg, FRG). After washing again five times with phosphate buffered saline, the stained tissue sections were preserved by embedding in Entelan (MERCK, Darmstadt, FRG). For all tissues, controls were performed by treatment with whole pre-immune serum or chromatographically purified IgG.

RESULTS

The structural components of the normal alveolar septa are deposited in a thin filamentous backbone. Collagen types I and III were found to be co-distributed. Light microscopically elastin was observed in similar structures as revealed by collagen staining. Collagen type I and type III obviously were associated with elastin fibres. The glycoprotein fibronectin was additionally visible in laminar structures representing either the epithelial or the subendothelial basement membranes. Proteodermatan sulfate was present not only in the interstitial spaces but was also observed close to basement membranes and all surfaces. In lung fibrosis the alveolar septa become enlarged due to higher amounts of connective tissue components. Collagen type I and type III now enveloped the larger elastic fibres. These fibres were additionally covered with fibronectin. The denser connective tissue matrix reduced the capillaries in the alveolar walls visuable by the reduction of basement membrane material laminus. In this stage of fibrosis, sometimes fibronectin was accumulated in alveolar spaces, opsoniering carbon or other dust particles. In further development of lung fibrosis especially in pneumoconiosis granuloma formation is visible. Although the connective tissue exhibited a dense structure, collagen type I and type III were decreased in pericentral areas while elastin seemed to be increased. Also fibronectin or laminin were either diminished or not further recognizable in central parts of granulomas.

DISCUSSION

The present results show the participation of different connective tissue components, especially collagen type I, type III, elastin, fibronectin and laminin in the formation of fibrous material in alveolar walls. Collagen types IV and V were not separately shown. Both collagen types are either in basement membranes (type IV) or co-distributed with collagen type I and type III or with fibronectin. In further development of fibrosis collagen type I and type III depositions were increased. However, in granuloma formation their central parts contermined predominantly elastin. These results indicate that analysis of collagen content of a tissue sample depends partially on the stage of disease.[6] The distribution of the glycoprotein laminin was mainly visible in either epithelial or subendothelial basement membranes. The specific fluorescence for laminin was diminished in later stages of fibrosis indicating a reduced microcirculation. Thus, the functional properties of the lung are totally disturbed. The increase and decrease of connective tissue components reflect their regulation by different cells. In recent years the *in vitro* investigations elaborated different cytokines which in cooperation with proteases may influence the formation of fibrous material.[7,8] New therapeutic approaches should include these cellular factors.

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STUDY OF FIBROGENIC EFFECTS OF POLYPROPYLENE AND POLYTHENE ON RAT LUNGS

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ABSTRACT

Polypropylene and polythene are macromolecular compounds and typical synthetic organisms. In order to research their fibrogenic effects, 128 rats (half males and half females) were selected and 50 mg of the polypropylene or polythene dusts was injected intrachacheally into each rat. The observation was made for 18 months.

The results showed that in the early stage the prominent histopathological changes in the lungs were foci of dust-granuloma (polythene group showed polynucleo-macrophage granuloma) and hyperplasia of reticular fibers. At the 18th month after injecting the dust, in experiment groups pronounced hyperplasia of reticular fibers as well as collagen fibers were seen in these foci and around bronchi. Collagen content of the lungs in experiment groups was higher than that in control groups (treated with normal saline). The author indicated that the slight fibrogenic effect on the rat lung was caused by both polypropylene and polythene dust.

See Table of Contents, Part II, for Paper.

CHEMOTACTIC RESPONSES OF LEUKOCYTES FROM THE BRONCHOALVEOLAR SPACE OF RATS EXPOSED TO AIRBORNE QUARTZ, COALMINE DUSTS OR TITANIUM DIOXIDE

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INTRODUCTION

Studies on humans and in laboratory animals have revealed that bronchoalveolar deposition of dusts commonly associated with pneumoconiosis, results in recruitment of leukocytes to the lung parenchyma.[1,2] In view of the important role of the leukocytes in mediating both injury and mesenchymal cell proliferation, the resulting alveolitis is considered to be an important factor in determining the progress of disease.[3,4] During inflammation leukocytes are known to marginate and then migrate from the capillaries to the interstitium and alveolar space under the influence of chemotactic factors generated in this region. As part of a study on leukocyte recruitment into the lungs of rats exposed, by inhalation, to pneumoconiosis-producing dusts,[5] we examined the chemotactic activity of bronchoalveolar leukocytes lavaged from these animals. We report here on the chemotactic activity of bronchoalveolar leukocytes from the lungs of rats exposed to 10 mg/m^3 or 50 mg/m^3 airborne mass concentration of; (a) the pathogenic particulate quartz, which causes silicosis; (b) dusts collected from the air of coalmines mining anthracite, high rank coking coal and low rank bituminous coal; (c) as a negative control, titanium dioxide, a fine particulate of respirable size which is not associated with pneumoconiosis.

MATERIALS AND METHODS

Rats

Syngeneic, PVG rats, SPF maintained and fifteen weeks of age at commencement of exposure, were used.

Minerals

The dusts used in the study were (a) titanium dioxide (Rutile), obtained from Tioxide Limited, Stockton-on-Tees; (b) the quartz standard DQ_{12}; (c) coalmine dusts collected from the air of British collieries mining anthracite, high rank (coking) coal and low rank (bituminous) coal. Airborne coalmine dust samples were collected on dry Bondina socks mounted in the return roadway of a single face at each of the three collieries; full details of this procedure are given elsewhere.[5] Details of the mineralogical composition of the samples used are shown in Table I.

Inhalation Exposure

Groups of 48 rats were exposed to airborne dust for 5 days per week, seven hours per day in exposure chambers described by Beckett.[6] The dusts were dispensed using either Wright or the dust dispensers. The concentration of dust in the chambers was monitored as the mass concentration of respirable dust defined by the BMRC Johannesburg sampling criterion[7] using a Casella MRE 113A dust sampler. Full details of the exposure system are described in full elsewhere.[5]

Bronchoalveolar Lavage

At 8, 32 and 75 days into exposure, groups of four rats, and two control rats maintained in room air, were removed from the chamber and subjected to bronchoalveolar lavage. The method is described in detail elsewhere[5] but involved removal of the lungs, exsanguination, followed by lavage of the bronchoalveolar space with 4 × 8 ml volumes of saline at 37°C. The bronchoalveolar leukocytes, so obtained, were concentrated by centrifugation, counted and the proportions of the different leukocyte types assessed by differential counting of May-Grunwald Giemsa stained cytospin preparations.

Assay of Bronchoalveolar Leukocyte Chemotaxis

Chemotaxis was assessed using Blindwell chambers. Three hundred microlitres of 10% zymosan-activated serum (ZAS) (high in the chemotactic complement component C5a), were placed in the lower compartment and a filter (Nuclepore, Pleasanton, California) placed on top. The top compartment was screwed down and 6 × 10^5 alveolar macrophages in 400 µl of RPMI medium (Gibco, Paisley) were placed in the upper compartment. The filters used were 5 µm pore size and incubation was for 3.5 hours at 37°C in 5% CO_2 to allow migration of cells through the filter towards the chemotactic material in the lower compartment. At the end of the incubation period the filter was removed from the chamber, washed, stained and allowed to dry before being mounted on a slide in plastic mountant. Two chambers were set up for each condition and the number of migrated cells in 5 high power fields (x1000) were assessed for each filter.

Table I
Mineralogical Composition of Dusts Used in the Study

DUST	CLASSIFICATION	% ASH	% IN DUST KAOLIN	MICA	QUARTZ
Coalmine dust A	Anthracite	10.6	0.8	4.3	1.4
Coalmine dust H	High rank	13.2	0.6	0.5	1.0
Coalmine dust L	Low rank	53.2	18.1	0.0	6.7
Quartz	DQ_{12} Standard	NOT APPLICABLE - PURE QUARTZ			
Titanium dioxide (TiO_2)	Rutile	NOT APPLICABLE - PURE TiO_2			

Statistical Analysis of Results

Results were obtained from four experimental and two control rats at each time point. Data were analysed by analysis of variance using the Genstat computer package and comparisons made using a 't' test.[5]

RESULTS

Chemotaxis versus Chemokinesis in Leukocyte Migration

To ensure that chemotaxis was the dominant activity being measured in each sample, and not chemokinesis, we used a modified "checkerboard" method:—(mean ± standard deviation migrated cells/high power field); spontaneous migration 0.0 ± 0.0; chemokinesis (measured as migration with 5% ZAS in both the upper and lower compartments) 14.8 ± 6.6; chemotaxis (measured with 5% ZAS in the lower compartment) 46.4 ± 4.8. These results confirm that the majority of the migration was in fact chemotaxis and migration in the Blindwell Chambers will henceforth be referred to as chemotaxis.

Effect of Dust inhalation on Chemotaxis of Bronchoalveolar Leukocytes

Figure 1 shows typical data obtained for chemotaxis experiments with leukocytes from rats exposed, by inhalation, to 10 mg/m^3 of the five dusts. This data clearly shows that inhalation exposure to TiO_2 had very little effect whereas exposure to quartz and the coalmine dust was associated with a marked reduction in the ability of the bronchoalveolar leukocytes to chemotact.

Figure 2 shows the data, from all experiments at 10 mg/m^3 airborne mass concentration, expressed as percentage inhibition of chemotaxis compared to the controls on that day, to more clearly highlight the effect of dust exposure. It is clear that, although inhibition of 30% was present with TiO_2 at 8 days, thereafter the inhibitory effect of TiO_2 did not exceed 17%. In the case of quartz, however, this was as great as 89.4% by day 75. All three coalmine dusts tended to show a gradual rise in the impairment of chemotaxis shown by the bronchoalveolar leukocytes as time of exposure progressed, reaching 50–70% inhibition by day 75.

Figure 3 documents the effects of increasing airborne mass concentration of coalmine dust, on the inhibition of chemotatic activity. The increase from 10–50 mg/m^3 airborne mass concentration was associated with a marked increase in the impairment of chemotaxis, observable in the coalmine dust-exposed bronchoalveolar leukocytes, reaching 70–90% at 50 mg/m^3.

Attempts to Elucidate the Mechanism of Dust-Related Impairment of Leukocyte Chemotaxis

Limited experiments were carried out to try and elucidate the mechanism whereby dust deposition in the lungs of rats, as described above, caused loss of ability to chemotact. (a) Effect of ingested dust on macrophage chemotaxis. Control rat alveolar macrophages were allowed to adhere to filters and then incubated with quartz or TiO_2 for 1 hour to allow phagocytosis. A chemotaxis gradient was then set up by placing the filters in a chamber with ZAS in the bottom compartment. We then allowed chemotaxis to proceed:—all data given as migrated cells/high power field mean ± standard deviation; untreated macrophages, with no phagocytic burden 54.4 ± 11.3, TiO_2-exposed 51.8 ± 6.2, quartz-exposed 59.8 ± 6.0. Clearly merely having a phagocytic burden inside the macrophages was not sufficiently detrimental to cause impairment of chemotaxis. (b) Effect of incubation for 4 hours on chemotaxis. Allowing dust-exposed macrophages with impaired chemotaxis (obtained after 75 days of exposure to coalmine dust L) to incubate for 4 hours in medium to allow recycling of chemotaxin receptors had no effect on the impaired ability of the cells to chemotact:—control alveolar macrophages, freshly derived 55.0 (7.0)—incubated for 4 hours 48.2 (11.0); dust-exposed bronchoalveolar leukocytes, freshly derived 12.6 (3.6)—incubated for 4 hours 9.1 (2.4). (c) Relationship between % neutrophils in the lavage and % inhibition of chemotaxis. Since neutrophils were present to substantial proportion in some samples of bronchoalveolar leukocytes we assessed whether the presence of neutrophils was related to impairment of chemotaxis. There was no clear relationship between the proportion of neutrophils present in any bronchoalveolar leukocyte sample and impairment of chemotaxis—10–60% inhibition was caused with <10% neutrophils while increasing the percentage of neutrophils

to between 10 and 50%, only caused a maximum further 20% inhibition.

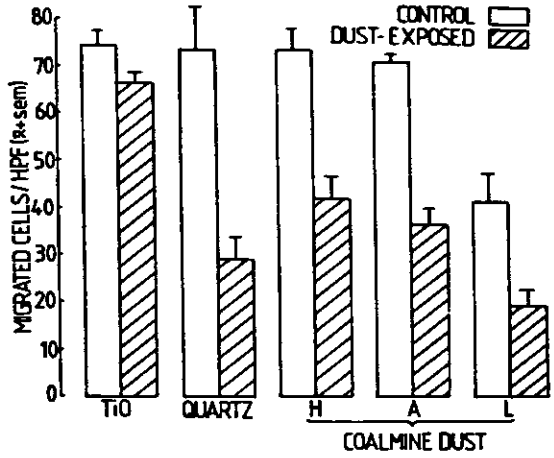

Figure 1. Chemotactic response of bronchoalveolar from rats exposed to the indicated dusts at 10 mg/m^3. Data derived as mean + sd of pooled results obtained for days 8, 32 and 75 (6–12 rats per group). Significant differences dust-exposed v control for all except TiO_2.

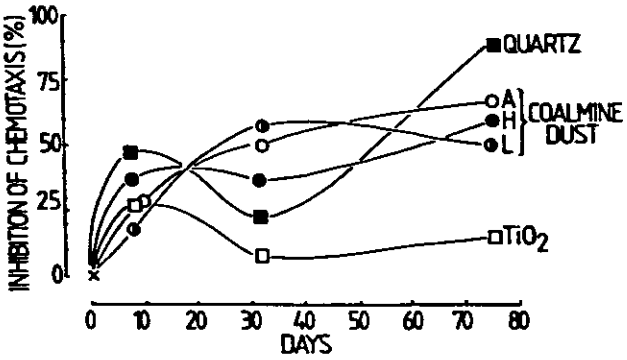

Figure 2. Mean percentage inhibition of chemotaxis shown by bronchoalveolar leukocytes from dust-exposed compared to control rats exposed to 10 mg/m^3 of the indicated dusts. Mean percentage inhibition obtained as:

$$100 - \frac{\text{mean migration of dusted bronchoalveolar leukocytes}}{\text{mean migration of control bronchoalveolar leukocytes}} \times 100$$

Raw data obtained from 2 control and 4 dust-exposed rats.

DISCUSSION

TiO_2 is a fine particulate used extensively in industry and is not associated with pneumoconiosis in exposed populations.[8] It causes minimal response in rats when given by inhalation or intraperitoneal injection.[2,9] Coalmine dust and quartz both cause pneumoconiosis and 3 coalmine dusts of

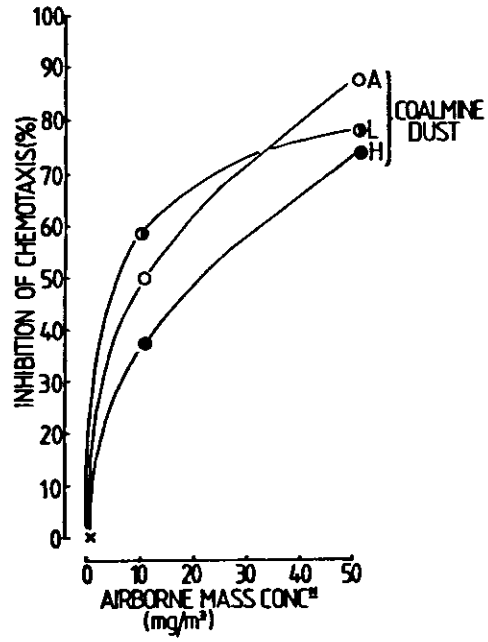

Figure 3. Airborne mass concentration dependence of the chemotaxis inhibition present in bronchoalveolar leukocytes from rats exposed for 32 days to the indicated dusts; no 50 mg/m^3 data available for quartz or TiO_2. Data derived as described in the legend to Figure 2.

different mineralogical composition, including quartz content, were included in order to test whether such differences would contribute to differences in leukocyte recruitment. These studies are reported in detail elsewhere[5] but revealed alveolitis in rats exposed to quartz and all 3 coalmine dusts and failure of TiO_2 to elicit any substantial leukocyte response except at high dose following a long period of exposure.

The studies on the chemotactic activity of bronchoalveolar leukocytes reported here show impairment of chemotaxis in line with the ability of the dust to cause inflammation, i.e., (a) titanium dioxide which caused minimal inflammation caused least impairment of leukocyte chemotaxis; (b) quartz, caused large scale inflammation and the bronchoalveolar leukocytes of the alveolitis had impaired chemotactic activity; (c) coalmine dusts were intermediate in response between TiO_2 and quartz in ability to cause inflammation and impair chemotactic responses. There were no well defined differences between the three coalmine dusts with different mineralogical composition, in terms of their ability to impair chemotaxis.

The results described here do show that chronic deposition of titanium dioxide, a dust not associated with pneumoconiosis did cause a measure of loss of impairment of chemotactic activity. In the cases where quartz and coalmine dusts caused impairment of chemotaxis there was

clear dose dependency in terms of the airborne mass concentration to which the rats were exposed. The data described here was obtained as counts of all migrated leukocytes which included both macrophages and neutrophils in inflammatory populations. However the decreased number of migrated leukocytes present in dust-exposed populations could not be explained on the basis of the neutrophils present, either as different migration characteristics compared to macrophages or effects of neutrophils on macrophage ability to migrate. This was evident since (a) profound inhibition was present even with low percentages of neutrophils;[5] (b) in a limited number of cases differential count of the migrated cells were carried out (data not included) revealing, in some cases, similar proportions of macrophages and neutrophils in the migrated cells to those in the cells as lavaged; in some cases the proportion of neutrophils was decreased but this was never sufficient to explain the overall reduction in migration shown by the inflammatory population and impairment of macrophage chemotaxis must have been present. From this it is clear that macrophages from dust-exposed lung have impaired chemotactic activity and that neutrophils from dust-exposed lung have less chemotactic activity than control alveolar macrophages, at least under the conditions of the assay. The net effect of this is that the ability of the leukocytes to clear dust from dust-inflammed alveoli is likely to be severely impaired.

We have shown that the biological mechanisms underlying the loss of ability to chemotact do not include mere difficulty encountered by dust-loaded cells in trying to pass through the pores of the filter towards the source of chemotaxin. Since the leukocytes lavaged from the bronchoalveolar space have exudated in response to a chemotactic stimulus, it seemed possible that chemotaxin receptors might already be occupied. However, experiments allowing chemotaxin receptors to regenerate, by incubation for 4 hours, produced no effect and impairment was maintained. Other studies from our Institute have suggested that neutrophils could cause some inhibition of the chemotactic activity of macrophages.[10] However plotting % inhibition against % neutrophils in the lavage failed to show any clear relationship between numbers of neutrophils and loss of chemotaxis.[5]

We believe that leukocytes from dust-exposed lung have impaired expression of chemotaxin receptors or inhibition of the cytoskeletal proteins involved in cell movement, or their energy supply. Myrvik[11] reported inhibition of migration of rabbit alveolar macrophages which had phagocytosed asbestos *in vitro*; whilst the impairment of chemotaxis could not be attributed to toxicity in this study, unfortunately inert control dusts were not included. Following exposure *in vivo* and bronchoalveolar lavage, Warheit et al.[12] reported impairment of chemotaxis with asbestos whilst Dauber et al.,[13] and Martin et al.,[14] both described impairment of leukocyte chemotaxis following inhalation exposure to silica. The present response is the first, to our knowledge, showing that coalmine dusts also cause profound impairment of bronchoalveolar macrophage chemotaxis. It was noteable that inhibition of chemotaxis was present following chronic inhalation exposure at an airborne mass concentration of 10 mg/m^3 approximating to the maximum allowable level in British collieries (7 mg/m^3).

The fact that impairment of migration in bronchoalveolar leukocytes was much less with the inert dust TiO_2 than with the two pneumoconiosis-producing dusts suggests that this phenomenon may be important in contributing to lung damage and pathological change in pneumoconiosis. This could be brought about by the pneumoconiosis-producing dusts being allowed to persist in the bronchoalveolar region within alveolar macrophages chronically stimulated by the ingested pathogenic dust. Such stimulated macrophages, refractory to the normal chemotactic gradients which govern their movements, could persist in the alveolar region, releasing injurious agents such as proteases and oxidants and growth factors such as interleukin 1 and tumour necrosis factor, leading to fibrosis.

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PATHOPHYSIOLOGICAL EVIDENCE IN MODIFICATION OF COAL-INDUCED LESIONS BY JAGGERY IN RATS

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INTRODUCTION

Inspite of rapid technological advancements made during the twentieth century, occupational lung diseases due to inhalation of airborne particulate or fibrous matters continue to constitute exceptionally high incidence among industrial workers. Pulmonary dust diseases, in general, are not curable in true sense because the usual therapy of destroying or removing the morbific agent from lung has not proved efficaceous as is possible with bacterial or viral infections of the lungs. Apart from protective devices, as designed by engineers and put into actual use, various experimental approaches for the treatment of pulmonary dust diseases were also extensively made in the past with partial success using different types of aerosol therapy, hormonal therapy, vitamin therapy and other substances including dietetic factors.[17] The discovery of antisilicotic drug-PVNO and its efficacy both under *in vitro* and *in vivo* situations demonstrated its usefulness not only against experimental silicosis but also against the pathogenic effects of a mixture of coal and quartz dust in the lungs of rats.[11] In 1975, Chinese investigators demonstrated the therapeutic and preventive effect of Tetrandrine—an alkaloid of bisbenzyl isoquinoline (*Stephania tetrandra* S.) on experimental silicosis in rats and monkeys as well as marked improvement in symptoms and chest X-ray of human silicotics seen with tetrandrine treatment.[3] Beletsky and Coworkers[1] have reported some success with alkali inhalation (aerosol of potassium carbonate) by industrial workers before and after work shift, indicating reduction of silicosis incidence up to 28%. Hydrolysed dextran or glutamate have also helped in bringing about significant prevention of silicosis.[8,13] However, all these agents have also shown to be associated with various harmful side effects.

Many therapeutic properties have been attributed to jaggery in the Ayurvedic system of medicine. Regular consumption of jaggery conferred great symptomatic relief of industrial mine workers in mining and industrial establishments of India. Our earlier work[9,10] and this report indicates the beneficial effects of jaggery, a nutritive substance of considerable potential and without any harmful side effects, on coal mine dust induced lesions in rats.

MATERIALS AND METHODS

Jaggery

A solidified form of the product obtained on boiling in open pan and concentrating sugarcane juice (*Saccharum sinense* Roxb.) is an indigenous edible item which is produced in all parts of India and is consumed as such or as confectionaries. The production of gur involves extraction of juice from cane, purification by straining, boiling and treating with vegetable clarificant followed by further boiling and concentration into a thick semi-solid mass which solidifies on cooling. Usually jaggery contains all the soluble constituents of sugarcane but the exact composition depends upon the variety and age of canes and nature of the soil on which they are cultivated. The chemical composition of jaggery[6,7,12] is given in Table I.

Coal Mine Dust

The respirable size (5 μm diameter) with fairly well defined chemical composition was obtained from Environmental Monitoring Section of Industrial Toxicology Research Centre, Lucknow. To increase fibrogenic potential of coal mine dust, it was supplemented with quartz up to 10% of the total mixture.

Experimental

Male albino rats (108) were procured from ITRC animal breeding facility and maintained on normal laboratory conditions, on standard pellet diet (Gold Mohur, Lipton India Ltd.) and water *ad libitum*. Animals were divided into 5 groups as shown in Experimental Protocol (Table II). The dose of jaggery in rat was based on its average daily consumption of mine workers in India. Following treatment from first day, 6 animals from each group were weighed individually and sacrificed at the end of 30, 60 and 90 days.

Hematology

Blood was collected from jugular vein in heparinized tubes for RBC and WBC counts and estimation of hemoglobin. RBC and WBC were counted on Cell Counter 2041 Labora Manheim GmBH, Germany. Haemoglobin was estimated according to the method of Dacie and Lewis.[4] Fresh blood

Table I

General Composition of Indian Jaggery (Gur) Compiled from Reference 6, 7 and 12

Content	Value (range)
Moisture (%)	3.9–7.2
Protein (%)	0.35–0.40
(a) Non-protein nitrogen (mg/100 g)	19.6–42.9
(b) Protein nitrogen (mg/100 g)	13.7–17.6
Carbohydrate (%)	83.5–95.0
(a) Sucrose (%)	72.8–80.3
(b) Reducing sugar (%)	6.8–14.2
Minerals (%)	0.6–2.6
(a) Calcium (%)	0.2–0.36
(b) Chloride (%)	0.2–0.34
(c) Phosphorus (%)	0.03–0.22
(d) Potassium (%)	0.10–0.16
(e) Sodium (%)	0.006–0.025
(f) Iron (%)	0.005–0.020
(g) Magnesium (%)	0.008–0.105
(h) Copper (%)	0.007–0.010
(i) Cobalt, Nickel and Molybdenum (%)	0.001–0.008
Vitamins	
(a) Thiamine (mg/100 g)	0.018–0.030
(b) Riboflavin (mg/100 g)	0.042–0.046
(c) Nicotinic acid (mg/100 g)	3.92–4.50
(d) Vitamin C (mg/100 g)	5.20–30.00
Carotene (µg/100 g)	155.0–168.0
Phenolics (mg/100 g)	280.0–320.0
Fat, Wax, Pectin and Organic acids (%)	0.10–0.60

Table II
Experimental Protocol

Group	Number of rats used	Treatment	
		Coal[a]	Jaggery[b]
I	22	+	-
II	22	-	+
III	22	+	+
IV[c]	22	+	+
V[d]	20	-	-

[a]Coal dust (50 mg/1 ml of 0.15 M NaCl solution, sterile suspension) was injected intratracheally.

[b]Jaggery (500 mg/1 ml of sterile distilled water) given orally (po) 5 days/week for 90 days (termination of the study).

[c]Animals were first treated with gur (po) for 2 weeks followed by coal dust (intratracheally) and gur (po) treatment for 90 days (termination of the study).

[d]The control animals were treated orally (po) 1 ml of sterile waters 5 days/week for 90 days (termination of the study).

was used for making blood films to enmurates differential leukocytes after Leishman's staining.

Relative Organ Weights and Lymphoid Cell Counts

At 30, 60, and 90 days post treatment, body weight, weights of thymus, spleen, peripheral (axial a popliteal lymph nodes) and tracheobronchial lymph nodes, adrenal glands, kidney, liver and lung were determined from individual rats and relative organ weights calculated. Thymus, spleen, peripheral and tracheobronchial lymph nodes cell counts were counted as number of nucleated cell per organ in Counter 2041 after making cell suspension. Viability of cells was determined by Trypan Blue exclusion method.

Histological

Lungs were inflated *in situ* with 10% buffered formalin while other organs were used for estimation of collagen content. After preliminary fixation, the blocks were selected on the fixed positions along with the long axes of both the lung at the level of the hilum to include the maximum area of the lung. Tracheobronchial lymph nodes were excised carefully and fixed in Bouin's solution. Other visceral organs were also fixed in formalin. The paraffin section of 5 μm thickness were prepared and stained with hematoxylin and eosin, silver impregnation for reticulin and Van Gieson's stain for collagen.

Collagen and Sulphydrol Content

Lung Collagen content was estimated by measuring hydroxyproline levels. In brief, dry lung tissues were hydrolysed with 6 N HCl in sealed glass tubes at 110°C for 16 hrs. The hydrolyate was titrated to pH 7 and diluted with distilled water. Hydroxyproline content was then assayed according to Woessner.[15] Concentration of total and free Sulphydryls in lung homogenates prepared in 0.25 M sucrose containing 0.005 M EDTA and free Sulphydryls in blood was determined using the Ellman procedure.[3]

RESULTS

Gross Observation

The visceral organs of rats of different groups did not reveal any significant macroscopic changes up to 90 except in lungs and tracheobronchial lymph nodes of rats receiving coal dust. The lungs of group 1 at 60 days showed black pin point patches of coal dust on the lobes and by 90 days these patches

became more prominent. Black patches of the coal dust were also seen in group III and IV at 90 days but they were less prominent than in group I judged from visual observation. In the early phase in group I, III and IV, the tracheobronchial lymph nodes became prominent and black in colour. However, in group III and IV at 90 days, a marked lymphadenopathy was observed. Tracheobronchial lymph nodes of Group I animals showed some macroscopic changes.

Relative Weight

The relative weight of lungs at 30 days showed marked increase in groups I, III and IV. At 60 and 90 days relative weight of lungs in group I increased significantly (51% and 41% respectively) in comparison to controls while relative lung weight of lungs in group III and IV were almost similar to that of control. The relative weight of tracheobronchial lymph nodes (TLN) of coal dust exposed group (I) showed 61-74% increase. In general the relative weight of lung, TLN, liver and spleen showed an increase at 30 days and a decline at 60 and 90 days.

Hematological Changes

RBC counts increased significantly in all the experimental groups. Concomitantly jaggery treatment in group III and IV significantly increased the RBC counts at different periods. At 90 days the values were higher than those of group I.

At 30 days in coal exposed and jaggery treated group (III and IV) the increase in WBC count was over 50%. A time dependent increase was further observed in these groups with maximum increase of 76% ($P < 0.001$) at the end of 90 days.

The haemoglobin content in group I was more or less the same at all periods but slightly higher than those of controls. However, the percent haemoglobin increased (45–50%; $P < 0.05$) in all the three jaggery receiving groups (II, III and IV) at 30, 60 and 90 days.

Cellularity of Lymphoid Organs

Animals treated with coal and jaggery group III and IV indicated 18-20% (P 0.05) increase in thymocyte counts at all periods. At the termination of experiment (90 days), a decline in splenocyte counts (16% and 33%; P 0.05 respectively) was observed in group I and II animals. The cell counts of tracheobronchial lymph node indicated an increase in group I, III and IV in a time dependent manner at the end of 90 days. Peripheral lymph nodes cell counts indicated significant increase in group III and IV at 60 and 90 days (25–45%; $P < 0.05$).

Histological findings

In group I at 90 days typical coal-induced focal areas of fibrosis was seen which upon silver impregnation showed presence of thick reticulin fibres enclosing coal dust mass. Lung of animals treated orally with jaggery did not reveal any significant histopathological alteration at 30, 60 or 90 days. In group III (coal and jaggery simultaneously) at the termination of study (90 days), the alveolar parenchyma, in general, showed widely scattered and partly unphagocytosed coal particles with minimal cellular reaction and less fibrogenic response upon silver impregnation in comparison to group I.

In group IV (pretreatment with jaggery followed by coal plus jaggery) at 90 days there was hardly any indication of the development of characteristic coal-induced lesions except there was mild thickening of alveolar Septa (Figure 1). Moreover, minimal cellular proliferation around coal deposits in the parenchyma as well as small aggregates of coal particles in the lumen of alveolar duct respiratory and terminal bronchioles as was seen in group III. The changes in tracheobronchial lymph nodes: the nodes were slightly enlarged with diffuse distribution of coal particles in the paracortical regions. Silver impregnation revealed presence of dense fibres along with thick branches of reticulin enclosing coal aggregates. In group III at 90 days there was minimal reaction provoked by coal aggregates which were rather focally distributed and not diffusely as in group I. Focal areas of coal aggregates did not reveal any significant fibroblastic reaction. In group IV and 90 days, the enlarged lymph nodes demonstrated many scattered focal areas of coal aggregates with minimal reaction (Figure 1). In spleen the fibroblastic reaction was seen in red pulp in group I at 90 days while very mild reaction was observed in group III and IV at same period. Histological examination of other organs did not show any significant alterations in their structures in various treatment groups at 90 days.

Lung Collagen

Lung collagen as measured by hydroxyproline content in various treatment groups (I to V) up to 90 days is shown in Figure 2. A time dependent increase was seen in hydroxyproline content of group I animals. Animals of group II, however, did not show any alteration in the lung hydroxyproline content up to 90 days. Group III animals also did not exhibit any initial increase in hydroxyproline content at 30 days but at later periods (60 and 90 days) 10% increase (P 0.001) did occur. Interestingly, hydroxyproline content of lung from animal of group IV remained unaltered and were within the limits of normal variation up to 90 days.

Total and Free Sulphydryl Content of Lung

The jaggery treatment group III and IV showed an elevated level of their lung-SH content. Free SH-contents of the jaggery treated animals (group III and IV) were exceptionally high at 90 days.

Free Sulphydryl Content of Blood

Coal dust instillation and oral treatment of jaggery (group I and II) did not change the free SH-content of blood. In group III and IV the SH-content increased in initial stage (30 days) but an increase became evident at 60 and 90 days in group IV.

DISCUSSION

The result of the present experiments showed significant inhibition of fibrotic changes in the lungs at 90 days in coal treated rats which received prior treatment of jaggery. Moreover the initial reaction of the coal induced cytotoxicity, phagocytosis as well as fibroblastic reaction in lungs remained less prominent and did not damage the lung archi-

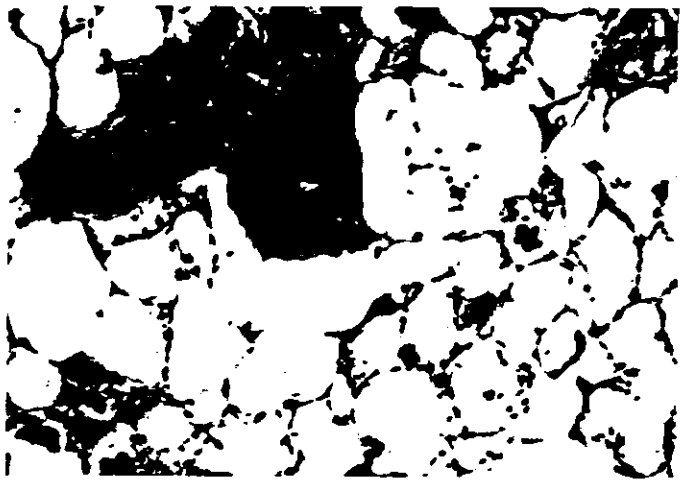

Figure 1A. Rat lung after treatment of Coal alone (group I) at 90 days, thick reticulin fibrosis upon silver impregnation, X 128.

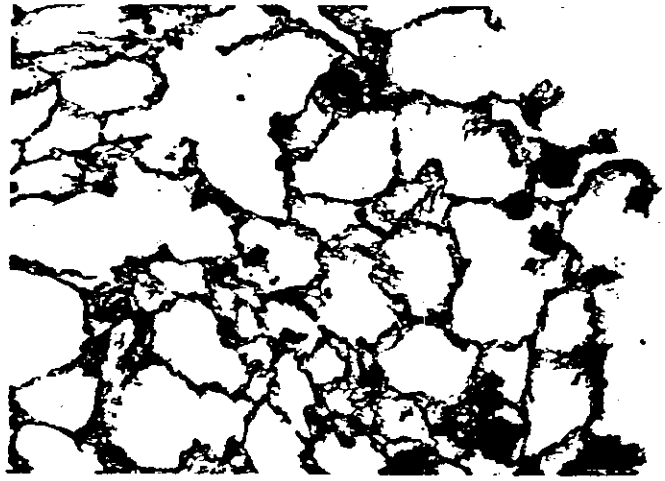

Figure 1B. Rat lung, pretreatment with Jaggery and Coal + Jaggery (group IV) at 90 days, upon silver impregnation showing mild thickening of alveolar septa, X 104.

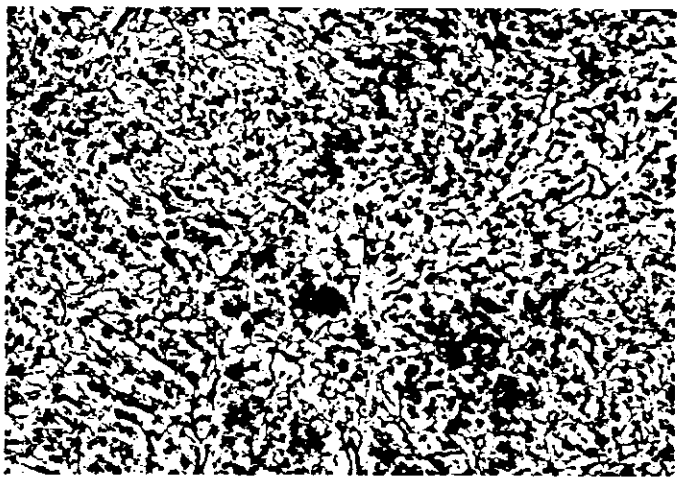

Figure 1C. Tracheobronchial lymph node after treatment of Coal alone (group I) at 90 days upon silver impregnation showing dense reticulin fibres and coal particles, X 104.

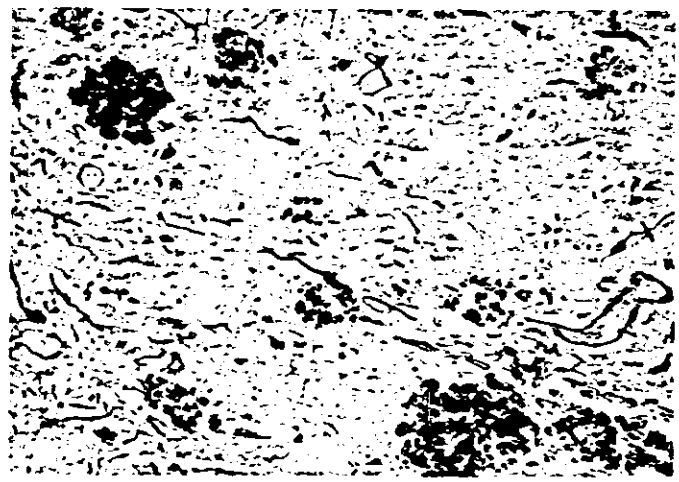

Figure 1D. Tracheobronchial lymph node, pretreated with Jaggery and Coal + Jaggery (group IV) upon silver impregnation, few reticulin fibres along with coal particles, X 104.

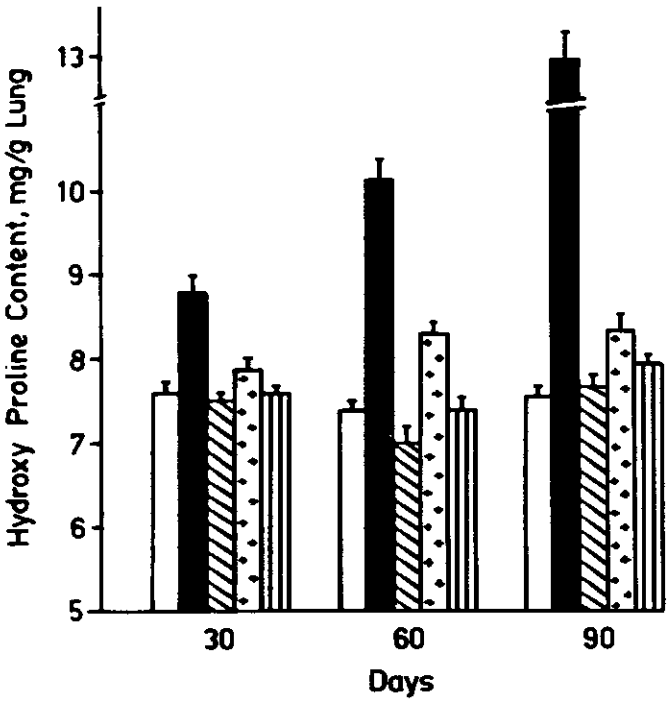

Figure 2. Changes in Hydroxyproline content of rat lung of different groups at 30, 60 and 90 days. □ — Control; □ — Coal alone (group I); ▨ — Jaggery alone (group II); ▦ — Coal and Jaggery simultaneous treatment (group III); ▥ — Pretreatment with Jaggery and Coal + Jaggery (group IV).

tecture. In addition to histologic evidence in lungs, pretreatment of jaggery prevented the increase in the hydroxyproline content (collagen) of lungs. Significant changes in the relative weights of lungs, liver, TLN and spleen of coal exposed rats were observed following jaggery treatment. The WBC counts and haemoglobin contents were significantly higher in all the jaggery treated groups. Concomitantly, the cell counts of lymphoid organs were also elevated. These findings indicate that jaggery treatment presumably increased the physiological status of almost every important organ and cells of the body suggesting that dust clearance from lung could be by the enhanced physiological pathway.

Our earlier studies[9] following jaggery treatment have shown that pathological pathway of clearance is also effectively operative in these groups as dust can be observed in TLNs.

Although it has been reported that protein is essential for fibrogenesis,[2,14] multideficient or protein deficient diets did not modulate silicotic fibrogenesis.[17] In the pre-fibrogenesis stage, there is likely to be proliferation of endoplasmic reticulum leading to enhanced-SH levels. If fibrosis is retarded, as in the jaggery treated groups as evident histopathologically, hydroxylation is initiated with affecting the endoplasmic reticulum. In that case SH is likely to increase. The enhancement of sulphydryl content of coal exposed rat lung following jaggery treatment suggest that jaggery or its microingredient(s) play some protective role in the release of these toxic biologically active substances.

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IMMUNOLOGIC FEATURES OF THE BRONCHOALVEOLAR LAVAGE FLUID OF RATS WITH SILICO-PROTEINOSIS

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ABSTRACT

We provoked silico-proteinosis in specific pathogen free Fisher 344 rats by exposing them to 10 mg/m^3 respirable free crystalline silica for 3 months (6 hrs./day, 5 days/wk) and compared the immunologic features to a group of non-exposed rats. Bronchoalveolar lavage fluid (BALF) return, total cell count, differential cell count, and BALF and serum IgG, albumin, and IgA levels were measured and expressed as mean ± S.E.M.

Percent fluid recovered was no different in the silica exposed and non-exposed rats (51.6±6 v. 64±8). Total cells recovered (x10^6)(64±17 v. 3.1±1.0), % macrophages (67.4±3.0 v. 94.8±0.5), % neutrophils (5.9±1.4 v. 1.3±0.8), and % lymphocytes (26±2 v. 4.5±0.6) were significantly different in the silica versus non-exposed rats, respectively.

IgG (g/dl) was significantly increased in the serum (2.0±0.2 v. 1.2±0.3) and BALF (0.7±0.01 v. 0.02±0.01) of the exposed rats. Serum albumin (g/dl) was not significantly different in the 2 groups but BALF albumin (g/dl) was significantly increased in the silico-proteinosis group (0.20±0.02 v. 0.03±0.01). IgA levels did not significantly differ in the serum and were below detectable limits in both of the groups.

A dramatic influx of humoral and cellular components occurs into the bronchoalveolar lavage fluid of rats with silicoproteinosis, reflecting the extensive inflammatory response associated with this disease.

No Paper provided.

OCCUPATIONAL ASBESTOSIS AND ASBESTOS RELATED DISEASES AMONG WORKERS EXPOSED TO ASBESTOS, 1987, THAILAND

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BACKGROUND

Occupational exposure to asbestos minerals constitutes a major health hazard in most industrialized nations of the world.[1]

Early case reports stimulated concern and in 1928 the detailed epidemiologic study of asbestos workers was undertaken by the Ministry of Labour in Great Britain. This was a cross-sectional chest X-ray study of 363 workers engaged in production of asbestos textiles. Of this group, 95 (26.2%) were found to have pulmonary fibrosis and the prevalance of fibrosis with 20 or more years employment was over 80%.[2]

Asbestosis is the name of the pneumoconiosis produced by the inhalation of asbestos fibers. It is characterized by diffuse interstitial fibrosis of lung parenchyma, often accompanied by thickening of the visceral pleura. Clinical findings include dyspnea on exertion, non productive cough, rales at the lung bases, bronchi, and in advanced cases, finger clubbing. Lung function measurements usually demonstrate a restrictive impairnent with reduced diffusing capacity.

The radiographic findings of asbestosis and asbestos related pleural plaques and thickening are best described through systematic application of the ILO-1980 Classification for interpretation of the pneumoconioses.[3] The small irregular opacities of asbestosis are most commonly distributed in the mid and lower lung zones.

Each year, Thailand imports about five million metric tons of asbestos to be used in friction and fire resistant materials. Industries include brake lining, clutch facing asbestos ceiling tiles, asbestos floor tiles, asbestos cement pipe and car undercoating.

These products are widely used in Thailand, but their hazards are not well-known here. They are exported to bring in money every year, but the employees do not know how hazardous asbestos is. More and more workers have been exposed to this potential health hazard while manufacturing asbestos products. It was claimed that there were no cases of asbestosis in Thai workers. The health status of exposed workers remains undescribed.

To find out whether there were asbestosis and asbestos related diseases among Thai workers, and to prepare the baseline data for the surveillance of asbestos related disease among the group of workers exposed to asbestos, thus we carried out a study concerned with this problem. The objectives of this study are, to study the prevalence of asbestos related diseases, to determine epidemiological distribution of asbestos related diseases, to survey knowledge, attitude and practice of workers in prevention of asbestos related diseases, to identify risk factors associated with asbestos related diseases, and to provide the knowledge in appropiate preventive and control measures of asbestos related diseases for all workers exposed to asbestos and all industries using asbestos.

METHODS

We conducted a descriptive epidemiological study, a survey of knowledge,attitude and practice in prevention of asbestos related diseases and a case-control study.

The descriptive study was done by surveying all 24 factories registered by ministry of industry that use asbestos in a production process. There are six provinces where this type of manufacturing is located. A11 are included in this study. All workers in these plants constitute the study group.

The workers were interviewed using questionaires that asked information regarding the examination with their work history and history of illness, knowledge and attitude prevention of asbestos related diseases. Chest radiograph, and lung function tests were carried out. The case definition was a worker exposed to asbestos for more than six months with chest radiograph change falling into a possible case and a definite case. A possible case of asbestos related disease had to have chest radiograph changes in parenchymal profusion of 1/0 together with at least one of the other abnormalities consistent with pneumoconiosis classified by international classification of puenmoconiosis-ILO-1980.[3] A definite case had to have chest radiograph changes in parenchymal abnormality profusion at 1/1 and above. The chest radiographs were read by a radiologist and an occupational health physician.

RESULTS

We surveyed twenty-four factories and performed 1,013 interviews, physical examinations, especially the respiratory system and lung function tests to workers. Six hundred and sixty chest posteroanterior radiographs were carried out.

There were thirty four cases that met our case definition. Thirty one cases were possible and three were definite cases

of asbestos related diseases, giving the prevalence rate of 5.1% among the whole group. All cases were male. The sex specific male prevalence rate was seven percent. Half of the cases were smokers. The mean age of the cases was 40 years old (range=21–53). Mean duration of exposure was 8.5 years (range=1–22).

Forty one percent of cases had symptoms including dyspnea, chest pain, chest tightness and weight loss. There were 50% of cases that had abnormal signs such as, diminished chest expansion and clubbing fingers. Mean forced expiratory volume in one second by forced vital capacity was 84%, and forced vital capacity by predicted FVC of a normal person at the same age, sex and height was 98%. All components of mean pulmonary function seem to be within normal limits. Forty four percent of cases had abnormal pulmonary function by the prediction equation of Crapro and coworker.[4] The predicted values were corrected with 0.85 for non caucasian people. Most of them (73%) were restrictive ventilatory defects. The chest expansion was 3.9 cm in average.

The three definite cases had chest radiographs of s and t in shapes and sizes with the small opacity parenchymal profusion of 1/2, 2/2 and 3/3. For the large opacity, there was one case of catagory 'B'. When it was considered in terms of other abnormalities, there were effusion(ef) of 5.8%, ill-defined diaphragm(id) of 5.8%, pleural thickening(pi) of 52.9%, pneumothorax(px) of 2.9%, calcification in small pneumoconiotic opacity (cn) of 11.76%, other significant abnormalities of volume loss at 5.8% and tuberculosis(tb) of 20.58%.

The highest prevalence rate of asbestos related disease was among workers in asbestos-cement pipe factory. The rate was 20%. The prevalence rate of asbestos related diseases among the workers in floor-tile was 5.3%, followed by 5.1% in ceiling tile, 4.7% in car undercoating and 2.1% in brake and clutch plants.

Asbestos-mixers had the highest prevalence rate of 23.5%, when it was analysed by job specific prevalence rate. There were 14.7% of prevalence rate among those who were tile machine operators, in addition with 14.7% in material deliverers, 11.8% in tile and pipe cutters, 5.9% in quality control personnel, 2.9% among the group of supervisers,and 2.9% in maintenance machanists.

The concentration of asbestos fibers collected by both area and personal samplings averaged at 2.5 fibers/ml and 5 fibers/ml, respectively. The maximum fiber concentration was 58.5 fibers/ml in one of brake-manufacturing plants. The recommended exposure limit by NIOSH of 0.1 fiber/ml was used to calculate the excess amount of fiber concentration in working atmosphere.[5] Such that maximum concentration was 585 times of REL. The asbestos used was mostly chrysotile, with some crocidolite and amosite.

In survey of knowledge, attitude, and practice, we found that only a third of the workers had been educated in preventive measures. Six percent said that they would continue their work, even if they were ill with an asbestos related condition. Ninety six percent of respondents wanted factories to provide protection. Almost all would use special masks if they were made available. Only thirteen percent of workers had annual medical examinations, and 1 % currently used masks approved by NIOSH. Twenty six percent of workers had ever received 16*17 inches films.

In the case-control study, cases and controls were not different in age, but significantly different in duration of exposure, vital capacity and forced vital capacity by predicted forced vital capacity ($p<0.05$ by student's t-test). Cases and controls were significantly different in proportions with restrictive lung defects. Cases and controls had similar smoking habits. Cases were significantly more likely to be asbestos mixers. The odds ratio was 21.3 with a 95% confidence interval limit that excluded zero.

DISCUSSIONS AND RECOMMENDATIONS

The study concluded that there were thirty four cases of asbestos related diseases attributable to work exposure. Prevalence was 5.1%. The workers most at risk were asbestos mixers and those who had long exposure to asbestos. Workers's knowledge, attitude and practice about the hazards of asbestos and prevention of asbestos related disease was very inadequate. The working conditions were also unsafe. When compared to the prevalence of asbestosis among railroad workers in the United state,[6] the prevalence in this study was three times higher. Morbidity and mortality analysis by Lacquet et al. (1979) of workers in a Belgian asbestos cement factory revealed a strong dose-response relationship for asbestosis, and pleural and parenchyma lung changes. Pleural thickening and adhesions began occurring in the lowest dose category (0-49 fibers/cc-year).[7] The concentrations in air of asbestos in this study were in the same range of that Belgium cement pipe in 1979 which could cause abnormalities in chest radiographs. The corresponding results led us to know for certain about the outcome of this study. This study did not include workers outside the plant that used asbestos even when they were part of the same workplace. These workers should be prospective to assess long term risk. Available epidemiologic data support a linear, no threshold dose-response relationship between asbestos exposure and the risk of lung cancer. And in additiona, no threshold has been convincingly demonstrated for non-malignant respiratory diseases associated with asbestos exposure. Thus, any asbestos exposure that carries with it some increased risk of asbestos exposure should be eliminated or reduced to the lowest level possible.

Appropriately designed and maintained engineering techniques are the control method of choice where asbestos substitutes cannot be used. Processing of asbestos in a wet state has been shown to be an effective control method in many asbestos processing industries, including the asbestos textile industry. The most commonly used control measure in asbestos processing plants is local exhaust ventilation whereby liberated dust is collected at the dust source and removed from the breathing zone of workers.

In this study, the control measures provided during and after the survey included reduction of asbestos dust in the workplace by the use of local hood ventilation and the establishment of better occupational health services. A better canteen was established to avoid having workers eat lunch on the piles of asbestos bags.

Periodic medical examinations were begun. Adequate and approved protective masks were providing along with training on how to use them effectively. Such measures should avoid the inadequate dust control measures now taken by workers.

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RESPIRATORY MORBIDITY IN PLUMBERS AND PIPEFITTERS: THE RELATIONSHIP BETWEEN ASBESTOS AND SMOKING

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INTRODUCTION

Plumbers and pipefitters, along with other building trades workers, have been shown to be at risk for asbestos-related lung diseases including lung cancer,[1,2] mesothelioma,[3,4] and interstitial fibrosis.[5] In the present cross-sectional study, an Upstate New York chapter of a plumbers and pipefitters union was evaluated for evidence of asbestos exposure and disease. Our purpose was to better define the relationship among the clinical endpoints used to characterize asbestos exposure and non-malignant disease as well as the interactive effects of smoking.

METHODS

All active and retired members with pension eligibility received a mailed offer of free asbestos screening examinations. The voluntary evaluations, conducted over a four month period in 1986-1987, included an interview, physical examination, spirometry, and chest radiograph. Out of the total union membership of 975, 797 persons were eligible. Of these, 343 (43%) accepted the offer. Those who did not respond tended to be older, retired, and living out-of-state; hence the study group represented a younger, more active, and perhaps healthier subset.

Trained interviewers took a detailed occupational and medical history, with smoking and respiratory questions obtained from the Epidemiology Standardization Project.[6] The physical examination sought evidence of rales and clubbing. Dyspnea was graded according to the Medical Research Council criteria.[7] On spirometric examination, 3 maximum expiratory flow volume loops were obtained, using the Eagle Three Survey Spirometer (W.C. Collins). Forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1), flow at 75% of vital capacity (FEF_{75}), and late expiratory flow volume (FEF_{75-85}) were measured. Computations were based on the largest values for FVC and FEV_1. Maximum ventilatory volume (MVV) was also tested. Predicted values based on sex, age, and height for FVC, FEV_1, FEF_{75}, FEV_1/FVC, and MVV were computed using the regression equations of Crapo et al.[8] The Mt. Sinai algorithm as described by Miller[9] was used to define obstruction, restriction, and small airways abnormality.

Posteroanterior, lateral, and oblique chest radiographs (16" x 17") were taken at maximal inspiration and were interpreted by one "B" reader according to the ILO/UC Classification of Radiographs.[10] Pleural change consistent with asbestos exposure was defined as any pleural thickening, diffuse or circumscribed, bilateral or unilateral, excluding changes clearly due to factors not related to asbestos. Parenchymal change considered positive for possible asbestosis was defined as the presence of opacities of size s or t and profusion 1/0 or greater.

Analyses used the Statistical Analysis System (Cary, N.C.). Univariate tests evaluated the prevalence of pulmonary findings. Two-way analyses looked at age, duration of exposure, and other characteristics. Differences between groups were tested using frequency x^2 and t-tests.[11] Multivariate linear regression evaluated the predictive power of age, latency, and smoking in determining FVC and % predicted FVC.[12] Unconditional logistic regression models were used to control simultaneously for several independent variables that affected the probability of pleural or parenchymal change.[13] Two logistic regression models were developed, potentially including age, pack years, and years since first exposure as independent variables. The first model compared the characteristics of those subjects with only pleural change to those classified as normal. The second model compared the characteristics of those with parenchymal change (s,t > 1/0) to normals and to those with pleural change only.

RESULTS

Of the 343 participants, all were male, the mean age was 47, and mean years in the union was 22. 12.5% were retired. 38% were current smokers, and 39.5% were ex-smokers. Job experience was heterogenous, with numerous work sites, many contractors and conditions, and a variety of tasks. Virtually all workers reported a history of tasks that included asbestos exposure. The variation in work history precluded estimation of dose. Our analyses used years-since-first-exposure as a measure of latency.

Current smokers showed lower mean and percent predicted function for all measurements of pulmonary function, while ex-smokers (who on average were older than current smokers) were generally intermediate between smokers and non-smokers. (Table I) Ex-smokers showed the highest prevalence of obstruction, restriction, and small airways abnormality. (Table II) However, because more than 25% of these ex-smokers reported quitting less than five years prior to the screening, these data may reflect a subset who quit because of respiratory symptoms or diagnosed lung disease.

Table I
Mean Lung Function Value by Smoking Category

Smoking Status	Age	FVC (% Pred)	FEV_1 (% Pred)	FEF 75 (% Pred)	FEV_1/FVC (% Pred)
Never (n=72)	43.0	4.66 (94)	3.94 (98)	4.36 (107)	84.6 (104)
Former (n=139)	50.2	4.30 (90)	3.53 (92)	3.79 (99)	81.8 (102)
Current (n=121)	43.4	4.37 (89)	3.55 (89)	3.61 (89)	81.0 (100)

Table II
Diagnosis of Lung Impairment

	N	OBSTRUCTION (%)	RESTRICTION (%)	SMALL AIRWAYS ABNORMALITY(%)
Nonsmokers	72	1 (1.4)	6 (8.3)	7 (9.7)
Ex-smokers	139	4 (2.9)	28 (20.1)	49 (35.3)
Smokers	121	1 (.8)	23 (19.0)	33 (27.3)
TOTAL	332	6 (1.8)	57 (17.2)	109 (26.8)

In linear regression analyses, age, pack-years, years-since-first-exposure to asbestos, and parenchymal change (s,t > 1/0) were potentially included in a model to predict actual FVC. However, since most subjects had spent their working lives mainly in the trade, age and years-since-first-exposure were highly correlated (r=.89). Because it is difficult to interpret the independent effect of either factor when both are included in the model, and because age is a strong predictor of pulmonary function, age rather than latency was included in subsequent models. FVC showed a negative relationship with age ($p < .0001$), pack-years ($p < .0001$), and presence of parenchymal change ($p < .004$).

Nearly one-third of the study subjects showed either pleural and/or parenchymal change consistent with asbestos exposure. (Table III) 79 subjects (23%) had pleural change; 53 of these (67%) were bilateral. Two-thirds of the 42 subjects with parenchymal change had the lowest level of profu-

Table III
Characteristics of Those with Radiographic Abnormalities

Characteristic		Normal	Pleural Only	p	Parenchymal Only	p	
Age				<.001		<.001	a
	<40	116 (47)	5 (9)		2 (5)		
	41-60	119 (49)	36 (65)		24 (57)		
	>60	9 (4)	14 (26)		16 (38)		
Latency				<.001		<.001	a
	<15	82 (34)	3 (6)		5 (12)		
	16-25	89 (37)	12 (22)		3 (7)		
	26-35	51 (21)	17 (31)		14 (33)		
	>35	22 (9)	23 (42)		20 (48)		
Ever Smoker		181 (75)	48 (87)	.031	38 (91)	<.016	c
Dyspnea		50 (21)	14 (28)	.196	22 (55)	<.001	c
Rales		6 (3)	3 (5)	.218	12 (29)	<.001	b
Clubbing		4 (2)	4 (7)	.038	9 (22)	<.001	b
Restriction		25 (11)	11 (21)	.051	20 (49)	<.001	c

a t-test, comparing mean value (not shown)
b Fisher's exact test, comparing each abnormal group to normal group
c x^2 test, comparing each abnormal group to normal group

sion considered positive for possible asbestosis (1/0), while the rest had profusion from 1/1 to 2/1. Twenty-four men (7%) had both pleural and parenchymal change.

The likelihood of having either pleural or parenchymal change increased with the number of years since first exposure. (Figure 1) Among those with latency >25 years, the prevalence of pleural change was nearly 50%, while 66% had either pleural or parenchymal change. Those with parenchymal change were more likely to be older, current smokers, and to have other pulmonary findings (dyspnea, rales or clubbing, restriction, and small airways abnormality) than those with normal radiographs or with pleural change only.

After controlling for age using logistic regression modeling, latency did not remain a significant predictor of either parenchymal or pleural change. Smoking measured as a categorical variable (current, never, or former smoking) was significantly ($p=.04$) related to the presence of parenchymal change after controlling for age. However, if pack-years was included in the model with age instead of smoking category, the term did not attain statistical significance ($p=.14$). After controlling for age, neither pack-years nor smoking category predicted pleural change.

Dyspnea and pleural change were the most prevalent endpoints overall. (Table IV) Because, in the absence of pathological evidence, parenchymal change is considered the most important diagnostic criterion for asbestosis,[14] we sought its best predictors. In this study, rales and clubbing had the highest predictive value but were the least sensitive measures. Dyspnea and/or restriction were most sensitive, but even these parameters identified only about half of those with radiographic evidence of significant fibrosis.

DISCUSSION

The high prevalence of possible asbestosis and other respiratory morbidity potentially associated with asbestos exposure in this study is consistent with other cross-sectional studies of plumbers and pipefitters. In our group (mean age 47), 12% showed parenchymal change consistent with possible asbestosis, and an additional 16% showed only pleural changes. Sprince at al.[5] described parenchymal opacities (> 1/0) in 8% of a similarly aged group of plumbers and pipefitters where 17% showed pleural change. In a slightly younger group (mean age 42), Schwartz et al.[15] found 29.5% had bilateral pleural change and/or parenchymal opacities.

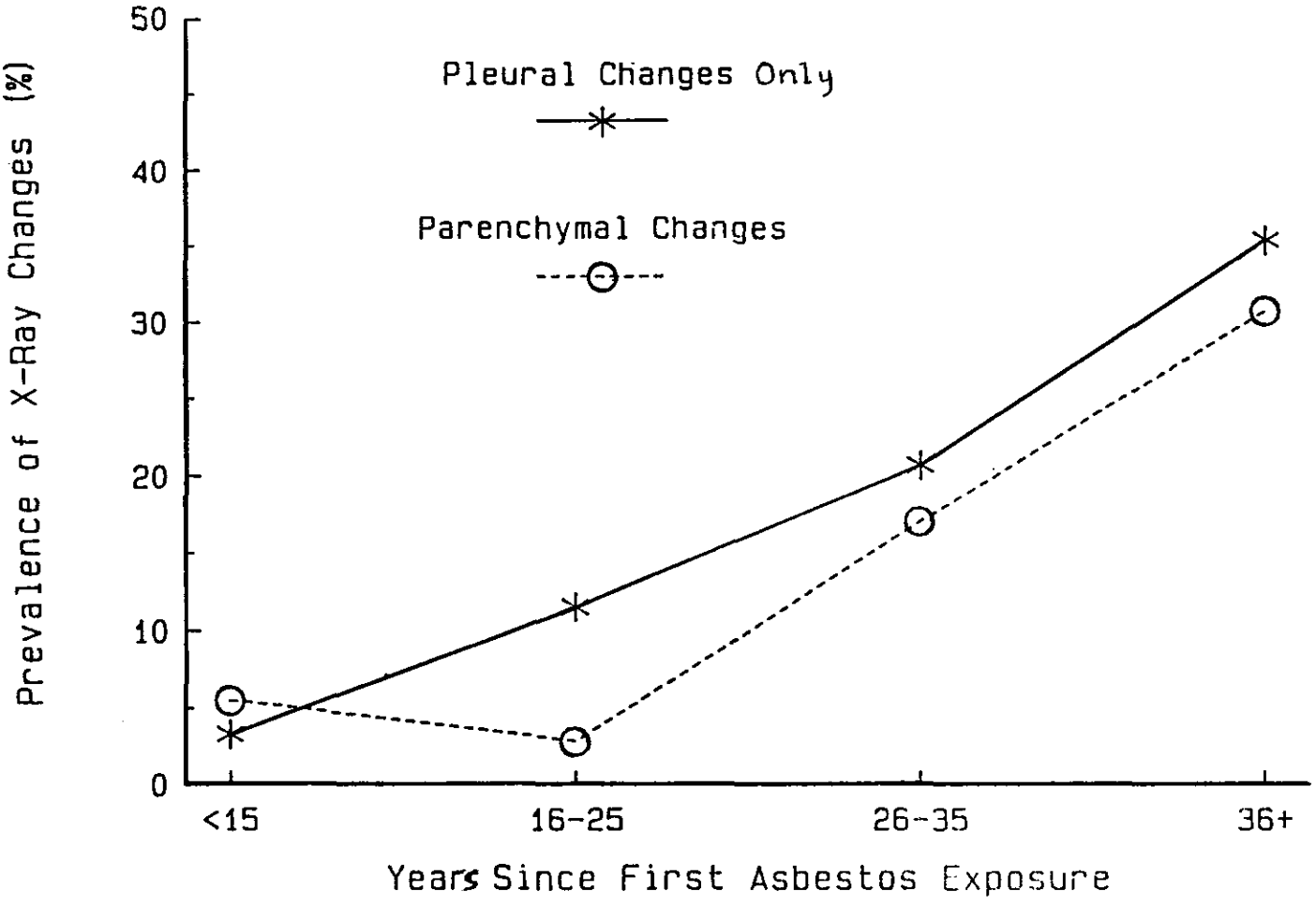

Figure 1. Prevalence of X-ray changes by years since first exposure.

Assessment of past exposure in the building trades is difficult. Given any history of exposure, age is the strongest predictor of asbestos-associated morbidity. But there are at least three other factors, systematically associated with age, which obscure the effect of age: (a) the lessening intensity of asbestos exposure over time, suggesting higher doses in older workers; (b) the secular trend in smoking habits; and (c) the collinearity with age of years-since-first-exposure.

Weiss[16] has argued that smoking is an independent cause of pulmonary fibrosis. Kilburn et al.[17] modified this view, suggesting that, while smoking alone does not produce fibrosis, it seems to have an additive effect to exposure to asbestos. Univariate analysis in the present study showed a relationship between smoking and the presence of parenchymal opacities. However, after controlling for age using logistic regression analysis, smoking was significantly associated with parenchymal change only when considered categorically (never, former, current), and not when pack-years was used as the smoking measure. This discrepancy may indicate a weak or non-existent association, the presence of an unknown confounder, or misclassification. Or it might illustrate the problem of using pack-years as a meausre of dose.

Each of the parameters studied here (history, physical examination, spirometry, and chest radiograph) has been used in the absence of pathological evidence to infer the presence of possible asbestosis. Evaluated alone, each parameter would identify a slightly different subset of subjects as potentially diseased. Even those persons with radiographic evidence of fibrosis did not consistently show other deficits; only 55% reported dyspnea, and only 56% had spirometric evidence of restriction. Conversely, the study identified a group of workers who had one or more of the criteria for the diagnosis of asbestosis (restriction, clubbing, rales, dyspnea) but who lacked radiographic evidence. These diagnostic problems were discussed by Murphy et al. a decade ago[18] but our study demonstrates that they are still incompletely resolved. Our examination of the relationship between smoking and interstitial change in an asbestos-exposed population illustrates an additional problem in classification: the differing conclusions resulting from the

Table IV
Clinical Endpoints

	Parenchymal Change	Pleural Change	Restriction	Clubbing	Rales	Dyspnea	N
Parenchymal Change		24(57)	20(49)	9(22)	12(29)	22(55)	42
Pleural Change	24(30)		24(30)	10(12)	10(13)	25(34)	79
Restriction	20(36)	24(43)		6(11)	11(19)	32(56)	57
Clubbing	9(53)	10(59)	6(35)		5(29)	11(65)	17
Rales	12(57)	10(48)	11(55)	5(24)		11(52)	21
Dyspnea	22(26)	25(29)	32(39)	11(13)	11(13)		26

use of smoking category or pack-years. Future studies of asbestos-exposed populations should carefully examine these issues.

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RADIOGRAPHIC ABNORMALITIES IN A LARGE GROUP OF INSULATORS WITH LONG TERM ASBESTOS EXPOSURE: EFFECTS OF DURATION FROM ONSET OF EXPOSURE AND SMOKING

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ABSTRACT

Chest radiographs and spirometry were evaluated in active and retired asbestos insulators selected to be ≥20 years since entry into the trade (DURONSET). Testing was performed in 19 cities in the U.S. and Canada during the years 1981–1983. Complete demographic, smoking, clinical, and radiologic data were obtained for 2790 workers. The total of 2790 insulators is the largest which has been reported: 548 (19.7%) were nonsmokers, 942 (33.9%) current smokers and 1300 (46.6%) past smokers.

Only 439 (15.7%) had no radiographic evidence of asbestos-related disease (normal); 1358 (48.7%) had both parenchymal and pleural fibrosis, 668 (23.9%) had pleural fibrosis only and 325 (11.6%) parenchymal fibrosis alone. The prevalence of radiographic abnormalities for parenchymal changes increased from 38.6% (DURONSET <30 years) to 70% (≥40 years). For pleural changes the respective prevalences were 55% and 82%.

Nonsmokers were more likely to have normal films than current and ex-smokers (19.2% vs 15.0%) and less likely to have parenchymal fibrosis (36.3% vs 51.3%). Current smokers were least likely to have normal films (14.4%) and most likely to have parenchymal fibrosis (69.7%); ex-smokers were intermediate but closer to current smokers. These findings were not explainable by the minor differences in age or DURONSET.

Dyspnea (MRC grade 3 and higher) was significantly more prevalent when pleural fibrosis was associated with interstitial pulmonary fibrosis (at all profusion levels of small opacities).

a. parenchymal abnormalities associated with pleural abnormalities
b. total pleural abnormalities and
c. total parenchymal abnormalities.

Small Irregular Opacities indicating the Presence of Interstitial Pulmonary Fibrosis were found with higher prevalence as duration from onset of exposure increased. Within each category of duration from onset of exposure (DURONSET) less than 29 years, 30 to 39 years, 40 years and over, prevalence of interstitial pulmonary fibrosis was consistently higher in persons with a positive smoking history than in workers who had never smoked (Figure 1 and Table III).

Profusion category increased with duration from onset of asbestos exposure; within each DURONSET category smokers had higher prevalence rates for more advanced interstitial fibrosis (Figure 2).

Thus, **cigarette smoking had a demonstrable effect on both prevalence of interstitial pulmonary fibrosis and on severity of interstitial pulmonary fibrosis.**

Pleural fibrosis (chest wall, in profile and/or face on) was a frequent finding. Prevalence rates increased with DURONSET; in contrast with parenchymal abnormalities the prevalence of pleural thickening did not differ significantly in those with a positive smoking history when compared to those who had never smoked (Figure 3).

Similar relationships were found for diaphragmatic pleural plaques; their prevalence increased with DURONSET, while no effect of smoking status could be detected (Figure 4).

Table I

Chest X-ray Findings in Asbestos Insulation Workers with Long Term Exposure

	N	%
Normal chest x-ray	439	15.7
Parenchymal changes only	325	11.6
Pleural changes only	668	23.9
Parenchymal and pleural changes	1358	48.7
Total parenchymal abnormalities	1683	60.3
Total pleural changes	2026	72.6

Table II

Radiologic Changes and Years from Onset of Asbestos Exposure

	Time from onset of asbestos exposure(years)					
	Less than 29		30-39		40 and over	
	N=368		N=1712		N=710	
Radiologic abnormalities	N	%	N	%	N	%
Parenchymal only	44	12.0	222	13.0	59	8.3
Pleural only	106	28.8	413	24.1	149	21.0
Parenchymal and pleura	98	26.6	824	48.1	436	61.4
Total pleural abnormalities	204	55.4	1237	72.3	585	82.4
Total parenchymal abnormalities	142	38.6	1046	61.1	495	69.7
Normal chest x-ray	120	32.6	253	14.8	66	9.3

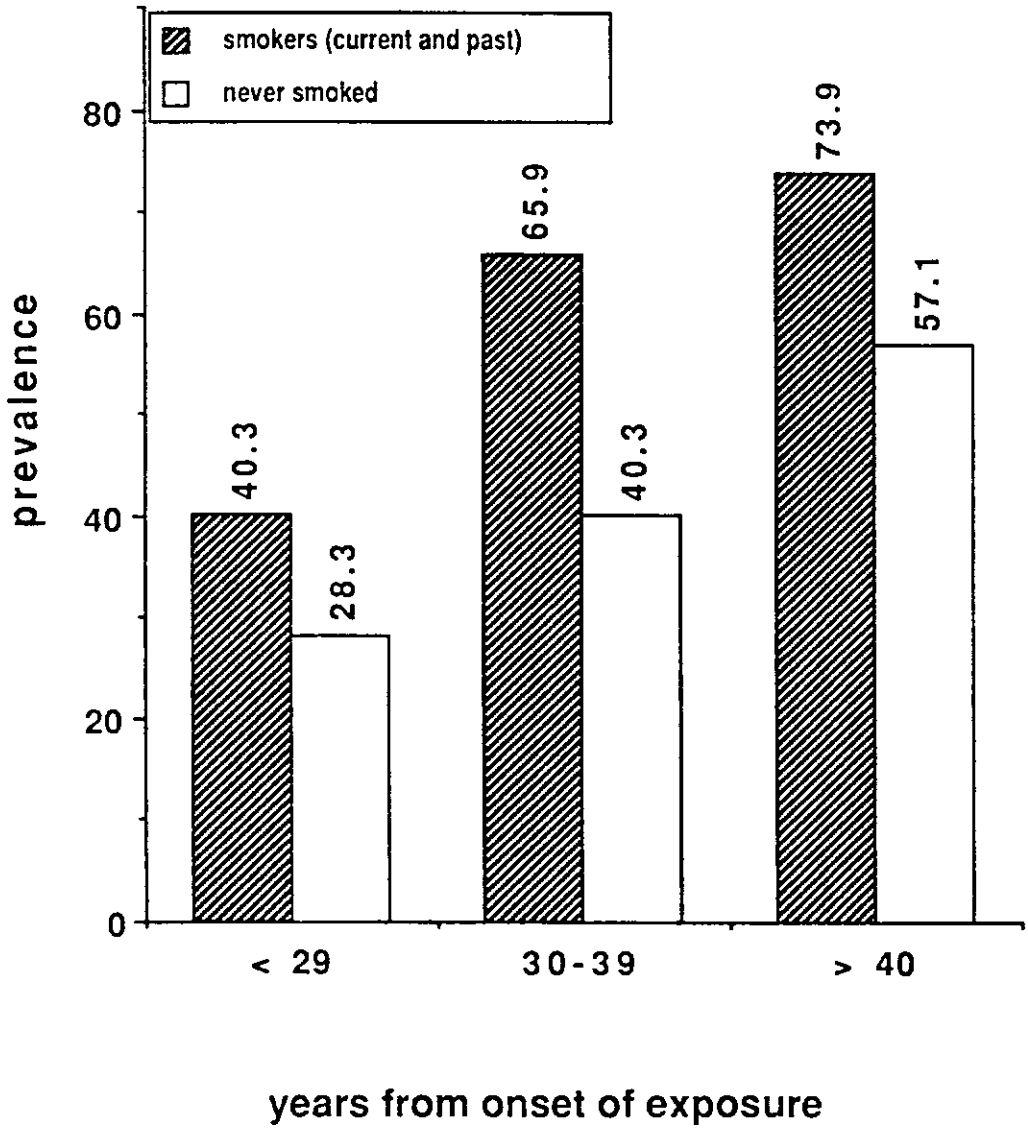

Figure 1. Interstitial pulmonary fibrosis (parenchymal small opacities) relationship with duration from onset of exposure and cigarette smoking.

Pleural calcifications showed an identical trend; increase of prevalence with DURONSET and no detectable effect of smoking status (Figure 5). Pleural calcifications extent grade 2 and grade 3 steadily increased with profusion of small opacities (Table IV).

The prevalence of pleural fibrosis was influenced by time from onset of asbestos exposure; smoking status did not seem to affect the development of pleural fibrosis.

The prevalence of total pleural abnormalities (pleural fibrosis, diaphragmatic plaques and pleural calcifications) increased with profusion of small opacities (Figure 6). Interestingly, more than half (60.3 percent) of those without radiologically detectable interstitial fibrosis (0/0–0/1) had pleural fibrosis.

Cigarette smokers were found to have more interstitial pulmonary fibrosis (as the only finding or associated with pleural fibrosis) than did nonsmokers; pleural fibrosis only was a considerably more frequent finding in nonsmokers than in smokers. Normal chest X-rays were also more frequent in non smokers (Figure 7 and Table V).

Regression techniques were used to assess the significance of the variables age, DURONSET, duration of exposure and smoking on the outcome parenchymal interstitial fibrosis (only and total i.e. associated with pleural fibrosis) and pleural fibrosis (only and total, i.e., associated with parenchymal fibrosis). The significant contribution of smoking to the finding of parenchymal abnormalities was demonstrated (Tables VI, VII). The variable DURONSET was very closely

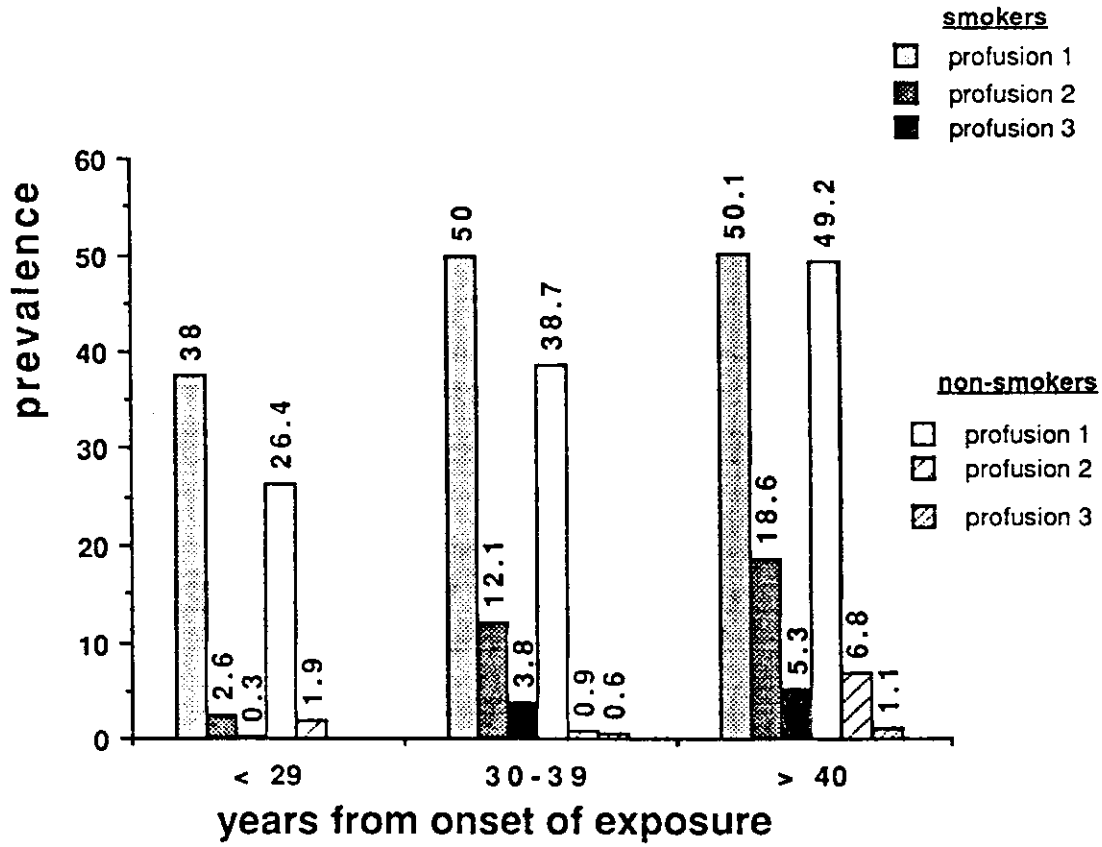

Figure 2. Parenchymal small opacities (profusion) relationship with duration from onset of exposure and cigarette smoking.

correlated with age ($r=0.79$, $p<0.0001$); when age was removed from the model, years since first exposure contributed significantly to parenchymal abnormalities.

Regression analysis demonstrated that, in contrast to parenchymal abnormalities, smoking made no contribution to pleural abnormalities. DURONSET was a significant factor even when age was in the model (Tables IX and X, XI and XII).

The presence and severity of the cardinal symptom of asbestosis, dyspnea on exertion, was assessed by questionnaire (MRC). Prevalence of dyspnea (grade 3 and over) was found to be higher in the subgroup with parenchymal interstitial fibrosis associated with pleural fibrosis than in that with parenchymal fibrosis only, at all three levels of profusion of small opacities (1/0–1/2; 2/1–2/3; 3/2–3/4). The difference in prevalence (Table XIII) was found to be statistically significant ($x2=5.09$, $p=0.024$).

Logistic regression analysis of dyspnea indicated, in addition to the significant contribution of DURONSET and years exposed, that the presence of pleural and parenchymal abnormalities was a significant explanatory variable, although parenchymal abnormalities only was not. The variable profusion of small opacities showed similar relationships, i.e., a highly significant contribution to dyspnea when associated with pleural abnormalities (Tables XIV and XV).

These results indicate that asbestos induced pleural fibrosis significantly contributes to dyspnea.

CONCLUSIONS

Pleural fibrosis is a very frequent effect of asbestos exposure. With lower levels of exposure than those of asbestos insulation workers the ratio of pleural fibrosis prevalence to interstitial fibrosis has been found to be higher.[4,5,6,7,8,9]

The results of this study indicate that pleural fibrosis contributes to dyspnea; this is in concordance with data reported by other investigators.[6,8,10,11,12,13,14] Thus, evidence has accumulated indicating that pleural fibrosis is an asbestos induced pathologic process, which after reaching a certain level/extent, adversely affects respiratory function, resulting in dyspnea.

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Table III

Interstitial Pulmonary Fibrosis (Profusion of Small Opacities) Relationship with Duration from Onset of Exposure and Smoking Status

Years from onset of exposure	Smokers		Never Smoked		
Less than 29 years					
Small opacities Profusion	N	%	N	%	p-value**
grade 1	118	93.0	14	93.3	n.s.
grade 2	8	6.3	1	6.6	n.s.
grade 3	1	0.8	0	_	n.s.
30-39 years					
	N	%	N	%	
grade 1	697	75.9	123	96.1	<0.0001
grade 2	168	18.3	3	2.3	<0.0001
grade 3	53	5.7	2	1.6	0.004
40 + years					
	N	%	N	%	
grade 1	267	67.8	87	86.1	<0.001
grade 2	99	25.1	12	11.9	<0.0001

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Table IV

Pleural Calcifications and Profusion of Small Opacities in Asbestos Insulation Workers with Long Term Exposure

Parenchymal radiologic abnormalities category	Total N	PLEURAL CALCIFICATIONS GRADE 1 N	%	2 N	%	3 N	%	Total N	%
0/0-0/1	1107	89	8.0	160	14.5	91	8.2	340	30.7
1/0-1/2	1306	146	11.2	235	18.0	216	16.5	597	45.7
2/1-2/3	291	37	12.7	61	21.0	69	23.7	167	57.4
3/2-3/4	86	8	9.3	22	25.6	21	24.4	51	59.3
TOTAL	2790	280	10.0	478	17.1	397	14.2	1155	41.4

Table V

Distribution Patterns of Radiographic Abnormalities by Smoking Category

Radiologic Abnormalities	Non smokers N=548		Current smokers N=942		Ex smokers N=1300	
	N	%	N	%	N	%
Parenchymal only	45	8.2	154	**16.3**	126	9.7
Pleura only	199	**36.3**	149	15.8	320	24.6
Parenchyma and Pleura	199	36.3	503	**53.4**	656	**50.5**
Any Parenchyma	244	44.5	657	69.7	782	60.2
Any Pleura	398	72.6	652	69.2	976	75.1
Normal	105	19.2	136	14.4	198	15.2
Age (mean ± SE)	58.7±.373		55.2±.244		58.7±.223	
Years from onset of exposure (mean ± SE)	36.4±.333		33.2±.217		36.0 ±.200	

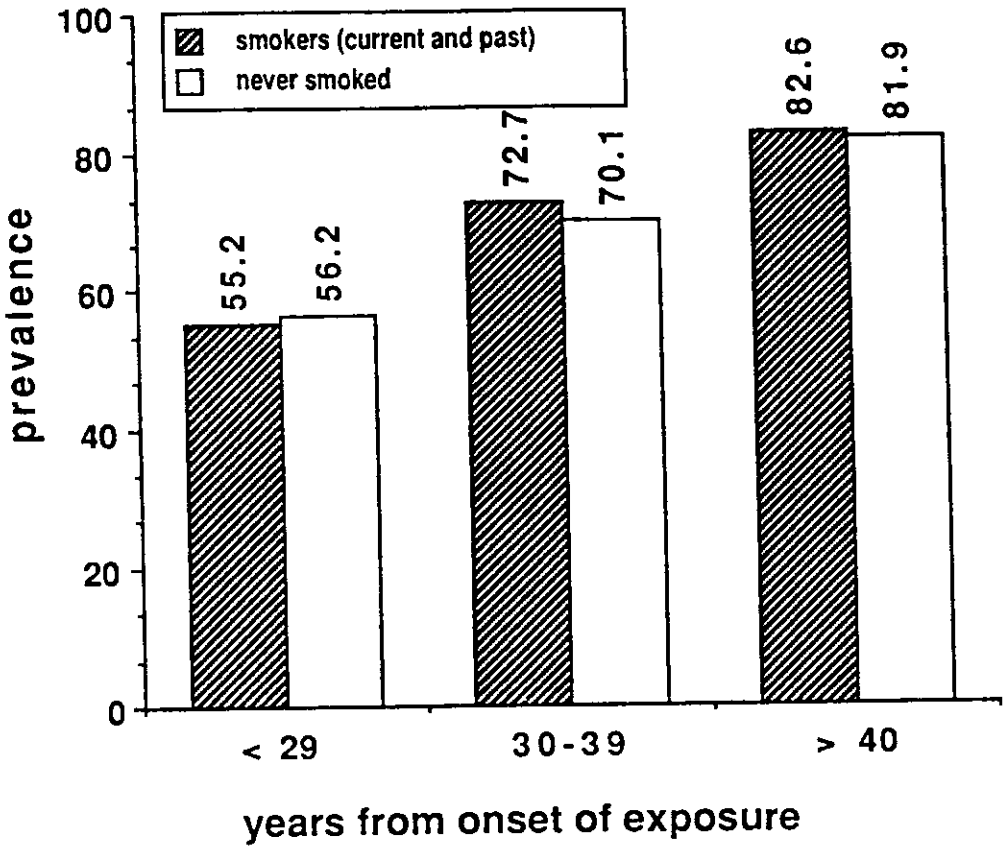

Figure 3. Pleural fibrosis relationship with duration from onset of exposure and cigarette smoking.

Table VI
Logistic Regression Analysis of Parenchymal Abnormalities (Only)

Explanatory Variable	Regression Coefficient (±S.E.)	Chi-square	P-value
Intercept	-4.203 (.557)	57.02	.0001
Age	.054 (.015)	13.17	.0003
Years since first exposure	-.005 (.021)	.06	.8113
Years exposed	.022 (.014)	2.33	.1265
Packyear	.013 (.003)	22.21	**.0001**
MODEL EXCLUDING AGE			
Intercept	-2.80 (.383)	53.33	.0001
Years since first exposure	.047 (.015)	9.13	**.0025**
Years exposed	.017 (.014)	1.53	.2165
Packyear	.014 (.003)	25.23	**.0001**

Table VII
Logistic Regression Analysis of Parenchymal Abnormalities (Total)

Explanatory Variable	Regression Coefficient (±SE)	Chi-square	P-value
Intercept	-3.604 (.315)	130.85	.0001
Age	.0471 (.008)	33.10	.0001
Years since first exposure	.012 (.011)	1.19	.2748
Years exposed	.014 (.007)	4.20	.0404
Packyear	.015 (.002)	90.52	**.0001**
MODEL EXCLUDING AGE			
Intercept	-2.34 (.221)	111.94	.0001
Years since first exposure	.057 (.008)	53.25	**.0001**
Years exposed	.010 (.007)	1.92	.1659
Packyear	.015 (.002)	96.83	**.0001**

Table VIII

Logistic Regression Analysis of Parenchymal Abnormalities* (Profusion Categories)

Explanatory Variable		Regression Coefficient (±S.E.)	Chi-square	P-value
Intercept(	prof0 vs. prof3)	6.656 (.624)	113.85	.0001
	(prof1 vs. prof3)	4.475 (.611)	53.59	.0001
	(prof2 vs. prof3)	.682 (.670)	1.03	.3096
Years since first exposure	(prof0 vs. prof3)	-.102 (.019)	30.22	**.0001**
	(prof1 vs. prof3)	-.053 (.018)	8.58	**.0034**
	(prof2 vs. prof3)	-.023 (.020)	1.25	.2627.
Years exposed	(prof0 vs. prof3)	.012 (.017)	.47	.4908
	(prof1 vs. prof3)	.020 (.017)	1.43	.2313
	(prof2 vs. prof3)	.041 (.019)	4.54	.0332
Packyear	(prof0 vs. prof3)	-.024 (.003)	47.34	**.0001**
	(prof1 vs. prof3)	-.011 (.003)	11.53	**.0007**
	(prof2 vs. prof3)	.00063 (.004)	.03	.8576

* Age excluded from the model

Table IX
Logistic Regression Analysis of Pleural Abnormalities (Only)

Explanatory Variable	Regression Coefficient (±S.E.)	Chi-square	P-value
Intercept	-2.466 (.451)	29.86	.0001
Age	.028 (.013)	4.50	.0338
Years since first exposure	.041 (.017)	5.55	**.0185**
Years exposed	.001 (.011)	.02	.8911
Packyear	.002 (.003)	.39	.5320
MODEL EXCLUDING AGE			
Intercept	-1.784 (.310)	33.06	.0001
Years since first exposure	.068 (.012)	29.29	**.0001**
Years exposed	.00002 (.011)	0.00	.9982
Packyear	-.001 (.002)	.17	.6764

Table X
Logistic Regression Analysis of Pleural Abnormalities (Total)

Explanatory Variable	Regression Coefficient (±S.E.)	Chi-square	P-value
Intercept	-2.392 (.327)	53.57	.0001
Age	.028 (.009)	10.51	.0001
Years since first exposure	.048 (.012)	15.87	**.0001**
Years exposed	.0002 (.008)	0.00	.9797
Packyear	.003 (.002)	2.66	.1026
	MODEL EXCLUDING AGE		
Intercept	-1.646 (.231)	50.70	.0001
Years since first exposure	.076 (.009)	72.49	**.0001**
Years exposed	-.003 (.008)	.10	.7469
Packyear	.003 (.002)	3.58	.0584

Table XI
Logistic Regression Analysis of Radiologic Abnormalities

Explanatory Variable		Regression Coefficient (±S.E.)	Chi-square	P-value
Intercept	(paronly vs. normal)	-4.203 (.557)	57.02	.0001
	(pleonly vs. normal)	-2.466 (.451)	29.86	.0001
	(parpleu vs. normal)	-5.196 (.443)	137.75	.0001
Age	(paronly vs. normal)	.054 (.015)	13.17	.0003
	(pleonly vs. normal)	.028 (.013)	4.50	.0338
	(parpleu vs. normal)	.060 (.012)	31.07	.0001
Years since first exposure	(paronly vs. normal)	-.005 (.021)	.06	.8113
	(pleonly vs. normal)	.041 (.017)	5.55	**.0185**
	(parpleu vs. normal)	.049 (.016)	9.28	**.0023**
Years exposed	(paronly vs. normal	.022 (.014)	2.33	.1265
	(pleonly vs. normal)	.001 (.011)	.002	.8911
	(parpleu vs. normal)	.013 (.016)	1.70	.1919
Packyear	(paronly vs. normal)	.013 (.014)	22.21	**.0001**
	(pleonly vs. normal)	-.002 (.003)	.39	.5320
	(parpleu vs. normal)	.014 (.010)	37.27	**.0001**

Table XII
Logistic Regression Analysis of Radiologic Abnormalities

Explanatory Variable		Regression Coefficient (±S.E.)	Chi-square	P-value
Intercept	(paronly vs. normal)	-2.798 (.383)	53.33	.0001
	(pleonly vs. normal)	-1.78 (.310)	33.06	.0001
	(parpleu vs. normal)	-3.420 (.307)	124.50	.0001
Years since first exposure	(paronly vs. normal)	.047 (.015)	9.13	.0001
	(pleonly vs. normal)	.067 (.012)	29.29	.0001
	(parpleu vs. normal)	.113 (.012)	91.38	.0001
Years exposed	(paronly vs. normal)	.017 (.014)	1.53	.2165
	(pleonly vs. normal)	.00002 (.011)	0.00	.9982
	(parpleu vs. normal)	.008 (.010)	.53	.4660
Packyear	(paronly vs. normal)	.014 (.003)	25.23	.0001
	(pleonly vs. normal)	-.001 (.002)	.17	.6764
	(parpleu vs. normal)	.014 (.002)	42.45	.0001

Table XIII

Dyspnea on Exertion (MRC Grade 3 and Higher) and Profusion of Parenchymal Small Opacities (with and without Associated Pleural Changes)

Chest x-ray Profusion of small opacities	Parenchymal changes only			Parenchymal and Pleural changes		
	Total N	Dyspnea gr 3 & higher		Total N	Dyspnea gr 3 & higher	
		N	%		N	%
1/0-1/2	282	50	17.7	1024	199	19.4
2/1-2/3	36	8	22.2	255	88	34.5
3/2-3/4	7	1	14.3	79	39	49.4
Total	325	59*	18.2	1358	326*	24.0

* The difference in prevalence statistically significant $x^2=5.09$ $p=0.024$

Table XIV
Logistic Regression Analysis of Dyspnea

Explanatory Variable	Regression Coefficient (±S.E.)	Chi-square	P-value
Intercept	-3.285 (.448)	53.82	.0001
Age	.024 (.010)	6.59	.0103
Years since first exposure	.012 (.012)	0.98	.3222
Years exposed	-.015 (.008)	3.50	.0615
Packyr	.005 (.002)	12.51	.0004
Parenchymal abnormlaities only	-.072 (.220)	.11	.7425
Pleural abnormalities only	-.101 (.086)	1.38	.2409
Pleural and Parenchymal abnormalities present	.244 (.106)	5.32	**.0210**
Profusion of small irreg. opacities (parenchymal abnormalities only)	.002 (.337)	0.00	.9970
Profusion of small irreg. opacities (parenchymal and pleural abnormalities)	.067 (.104)	11.22	**.0001**

Table XV
Logistic Regression Analysis of Dyspnea

Explanatory Variable	Regression Coefficient (±S.E.)	Chi-square	P-value
Intercept	-2.585 (.350)	54.42	.0001
Years since first exposure	.035 (.009)	16.03	**.0001**
Years exposed	-.018 (.008)	5.08	**.0242**
Packyr	.006 (.002)	13.08	.0003
Parenchymal abnormlaities only	-.089 (.220)	.16	.6854
Pleural abnormalities only	-.109 (.086)	1.61	.2038
Pleural and Parenchymal abnormalities present	.236 (.106)	5.00	**.0254**
Profusion of small irreg. opacities (parenchymal abnormalities only)	.00005 (.337)	0.00	.9986
Profusion of small irreg. opacities (parenchymal and pleural abnormalities)	.684 (.103)	43.73	**.0001**

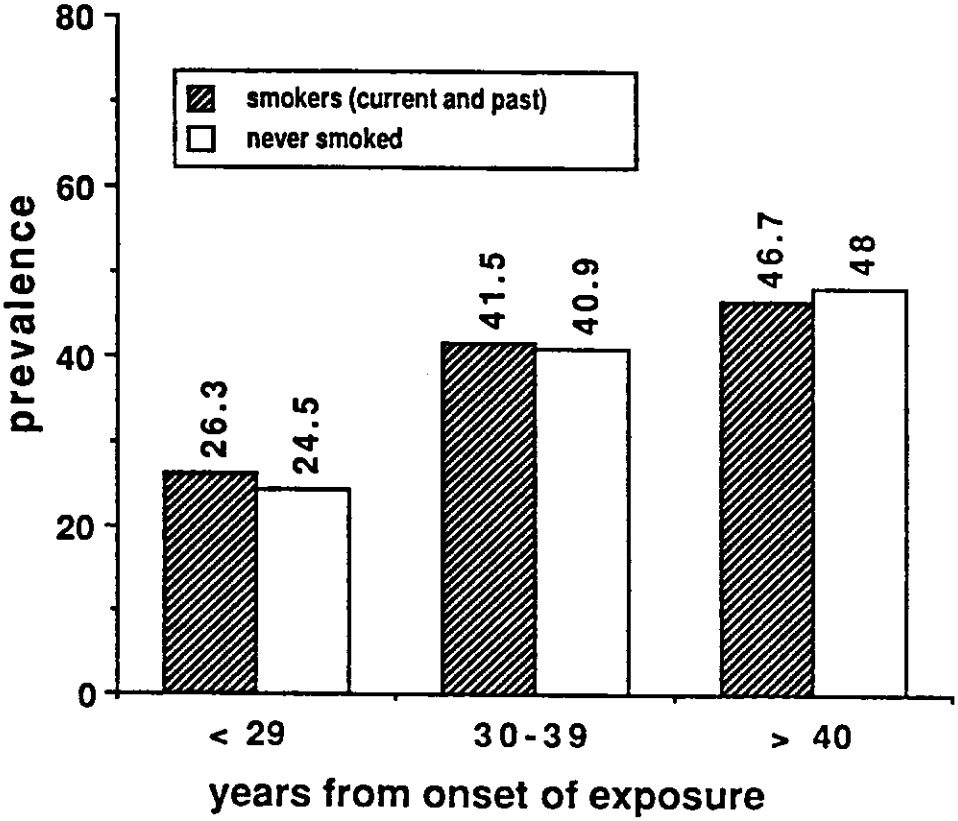

Figure 4. Diaphragmatic pleural plaques relationship with duration from onset of exposure and cigarette smoking.

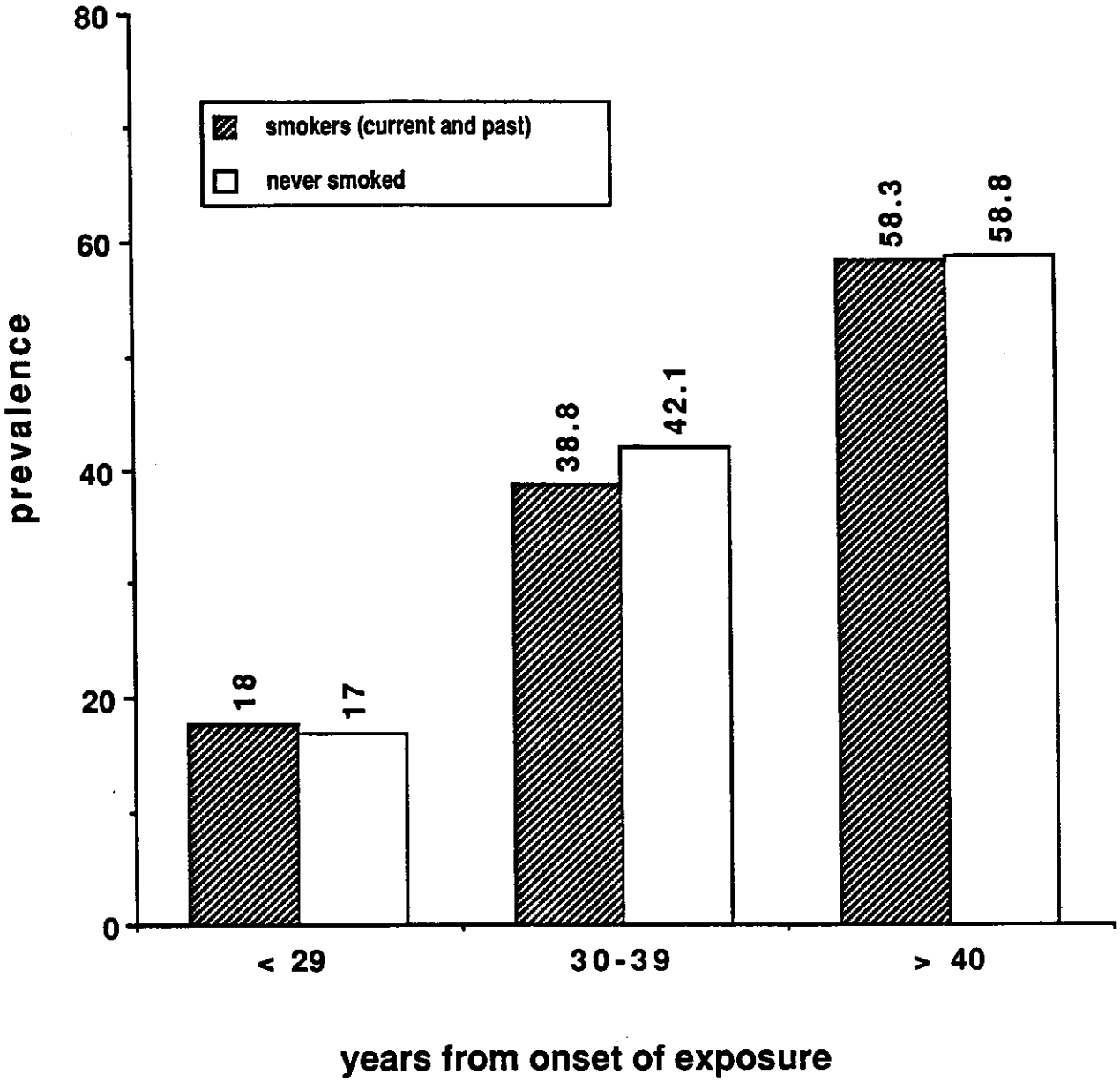

Figure 5. Pleural calcifications relationship with duration from onset of exposure and cigarette smoking.

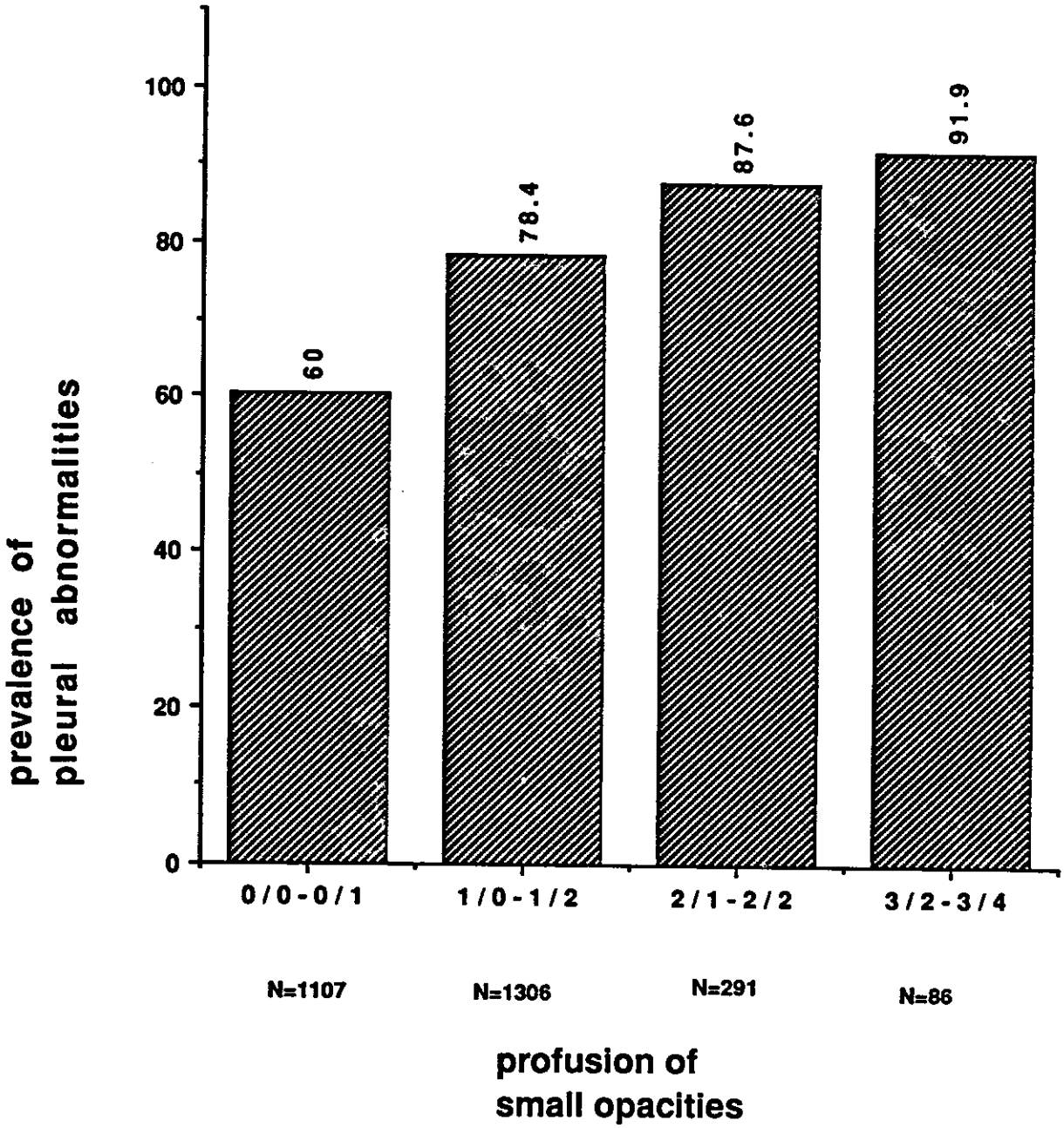

Figure 6. Relationship between interstitial pulmonary fibrosis (profusion category) and prevalence of pleural abnormalities (pleural fibrosis, plaques and calcifications).

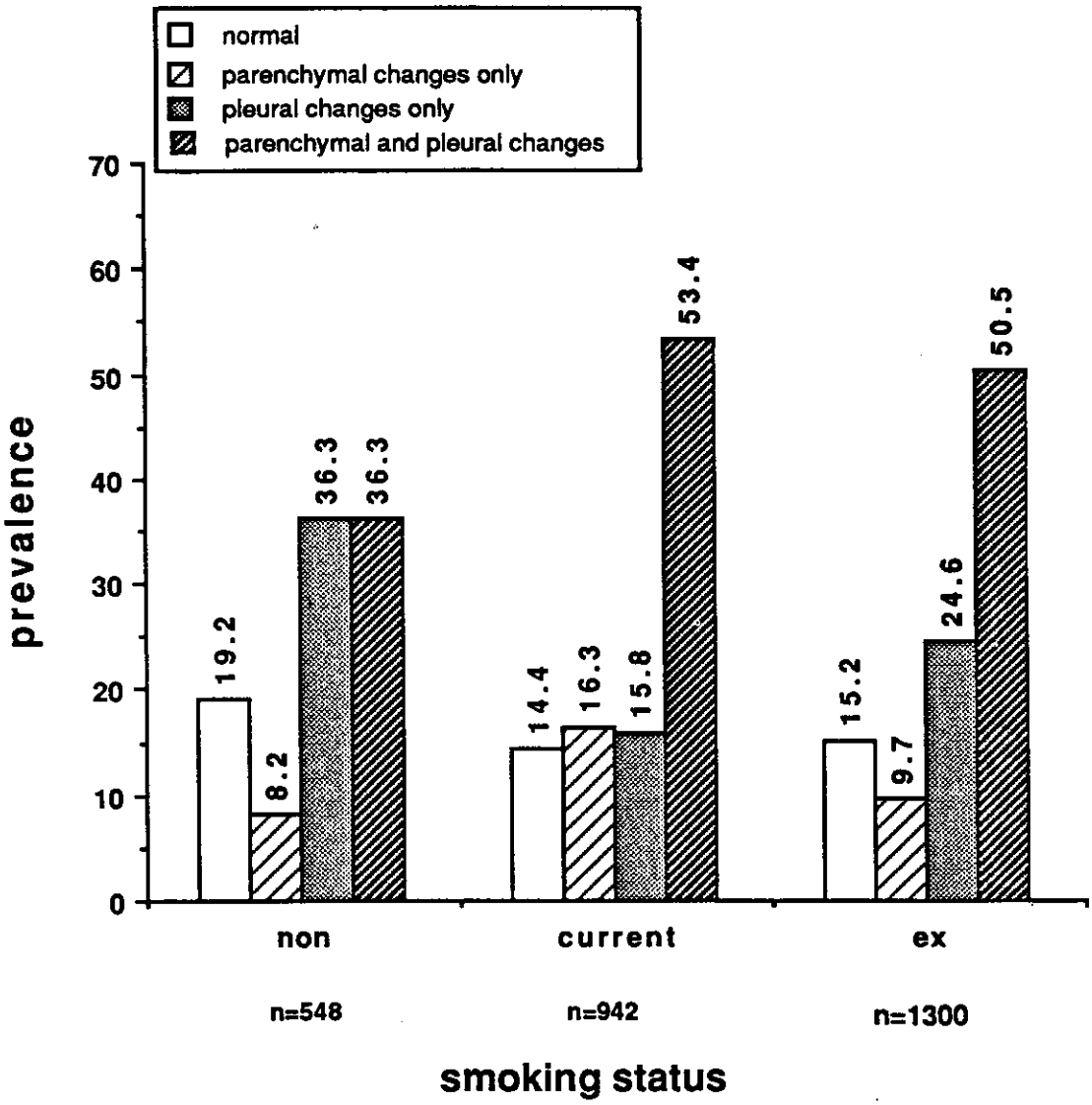

Figure 7. Distribution pattern of radiographic abnormalities by smoking category.

A STUDY ON ASBESTOS-ASSOCIATED LUNG DISEASES AMONG FORMER U.S. NAVAL SHIPYARD WORKERS

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INTRODUCTION

We have had opportunities of studying health conditions of a former U.S. Naval shipyard in Yokosuka, Japan. The examinations were carried out once a year from 1984. All were volunteers who had worked more than 30 years on an average in the U.S. Naval shipyard. The workers except two female workers, who had been engaged in office work, had been exposed to asbestos directly or indirectly. The exposure information was collected through referring to them for working environment and workshops they had belonged to. There were a few subjects who underwent the health examinations four times until 1987. The latest data for the subjects who underwent twice or more were used for the present analysis. During the 4 years there were no remarkable changes in radiographic findings. We will discuss roentgenological manifestations of effects of asbestos dust exposure on the subjects. Each chest radiograph was interpreted according to the International Classification of Radiographs of Pneumoconiosis (ILO/UC).

Distributions of Age and Years Since First Exposure of Asbestos

We studied 248 former U.S. Naval shipyard workers. They were classified into the following two groups (Tables I and II): 1) workers of group A were exposed only in the U.S. Naval shipyard; and 2) workers of group B had been already exposed in other workplaces before employment of the U.S. Naval shipyard. The number of group A workers was 148 and the number of group B was 100. The average age was 62.1 years (61.8 years for group A and 62.6 years for group B). The mean job duration in the U.S. Naval shipyard was 33.2 years (32.0 years for group A and 33.2 years for group B). The job duration of dusty work except the U.S. Naval shipyard for group B was 9.5 years on an average.

Parenchymal Fibrosis

Not only small irregular opacities characteristic of asbestos exposure, but also small nodural opacities were observed to some extent on most of the chest radiographs. It can be considered that these small opacities depended on welding, sandblasting and other dusty work in ship repair and/or building work. Therefore the development of parenchymal fibrosis was interpreted as combined profusion.

We classified all the subjects of groups A and B into 4 subgroups: 1) workers having worked almost always in ships (subgroup 1), 2) workers having had their tasks around ships and/or in factories (subgroup 2), 3) workers having worked both in ships and on shore (subgroup 3), and 4) workers having been engaged in office work (subgroup 4).

The reason why all the subjects were classified into 4 subgroups was based on different intensities of asbestos exposure. Distribution of parenchymal fibrosis by category was as follows: the number of category 1 or more in group A amounted to 136 of 148 persons or 92.0%; the number of category 1 or more in group B also amounted to 96 of 100 persons or 96.0%. 232 persons of pneumoconiosis in groups A and B comprised 119 persons of subgroup 1 (48.0%), 42 persons of subgroup 2 (16.9%), 68 persons of subgroup 3 (27.4%) and 3 persons of subgroup 4 (1.2%).

The prevalence of pneumoconiosis was highest in subgroup 1, followed by subgroup 3, subgroup 2 and subgroup 4 in this order. These data clearly reflected different exposure intensities by subgroup. On the other hand, the prevalence of category 2 was highest in group B (44 persons or 44.0%) and that of category 2 was lower in group A (38 persons or 25.7%). This fact might be related to 9.5 years' work in other workplaces before employment of the U.S. Naval shipyard.

Pleural Abnormalities

Distribution of pleural abnormalities in the subjects is shown in Tables III, IV, and V.

The prevalence of pleural abnormalities by subgroup was similar to the case of parenchymal fibrosis. Pleural abnormalities amounted to 197 of 248 persons or 79.4% and no pleural abnormalities to 51 persons or 20.6%.

The prevalence of roentgenographic pleural abnormalities by age was as follows: number of different kinds of the abnormalities was 1.5 in the age of 70 years or more (18 findings in 12 persons), 1.08 in the age of 60s (194 findings in 175 persons), 0.92 in the age of 50s (54 findings in 59 persons) and 1.0 in the age of 40s (1 finding in 1 person). The prevalence of pleural abnormalities increased with age.

Plaques

Pleural thickening of over 5 mm was adopted as the evidence of plaques in profile. En face plaques were naturally included in the data.

Table I

Distribution of Age and Years Since First Asbestos Exposure in Group A

Age	Years since first asbestos exposure (since onset of employment in US Naval shipyard)						
	<10	10-19	20-29	30-39	40-49	50≦	total
49	0	0	0	0	0	0	0
50-59	1	2	1	28	8	0	40
60-69	1	4	15	81	3	0	104
70	0	0	3	1	0	0	4
	2	6	19	110	11	0	148

Table II

Distribution of Age and Years Since First Asbestos Exposure in Group B

Age	Years since first asbestos exposure at other workplaces before US Naval shipyard						
	<10	10-19	20-19	30-39	40-49	50≦	total
49	0	0	1(1)	0	0	0	1
50-59			0(2)	3(15)	14	0	17(17)
60-69	(1)	(4)	3(5)	8(62)	63(2)	0	74(74)
70		0	1(7)	3(1)	4	0	8(0)
	(1)	(4)	5(15)	14(78)	81(2)	0	100(0)

( )=Years since first exposure in the US Naval shipyard

Table III Group A

	NO pleural abnormalities by category parenchymal fibrosis					Pleural abnormalities by category parenchymal fibrosis					
SUBGROUP	0	1	2	3	Total	0	1	2	3	Total	
1	0	4	3	0	7	3	32	19	2	56	63
2	4	4	2	0	10	0	15	7	0	22	32
3	1	9	3	0	13	3	27	4	2	36	49
4	1	1	0	0	2	0	2	0	0	2	4
Total	6	18	8	0	32	6	76	30	4	116	148

Table IV Group B

SUBGROUP	0	1	2	3	4	Total	0	1	2	3	total	
1	1	2	4	0	0	7	2	27	25	1	55	62
2	1	4	3	0	1	9	0	5	1	0	6	15
3	0	2	1	0	0	3	0	9	10	1	20	23
4	0	0	0	0	0	0	0	0	0	0	0	0
total	2	8	8	0	1	19	2	41	36	2	81	100

Table V Groups A and B

SUBGROUP	0	1	2	3	4	Total	0	1	2	3	total	
1	1	6	7	0	0	14	5	59	44	3	111	125
2	5	8	5	0	1	19	0	20	8	0	28	47
3	1	11	4	0	0	16	3	36	14	3	56	72
4	1	1	0	0	0	2	0	2	0	0	2	4
total	8	26	16	0	1	51	8	117	66	6	197	248

Table VI Group A

	Extent of Parenchymal Fibrosis				
Subgroup	0	1	2	3	total
1	3	36	22	2	63(42.6%)
2	4	19	9	0	32(21.6%)
3	1	36	7	2	49(33.1%)
4	1	3	0	0	4(2.7%)
	12	94	38	4	148(100.0%)

Table VII Group B

	Extent of Parenchymal Fibrosis				
Subgroup	0	1	2	3	total
1	3	29	29	1	62(62%)
2	1	9	4	0(1)*	15(15%)
3	0	11	11	1	23(23%)
4	0	0	0	0	0(0%)
	4	49	44	2(1)*	100(100%)

Table VIII Both Group A and B

	Extent of Parenchymal Fibrosis				
Subgroup	0	1	2	3	total
1	6	65	51	3	125(50.4%)
2	5	28	13	0(1)*	47(19.0%)
3	4	47	18	3	72(29.0%)
4	1	3	0	0	4(1.6%)
	16	143	82	6(1)*	248(100.0%)

*: Large opacities

1. Hyaline plaques

   Interval since first exposure of asbestos appeared to be the factor that determined the prevalence of hyaline plaques. On the other hand, the prevalence rate of hyaline plaques was higher in 50s and 60s age groups than in 70s group. This will be discussed later. A total number of hyaline plaques among the subjects was 76 findings (30.6%).

2. Calcified plaques

   There was no definite relationship between the prevalence of calcified plaques and interval since first exposure of asbestos. However, it was clear that the prevalence of this type of plaques increased with age. A total number of calcified plaques was 60 findings (24.0%).

   A total number of the plaques amounted to 136 findings (54.8%). The prevalence rate of the plaques became higher not only with age but also with duration of the exposure, as shown in Figure 1.

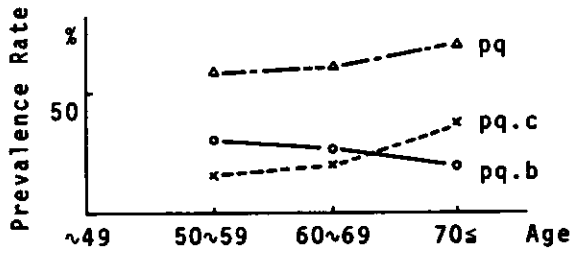

Figure 1. Prevalence of parenchymal fibrosis by exposure.

Radiographic Findings of a Control Group

Of those retired workers registered in an employment agency called "Grey Human Resources Bank" for people of 60 years or more in Yokosuka, 40 persons having not experienced occupational asbestos exposure were examined as a kind of control group in November 1987. The mean age was 67.2 years. 18 persons or 45.0% had no pneumoconiosis changes on their chest X-rays, but 22 persons or 57.0% of the subjects had pneumoconiosis of category 1. A number of pleural abnormalities except tuberculous pleuritis was 12 (30.0%), including 1 person with hyaline plaques, 1 with calcified ones and 6 with costophrenic angle obliterations. 24 persons or 60.0% had no pleural abnormalities on their chest X-rays.

DISCUSSION AND CONCLUSION

The prevalence of the former U.S. Naval shipyard workers with radiographic abnormalities characteristic of asbestos exposure was extremely higher than that of the control group.

The prevalence of parenchymal fibrosis and pleural abnormalities increased with age. Such radiographic changes were also influenced by interval since first exposure of asbestos dust.

The prevalence of pneumoconiosis was also influenced by intensities of asbestos exposure in terms of 4 subgroups.

In the age group of 70 years or more, the prevalence rate of calcified plaques was higher than that of hyaline plaques. The prevalence rate of hyaline plaques was lower in 70 years or more than in 50s and 60s age groups. These are perhaps because hyaline plaques had developed into calcified plaques.

Among the subjects, a case of lung cancer and a case of stomach cancer were found in these four years.

The subjects examined in the present study were only part of the retired workers from the U.S. Naval shipyard. Therefore, it was a tip of an iceberg that was examined by us.

As you know, the U.S. Navy has already adopted stringent occupational health and environmental protection regulations for control of asbestos. However, the Japanese Government is basically responsible for health of Japanese workers employed in the U.S. military facilities in Japan. According to the Pneumoconiosis Law and the Specific Chemical Substance Control Regulation, only those workers of category 3 or more are being followed up after retirement. We strongly insist on a revision of this legislation. For the time being, retired shipyard workers are surely important targets for the specific health examination.

ASBESTOS EXPOSURE, SMOKING AND LUNG CANCER—RESULTS OF A COHORT STUDY IN THE ASBESTOS CEMENT INDUSTRY

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INTRODUCTION

The following paper presents preliminary results of a historical-prospective cohort study which has been conducted in the oldest asbestos-cement factory of the world, in a region in which the diagnoses of death certificates rely on autopsy in every third case of death (Vöcklabruck, Upper Austria). Cohort and reference population have been described earlier.[8,10,11]

BACKGROUND

In Austria asbestos consumption relies on imports which (after exhaustion during World War II) increased to 39.583 (metric) tons in 1973[4] when 28.063 tons (70%) were used by the asbestos cement factory investigated. In 1985 approximately 18.000 tons (90%) of imported asbestos were used by this company.

In Vöcklabruck predominantly chrysotile was used (since 1895). From 1920 to 1977 also crocydolite was used in the pipe factory. Amosite (used for certain products in 1970–1986) played no role for the exposure of employees. The dust supply of asbestos in jute-sacks was stopped in 1960–1970. Open edge mills (kollergangs) were still a major source of exposure up to 1965. Most persons exposed to high levels derived from the period of increased production after 1945, when work was carried out until the mid 60's without appropriate dust removal and high-speed machines had been introduced in the finishing area. A satisfactory extraction of respirable dust was functioning since 1969 and in 1975 a new high-performance dust-suction system was put into operation.

METHODS

From 1950 we found a stabilized population and workforce, and the records for classification of individual exposures. Therefore we included in the cohort all persons employed (for at least 3 years) in the asbestos cement plant Vöcklabruck from 1950–1981. Before 1969 (the decisive year in improving dust situation) 82% of our cohort members had been employed, most of them around 20 years of age, but older persons were also given jobs, especially in the period of full employment. Details of exposure- and age-distributions have been reported.[11] Individual exposures were estimated since 1973 from personal records on duration of exposure at different workplaces, dust level estimations until 1965, dust measurements mainly by conimeter method until 1975 and by personal air samplers and membrane filter method.[1] Independent of the exposure study of the factory carried out by the safety engineers in cooperation with the Austrian Dust and Silicosis Control Office, we sent trained interviewers to all cohort members who had left the plant after 1950 and were still alive in 1982, to obtain data on occupational exposures and smoking by standardized questionnaire. The coding of tobacco exposure was carried out similarly to that of asbestos exposure according to time periods, changing number of cigarettes smoked and tar content. The minimum information "smoker, non-smoker, ex-smoker" was also obtained from deceased persons via relatives and (independently of this) from four work mates.

Completely separated from the exposure enquiries was the follow-up investigation with the government registration offices and the determination of the cause of death with the aid of the death registries, physicians and pathologists.

RESULTS

Of the 2816 persons eligible for the study we found 2155 alive and 540 dead in 1987. 121 persons had been lost, mainly by emigration. Altogether, 51,218 personyears were available for analysis. These included 24,897 observation years above the 40th year of life which are relevant for the assessment of the risk of lung cancer. Table I shows official diagnoses on underlying cause of death from 535 death certificates used for comparison with the general population mortality. The best available information on the main cause of death after enquiries in hospitals, pathological institutes and social insurance are given in brackets. They were used for comparisons within the cohort. Subsidiary causes of death or other important diseases which were diagnosed besides the main disease leading to death are listed under "additional diagnosis."

Lung cancer (SMR 1.7) and stomach cancer (SMR 1.5) were found significantly more frequent than in the general population of Upper Austria corresponding in age and sex. Also pleural and peritoneal cancer occurred more frequently and even if taking into account that some of them turned out to be non-mesotheliomas (e.g., pleuritis carcinomatose in adenocarcinoma of the lung, carcinosis peritonei in pancreatic carcinoma) the 5 cases from best available information (4 of them verified by autopsy and histology) showed an overly high relative risk, since the corresponding rates of histologically verified cases in Austria were found orders of

Table I

STEM-Analysis of Fibrous Adsorption Granulates Containing Sepiolite and Attapulgite

Four samples consisting of relatively long fibres and 1 sample composed of comparatively short fibres were selected; in previous studies (by the use of X-ray diffraction and differential thermoanalysis) 3 of these samples proved to be sepiolite and 2 to resemble attapulgite.

STEM-analysis of adsorption granulates							
main mineralogical component	presence of long fibres	fibre dimensions median values of 100 fibres any length*)			fibre concentr. of any length*)		L ≥ 5 um**)
		L [um]	D [um]	L/D	$x10^9$ [F/mg]	n	$x10^6$ [F/mg]
sepiolite	+	1.0	0.03	26	135	25	12.7
sepiolite	+	1.1	0.04	28	111	54	12.2
attapulgite	+	1.3	0.05	29	71	26	26.4
attapulgite	-	0.7	0.03	20	110	25	1.8
sepiolite	++	1.0	0.03	29	120	68	1240

*) STEM, 29000x
**) TEM, 10000x

magnitude lower.[5,9] Pneumoconioses are registered mainly as additional causes of death. Of the illnesses of the circulatory system the deaths from cor pulmonale are of interest in this connection. The cause of death could not be determined in 5 cases (0.9%). The overall mortality was not significantly higher than in the corresponding general population of Upper Austria (SMR 1.04).

Table II shows the increase in lung cancer in comparison to this age- and sex-corresponding reference population (4 census results and migration-corrected interpolations from births and deaths in years between censuses have been used for calculation of expected). If the calculation of expected values takes smoking habits into account, however, an adjusted SMR of 1.04 results, which is not significantly raised. For this adjustment the age- and sex-specific results of microcensus on smoking in Upper Austria[6] and a lung cancer risk factor 8 times as high as that for non-smokers was used for the smokers.[13] From the lower part of Table II no higher lung cancer rate can be seen in workers who cumulated more than 25 fibers/ml.year. Lung cancers observed in persons with lower cumulative doses included also 2 cases who died after only 4 years of employment.

A life table analysis with best available diagnoses showed the expected differences between smokers and non-smokers: the overall probability of survival of smokers was 1.7% at the end of observation and 64.1% at age 65 (95% confidence interval: 59.6–68.2%). Survival of never smokers was 7.9% and 67.1% at age 65 (confidence 58.9–75.3%). Survival from lung cancer was 78.4% for smokers (93.7% at age 65, confidence 91.0–96.4) and 96.0% for never smokers (99.2% at age 65, confidence 97.7–100.0). These differences were statistically significant (Poisson, $p < 0.01$). The same life table calculation for groups with different asbestos exposures (according to cumulative doses and according to exposure class at begin of work) revealed no systematic relation to the probability of surviving from lung cancer.

DISCUSSION

The excess lung cancer mortality which we found in asbestos cement workers compared to the general population of corresponding age and sex could be explained by the higher tobacco consumption of the workers compared to the general population. An additional influence of asbestos exposure could not be proven up to now. From our sample size we can exclude a relative lung cancer risk of more than 1.34 (Poisson, one-sided). This result is in agreement with those from similar factories and industries using mainly chrysotile[2,12,13] without extreme exposures. Figure 1 compares cumulated doses of 56 deaths from lung cancer and mesothelioma with those of 464 non asbestos associated

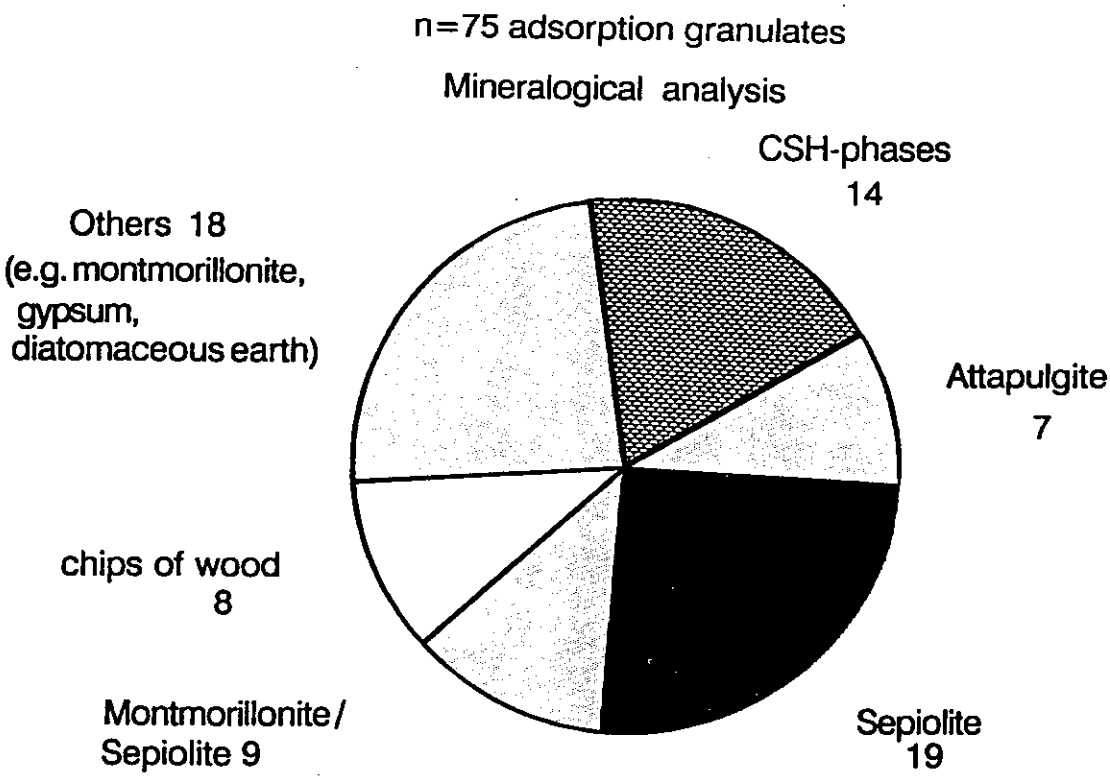

Figure 1. Mineralogical composition of 75 commercially available adsorption granulates used in animal keeping.

deaths. The resulting cumulative frequencies were nearly identical up to a cumulative dose of 50 fibers/ml.year. This result would be compatible with a threshold for lung cancer between 25 and 100 fibers/ml.year[3] and a nongenotoxic action of asbestos on the bronchial epithelium. For mesothelioma, however, asbestos could be a complete carcinogen with much lower fiber doses sufficient to initiate the tumor. The lowest dose we registered in a woman who was only exposed from 1958–1963 to an average of approximately 1 fiber/ml (range up to 10 fibers/ml), corresponding to 5 fibers/ml.year. But she was exposed to crocidolite in pipe production (exposure level staged as "medium"). In a nested case-control study the 4 deaths from mesothelioma verified by autopsy had been matched to 16 controls by sex and as close as possible by year of first employment, length of employment and year of birth. Crocidolite exposure level (disregarding duration) was staged without knowledge of the diagnosis from existing records. All verified mesotheliomas were found to have had medium to high crocidolite exposure whereas controls alive in 1987 had negligible to medium exposures (Table III). The crocidolite exposures of the 4 mesothelioma cases and the 16 matched controls were statistically significant (Miettinen $Chi^2 = 2.8125$, $p < 0.05$). This result is compatible with other studies[2,4] and also with our own experience from a population-based case-control study on 120 verified mesotheliomas in Austria.[5,9] Our results confirm that the absolute risk of mesothelioma in asbestos-cement production is low, but that there is a high relative risk, probably associated with the use of crocidolite.

According to latency we expect some more cases of mesothelioma in our cohort and cannot exclude the occurrence of asbestos induced lung cancers in the near future, because 148 surviving members of our cohort have had exposures of more than 50 fibers/ml.year. But from present working conditions at much lower levels of chrysotile (the use of crocidolite in pipe production has been stopped completely) we do not expect any more occupational cancer in the asbestos cement industry.

SUMMARY

In the oldest asbestos cement factory a historical prospective cohort study set up in the 1970s included all persons employed in 1950-1981 and for at least 3 years. From 2816 persons eligible for the study record-based estimates and measurements of dust and fibers and interview based smoking histories were used to calculate person-related exposures over time. After observation of 51,218 personyears and registration of 540 deaths underlying causes were compared with the regional population on the basis of death certificates.

Lung cancer in asbestos cement workers was raised (SMR 1.7), but not significantly after adjustment for age- and sex-specific smoking habits (SMR 1.04). Using the best available evidence (including autopsy records) 52 deaths were assigned to lung cancer and 5 to mesothelioma. Their cumulated dose-distribution differed from cases not associated with asbestos, for exposures >50 fibers/ml.years. Life table analyses confirmed the predominant influence of smoking on lung cancer.

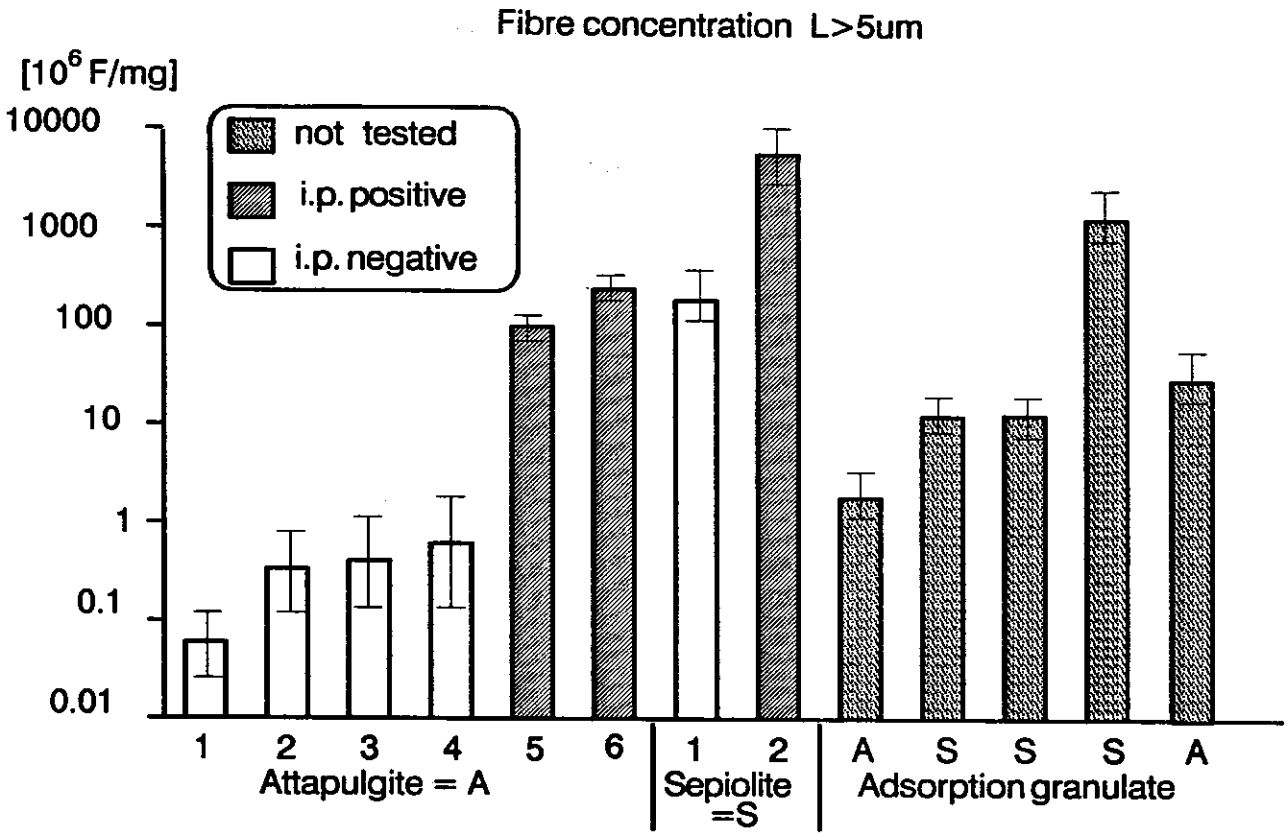

Figure 2. Number of fibres with a length of L ≥ 5 μm in 5 selected adsorption granulates as revealed by TEM at a magnification of 10,000x. Comparison of samples of attapulgite (Georgia 1, 2, Mormoiron 3, Lebria 4, Torrejon 5, Cacéres 6) and sepiolite (Spain 1, Finland 2) examined in animal experiments, c.f.[4]

Mesothelioma was associated with the use of crocidolite in pipe production. A relative lung cancer risk of >1.3 can be ruled out in the given dose-range with predominant use of chrysotile.

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Tables II and III not provided.

PULMONARY FIBROSIS AS A DETERMINANT OF ASBESTOS-INDUCED LUNG CANCER IN A POPULATION OF ASBESTOS CEMENT WORKERS

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INTRODUCTION

It has long been recognized that workers exposed to asbestos are at increased risk of both asbestosis and lung cancer (as well as mesothelioma), and that these effects are dose-related. It is not clear, however, if these two lung diseases are separate, independent consequences of exposure or if asbestos is a lung carcinogen because of its fibrogenicity. Some authors have concluded that, although the evidence is not conclusive, asbestos-induced lung cancer may, in fact, be a complication of asbestosis.[12,2] Others have questioned the plausibility of this view.[5]

Evidence in support of fibrosis being a precursor to asbestos-induced lung cancer includes two studies[9,11] of lung cancer cases among asbestos workers which found high percentages (100% and 90%) to have histologic evidence of fibrosis; one of these studies found 82% to have X-ray evidence.[9] If asbestosis and lung cancer are unrelated processes, then some of the asbestos-related, as well as the smoking-related, cases would be expected to be free of fibrosis.

Elevated lung cancer risk could be the non-specific result of lung fibrosis in general, a view supported by the observation of a considerable lung cancer excess among patients with other fibrotic diseases such as cryptogenic fibrosing alveolitis and pulmonary systemic sclerosis.[13]

Possibly the most important evidence suggesting a relationship between asbestos-induced lung cancer and fibrosis are several studies demonstrating that asbestos workers with lung fibrosis were at increased risk of lung cancer relative to a comparison population.[10,1,6,4,3] The difficulty in making this interpretation, however, is that the asbestotics have generally had greater asbestos exposure than the comparison groups, so that the elevated lung cancer risk may have been due to the exposure; the occurrence of asbestosis may have been a separate, unrelated condition serving primarily to identify a group with substantial asbestos exposure.

The purpose of this study was, therefore, to compare the mortality experience of asbestos workers with and without fibrosis, while accounting for asbestos exposure.

DESCRIPTION OF THE STUDY POPULATION

In 1969, chest X-rays and interviews were obtained on 908 workers in two New Orleans asbestos cement plants.[14] In the current, follow-up study, the 36 women, the 32 men who had retired prior to 1968, and the one man with an unreadable chest film have been excluded, leaving a study population of 839 men. All were employed in 1969 or recently retired.

Exposure information for these two plants has been described elsewhere.[8] Although chrysotile was the primary type of asbestos used in both plants, most of the workers in the current study were also exposed to crocidolite; many of those from Plant 1 were also likely to have had some amosite exposure. Job histories were available and an estimated asbestos profile calculated for each worker.

Mean age for workers from both plants was approximately 45 years, ranging from 21 to 68. Approximately 52% were current cigarette smokers in 1969, 26% ex, and 22% never. The prevalence of cigarette smoking was very similar to the 55% reported for all male U.S. blue-collar workers aged 20–64 in 1970.[7]

X-RAY FINDINGS

Chest films were read in 1972 by three experienced readers using the ILO U/C International Classification for the Pneumoconioses (1971). Median readings were used to classify each film into one of several mutually exclusive X-ray categories (Table I). Films for 79 workers had no large opacities, but had profusion of small opacities of Category 1 or higher (61 Category 1, 18 Category 2 or 3). For 89 workers, the profusion of small opacities was 0/1. A total of 72 workers had no large or small opacities, but had pleural plaques, diffuse pleural thickening or costophrenic angle obliteration (see Table I). Because of the small number, the four workers with large opacities will be excluded from analyses.

Using multiple logistic regression, presence of small opacities (of any profusion level) was found to be related to age ($p < .001$) and cigarette smoking (either pack-years [$p < .001$] or ever/never [$p = .01$]); after accounting for these variables, plant was also a significant factor (a higher prevalence in Plant 2 than in Plant 1, $p < .01$). After these variables, estimated cumulative asbestos exposure was also significant ($p < .001$). The same results were found when analyses were restricted to workers with at least 20 years of follow-up since hire.

Table I
Distribution of Workers by X-ray Category (Median Reading)

Category	Number (%)
No Abnormalities	595 (71%)
Unilateral Costophrenic Angle or Diffuse Pleural Thickening	27 (3%)
Bilateral Costophrenic Angle or Diffuse Pleural Thickening	10 (1%)
Pleural Plaque	35 (4%)
Small Opacities 0/1	89 (11%)
Small Opacities $\geq$1/0	79 (9%)
Large Opacities	4 (0.5%)
	839 (100%)

MORTALITY RESULTS

The mortality experience of this population was first compared to that expected on the basis of Louisiana death rates, using the usual person-years approach. In order to allow for 20 years' latency, each worker began contributing person-years in June, 1970, or 20 years from his hire date, whichever was later.

There were 646 workers with follow-up 20 or more years from hire. Among these, there were 135 deaths, including 26 lung cancers, eight mesotheliomas (another mesothelioma occurred in 1984, after the end of follow-up), and six with asbestosis. All of those with lung cancer were either current or ex-smokers in 1969. Four of these workers had large opacities (including one of the lung cancers), and will not be included in the following analyses. A description of these workers by X-ray category appears in Table II; those with plaques, diffuse pleural thickening and costophrenic angle obliteration have been combined into one group. Differences between those with small opacities and the other workers are as expected based on the X-ray findings reported above. In particular, the 77 with small opacities $\leq$1/0 were slightly older than the 421 with no abnormalities (median ages of 53 and 47, respectively), with a slightly lower percentage of never-smokers, and higher pack-years of smoking. Concerning exposure indices, median years employed were similar, but there was a lower percentage employed for less than 18 years among those with small opacities. Estimated cumulative asbestos exposure, as well as average concentration of exposure, were also somewhat higher.

The ratios of the observed to expected deaths for selected causes for these X-ray groups appear in Table III. Among those with no abnormalities, there was no excess of all malignancies combined or of respiratory cancer, although there were five mesotheliomas. By contrast, among those with small opacities $\geq$1/0, there was a significant excess of cancer, all of it from lung cancer (9 observed, 2.1 expected).

Those with no abnormalities were subdivided into two groups: 244 workers employed less than 22 years (the approximate median duration for this category) and 177 employed at least 22 years. There was no significant excess lung cancer in either group: 5 observed versus 4.5 expected, and 5 observed versus 5.3 expected, respectively. The median estimated cumulative asbestos exposure in the second group was 140 mppcf-yrs, making this group comparable in exposure estimates to those with small opacities $\geq$1/0.

There was a small excess of lung cancer among those with small opacities 0/1 (4 observed, 2.3 expected), but a significant excess of "other" cancers (4 observed, 0.6 expected). Three of these cases (all current or ex-smokers in 1969) listed only cancer as the cause of death, without specification of site; the remaining case, a non-smoker, listed the cause as "generalized abdominal carcinoma," raising the possibility of a mesothelioma.

Since age-specific rates were used to calculate expected numbers, the substantial difference in the lung cancer experience of workers with small opacities $\geq$1/0 and those without abnormalities could not be due to age differences.

Table II

Description of Workers* with Follow-up ≥20 Years, by X-ray Category in 1969

	No Abnormalities	Plaques, etc. No Opacities	Small Opacities 0/1 No Large Opacities	Small Opacities ≥1/0 No Large Opacities
n	421	62	82	77
Age	47	48	51	53
Cigarette Smoking				
Current	48%	45%	52%	47%
Ex	27%	24%	32%	36%
Never	25%	31%	16%	17%
Years Smoked	27	28	29	33
Pack-Years	23.0	26.0	26.3	33.5
Average Packs/Day	.92	.87	.94	1.00
Years Employed	21.6	22.0	22.5	22.6
<18	20%	10%	9%	4%
18–29	76%	85%	82%	91%
≥30	3%	5%	10%	5%
Estimated Average Exposure Concentration (mppcf)	5.0	4.7	5.2	5.8
Estimated Cumulative Exposure (mppcf-yrs)	105	113	123	135
Years of Follow-Up Since Hire	35.6	35.7	36.3	36.0

*medians and percentages

It is unlikely that the small differences in smoking and exposure distributions of these X-ray groups could account for their marked differences in lung cancer mortality. However, in order to explicitly account for these factors, two other methods of analyses were used to analyze the mortality experience of these 642 workers: survival and case-control.

SURVIVAL ANALYSIS

Cox's Proportional Hazards model was used to determine if death due to lung cancer differed between two X-ray groups: those with small opacities ≥1/0 and all other groups combined. The logarithm of pack-years and age were the most significant factors ($p < .01$); after accounting for these factors, only X-ray category was significant (one-tailed $p = .026$). Plant and the various exposure indices were not significant.

To see if the inclusion of never-smokers, none of whom had lung cancer, influenced these results, the analysis was repeated on smokers only; the results were essentially identical.

In these analyses, after accounting for pack-years and age, the estimated relative risk for lung cancer for those with small opacities ≥1/0 compared to the other groups combined was 2.4.

CASE-CONTROL ANALYSIS

Each of the 25 lung cancers occurring 20 or more years after hire (and excluding the case with large opacities) was matched to four controls. For each case, the four controls were selected randomly from the set of all workers who: 1) were approximately the same age as the case (most within one year), 2) were of the same race, 3) were alive when the case died, and 4) were either a current or ex-smoker (since all cases had been smokers).

A description of the cases and controls appears in Table IV. Compared with the controls, the cases had a higher percentage of current smokers (68% versus 58%), had started smoking at an earlier age, on average, and had a higher mean pack-years. Mean durations of employment were similar, but the cases had higher median concentration and cumulative exposure. Concerning X-ray category, the cases had a higher percentage with small opacities ≥1/0 (36% versus 16%), although a slightly lower percentage with 0/1 (16% versus 22%).

Ignoring other factors, the odds ratio for lung cancer from having small opacities ≥1/0 compared with all others combined is 2.95 (84[9]/16[16]).

Table III

Observed and Expected Deaths 20 or More Years After Hire, During 6/1970–12/1983, by X-ray Category in 1969

	No Abnormalities	Pleural Thickening and/or Plaques No Opacities	Small Opacities 0/1	Small Opacities ≥1/0
All Malignancies	22/24.8 88.9	5/3.9 126.8	12/5.7 210.2*	12/5.4 221.5†
Respiratory Cancer	10/ 9.8 102.2	2/1.5 129.7	4/2.3 176.7	9/2.1 424.3†
Other Cancer	** 2/ 2.7 73.1	** 1/0.4 232.0	†† 4/0.6 653.6†	0/0.6 0
Mesothelioma	5	1	2	0

*p < .02 based on Poisson distribution
†p < .01 based on Poisson distribution
**Includes one liver cancer.
††Three with site unspecified; one "generalized abdominal carcinoma".

Multiple logistic regression analysis for a matched design (using the PHLGM procedure in SAS) was used to compare the cases with the controls. The most important factor was pack-years of smoking (p = .01). After pack-years, average concentration of exposure was marginally significant (one-tailed p = .051), as was cumulative exposure (one-tailed p = .062). After accounting for pack-years, concentration, cumulative exposure and cigarette smoking status, X-ray category (small opacities ≥1/0 versus all others combined) was statistically significant (one-tailed p = .024).

In the full model, the estimated odds ratio for lung cancer risk for those with small opacities ≥1/0 was 3.0. If the odds ratio is considered to be an approximate estimate of relative risk, then this estimate is somewhat higher than the estimate of 2.4 obtained in the survival analysis.

DISCUSSION

As would be expected, this population of asbestos cement workers, most of whom had substantial, long-term asbestos exposure, has experienced the major health risks known to be related to asbestos exposure: asbestosis, excess lung cancer and mesothelioma.

The excess lung cancer risk, however, was found to be restricted to those workers with X-ray evidence of asbestosis, as determined by a panel of three independent readers. No excess lung cancer risk was observed among those with no evidence of asbestosis, not even among the sub-group employed at least 22 years, for whom exposure indices were comparable to those with small opacities ≥1/0 on X-ray.

We conclude that the mortality experience of this population supports the view that asbestos is a lung carcinogen because of its fibrogenicity; lung cancers occurring among those without X-ray evidence of asbestosis can be attributed to smoking rather than asbestos exposure. If these findings are confirmed in studies of other asbestos-exposed populations, then workplace exposure levels which are effective in preventing asbestosis would be expected to also prevent detectable increases in lung cancer risk in the future.

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Table IV

Description of the 25 Lung Cancer Cases* Occurring ≥20 Years After Hire and the 100 Matched Controls

	Controls	Cases
Mean Age	53.6	53.7
Cigarette Smoking		
Current	58 (58%)	17 (68%)
Ex	42 (42%)	8 (32%)
Mean Age Started	18.7	16.6
Mean Pack-Years	29.6	40.0
Mean Years Employed	23.1	22.5
Estimated Asbestos Exposure (medians)		
Concentration (mppcf)	4.8	5.8
Cumulative (mppcf-yrs)	115	145
1969 X-Ray Category		
No Abnormalities	55 (55%)	10 (40%)
Pleural Thickening, +/- Plaques	7 (7%)	2 (8%)
Small Opacities 0/1	22 (22%)	4 (16%)
Small Opacities ≥1/0	16 (16%)	9 (36%)

*excluding the case with large opacities on 1969 x-ray

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SMALL AIRWAY IMPAIRMENT FINDINGS AT THE SCREENING OF 639 ASBESTOS WORKERS WITH EXPOSURE HISTORY OF 20 YEARS

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Small airway impairment was observed and first reported by Leuallen and Fowler[3] in 1955 as a sensitive parameter in early detection of expiratory airflow obstruction.

Early pathophysiological findings by Wright and Colleagues[8] stated that inflammation in both respiratory and membranous bronchioles, goblet cells metaplasia of the epithelium in membranous bronchioles are the pathologic features resulting in impairment of FEF_{25-75} volumes.

Not many in literature but few authors investigations postulate that the Small Airway Disease (SAD) represents significant airway obstruction in peripheral bronchioles and such may represent an early manifestations of chronic lung disease when it may be amenable to treatment.

Peripheral airway are the quiet zone and the early insult to this area by offending factors such as mixed solvents, chemical dust, gases, fumes, vapors, moldy hay, moldy air particles, polycyclic aromatic hydrocarbon, man-made fibers were documented.

This concept supported by Petty[7] and coworkers' investigations in small airway impairment and also Myint and Myint[4] postulated the early findings of FEF_{25-75} impairment with mixed chemical exposures.

MATERIALS AND METHODS

This paper intends to discuss the findings of small airway impairment in asbestos workers with different trades. This paper also discusses a crucial point that these workers are exposed to NOT ONLY ASBESTOS but ASBESTOS contaminated with ENVIRONMENT CHEMICALS, COMBUSTIBLE PRODUCTS and many other offending factors as STONE DUST, CEMENT DUST, SO_2 GAS, FIBREGLASS DUST, CIGARETTE SMOKE, GASES AND FUMES.

During the period of 1986–87 asbestos workers with exposure history to asbestos more than 20 years were included in this study. The total of 639 asbestos workers with different trade unions were 200 sheet metal workers, 110 pipefitters, 70 insulators, 120 boiler makers, 60 bricklayers, 70 iron workers, and 20 others were electricians, plasterers, and millwright exposed to asbestos fibers. Among them were cigarette smokers, cigarette non-smokers, and ex-cigarette smokers.

Asbestos screening physicals included vital signs, chest X-ray PA view using International Labour Organization (ILO) Standard criteria technique and interpretation, Pulmonary Function Test (PFT) performed on Jones Pulmonar II in standing position with good effort and cooperation. The Standard Criteria of American Thoracic Society 1979 was used. Results obtained were FVC, FEV_1, FEF_{25-75} and FEV_1-FVC ratios. Predicted values of Knudson were preferred. Due considerations were given to ethnic factor calculation. Seventy-five percent of the predicted value readings was taken as the normal range. The values were corrected to BTPS. The best of at least three spirograms was chosen. Testing was performed by trained and qualified technicians. And the last test included Hemocult Stool Test. The results of these findings were dictated and reported to their attending physician. Many of their union officials distributed education materials on asbestosis and addresses of cigarette smoking cessation clinics were given.

RESULTS

Table I shows number of asbestos workers in different trades and number of cigarette smokers, non-smokers and ex-smokers in each trade. The total numbers of 148 non-cigarette smokers, 336 cigarette smokers and 155 of ex-cigarette smokers were analyzed.

Table II indicates the prevalence of Small Airway Disease (SAD) among asbestos workers who participated in this study. It is interesting to note that those who do not smoke cigarettes; of 154 workers of which 37.01% had Small Airway Disease (SAD). The reading of FVC, FEV_1 and FEV_1-FVC ratios were within normal range in this group of non-smokers. Again cigarette smokers 314 had 50.63% of SAD, whereas ex-smokers of cigarettes 151 shows 40.39% SAD.

Table III information about the incident of asbestosis in chest X-ray profusion between 1/1-3/3 according to ILO Classification of Film 1980. Cigarette smokers have higher incidence of parenchymal scarring as had been previously documented by many researchers on synergistic action of cigarette smoking and asbestos exposure.

Table I

Screening of Asbestos Workers Belonging to Different Unions

UNION	NON SMOKERS CIGARETTES	SMOKERS CIGARETTES	EXSMOKERS CIGARETTES
200 SHEET METAL	40	130	30
50 INSULATORS	16	24	10
110 PIPE FITTERS	23	51	36
120 BOILER MAKERS	27	67	26
60 BRICK LAYERS	19	21	25
70 IRON WORKERS	19	31	24
20 OTHERS ELECTRICIAN, PLASTERER, MILLWRIGHT	4	12	4
TOTAL	148	336	155

Table II

Prevalence of Small Airway Diseases (SAD) Among Asbestos Workers Exposure History Over 20 Years

NON SMOKERS OF CIGARETTES 154	37.01%
CIGARETTE SMOKERS 314	50.63%
EXSMOKERS OF CIGARETTES 151	40.39%

INSULATORS, SHEET METAL WORKERS, PIPE FITTERS, BOILER MAKERS, BRICK LAYERS, IRON WORKERS

Table III
Incident of Asbestosis Classified as 1/1 to 3/3 Reference to ILO Classification Film 1980

CIGARETTE SMOKERS	34.71%
NON SMOKERS OF CIGARETTES	20%
EXSMOKERS OF CIGARETTES	23%

Figure 1 illustrates clearly that due to synergistic action, the less smoking history of cigarettes, the higher the percentage of normal chest X-ray findings among 200 sheet metal workers union members.

Slides I, II, and III show with asbestos suit how they are contaminated with combustion products, grease, and chemicals in removal jobs. One can imagine the beginning of their trade before the stringent regulations the inhalation of various toxic offending factors as mentioned above in addition to notorious asbestos victim.

DISCUSSIONS

Many questions raised in this study were: (1) is this abnormal small airway performance related to asbestos exposure alone or mixed inhalation of offending agents contaminated to asbestos fibers, and in addition to environment where they work exist many factors which can also insult small airway volumes.

The small airway has been shown to be a more reproducible and sensitive measure and it relates closely to the closing volume at which the small bronchioles at the bases of the lungs closed during forced expiration.

Another question raised: (2) is small airway impairment in asbestos exposed populations possibly early sign to observe and prevent chronic lung diseases?

The results of these findings clearly demonstrates that non-cigarette smokers have considerable prevalence of abnormal FEF_{25-75} performance.

Therefore, the insult done to small airways is coming from either asbestos or asbestos fiber coated with other by-product chemicals. One cannot completely rule out that boiler makers were heavily exposed to other irritants such as SO_2, gases, stone dusts, cement dusts. Similarly sheet metal workers are exposed to welding fumes, fibreglass dust in addition to asbestos.

As this study indicates a signal parameter involved. It requires further confirmation before it is assumed that SAD is an early indicator of PFT impairment in asbestos workers, therefore, future epidemiologic studies should be taken with a larger population.

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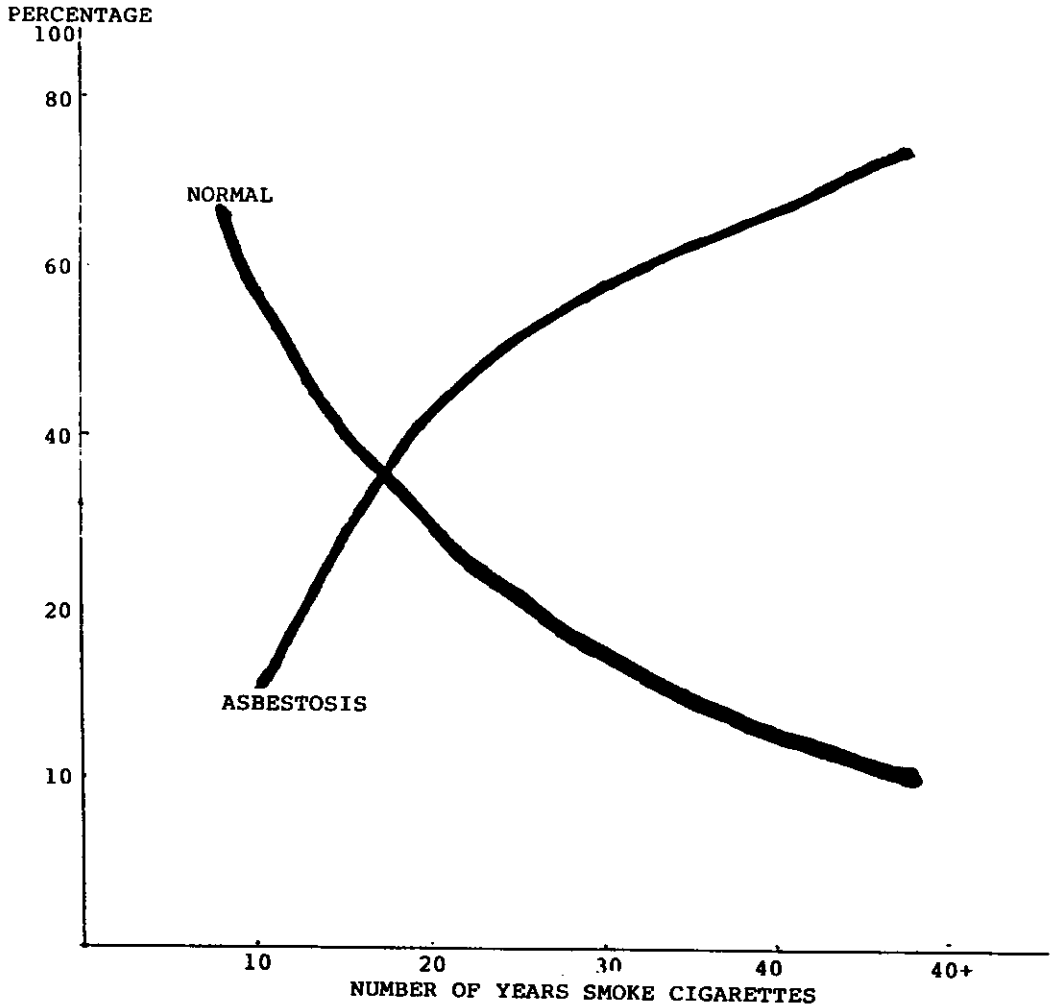

Figure 1. Sheet Metal Workers Union Central Florida, asbestos screening February/March 1987.

Table IV
Prevalent of Small Airway Diseases in Different Asbestos Trades

UNION	NON SMOKERS CIGARETTES SAD	SMOKERS CIGARETTES SAD	EXSMOKERS CIGARETTES SAD
200 SHEET METAL			
50 INSULATORS	16 - 8 - 50%	24 - 9 = 37.50%	10 - 4 = 40%
110 PIPE FITTERS	23 - 9 = 39%	51 - 22 = 43.13%	36 - 17 = 47.22%
120 BOILER MAKERS	27 - 11 = 40.7%	67 - 34 = 50.74%	26 - 8 = 30.76%
60 BRICK LAYERS	19 - 5 = 26.3%	21 - 9 = 42.85%	25 - 12 = 48%
70 IRON WORKERS	19 - = 26.3%	31 - 13 = 41.93%	24 - 7 = 29%
20 OTHERS, ELECTRICIAN, PLASTERER, MILLWRIGHT			
TOTAL	148	336	155

LUNG FUNCTION AND LUNG SYMPTOMS IN RAILROAD EMPLOYEES WITH ASBESTOS EXPOSURE—A 5 YEAR FOLLOW-UP STUDY

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ABSTRACT

175 male employees of railroad service and repair shops were examined in 1981 and 1986 by questionnaire/interview (occup. history, smoking, lung symptoms) and measurement of lung function by Vitalograph. (See other abstract for result of X-ray study).

Asbestos exposure of low to moderate intensity has occurred mainly between 1940 and 1960. On the basis of occupational history a cumulative index of asbestos exposure has been established for each study person. The whole group was divided into 4 exposure groups.

Results: Mean age was 65.1 years. FVC and FEV_1 fell significantly and were negatively related to asbestos exposure. The annual fall for FVC AND FEV_1 was 90 and 86 ml respectively. Smokers had lower lung function values than non-smokers, but the 5-year decrease was not different between the subgroups. Prevalence of dyspnoea (grade 2 and more) was 64% in the highly exposed group against 35% and below in the other exposure groups. Neither cough nor cough and sputum were related to asbestos exposure.

Conclusion: The results support the hypothesis, that asbestos related lung disease might progress even many years after mild to moderate exposure has taken place. The result should however be taken with caution because of the short observation period and the relatively advanced age of the examined men.

No Paper provided.

CHEST RADIOGRAPHS IN RAILROAD EMPLOYEES WITH ASBESTOS EXPOSURE —A 5 YEAR FOLLOW-UP USING ILO 1980 CLASSIFICATION

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INTRODUCTION

Radiological signs of pleural asbestosis indicate previous asbestos exposure. The presence of only pleural changes without fibrosis is generally considered to occur many years after low level asbestos exposure has taken place. A dose-effect relationship for purely pleural asbestosis has not yet been established.

While it is known that pleural changes progress over the years[3] the risk for a higher incidence of parenchymal changes in cases with pleural asbestos is still disputed.

Some authors have suggested that lung fibrosis might develop in patients with pleural asbestosis.[2,6,7] In order to study more closely the above mentioned questions a cohort of railway employees with a previously established history of exposure to asbestos has been examined with a 5 year interval (1981 and 1986).

MATERIAL AND METHODS

In 1978 263 men were selected out of 1192 employees at the repair and maintenance workshops of the Danish Railroads. Among the selected were 87 men who previously had been reported for pleural asbestosis and 176 controls. 209 accepted to participate in the study of 1981, in 1986 there were 175 (84%). Thirteen had died and 21 did not wish to participate again. This report will concentrate on the results of the examination of 175 men in 1981 and 1986.

Exposure to asbestos dust has mostly occurred between 1945 and 1965. An individual index of asbestos exposure had been established in 1981 on the basis of work history concerning 28 different working procedures at the workshops. The exposure index was updated for the 5 year period.

Chest radiographs were made posteroanterior and lateral view) by the same technique in 1981 and 1986. The quality of the films was controlled immediately. If necessary, the radiographic examination was repeated.

Two experienced readers read pairs of the blinded radiographs for each participant. The films were presented on the viewcase at random order. The ILO 1980 Classification of radiographs of the pneumoconioses was used for recording following standard instructions and using standard radiographs for comparison.[5] For each person two columns on the classification sheet were used. Data from the classification sheet were first analyzed for each reader separately. Then the two readers results were compared with each other for each feature on the classification. Only when both readers agreed on bilateral changes for a particular feature it was considered to be a positive finding; otherwise it was considered negative. Small opacities were pathological (fibrosis) with profusion 1/1 or greater in at least both lower zones. For pleural calcifications extent was registered for each site separately.

The combined results were analyzed for prevalence in 1981 and 1986, for 5-year incidence and finally for a possible relation to asbestos exposure index.

RESULTS

Table I shows asbestos exposure index and the distribution into 4 exposure groups in 1981 and 1986. Index 200 corresponds roughly to one year (200 days) of daily asbestos exposure. Only a few participants had been exposed to asbestos after 1981. Groups I and II have had low level, group III and IV high level exposure.

The time period since first exposure was more than 40 years for 32% and more than 30 years for 47% of all men in the cohort. Mean age was 65.1; 72% of the men were between 60 and 70 years old.

Quality

All radiographs were readable. Most were of good, a few of acceptable quality. The pleura was not clearly visible in 2 cases in 1981 and in 1986.

Small Opacities

Table II shows profusion divided into 3 categories for 1981 and 1986, profusion 1/1 to 2/1 belonging to the same category. Profusion of grade 1/1 and higher was found in 7 cases in 1981. Two of these were in 1986 found in category below 1/1 and one of these in a higher category. Sixteen new cases of category 2 were diagnosed in 1986 which means a total of 21 cases of fibrosis in 1986 against 7 in 1981. Table III shows the prevalence of profusion category 2 and 3 in relation to exposure groups. A correlation between profusion of small opacities and increasing dose can be seen. Table IV shows the prevalence of tick (v) for small opacities in the 3 lung zones in 1981 and 1986 distributed among the exposure groups. An increase for middle and lower zones is

Table I

Asbestos Exposure in Railroad Employees. Index and Distribution into 4 Exposure Groups in 1981 and 1986

Exposure group	Asbestos Index	1986 Number of persons	1986 %	1981 Number of persons	1981 %
I	0 - 15	19	10.9	23	11.0
II	16 - 559	62	35.4	81	38.8
III	560 - 3150	68	38.9	74	35.4
IV	3151 - 22000	26	14.8	31	14.8
		175	100.0	209	100.0

Table II

Profusion of Small Opacities in Chest Radiographs of Railroad Employees in 1981 and 1986

		1986 0/- - 1/0	1986 1/1 - 2/1	1986 2/2 - 3/+	1986 N
1981	0/- - 1/0	152	16	0	168
	1/1 - 2/1	2	4	1	7
	2/2 - 3/+	0	0	0	0
	N	154	20	1	175

shown in all exposure groups. Both readers recorded almost exclusively small opacities of irregular type and small size (type s,t). The most frequent letter combination was "s-t" which was registered by both readers 11 times in 1981 and 21 times in 1986.

No large opacities were registered.

Pleural Thickening

The number of positive findings of pleural thickening is presented for 1981 and 1986 in Table V. Bilateral pleural thickening of the diaphragm and of the costophrenic angle was recorded in 18 and 11 cases in 1981 and in 22 and 14 cases in 1986. Special attention was placed on diffuse pleural thickening and pleural plaque, as shown on Table VI. An increase of prevalence for both pleural changes over the 5 year period and a positive relation to exposure, except for exposure group IV was observed. The dose-effect correlation was significant. The recordings of width and extent for diffuse pleural thickening showed an increase between 1981 and 1986 for all symbols a,b,c and 1,2 and 3 respectively. These results were not analyzed more closely.

Table III

Profusion of Small Opacities 1/1 and Higher on Chest Radiographs of Railroad Employees; Prevalence in 1981 and 1986 in 4 Exposure Groups (%); Actual Numbers of Participants in Each Exposure Group

	EXPOSURE GROUPS			
	I	II	III	IV
1981	0	3	3	12
1986	0	10	12	27
N	19	62	68	26

Table IV

Profusion of Small Opacities in Three Zones on Chest Radiographs of Railroad Employees; Prevalence (%) in 1981 and 1986 Among Exposure Groups

	EXPOSURE GROUPS							
	I		II		III		IV	
	81	86	81	86	81	86	81	86
UPPER	0	0	2	2	0	7	8	8
MIDDLE	0	16	5	16	4	20	24	28
LOWER	0	21	8	23	7	28	20	36

Table V

Pleural Thickening on Chest Radiographs of Railroad Employees in 1981 and 1986; Number of Cases

	1981	1986
Pleural thickening diffuse (A)	34	38
Pleural thickening plaque (B)	7	8
Pleural thickening (A) + (B)	14	19
Total pleural thickening	55	65

Table VI

Pleural Thickening on Chest Radiographs of Railroad Employees; Prevalence (%) in 1981 and 1986 Among 4 Exposure Groups

			EXPOSURE GROUPS				
		N	I %	II %	III %	IV %	
Pleural thickening	1981	84	11	36	54	89	***
	1986	102	16	47	65	85	***
Pleural th.diffuse	1981	48	0	16	35	54	***
	1986	57	0	24	43	50	***
Pleural plaque	1981	21	5	10	9	31	*
	1986	27	5	11	13	39	**
N Total		175	19	62	68	26	

Chi² for trend:
*** p = 0.001
** p = 0.003
* p = 0.020

As a rule when pleural thickening was recorded on the lateral chest wall it was always situated in the middle and lower zones.

Pleural Calcifications

The total number of pleural calcifications on the diaphragm and the chest wall recorded in 1981 and 1986 and distributed among exposure groups is shown on Table VII. An increase over the 5-year period as well as a positive relation to exposure can be seen.

Symbols

Only few symbols were recorded, and have not yet been analyzed.

DISCUSSION

For this radiological study severe diagnostic criteria for positive radiological findings were applied. These were in total agreement between readers on individual bilateral changes and a profusion of small opacities of at least 1/1 for the

Table VII
Pleural Calcification on Chest Radiographs of Railroad Employees;
Prevalence (%) in 1981 and 1986;
Distribution Among Exposure Groups

		EXPOSURE GROUPS			
	N	I	II	III	IV
1981	22	0	8	15	27
1986	28	5	8	21	31

diagnosis of fibrosis. Pleural changes and fibrosis were recorded in 58 and 12% respectively of the cohort. Pleural calcifications were found in 16%.

These figures partly confirm the results on radiological changes recorded in railroad employees[6,7] and in other trades with comparable exposure to asbestos.[4,9] In several studies though a higher prevalence of fibrosis was recorded in high exposure groups. The rather high prevalence for pleural changes can be due to the initial selection of cases when the cohort was established.

In this cohort with mainly pleural changes, more than 30 to 40 years after first exposure, a 5-year increase of fibrosis from 7 to 21 cases is surprising. The prevalence and 5 year incidence of fibrosis is clearly dose related (see Table III). This indicates a long latency for the appearance of asbestos related lung fibrosis. Others have suggested the presence of a mild form of lung fibrosis in older patients with pleural asbestosis,[1,8] while it seems to occur extremely seldom as a form of premature aging process according to others.[3]

Lung fibrosis was mostly combined with pleural thickening. But in a few cases it occurred isolated (one case in 1981 and 3 in 1986).

In agreement with other reports some progression of the pleural changes was observed over the 5-year period as well for the number as for the extent and width of pleural thickening and of pleural calcification.[3]

The radiological changes on the lateral chest wall seem to be more suitable for recording and follow-up than the changes on the diaphragm and costophrenic angles.

The dose effect correlation for pleural thickening is noteworthy. The results indicate that progression of pleural changes is most pronounced in the groups with high exposure. There is no explanation for this unusual result which is in contradiction to the generally accepted view that radiological changes in pleural asbestosis are dose independent but related to age and time since first exposure. Age difference between the exposure groups was minimal. Furthermore there was no association between age and exposure index.

The results of this study are only applicable for this selected cohort which—besides an overrepresentation of cases with pleural changes—is characterized by heterogeneity in degree and duration of exposure and by heterogeneity in attrition.[10] Taking these bias into consideration one can expect that the results probably overestimate the true prevalence/incidence of the recorded radiological changes.

CONCLUSION

In a heterogenous cohort of elder railway employees with more than 30 years after first exposure to asbestos dust pleural asbestosis developed in a way similar to what is described by others. Surprisingly the progression of these pleural changes is dose related.

The incidence of fibrosis has increased in this cohort with mainly pleural asbestosis.

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RADIOGRAPHIC PROGRESSION OF ASBESTOSIS WITH AND WITHOUT CONTINUED EXPOSURE

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Early in this century asbestosis in the textile industry was recognized as a rapidly progressive disease, with death often in less than 7 years. By 1933, Merewether,[13] a most astute observer, concluded ". . . since unaltered asbestos fibers also can be found in the lungs years after last exposure, it is evident that asbestos dust trapped in the lungs remains and continues to exert its fibrosis-producing power for at least many years." He was also the first to recognize a latent period: ". . . a certain minimum fibrosis-producing amount, as it were, of asbestos dust must be trapped in the lungs . . . and also a certain "maturation" period must elapse before that amount of fibrosis is developed." Finally, he predicted that ". . . preventive measures which have applied for 17 years . . . have lengthened the period before fibrosis becomes fully developed." Over the next 30 years his observations were confirmed such that by 1964 asbestos-related manifestations generally were not seen less than 20 years after initial exposure.

Asbestosis has been referred to as a relentlessly progressive disease, even after exposure has ceased, a dictum often restated in textbooks, by medical section reports, by commissions and in reviews. Indeed, Gilson,[7] summarizing the 1964 New York Academy Meeting, proposed research to determine whether there is a detectable stage of asbestosis at which progression ceases after removal from dust. Later still, in 1977, Wagner[23] concluded that ". . . at present there is no published evidence that removal from exposure will prevent progression of asbestosis." Recently some studies have suggested that progression is not inevitable.[2,8,16,17,19,22]

During the past 12 to 22 years we have studied prospectively at yearly intervals groups of employees in six plants, to observe the earliest manifestations of pulmonary fibrosis, to study the physiologic effects of pleural disease, and to address the question of progression. When we presented preliminary results two years ago it was noted that the group no longer exposed was older, and had first exposure earlier than the group with continued exposure.[6] Also, questions were raised concerning smoking histories, the prognostic implications of initially low profusion and the incidence of "attacks" as opposed to true profusion. We now present updated results, groups matched for age, years since first exposure, and for smoking habits, and details concerning low profusion and "attacks."

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METHOD

Survey Studies

Annual examination included a medical and detailed occupational history, a physician-administered questionnaire, chest physical examination, forced vital capacity and flow derivatives, single breath diffusing capacity and anteroposterior and lateral chest roentgenograms sometimes supplemented by oblique views.

Radiographic Interpretation

Films were interpreted by two "B" readers only one of whom was aware of the timing and nature of the exposure. Generally, interobserver agreement was good.[11] Recordings since 1980 were made according to the most recent ILO scheme[9] and earlier readings were translated by comparison of standard films.[14,21] Two interpretations were available as described for coalworkers pneumoconiosis.[1,10,15] Prospectively, films were categorized at each visit without recourse to other films, to be referred to as "apart reading." For this project, the entire series of films was displayed in order of date, and profusion recorded once more, this to be called the "side-by-side" reading.

Employment and Exposure

These are summarized in Table I. The shipyards had large employment, occupations generally did not change, and we followed only selected groups such as pipecoverers, shipfitters, welders, guards and painter-sweepers. At the paper plants and asbestos products plant we followed all employees most of whom eventually participated in nearly all of the available tasks. Paper A manufactured mostly filter paper for gas masks, and automotive products; and from 1952 to 1956 they made a non-paper web on a carding machine for cigarette filters.[5] Paper B made mostly gaskets, and Paper C manufactured electrical insulation paper. The asbestos plant specialized in insulation board.

Extent and Type of Exposure

Detailed exposure data were available only for Ship A where

Table I
Survey Plants and Type and Duration of Exposure

Plant	Known Asbestos Exposure Type	Years & Amount	Survey Years First	Total
Ship A: New Naval Ship	Mixed[X]	45-72 < 5 mppft;[#]	1966	19[*]
Ship B: Submarine	Mixed[X]	To 72 Decreasing;[#]	1976	10[*]
Paper A: Filter, Gaskets	Chrocid.	To 72 Severe, None Since	1971	16
Paper B: Filter, Gaskets	Chrys.	61 to Present: Slight;[#]	1973	16
Paper C: Insul. Paper	Chrys.	To 72 Moderate;[#]	1976	12
Plant: Insul. Board	Mixed[X]	To 72 5 mppft,[#]	1970	18

[#] Since 1972 <2 f/cc [*] Selected Groups Not Seen Annually [X] With Amosite

pipecovering exposures had been kept below 5 mppft since 1945.[14] At other plants data available since 1972 indicated exposures below 2 f/cc. Fiber mix at the shipyards and asbestos plant included a good deal of amosite because of U.S. Navy specifications.[4] At Paper A, only crocidolite imported from South Africa and Bolivia was used, and asbestos use was discontinued in 1972.[5] At Paper B and C only Canadian chrysotile was used. Because retired persons and those now employed elsewhere were encouraged to return for examination we were able to follow some persons who were no longer exposed.

Case Selection and Definition

For this study analysis was limited to parenchymal disease. We reviewed "apart readings" of all 1764 persons, and for study of progression we selected only those 522 who had been followed for six or more years (Table II). The others were lost to follow-up, had died, or had been hired more recently. Roentgenograms for this smaller group were then displayed for "side-by-side" readings. "Progression" or "regression" was recorded when there was a 2-step or greater change of the 11-step ILO scale. (We did not use the lowest reading of 0/−.)

RESULTS

Prevalence of Asbestosis

This study confirmed our impression that asbestosis is a disappearing disease. Figure 1 shows that among persons first exposed before 1950, 47.6% had developed fibrosis. This decreased to 18.0% for 1950–1959, and among those first exposed after 1959 only 2.0% had developed asbestosis. Furthermore, among those first exposed during the past 38 years only 1 developed advanced disease. However, even in the group with the shortest follow-up, the earliest exposure was 28 years ago. Asbestosis varied also for different employments. At one extreme, among those first employed at Ship A before 1950, the prevalence to date has been 65%. At the other end of the spectrum, at Paper B and C, with work largely with encapsulated chrysotile, only 6% and 8% respectively had asbestosis and this was always of minimal degree.

Progression and Regression

The 522 persons followed for 6 or more years had a mean age of 52 ± 11 years and were followed for 11 ± 3 years (Table II). Concerning progression, once more the type of employment was important: Worsening of 2 or more steps varied from 3.9% for Paper C to 39.0% for Ship A. Interestingly, among those with no further exposure progression was much more frequent (36%) than among those with continued exposure (9%).

It was suggested that progression was more common among those no longer exposed was because they were 9 years older, had been exposed for 9 more years and were followed 4 years longer (Table II). Therefore we displayed the mean years since first exposure against the percent of cases progressing for each of the 8 groups (Figure 2). There was a striking correlation ($r=0.76$). To exclude this variable, we selected two subgroups matched for age and years since first exposure, with and without further exposure. This matching of 74 pairs greatly reduced the difference with respect to progression, now 30% and 23% respectively (Table III). The remaining difference could be explained from data shown in Table II: The 3 groups that were no longer exposed historically all had had occupations with known heavy exposure, largely as pipecoverers and with crocidolite carding. By contrast, most of those with continued exposure had worked largely with encapsulated chrysotile.

Because smoking may affect progression we matched 60 pairs of smokers and nonsmokers for age and years since first exposure. They also matched exactly for years exposed and for years followed up (Table III). Among the smokers there was a significantly higher proportion who progressed.

A distinction has been made between a situation referred to as "onset," "first appearance of an abnormality," or "at-

Table II

Age, Exposure and X-ray Changes of Group Followed for >6 Years

Plant	Expos.	Total #	6 Plus Yrs.	Last Mean Age	Years First Expos.	Years Follow Up	Radiographic* No Change	Pro-gress	Re-gress
Ship A:	Discont	41	41	58±12	28±10	14±6	24	16 (39%)	1
	Low	148	107	53± 9	24± 8	11±5	80	21 (20%)	6
Ship B:	Low	665	65	51±11	22± 9	7±1	56	1 (2%)	8
Paper A:	Discont	260	66	56± 9	30± 7	14±3	39	24 (36%)	3
Paper B:	Low	306	116	51±13	21±13	11±3	103	5 (4%)	8
Paper C:	Low	163	51	49±12	20± 9	8±1	49	2 (4%)	0
Plant:	Discont	28	22	68± 7	39± 9	11±3	15	7 (32%)	0
	Low	153	54	45±11	16± 8	11±3	47	5 (9%)	2
Mean	Discont	329	129	59± 9	31± 9	14±4	78(61%)	47 (36%)	4 (3%)
Mean	Low	1,435	393	50±11	22±10	10±3	335(85%)	34 (9%)	24 (6%)
Total		1,764	522	52±11	24±10	11±3	413(79%)	81 (16%)	28 (5%)

* "Separate Reading"

Table III

Subgroups Matched for Exposure, Age and Smoking

Exposure	#	Last Mean Age	Yrs. First Expos	Mean Yrs. Expos	Yrs. Follow Up	Radiographic Unchang #	Unchang %	Progres #	Progres %
Matched for age and years since initial exposure									
Discont.	74	57±10	29± 9	19±10	12± 5	52	(70)	22	(30)
Low Level	74	57± 9	29± 9	29± 9	11± 5	57	(77)	17	(23)
Matched for smoking , age and years since initial exposure									
Smokers	60	53±12	25±11	22±11	9± 4	49	(82)	11	(18)
Nonsmok.	60	52±12	25±11	23±11	9± 3	53	(88)	7	(12)

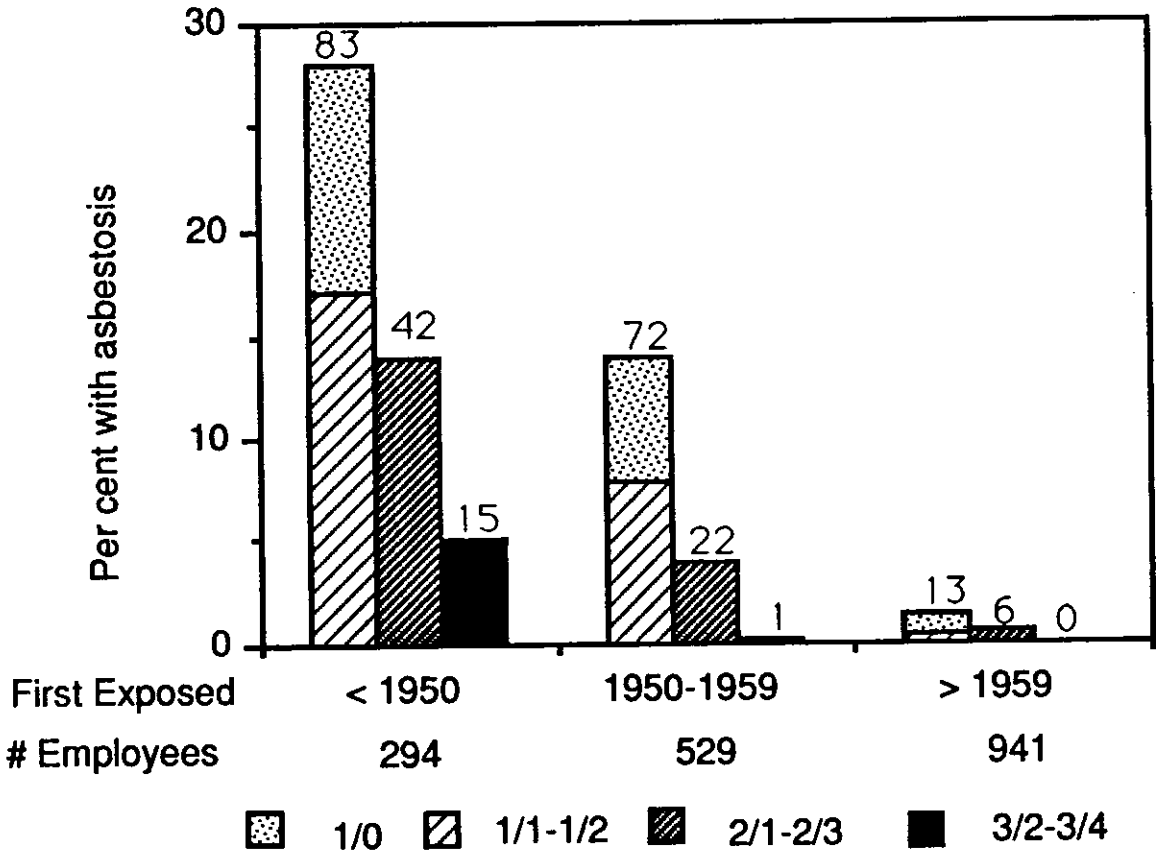

Figure 1. Prevalence and profusion of irregular small opacities at last visit of 1,764 employees seen during industrial surveys. There were 254 (14.4%) with presumed asbestosis. The prevalence decreased from 47.6% for those first exposed before 1950 to 18.0% for 1950–1959, and was only 2.0% for those first exposed during the past 28 years. Exclusion of 1/0 readings would have reduced these three figures to 36.4%, 10.2% and 0.6% respectively.

tack" where the previous film was normal, as opposed to "true progression," that is, a worsening compared to a previous less-than-normal film.[10,15] This is analyzed in Table IV. *Numerically,* "attack" was more frequent (25 vs. 12 for continued exposure, and 31 vs. 17 for discontinued exposure), largely because initially asbestosis was uncommon. However for *percentages* the reverse was true: About one-half of the patients with initially moderate disease progressed.

We defined progression as a 2-step or greater change in the 11-step ILO scale in accord with others.[2] In Table IV, we also compared the frequency of 2-step progression to 3 or more step changes: The two were about equally common, 19 vs. 18 cases for low exposure, and 22 vs. 26 cases for discontinued exposure.

The prognostic significance of different low level readings has been questioned. Table V shows no impressive difference: Among those with continued exposure progression was 15% for 0/1 and 16% for 1/0; and for discontinued exposure these figures were 44% for 0/1 and 30% for 1/0. However, an initial reading of definite minimal asbestosis, that is 1/1, had a somewhat worse prognosis in relation to progression particularly among persons still working.

The possibility of "regression" has been discussed in relation to coalworkers pneumoconiosis.[1,10,15] In other studies of asbestos-exposed persons "regression" was seen sometimes when only 2 films were available for comparison[2] but was not seen when there were serial films.[3] In our series "regression" was recorded in Table II for 28 persons (5%), but our Table II was derived from "apart readings." Subsequently we displayed all annual films for "side-by-side" reading and then there usually was an obvious explanation for an earlier higher reading (Table VI). As a result, for all subsequent analyses we incorporated this group into the "no change" category.

DISCUSSION

The effect of continued low exposure in a shipyard was detailed by Rossiter et al.[16] Their results were comparable to our shipyard experience: During 9 years 25% of laggers and 16% of asbestos sprayers progressed but there was little change among other employees. Other reports of progression all concerned retired miners: Among often briefly ex-

Table IV

"Attack" versus True Progression

(522 Cases Observed ⩾ 6 Years)

Initial ILO	Total Number		Progression: 2 Step # (%)	⩾ 3 Step # (%)	Total # (%)
Continued Low Level Exposure (393)					
0/0-0/1	328	"Attack"	13 (4.0)	12 (3.6)	25 (7.6)
1/0-1/2	56	Progress.	4 (7.1)	5 (8.9)	9 (16.0)
2/1-2/3	9	Progress.	2 (22.2)	1 (1.1)	3 (33.3)
3/2-3/4	0	Progress.	0	-	0
Total	393		19 (4.8)	18 (4.6)	37 (9.4)
Discontinued Exposure (129)					
0/0-0/1	86	"Attack"	15 (17.4)	16 (18.6)	31 (36.0)
1/0-1/2	30	Progress.	2 (6.6)	8 (26.7)	10 (33.3)
2/1-2/3	12	Progress.	5 (41.7)	2 (16.7)	7 (58.4)
3/2-3/4	1	Progress.	0	-	0
Total	129		22 (17.1)	26 (20.2)	48 (37.3)

Table V

"Regression" from Apart Reading

Explanation from "Side-by-Side" Reading	
"Regression" among 522 Cases	28
Technical	
Underexposed, Poor contrast	10
Inadequate Inspiration	3
Pleural Disease	
Regressing Effusion	2
Confusion with Face-on Plaques	4
Decreasing Congestive Failure	3
Progressing Emphysema	3
Decreasing Obesity	2
Comparison Film Lost	1

posed Canadian chrysotile miners, 9.3% showed definite 2-step progression after 17 years,[2] while chrysotile miners in Italy[17] and Corsica,[22] with longer and heavier exposure, showed progression in 32.1% to 46%, respectively. Findings concerning Australian crocidolite miners are obscured by a statistical treatment dealing with "relative rates of progression."[3] Also, their results are not like any others: Median exposure was only 4 months, and asbestosis was sometimes seen only one year after initial exposure. Progression among those who developed asbestosis in 0–9 years was 8 times more common than when fibrosis first appeared after 20 years. Clearly, crocidolite is a bad actor also with respect to asbestosis. Next to fiber type and occupation, years since first exposure was the most relevant variable, and others have found the same.[2,3,8] Most likely this is due to obviously heavier exposure many years ago, and not because of relentless progression of any degree of asbestosis. Most observers[19,22] but not all[8] have found more progression with initially more severe grades of asbestosis. Our finding of more progression among smokers was shared by Rossiter et al.[16] who found progression among 9% of smokers and ex-smokers while there was no progression among 33 nonsmokers. In other smaller series ex-smokers tended to

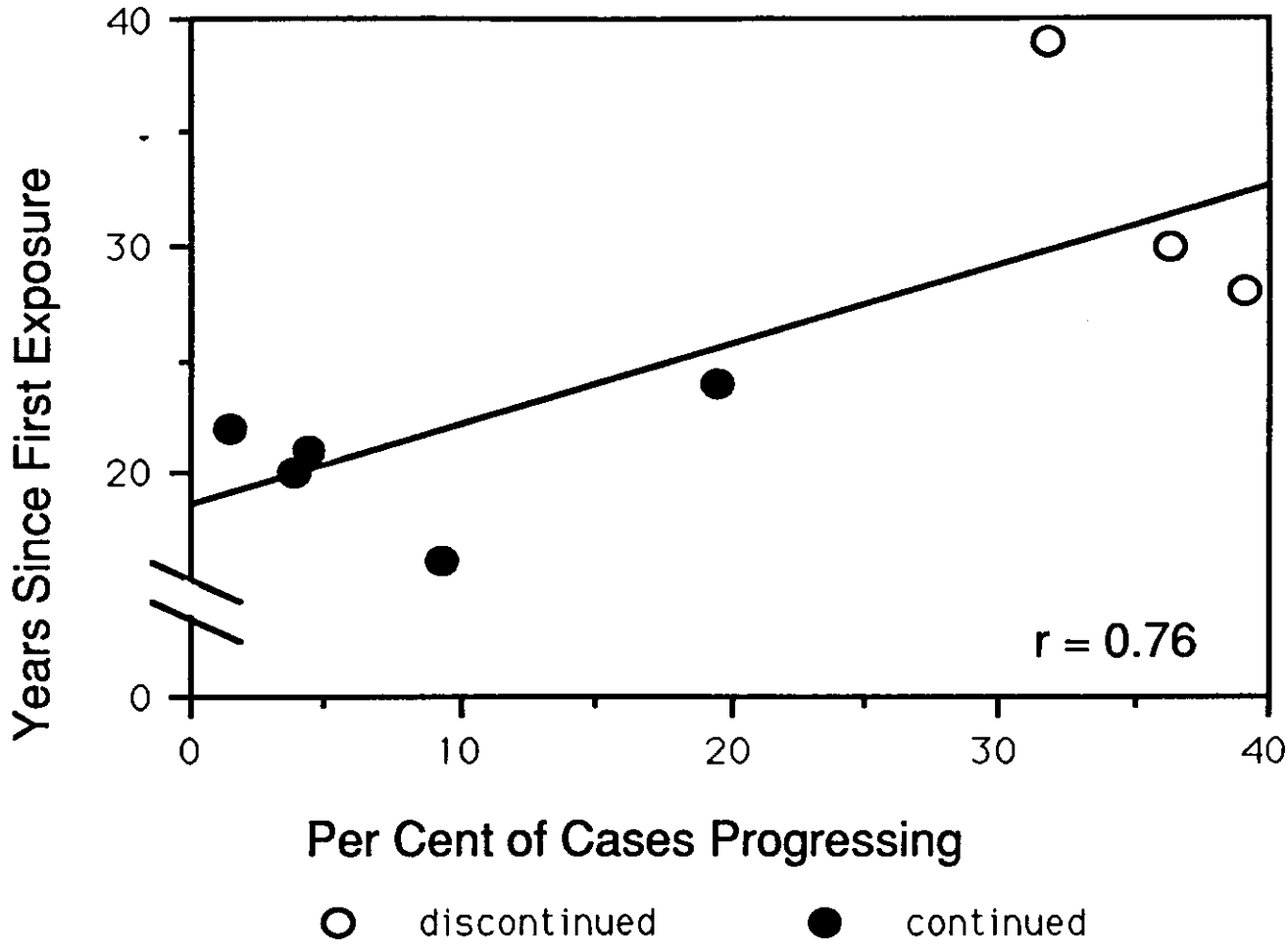

Figure 2. The percent of cases who progressed by 2 or more steps on the 12-step ILO scale during an observation period of 11±3 years are compared to mean years since first exposure for 8 groups of employees. There was much less progression among the 5 groups who continued to have low level (<2 f/cc) exposure during the period, but their first exposure was also more recent than for the 3 groups who had no further exposure.

fare worst.[19,22] A profusion of 1/1 is helpful for diagnosis in the clinical context.[20] Here we have elected a profusion of 1/0 to denote possible minimal fibrosis because this reading may have some significance for epidemiologic studies. However, referring to Figure 1, a profusion of 1/0 accounted for 29% of all of our cases of asbestosis, and a choice of 1/1 to denote minimal disease would have changed our results considerably.

SUMMARY

Asbestosis appears to be a disappearing disease in that the prevalence has decreased from 47.6% with exposure prior to 1950 to 2.0% among those first exposed since 1960. Follow-up averaging 11 ± 3 years of 522 persons indicated progression among 9% of those with continued exposure and among 36% of those with no further exposure. More frequent progression in the latter group was related to both earlier and more severe exposure, and to a slightly longer period of follow-up. "Attack," as opposed to worsening of previous disease, accounted for two-thirds of all cases. Progression rates did not differ with initially low profusion readings of 0/0, 0/1 or 1/0, but a 1/1 reading carried a somewhat worse prognosis. Among 60 pairs matched for age and years since first employment, there was significantly more progression among 60 smokers than 60 nonsmokers.

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Table VI

Prognosis with Initial Low Profusions

Initial ILO	Total #	Progression 2 Step #	(%)	⩾ 3 Step #	(%)	Total #	(%)
Continued Low Level Exposure							
0/0	280	9	(3)	8	(3)	17	(6)
0/1	48	3	(6)	4	(8)	7	(15)
1/0	25	1	(4)	3	(12)	4	(16)
1/1	22	3	(14)	3	(14)	6	(27)
Discontinued Exposure							
0/0	68	11	(16)	13	(19)	24	(35)
0/1	18	5	(28)	3	(17)	8	(44)
1/0	10	0		3	(30)	3	(30)
1/1	15	2	(13)	5	(33)	7	(47)

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THE RELATIONSHIP BETWEEN PULMONARY FUNCTION AND MORTALITY IN MEN SEEKING COMPENSATION FOR ASBESTOSIS

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INTRODUCTION

Exposure to asbestos dust may carry a risk of shortened life expectancy associated with increased mortality rates from respiratory diseases and cancer. A variety of epidemiologic studies have demonstrated dose-response relationships between estimates of personal exposure to asbestos dust, expressed either as cumulative exposures or as time-weighted exposures, and mortality risk.

It may sometimes be desirable to be able to assess the asbestos-associated risk for individuals or groups. Dose-response relationships in the literature may be used to make predictions when it is feasible to calculate estimates of personal or group exposures. For most individuals exposed to asbestos, however, personal exposure records or records of airborne asbestos levels will not exist, and such a calculation will not be possible. In these circumstances, it would be useful if one could find a surrogate for the exposure record for the purpose of prognosis.

It has been demonstrated that the results from two commonly used clinical tests, namely the chest radiograph and pulmonary function tests, are associated with measures of exposure to asbestos dust, with the test result worsening in response to increasing exposure.[1,2] It would thus be expected that these clinical test results might serve as surrogates for missing exposure histories in a mortality dose-response relationship. It has indeed been shown that mortality risk is associated with radiographic scores.[1] It is the purpose of this paper to demonstrate that the results of pulmonary function testing are also predictive of the risk of death from asbestos-associated diseases.

MATERIALS AND METHODS

Subjects in this study were 161 men who had been examined by the physicians of an Advisory Panel to the Ontario Workers' Compensation Board in the years 1962 through 1978, in connection with claims for compensation for asbestosis. Workers were examined in the Laboratory of the Occupational Chest Disease Service of the Ontario Ministry of Labour and underwent medical, radiographic, and pulmonary function examinations. Occupational, medical, and smoking histories were obtained by the examining physician. Any man known to have a malignancy at the time of the index examination was excluded from the present analysis.

Eighty-eight (55%) of the applicants were awarded a disability pension for asbestosis at the time of the index examination, 33 (20%) were awarded a pension at subsequent examinations, and 40 (25%) have not been awarded a disability pension to this date. The results of lung function testing at the time of the initial disability examination provide the data for this analysis.

The claimants were given a standard spirometric examination and the Morris reference equations were used to standardize the results of FVC and FEV_1 for age and height.[3] Workers were followed-up for mortality through the end of 1986. For examination of the association between test results and mortality rates, subjects were divided into 4 groups according to the quartile of the study population in which the test result fell.

Person-years at risk, from the time of the entry examination until death or the end of follow-up, were calculated with the Person-Years computer program.[4] An examination of the age distribution of the person-years at risk indicated that they were similar across pulmonary function quartiles, indicating that a direct comparison of Standardized Mortality Ratios (SMR) was valid. The Person-Years program was thus used to compute SMRs using the general male population of Ontario as the reference population. Poisson regression analysis was used to model the relationships between pulmonary function percentiles and SMRs.[5]

RESULTS

Ninety-nine (61%) of the 161 claimants had worked in the asbestos-cement industry, 38 (24%) had worked as insulators, and the remainder (15%) had worked in a variety of other asbestos-exposed occupations.

The mean age at examination was 54.2 years, with a range from 35 to 75 years. Fifty-eight of the claimants had died by the end of 1986, while 27.9 deaths would have been expected in the general population (SMR = 194).

Table I gives the SMRs for various causes for the 4 quartiles of FVC (Percent Predicted) in the study population. The age distributions are similar in the 4 groups so that the SMRs may be legitimately compared. Most of the subjects were smokers, with only 7% claiming never to have smoked, and the distribution of smokers was similar across the quartiles. There is a monotonic increase in the All Causes SMR across

Table I

The Relationship Between FVC (Percent Predicted) and Mortality Ratios

	GROUP 1 (N=41)			GROUP 2 (N=40)			GROUP 3 (N=40)			GROUP 4 (N=40)		
Mean Age (Standard Deviation)	52.4 (8.6)			54.7 (9.1)			55.8 (8.2)			53.9 (9.5)		
Range of FVC Percent Predicted	84.3 - 125			74.6 - 83.9			64.1 - 74.5			28.5 - 63.9		
Mean FVC% (Standard Deviation)	94.1 (8.9)			78.9 (3.1)			69.5 (3.5)			53.0 (9.4)		
	OBS	EXP	SMR	OBS	EXP	SMR	OBS	EXP	SMR	OBS	EXP	SMR
ALL CAUSES OF DEATH	4	6.45	62	10	9.44	106	19	6.38	298	25	5.68	440
ALL MALIGNANCIES	1	1.84	54	6	2.46	244	9	1.75	514	8	1.49	537
CHEST MALIGNANCIES+	0	0.68	0	3	0.85	353	5	0.64	781	4	0.53	755
ABDOMINAL MALIGNANCIES+	0	0.55	0	3	0.76	396	3	0.54	559	2	0.47	429
RESPIRATORY DISEASES	0	0.35	0	1	0.69	145	4	0.39	1030	10	0.43	2350
CIRCULATORY DISEASES	3	3.13	96	0	4.84	0	4	3.21	125	3	3.27	92

NOTES: +Chest Malignancies includes Lung Cancer and Pleural Mesothelioma

+Abdominal Malignancies includes ICD 150.0 to ICD 159.9

quartiles, with the most spectacular changes occurring in the SMRs for Respiratory diseases. No respiratory deaths were observed in the group with the best FVC while there was a 23-fold excess of respiratory deaths in the group with FVC averaging 53% of predicted.

The relationship between the All Cause SMRs and Mean FVC (Percent Predicted) was modelled with Poisson Regression analysis. There was a strongly significant linear association (Chi-Squared = 24.2; df = 1; $P < 0.001$) and the best fitting equation was:

$$SMR = 834 - 8.36 * FVC\%.$$

There were also strong associations between the Mean FVCs and the SMRs for malignant diseases and respiratory diseases.

The test results for FVC and FEV_1 were highly correlated ($r = 0.86$), so it is not surprising that the findings for the relationships between quartiles of FEV_1 and SMRs had a similar structure (Table II). There was again a highly significant linear association between Mean FEV_1 (Percent Predicted) and All Cause SMRs (Chi-Squared = 25.2; df = 1; $P < 0.001$) and the best fitting equation was:

$$SMR = 787 - 7.27 * FEV_1\%.$$

Various authors have proposed criteria, which combine information from several tests, for grading impairment of pulmonary function. One such proposal appears in the text by Morgan and Seaton.[6] Table III compares the SMRs of those without impairment (Group 1: FVC and FEV_1 *both* at least 80% of predicted) with the SMRs of those with varying degrees of impairment. Group 2 consists of all those not in Group 1. Group 3 consists of those with FVC and FEV_1 *both* 70% or less of predicted and group 4 of those with FVC and FEV_1 *both* no more than 60% of predicted. Groups 2, 3, and 4 are not mutually exclusive and contain overlap in membership. Those without impairment had a favorable mortality experience in comparison with the general population (possibly an example of the "healthy worker effect") while the most severely impaired had a marked increase in mortality rates.

DISCUSSION

This analysis has demonstrated that the results of pulmonary function testing were predictive of mortality risk in a group of 161 men examined because of workers' compensation claims for asbestosis. About half of the claimants were awarded compensation at the time of the index examination while a quarter have not yet been classified as having a disability due to asbestosis. Mortality risk was found to be strongly associated with reductions in FVC and FEV_1 and regression equations were fitted to the data. The risk coefficients are derived from relatively small numbers of men and need to be replicated in other groups of asbestos-exposed workers before the quantitative result can be generalized.

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Table II

The Relationships Between FEV_1 (Percent Predicted) and Mortality Ratios

	GROUP 1 (N=42)			GROUP 2 (N=39)			GROUP 3 (N=40)			GROUP 4 (N=40)		
Mean Age (Standard Deviation)	53.9 (9.3)			54.2 (9.0)			54.2 (8.7)			54.5 (8.8)		
Range of FEV1 Percent Predicted	93.7 - 130			79.8 - 93.5			65.0 - 79.2			26.6 - 64.0		
Mean FEV1 (Standard Deviation)	101.3 (7.5)			86.1 (4.2)			71.1 (4.2)			50.4 (9.2)		
	OBS	EXP	SMR	OBS	EXP	SMR	OBS	EXP	SMR	OBS	EXP	SMR
ALL CAUSES OF DEATH	4	8.90	45	14	6.06	231	15	7.35	204	25	5.64	444
ALL MALIGNANCIES	2	2.42	83	8	1.67	479	7	1.95	359	7	1.50	467
CHEST MALIGNANCIES+	1	0.86	116	5	0.61	820	3	0.69	437	2	0.54	373
ABDOMINAL MALIGNANCIES+	1	0.74	135	1	0.51	196	4	0.60	666	2	0.47	429
RESPIRATORY DISEASES	0	0.58	0	1	0.37	270	4	0.49	816	10	0.35	2864
CIRCULATORY DISEASES	1	4.46	22	2	3.01	67	3	3.73	80	4	2.88	139

NOTES: +Chest Malignancies includes Lung Cancer and Pleural Mesothelioma

+Abdominal Malignancies includes ICD 150.0 to ICD 159.9

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Table III

The Relationships Between Various Impairment Criteria and Mortality Ratios

IMPAIRMENT CATEGORIES NOTE THAT CATEGORIES 2, 3, AND 4 ARE NOT MUTUALLY EXCLUSIVE	GROUP 1 (N=51) FVC PERCENT >= 80 AND FEV1 PERCENT >= 80			GROUP 2 (N=110) NOT GROUP 1 FVC PERCENT AND FEV1 PERCENT BOTH NOT >= 80			GROUP 3 (N=48) FVC PERCENT <= 70 AND FEV1 PERCENT <= 70			GROUP 4 (N=23) FVC PERCENT <60 AND FEV PERCENT <60		
	OBS	EXP	SMR	OBS	EXP	SMR	OBS	EXP	SMR	OBS	EXP	SMR
ALL CAUSES OF DEATH	6	10.43	58	52	17.51	297	26	7.68	339	17	2.94	577
ALL MALIGNANCIES	3	2.84	106	19	4.70	404	9	2.06	437	4	0.75	533
CHEST MALIGNANCIES+	2	1.01	197	7	1.68	417	4	0.74	541	2	0.26	769
ABDOMINAL MALIGNANCIES+	0	0.87	0	8	1.45	552	2	0.64	313	1	0.24	420
RESPIRATORY DISEASES	0	0.68	0	15	1.12	1339	9	0.49	1837	6	0.20	3000
CIRCULATORY DISEASES	2	5.22	38	8	8.86	90	3	3.92	77	2	1.54	129

NOTES: +Chest Malignancies include Lung Cancer and Pleural Mesothelioma

+Abdominal Malignancies include ICD 150.0 to ICD 159.9

ASBESTOS-RELATED DISEASE IN CROCIDOLITE AND CHRYSOTILE FILTER PAPER PLANTS

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Crocidolite first achieved some notoriety with delineation of its relationship to mesothelioma in South Africa.[17] A short time later this tumor was related to other types of asbestos as well. The relative danger of different fibrous minerals has been difficult to establish because for most applications mixtures have been used. Nevertheless, in man there is increasing evidence for a gradient of mesothelioma-producing potential from crocidolite to chrysotile with amosite in an intermediary position,[11] though this issue remains controversial.[14] It may be that this gradient of risk applies not only to mesothelioma, but also to asbestosis and lung cancer, but this has been even more difficult to establish with any degree of certainty.[14]

Some now believe that chrysotile does not ever cause mesothelioma, and that the rare reports of this tumor in miners, or when chrysotile was used alone are the result of tremolite contamination.[3,9,14,15] If there is some difference in activity then most likely it is related to the physical properties of these minerals, and also because chrysotile, unlike the amphiboles, is cleared from the lungs rather quickly.[3,15] In many countries threshold limit values for crocidolite are now lower than for other asbestos, and in some the importation and use has been prohibited entirely.[14]

Mortality from mesothelioma in a few small cohorts briefly exposed only to crocidolite in gas mask manufacture in Canada[12] and Great Britain[1,18] has been higher than with most other exposure. We have found no reports of the effect of pure crocidolite exposure in this country.

Some 28 years ago we encountered two patients with advanced pulmonary fibrosis, a policeman and a wool textile worker. Lung biopsy established the diagnosis of asbestosis.[2,5] Subsequently, both men reported that, 18 years earlier, for a few months, they had worked on a carding machine mixing asbestos cigarette filters. A visit to the plant revealed that from the beginning in 1943, only crocidolite had been used. We embarked upon a longitudinal study of all employees, and, because the same company owned another plant nearby where from the beginning only chrysotile had been used, we were persuaded to follow the employees of that plant as well. Exposure intervals, methods of manufacture, and industrial hygiene at the two plants had differed. Nevertheless, now that the two cohorts have been exposed for a minimum of 15 years, with further longitudinal follow-up for up to 30 years, we believe that a preliminary report may be of some interest at this conference.

METHODS

Clinical Studies

All employees at both plants, including research and supervisory personnel, but not office workers, had detailed medical and occupational histories, chest physical examination and lung function studies including spirometry and single breath diffusing capacity. Frontal roentgenograms were interpreted according to the 1980 ILO scheme by two "B" readers. Details of annual examinations have been described elsewhere at this conference.[4] Interval or subsequent reports of major chest illness or any cancer were confirmed by review of hospital records and X-rays. Pathologic material was reviewed by one of two lung pathologists, Chairman and member respectively of the National Mesothelioma Panel (Dr. C.B. Carrington of Stanford University and Dr. Thomas V. Colby of the Mayo Clinic). We believe that all persons no longer employed because of illness or death have come to our attention. Employees who left for positions elsewhere or retired were invited to return for annual examination but our follow-up in this regard is incomplete.

Exposure

Both plants are small old paper mills in the countryside engaged in the manufacture of specialty and filter papers. *Plant A* was selected in 1943 by the Naval Research Laboratory for an experimental project to make the filters for military masks, and crocidolite was the material of choice. After 1945, filter media continued to be made for civil defense and the Atomic Energy Commission. Around 1952, at the request of a cigarette manufacturer, a British process was developed for the production of filters hoping that crocidolite would remove noxious particles.[6] This was a dry method where asbestos was mixed with cellulose in a carding machine and the resulting web was deposited on crepe paper to form a sandwich. Employees describe a constant blue haze in the room. In 1953, the Massachusetts Division of Occupational Hygiene listed 35 persons engaged in this work at a subsidiary of Plant A, and found safe dust levels of <5 mppft.[16] The cigarette filter project was abandoned in 1956, partly because the Federal Trade Commission prohibited further health claims, and partly because cheaper synthetic fibers were equally effective. Crocidolite continued to be used for air, oil and other filters until 1972 when microglass was substituted for all applications.

At *Plant B*, only Canadian Chrysotile was used beginning

in 1961 and escalating in amount to seven million pounds per year by 1974, largely for manufacture of gaskets. Unlike at Plant A, where crocidolite was delivered in burlap bags and used openly, at Plant B chrysotile was delivered encapsulated in pulp sheets and latex polymer and placed unopened into beaters. Records indicate in all locations less than 2 f/cc since 1971.

RESULTS

Dates and type of exposure are summarized in Table I. At Plant A, we examined at intervals since 1971 a total of 265 persons. Of these we included here only those 136 who had been exposed prior to 1972 when asbestos use was discontinued. These 136 persons were further divided into a *Group I* of 74 who were first exposed 15-27 before 1988 comparable to exposure at Plant B, and a *Group II* of 62 persons first exposed 28–45 years ago (Table I). At Plant B we followed 306 employees from 1971 to 1988, but we included here only those 67 who were first exposed 15–27 years after 1961 when asbestos was first used.

Asbestos-related radiographic abnormalities are indicated in Table II. Comparison of the two more recently exposed groups shows that the crocidolite Group I had 47.3% abnormal findings—14.9% plaques and 32.4% asbestosis, whereas the chrysotile group had only 13.5% asbestos-related changes with 4.5% asbestosis, and this was always minimal. The crocidolite Group II had the worst experience that has ever come to our attention: 95.1% had abnormal radiographs, 14.5% plaques alone and 80.6% asbestosis of which one-third was advanced disease (Table II).

Asbestos-related deaths are detailed in Table III. Again, there was marked difference between the chrysotile group and crocidolite Group I. With chrysotile, there were no deaths from asbestosis, no mesotheliomas and no lung cancers, even though this group was older (58.4 years as opposed to 49.9 years for crocidolite Group I). In the crocidolite Group I there were 10.9% deaths, 3 from asbestosis, 1 mesothelioma and 4 lung cancers. In the older crocidolite Group II, nearly one-half died of asbestos-related disease: 11.9% each of asbestosis and of lung cancer, and 16.4% of mesothelioma. Among the 12 mesotheliomas, 8 were abdominal lesions. Not included is one wife who, like her husband, died of abdominal mesothelioma. The mesothelioma in Group I occurred rather early, 21 years after initial exposure, and the average latent period of 30.1 years for the other 11 in Group II also was rather short. Among the lung cancer patients in Group I, 1 of 4 also had asbestosis and in Group II, 7 of 8 had asbestosis (Table III). Comparing the entire cohorts of plants A and B, there were 25.7% asbestos-related deaths among the crocidolite workers, and none in the chrysotile groups.

Lung function of the two cohorts is compared in Table IV. We included as controls 100 normal men over age 40 with no previous exposure who were seen for pre-employment examinations.[4] Their FVC, FEV_1 and D_L was about 5% lower than the predicted for nonsmokers. Employees of Plant B had function similar to the controls in most respects. For Plant A, all values were about 10% lower. However, several of the retirees with advanced asbestosis could no longer participate in the breathing tests.

DISCUSSION

Evidence concerning a possible gradient of danger of various asbestiform minerals has been reviewed in detail by the Ontario Royal Commission.[14] They introduced their lengthy review of testimony and publications by stating: "There is perhaps no issue related to the health effects of asbestos that has evoked as much debate as the issue of whether the amphiboles, and particularly crocidolite, are more hazardous

Table I
Exposure and Case Selection

Plant A:		
Crocidolite Paper (Wet)	1943-1972	
Crocidolite Web (Dry)	1952-1956	
Micro Glass Only	1973-	
Total Employees Examined (1971-1988)		265
Exposed ≥ 15 Years Before 1988		136
Group I: Exposed 15-27 Years Ago		74
Group II: Exposed 28-45 Years Ago		62
Plant B:		
Chrysotile Paper (Wet)	1961-	
Total Employees Examined (1971-1988)		306
Exposed 15-27 Years Ago		87

Table II
Asbestos-Related Radiographic Abnormalities

Plant A: Crocidolite			
Group I Exposed 15-27 Years Ago (74 Persons)		#	%
Asbestosis 1/0-1/2	(Plaques 10)	15	(20.3)
2/1-2/3	(Plaques 4)	8	(10.8)
3/2-3/4	(Plaques 1)	1	(1.3)
Total Asbestosis		24	(32.4)
Circumscribed Plaques Only		11	(14.9)
Total Abnormalities		35	(47.3)
Group II Exposed 28-45 Years Ago (62 Persons)			
Asbestosis 1/0-1/2	(Plaques 27)	33	(53.2)
2/1-2/3	(Plaques 10)	11	(17.7)
3/2-3/4	(Plaques 5)	6	(9.7)
Total Asbestosis		50	(80.6)
Circumscribed Plaques Only		9	(14.5)
Total Abnormalities		59	(95.2)
Plant B: Chrysotile			
Exposed 15-27 Years (67 Persons)			
Asbestosis 1/0-1/2	(Plaques 2)	3	(4.5)
2/1-2/3		0	(0.0)
3/2-3/4		0	(0.0)
Total Asbestosis		3	(4.5)
Circumscribed Plaques Only		6	(9.0)
Total Abnormalities		9	(13.5)

than chrysotile..." Exclusive use of but one fiber type has been rare and therefore there are few epidemiologic studies suitable for analysis.

It is clear that long-term exposure to "pure" chrysotile rarely causes mesothelioma. For example, among 11,379 long-term chrysotile miners and millers there were only 11 mesotheliomas (0.26% of 4,247 deaths), all of the pleural type.[10] Similarly, multiple studies of a South Carolina asbestos textile workers revealed only 1 possible mesothelioma even though there was a steep linear exposure-response for lung cancer which was 50-fold greater at similar accumulated dust exposures than for the chrysotile miners.[9] There were no deaths from mesothelioma in a large group of Connecticut friction product workers who used only chrysotile.[7]

Experiences with cohorts exposed to products containing amphiboles has been quite different. Admixture of some amosite or crocidolite almost always resulted in a number of deaths from mesothelioma.[13] Insulators have been especially vulnerable with as many as 10% of all deaths due to mesothelioma, often with abdominal lesions predominating. However, there have been only a few small cohorts largely exposed to crocidolite, all in gas mask manufacture.[1,12,18] Our cohort from Plant A differed in many respects from these earlier accounts where exposure was quite brief and stopped in 1945 whereas exposure in our men did not begin until 1943 and continued for 29 years. The origin of the crocidolite also was different: In Great Britain the material came from Western Australia while our plant B ought mostly from Bolivia and sometimes South Africa. Furthermore, in the plants reported previously, both chrysotile and crocidolite was used, and cohorts primarily exposed to crocidolite were reconstructed from historical accounts, while in our plant

Table III
Asbestos-Related and Other Cancer Deaths

	#	%
Plant A: Crocidolite		
Group I: Exposed 15-27 Years Ago (74 Persons)		
Asbestosis	3	(4.1)
Mesothelioma	1	(1.4)
Bronchogenic Carcinoma (With Asbestosis: 1)	4	(5.4)
Total Asbestos Deaths	8	(10.9)
Other CA: 1 Colon, 1 Esophagus,1 Myeloma		
Group II: Exposed 28-45 Years Ago (62 Persons)		
Asbestosis	8	(11.9)
Mesothelioma	11*	(16.4)
Bronchogenic Carcinoma (With Asbestosis: 7)	8	(11.9)
Total Asbestos Deaths	27	(40.3)
Other CA: 1 Esophagus		
Plant B: Chrysotile		
Exposed 15-27 Years Ago (67 Persons)		
Asbestosis	0	
Mesothelioma	0	
Bronchogenic Carcinoma	0	
Total Asbestos Deaths	0	
Other CA: Followup Incomplete		

* Additionally one employee's wife

Table IV
Lung Function, Two Paper Mills

Cohort	No.	Age Yrs.	Exposed Yrs.	FVC %	FEV_1 %	D_L %
Normal*	100	51.8	0	94.5	96.9	95.3
Plant B	67	58.4	20.4	92.5	97.5	98.7
Plant A	136	54.4	27.1	87.0	90.1	85.1

* Unexposed, Pre-employment, Over Age 40

this was the only asbestos ever used. Finally, the earlier reports dealt largely with women, which introduced the confounding factor of cancer of the ovaries while we studied only men.[1,18] Mortality from mesothelioma in these previous reports ranged from 1.1% (6/570) to 2.6% (13/500) among female gas mask assemblers in Great Britain to 4.5% (9/199) in Canada.[1,12,18] The much higher prevalence of 16.4% (11/62) in our group II with similar length of followup probably has several explanations. Exposure of our workers was much longer, and extensive use of carding machines, as opposed to packing and assembling, probably caused more dust.[8,9] Also, previous reports have relied largely on death certificates whereas we had biopsy or autopsy material which sometimes resulted in reclassification to mesothelioma, a factor mentioned by others.[13] Finally, as was true with other crocidolite studies, our followup of workers who left many years ago for other jobs is incomplete, which reduced the total number of persons observed. Because of this preliminary nature of our study we have not attempted to calculate standardized mortality ratios. However, followup has been completed for a cohort of 35 persons making cigarette filters in a subsidiary of Plant A.[16] Among these there were 8 lung cancer deaths for an observed/expected ratio of 13.3, and 5 mesotheliomas for a ratio of 454. The highest mortality from mesothelioma as a percentage of all deaths previously reported has been 16%[12] whereas at our Plant A, where Group II was followed for a similar period, 27.5% (11/40) of all deaths were due to mesothelioma, and two-thirds of deaths (27/40) were asbestos-related.

Previous crocidolite studies have not dealt with radiographs. Serial films in our Group II showed a prevalence of asbestosis of 80.6%, which appears higher than any previously documented, and this may lend some credence to the suggestion that crocidolite is more toxic not only with respect to cancer but also with respect to asbestosis.

Our two groups exposed 15–27 years to crocidolite and chrysotile respectively were quite similar with respect to age, sex, geographic location, manner of yearly clinical examination, and minimum latent period of 15 years. Also, the crocidolite Group I was never involved in the dry carding process because this was discontinued in 1956. (Table I) It was thought that, in selecting two cohorts with latent periods of only 15 to 27 years, and inasmuch as crocidolite Group I had no further exposure after 1972, diseases with a relatively low incidence and long latent period would be excluded in both groups. Nevertheless, there was a striking difference between exposure to the two minerals even during this short period: In the crocidolite group study there were 3 deaths from asbestosis at 17, 17 and 18 years after first exposure, one died of mesothelioma at 21 years, and the 4 lung cancer deaths occurred at 21,23,24 and 26 years. There were no asbestos-related deaths among the chrysotile workers though that group was older, and though exposure continued until last examination in 1988. Thus it appears that, even in these two more recently exposed groups, those exposed to crocidolite had a much worse experience with respect to all three, asbestosis, lung cancer and mesothelioma.

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ASBESTOS RELATED PLEURAL PLAQUES AMONG SEAMEN

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PURPOSE OF STUDY

This study was conducted to investigate the prevalence of asbestos related pleural plaques among seamen. A high prevalence of such plaques has been reported among building and factory boilermen as well as among steam locomotive engineers and repairshop workers.[1,2] We had experienced cases with pleural plaques among engineers on warships also.[3] In 1986, the Collegium Ramazzini headed by I. Selikoff held a symposium on asbestos exposure on merchant ships.

SUBJECTS AND METHODS

An investigation was made of seamen over age 50 who were reported to have worked in uncontrolled environments on board ships and who certainly exceeded the latent period for the development of pleural plaques, which usually manifest 20 or 30 years after the first exposure. Under the life time employment system in Japan, almost all the these subjects had gone to sea soon after leaving school at the age of 18 to 22 depending upon their job. They had received annual X-ray examinations according to government regulations, usually using film size of 100 × 100 mm. Two experienced readers, one of whom was a U.S. B-reader, reviewed blindly all films on five rolls which had been taken in 1983 to code for pleural abnormalities. The films of seamen were identified later from the film ID numbers.

RESULTS

Among 90 members in the engineer group, nine (10%) were found to have plaques. Their duration of work had been 27 to 39 years, average 35 years, except for one whose duration of work could not be determined. (Figure 1) On the other hand, plaques were found in only three (2.0%) out of 136 deckmen and stewards whose duration of work ranged from 28 to 37 years, average 34 years. This difference in prevalence between the two groups was significant ($p < 0.05$). Age-sex-matched positive and negative controls also were investigated. Plaques were found in 20 (13.7%) out of 146 workers at steam locomotive repairshops but in none of the 100 clerical staff of the same company. No pulmonary parenchymal fibrosis was found in any of these workers. The seamen with pleural plaques are listed in Table I by job, age and at the time they had gone to sea. The radiographic patterns are shown in Figure 1. Of the three deckmen with pleural plaques, one had exclusively worked as a wireless radio operator, while the other two had engaged in miscellaneous work before promotion to deckman. The X-ray picture of case #201, an engineer, is shown in Figure 2. He is a 55-year-old-male who had entered the company as a fireman in 1948 and worked for 36 years. Prominent bilateral en face and profile plaques are seen with left diaphragmatic protrusion.

DISCUSSION

The radiological diagnosis of pleural plaques has not been standardized internationally. Some readers record only definite changes while others even the slightest changes. Thought the ILO Classification of Radiographs of Pneumoconioses included the coding of pleural plaques in 1971, of even greater importance is the actual procedures followed in reading the films. To avoid a bias in the results, this study used both positive and negative controls. Even if there were disagreements with the reading criteria used in our study, a comparison of such abnormalities is possible among groups. All of the ships on which these subjects had worked were replaced during the 1960s with ships equipped with modern, remote controlled engine systems. Therefore, exposure to asbestos probably was limited to the period prior to that time when the engineers probably worked in rooms where much of the apparatuses were wrapped with asbestos sheets. In Japan, civil seamen numbers 195,000 in 1960 even though there were only 1,600 civil ships in 1964. (Tables II, III) Though the number of ships decreased, the number of seamen remained stable until the early 1980s when the number increased. The younger seamen were probably less contaminated with asbestos. There has been controversy over the question of whether the pleural plaques increase the risk of lung cancer or mesothelioma. Our previous data on workers in steam locomotive repairshops suggested a somewhat higher incidence of lung cancer in asbestos related workers than in the control group.[4] Older seamen or retired seamen should be followed up carefully in every ocean-going country.

CONCLUSION

A higher prevalence of pleural plaques was found on 100 × 100 mm miniature X-ray films of seamen over the age of 50; in nine (10%) of 90 engineers, and in three (2.0%) of 126 deckmen and stewards. The prevalence among the age-sex-matched controls was found to be 20 (13.7%) out

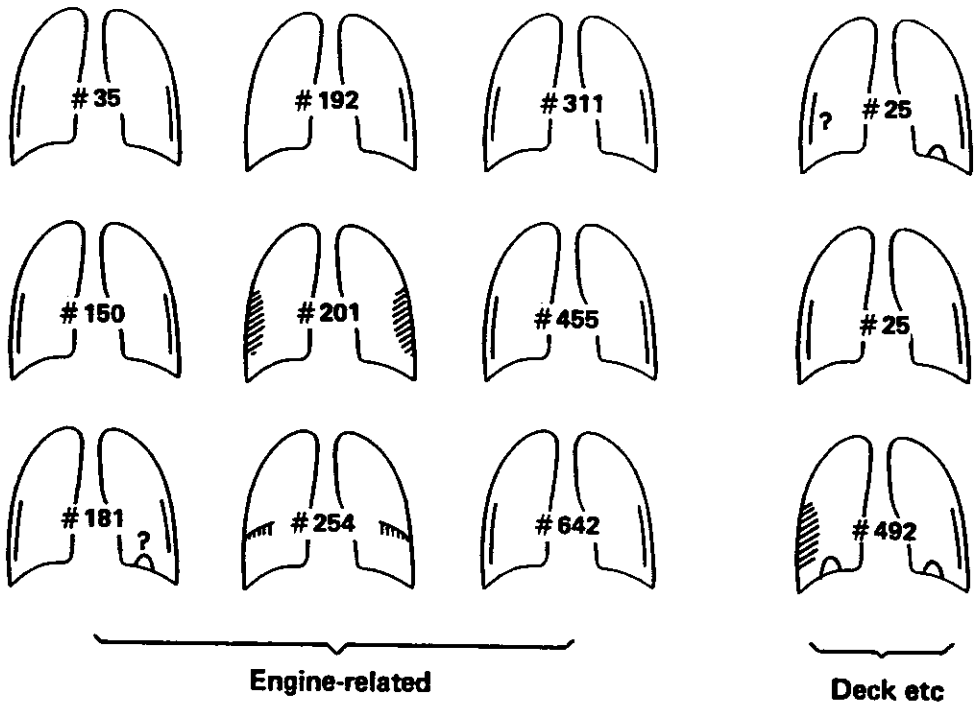

Figure 1. Plaque cases according to jobs.

Table I
Individuals with Pleural Plaques

Job	Film No.	Age (yr)	Work Duration (yr)	Entry to Sea
Engineers	# 35	55	32	1944
	#150	55	38	1944
	#181	55	39	1944
	#192	54	38	1945
	#201	55	36	1948
	#254	54	27	1957
	#311	55	37	1947
	#455	54	36	1947
	#642	54	?	19 ?
Deckmen	# 25	56	37	1944
	#232	54	28	1955
	#492	52	37	1947

Table II
Number of Merchant Marine Ships in Japan

Year	Number
1964	1,600
1970	13,200
1975	14,400
1980	15,100
1985	9,100

Table III
Number of Merchant Marine Seamen in Japan

Year	Number
1960	195,000
1966	94,000
1970	112,000
1975	234,000
1981	187,000
1985	172,000

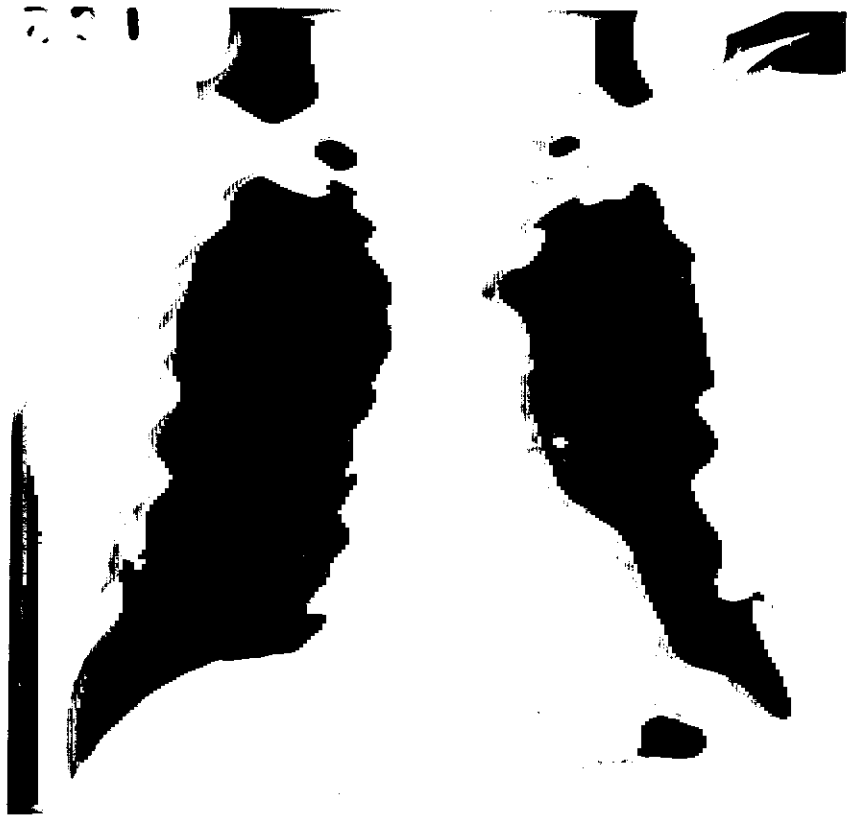

Figure 2. A 55-year-old male who had entered the company as a fireman in 1948 and worked for 36 years.

of 146 workers in steam locomotive repairshops but nil among 100 clerks of the same company. Older seamen or retired seamen should be followed up carefully in every ocean-going country.

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CLINICAL, RADIOLOGICAL AND FUNCTIONAL ABNORMALITIES AMONG WORKERS OF AN ASBESTOS-CEMENT FACTORY

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The purpose of this paper is not to report an epidemiological study but to throw light on the problems of asbestos related effects in a factory in the North of France which is mainly producing fibrocement pipes and roofing components. In this factory a population of 1800 workers had been employed in 1965 but the total number was reduced to 476 in 1987. Among the different kinds of asbestos, actinolite was never used and crocidolite unused after 1980. If several projects were already under way as early as 1952, preventive measures concerning asbestos related diseases became really effective about 1975. Notifications of occupational diseases were not frequent until 1984 but the three following years 106 cases were reported. This study relates clinical, radiological and functional abnormalities among 92 workers investigated the two last years within an expert evaluation.

SUBJECTS AND METHODS

The study was carried out in 92 male subjects with following biometric characteristics (mean and standard deviation) : age : 54 ± 9.4 years, weight : 77 ± 17.5 kg and height : 1 7 ± 0.06 m. Forty three subjects (47 p.100) were still working in the asbestos-cement factory at the time of examination and the others were recently retired. The risk exposure was 32 ± 7.3 years and it was generally the first notification of disease. Each patient was submitted to clinical, radiological and respiratory function investigations. The subjects answered a questionnaire mainly intended to specify risk exposure, smoking status, breathlessness and symptoms of bronchitis according to the usual criteria.[1] Radiological examination consisted of a chest radiograph (standard postero-anterior and lateral views) and CT scan if necessary. Respiratory function tests included lung volumes measurement, transfer factor determination and blood gas analysis. Vital capacity (VC), forced expiratory volume in one second (FEV_1 and functional residual capacity (CRF) were measured with a Gould Pulmonet III and FRC computer. Carbon monoxide transfer factor was obtained using single breath (TlCO SB) and steady-state (TlCO StSt) methods with respectively a Morgan Transfer test autolink and a SNIAS Syscomoram R. The predicted values were those of CECA[7] for lung volumes, those of BATES and all[2] for TlCO SB and DECHOUX and all[8] for TlCO StSt. Arterial blood was sampled in the patients at rest in sitting position, and analysed on a Corning 178 pH/blood gas system or an IL Meter 1306 apparatus. The predicted values for PaO_2 were evaluated according to SORBINI and all.[28]

RESULTS

In the population of 92 workers, 12 subjects had normal chest roentgenograms. Among the radiological abnormalities we found 5 pulmonary fibrosis, 9 benign pleural thickenings and 57 associated pulmonary fibrosis and non malignant pleural changes. Diagnosis of malignant pleural mesothelioma was established in 8 cases. For one patient there was a bronchial carcinoma with concomitant asbestosis and pleural plaques. The number of smokers and ex-smokers was important : 67 subjects (73 p.100). Twelve subjects (22 p.100) were suffering from symptoms of chronic bronchitis.

Asbestos-related occupational disease was recognized in 80 subjects but in our results we did not include mesotheliomas because functional respiratory investigations were not ever complete in these patients. The variance analysis showed that it was possible to express data for a population grouping together pulmonary, pleural and associated forms. In these 72 subjects, age (yr) was 55 ± 7.4 and risk exposure (yr) 33 ± 7.3 (m ± SD). Active life, smoking habits, chronic bronchitis were respectively observed in 50, 79 and 24 p.100 of the patients. Abnormal spirographic values were measured in 60 cases (83 p.100) with restrictive syndrome predominancy (58 p.100). Residual volume was always found in the predicted limits. TlCO steady-state was decreased in 76 p.100 of the group, DuCO (fractional uptake) in 50 p.100, TlCO single breath only in 29 p.100 and TlCO/VA (transfer factor by alveolar volume) in 14 p.100. Arterial hypoxemia was showed up in 35 cases (49 p.100) with $PaO_2 = 9.2 \pm 0.81$ KPa (0.88 predicted) and mild hypercapnia was found only in 6 cases (8 p.100). The values of the respiratory function indices are listed in Table I.

There was no significant difference in age, risk exposure, smoking habits, TlCO and hypoxemia between subjects suffering or not from a chronic bronchitis. However as shown in Table II they were different in VC, FEV_1 and FEV_1/VC values.

With regard to the 12 free of asbestos-related disease subjects according to chest radiograph, age and risk exposure were respectively 52 ± 6.6 and 27 ± 6.0 years. The frequency of active life, smoking habits and chronic bronchitis was the same we observed in the total population. There were functional abnormalities with decreasing in VC (0.85 ± 0.180 predicted), FEV_1 (0.79 ± 0.274 predicted), TlCO

Table I
Respiratory Function Tests in Asbestos-Related Disease (n = 72)

VC/pred	0.84 ± 0.150
FEV 1/pred	0.84 ± 0.209
FEV 1/VC	0.69 ± 0.141
TlCO StSt/pred	0.73 ± 0.307
DuCO (FuCO)	0.42 ± 0.109
TlCO SB/pred	1.03 ± 0.305
PaO_2/pred	0.97 ± 0.169

X ± SD

Table II
VC, FEV_1, FEV_1/VC Values in Asbestos-Related Disease

	A (n=17)	B (n=55)
VC/pred	0.74 ± 0.167*	0.87 ± 0.132
FEV 1/pred	0.67 ± 0.183*	0.89 ± 0.188
FEV 1/VC	0.64 ± 0.155*	0.71 ± 0.100

X ± SD. A = with chronic bronchitis, B = without chronic bronchitis. * P < 0.001

StSt (0.71 ± 0.275 predicted) and TlCO SB (0.96 ± 0.210 predicted). Hypoxemia was present in 3 cases.

DISCUSSION

Epidemiological investigations had demonstrated causal relation between asbestos exposure and non malignant pleuropulmonary pathology, mesothelioma and bronchial carcinoma.[31] Several studies attempted to determine nature and characteristics of the responsible fibres and to establish a dose-effect relationship.[25,3,26,30,11] As said in introduction our study was not an epidemiological one and an endeavour to do correlations between risk exposure and asbestos-related effects did not appear justified. Only some studies had underlined that it was very difficult to have a precise evaluation of exposure.[9,10,23,5] In fact, asbestos fibres inhalation by the workers had been varying in quality and quantity through the years. However it was possible to relate the occupational diseases to a very important dust pollution in the factory before 1975s. Furthermore the classical long delay from exposure to radiological diagnosis and the frequency of smoking habits were evident.

The repartition of the subjects according to exposure-related effects indicated few isolated fibrosis and non malignant pleural pathology with predominancy of associated pleuropulmonary disease. These findings were not surprising because the association of pulmonary asbestosis and pleural plaques, though still remaining controversial, can be shown in patients.[18,16,27,14,17] The lung fibrosis was more often a slight one on the radiographs. The frequency of "occupational bronchitis" was found important in our patients including the free of asbestos-related disease subjects.[21,19,4] It would be reasonable to suggest a synergistic effect between dust exposure and cigarette smoking to explain these results. Indeed, after retired, a number of patients saw that their symptoms had decreased or disappeared with no change in smoking habits.

Abnormalities in respiratory function tests frequently occurred without a clear relationship to put forward dyspnea. A restrictive function pattern was found in half the population, normal spirographic values in 20 p.100 and a mixed picture of restriction and obstruction in about 30 p.100 of the cases. These observations are not in opposition to the data of the literature.[12,24,22,32,13,29,6,20] Non uncommon impairment of gas exchange was indicated by decreasing in transfer factor, more frequently in TlCO steady-state and DuCO than in TlCO single breath and TlCO/VA, and attested by blood

gas analysis. This investigation detected at rest an arterial hypoxemia about one time out of two and also a mild hypercapnia in 8 p.100 of the subjects. Such disorders do not appear commonly described in predominant pleural asbestos effects but were found with the same frequency in coal miners.[15]

Bronchitis brought about alterations in spirographic values but no significative modification in transfer factor and blood gases. For the same biometric characteristics, risk exposure and smoking habits, VC, FEV_1, FEV_1/VC were more decreased in bronchitic than in non bronchitic subjects and restrictive and obstructive lung function profile was underscored.

At last in the absence of typical radiological changes, asbestos workers were not free of probably linked to dust exposure functional abnormalities.

Our study reported pathological effects in relation to an important asbestos exposure. At present time, with preventive measures, the risk has become less worrying in asbestos-cement factories. However environmental measurements remain fundamental for defining safe working dust levels to avoid occupational diseases.

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AIRWAY OBSTRUCTION IN ASBESTOSIS STUDIED IN SHIPYARD WORKERS

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ABSTRACT

Airway obstruction was measured by spirometry in 296 boilermakers with shipyard exposure to asbestos for 15 or more years. Percent of predicted was used to adjust each worker's pulmonary function values for height (mean 174 cm.), age (mean 52.5 years) and cigarette smoking (mean 23.3 years). Mean values were significantly ($P<0.05$) below predicted for FVC 4.23 L 94.2%, FEV_1 3.06 L 89.3%, FEF_{25-75} 2.51 L/sec 82.3%, and FEF_{75-85} .574 L/sec 77.8%. Corresponding values for the 106 men with pulmonary asbestosis (ILO profusion of opacities 1/0 or greater) were below these levels. Correlation coefficients for pulmonary functions with ILO categories of asbestosis (profusion of irregular opacities) were: FVC −.2381, FEV_1 −.2494, FEF_{25-75} −.2403 and FEF_{75-85} −.1629. All were significant $P<0.05$. The subgroup with radiographic asbestosis (ILO 1/0 or greater) had more functional loss. Data on this large cohort of asbestos exposed workers establish that airway obstruction occurs with the slightest profusion of asbestosis scarring in the lungs of shipyard workers and progressively worsens with greater profusions of irregular opacities.

INTRODUCTION

The pattern of pulmonary functional impairment due to asbestosis, particularly the nature and severity of airway obstruction during the development of pulmonary fibrosis, is unclear despite many published studies.[1] Although small airways, the terminal and respiratory bronchioles, were identified as the locus of asbestos damage by Gloyne[2] half a century ago, in the past decade or two standard practice has been to attribute the airway obstruction observed in asbestos workers to cigarette smoking. In fact, the presence of airway obstruction, even in the presence of radiographic evidence of pulmonary asbestosis manifested by fine irregular opacities, has been considered as evidence against asbestosis.[3,4] In an earlier study of nonsmoking asbestos insulators we showed evidence for airway obstruction.[5] In contrast, active and retired shipyard workers[6] showed less convincing evidence for airway obstruction after adjusting for the effects of cigarette smoking. The relatively small group of nonsmokers showed little functional impairment, but they were older men who had less severe asbestosis. A subsequent review of the literature showed that too few nonsmokers with asbestosis had been studied to generalize about the effects, except in clinically advanced pulmonary asbestosis with its classic triad of decreased lung volume, vital capacity and diffusing capacity.[1] The age ranges were different in these studies and the shipyard study population contained older survivors. This study was designed to measure the degree of airway obstruction in asbestos exposed workers in ship construction, and repair and to relate it to the signs of asbestosis on chest radiographs.

METHODS

Measurements of pulmonary function were made in 296 male boilermakers who had been exposed to asbestos for more than 15 years. They were members of a local union of the International Brotherhood of Boilermakers, Iron Shipbuilders, Blacksmiths, Forgers and Helpers. The 296 men were or had been employed mostly in ship repair but some had built new ships as well. The presence and profusion of irregular pulmonary opacities of asbestosis was graded numerically using the ILO[7] criteria applied to posteroanterior radiographs taken at full inflation of the chest. Lateral chest radiographs were also obtained at full inflation to examine for dorsal pleural plaques and retrocardiac disease, and to measure lung volume.[8]

To express the severity of asbestosis in usable numbers for calculation, the ILO profusion categories were converted to integers as follows: 0/0=1, 0/1=2, 1/0=3, 1/1=4, 1/2=5, 2/1=6, 2/2=7, 2/3=8, 3/2=9, 3/3 and greater =10. These numbers were used as independent variables in regression equations to calculate correlation coefficients.

An occupational diary and exposure questionnaire was completed and questions answered with interviewer assistance on chronic bronchitis, wheezing, and shortness of breath

which were adopted from DLD-78.[9] The questionnaire inquired about pneumonia, respiratory illness, work loss and chest pain or heaviness and about workshift symptoms including feverishness, chills, thirst, taste, headaches, hoarseness or sore throat along with chest tightness, cough, phlegm and wheezing. Trained interviewers assisted the welders in answering questions and checked questionnaires for completeness.

Spirometry was done by recording sequentially forced expiratory flows on rolling seal spirometers until a pair agreed within 5%. Spirometers were calibrated repeatedly with a 3 liter syringe during the study. Spirometry was measured with subjects standing wearing a nose clip and following the American Thoracic Society Standardization.[10] The best effort was digitized and values computed for forced vital capacity, forced expiratory volume in 1 second, FEF_{25-75} and FEF_{75-85}. These values were compared to those from a stratified random population of Michigan, and comparisons were made smoking specific to current and ex-smokers of cigarettes and non-smokers.[11] This meant that a smoking duration (years) adjustment of -0.0094 for FEV_1. Total lung capacity was measured -0.0052 for log FEF_{25-75} from posteroanterior and lateral chest X-rays at full inflation and -0.0112 for log FEF_{75-85} using the method of Harris et al.[8]

The individual pulmonary function values were summed and means calculated from individual data for comparisons of values and percentage of predicted. Data was entered into a Hewlett-Packard 9816 computer and standard statistical analyses and regression analysis done with the HP statistical library. A p value of 0.05 or less was considered statistically significant.

RESULTS

The mean age of the 296 southeastern shipyard workers was 52.5 years. They were 68.5 inches in height, had smoked an average of 23.3 years and averaged 23.6 cigarettes per day. They had 27.3 (mean) $\pm$ 11.6 (s.d.) years of exposure to asbestosis, Table I. Chronic bronchitis was diagnosed in 22.6% and 13.5 had a history of intermittent wheezing relieved spontaneously or by medications which was classified as asthma. They had reductions of FVC to 94.2% of predicted, FEV_1 to 89.3% of predicted, and FEF_{25-75} and FEF_{75-85} to 82.3% and 77.8% of predicted, respectively. All reductions were significant. The 106 men with asbestosis had lower FVC and flows than the entire group and these differences were all significant. Thus in the men with pulmonary asbestosis (ILO profusion 1/0 and greater) percent of predicted for vital capacity averaged 8% lower, for FEV_1 was 11% lower, midflow was 19% lower and terminal flow was 14% lower than in those without asbestosis. All differences were significant, $p<0.05$. There was a 12 year age difference from this division, but comparisons based on percentage predicted adjusted for the difference.

The correlation coefficients of pulmonary functions as dependent variables against ILO category score as the independent variable showed $-.2381$ for FVC, $-.2494$ for FEV_1, $-.2403$ for FEF_{25-75} and -1629 for FEF_{75-85} were all significant, Table II. The r^2 values showed that 2.65% to 6.22% of the variance in vital capacity and flows was accounted for by asbestosis. The regression lines with their confidence intervals show a continuum of change in each function from no asbestosis to severe asbestosis, ILO profusion 3/3, Figure 1 panels A-D. When the correlation coefficients were calculated for the 106 subjects with asbestosis, ILO profusion 1/0 and greater the respective coefficients were for FVC $-.1919$, for FEV_1 -2832, for FEF_{25-75} $-.2918$ and for FEF_{75-85} $-.2483$. Again all were significant. The two sets of regression equations for all shipyard workers and those with asbestosis produced similar estimates of reduction of vital capacity and of flows at 1/0[3] and 2/1.[6]

DISCUSSION

By collecting spirometric measurements of pulmonary function by uniform protocol on 296 asbestos exposed shipyard workers and adjusting the data for height, age, ethnicity and cigarette smoking duration, we found that pulmonary parenchymal asbestosis is correlated with worsening airway obstruction. Increasing profusions of irregular opacities of asbestosis are associated with more obstruction. This observation was anticipated in 1933 by the original observation of the pathologic findings of peribronchiolar cuffing by Gloyne. However, the physiologic impairment of late or advanced disease has focused on restriction, i.e. reduced lung volume (TGV), FVC, and diffusing capacity. In contrast, the airway obstruction in workers with a high proportion of cigarette smokers has been attributed to smoking. By adding a standard adjustment for duration of smoking to the regression equations for FVC, FEV_1 and flows this confounding was removed.[11] Thus, the effect of asbestosis on FEV_1 and flows was clearly revealed.

This approach may lend itself equally well to analysis of the effect of other occupational and environmental exposures when the population lacks sufficient nonsmokers to make it possible to analyze effects in them alone. It appears to adjust effectively for the contribution of smoking. One reality which may interfere with such analyses is the age dependence and thus, concordance between age, years of smoking and years of exposure. By using a quantitative effect estimate of asbestosis based on the profusion of irregular opacities in the lung fields, the estimate of effect was independent of years and thus avoided this problem.

These findings establish an observational continuum between observations of airway obstruction especially of small airways in insulators who were heavily exposed to asbestosis but had not yet showed asbestosis on chest radiographs[5] and advanced asbestosis[6] in which FVC and diffusing capacity are reduced. It also avoids the survivor bias which was observed when elder men, most nonsmokers were studied earlier.[6,12] It appears that as increasing numbers of small airways are permanently obstructed FVC progressively decreases. As the process worsens, so many small airways are obstructed that the slowly ventilated space is lost and VC is small but quickly emptied so FEV_1 is restored together with flows. Diffusing capacity is closely tied to alveolar volume and remains so until it is critically reduced.

There may be a greater functional pulmonary impairment of shipyard workers compared to construction workers.[13] This was evident when the two segments of a midwestern

Table I

Comparison of Pulmonary Functions, Means and Standard Deviations for 296 Southern Shipyard Workers and the Subgroup with Asbestosis Compared as Percentage Predicted to the Michigan Male Population Sample

	ALL SHIPYARD	ASBESTOSIS	NO ASBESTOSIS
Number	296	106	190
Age - years	52.5 + 11.0	57.9 ± 8.2	49.5 ± 11.2
Ht - cm.	174.0 ± 7.1	173.7 ± 6.8	174.2 ± 7.4
Smoked - years	23.3 ± 16.7	27.7 ± 16.8	20.8 ± 16.1
Cig per day	23.6 ± 18.1	25.5 ± 16.7	22.6 ± 18.8
Asbestos - years	27.3 ± 11.6	31.3 ± 10.7	25.0 ± 11.5
Ch. Bronchitis	22.6	26.4	20.5
Asthma history	13.5	15.1	14.2
FVC L	4.23 ± .93	3.91 ± .90	4.42 ± .89
% pred	94.2 *	89.4 *+	96.9 *
FEV_1 L	3.06 ± .91	2.73 ± .82	3.25 ± .90
% pred	89.3 *	84.0 *+	92.3 *
FEF_{25-75} L/sec	2.51 ± 1.53	2.00 ± 1.23	2.79 ± 1.60
% pred	82.3 *	71.8 *+	88.2 *
FEF_{75-85} L/sec	.57 ± .46	.42 ± .34	.65 ± .50
% pred	77.8 *	71.0 *+	81.6 *
TGV L	7.69 ± 1.03	7.63 ± 1.04	7.72 ± 1.02
% pred	98.0	97.0	98.3

* Significant difference $p<0.05$ compared to predicted.
\+ Significant difference $p<0.05$ compared all shipyard workers.

Table II

Correlation Coefficients, R^2 and Regression Analysis for Pulmonary Function Against Category of Asbestosis (ILO) for 296 Southeastern Shipyard Workers and for the 106 with Asbestosis, ILO Category 1/0 or Greater

Percent Predicted	EXPOSED ASBESTOS		ASBESTOSIS	
Number	296	r^2	106	r^2
FVC	-.2381 *	.0567	-.1919 *	.0368
FEV_1	-.2494 *	.0622	-.2832 *	.0818
FEF_{25-75}	-.2403 *	.0577	-.2918 *	.0852
FEF_{75-85}	-.1629 *	.0265	-.2483 *	.0616

* P<0.05

REGRESSION EQUATIONS FOR ILO PROFUSION CATEGORY OF ASBESTOSIS AND PULMONARY FUNCTION AS PERCENT PREDICTED FOR 296 SOUTHEASTERN SHIPYARD WORKERS.

			ILO CAT 3 6
Percent pred. FVC	=	98.87 - 02.11 x ILO category	= 92.5/86.2
Percent pred. FEV_1	=	95.50 - 02.78 x ILO category	= 87.2/78.8
Percent pred. FEF_{25-75}	=	94.63 - 05.56 x ILO category	= 78.0/61.3
Percent pred. FEF_{75-85}	=	87.54 - 04.39 x ILO category	= 74.4/61.2

REGRESSION EQUATIONS FOR ILO PROFUSION CATEGORY OF ASBESTOSIS AND PULMONARY FUNCTION AS PERCENT PREDICTED FOR 106 SHIPYARD WORKERS WITH ASBESTOSIS.

			ILO CAT 3 6
Percent pred. FVC	=	96.27 - 01.64 x ILO category	= 91.4/86.4
Percent pred. FEV_1	=	96.35 - 02.98 x ILO category	= 87.4/78.5
Percent pred. FEF_{25-75}	=	96.02 - 05.83 x ILO category	= 78.5/61.0
Percent pred. FEF_{75-85}	=	95.95 - 06.01 x ILO category	= 77.9/60.0

population were compared to this southeastern group. The usual causes of differences including methodological ones have been eliminated. The ambient environments were urban and varied only slightly and all groups had equal exposure to welding. It is suggested that the greater impairment in shipyard workers reflects the hours of work in a container of limited volume into which are generated effluents of welding, insulating, metal grinding and polishing (still including sandblasting), painting, and other surface coating. These within ship and shipyard shops atmospheres appear richer and potentially more harmful to pulmonary function than is the outdoors or the interior of most buildings during construction.

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FIBROUS SUBSTITUTE MATERIALS FOR ASBESTOS —EVALUATION OF POTENTIAL HEALTH RISKS

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ABSTRACT

Increasing restriction of the use of asbestos has led to considerable effort to develop suitable substitute materials, many of which are also fibrous. Since available data indicate that fibre size and shape are important determinants of asbestos-related disease, there is concern that materials with fibre sizes within the range of those of asbestos may present similar risks to health. There is a need, therefore, to develop suitable toxicological testing protocols for these materials.

We have recently reviewed the relevant data on one group of these materials, the man-made mineral fibres (MMMF), for the International Programme on Chemical Safety. This review was conducted to provide background information for assessment, by a Task Group of experts, of the potential risks to health associated with exposure to these materials in the occupational and general environments. The principal observations which formed the basis for this evaluation will be discussed.

In particular, difficulties in interpretation of the toxicological data on MMMF will be addressed. The implications of these difficulties in the assessment of potential health risks associated with exposure to new fibrous materials for which there are relatively fewer relevant data, will be discussed. Initiatives of the Department of National Health and Welfare to attempt to obtain some consensus concerning appropriate toxicological testing protocols for these materials will be described.

No Paper provided.

AN EARLY INDICATOR FOR PULMONARY FIBROSIS IN ASBESTOS EXPOSURE: THE SERUM LEVEL OF TYPE III PROCOLLAGEN PEPTIDE

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SUMMARY

Serum type III procollagen peptide (PIIIP) levels were measured in 29 asbestos-exposed workers and in 29 healthy controls. Mean serum PIIIP level was 16.9 ± 2.9 (SD) ng/ml in exposed workers and 11.6 ± 2.9 (SD) ng/ml in the referent group, the difference being highly significant. Mean serum PIIIP level in moderately exposed subjects (<0.1–0.2 fibres/ml) was significantly higher than in controls; PIIIP values in workers exposed to a higher air fibre concentration (0.2–3.8 fibres/ml) proved significantly elevated in comparison to controls and moderately exposed subjects, thus suggesting a dose-effect relationship. In 12 workers personal monitoring of exposure showed a clear correlation (r=0.69) between estimated asbestos dose (fibres/ml x years of exposure) and serum PIIIP levels. Moreover levels of PIIIP in the serum were found to be on average significantly higher in workers with reduced forced vital capacity. Serum PIIIP level seems to be a promising index for monitoring early asbestos-induced pulmonary fibrotic effects.

INTRODUCTION

The diagnosis of asbestos related non-malignant lung disease is based upon clinical signs, impairment of lung function tests and radiographic findings.

Radiological and clinical evidence has been reported to be less sensitive to the presence of asbestosis and other interstitial fibrosis than histopathological examination.[4,6] On the other hand, only very early detection of the pulmonary fibrogenic response may prevent progression to severer stages of asbestosis.

Recent studies suggest that the pathogenesis of pulmonary fibrosis might be related to changes in the structure and function of pulmonary collagen rather than to an increase of its absolute amount.[6] An increase of type III collagen has been observed in bioptic lung samples taken from patients in early stages of cryptogenic pulmonary fibrosis[6] and from subjects with active fibrotic disease.[2] However, type III collagen was reduced in post-mortem lung samples taken from patients who had died from pulmonary fibrosis[7] and from patients with a longer duration of the disease.[6]

These findings suggest the hypothesis of an increased synthesis of type III collagen during the early stages of the disease followed by a decrease later.

Type III collagen is synthetized within the collagen producing cells in a precursor form as procollagen with specific N-terminal and C-terminal extension peptides at the ends of the molecule. These peptides are cleaved in stoichiometric amounts by specific peptidases during secretion of the newly formed collagen from the cell.[3]

N-terminal peptide can be measured in serum and its level shows a positive correlation to the type III/type I collagen ratio measured biochemically in lung tissues.[6]

Our study aimed to measure PIIIP serum levels in subjects exposed to asbestos in order to investigate the usefulness of the test in the biological monitoring of asbestos exposure.

MATERIALS AND METHODS

29 male workers occupationally exposed to asbestos fibres and employed in two factories producing cement-asbestos products were examined. All the subjects, whose mean age was 36 years, were currently exposed at the moment of the study and their mean exposure time was 7.9 years (range 1–25 years).

Airborne asbestos fibre exposure was evaluated by stationary and/or personal sampling according to the AIA 1979 reference method.[1] The workers were mainly exposed to chrysotile, but in one factory crocidolite was also present (up to 30% of the total airborne asbestos).

According to the air sampling data the subjects were divided into two groups: group 1 comprising 17 workers exposed to low concentrations (up to 0.2 fibres/ml) and group 2 including workers also exposed to crocidolite and to a higher concentration of total asbestos fibres (range 0.2–3.8 fibres/ml). 2 workers were considered exposed but not assigned to either group since air determinations for their specific job were lacking.

Cases were compared to a reference group of 29 healthy male subjects matched for age, tobacco and alcohol consumption.

A standardized questionnaire was used and appropriate biochemical indices performed on cases and controls to rule out liver and/or collagen diseases, which could influence the results of the test.

Serum PIIIP measurements were performed by the radioimmunoassay method described by Rhode et al.[8] The mean recovery at different PIIIP concentration varied between 89 and 104% and the coefficient of variation within run ranged between 7–15%.

RESULTS

The level of serum PIIIP in the exposed subjects and in the referent group is reported in Table I. The mean value was 11.6 ± 2.9 (SD) ng/ml in controls and 16.9 ± 2.9 (SD) ng/ml in the exposed subjects. The difference between the means is highly significant.

Neither in cases nor in controls was a significant difference in serum PIIIP levels found between smokers and nonsmokers or between alcohol drinkers and non-drinkers. It must be stressed that in both groups alcohol assumption was moderate.

When subjects with low and higher exposure were separately considered again a significant increase of serum PIIIP values was found in comparison to the referent group. The workers exposed to higher levels of airborne asbestos fibres showed the highest values of PIIIP in serum (Table II). From these data it seems possible to infer a dose-effect relationship between the exposure to asbestos fibres and serum PIIIP values.

To verify this hypothesis we compared the serum PIIIP level and the individual "dose" expressed as fibres/ml/years in 12 subjects, monitored repeatedly by personal air samplers and taking into account the years of duration of exposure (Figure 1). A significant regression line was found with a coefficient of correlation of 0.69 ($p < 0.01$). This relationship should be considered valid for short-term exposure periods, since all the 12 subjects studied were exposed for less than 5 years.

To evaluate whether the concentration of PIIIP in serum bears some relationship to possible asbestos related effects, we measured the forced vital capacity (FVC) and the volume expired in the first second (FEV_1) in the exposed subjects. In the workers with a reduced FVC and FEV_1 a significant increase as a mean of the serum PIIIP was evident when compared to the workers showing no impairment of lung function tests (Table III).

Since, according to our results, tobacco and alcohol consumption is not related to serum PIIIP values, and possible age-related effects have also been ruled out by matching criteria, the difference in serum concentration of PIIIP seems to be ascribable only to the exposure to asbestos fibres. The different level of the PIIIP in groups with different exposure intensity suggests a dose-dependent increase as demonstrated further by the clear relationship between the number of fibres/ml/years and the serum levels of PIIIP.

It must also be stressed that a significant increase of PIIIP is already evident at exposure levels of 0.2 fibres/ml or less, a finding which suggests the need to reconsider the threshold for asbestos related pulmonary effects.

Further studies are certainly needed on the biological meaning of serum PIIIP levels, but our results suggest that the test may represent a promising index for early asbestos induced fibrotic effects and should be considered for the biological monitoring of exposed workers.

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Table I

Serum PIIIP Values in Controls and in the Exposed Workers

	number of subjects	serum PIIIP (ng/ml) mean	DS	significance of the difference
CONTROLS	29	11,64	2,92	
				p < 0,0001
EXPOSED WORKERS	29	16,86	2,91	

Table II
Serum PIIIP Values in Controls and in the Exposed Workers

	number of subjects	serum PIIIP (ng/ml) mean	DS	significance of the difference vs controls
CONTROLS	29	11,64	2,92	
EXPOSED WORKERS				
Group 1	17	15,23	2,70	$p < 0,005$
Group 2	9	19,00	4,39	$p < 0,003$

Significance of the difference between group 1 and group 2 : $p < 0,05$

Group 1: low exposure workers (<0,1-0,2 ff/ml)

Group 2: higher exposure workers (0,2 - 3,8 ff/ml)

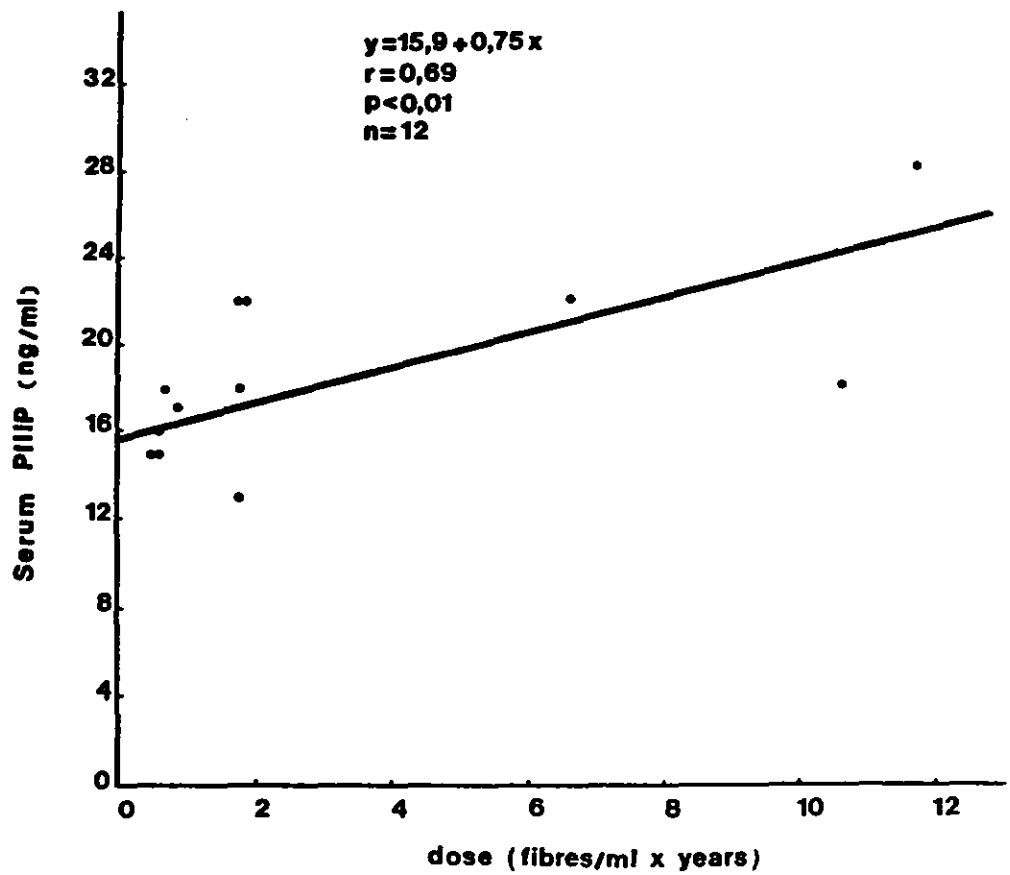

Figure 1. Relationship between asbestos dose (fibres/ml × years of exposition) and serum PIIIP values in the exposed workers.

Table III

Serum PIIIP in Asbestos Exposed Workers Subdivided According to Pulmonary Function Test Results

	Number of subjects	serum PIIIP (ng/ml) mean	DS	significance of the difference
FVC ≥ 100% ref. value	15	14,93	2,12	p < 0,005
FVC < 100% ref. value	12	19,25	4,14	
FEV1 ≥ 100% ref. value	12	15,17	2,04	p < 0,03
FEV1 < 100% ref. value	15	18,20	4,38	

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UPPER LOBE CHANGES AND EXPOSURE TO ASBESTOS

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ABSTRACT

Asbestosis is classically a disease which mainly affects the lower lobes. However, it has been known for many years that sometimes the upper lobes are affected and indeed severely so, even if this is a rare occurrence. There have been discussions on whether these lesions are indeed due to asbestos or some other disease. In particular, many cases have been labelled tuberculosis and treated as such.

In the county of Uppsala, Sweden, we have been interested in the asbestos problem for more than a decade and have now collected more than 1500 persons with asbestos-related pleural and/or parenchymal disease which we follow. Most of these have had comparatively light exposure. Among those workers, 40 patients have been seen with typical upper lobe changes.

These 40 persons have had intermittent exposure for in the mean 25 years (2 to 46 years). The latency time from first exposure was in the mean 34 years with a range of 5 to 51 years. The upper lobe is sometimes severely affected with a pleural thickening of up to 40 mm (mean 21 mm) and an obvious shrinkage of the lobe with the hilus drawn upwards and the trachea deviating to the affected side. In 4 patients (10 percent) the left upper lobe only was affected, in 21 the right, and in 15 both sides. The disease often progresses fairly rapidly within 5 to 10 years and is in almost all cases part of a general pleuroparenchymal disease. Hence, the lung function is severely affected. VC was in the mean 62% of predicted and TLC 69%.

See Table of Contents, Part II, for Paper.

OCCUPATIONAL SILICOSIS AMONG WORKERS IN AN ORE MILL, THAILAND

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BACKGROUND

In July, 1986, the chest disease hospital in Nonthaburi reported a death to the divisions of occupational health and epidimiology of the ministry of public health. The death occurred in a 27 year-old female worker with a diagnosis of silicosis. The patient had a long history of dyspnea treated at numerous clinics. Two weeks prior to her death she was admitted to the Nakorn patom provincial hospital with fever, dyspnea, cough, and crepitation in both lungs. Her chest X-ray was abnormal with marked reticulo-nodular infiltration. The index case worked in a mill in Nakorn patom province, located 60 kilometers southwest of Bangkok.

The factory ground minerals such as quartz, feldspar, flint, talcum, clay, dolomite, and phosphate, as seen here before the crushing process. The process of grinding very fine granules 300 mesh of these ores.

The effects of silicosis, the chronic fibrosis of the lungs produced by prolonged and extensive exposure to free crystalline silica, have been recognized for centuries. Pulmonary disease produced by dust is mentioned by Agricola in his Treatise on Mining and is described in stonecutters by Van Diemerbroeck Ramazzini.[1] Clinical evidences of previous exposure to free silica in old mines, abandoned quarries, and ancient flint tools and weapons were demonstrated.[2] Silicosis is caused by the inhalation and retention of dust containing silica in occupations such as mining, tunnelling, quarrying, stone dressing, sandblasting, fettling, boiler scaling, and in pottery, ceramics and brick manufacture.[3] Symptoms of silicosis cases are increasing dyspnea, non productive cough and chest pain, progressing to compensatory emphysema and cor pulmonaly.[4] There was a report of silicosis among miners which the prevalence of 19.48% (5,366/27,553) together with pulmonary tuberculosis of 13.83% (742/5,366).

In order to carry out the investigation of this fatal case, and to search for other possible cases, meetings were held with officials from various other goverment agencies, including the ministry of interior and ministry of industry.

The objectives of our investigation were (1) to establish whether or not there was an epidemic of silicosis among the workers in the factory; (2) to find the epidemiological distribution of silicosis; (3) to identify risk factors for silicosis disease; and (4) to develop appropriate preventive and control measures.

METHODS

The methods included (1) describing the epidemiology of the problem; (2) a case-control study for risk factors for disease; and (3) studying the environment of the factory.

To describe the problem, we interviewed all 80 workers in the plant with questionnaires about work histories and history of illness, and performed physical examinations included chest auscultation, chest percussion, and measurement of chest expansion. All 80 workers received posteroanterior chest radiographs. All 80 workers underwent pulmonary function testing. Capro's prediction equation was used to find predicted values.[5] The predicted values were corrected with 0.85 for non-caucasian people.

A case of silicosis was defined as any worker in plant whose chest radiograph change by ILO-1980 international classification of pneumoconiosis at 1/1 profusion of lung parenchyma.[6] Four controls for each case in the case-control study were selected by simple random sampling from non-case workers in the mill.

The environmental survey included a walk-through of the plant. We measured dust concentrations at various sites in the plant. We also observed the workers performing their jobs, and we attached portable dust concentration measuring devices top selected workers.

RESULTS

The mill was divided into three plants. Plant number one ground feldspar and phosphate. Plant number two usually ground quartz and flint, and on occasion would grind feldspar and phosphate. Plant number three ground clay, only. Of the total of 80 workers in the plant, we found 10 workers or 12.5% with silicosis,including the fatal index case. This index case was the only worker to have died in the previous year, for a mortallity rate of 1.2 percent, and a case-fatality rate of 10 percent.

Chest radiographs revealed the small opacities of parenchymal profusion of 1/1 at 20%, 2/1 at 30%, 3/3 at 50%. Most of the sizes and shapes of such abnormalities were p and q. One case had large capacity catagorized as "B".

Pulmonary function tests were normal in five, or half of the cases. The five cases with abnormal pulmonary function generally had a restrictive ventilatory defect. Clinical symptoms and sign in the case included dyspnea, chest pain,

chronic cough, restriction of lung expansion, and decreasing breath sounds.

The mean age of the 10 cases was 34.9 years with a range from 34 to 49 years. The duration of working in the plant averaged 8 years before our study,with a range of 1 to 14 years of exposure.

The attack rates for silicosis by job category were highest in two housekeepers whose job was to sweep up the dust which accumulated in the working areas. The second highest attack rate was in ore-grinders at rate of 33% (7/21).

Attack rate by job location were highest in plant number two, where quartz and flint were ground. The attack rate was 3.5%. This is the plant where the fatal case worked. The attack rate was 10.7% in plant number one, where feldspar and phosphate were ground. There were no cases in plant number three, where clay was ground. There were no cases in office workers, but there were two cases among foremen, who were exposed to dust in all the plant areas.

For the environmental inspection, we tested the mineral content of the ores used in the plant. Silica is the mineral ingredient of greatest hazard. Quartz and sand had the highest silica content, at 45.7%.

We found no engineering dust control measures in use; no hoods and no protective dust enclosures. A few workers tried to avoid breathing the hazardous dust with cloths over their face, but this is very ineffective. Our inspection revealed very hazardous levels of dust being created by the grinding process. No occupational health services were provided for workers in the plant, as required by regulations.

The Thai ministry of interior's maximum permissible level of respirable dust in workplace air is 5 mg/cubic meter. We measured an average concentration of respirable dust in the breathing zones of ten workers of 437.7 mg/cubic meter of air, 87 times the permissible level.

In the case-control study, the workers with a duration of exposure of greater than 5 years had odds ratio of 16 times the likelihood of being a case than workers with less exposure.

The case-control study also found that workers in the grinding and packing areas of the mill had an odds ratio of 12 times the likelihood of being a case than workers in other areas of the plant.

When it was analyzed by the measured amounts of dust in various work areas, we found that workers in areas with dust exceeding permissible exposure limit had an odds ratio of 11 times the likelihood of having silicosis, compared to workers in areas with dust within regulation limits.

When we measured amounts of silica contained in the dusts, we found that workers in areas with dust containing 33% or more of silica had an odds ratio of eight times the likelihood of having silicosis than workers in areas with dust containing less than 33% silica.

DISCUSSIONS AND RECOMMENDATIONS

This investigation revealed 12.5% of silicosis prevalence rate with one dead case. It is a quite severe situation. To prevent workers from exposure to silica is among the highest priorities in protecting the health of the workers. Silicosis is not reversible. If one gets the disease, one will be affected for the rest of one's life. Thus, this epidemiological study aimed ultimately to such prevention, as one definition of epidemiology is the study of distribution and determinants of the disease. The classical process consists of examining a series of variables to ascertain causation including age, sex, socioeconomic status and other. Since it is known that silica causes silicosis, but there are several major difficulties involved in attempting to do this, which were difficulties in the accurate determination of exposed dose, difficulties in the accurate determination of the health effects and difficulties in dealing with competing variables such as cigarette smoking and host susceptibility.[7]

As the epidemiological data show that the housekeepers and the ore-grinders were the highest risk group to develop silicosis. This group should be firstly provided preventive measures, if there were any constraints.

At the conclusion of the investigation, we gave essential health education lectures to all the workers about the hazards of silica and how to avoid it by using NIOSH-approved masks. We advised the owners how to make engineering changes that would make the workplace safer. The report was provided to the ministry of industry, which closed down the factory for 6 months because of the health dangers. A joint meeting of the ministries of industry, interior, and public health was held with many owners and operators of ore and stone grinding plants throughout Thailand to tell the plant operators about the dangers of silica, and how to prevent workers from developing silicosis.

This plant was reopened after making recommended changes in workplace practices, including (1) building covers and hoods over grinding machines to prevent escape of dust, (2) providing approved masks for exposed workers, (3) offering medical care for workers, and (4) tranferring those with lung problems to safer parts of the plant.

This plant was inspected about six months after the original investigation. Dust levels were found to be below permissible limits and workers were wearing approved masks.

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SILICOSIS AND LUNG CANCER: PRELIMINARY RESULTS FROM THE CALIFORNIA SILICOSIS REGISTRY

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ABSTRACT

Exposure to silica (SiO_2) causes silicosis and silicotuberculosis; now there is new concern about its carcinogenicity (see IARC Monograph on Silica, 1987). The California Silicosis Registry was created to examine the mortality of silicotics (individuals with high SiO_2 exposures) among state Workers' Compensation Appeals Board claimants. The authors used proportionate mortality ratios (PMRs) to assess the risks among 212 while male silicotics who filed claims between 1945 and 1963 and were followed until 1984. The PMRs (and 95% confidence intervals [$Cl_{95\%}$]) indicated that silicotics had excesses of cancer of the lung (PMR=2.22; $Cl_{95\%}$=1.30, 3.37), tuberculosis (PMR=9.75; $Cl_{95\%}$=6.58, 13.92), and nonmalignant respiratory diseases (PMR=4.18; $Cl_{95\%}$=3.10, 5.51). Removing tuberculosis deaths from the analysis produced a lung cancer PMR of 2.53. There was no excess risk for gastrointestinal or lymphatic cancers. These preliminary findings from the Registry suggest that silicotics in California have a significant respiratory cancer risk. This risk is consistent with findings from many international studies and strongly suggests that silicosis acts as a precursor lesion for lung cancer.

BACKGROUND

Since the 1930s there has been unsubstantiated conjecture that silicosis predisposes to cancer of many sites. It is established that silica exposure causes silicosis, silicotuberculosis, cor pulmonale, and perhaps nephritis. However, that silica may be a carcinogen or that silicosis may increase the risk of bronchogenic cancer (Goldsmith et al., 1982; Goldsmith et al., 1986; IARC, 1987) has been seriously considered only in the past seven years and challenges a great deal of expert medical opinion (see Heppleston, 1985; Selikoff, 1978; Ziskind et al., 1976).

The following is a summary of the scientific evidence of silica's carcinogenicity and the relationship between silicosis and respiratory cancer:

1. Very recent evidence shows that silica produces mutations and premalignant hyperplasia *in vivo* (Hesterberg et al.; 1986, Gibson et al., 1986; Saffiotti, 1986).

2. Since 1980 silica (as Min-U-Sil) has been shown to be a pulmonary carcinogen in five lifetime rat studies using both intratracheal and inhalation methods (Holland et al., 1983; Groth et al., 1986; Dagle et al., 1986; Wagner et al., 1980; Muhle et al., 1989). Muhle et al.'s research on rats shows that quartz is a carcinogen at a level of 1 mg/m^3. Although the tumorigenic results were not replicated in hamsters (Holland et al., 1983; Saffiotti, 1986), this is the first time that pulmonary tumors were induced using inhalation (Dagle et al., 1986; Muhle et al., 1989; Holland et al., 1986), paralleling the human route of exposure.

3. Workers in dusty trades with known high exposure to crystalline silica, including sandblasting, firebrick manufacture, ceramics, granite and stone work, and tunneling have statistically significant excess mortality from lung cancer (reviewed in Goldsmith et al., 1986; IARC, 1987; Lynge et al., 1986). Smoking was not controlled in most of the studies, however its lack of adjustment cannot completely explain the high lung cancer risk ratios (Axelson, 1978, Fletcher and Ades, 1984). By way of contrast, Goldsmith and Guidotti (1986) presented evidence that smoking may be synergistic with silica exposure in the risk of lung cancer.

4. Paralleling the lymphatic malignancies induced by silica in animals (Wagner et al., 1980), there are several studies indicating an elevated risk in humans (Brown et al., 1986; Kurppa et al., 1986; Redmond et al., 1981; Mirer et al., 1986). In addition there are several studies indicating excess mortality from stomach cancer among workers in which silica exposure predominated (reviewed by Greenberg, 1986).

5. Similar to the observations of pulmonary tumors adjacent to silicotic nodules in rats, lung cancer excesses have been reported consistently in studies of silicotics (reviewed by Goldsmith et al., 1988). The risk measures range from 1.4 to 5.9 and have been reported from Sweden (Westerholm, 1980), Ontario (Finkelstein

et al., 1982, 1987), Switzerland (Schuler and Ruttner, 1986), Austria (Neuberger et al., 1986), Finland (Gudbergsson et al., 1984; Kurppa et al., 1986), Italy (Forastiere et al., 1986; Rubino et al., 1985; Zambon et al., 1986), U.S. (Steenland and Beaumont, 1986), and Japan (Chiyotani, 1984).

EXPERIMENTAL DESIGN AND METHODS

Background of This Study

In 1986 and 1989 we received funding from the California Thoracic Society and the Centers for Disease Control, respectively, to create the California Silicosis Registry. Its purpose is to provide a registry of all claims for silicosis (and claims for other occupational pulmonary disease) within California, and to provide a basis for testing the association beween silicosis and cancer. This paper will describe the proportional mortality ratio (PMR) findings from a partial and preliminary examination of the registry.

Methods

Patients having claims for silicosis diagnosed in California who were state residents from January 1, 1946 to December 31, 1980 are being identified. We are using the files of the California Workers' Compensation Appeals Board (WCAB). The following data are being extracted from the archived records of WCAB: name, address, sex, Social Security number, date of birth, name and address of primary physician, date of claim, type of injury alleged, and employer's name and address. There are three types of controls being selected (excluding fatal injuries): one, matched for age (± 2 years), year of claim, region and sex; second, the next noncase in the files after a lung disease claim is found; the third control is a random selection of one claim from every 12 boxes of files (approximately 1 per 400 sample). These cases of silicosis and controls constitute the California Silicosis Registry.

All subjects are being traced up to December 31, 1984 to determine their vital status. Using California Department of Motor Vehicles (DMV) records, tracing is now being carried out to determine last known address if alive. Deceased subjects are being identified and information extracted from the California Vital Statistics Section of the Department of Health Services.

We used a proportionate mortality ratio (PMR) analysis program developed by Maizlish (1986) to provide a preliminary assessment of mortality between silicosis and respiratory disease claims whose death certificates (up to 1984) could be abstracted from California vital records. Expected values are from U.S. white male rates according to the 8th revision of the International Classification of Diseases. The major advantage is that this approach uses all the deaths obtained in the registry to date and provides a useful indication of any excesses relevant to the hypotheses under evaluation in this study.

RESULTS

This paper will examine only those data from the San Francisco district in a preliminary follow-up. All claims listing either silicosis, silicotuberculosis, anthracosilicosis, pneumoconiosis, dust diseases of the lung, or any lung illness (not accidents) are being extracted from the files of WCAB.

Table I shows the number of WCAB files examined, the number of lung disease claims found and the proportion of cases found per 1,000 records. These preliminary results indicate that about 5 of every 1,000 files reviewed contains a WCAB claim for occupational respiratory disease. As of May, 1988, over 130,000 individual files had been reviewed, and nearly 700 pneumoconiosis claims (plus controls) have been extracted. For this study we focused only on white males because fewer than 5% of the deaths occurred among nonwhites or females.

Tables II and III presents PMRs for white male cases dying from nonmalignant and malignant diseases, respectively. As expected, the cases have a striking excess mortality from tuberculosis (TB), a frequent complication of silicosis (PMR = 9.75; 95% CI = 6.58, 13.92). There is a significant deficit of mortality for all circulatory diseases, PMR = 0.60; 95% CI = 0.47, 0.75. Nonmalignant respiratory disease mortality showed the expected pattern with claimants having a clear excess PMR of 4.18; 95% CI = 3.10, 5.51. Cirrhosis of the liver showed a nonsignificant PMR of 1.39. Accidental deaths among lung disease claimants had a borderline significant deficit PMR of 0.42, and there was no excess mortality for suicide.

Table III indicates that the silicosis claimants have a PMR of 1.07 for all malignant neoplasms. In contrast to the recent findings of Finkelstein et al. (1987), there was no excess of cancer of the gastrointestinal tract among cases (PMR = 0.91). An excess risk for lymphopoeitic cancers was not born out among these pneumoconiotics, PMR = 0.90. There was also a PMR of 2.32 for pancreatic cancer (based on only 5 deaths).

Malignant neoplasms of the respiratory system were significantly elevated for lung disease claimants (PMR = 2.16; 95% CI = 1.37, 3.24). For cancer of the trachea, bronchus and lung, the pneumoconiotics had a PMR of 2.22; 95% CI = 1.39, 3.37. Removing the deaths from tuberculosis, produced a PMR of 2.53 for pulmonary cancer among silicotics.

DISCUSSION

In this preliminary PMR analysis (with the known weaknesses of PMR data acknowledged), respiratory disease claims showed an expected striking excess risk for TB and nonmalignant pulmonary disease mortality. In addition, we demonstrated a significant doubling of respiratory system cancer among claims for occupational lung disease (cases). Because we could not adjust for smoking, this finding can only be considered preliminary. However, these findings support the association between silicosis and lung cancer mortality risk described by Goldsmith et al. (1988), and the consistency of this association suggests that silicosis may act as a "precursor lesion" in the risk of pulmonary cancer (Goldsmith et al., 1983). The nature of the association will become clearer as the research on the California Silicosis Registry progresses.

Table I

Number of Files Examined, Number and Proportion of Claims for Lung Disease Found from the San Francisco Office of WCAB, 1945 to 1965

Years of claim	# Files Reviewed	Claims found	Proportion/1,000
1945-49*	27,242	174	6.4
1951-55	33,321	122	3.7
1956-60	21,931	112	5.1
1962-65	18,776	57	3.0
TOTAL	101,270	465	4.6

* 1950 and 1961 are missing from current files

Table II

PMR Findings from the California Silicosis Registry: Claims of Pneumoconiosis from 1945 to 1963 Followed until 1984 (Nonmalignant Diseases Among White Males; N = 171)

CAUSE OF DEATH	OBS	EXP	PMR	95% CON INT
Tuberculosis	30	3.1	9.75	6.58, 13.92
All Circulatory Diseases	71	119.2	0.60	0.47, 0.75
All Respiratory Diseases	50	12.0	4.18	3.10, 5.51
Cirrhosis of Liver	5	3.6	1.39	0.44, 3.20
All Accidents	4	9.5	0.42	0.11, 1.07
Suicide	0	3.4	000	--- ---

Table III

PMR Findings from the California Silicosis Registry: Claims of Pneumoconiosis from 1945 to 1963 Followed until 1984 (Malignant Neoplasms Among White Males; N = 41)

CAUSE OF DEATH	OBS	EXP	PMR	95% CON INT
All Malignant Neoplasms (MN)	41	38.4	1.07	0.77, 1.45
MN of Digestive Tract	12	13.2	0.91	0.47, 1.59
MN of Pancreas	5	2.2	2.32	0.74, 5.42
MN of Respiratory System	23	10.6	2.16	1.37, 3.24
MN of Lung	22	9.9	2.22	1.39, 3.37
MN of Lymphopoietic System	3	3.3	0.90	0.18, 2.65

CONCLUSION

This preliminary assessment of the proportionate mortality risk for silicosis claims has confirmed the finding of an elevated risk for pulmonary cancer. Because this finding is preliminary and because it only represents a minority of cases expected to be in the registry when finished, some caution is needed in drawing definitive conclusions. Spoecifically, adjustment for smoking is needed, and industry-specific risks should be calculated in order to see if the risk differs according to whether there is confounding from asbestos (in construction and shipbuilding), from pyrolosis products and metal fumes (in metallurgical industries), or from radon (in mining).

In the United States there are over 3,000,000 workers exposed to silica (Frazier and Sundin, 1986) and over 100,000 patients suffering from silicosis (Wegman, 1983). In spite of the limitations of this study, several activities can and should now be undertaken:

1. Physicians who now care for silicosis patients must become aware of the consistent findings of excess lung cancer risk and transmit this information to their patients.
2. Occupational health agencies, including NIOSH, OSHA, and other public health agencies, should reexamine the current standards for silica (0.1 mg/m^3 TWA) in order to factor in the consequences of its being labelled as a probable human carcinogen by IARC (1987).
3. Additional research should now be undertaken among silica-exposed workers in order to prevent new cases of fibrotic lung disease, and to assess their risk for cancer in the absence of silicosis.

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OCCUPATIONAL ASTHMA FROM MADRAS: SOUTH INDIA

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48 cases of asthma of occupational origin were studied from industrial workers of Madras City over a period of two years. They were all from Ambathur Industry, Guindy Industrial Estate and Manali Chemical Industries. The maximum age group was 20–29 years (52%). Cotton dust, flower mills and chemicals formed 62%, 30% and 8% respectively. Lung function tests showed obstructive type of ventilatory defects. Prevention and drug therapy are discussed.

INTRODUCTION

Asthma of occupational origin is of importance, *medically* because new techniques have resulted in increased knowledge of physiopathological mechanisms involved, *occupationally* because of introduction of new chemicals.

Asthma is defined as a reversible reduction in the diameter of the bronchi which by muscular contraction hinders the passage of air. Occupational asthma is brought about by a single or repeated exposure to an active substance present in the working environment.

MATERIALS AND METHODS

About 70 doctors refer to the cases of asthma for investigation and treatment from E.S.I. Dispensaries, Madras. Cases were admitted and detailed history and clinical examinations were done—Atopy type of job, work environment and treatment already had. Blood count investigations, blood and sputum eosinophilia, chest X-ray and lung function tests were done. Intradermal skin tests were also done in the majority of the cases. Treatment with bronchodilators—oral, parenteral, aerosols were given. Desensitization of the allergen was also done. Of the total hospital admission cases, 10% were asthmatic; 10% were occupational.

Table I

Age	Male	Female	Total	%
20–29	10	15	25	52%
30–39	15	2	17	27%
40–49	6	—	6	13%
	31	17	48	

Of the 48 cases 52% were in the age group of 20–29 years, 27% were in the age of 30–39 years.

Occupations involved are tabled as:

Table II

	No.	Percentage
Cotton Dust	30	62%
Flower Mills	14	30%
Chemicals (Isocyanates)	4	8%

62% were working in cotton mills and export cotton industries.

Table III

Symptoms	No.	Percentage
Dyspnea	40	83%
Cough	18	100%
Wheezing	48	100%

Table IV

INVESTIGATION: Showed Blood and Sputum Eosinophilia

—Leukocytosis	24	50%
—Blood—Eosinophilia	48	100%
—Sputum Eosinophilia	48	100%
—Chest X-rays		
Over inflated	40	83%
Pneumothorax	2	4%
Normal	6	13%

Lung function tests were done because chest X-ray findings were not specific of asthma, and to assess the severity of respiratory impairments. It was observed that the obstructive type of ventilatory defects were due to narrowing of lung airways. The FEV_1/FVC ratio expresses the slowed expiration. Normal is 75%. Its reduction in airflow obstruction percentage results of lung function tests in cotton, flower mills and chemicals are shown in tables before and 10 minutes after solbutanol inhalation.

Table V

LFT	Cotton		Flower Mill		ChemicaL	
	B	A	B	A	B	A
FVC	1.2	1.25	1.65	1.75	2.10	2.5
FEV_1	0.67	0.67	0.90	0.90	1.65	1.75
FEV_1/FVC	57%	57	49%	59%	72	73
PER	2.2	3.3	2.3	3.4	2.4	3.6
FMEFR	0.4	0.5	0.4	0.4	0.8	0.4

Lung function tests which were done before and after exposure showed decrement of 20% predicted values in all the cases.

Treatment

Elimination of the causative agents from the environments is most ideal. Desensitization with cotton dust, flower mill dust is under trial. Routine bronchodilators with tablets, injections or aerosols, steroids and chromolynsodium are also being tried.

Occupational asthma is really a problem in our industrial country. Identifying the allergen in the working environment, removal of the causative agent and better healthier conditions of the industrial worker will augment the industrial output and the country will certainly prosper.

MANAGEMENT OF ASTHMA

Occupational asthma can be prevented by reduction of air-dusts in the workplaces by exhaust ventilation and hoods or enclosures. Reallocation to different works, though advised, is difficult because of the special training and the job skills they require. In the manufacturing process proteolytic enzymes may be added to change the allergen. Encapsulation into inert compounds and substitution for chemical powders by paste or solutions can be the ideal way of preventing occupational asthma.

Drugs used only for symptomatic relief of the attacks are:

1. Sympathomimatic (adrenergic) Epinephrine .5 ml. of 1:1000 by subcutaneously Ephedrine—50 mg. Orciprenaline sulphate—tab.10 mg. t.d.s. .5ml I.M. or I.V. drops.

2. Beta—adrenergic drugs—advantage it orally gives; sustained action, sympathomimatic side—effects are absent. Hence replaced sympathomimatic drugs. SALBUTAMOL —4 mg. tab. twice daily. Terbetaline sulphate 2.5 mg. tab.

3. Xanthenis are widely used: effective

Amino Phylline	.25 gm.	10 ml. I.V. twice daily
Theophylline	50 mg.	$\frac{\chi}{\chi}$ I.M. or I.V. twice daily
Etophyline	150 mg.	χ

4. Anticholinergic—Atropine sulphate given orally or in drip—Not used because of drying up of mucous secretion and further aggrevating bronchospasm.

5. Mast-cell Stabilizers—CROMOLYN SODIUM can be given for prophylaxis.

6. Corticosterods—oral prednisolone 30–60 mg. t.d.s. betamethazone .5 mg tab.

   4 mg/ml.—I.V. drip; Dexametha Zone 4 mg/ml. can be given; found to be less effective compared with Betamethazone studies; not effective for immediate reactions.

7. Inhalation—AEROSOL.

   Adrenaline by nebulizers or intermittent positive Breathing device (IPBD) inhalation.

   —SALBUTAMOL—100 mcg/per metered dose.
   —TERBETALINE—0.25 mg/per metered dose.
   —BETAMETHAZONE—50 mgg/inhalation
   —CROMOLYN SODIUM—inhalation.

8. ANTIBIOTICS, OPIATES, SEDATIVES, TRANQUILIZERS, EXPECTORANTS MUCOLYTIC AGENTS, I.V. FLUIDS can be used if needed.

9. Desensitization for the specific allergen can also be tried.

STATUS ASTHMATICUS: can be due to respiratory infections, respiratory depressants of early withdrawal of stands. Blood gas analysis, PH may help in addition to chest X-ray—Oxygen inhalations, adequate hydration, expectorants, antibiotics and physiotherapy will help these patients remarkably.

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LUNG MECHANICS IN ANTHRACITE COAL WORKERS' PNEUMOCONIOSIS

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INTRODUCTION

Anthracite has been traditionally in wide use both at home and in industry in Korea and, therefore, anthracite mining has always been one of the major sources of pneumoconiosis. The prevalence rate of pneumoconiosis in anthracite mines reaches at present 14.5% among coalface workers and even 24.3% among rock drillers. Coal mine dust from anthracite mines may have higher concentrations of silica than that found in bituminous coal mines. Morgan[1] reported the existence of higher prevalence rates for both simple and complicated coal workers' pneumoconiosis (CWP). The essential pathological lesion of CWP is the coal macula with its attendant focal emphysema and a little surrounding fibrosis. CWP in miners from the anthracite region is associated mainly with the presence of coal macula but also with smaller number of silicotic nodule.[2] As these lesions involve only the respiratory bronchiole, they could potentially compress or constrict the lumen of the bronchiole. Studies in coal miners with simple bituminous CWP have demonstrated small airway obstruction and slight changes in lung mechanics. However, these physiologic evidences are not detected in coal miners with simple anthracite CWP. The present study was planned to investigate the physiologic evidence of small airway obstruction and significant abnormalities of lung mechanics in anthracite coal miners with CWP.

SUBJECTS AND METHODS

The subjects of this study comprised 178 anthracite coal miners with CWP and 25 normal subjects as a control group. Miners with significant heart or lung disease were excluded. Miners with CWP were divided into two groups. The first group consisted of 148 miners with suspected or simple CWP. This group was selected on the basis of an absence of significant impairment of ventilatory capacity as defined by a $FEV_{1.0}$ to FVC ratio of not less than 70%. The second group consisted of 30 miners with progressive massive fibrosis (PMF). Many of these subjects had airway obstruction ($FEV_{1.0}$/FVC <70%).

Spirometry was performed using a waterless electronic spirometer attached to Autobox system (model CS-828 FC, Chest Co., Japan). Lung volumes and airway resistance were measured in a constant pressure (flow displacement type) both plethysmograph of Autobox system by the methods of DuBois et al.[3] and Woitowitz and Buchheim.[4]

Compliance was obtained as the ratio of the change in volume to the change in transpulmonary pressure. Transpulmonary pressure was obtained by electronically subtracting mouth pressure from esophageal pressure, which was measured by a 10 cm later balloon attached by polyethylene tube to a pressure transducer. The tip of the balloon was positioned approximately 40–45 cm from the nares. Static compliance was measured from the linear portion, just above FRC, of the expiratory limb of the pressure-volume curve obtained over the full VC range. Pulmonary recoil pressure at TLC (Pst TLC) was also obtained from this curve. The coefficient of retraction was calculated by dividing Pst TLC by TLC. Dynamic compliance was measured at respiratory rates of approximately 30 (0.5 Hz), 42 (0.7 Hz), 54 (0.9 Hz) and 72 (1.2 Hz) breaths/min, and calculated by dividing the change in volume by the corresponding change in transpulmonary pressure at points of zero flow over five respiratory cycles and taking the mean value. Frequency dependence of compliance was defined as a fall in Cdyn/initial Cdyn to less than 80%. All measurements were performed in the sitting position.

RESULTS AND DISCUSSION

The subjects with category 3 and PMF were significantly older than those with control and suspected CWP. The subjects with PMF had significantly worked longer underground than those with suspected CWP. (Table I)

Lung function datums of the subjects are illustrated in Table II. No significant differences were found for all measurements among the groups with control and each category of simple CWP. However, RV tended to be rather higher than predicted in all categories of simple CWP. Mean values of $FEV_{1.0}$ and $FEV_{1.0}$ /FVC were abnormally reduced in all categories of PMF, and those of RV and RV/TLC were significantly lower in PMF than in simple CWP. These findings might be related to the airway obstruction.

Mean results of lung mechanics of the subjects are recorded in Table III. Static compliance (Cst), specific compliance (SCst), pulmonary recoil pressure at TLC (Pst TLC) and coefficient of retraction in individual subjects are illustrated in Figures 1, 2, 3 and 4. In suspected or simple CWP, mean values of airway resistance, Cst, Pst TLC and coefficient of retraction were normal. There were no significant differences in these measurements between control group and CWP group. Static compliance was not related to the category of simple CWP and also, no relationship was observed between specific compliance and increasing

Table I

Characteristics of the Subjects by Radiographic Finding of Coal Workers' Pneumoconiosis

(Mean±SD)

Radiographic finding	No. of subjects	Age (yr)	Height (cm)	Weight (kg)	BSA (m^2)	Cigarettes (pack yr)	Time underground (yr)
Controls	25	41.0 ±11.3	168.4 ±5.5	59.8 ±6.8	1.68 ±0.11	17.9 ±12.3(19)	
Suspected	24	43.9 ±6.6	165.2 ±5.0	60.6 ±6.4	1.66 ±0.09	13.6 ±6.6(19)	14.4 ±6.3
SRO	124	45.5 ±7.2	165.2 ±5.5	59.9 ±6.9	1.66 ±0.10	15.3 ±9.7(105)	16.4 ±6.2
Category 1	66	44.9 ±7.5	164.8 ±5.7	59.9 ±6.4	1.65 ±0.10	15.0 ±7.7(56)	15.9 ±6.3
2	41	45.1 ±7.0	165.1 ±5.2	60.3 ±8.0	1.66 ±0.11	16.5 ±11.2(35)	16.3 ±6.1
3	17	48.9 ±5.5	166.7 ±5.4	59.1 ±6.0	1.66 ±0.09	13.7 ±7.3(12)	19.0 ±5.0
LO	30	51.3 ±5.4	164.4 ±6.0	57.8 ±8.0	1.63 ±0.13	9.3 ±10.7(12)	18.2 ±6.4

BSA: body surface area, SRO: small rounded opacity, LO: large opacity, Pack yr: packs of cigarettes per day×smoking years. Parentheses indicated the number of current smoker.

Table II

Lung Function Data in Controls and Miners with Coal Workers' Pneumoconiosis

Radiographic finding	No. of subjects	VC (% pred.)	$FEV_{1.0}$ (% pred.)	$FEV_{1.0}$/FVC(%)	FRC (% pred.)	RV (% pred.)	TLC (% pred.)	RV/TLC (%)	RV/TLC (% pred.)
Controls	25	107.9 ±9.1	100.8 ±11.1	83.7 ±5.6	104.3 ±9.1	129.2 ±25.8	106.4 ±9.1	30.7 ±6.5	107.0 ±15.8
Suspected	24	109.1 ±11.6	100.0 ±10.5	80.6 ±5.9	110.3 ±18.5	139.2 ±32.4	111.4 ±15.4	32.1 ±6.2	109.3 ±18.9
SRO	124	107.7 ±12.5	99.0 ±12.3	79.6 ±5.7	110.1 ±13.3	137.8 ±27.1	107.9 ±10.2	32.7 ±5.7	109.3 ±18.2
Category 1	66	109.6 ±11.6	100.5 ±12.0	79.9 ±5.9	110.6 ±12.1	138.4 ±27.7	109.2 ±9.3	32.2 ±5.8	108.3 ±18.9
2	41	106.3 ±12.8	96.1 ±11.5	78.3 ±5.3	110.1 ±15.5	136.6 ±27.0	106.5 ±11.6	32.6 ±5.3	109.7 ±17.2
3	17	103.9 ±14.7	100.4 ±14.5	81.8 ±5.4	108.3 ±12.4	138.2 ±25.9	106.3 ±9.8	35.0 ±6.1	112.0 ±18.9
LO	30	91.2 ±19.3	66.7 ±25.2	62.5 ±15.9	109.8 ±18.1	159.6 ±43.1	103.6 ±14.7	41.8 ±9.3	128.9 ±27.2
Category A	12	93.1 ±21.2	73.0 ±23.4	66.2 ±13.6	106.5 ±23.3	157.7 ±52.3	104.1 ±17.4	40.4 ±10.0	126.4 ±31.3
B	12	91.8 ±18.2	70.4 ±28.8	64.4 ±15.5	111.9 ±13.6	159.1 ±38.1	104.1 ±12.7	41.7 ±8.8	130.6 ±25.8
C	6	86.1 ±20.0	47.0 ±8.9	51.8 ±18.5	112.5 ±16.1	164.5 ±39.1	101.6 ±15.1	44.7 ±9.6	130.6 ±25.1

Table III

Lung Mechanics in Controls and Miners with Coal Workers' Pneumoconiosis

Radiographic finding	Raw ($cm H_2O/l/sec$)	MBC (% pred.)	Cst ($l/cm H_2O$)	SCst ($l/cm H_2O/l$)	Cdyn ($l/cm H_2O$)	Pst TLC ($cm H_2O$)	Coeff. retract. ($cm H_2O/l$)
Controls	1.16 ±0.24		0.222 ±0.050	0.062 ±0.020	0.186 ±0.053	29.19 ±7.12	4.850 ±1.210
Suspected	1.32 ±0.46	112.5 ±11.5	0.244 ±0.061	0.067 ±0.011	0.187 ±0.058	26.93 ±7.11	4.517 ±1.419
SRO	1.25 ±0.29	107.3 ±14.5	0.229 ±0.069	0.062 ±0.016	0.179 ±0.054	30.30 ±11.51	5.177 ±2.211
Category 1	1.25 ±0.29	109.6 ±14.9	0.239 ±0.067	0.064 ±0.015	0.182 ±0.049	27.52 ±8.79	4.627 ±1.613
2	1.27 ±0.34	104.0 ±13.3	0.225 ±0.072	0.061 ±0.017	0.180 ±0.058	31.97 ±13.57	5.558 ±2.694
3	1.20 ±0.18	106.1 ±14.7	0.201 ±0.060	0.054 ±0.015	0.161 ±0.062	37.03 ±12.55	6.395 ±2.381
LO	2.96 ±2.35	76.7 ±26.6	0.185 ±0.080	0.046 ±0.020	0.132 ±0.068	34.65 ±13.77	6.510 ±3.447
Categery A	2.88 ±2.82	81.2 ±22.5	0.195 ±0.089	0.051 ±0.021	0.136 ±0.056	28.97 ±14.22	5.591 ±3.886
B	2.66 ±2.07	81.3 ±31.5	0.214 ±0.088	0.051 ±0.016	0.160 ±0.078	34.06 ±12.90	6.216 ±3.215
C	3.74 ±2.06	52.9 ±9.5	0.106 ±0.025	0.027 ±0.068	0.071 ±0.016	47.20 ±4.76	8.935 ±1.915

Raw: airway resistance, MBC: maximal breathing capacity, Cst: static compliance, SCst: specific compliance (Cst/FRC), Cdyn: dynamic compliance during quiet breathing (23 breaths/min), Pst TLC: static pulmonary recoil pressure at TLC, Coeff. retract: coefficient of retraction (Pst TLC/TLC)

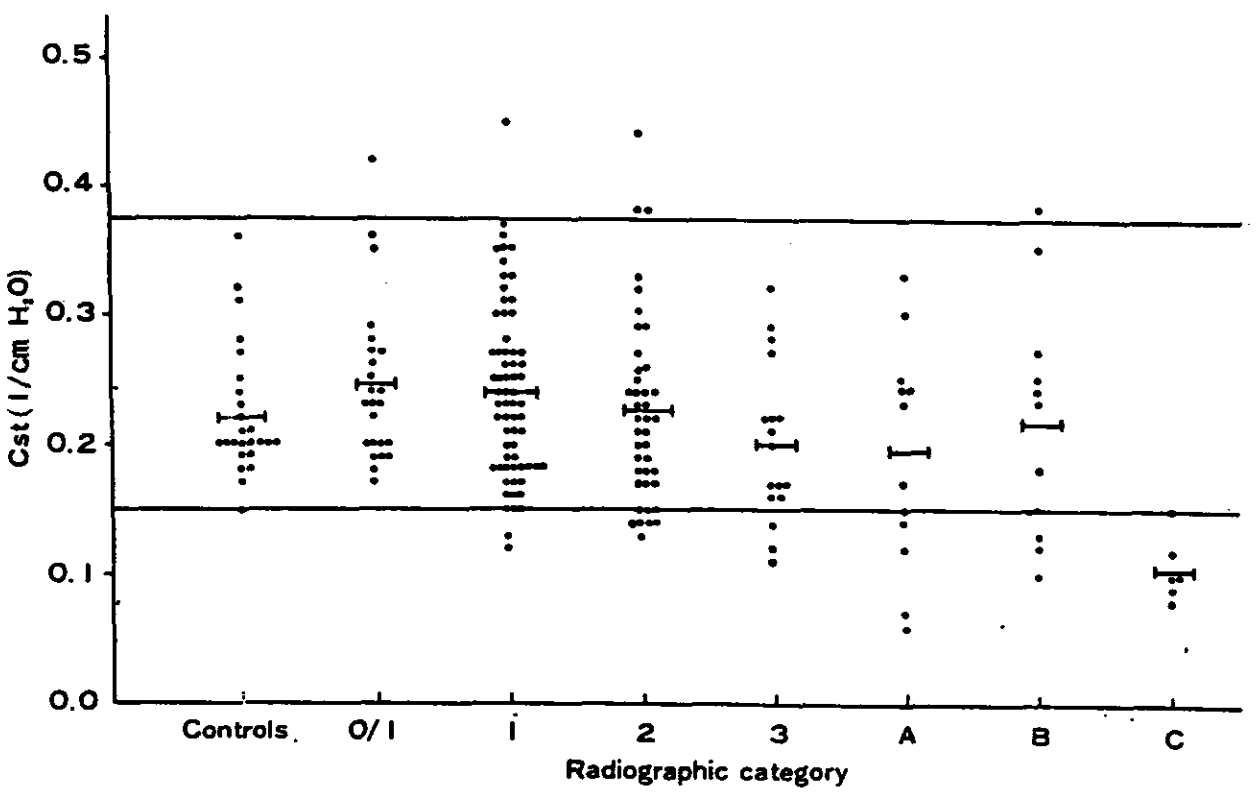

Figure 1. Static compliance in controls and miners with different radiographic categories of coal workers' pneumoconiosis (CWP). Horizontal line represented the normal range and horizontal bar represented the mean value.

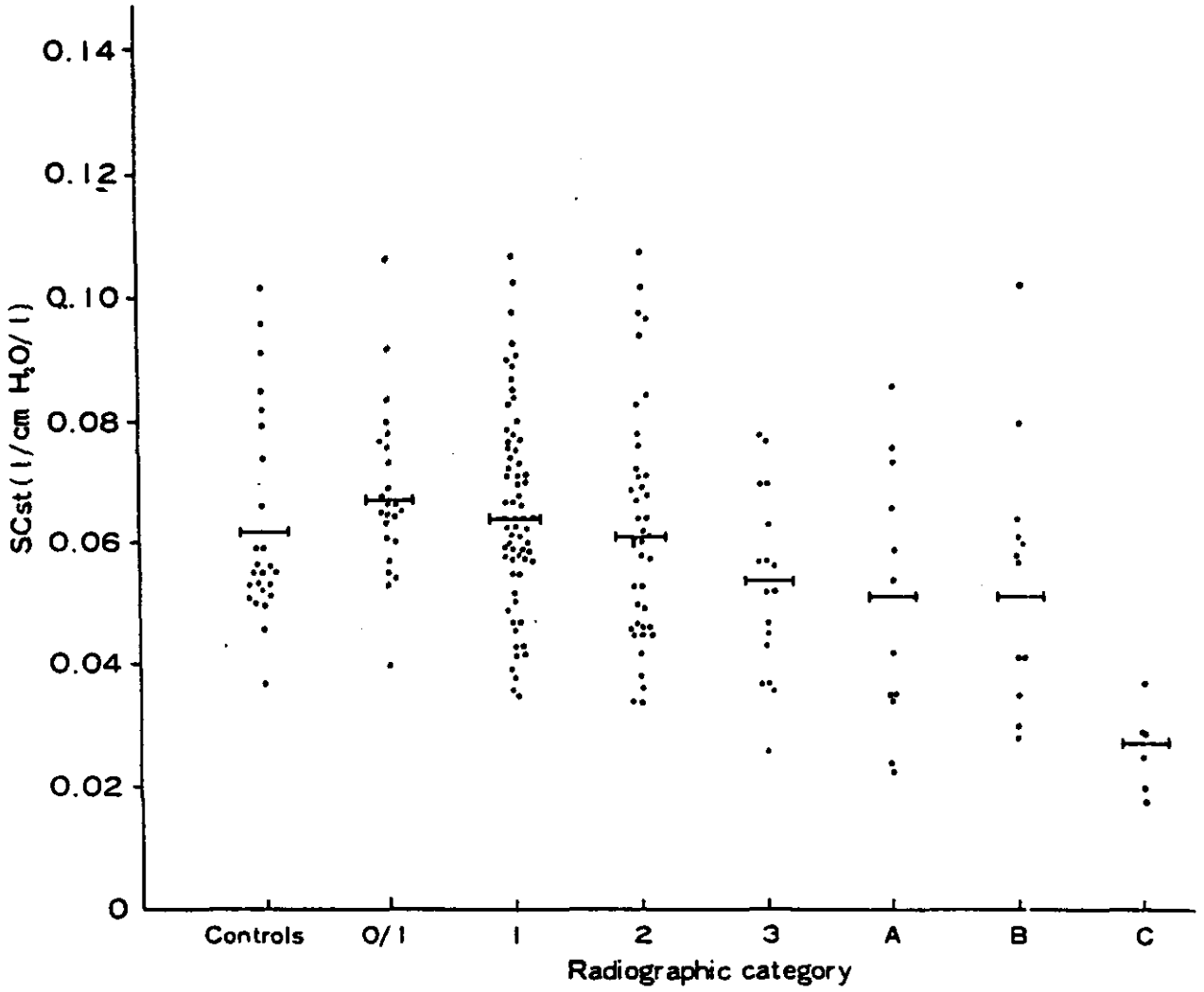

Figure 2. Specific compliance in controls and miners with different radiographic categories of CWP. Horizontal bar represented the mean value.

category of simple CWP. Dynamic compliance at quiet breathing tended to be somewhat lower than static compliance in all categories. Mean coefficient of retraction and number of individuals with higher coefficient tended to increase with increasing category. Subjects with abnormally high coefficient showed 9.1%, 14.6% and 41.2% in category 1, 2 and 3, and those with abnormally low coefficient 22.7%, 14.6% and 0% in category 1, 2 and 3. Pst TLC had the same tendency as coefficient.

In PMF, airway resistance was abnormally increased and mean values of Cst, Pst TLC and coefficient of retraction were normal except category C. A large number of miners fell outside the normal range of Cst and most of these showed values lower than normal, and this was most marked in miners with category C. Dynamic compliance at quiet breathing was lower than static compliance, as in suspected or simple CWP. Similarly, in category C, 5 and 4 of 6 miners showed values of Pst TLC and coefficient higher than normal.

Since the essential pathological lesion of CWP is the coal macula with its attendant focal emphysema and a little surrounding fibrosis, the physiological abnormalities might be detected by the measurements associated with emphysema. These might include an increase in RV and alterations in lung mechanics, such as a high compliance and a low pulmonary recoil pressure and coefficient of retraction. However, if significant interstitial fibrosis were present in the coal macula, these latter changes could be masked and demonstrate a low compliance and a high pulmonary recoil pressure and coefficient.

In a detailed study of lung mechanics in CWP, Ferris and Frank[5] found compliance to be somewhat reduced in subject with complicated CWP. In the subjects with no or simple CWP, there was a wide scatter of compliance value. Seaton et al.[6] studied the lung mechanics in bituminous miners with CWP. In the subject with simple CWP, static compliance was mostly in the normal range, whereas it was

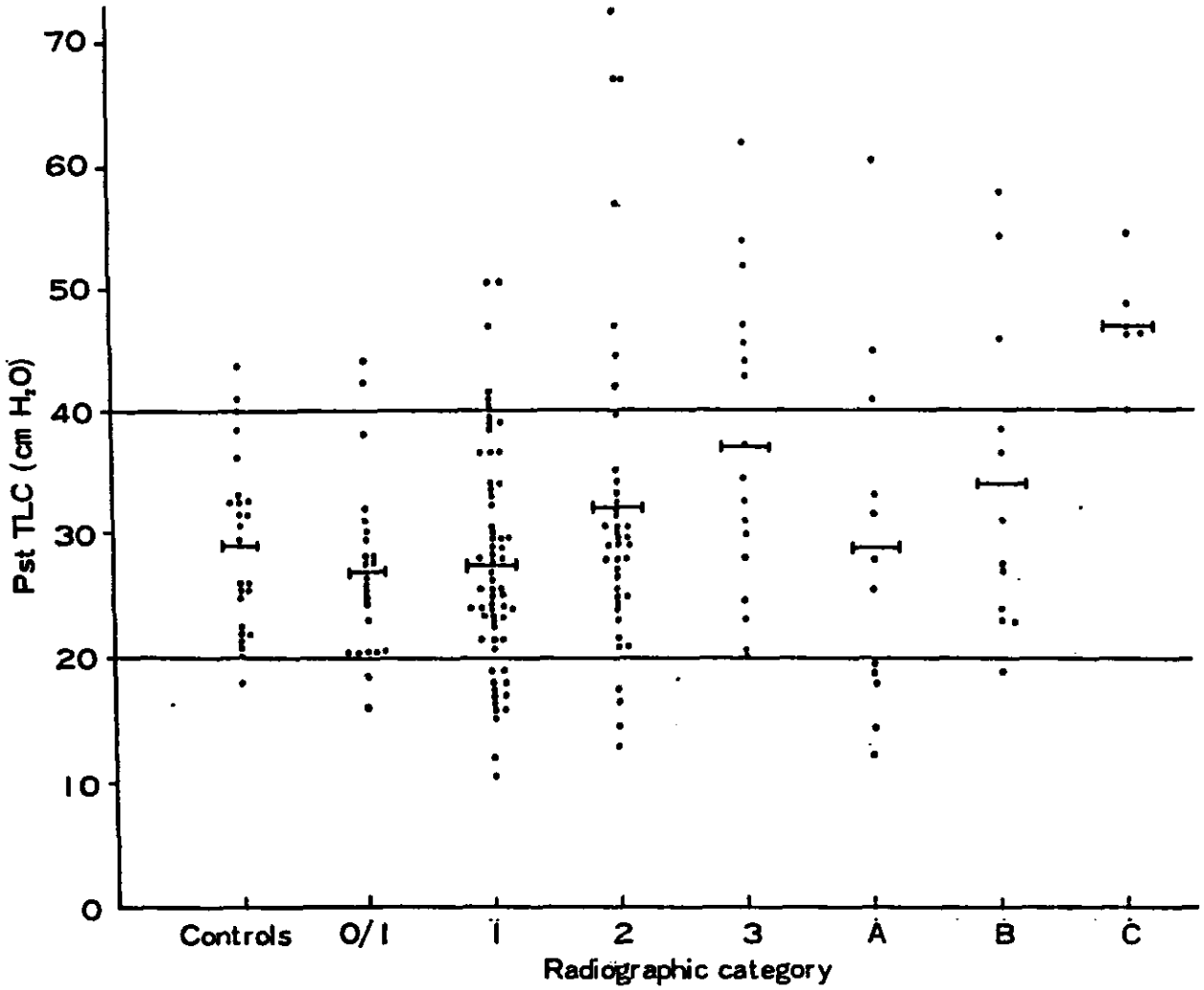

Figure 3. Static pulmonary recoil pressure at total lung capacity in controls and miners with different radiographic categories of CWP. Horizontal line represented the normal range and horizontal bar represented the mean value.

often reduced in complicated CWP. The coefficient of retraction was normal or reduced in most subjects except those with category B and C PMF. They noted that so far as simple CWP was concerned, abnormalities reflected emphysema rather than fibrosis and in severe PMF, changes suggesting fibrosis tended to predominate. Murphy et al.[7] studied a group of 20 miners with simple anthracite CWP and found no significant alterations in lung mechanics. They pointed out that the absence of decreased maximum expiratory flow, a normal coefficient, and a normal specific compliance made significant emphysema most unlikely.

Our findings studied anthracite miners with CWP were similar to the results obtained by the above authors and found a negative correlation between coefficient of retraction and RV, FRC and RV/TLC in miners with suspected or simple CWP. As these measurements correlated with the pathological demonstration of emphysema,[8] a low coefficient may well also be a guide to the presence of emphysema.

If interstitial fibrosis were the predominant change in miners, they should have demonstrated reduced compliance and elevated coefficient and pulmonary recoil pressure. Among the subjects with simple CWP, the number of individuals with abnormally reduced coefficient tended to be more than those with elevated coefficient in category 1 and individuals with elevated coefficient were more than those with reduced coefficient. Among the subjects with PMF, especially category C, most of them had reduced compliance and elevated coefficient. These findings suggested that in simple anthracite CWP, the abnormalities tended to reflect focal emphysema rather than fibrosis in category 1 and fibrosis rather than emphysema in category 3, and in severe PMF, fibrosis tended to predominate.

As the coal macula and the silicotic nodule which are characteristic histological findings of anthracitic CWP are found in relation to the respiratory bronchiole, they could potentially compress or constrict the lumen of the bronchiole.

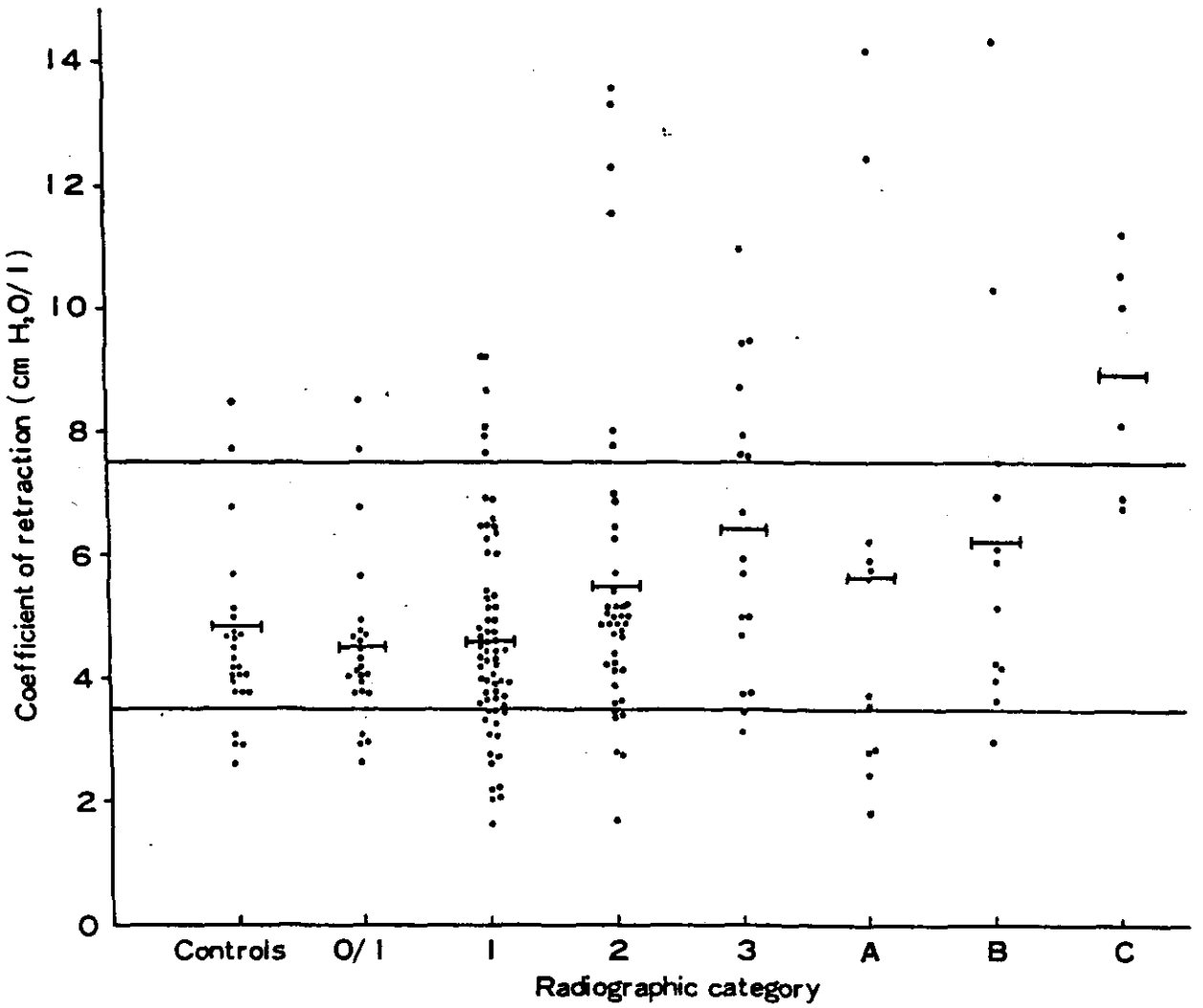

Figure 4. Coefficient of retraction in controls and miners with different radiographic categories of CWP. Horizontal line represented the normal range and horizontal bar represented the mean value.

The technique available to assess the presence of abnormal resistance to airflow through the small airways is the measurement of compliance at increasing respiratory rates.[9] It has been assumed that regional differences in elastic properties sufficient to cause a detectable fall in dynamic compliance at rapid respiratory rates should result in an abnormal static compliance curve. Thus, if a patient has normal pulmonary resistance, spirometry and static pressure-volume curve, a fall in dynamic compliance at faster rates of respiration (frequency dependence of compliance) is most probably due to peripheral airways obstruction. Seaton et al.[6] and Lapp and Seaton[10] noted that 17 of the 25 working bituminous miners with simple CWP demonstrated frequency dependence of compliance, and that this finding did not relate to bronchitis and type of opacity. However, Murphy et al.[7] were unable to detect significant changes in either small airway narrowing and lung mechanics in miners with simple anthracite CWP.

In our study, miners with simple anthracite CWP showed a fall (less than 80%) in dynamic compliance at faster rates of respiration, compared to those with control and suspected CWP. There was no relationship between a change in dynamic compliance at faster rates of respiration and category of simple CWP. (Table IV. Figure 5) In 96 suspected or simple CWP miners with normal spirometry and static pressure-volume curve, the frequency dependence of compliance was observed in 46.9% at 55 breaths/min and in 62.5% at 76 breaths/min. This finding appeared to be the result of increased resistance to airflow in small peripheral airways but was not related to the category of opacity. (Table V)

SUMMARY

The mechanical properties of the lungs were studied on 25 normal subjects, 148 anthracite miners with suspected or simple coal workers' pneumoconiosis (CWP) and 30 miners with progressive massive fibrosis (PMF). The mean values of

Table IV

Dynamic Compliance at Different Respiratory Rates in Controls and Coal Workers' Pneumoconiosis Miners with Normal Pressure-Volume Curve

(l/cm H_2O)

Radiographic category	No. of subjects	Respiratory rate (breaths/min)				
		23	31	43	55	76
Controls	21	0.185±0.054	0.176±0.055 (94.5±8.1)	0.169±0.057 (90.6±9.3)	0.161±0.052 (86.4±8.2)	0.151±0.051 (81.1±9.2)
Suspected	17	0.181±0.040	0.167±0.038 (92.5±8.5)	0.161±0.039 (89.4±15.9)	0.156±0.034 (87.2±15.9)	0.144±0.035 (80.2±16.1)
SRO	79	0.179±0.040	0.163±0.037 (91.4±11.7)	0.157±0.040 (87.8±13.7)	0.145±0.039 (81.2±15.8)	0.124±0.037 (69.4±15.8)
Category 1	46	0.179±0.038	0.165±0.037 (92.2±11.5)	0.159±0.039 (88.4±13.6)	0.142±0.038 (79.5±16.7)	0.120±0.033 (67.6±15.5)
2	26	0.178±0.041	0.159±0.034 (90.7±11.0)	0.154±0.038 (87.9±14.6)	0.147±0.039 (83.4±14.8)	0.126±0.040 (73.4±18.3)
3	7	0.187±0.050	0.166±0.047 (89.4±17.2)	0.157±0.052 (83.5±10.7)	0.156±0.047 (83.5±14.7)	0.137±0.049 (73.4±18.3)

Parentheses indicated the dynamic compliance expressed as a percentage of the initial (23 breaths/min) dynamic compliance.

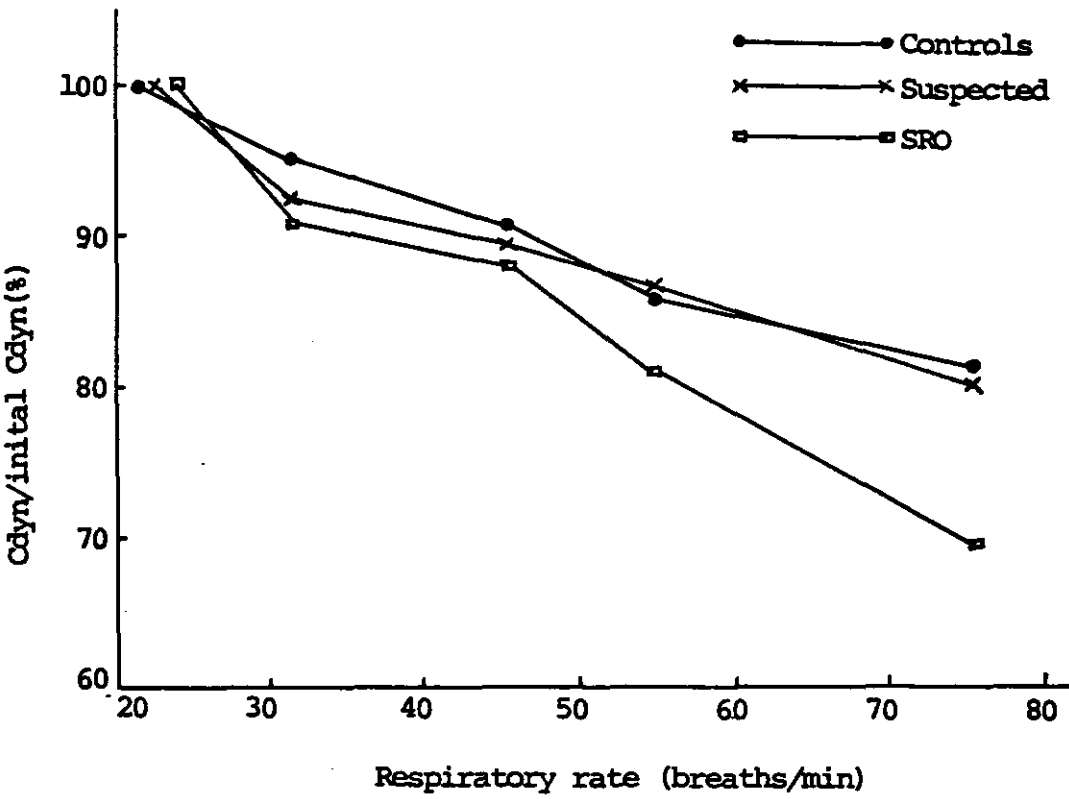

Figure 5. Dynamic compliance with different respiratory rates expressed as a percentage of the dynamic compliance during quiet breathing in controls and suspected or simple CWP miners with normal pressure-volume curve.

Table V

Number of Subjects with Frequency Dependence of Dynamic Compliance in Different Respiratory Rates by the Category of Coal Workers' Pneumoconiosis

Radiographic category	No. of subjects	Respiratory rate (breaths/min)			
		31	43	55	76
Controls	21	—	2 (9.5)	3(14.3)	5(23.8)
Category 0/1	17	1 (5.9)	6(35.3)	7(41.2)	10(58.6)
1	46	6(13.0)	9(19.6)	24(52.2)	32(69.6)
2	26	3(11.5)	8(30.8)	11(42.3)	14(53.8)
3	7	2(28.6)	2(28.6)	3(42.9)	4(57.1)
Subtotal	96	12(12.5)	25(26.0)	45(46.9)	60(62.5)

Frequency dependence of dynamic compliance was defined as a fall in Cdyn/initial Cdyn to less than 80 % (Seaton *et al.*, 1972a). Parentheses inidicated the percentage.

static compliance, pulmonary recoil pressure at total lung capacity and coefficient of retraction were normal in all categories of CWP. The static compliance was within normal range in most miners with suspected or simple CWP, whereas it was often reduced in miners with PMF, particularly in category C. The number of miners with higher coefficient of retraction tended to increase in parallel with the progression of pneumoconiosis in terms of the category of opacity. The coefficient of retraction was mostly elevated in miners with category C among PMF. In simple CWP, the abnormalities of lung functions concerned with gas exchange tended to reflect focal emphysema rather than fibrosis in category 1, and fibrosis rather than focal emphysema in category 3. In severe PMF (especially category C), fibrosis tended to predominate. In 96 suspected or simple CWP miners with normal spirometry and static pressure-volume curve, the frequency dependence of compliance was observed in 45 miners (46.9%) at 55 breaths/min and in 60 miners (62.5%) at 76 breaths/min. This finding appeared to be the result of increased resistance to airflow in small peripheral airways.

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BRONCHOALVEOLAR LAVAGE AND SILICOSIS PATHOGENESIS

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INTRODUCTION

Inhalation of silica can lead to chronic inflammatory interstitial lung injury susceptible to progress to silicosis with clinical expression.

The modern theories about pathogenesis of silicosis are clearly synthesized by Davis[7] and consider that the silica-laden alveolar macrophages maintain viability and phagocytotic ability and once activated by the noxious dust produce pro-inflammatory mediators which are able to initiate the disease pathogenic pathways, such as interleukin, chemotaxis, macrophage derived growth factor.

The alveolar macrophage of these patients is also able to release or provoke the releasing of Paf-acether[15] and histamine mediators that also interfere in the disease process.

As the silica is indestructible and the lung tissue clearance of silica dust is very slow[4] the chronically activated silica-laden macrophages perpetuate the inflammatory process, continuously releasing the above mentioned mediators.

In these patients, besides the inflammatory process, there are immumologic mechanisms locally expressed by an increasing in the T-lymphocytes.[3,7,17]

All these facts suggests the existence in the chronic silica exposed workers of an alveolitis what had been confirmed by different authors[14,12,7,13] and evoke the interest of the bronchoalveolar lavage in their study.

In this article we studied a group of 34 long-term silica-exposed workers with a broad spectrum of disease manifestations through clinical chest X-ray, Functional and Bronchoalveolar lavage fluid investigations in order to achieve a better comprehension of the disease pathogenesis and evaluate the eventual correlation between the BAL data and clinical manifestations.

MATERIALS AND METHODS

Patients

Thirty-four patients were studied being 27 males and 7 females with ages ranging between 31 and 78 years old ($\bar{X} = 48 \pm 13$). Fifteen of the patients were smokers and none of them had previous history of any other pulmonary disease. All were current workers in industry with exposition at least in the week prior to evaluation.

As generally accepted[7] the diagnosis of silicosis was based on a history of a prolonged exposure to silica dust and a chest X-ray showing shadows compatibles with silicosis in category 1 or above according to ILO classification.[8]

All patients were submitted to a standard posterior anterior chest X-ray, read by 3 observers according to ILO classification and to a functional study by global body plethysmography.

The patients were divided in two groups. The group I,was composed of 22 patients without or only with bronchial complaints, radiograph of the category 1 and normal functional tests or with a mild obstructive syndrome. The group II was constituted by 12 patients with complaints suggesting interstitial involvement, chest X-ray above category 2 and frequently with coalescence of lesions and functionally with volumetric restriction.

Controls

As controls we used 6 normal volunteer without exposition to silica containing dust, with a distribution by sex and ages similar to patients. Two of the controls were smokers.

Bronchoalveolar Lavage (BAL)

The BAL procedures and analyses have been previously described.[11] Briefly bronchoalveolar lavage was performed by slow infusion of 4 × 50 ml 37°C aliquots of saline solution through a 50 ml Luer-lock Syringe attached to the bronchofiberscope, followed by gentle syringe aspiration of the effluent. The BAL was performed in one of the middle lobe sub-segments.

After remotion of mucus cells were counted in a hemocytometer and cytocentrifuge smears were prepared and stained by May-Grunwald Giemsa for identification of the cellular population.

The cellular pellet was obtained by centrifugation, 500 G at 40°C during 20 minutes, washed twice with PBS solution and resuspended in PBS solution at the final concentration of 5×10^6 cells/ml. Then the T-Lymphocytes and its subpopulation were characterized by indirect immunofluorescence after banding to specific monoclonal antibodies.

The BALF supernatants were concentrated 25 folds by ultrafiltration and the IgA and IgG dosed by radial immunodifusion (Mancinni technique).

In order to evaluate the eventual modification of the surfactant in patients and the release of active lipidic molecules, the lipidic composition of the supernatants of 8 of the patients and 4 controls were studied by thin layer chromatography and phosphorous analysis[9] and the etherlipids and Lyso-Paf-acether were assayed by washed rabbit platelet aggregability, method of Benveniste.[2]

RESULTS

The chest radiographs were classified in category pl in 65% of the patients and in above categories in 35% of the cases. Fifteen per cent of the patients presented coalescence of opacities and 30% stated hilar involvement (Table I).

The ventilatory tests were normal in 41% of the patients; 32% had obstructive syndromes, 19% restrictive syndromes and 14% combined ventilatory syndromes (Table II).

Under the defined criteria 65% of the patients must be included in category I and 35% in category II.

From the analysis of the cellularity of patients BAL effluents appears the increasing number of cells per ml, statistically significant in category II patients (Table III).

In this category of patients is almost constant the existence of an alveolitis depending on an increasing of the macrophages and Lymphocytes, mainly of these last ones which are 9 folds above the normal values. It appears also that even in category I there is a significant increase of the number of lymphocytes. Finally the number of cells, macrophages and lymphocytes is significantly higher in category II patients than in category I.

The analysis of the lymphocytic populations through monoclonal antibodies shows in category II a significant increase of the T lymphocytes, T helper lymphocytes and much more striking of the T suppressors. However percentually there is a decrease of the T helper and increase of the T suppressors leading to an inversion of T_h/T_s ratio (Table IV). The increasing of T suppressors and the inversion of T_h/T_s ratio is also evident in category I patients.

The IgA is slightly and the IgG significantly higher among patients of category II than of category I (Table V).

The analysis of the lipidic composition of surfactant makes evident a significant diminishing of the phosphatidylcholine among patients, correlating inversely with the numbers of macrophages and lymphocytes (Tables VI and VII).

In none of the studied BAL effluents Paf-acether was found. However in the patients there was a significant increase of its percursor the Lyso-Paf-acether as compared to normal controls and an exponential correlation with the number of lymphocytes was found in patients (Table VIII). No correlation between Lyso-Paf-acether and phosphatidylcholine rates was found.

DISCUSSION

From the results of BAL studies of workers exposed to silica we had studied, appear that the composition of lower respiratory tract fluid clearly reflect the clinical spectrum of the respiratory disease caused by chronic inhalation of silica containing dust.

Table I
Chest Radiographs

p = 1	65%
p > 1	35%
CONFLUENCE	15%
hi	30%

Really it had been in BAL effluents of category II patients that we had found the most impressive increasings of immunological and inflammatory effectors cells and it had been in the patients with alveolitis that the ventilatory impairment is more frequent and important.

These data are in agreement with those referenced in literature reporting either to cases with history of exposition but without disease, either to complicated forms of silicosis, being possible, in both cases, to disclose the existence of an alveolitis.[3,5,6]

Once more the central role of Alveolar Macrophage in the chronic inflammatory lung process remains evident through its potent immuno-modulatory action, its capacity of secret fibro regulatory compounds[3,10,12] and Paf-acether, once activated by occupationally relevant stimulus.[1,15,18] Indeed in category II patients there is a significant increase of the A.M. number and in both categories signs of cellular activation: increased number of A.M. with two or more nuclei and of foamy cells, spontaneous formation of rosettes A.M.—Lymphocytes and a percentage of giant cells above 2%.

This evidence of activation becomes more important once accepted the hypothesis that the silica stimulated A.M. releases in vivo Il_1. Then the T-lymphocytes activated by Il_1 enhances the secretion of macrophage activating factor, migration inhibition factor and other molecules leading to the recruitment of peripheral blood monocytes and to the proliferation of resident macrophages, amplifying and perpetuating the local inflammatory response, even after ceasing of the silica containing dust exposition.[12] This hypothesis is also corroborated by the increased number of OKM_1 positive cells we had found in BAL fluids of patients with occupational respiratory diseases caused by mineral containing dust inhalation.[6]

Another important fact to be stressed is the evidence of local cellular and humoral immune abnormalities in silicotic patients.

It is reasonable to think that the T lymphocyte stimulated by the activated A.M. releases Il_1 leading to a T-helper local proliferation. Simultaneously the A.M. also perhaps secret molecules with inhibitory functions causing an increasing in the number of T suppressor cells[12] with the objective of

Table II
Ventilatory Function

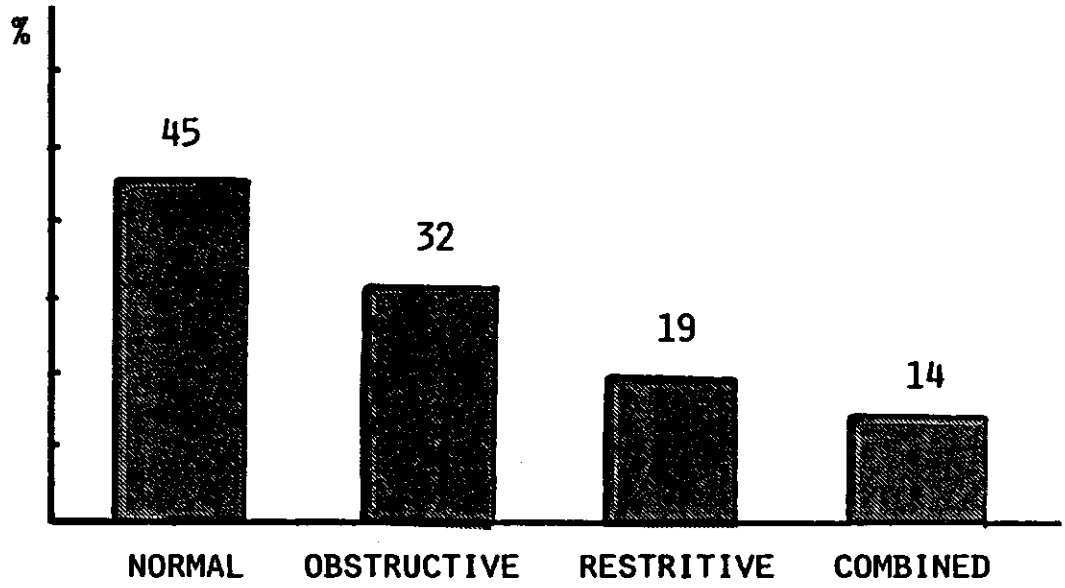


Table III
Number of Cells × 10^4/ML

	TOTAL CELLS	MACROPHAGES	LYMPHOCYTES	P.M.N.
CATEGORY I n = 6	16,7± 7,7	13,4± 6,9	3,7±2,2	0,3±0,6
CATEGORY II n = 6	44,7±14,5	28,6±13,4	15,1±5,3	1,1±2,6
CONTROLS n = 6	17,4± 4,1	15,8± 3,8	1,6±0,6	0,2±0,1

CONTR.-CAT. I	N.S.	N.S.	p < 0,02	
CONTR.-CAT.II	p < 0,001	p < 0,05	p < 0,001	N.S.
CAT.I - CAT.II	p < 0,001	p < 0,001	p < 0,001	

T - STATISTIC ANALYSIS

Table IV
T-Lymphocytes (Cells × 10^3/ML

	T_3	T_4	T_8	T_4/T_8
CATEGORY I n = 6	14,5±10,2	10,2± 5,7	16,1± 7,6	0,8±0,4
CATEGORY II n = 6	106,1±34,7	37,7±14,1	64,4±26,6	0,6±0,2
CONTROLS n = 6	10,9± 3,4	6,6± 1,9	4,1± 1,3	1,6±0,1

CONT.-CAT. I	N.S.	N.S.	$p < 0,01$	$p < 0,001$
CONT.-CAT.II	$p < 0,001$	$p < 0,001$	$p < 0,001$	$p < 0,001$
CAT.I-CAT.II	$p < 0,001$	$p < 0,01$	$p < 0,01$	N.S.

T - STATISTIC ANALYSIS

braking the immune local reaction. In mild forms of disease this equilibrium seems to be sufficient.

In complicated silicosis there are simultaneously increased number of T helper and T suppressor cells and it is possible to speculate that these immunoabnormalities contribute to the pathogenic mechanisms.

The modifications in the composition of surfactant phospholipids suggest that silica, through its cytotoxic action, damage the type II Pneumocyte with perturbation of normal surfactant functions. Once that it seems[20] that the surfactant improves the mucus transport in airways, it is possible that this is one of the responsible mechanisms for the high frequence of bronchial complaints among silicotic patients. This hypothesis is reinforced by the data of the Louisiana study on workers with complicated silicosis in which increased number of type II Pneumocyte in lavage were found.[14]

Although Paf-acether wasn't found in lung lavages of patients our data provides some evidence of an activation of the Paf-acether pathway based in the great increase in Lyso-Paf-acether rates (percursor of Paf-acether) and its correla-

Table V
Immunoglobulins

	IgG	IgA
CATEGORY I n = 6	2,3±2,6	2,1±2,8
CATEGORY II n = 6	7,5±4,3	2,0±0,7
CONTROLS n = 6	1,1±1,1	0,7±0,8

CONTR.-CAT. I	N.S.	N.S.
CONTR.-CAT.II	p < 0,001	p < 0,02
CAT.I -CAT.II	p < 0,05	N.S.

T - STATISTIC ANALYSIS

Table VI
Surfactant Phospholipids

	PHOSPHOLIPIDS TOTAL µg/ml	PHOSPHATIDILCHOLINE (%)
CONTROLS	25.4±7,8	28.2±5.9
		S**
SILICOSIS	21.6±4.0	16.5±3.6

S** p < 0,02

Table VII
Surfactant Analysis

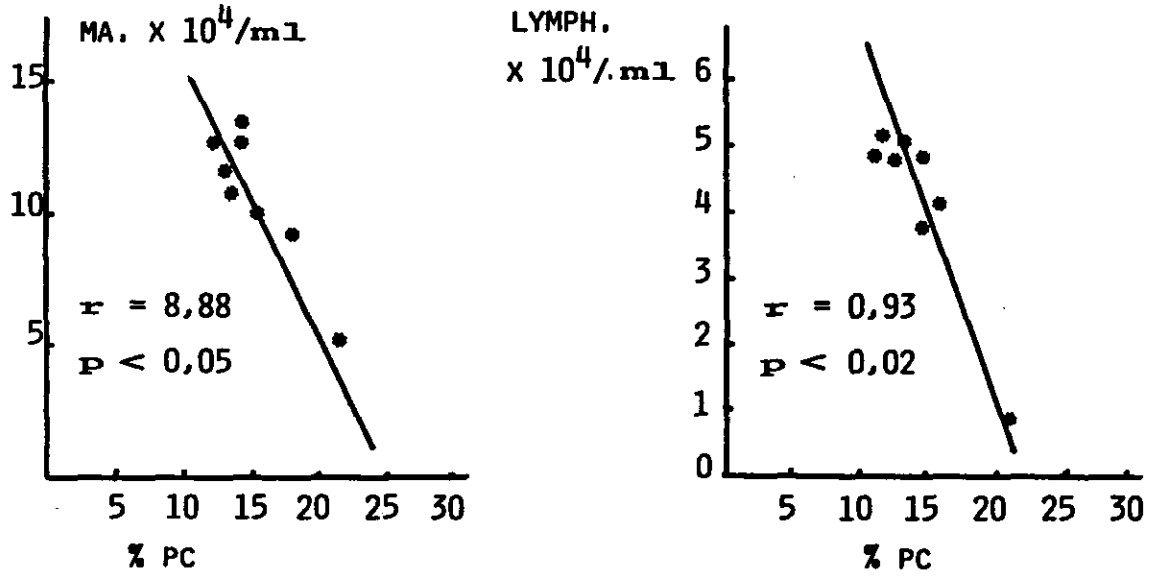
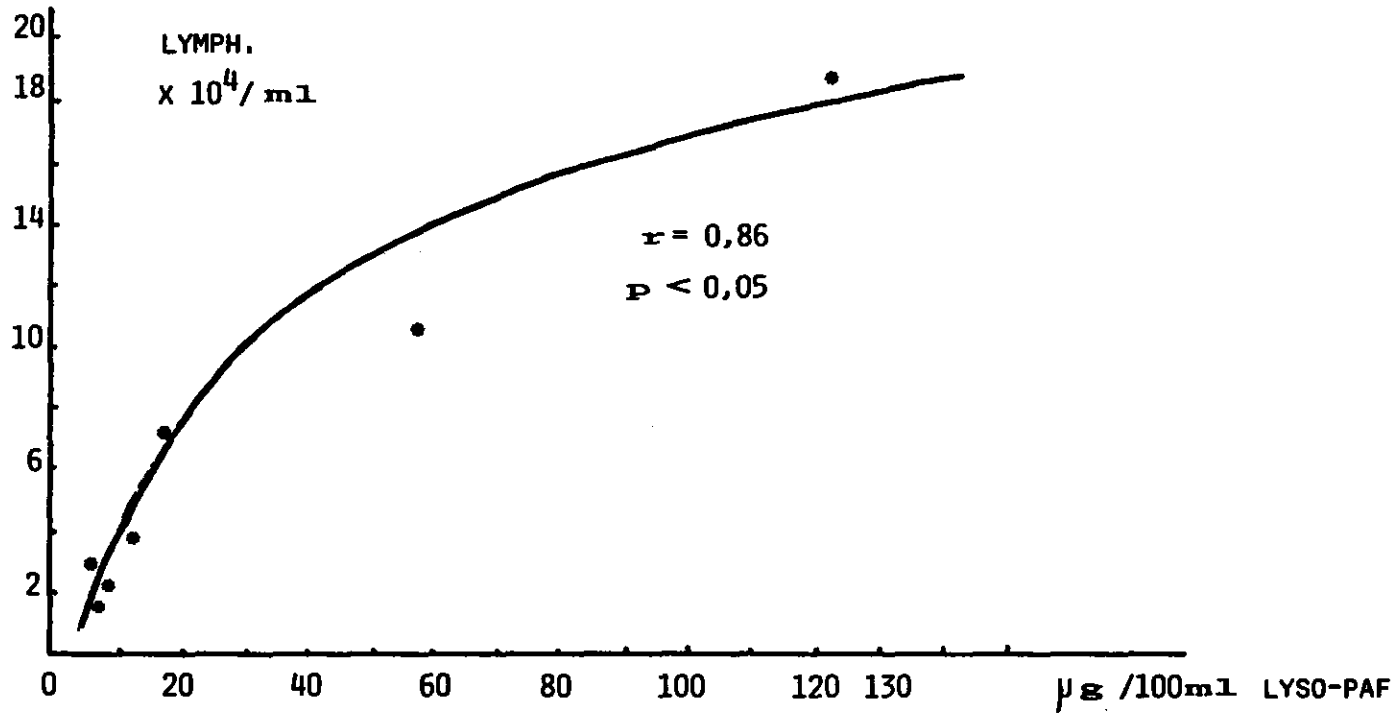


Table VIII



tion with the number of lavage lymphocytes. This hypothesis is reinforced by our previous demonstration that the A.M. of patients with occupational diseases caused by mineral containing dust releases, in vitro, Paf-acether when stimulated by the responsible dust through a mechanism uncompletely understood.[15] However we think that the above mentioned mechanism of perpetuation of the A.M. activation plays an important role in the synthesis of this lipid mediator.

Once admitted that in silicosis there is, in vivo, a chronic secretion of Paf-acether certainly it will play a role in the clinical picture of these patients either through its proinflammatory or bronchoconstrictive effects.[1,18]

In conclusion in silicosis there are, almost constantly, modifications in the composition of the lower respiratory tract fluid and the degree of alveolitis correlate reasonably with the gravity of disease, the complaints and the functional defects.

Moreover from the obtained data arises the central role of perpetually activated alveolar macrophage in Silicosis pathogenesis, either through the secretion of mediators, either to it ability to modulate other cells. Among these ones emerges the T-Lymphocyte and its subclasses importance. Finally the role of type II Pneumocyte must be referred due to its function of surfactant secreting cell.

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INHALED CORTICOSTEROIDS IN THE TREATMENT OF OCCUPATIONAL RESPIRATORY DISEASES (O.R.D.)

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INTRODUCTION

The Occupational Respiratory Diseases (O.R.D.) are nosological entities for which it is possible to find a relationship between the dust, gas and aerosols inhalation in the work environment and the disease emergence.

The O.R.D. can display as an interstitial lung disease or a chronic air-flow obstruction. Frequently, the two syndromes overlap[1,2,3,8] and the basic pathogenic mechanisms are similar in both cases depending upon the clinical differences in the characteristics of the inhaled noxious substance and the individual behaviour.

In the pathogenic pathways of O.R.D. the alveolar macrophage fulfils an important role. Its stimulation releases Il_1, activating the T-lymphocyte with release of Il_2, peripheral monocyte recruitment, local T cell proliferation and a B cell stimulation leading to the granuloma formation.[5]

The perturbation of the macrophage cell membrane by stimulus, antigenic or others, causes the activation of the Phospholipase A2, interfering with the membrane phospholipids and leading to the release of arachidonic acid molecules and its metabolites.[11,14] The release of Paf-acether by the alveolar macrophages of these patients,[10,14] and of toxic 02 species has also been demonstrated.

The activated alveolar macrophage also releases fibronectin and Macrophage Derivated Growth Factor, important mediators in the fibrotic process.[1,3,8]

From the destruction of the alveolar macrophage by the cytotoxity of the noxious substance and from incomplete lysosomes results the release of enzymes—elastase and collagenase—contributors to the interstitial lung damage.[8,11]

Also the neutrophils are increased in the alveolar spaces and when stimulated by immune complexes liberate noxious enzymes.[8,11]

Finally in O.R.D. patients, as it happens in other fibrotic diseases, there is an increased number of mastocytes in the interstitial spaces and the released histamine would perhaps have a proinflammatory effect besides its bronchoconstrictive action.[13,15]

From the above mentioned emerges the justification to the use of corticosteroids in the treatment of some O.R.D. patients through its capacity to blockade the interleukins and other mediators release, to inhibit the Phospholipase A2, to diminish the neutrophils adhesivity and chemotaxie and to inhibit the production of histamine.

In clinical trials we had already confirmed that the improvement of the O.R.D. patients under corticotherapy is accompanied by a significant diminishing of the number of T-lymphocytes and rates of Lyso-Paf-acether (the percursor of Paf-acether) and histamine.[13,14]

As the local of the pathogenic process is the epithelial alveolar surface, it seems reasonable to think that the inhaled corticosteroids could perhaps stop them and be useful in the treatment of these O.R.D. patients requiring the use of drugs for their management.

The aim of this study is to evaluate the effectiveness of the inhaled corticosteroids in the treatment of the occupational respiratory diseases.

PATIENTS AND METHODS

We have studied 15 patients with ages ranging between 28 and 66 years, mean age 49 years. Ten of the patients were males and 5 females and two of the men were smokers (Table I).

Nine of the patients had a consistent occupational history of exposition to mineral dusts (5 to silica, 3 to iron and 1 to asbestos) and 6 to organic dust (3 to corck dust and 3 to pigeon dregs)—Table II.

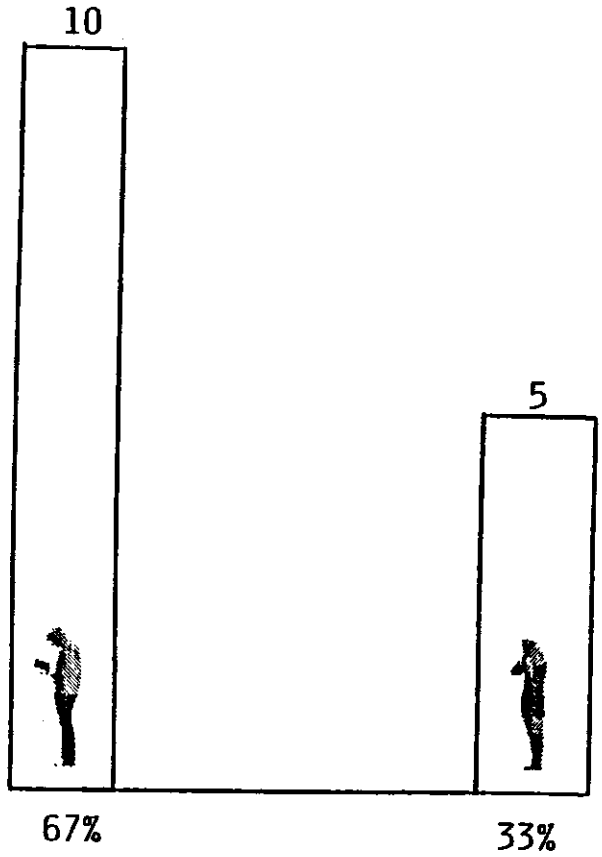
All of them had the disease confirmed through the usual clinical, functional, immunological and histological criteria.

All the patients had been submitted to a clinical inquiry, a standard chest X-ray and a complete functional respiratory study (global body plethysmography) previously to the treatment. The same study has been repeated every three months during one year.

The patients without evidence of ventilatory obstruction were submitted to bronchoalveolar lavage in a subsegment of the middle lobe with 4 syringes of 50 ml of saline serum warmed up to 37°C by a usual technique.[1] In 3 of the patients the bronchoalveolar lavage has been repeated 6 months after the beginning of the treatment.

The patients were submitted to a therapeutic with Budesonide 4 × 200 μg twice a day, via a 750 ml spacer.

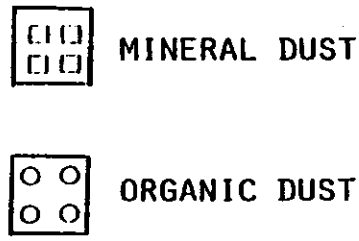
Table I
Patients

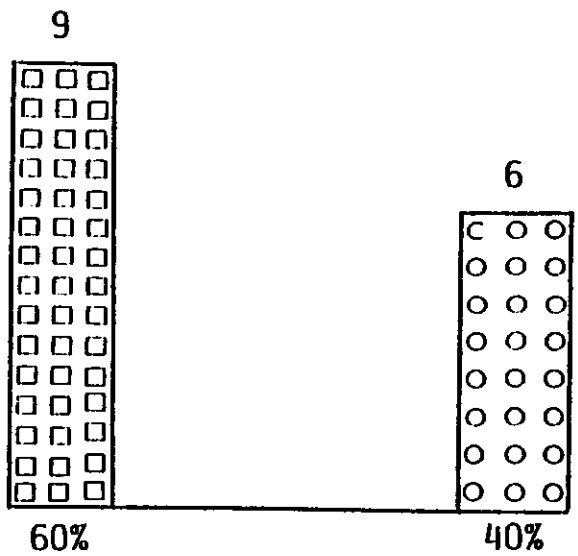


TOTAL - 15

MEAN AGE - 49
MAX. " - 66
MIN. " - 28

Table II
Exposition





As concomitant medication we used in 7 patients inhaled bronchodilators. None of the patients had concomitant or previously oral corticosteroids. All were kept away from their workplace.

As comparison terms we considered a control group of 5 other O.R.D. patients with similar clinical, radiological and functional patterns, also kept away from the workplace in which only oral bronchodilators had been prescribed.

For statistic analysis we used the T test for paired data, differences method.

RESULTS

Before treatment all patients had complaints of exertion dyspnoea, 14 (93%) had cough, 8 (53%) expectoration and 7 (46%) wheezing (Table III).

After the first 3 months of treatment the clinical evaluation stated an improvement of the complaints in 12 (80%) of the patients, increasing progressively throughout the complete period of study.

The only side effects reported were two cases of mild sore throats and one of hoarseness, not being necessary to stop treatment.

In the control group only 3 out of the 5 patients (60%) improved.

All patients of both groups had chest X-ray before treatment evocating interstitial lung involvement expressed by linear and round shadows classifiable as, at least, of the type p 1/1 (UICC/Cincinnati classification). These aspects did not modify throughout the period of the study. However, in three patients with confluent shadows this aspect disappeared during the treatment.

At the beginning of the treatment 4 of the patients had functional obstructive defects, six restrictive defects and 5 had a normal pattern.

From the observation of Table IV it is clear that the Vital Capacity improved during the treatment in 12 of the patients (80%) and from the 3 that did not improve 2 had previously normal values. This improvement is significant ($p < 0.001$).

In what concerns the Total Lung Capacity only 9 of the patients improved (60%) and the difference is not significant (Table IV).

In Table IV the FEV_1 values are analyzed and it is verifiable that there is a significant improvement during the treatment ($p < 0.05$).

On the contrary the Tiffeneau index did not modify significantly with the treatment (Table IV).

In the control group there is no significant modification in any of the studied parameter (Table V).

The eight patients without evidence of bronchial obstruction were submitted to bronchoalveolar lavage. In 4 of them we verified the existence of an alveolitis ($74.5 \pm 71.3 \times 10^4$ cells/ml) and in both groups a significant increase of the lymphocytes percentages—three folds the normal values—(Table VI).

All patients of this group referred improvement in complaints during the treatment and ventilatorily and a significant increase in the values of Total Lung Capacity and Vital Capacity has been found (Table VII).

The three patients in which a second lavage had been performed showed 6 months after the beginning of the treatment, a decrease in the total cell count and in the number of lymphocytes as it is demonstrated in Table VIII.

DISCUSSION

First we must emphasize the difficulty to take conclusions from such a heterogeneous population in what concerns the type of inhaled agressor and the clinical manifestations.

By obvious reasons in a preliminary study we had chosen patients with a relatively mild disease, in which a sufficient

Table III

Complaints

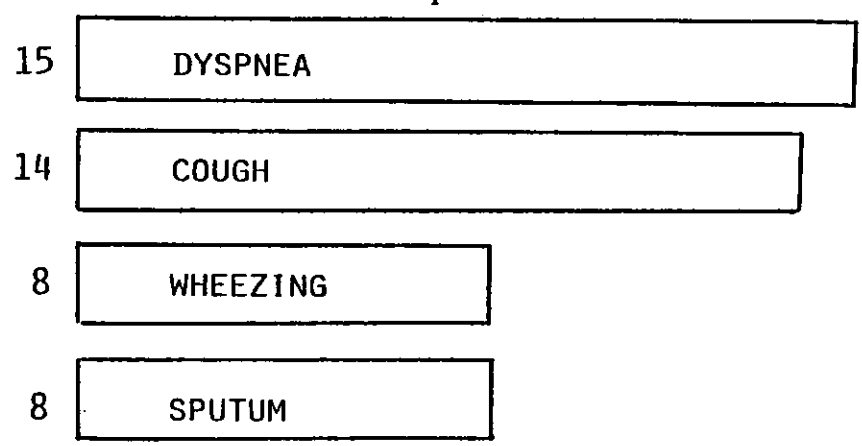
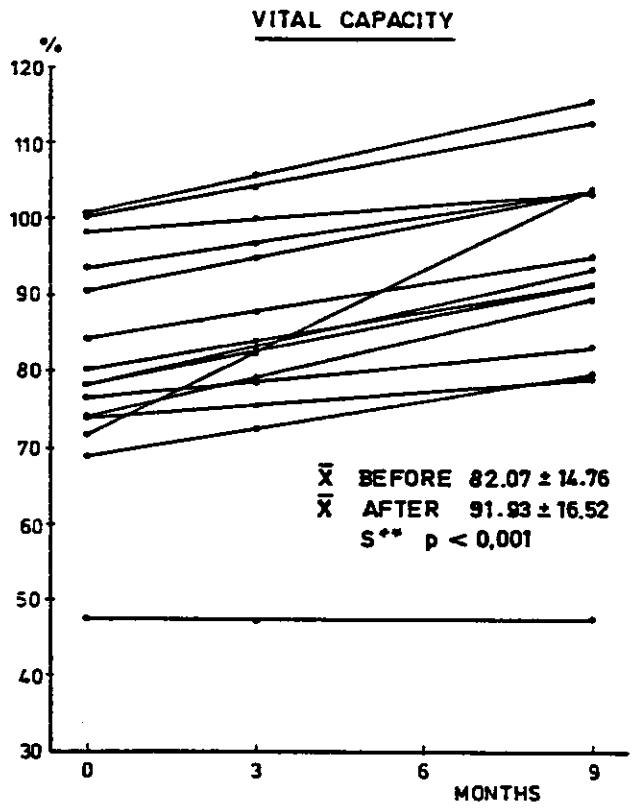
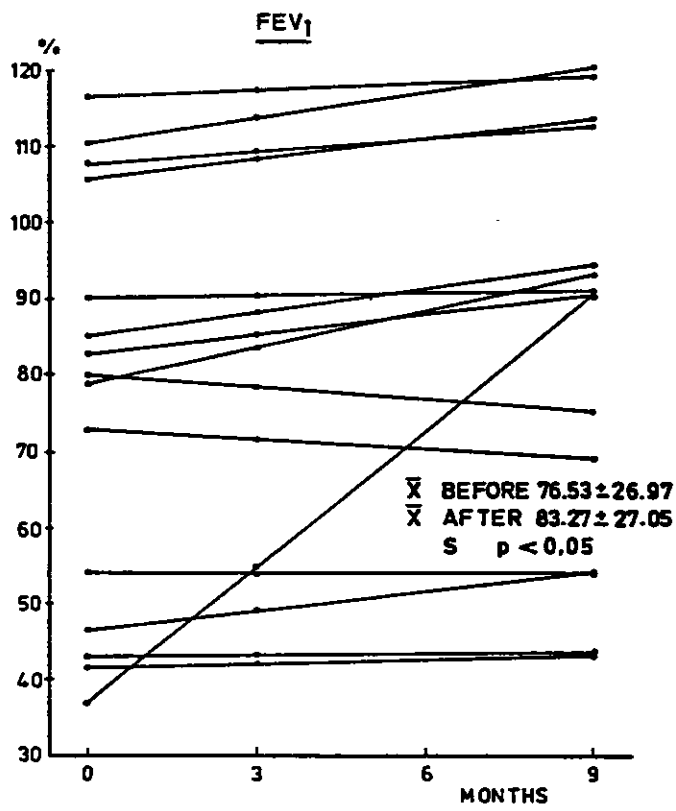
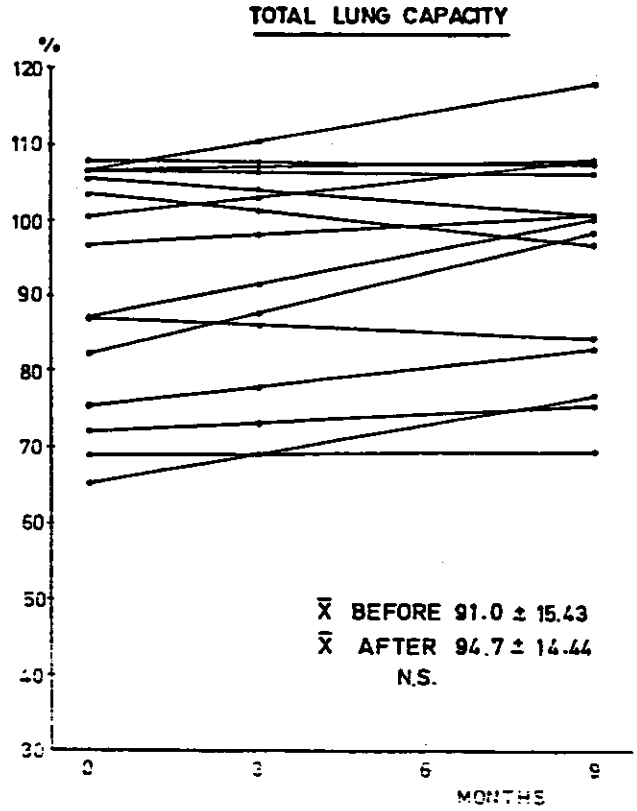


Table IV


VITAL CAPACITY
%
120
110
100
90
80
70
60
50
40
30
0
3
6
9
MONTHS
X̄ BEFORE 82.07 ± 14.76
X̄ AFTER 91.93 ± 16.52
S** p < 0,001


FEV1
%
120
110
100
90
80
70
60
50
40
30
0
3
6
9
MONTHS
X̄ BEFORE 76.53 ± 26.97
X̄ AFTER 83.27 ± 27.05
S p < 0,05


TOTAL LUNG CAPACITY
%
120
110
100
90
80
70
60
50
40
30
0
3
6
9
MONTHS
X̄ BEFORE 91.0 ± 15.43
X̄ AFTER 94.7 ± 14.44
N.S.

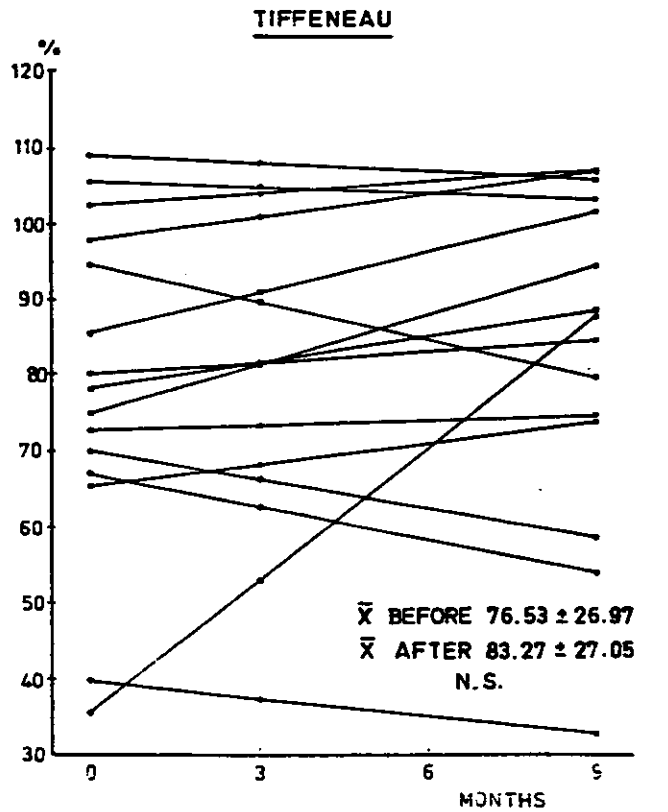
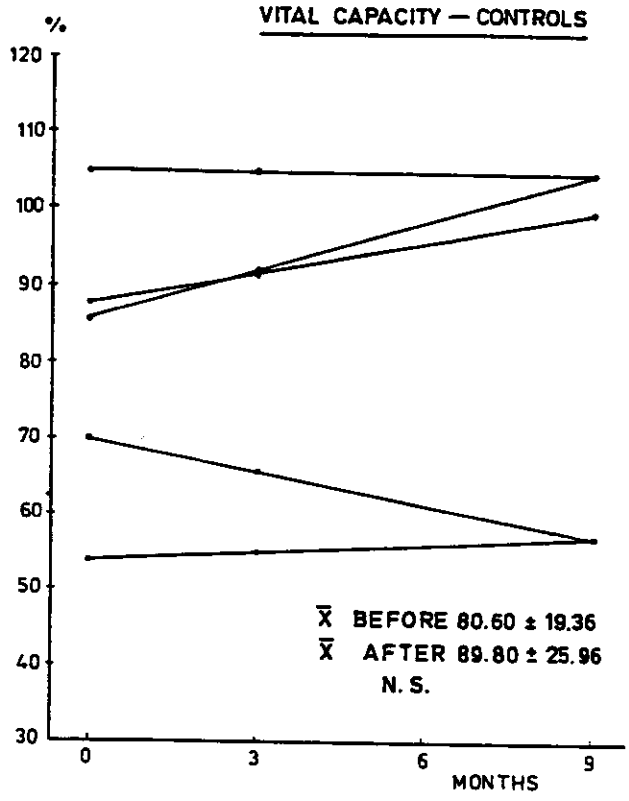
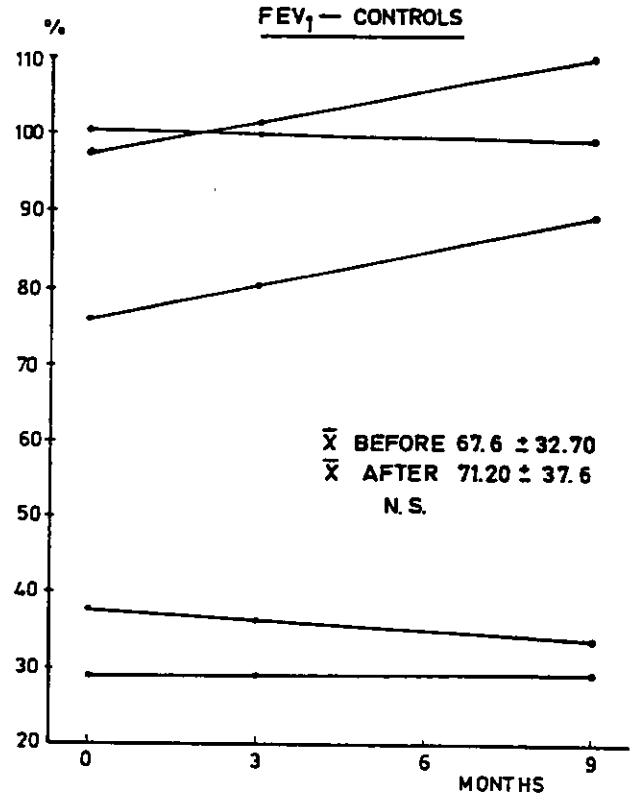
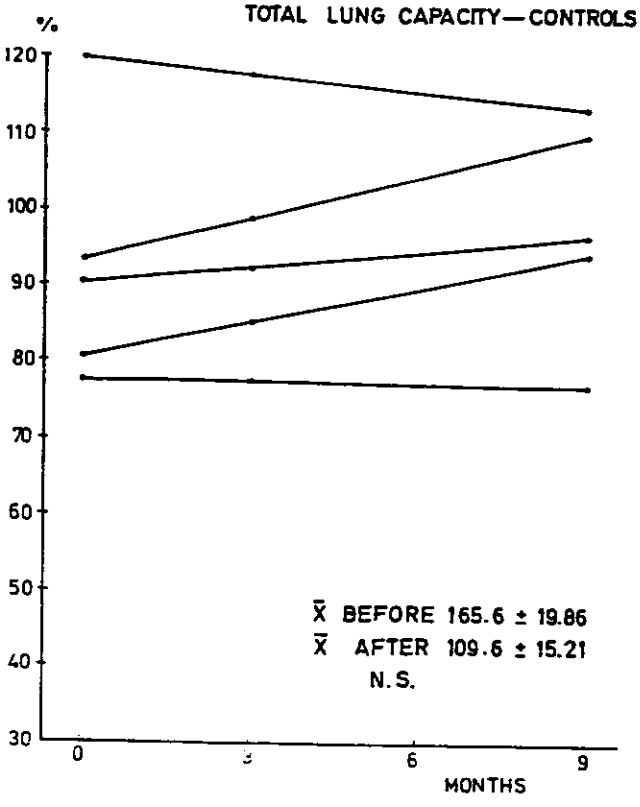
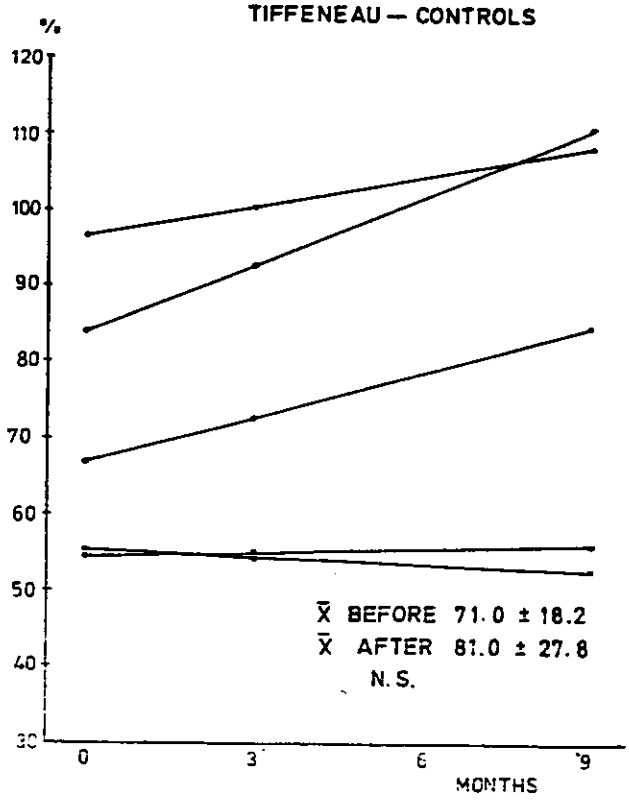

TIFFENEAU
%
120
110
100
90
80
70
60
50
40
30
0
3
6
9
MONTHS
X̄ BEFORE 76.53 ± 26.97
X̄ AFTER 83.27 ± 27.05
N.S.

Table V


VITAL CAPACITY — CONTROLS
%
120
110
100
90
80
70
60
50
40
30
0
3
6
9
MONTHS
X̄ BEFORE 80.60 ± 19.36
X̄ AFTER 89.80 ± 25.96
N. S.


FEV1 — CONTROLS
%
110
100
90
80
70
60
50
40
30
20
0
3
6
9
MONTHS
X̄ BEFORE 67.6 ± 32.70
X̄ AFTER 71.20 ± 37.6
N. S.


TOTAL LUNG CAPACITY—CONTROLS
%
120
110
100
90
80
70
60
50
40
30
0
6
9
MONTHS
X̄ BEFORE 165.6 ± 19.86
X̄ AFTER 109.6 ± 15.21
N. S.


TIFFENEAU — CONTROLS
%
120
110
100
90
80
70
60
50
40
0
3
6
9
MONTHS
X̄ BEFORE 71.0 ± 18.2
X̄ AFTER 81.0 ± 27.8
N. S.

clinical, radiological or functional support of an interstitial involvement had been found; however, this group included an important number of patients with simultaneous chronic airflow obstruction, sometimes even prevalent.

Supporting the favourable clinical evolution of the patients under inhaled corticotherapy the functional ventilatory parameters that more consistently improved were those related with the interstitial involvement rather than those related with airflow obstruction.

The suggestion of the interest of these drugs in O.R.D. patients is reinforced by the favourable clinical evaluation of the patients with alveolitis, confirmed by bronchoalveolar lavage (BAL) and by the improvement of the cellular parameters of their BAL fluid during the treatment.

The anarchical response of obstructive parameters to the therapeutic measures suggests the interference of other factors in bronchoconstriction independently of corticosteroids action: tobacco, infection, etc.

Besides the interest of inhaled corticosteroids in diseases with airflow obstruction[7,9] it has already been demonstrated in Sarcoidosis that the inhalatory therapy with Budesonide is able to transform the initial cellular, biochemical and immunological abnormalities in the direction of normalization and that the clinically useful doses result in tissue concentrations high enough to be efficacious.[9]

These two perspectives are very important in O.R.D. patients.

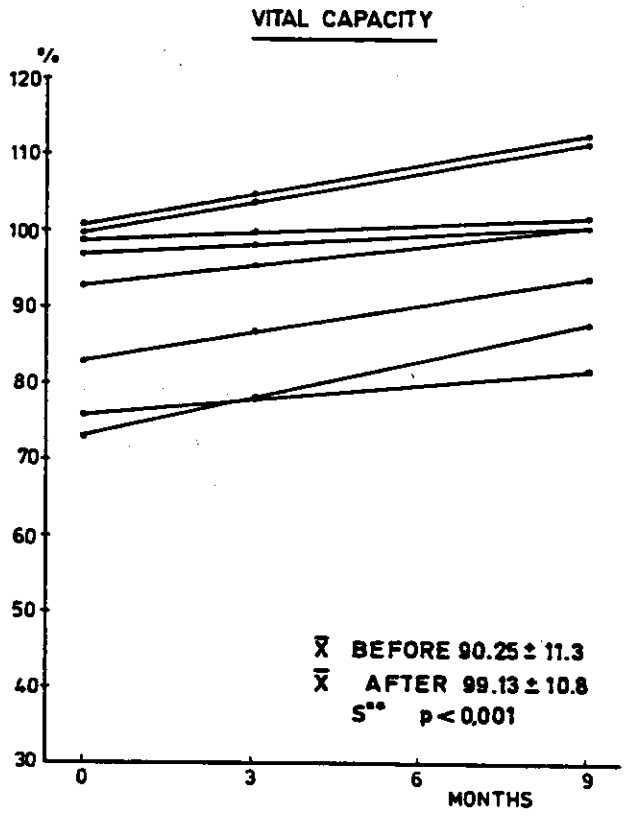
In fact a drug sufficiently efficient to reach the alveoli and stop the release of mediators by the immunological and inflammatory effector cells, and simultaneously to persist in the interstitium braking the pathogenic mechanisms due to the persistence of the aggressive particle, would surely have a place in the management of these diseases.

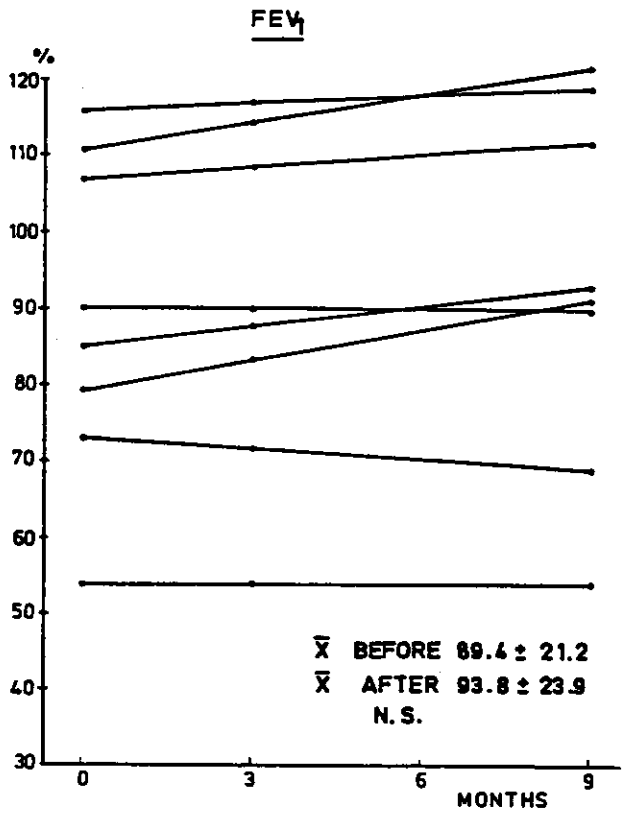
The obtained results seem to provide some evidence of the effectiveness of the purposed treatment, mainly in the interstitial occupational respiratory diseases which is not surprising once admitted the pathogenic mechanisms described above.

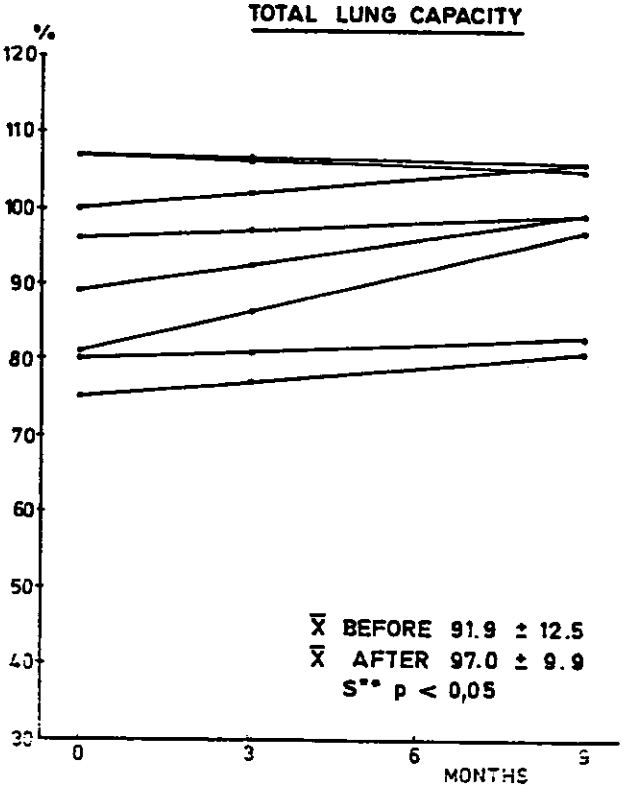
Table VI
Bronchoalveolar Lavage

	CELLS	MA	LYMPH.	P.M.N.
WITH ALVEOLITIS n = 4	74,5±71,3	53,8±32,5	39,5±23,2	1,75±1,5
WITHOUT ALVEOLITIS n = 4	18,3± 6,9	63,3±28,6	36,3±28,6	1,0 ±1,4

Table VII
Patients with B.A.L.







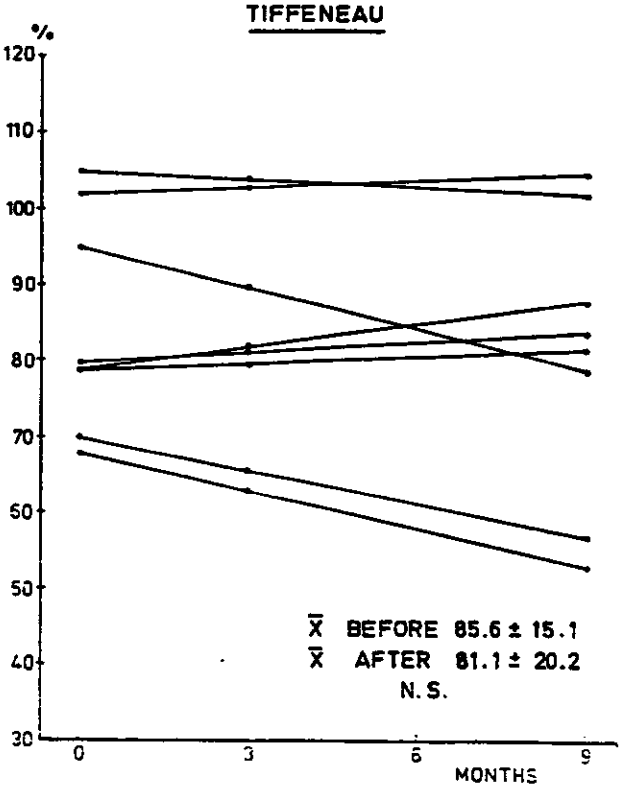
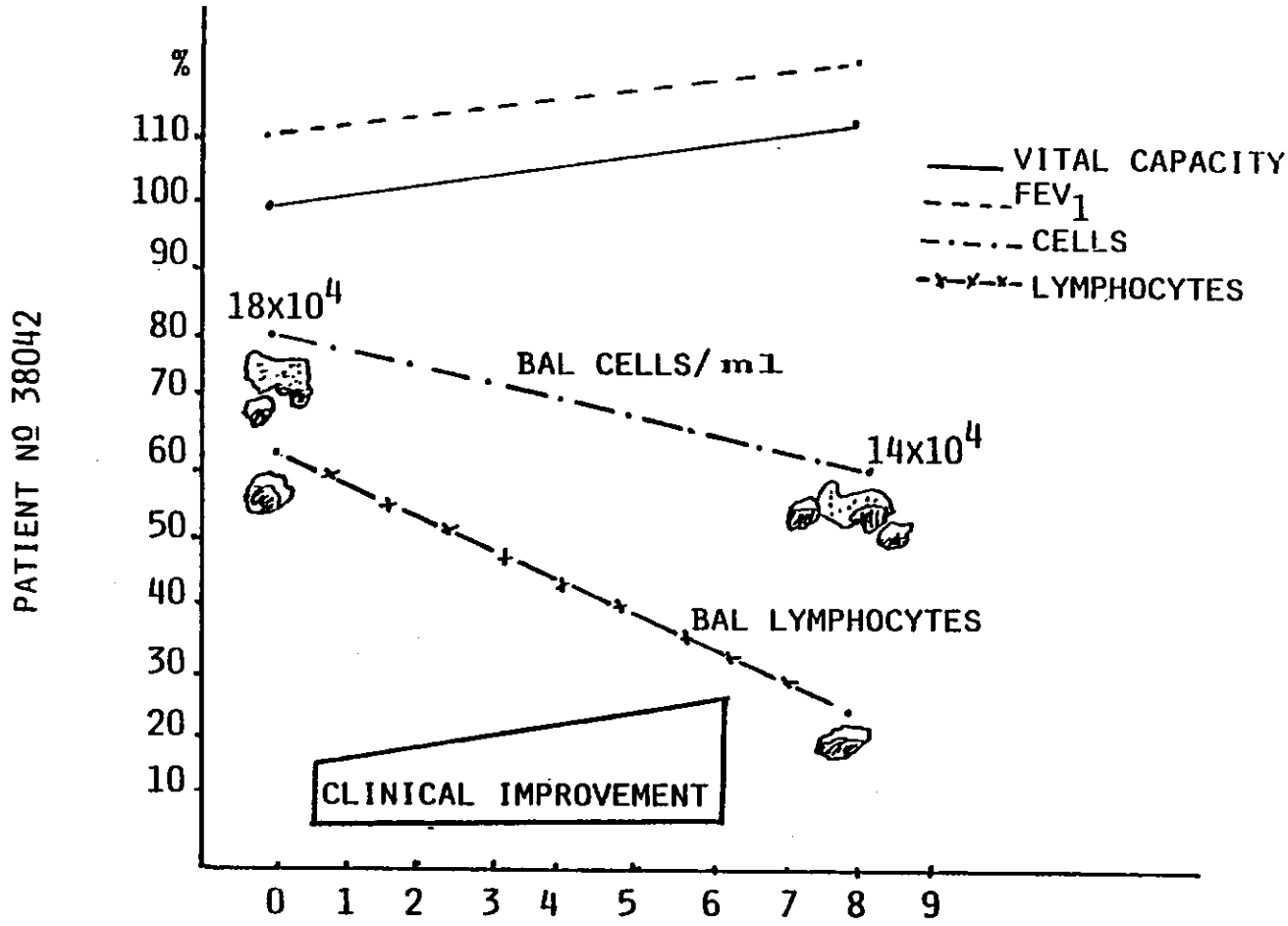


Table VIII



Thus when it is necessary to consider the use of corticosteroids the inhalatory therapy can represent an alternative or a complement to oral corticosteroids. This alternative becomes more important if one considers that inhaled corticosteroids rarely cause systemic side effects and do not reach immunosuppressive levels,[2] which is of a great interest in patients with susceptibility to infections such as the case of Silicosis.

Further studies will be necessary to define the real usefulness of Budesonide in the treatment of these patients, which are the parameters necessary to define when it can be used as the unique therapeutic measure, besides the evication from the aggressive noxious, and when it must be used as a complement to oral corticosteroids, permitting a significant dose reduction.

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ANALYSIS OF FATTY ACIDS FRACTIONS OF PHOSPHOLIPIDS AND NEUTRAL LIPIDS FROM BRONCHOALVEOLAR LAVAGE FLUID (BALF) IN PATIENTS WITH OCCUPATIONAL LUNG DISEASES (OLD)

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INTRODUCTION

The pulmonary surfactant has caught the attention of numberless investigators since its discovery was reported by Pattle[1] and the primary characteristics of the substance were first described by Clements.[2]

Basically the pulmonary surfactant reduces surface tension of the interface air-liquid of the alveolus, maintaining mechanical stability and avoiding alveolar collapse particularly at small pulmonary volumes.[3,4,5] Other functions of this complex substance are the help on removal of particles from airways and on digestion of bacterias intra and extra cellulars, the inhibition of pulmonary edema and the transudation of fluids into the alveolus.[7,8,9]

Dipalmitoyl phosphatidylcholine (DPPC) is the predominant molecule of the pulmonary surfactant and of it depends, in great part, the tensio-active function of this compound.[3,5,6] The exact functions of the remaining components such as insaturated phosphatidylcholine, other phospholipids, neutral lipids, and specific proteins are incompletely studied.[3,10]

The pulmonary surfactant is produced in the pneumocyte type II, synthetized in its endoplasmic reticular system and transferred, by mechanisms not fully known, to the lamellar bodies and then secreted to the alveolar surface.[3,11]

Several enzymatic mechanisms are involved in the synthesis of phospholipids and there is evidence of a certain hormonal regulation—androgenes, corticosteroids, tiroxine and insulin.[11,3]

In the control of the secretion there seem to be involved cholinergic and B adrenergyc mechanisms. Chemical mediators such as prostagl; dines, physical factors such as the distortion of the alveolar membrane and hyperventilation can also interfere in surfactant secretion.[11,12]

The importance of surfactant defects is well established in the pathogenesis of diseases like neonatal and adult respiratory distress syndrome[13,14] and less well established in other situations of respiratory suffering in man.[5,6]

Since on occupational lung diseases there are important immunologic and inflammatory mechanisms occurring in the surface of the alveolus including changes in the alveolar microatmosphere, thickness and rigidity of the membranes and distortion of the structure,[15,16,17] an hypothesis was sought that this factor could condition changes in the composition of the pulmonary surfactant.

In order to attempt to prove it, we studied the lipidic composition—phospholipids, neutral lipids and fatty acids—of the extracellular compartment of the pulmonary surfactant, obtained through bronchoalveolar lavage in 15 individuals: 5 normal, 5 pigeon breeders and 5 silicosis patients.

MATERIAL AND METHODS

Patients

We studied 5 patients with silicosis and 5 with pigeon breeder's lung, diseases confirmed through usual criteria.

Both groups were homogeneous concerning age and sex. None of the patients smoked cigarettes and none was submitted to corticotherapy.

All were submitted to a clinical and functional study, a standard thorax X-ray and bronchoalveolar lavage.

As controls we used 5 normal volunteers, non-smokers with ages not differing significantly of those of the patients.

Bronchoalveolar Lavage

All individuals studied were submitted to BAL in one of the sub-segments of the middle lobe. Four fractions of 50 ml of saline at 37°C were instilled with a syringe adapted to the fibroscope and after a few seconds the liquid was retrieved. The mucus was separated, total cell count was performed by hemocitometry. The cellular component was separated by centrifugation at 500 G for 15 min. at 4°C. The supernatant was dried in a vacuum oven −50°C to −60°C for several hours and stored in a steam of nitrogen for further study.

PROCESSING AND ANALYSIS OF LIPIDS

Extraction of Lipids

The total lipids were extracted from the dried supernatant lavage fluid according to Bligh and Dyer method.[25]

Chromatographic Methods

Total lipids were separated by column chromatography on silica acid-Kieselguhr (BDH), in neutral lipids (NL) and phospholipids according to Cmelik and Fonseca.[26]

The neutral lipids (cholesterol, cholesterol esthers fatty acids and triglycerids fractions) were separated by thin layer chromatography (TLC) on silica gel G plates (Merck Chemical Co.) using petroleum ether/ethyl/acetic acid (70:30:1) as developer.

Phospholipids were separated by TLC on silica gel H (Merck) and Florisil (BDH 10-200 mesh) plates using chloroform/methanol/water (65:25:4) as a solvent.

NL fractions were hydrolyzed with a 5% potassium metoxide solution. After the extraction of the non-saponifiable part, fatty acids were extracted from the acidified solution with ethyl ether.

Phospholipids were hydrolyzed with HCl 6N in sealed tubes immersed in a boiling water bath for 4-6h.

Fatty acids were converted into methyl esters with a methanolic solution of Boron trifluoride BF_3[27] and analyzed on a Perkin Elmer 900 gas-chromatograph with a dual flame ionization detector. The columns were 2 m long with an 1/8 inch o.d. and were packed with 20% Diethylenoglycol Succinate (DEGS) and chromosorb W (DMCS) 80–100 mesh. The analysis was performed at programmed temperature (140°–170°C) with an increasing rate of 2°C minute, followed by isothermal operation. The nitrogen flow rate was 35 ml/min. Peak's identification was determined by comparing their relative retention time with that of known standards. The relative percentage of the peak areas was evaluated by an integrator from Hewlett Packard's 3.380 A).

Spots on analytical plates were visualized by spraying with concentrated sulfuric acid containing 0.1% of potassium dichromate and subsequent charring at 140°C. Spots of the phospholipids were identified by the use of respective standards and phosphatidylcholine (PC) and phosphatidylethanolamine (PE) were identified too by spraying the plates with Dragendorff and Ninhydrin reagents respectively.

Total cholesterol was determined by the use of a modified Lieberman-Buchard reagent.[28] Phosphorus analysis was performed by the method of Fiske and Subbarow[29] as modified by King.[30]

Total proteins were assayed by Lowry's method.[31]

RESULTS

Study of phospholipids revealed some differences on both groups of patients in relation with controls (Table I). Therefore on pigeon breeders a significant decrease of phosphatidylcholine was found as well as phosphatidylglycerol on silicosis patients.

On the other hand, in both groups we found significant increases of phosphatidylethanolamine and sphingomyelin.

As for neutral lipids, the fact that cholesterol was abundant in the 3 groups prevailed. Also in the 3 groups free fatty acids were detected (Table II).

In the composition on fatty acids of phospholipids, significant differences on both groups of patients were also detected by comparison with the controls (Table III), mainly the important decrease of C16:0 and increase of fatty acids insaturated in C16, C18 and C20. To be noted also the significant increase of arachidonic acid on pigeon breeders. From this results that the ratio between saturated and insaturated fatty acids is inferior to unity on patients and superior to 2 on controls (Table IV).

From the analysis of the composition in fatty acids of the neutral lipids once more highlights the important decrease of palmitic acid and the increase of insaturated fatty acids in patients, mainly in C16 and C18 (Table V). The ratio saturated/insaturated fatty acids results once again less than unity on patients and greater than 2 on controls (Table VI).

DISCUSSION

The 3 groups of individuals studied being comparable, it becomes evident that on patients with occupational diseases of the lung there are significant changes on the composition of the pulmonary surfactant.

On the whole, the changes encountered on both groups of patients are similar, suggesting partially common metabolic paths. This is in accordance with other data of the study of BAL liquid referring either to cellular elements or to chemical mediators.[17,19,20,21,22,23,24]

One of the more relevant conclusions of this study is the decrease of the phospholipids that form the molecules with tensio-active function generally accepted, especially phosphatidylcholine, as it is clear on Table I.[5,3] In parallel there are alterations of many other phospholipids, whose meaning is difficult to determine since its functions have not yet been clarified.

Even more interesting are the profound modifications on the composition of fatty acids related with phospholipids knowing that, for instance, the tensio-active properties of PC depend of the fatty acids in positions α or β.[7]

It is true that for a normal surfactant function a minimal quantity of DPPC is required and that some variations in fatty acids composition do not interfere with this function.[4] On these patients it is a field requiring further research, so much for the fact that we recognize that, in exposed individuals without the disease, the composition in fatty acids did not vary from controls; suggesting that the alterations follow the surge of the disease.

One word about the great amount of arachidonic acid found in pigeon breeders without forgetting that it is on the basis of leucotrienes, Prostaglandins and Paf-acether, mediators involved in the disease.[17,22,24]

Also in relation to the composition in neutral lipids, the alterations are profound and its meaning remains uncleared, given the lack of knowledge associated with its functions.[5,18] However we would like to point out that triglycerids are the preferential form of stock of the fatty acids which, by subsequent oxidation or sterification form other lipids.[18] Also the relative decrease in fatty acids found on some patients may contribute to explain the susceptibility to acquire respiratory infections which is widely accepted.[8,9]

So we find important disturbances on the metabolic path of the surfactant synthesis. What does it mean?

Table I
Bronchoalveolar Lavage

	PIGEON %	CONTROLS %	SILICOSIS %
PHOSPHATIDYLCHOLINE	52,1±2,5 * ↓	59,6±2,9	65,8±5,4 N.S.
PHOSPHATIDYLGLYCEROL	16,3±2,2 N.S.	23,4±5,6	9,9±3,5 *** ↓
PHOSPHATIDYLINOSITOL + PHOSPHATIDYLSERINE	9,2±4,2 N.S.	9,8±2,1	8,0±2,5 N.S.
PHOSPHATIDYLETHANOLAMINE	10,4±2,7 *** ↑	4,9±1,5	7,5±1,0 ** ↑
CARDIOLIPINE	6,1±1,6 N.S.	4,9±0,9	4,8±1,6 N.S.
SPHINGOMYELINE	7,0±1,3 **** ↑	1,3±0,6	7,9±3,1 ** ↑

* $p < 0,05$ *** $p < 0,01$

** $p < 0,02$ **** $p < 0,001$

Table II
Bronchoalveolar Lavage

	PIGEON	CONTROLS	SILICOSIS
CHOLESTEROL	++++	++++	++++
FREE FATTY ACIDS	+	+	+
TRIGLYCERIDES	++	++	++
CHOLESTEROL ESTER	+++	+++	+++

We have already mentioned that in these diseases there are changes in the structure and in the microatmosphere of the alveolus that may explain its origin.[11,12] Also, we must not forget that the alveolar macrophage (AM) which, in these patients, is permanently activated producing enzymes and chemical mediators whose interaction with the Pneumocite type II is not clarified.

In parallel the cellular membrane of the activated AM is a productive source of lipidic molecules[22,24] which may contribute for the constitution of the surfactant. In the end it is possible that the Pneumocite type II may be directly injured; Schuyler[21] found in the bronchoalveolar lavage fluid of unusual silicosis patients an a burdance of Pneumocites type II so far unexplained.

In the pathogenesis of occupational diseases of the lung there are mechanisms that may cause modifications in the synthesis and secretion of the surfactant.

We believe however these changes to be more than an epiphenomenon. It is probable that they condition functional changes of the pulmonary surfactant and therefore enable a positive loop of amplification of the processes in course.

Let us not forget that in the acute phases of the disease there is interstitial edema an alveolar transudation and that in other phases alveolar collapse appears. What is the role of surfactant alterations in these processes? Can these changes disturb its basic role in the muco-ciliar stair?

CONCLUSIONS

In patients with occupational diseases of the lung there are important alterations in the lipidic composition of the pulmonary surfactant. Future research will be necessary to establish up to which point these changes disturb its functions contributing to the clinical-pathological picture of the diseases.

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Table III

	PIGEON	CONTROLS	SILICOSIS
12:0	1,1±0,2 N.S.	1,4±0,6 N.S.	1,9±1,1 N.S.
14:0	1,1±0,2	2,1±0,8	4,5±0,9 * ↑
14:1	< 1	< 1	1,1±0,9
16:1	5,6±2,2 ↓ ***	59,7±2,8	25,9±2,9 ↓ ***
16:1	< 1	< 1	< 1
16:2	< 1	< 1	< 1
16:3	21,8±1,5 ↑ ***	< 1	13,8±1,3 ↑ ***
18:0] 18:1]	42,9±2,9 N.S.	24,5±7,4	30,2±2,2 N.S.
18:2	< 1 ↓ **	6,1±2,9	3,2±3,3
18:3	4,3±0,9 ↑ **	< 1	13,1±0,9 ↑ **
20:0] 20:1]	< 1	< 1	7,6±1,6 ↑ **
20:4	22,6±4,1 ↑ **	8,7±2,5	4,4±3,6 N.S.

* $p < 0,05$ ** $p < 0,01$ *** $p < 0,001$

Table IV

Ratio Total Saturated Fatty Acids/Total Unsaturated Fatty Acids

PIGEON		CONTROLS		SILICOSIS
0,3 ± 0,1 ←	S***	→ 2,3 ± 0,6 ←	S***	→ 0,7 ± 0,1

S *** $p < 0,001$

Table V

	PIGEON	CONTROLS	SILICOSIS
12:0	< 1 N.S.	< 1 N.S.	4,2±0,7 N.S.
14:0	< 1 ↓ **	6,4±2,2	4,6±0,7 N.S.
14:1	3,4±2,4 N.S.	3 ± 2 N.S.	1,8±0,4 N.S.
16:0	13,2±9,0 ↓ *	44,9±19,5	23,9±1,2 ↓ **
16:1	2,1±1,9	< 1	< 1
16:2	< 1	< 1	< 1
16:3	8,0±1,44 ↑ **	< 1	13,0±1,2 ↑ **
18:0] 18:1]	11,2±9,9 N.S.	21,8±18,2 N.S.	32,4±9,2 N.S.
18:2	13,7±2,4 ↑ **	< 1	< 1
18.3	< 1	< 1	13,1±0,6 ↑ **
20:0] 20:1]	14,4±3,1	13,8±3,4	< 1 ↓ **
20:4	19,8±7,5 N.S.	11,7±7,7 N.S.	8,1±0,8 N.S.
22:1	8,6±6,8 N.S.	9,25±8,6 N.S.	3,3±1,2 N.S.

S * $p < 0,05$ S ** $p < 0,02$

Table VI

Ratio Total Saturated Fatty Acids/Total Unsaturated Fatty Acids

PIGEON		CONTROLS		SILICOSIS
0,3 ± 0,2	S ***	← 1,9 ± 0,8 →	S **	0,8 ± 0,1

S *** $p < 0,01$ S ** $p < 0,05$

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THE TREATMENT OF OBSTRUCTIVE AIRWAY DISEASE OF COAL WORKERS WITH COAL WORKERS' PNEUMOCONIOSIS

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ABSTRACT

In categories B and C (ILO-classification 1980) coal workers develop more than twice as often obstructive airway diseases as persons of the same age who are not exposed to dust. The obstructive airway disease of coal workers responds in the same way on the same kind of treatment as the obstructive airway disease of non-exposed persons. Under a well-controlled treatment, the obstructive airway disease of coal miners, the most important complication of coal workers' pneumoconiosis, can be controlled, and life expectancy of these coal miners with coal workers' pneumoconiosis and obstructive airway disease is the same as that on non-exposed persons.

No Paper provided.

NUMBER, NATURE AND SIZE OF ASBESTOS BODIES IN BAL FLUIDS OF CHRYSOTILE WORKERS

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ABSTRACT

Bronchoalveolar lavage (BAL) fluids from 15 workers of the same brake lining factory (Group 1) were investigated with respect to their asbestos bodies (AB) content. Those subjects were only exposed to chrysotile. BAL fluids from 34 asbestos cement workeres (Group 2) were also examined for comparison. Group 2 was mainly exposed to amphiboles. AB concentration was ranging from 0.2 to 3168 AB/ml (mean: 263 ± 812) for group 1 and from 0.3 to 11,200 AB/ml (mean: 1028 ± 2326) for group 2. Repeated BAL were obtained for 3 subjects of group 1. There were no significant changes in AB concentrations even 10 months after cessation of exposure. Among 159 typical AB cores analyzed in 7 subjects of group 1, chrysotile was identified in 95.6%, amosite in 2.5% and 1.9% remained undetermined. Neither tremolite-actinolite nor anthophyllite were identified as AB cores in this group. This contrasts with the data obtained on 561 AB cores from 20 subjects of group 2 where 9.8% were built on chrysotile. Geometric mean length and diameter were respectively shorter and thinner for chrysotile AB cores than for amphibole ones but mean aspect ratio was higher.

We can conclude that 1) routine AB counting in BAL samples allows to disclose occupational exposures to chrysotile, 2) such exposures can lead to AB concentration in BAL comparable to those encountered with occupational exposures to amphiboles, 3) size characteristics of AB on chrysotile are different from those of AB on amphiboles and 4) mechanisms of chrysotile fibers clearance does not substantially affect chrysotile AB concentrations in BAL for at least 10 months after cessation of exposure.

No Paper provided.

ASBESTOS BODIES IN BRONCHOALVEOLAR LAVAGE FLUID IN VIEW OF OCCUPATION, PLEURAL CHANGES, AND BRONCHOGENIC CARCINOMA

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The asbestos content of lung tissue reflects the asbestos exposure during life. One finds both naked or uncoated fibres, and fibres coated with a ferroproteinous material also called ferruginous bodies or asbestos bodies (AB's).[1,5] The great majority of the AB's contain an amphibole in its core.[2] AB's can easily be identified in bronchoalveolar lavage fluid.[4,6] Their number correlates with the number found in lung tissue.[3] The aim of the present study is to explore the relationship between AB concentration in bronchoalveolar lavage fluid, on the one hand, and the occupational history, the presence of benign pleural changes, and the presence of primary bronchogenic carcinoma, on the other hand.

MATERIAL AND METHODS

Bronchoalveolar lavage was performed during routine diagnostic bronchoscopy, under local anesthesia, in 275 consecutive patients (257 male, mean age 60.9 ± 9.2 yr) who could tolerate the procedure safely. A fiberoptic bronchoscope was securely wedged in a segment of either the middle lobe or the lingula, which was then washed with a minimum of two aliquots of 50 ml of normal saline solution. About 50% of the second aliquot was recovered and used for analysis.

About 20 ml of lavage fluid, mixed with 40 ml of bleach, was incubated at 40°C for 2 hours. The fluid was then sucked through a 0.45 micrometer pore size cellulose esters filter, subsequently rinsed twice with water and once with alcohol 25%. The filters, mounted and cleared, were examined at 400 × magnification under phase contrast. A known portion of the filter, approximately 400 fields, were examined for AB's, from which the original concentration of AB's could be calculated. The logarithmic means were used in all comparisons; one AB was added to all counts so that no concentration came out lower than 0.01/ml, which is an artifact.

Complete occupational and smoke histories were taken. The chest radiographs were read according to the ILO classification system for pneumoconioses. The following benign pleural changes were considered for analysis: pleural effusion, diffuse pleural thickening, markedly obliterated costophrenic angle, pleural plaques calcified or not.

Control groups consisted of an equal number of patients, matched for sex, age (± 4 yr), and smoking habit (± 50% of total cigarettes smoked). Asbestos workers, i.e. workers with explicit asbestos exposure, were eliminated from matched comparisons for fear of bias. Indeed most of these were referred explicitly for detection of AB's.

RESULTS

The concentrations of AB's in lavage fluid, range 0.01–130/ml, appear to follow a logarithmic distribution in this sample of 275 patients. The 257 male subjects could be categorized in five groups, unmatched for age and smoking history, according to occupation. These groups and corresponding mean AB concentrations are: (a) 11 asbestos workers, 21.9 ± 41/ml; (b) 50 metal workers, welders, plumbers, and heating workers, 1.4 ± 7.8/ml; (c) 47 coal miners, 1.4 ± 7.9/ml; (d) 103 other blue collar workers, 0.3 ± 5.4/ml; and (e) 46 farmers, staff, and other white collar workers, 0.1 ± 5.7/ml. The mean concentrations found in the first four groups are all significantly higher than in the one found in the last group.

Metal workers (n=25) also had significantly higher AB counts if compared, not with group (e), but with an equal number of matched controls (1.23/ml versus 0.34/ml, P=0.02). The same was found for coal miners (n=37, 1.78/ml versus 0.23/ml, $P=10^{-5}$).

Likewise, subjects with bilaterial pleural changes (n=50) had significantly higher AB counts than their matched controls (1.8/ml versus 0.3/ml, 2P=0.001). However, subjects with unilateral, pleural changes (n=31) did not differ significantly from the controls (0.7/ml versus 0.4/ml).

The patients with primary bronchogenic carcinoma (n=69) had a higher mean AB concentration than matched controls, but the difference was not significant (0.76/ml versus 0.44/ml, P=0.1).

DISCUSSION

It is not surprising that the highest AB concentrations were found in asbestos workers. Of more interest is the increased number of AB's found in people who, in the majority of cases, did not mention any contact with asbestos. They constitute nevertheless a group of workers with probable asbestos exposure: steel and foundry workers, metal construction workers, welders, plumbers, central heating workers, and other workers who may use asbestos as sealing or heat insulator. It is somewhat surprising that a similar distribution of AB concentrations was found in coal miners. The Belgian geological structures contain no asbestos, but the material has been applied in the past as fire protection, among other uses. Another possible explanation is that some of these AB's

have cores made of carbon fibre rather than asbestos. The present study cannot answer this.

We have distinguished a group of blue collar workers, who definitely had no explicit occupational exposure to asbestos, although sporadic contact remains possible. This group too had a significant, but small, increase of AB's, in comparison with the group of people with occupations outside of industry. These non-industrial workers have rather low AB concentrations: less than 1/ml in 67% of them, less than 3/ml in 84%, and less than 10/ml in 93%. Even this group shows some overlap with all other groups. We do not know for sure the source of occasional high AB counts, but in some cases the hobby activity may have been responsible.

It is known that asbestos exposure can cause any of the benign pleural changes we have considered in this study. We have treated these entities as a whole. Separating them is often difficult, as often they occur together, radiologically they may overlap, and finally one type of lesion can evolve into another (e.g. pleural effusion into pleural thickening). This study shows clearly, perhaps not surprisingly, that bilateral benign pleural changes (of any type are much more indicative of previous asbestos exposure than are the unilateral ones.

The relationship of substantial asbestos exposure and increased incidence of bronchogenic carcinoma is well established. We tested the more subtle hypothesis, that bronchogenic carcinoma in the general population might develop more frequently in the presence of a moderate level of asbestos impregnation of the lungs. To elucidate this, the group of 69 male patients with bronchogenic carcinoma was compared with a group of matched controls. The carcinoma cases indeed showed a higher mean AB concentration, but the difference was not significant although one might suspect a trend ($P=0.1$). This is in agreement with studies wherein the asbestos contents of lung tissue were compared.[7] A major influence thus of moderate asbestos impregnation on the incidence of lung cancer does not seem to exist. The final answer to this question must await the comparison of larger groups and identification of the cores of the AB's also would be desirable.

CONCLUSIONS

Our study of AB's in bronchoalveolar lavage fluid yields the following conclusions: (a) There is a gradation of AB concentrations related to occupational history; (b) increased AB concentrations correlate with the presence of benign pleural changes, when visible bilaterally on a standard chest radiograph; and (c) AB concentrations are not significantly increased in men, non-asbestos workers, with bronchogenic carcinoma.

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RELIABILITY OF EARLY DIAGNOSIS OF PLEUROPULMONARY LESIONS IN WORKERS EXPOSED TO ASBESTOS: THE EFFECT OF POSITION, RADIOGRAPHIC QUALITY AND STORAGE PHOSPHOR IMAGING ON DIAGNOSTIC ACCURACY

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A fortuitous combination of circumstances prompted us to undertake this analysis of a pilot group of workers with documented asbestos exposure:

1. The availability of high quality conventional chest radiography with oblique projections.
2. The recognition that a significant proportion of workers referred to us because of positive readings of outside films actually had no recognizable interstitial disease or pleural lesions.
3. The fact that an experimental high resolution storage phosphor radiographic digital imaging system was in place in our department, to be tested with emphasis on general chest radiography, and
4. The workers were evaluated in our institution clinically and by pulmonary function studies.

Radiographically, the majority of these workers had either minimal abnormal findings compatible with asbestosis, or clearly normal chests. It is in this grey zone of minimal or equivocal evidence of disease that the greatest degree of uncertainty arises, that most disagreements occur between readers, and that the accuracy of interpretation is most critical. In these cases, the likelihood of false positive and false negative diagnoses is highest, resulting in substantial potential inequities to the workers and to society, ethically, medically, and economically.

In this study, "radiographic accuracy" means the recognition of existing lesions (true positives) and the demonstration of normal lungs and pleura when no evidence of asbestos-related pathology exists (true negatives), i.e.: the sum true positives plus true negatives, divided by the total number of cases. The former requires, of course, a technique with the highest practical ability to detect even minor lesions. The latter can only be defined tentatively, in the absence of autopsy confirmation, since all of the 100 workers are still alive. Therefore, the conclusion "No radiographic evidence of pneumoconiosis" is less than totally reliable but, with exacting imaging technique, does carry a very high confidence ratio.

In clinical practice, it is often difficult to decide whether a given individual worker does or does not have asbestosis, when the objective findings are borderline. Yet an all-or-none type of diagnosis must be made, and the impact of the conclusion carries serious consequences.

Perhaps distinct from epidemiologic survey situations, the individual patient requires the maximal practical accuracy. We have, therefore, chosen high quality chest radiography with oblique films as the diagnostic standard, and correlated it with the accuracy of other modalities, and the clinical and functional data.

MATERIALS AND METHODS

Patients

This study consists of 100 consecutive workers (99 males, 1 female) with an occupational exposure to asbestos, mostly for 15 years or more, who were referred here for medical evaluation because of a prior "B" reader's report of characteristic pleural lesions and/or a profuseness of small interstitial opacities of 1/0 or greater according to the 1980 ILO-U/C system.

Clinical and Functional Evaluation

These patients were examined in the Occupational and Environmental Medicine Clinic by one physician (M.J.H.). Standard respiratory questions were asked: "usual" cough and phlegm production, wheezing (never, occasionally apart from colds, most days and nights), and grades of dyspnea were recorded. The presence of clubbing (softened nail beds or increased angle) and fine crackles were coded as present or absent.

Pulmonary function studies were performed either using 1) simple spirometry or 2) whole body plethysmography with lung volumes (51 cases) and single breath carbon monoxide diffusing capacity (DLCO) in 77 cases.

Classification

Individuals were classified as having asbestosis if they had a substantial asbestos exposure and two of three in-house

readers determined that interstitial fibrosis of 1/0 or greater was present on the basis of the complete set (PA, left lateral and both obliques) of in-house radiographs. A "B-reader diagnosis" of asbestosis was established by admitting one in-house B-reading and one outside B-reading classification of 1/0 or greater on PA films.

Conventional Radiography

In 98 patients, PA, left lateral and right and left 45 degree anterior oblique chest radiographs were obtained with 110 to 120 Kv and very short exposure times (0.005 to 0.010 seconds) depending on size and position, at 10 foot tube to film distance, with rare earth intensifying screens and Kodak OC or TMG radiographic film with a speed rating of 400, and automatic processing. The films were exposed, either on a dedicated chest unit with a 110 line, 10:1 grid and phototiming at 2.5 to 4 mas, or manual timing at 500 ma with a 6 inch air gap. The completed radiographs were checked immediately by the responsible radiologist for quality, position and completeness. Inadequate films were repeated as needed unless the patient had already left the department, or was of excessive body size to preclude optimal radiography. This technique affords wide contrast latitude, high detail, maximal image sharpness and facilitates detection of interstitial and pleural fibrosis, but soft tissue calcification is less obvious than with short contrast techniques. The oblique films were obtained with careful positioning to minimize obscuring the lung fields by the scapulae and shoulders, i.e.: both upper extremities elevated overhead in extension and internally rotated, instead of the more popular low shoulder position (Figure 1).

Figure 1. Patient's position for (anterior) oblique films.
A. Low shoulder position obscures lung and pleura.[2]

In 2 patients, only PA and left lateral projections were obtained, by clerical error, and 3 had technically unsatisfactory films (because of excessive body size) in the opinion of at least 2 of 3 in-house readers. Thus, 95 patients had complete sets of in-house radiographs of diagnostic quality.

Outside Films

In 60 patients, the films made elsewhere, on which the prior diagnosis of asbestosis was based, were available for review and identical copies made, except in 10 cases where the films were not copied and the originals seen only by in-house Reader No. 1.

Experimental Radiography

We had the opportunity to utilize an experimental general purpose chest radiography system, recently installed for trial in our department. This prototype storage phosphor digital radiography complex was described in a recent publication.[6] Whenever plates were available, the purpose and risks of one additional PA radiographic exposure, identical to the initial conventional PA film, were explained to the patients and a single PA storage phosphor plate was obtained when they signified their informed consent by signing an institutionally approved authorization form.

Figure 1. Patient's position for (anterior) oblique films.
B. Recommended position for optimal chest radiography.

This system is independent of over or underexposure within a wide range by virtue of its linear receptor response curve (Figure 2). It provides a wide contrast and resolution capability similar to computed tomography and, therefore, a nearly infinite spectrum of processing options by contrast expansion. In our case, the inherent contrast is 4096 shades of grey, and the approximate resolution is 5 lines/mm for the full size images, and 2.5 line/mm for the 2:1 minified images. The latter are produced by pixel interpolation, rather than optical reduction.

Available to us was a standard configuration of print-outs, illustrated in Figure 3, in the case of a very overweight asbestos worker, with previous right thoracotomy for lung abscess. His conventional chest radiographs were of marginal quality, with inconsistent readings for asbestosis. With one full sized print-out as reference, the selection of four minified images was designed empirically prior to our study by concensus among several general radiologists, primarily to facilitate recognition of nodules and visualization of mediastinal, retrocardiac, and retrophrenic spaces.

The resultant storage phosphor print-outs were classified technically as good, noisy, or unfit for diagnosis. The latter were discarded, leaving 50 film sets to be evaluated (35 technically good, and 15 usable but "noisy" print-outs). These films were then viewed and interpreted in the same manner as the conventional radiographs.

Interpretation of Radiographs

The radiographs of all 100 patients were evaluated in-house and scored according to the 1980 ILO U/C method by 2 experienced "B" readers (one chest radiologist and one pulmonary physician) and by 1 experienced chest radiologist, and re-read again by the latter after an interval of one to six months after his initial readings of the same cases. For each patient, each reader evaluated the images separately in this order:

1. In-house PA radiograph alone;
2. In-house combined set of 4 radiographs;
3. Previous outside PA film when available;

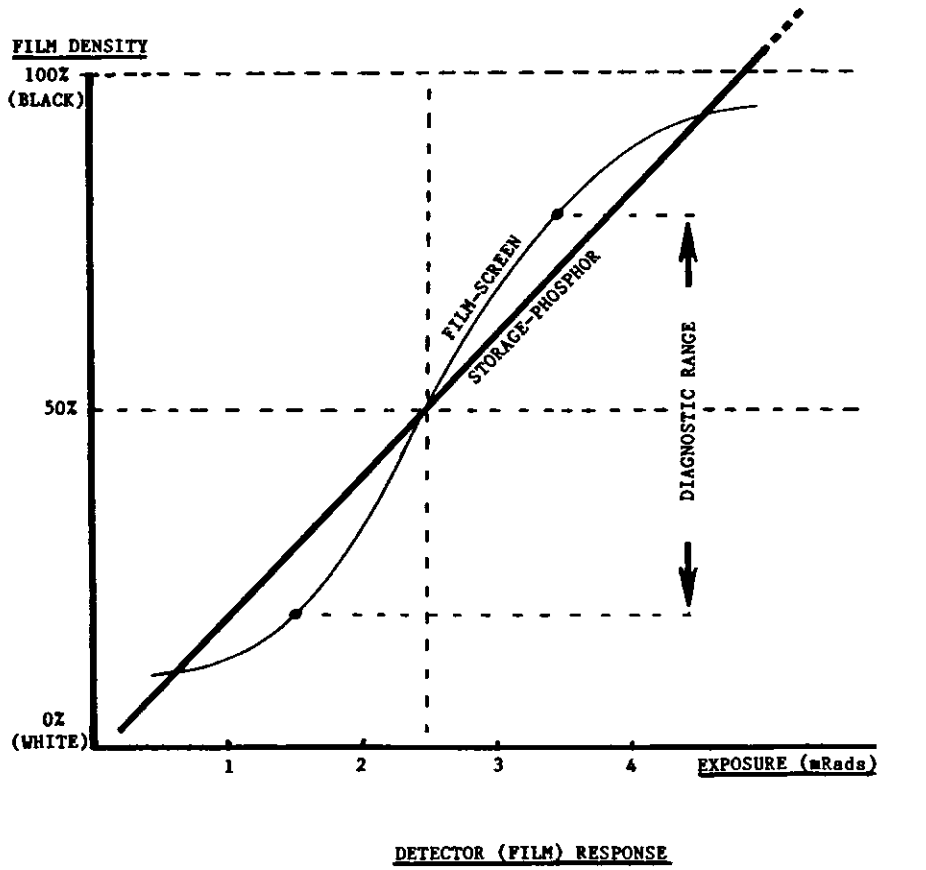

Figure 2. Comparison of detector response curve of film screen versus storage phosphor radiography.

Figure 3. Configuration of storage phosphor image print-outs of examination of a very large patient:
A. Full sized (12 × 14 inch) unprocessed.

4. Single PA full size unprocessed storage phosphor film when available; and
5. Combined set of 4 PA minified processed storage phosphor images when available.

This resulted in nearly 1,200 ILO U/C forms. From these, the following information was entered into the data base:

(a) Film quality: 1 Diagnostic; 2 Borderline readable; 3 Non-Diagnostic (faulty technique); and 4 Non-Diagnostic (faulty patient).
(b) Profuseness of small opacities compatible with pneumoconiosis.
(c) Pleural thickening consistent with pneumoconiosis.
(d) Pleural calcifications consistent with pneumoconiosis.

RESULTS

Because of the slower than anticipated presentation of workers for examination, the final readings were only completed one month ago. The statistical portion of this study is, therefore, incomplete and only preliminary.

In the absence of independent means for diagnosis, for the purposes of this study, as indicated previously, the diagnosis of asbestosis was made when at least two of three in-house readers reported a profuseness of interstitial fibrosis of 1/0 or greater on the set of 4 films, and was compared with a diagnosis of asbestosis based on concurrence of 1 outside B-reader with at least 1 in-house B-reader, on PA films only.

Of the 95 patients who had technically acceptable in-house films, 50 (52.6%) were interpreted by at least 2 in-house readers as having asbestosis. Table I lists the prevalence of symptoms, body mass index, and pulmonary function studies for individuals who did and who did not meet the criteria for asbestosis. Symptoms were generally not more frequent among individuals with asbestosis, with the possible exception of wheezing. Pulmonary function tests were compared between the two groups. Only mean percent of predicted DLCO was statistically significantly different between the two groups.

Table II illustrates that the diagnosis of asbestosis made by the two groups defined above differed significantly, indicating greater consistency of in-house readers, than concurrence without outside readers.

Diagnostic groupings were established, classifying cells by concordance and discordance of diagnosis. Table III presents

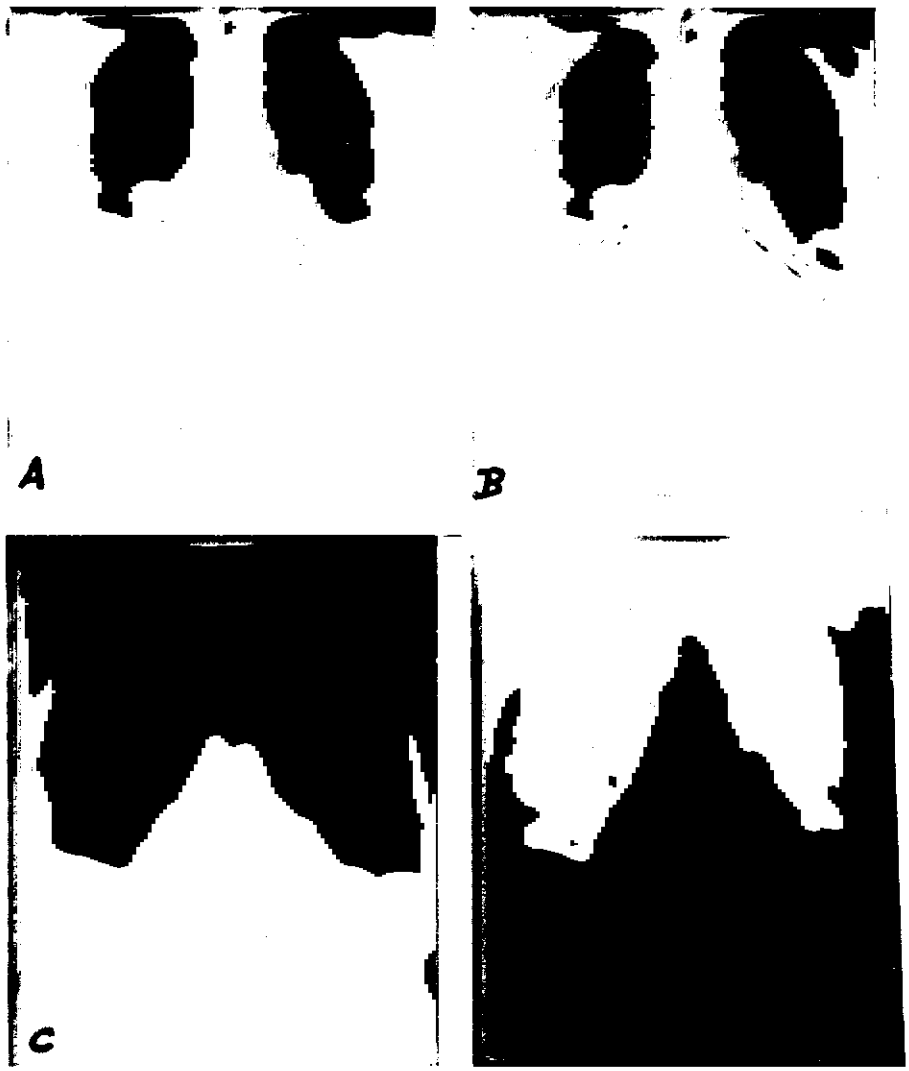

Figure 3. Configuration of storage phosphor image print-outs of examination of a very large patient:
B. 4 minified (6 × 7 inch) images:
(a) unprocessed, identical with A except for minification;
(b) mildly edge enhanced;
(c) mildly edge enhanced and contrast enhanced negative; and
(d) mildly edge enhanced and contrast enhanced positive ("black bone").

analyses of variance. DLCO was again the only variable which appeared unevenly distributed among groups, whereas age, symptoms, body mass index, and other pulmonary function studies were all random. While even DLCO only approached statistical significance, and the number of data is small, the trend supports the clinical impression that many outside films, which were of diagnostically acceptable quality, were erronously interpreted as positive.

Subsequently, each individual in-house reader's diagnostic interpretation of the PA film alone from the same set was compared with the readings of the complete set of in-house radiographs. Table IV presents the cross-classification of these results. Each individual reader disagreed in a substantial proportion of cases with his own diagnosis and with that of the combined in-house readings, in comparison with the diagnosis based on the complete set. This supports our thesis that PA films alone are an insufficient basis for the diagnosis of asbestosis in individual patients, although PA films are simpler to handle and may well suffice for epidemiologic purposes.[14]

Table I
Prevalence of Symptoms and Pulmonary Function Studies by the Diagnosis of Asbestosis

	Asbestosis	No Asbestosis	p-value
Age	57.2 (1.32)	58.9 (1.32)	0.324[1]
Body mass index	28.4 (0.798)	30.0 (0.778)	
Usual cough	35 (70.0)	25 (64.4)	0.7207[2]
Usual phlegm	32 (66.0)	32 (71.1)	0.8116[2]
Wheezing	46 (93.9)	34 (79.1)	0.0728[2]
DLCO (in percent of predicted	77.2 (2.97)	89.0 (3.386)	0.011[1]

[1] unpaired t-test
[2] chi-square

Table II
Asbestosis by "B-Reader Diagnosis of Asbestosis"

Diagnosis of asbestosis by

		in-house experts	
		Yes	No
B-readers	Yes	23	28
	No	9	40

chi-square = 7.023; p = 0.008

Table V summarizes the in-house readers' confidence in the tested modalities, for the conventional radiographs, and for our experience with interpreting asbestos related interstitial and pleural lesions with the storage phosphor films. This system has not yet been used in routine clinical practice, and the readers had no significant working familiarity with it. In our combined judgment, the experimental storage phosphor films used in this study were superior to the standard single PA radiograph only in the recognition of pleural calcifications, but not in diagnosing interstitial or pleural fibrosis. In contrast, the overall confidence rating in the reliability of the complete set of in-house radiographs was positive in all three regards.

Finally, Table VI lists the important unusual findings encountered in this group of patients, a by-product of substantial clinical significance.

DISCUSSION

The difficulty of recognition of minimal or early lesions is legendary, particularly concerning interstitial disease.[4,5,8,9,10] The threshold of recognition always depends on the stage of evolution of the lesions, the sensitivity of the detecting system, and the specificity of the process of interpretation. Clearly below this threshold are the histologically recognizable lesions which have not yet reached detectability

Table III
Analysis of Variance for Diagnostic Groups

Grouping	Single breath carbon-monoxide diffusing capacity (percent of predicted)
Asbestosis by in-house experts and by certified B-readers	77.7
Asbestosis by in-house experts but not by certified B-readers	76.7
Asbestosis not by in-house experts but by certified B-readers	86.0
No Asbestosis by in-house experts or by certified B-readers	89.9

F-value 2.311; p = 0.0835

Table IV
Cross-classification of Diagnostic Evaluation of Simple Posteroanterior Chest X-rays vs. the Diagnosis of Asbestosis on Complete Set of Films by at Least Two In-house Readers

Reader	Read	Diag. on full set: Positive	Diag. on full set: Negative	p-value by a chi-square test
Reader #1				
Asbestosis by PA only	Yes	31	16	0.0089
	No	20	33	
Reader #2				
Asbestosis by PA only	Yes	34	20	
	No	17	29	0.0168
Reader #3				
Asbestosis by PA only	Yes	34	5	
	No	17	44	0.0001

Table V

1988 ASBESTOSIS STUDY: Perceived Reliability of Tested Imaging Modalities Relative to Good Quality PA Radiographs Alone (Combined Valuation by 3 Readers)*

Modality	for interstitial disease	for pleural fibrosis	for pleural calcifications	Overall Confidence Rating
Complete Set (incl. obliques)	+1.3	+2.6	+1.3	+1.7
Exp'l Storage-Phosphor PA				
Single 14 X 17 unprocessed	-1.3	-1	-0.6	-1
Composite of 4 processed minified 4-in-1 films	-2	-1	+1.5	-1.5

*Valuation: Equal = 0, Better = +1 to +3, Worse = -1 to -3

Table VI

1988 Asbestosis Pilot Study: Significant Unusual Findings

1988 ASBESTOSIS STUDY

Significant unusual findings in 100 cases

Suspicious adenopathy or mass (R.O. CA)	12
Excessive pleural fibrosis (R.O. mesothelioma)	4
Bullous emphysema	6
Major cardiovascular abnormality	7
Mediastinal plaques	2
Pericardial plaques	5
Miscellaneous	6

by radiography.[10] A workable definition of a "threshold of detectability" needs to be established before much real progress is possible in this field. With time, lesions generally progress to a level where the recognition rate approaches 100%. Our concern involves the lower end of the spectrum, i.e.: borderline evidence of disease, where the errors in diagnosis abound. After a measure of the diagnostic error rate in general was ascertained over 30 years ago,[7,18] Morgan, et al.[13] first related it to pneumoconiosis and the use of the ILO U/C classification in particular. More recently, Rockoff and Schwartz[15] called attention to the underestimation of early asbestosis by the ILO classification, but because of lack of an independent "truth diagnosis,"[12] ROC analysis is not appropriate in this situation.

Diagnosis of Interstitial Lung Disease

The pulmonary interstitial markings are accentuated by certain technical factors, such as increasing contrast by low KV radiography, edge enhancement illustrated by the storage phosphor images, unsharpness (often due to prolonged exposure times as was the case in the majority of outside films with overinterpretation of interstitial patterns), or underexposure of the lungs (sometimes due to excessive body size) (Figure 3). By virtue of its linear response curve, deficiencies due to over or underexposure are characteristically reduced by the storage phosphor technique (Figure 2). Conversely, pulmonary interstitial markings can be minimized by overexposure of radiographs, deficiency of soft tissues, excessively deep inspiration, and by imaging techniques such as positive printing as illustrated by the positive image in the 4-in-1 storage phosphor print-outs (Figure 3B). The addition of oblique films affords substantially more correct evaluation of the interstitial patterns of the lungs, and increases the confidence of recognition of presence or absence of minor interstitial opacities (Figure 4).

Diagnosis of Pleural Fibrosis

Asbestos related pleural fibrosis occurs most frequently posterolaterally, and in our series, nearly 50% of typical pleural lesions were only detected on oblique films. This has

Figure 4. Oblique films generally allow more reliable evaluation of interstitial pattern.
A. PA film with accentuated interstitial pattern (1/1 profuseness of "t" irregular opacities on original film).

also been reported by others.[1,11,16] Oblique films also help in properly evaluating previously seen pleural lesions, but require some degree of experience. Furthermore, proper position is critical for a precise view of the pleura (Figures 1 and 5).

Although routine computed tomography of the chest was not included in our study, our experience and that of others,[9,17] indicates that pleural lesions, especially on the diaphragm, are most reliably recognized thereby. Probably, parietal pleural lesions will remain more easily recognizable by radiography with oblique projections, because of their predominantly craniocaudad orientation, while the diaphragmatic pleura as well as the areas of pleura normally obscured by the heart or diaphragm are more properly examined by computed tomography (Figure 6), where the right lower pleural mass probably represents a "rounded atelectasis."[3] Surprisingly, not a single patient in our series had pleural effusion.

Diagnosis of Pleural Calcifications

Calcifications, especially early, are not recognized radiographically unless a sufficient dimension of the calcified lesion lies parallel to the direction of the ray. Therefore, in a given population with various pleural calcifications, the detection rate will vary directly with the number of different projections. For instance, Figure 7 demonstrates diaphragmatic and substernal calcification, seen only in the lateral projection in this particular case. Calcifications are more readily demonstrable with relatively low kv and high contrast techniques, and with contrast enhancement (Table V).

RECOMMENDATIONS AND CONCLUSIONS

This pilot study confirms that increased reliability of the radiographic diagnosis of asbestos related pulmonary and pleural lesions varies directly with diagnostic quality, sharpness, contrast and positioning, and that, particularly in early cases, PA films alone do not suffice. In order to enhance

Figure 4. Oblique films generally allow more reliable evaluation of interstitial pattern.
B. Right anterior oblique film shows normal peripheral lung fields (no interstitial opacities on original film).

Figure 5. Effect of shoulder position on quality of oblique film:
A. Improper position (cf Figure 1A, low shoulder).

recognition of actual disease and minimize false positive diagnoses, the standard examination for individuals suspected of asbestos related disease should consist of PA, left lateral and both 45 degree anterior oblique projections with very short radiographic exposure, high kv technique, and proper positioning. Uncertainty concerning pleural and diaphragmatic lesions may be resolved by computed tomography. With the proper precautions, increase in individual radiation exposure to the chest, incurred by these diagnostic measures, is trivial, particularly in view of the medical and economic consequences of false diagnoses to the patient and to society. The potential for improving the diagnosis in asbestosis by alternative imaging procedures is illustrated by our experience with a new experimental storage phosphor technique, and warrants continued evaluation by using new imaging configurations, more suitable for interstitial and pleural disease.

Finally an objective detectability threshold for asbestos related pleural and pulmonary lesions is urgently needed.

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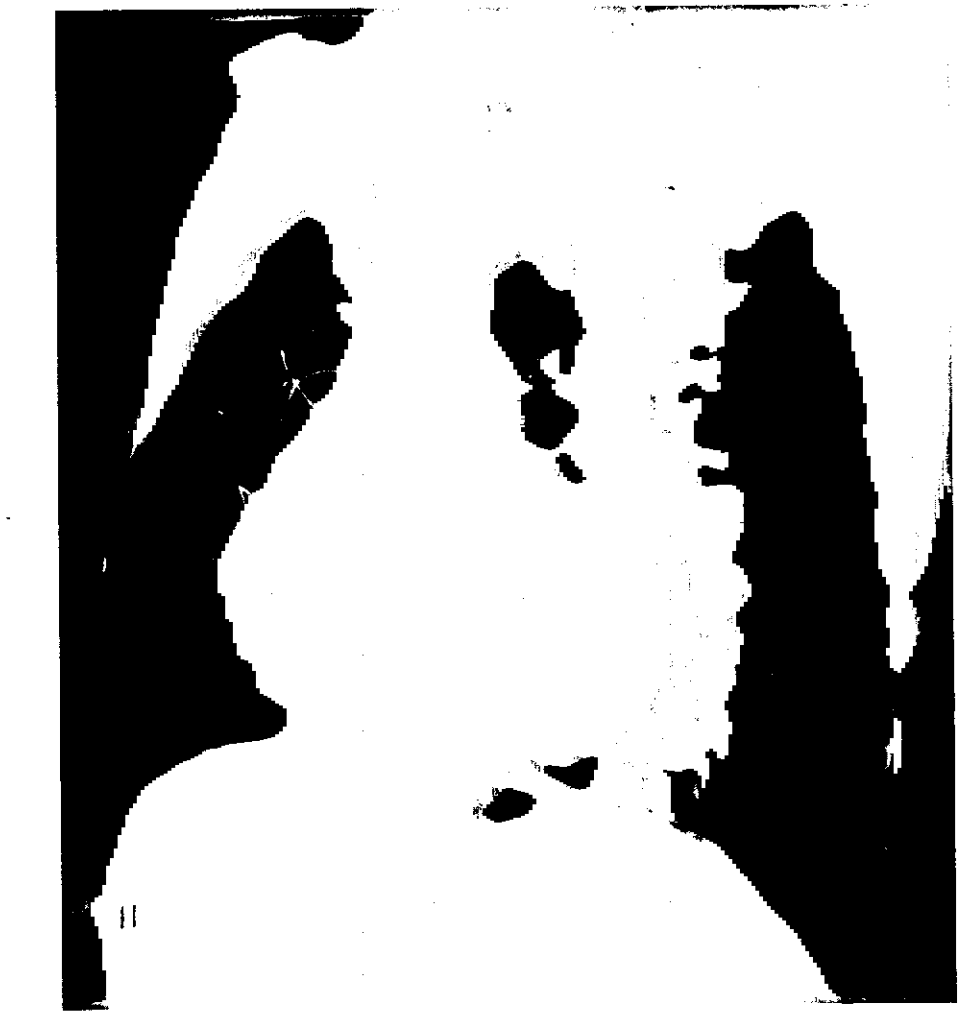

Figure 5. Effect of shoulder position on quality of oblique film: B. Correct position (cf Figure 1B, upper extremities elevated, extended and internally rotated.

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Figure 6. Role of computed tomography for detection of pleural lesions in certain anatomic areas:
A. PA radiography shows interstitial opacities, pleural plaques and right diaphragmatic calcification.

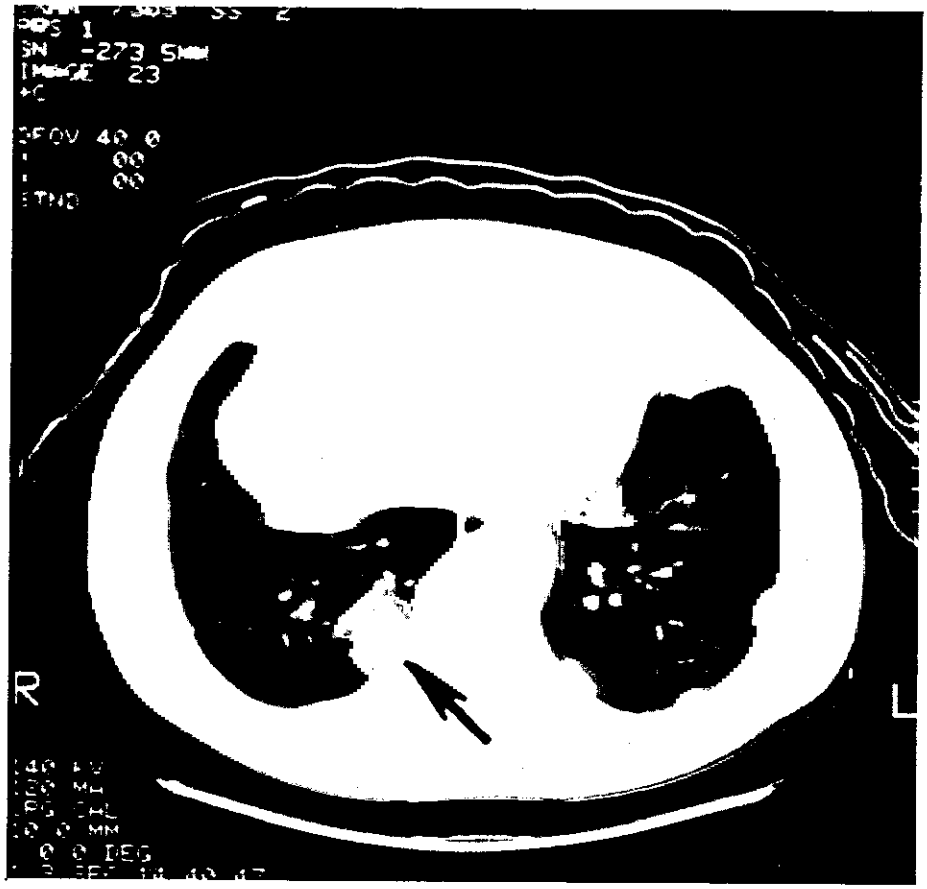

Figure 6. Role of computed tomography for detection of pleural lesions in certain anatomic areas:
B. Computed tomogram shows 4 cm right lower retrophrenic pleural mass, not seen on any of the conventional radiographs (probably a rounded atelectasis).

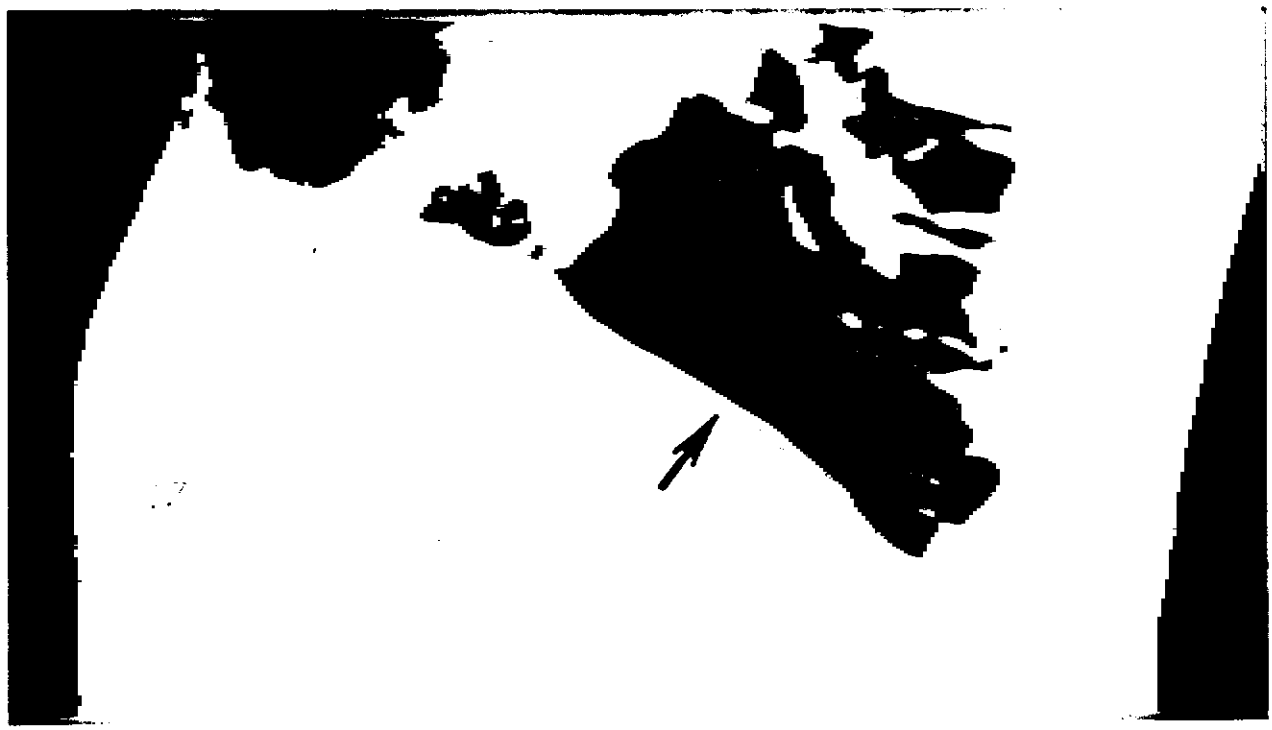

Figure 7. Diagphragmatic and substernal calcifications seen only on lateral radiograph.

PRESENT USE AND TRENDS IN THE DEVELOPMENT OF THE ILO INTERNATIONAL CLASSIFICATION OF RADIOGRAPHS OF PNEUMOCONIOSES

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The First International Classification of Pneumoconioses, based both on radiographical appearances and respiratory function impairment, was adopted as early as 1930 at the First International Pneumoconioses Conference, convened by the ILO in Johannesburg. Substantial work has been devoted to the further improvement of the Classification which has resulted in five successive revisions, the latest being the ILO International Classification of Radiographs of Pneumoconioses, (further ILO Classification) 1980.[7] Recently some proposals for further improvement of the ILO Classification and methodology of reading radiographs and subsequent handling of data have been published.[1,2,9] For this reason, we addressed the major users of the ILO Classification and asked their opinions about the potential need of its revision.

METHOD

A questionnaire was sent to institutions responsible for matters of pneumoconioses in a number of countries exploring the present use and trends for further development of the ILO Classification. Replies were received from the following 29 countries: Australia, Austria, Belgium, Brazil, Canada, Chile, China, Czechoslovakia, Denmark, Egypt, Finland, France, German Democratic Republic, Greece, Indonesia, Mexico, Netherlands, Nigeria, Norway, Peru, Poland, Rumania, Spain, Sweden, Uganda, USSR, United Kingdom, United States of America and Yugoslavia. The cooperation of institutes and individuals from these countries is highly appreciated.

RESULTS

Use of the ILO Classification

In almost all of the above countries, a standardized classification of pneumoconioses is used for general or for specific purposes. There are exceptions in a few countries in which pneumoconioses appear to be very rare diseases due to the limited extent of industries involving exposure of workers to fibrogenous mineral dust.

A casual review of published epidemiological studies of pneumoconioses clearly proves that the ILO Classification has been universally applied in these surveys. Its general use to this purpose has been endorsed by the WHO.[8] The guidelines for its use explicitly state that the ILO Classification does not imply definitions of pneumoconiosis for compensation purposes but has as an object to codify the radiographic abnormalities of pneumoconioses.[3] Nevertheless, the criteria of the ILO Classification have been routinely incorporated into national classifications of pneumoconioses for the compensation of sick workers. Besides, the symbols for pulmonary X-rays changes are frequently used in surveillance of health of individuals and in clinical diagnosis, replacing lengthy verbal descriptions of the type and extent of the changes. For the same reason, they have been found useful even for registration of disseminated shadows in chest X-rays in lung diseases other than pneumoconioses.[5]

National classifications of pneomoconioses usually define minimum radiographical changes considered as compatible with a definite diagnosis of pneumoconioses as well as the grading of the less and more advanced stages (Table I).[6]

In view of their principal use, i.e. compensation of the disease, the national classifications sometimes slightly modify the ILO Classification or include additional criteria, in particular respiratory function impairment (Australia, Belgium, Chile, China, Denmark, Egypt, Finland, Greece, Indonesia, Mexico, Poland, Spain, USSR, Yugoslavia). The USSR Classification also takes into account aetiological factors by distinguishing, e.g., silicosis, silicatosis or mixed-dust pneumoconioses, in the latter the effect of silica being modified by other components of rocks. Whereas the ILO Classification contains three major categories of profusion of small opacities and three categories of large opacities, in some countries the number of stages of pneumoconiosis is limited to three: initial fibrosis, pneumoconiosis with small and with large opacities, to which cilicotuberculosis is added in accordance with the ILO Injury Benefits Convention, 1964 (No. 121) (Chile, China, Czechoslovakia, German Democratic Republic, USSR). For codification of radiographical changes, the symbols of the ILO Classification are used even in such cases.

Therefore, a clear distinction must be made between the national classifications of pneumoconioses as diseases, and the international classification of radiographical appearances of pneumoconioses. Whereas it would be extremely difficult to internationally harmonize criteria for compensation purposes, it is feasible in the case of radiographical changes only. For this reason, the ILO Classification has omitted criteria

Table I

Radiographical Criteria for Notification of Pneumoconioses as Occupational Disease in Selected Countries[6]

COUNTRY	SMALL OPACITIES	
	PROFUSION	SIZE
Belgium	2	.
Bulgaria	2/2	p (s,t)
Czechoslovakia	3/2	.
France	1	.
FRG	3	.
GDR	1/1	p
Hungary	2/2	p
Poland	1/1	.
Sweden	2	.
UK	2/1	.

of respiratory function impairment since its first revision in 1950 and has limited itself to chest radiographs.

In most countries, the 1980 ILO Classification is used either exclusively (Australia, Austria, Finland, Indonesia, Mexico, Norway, Peru, USA) or together with one of the previous revisions, in particular the 1971 ILO Classification (Belgium, Brazil, Egypt, France, Poland, Spain, United Kingdom, Yugoslavia). However, there is a tendency to adopt the latest, i.e. the 1980 revision.

Nevertheless, for reasons of continuity in statistics and research, some cohort studies on miners which started even some decades ago continue to use the 1968 revision of the ILO Classification (France, United Kingdom).

A few of the countries which continue to use one of the older revisions of the ILO Classification indicated that the expense of providing all national centres responsible for evaluating pneumoconioses with new sets of standard radiographs of pneumoconioses prevented them from transition to the 1980 ILO Classification.

In some countries (China, Czechoslavakia, France, German Democratic Republic, Indonesia, Norway, Poland, Rumania, USSR), the use of a standardized national classification of pneumoconioses in compulsory for health services and social security institutions. In other countries, such as Australia (some states), Austria, Chile and Spain, social security enforces the use of a standardized classification for its own purposes. In the remaining countries, a standardized classification has been agreed upon by representative medical bodies or institutions specialized in occupational health, in particular in the field of pneumoconioses. In the USA, at least three Federal Agencies (Department of Labor, U.S. Navy and the National Institute for Occupational Safety and Health) have established the use of the ILO Classification, 1980.

Qualification of Readers and Organization of Reading of Radiographs

Only in some countries certificates are issued to physicians testifying their qualification for the evaluation of radiographs of pneumoconioses (Austria, Belgium, Egypt, German Democratic Republic, Indonesia, Rumania, Spain, USA, USSR). Qualification is achieved by participating in specialized post-graduate training courses or passing an examination. The most elaborated curricula for training of readers at two levels (A and B) have been established in the USA.

In the remaining countries, specialization in radiology, chest diseases or occupational medicine—exceptionally only a basic M.D. diploma—authorizes physicians to evaluate radiographs of pneumoconioses. Training is provided in short-term courses, in-house or as self-training.

Most of the specialized occupational health or social security institutions establish boards of specially trained readers, whose qualification has been tested and even re-tested.

In most countries there is a tendency to centralize the reading to a restricted number of special centres. This is facilitated by the fact that industries involving exposure to fibrogenous dust are frequently accumulated in certain areas close to mineral deposits (mines, quarries, ceramic industry) and that compensation claims concentrate in social security institutions.

Sometimes, large-scale screening is broadly decentralized, however, special boards or panels are used to confirm positive diagnosis of pneumoconioses or to settle widely divergent interpretations. There is no general rule about the size of the board or panel. The first screening is usually carried out by one reader, and the re-evaluation of the positive findings by two or more additional readers.

The on-going discussion concerning the potential use of specially trained lay-readers, instead of physicians, for the first screening or for epidemiological studies should be noted; there is no definite agreement on this point.[4]

Further Development of the ILO Classification

No classification can be considered to be a definite scheme and newly acquired knowledge may demand its modification. This need may be conflicting with the necessity for continuity of statistics or epidemiological cohort studies. The

respondents to the ILO questionnaire expressed their general satisfaction with the ILO Classification, 1980, and mostly preferred continuation rather than a revision, but some of them considered that regular reviews may be useful. Several institutions made suggestions which are summarized as follows:

More attention should be given to incipient changes by adding in the standard set instructive radiographs of early stages (Australia), namely borderline films 0/1 and 1/0 of rounded and irregular opacities and a clear standard 1/1 (Brazil), a standard of 0/0 taken on an obese person (Finland), and additional radiographs of the peripheral parts and vascular patterns (Mexico);

On the other hand, treatment of silicotics influences the development of large opacities and for this reason a subdivision of large opacities is found useful for research and therapeutical considerations (France);

The present standard radiographs are mid-category ones; boundary films should be considered to exemplify the middle reading between each of the major categories (China, United Kingdom, USA);

Improvements could be made in the Guidelines for the Use of the ILO International Classification of Radiographs of Pneumoconioses;[3] they should not only be a supplement to the films, but a firm guidance (France); the reading sheet should be modified or simplified (Brazil, Norway, USA); they should also contain instruction on recommended methods for epidemiological research and group surveillance (Brazil); a symbol for lung vessel congestion should be added (Austria);

Criticism has been expressed concerning pleural pathology, its grading and the descriptive text (Belgium, Brazil, Finland, United Kingdom, USA).

It is my expectation that the discussion at this Conference will give advice for further action.

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AN ANALYSIS OF X-RAY READER AGREEMENT: DO FIVE READERS SIGNIFICANTLY INCREASE READER CLASSIFICATION RELIABILITY OVER THAT OF THREE READERS?

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ABSTRACT

Five experienced readers, working independently and without exposure or other subject data, applied the ILO 1980 classification to the chest radiographs of 1,168 workers currently employed in the manufacture of man-made mineral fibers. To examine the effect of using five instead of three readers, we determined the difference in profusion of small opacities when using the median readings of all five readers, compared to the medians produced by each of the ten panels combining three of the readers. The distribution of small opacity profusion differed among individual readers, but most of the films were placed in low categories: fewer than one percent were above category 1/1. Readers also differed in their assessments of film quality, and showed differing sensitivities to radiographic effects of age and smoking. Despite these individual differences, the addition of two readers usually had little effect on median profusion judgments. For eight of the ten panels, five or fewer percent of films were classified differently; for all ten panels, fewer than two percent of films were reclassified beyond an adjacent category on the twelve-part scale. Eight panels were sensitive to radiographic effects of smoking, and three to effects of age; the five-member panel was also sensitive to smoking. We conclude that, when experienced readers are used, enlarging a panel from three to five members is unlikely to affect median small opacity profusion.

INTRODUCTION

The ILO 1980 Classification of Radiographic Appearances of Pneumoconioses is subject to inter- and intra-observer variability.[1] It has therefore been accepted practice to use several experienced readers—at least three—in order to minimize the chance of systematic bias.[3] The median reading for the readers has been used to summarize each film, since it is not affected by the values of the extreme readings, as would be the mean reading.[2] Although it is intuitively true that the accuracy of the summarized readings should increase with more readers, there is a question whether a significant proportion of readings would change if the number of readers was increased beyond three. In a study of a working population engaged in man-made mineral fiber manufacturing, ILO 1980 classifications of a set of chest X-rays by five readers were available for comparison with all possible subsets of three readers.

METHODS

The study materials consisted of the chest radiographs of 1,755 employees in seven plants. All five readers attempted to classify all films according to the ILO 1980 Classification. The readers concluded that a different percentage of these 1,755 films were of unreadable quality (0% to 8%). A total of 1,603 films were judged readable, and were classified by all five readers. At the time of this analysis complete smoking history was available for 1,168 subjects, and we will only consider this subset to assess the effect of age and smoking status on the classification of low-level opacities. The ages of the workers considered have a mean of 41 years, a standard deviation of 11 years, and a range from 19 to 76 years. Sixty-eight percent of the workers were either current or ex-smokers with pack years having a mean of 28, a standard deviation of 25, and a range from 0.2 to 168.

RESULTS

Most individual readings were concentrated in the lower profusion categories, as indicated in Table I. All readers classified between 82% and 98% of the films as 0/0, with only between 1% and 10% over 0/1. Two readers classified 0.5% of the films ½ or higher.

Table II considers the distribution of individual readings relative to the entire group. The entries in the table represent the percentage of times each individual reading deviates from the median reading for all five readers. For example, Reader A classified 3.5% of the 1,168 films one category higher than the classifications based on the median of all five readers. If we consider the number of times individuals rated

Table I
Distribution of Small Opacities Profusion in %, by Reader (N = 1,168)

Reader	Profusion 0/0	0/1	1/0	1/1	≧1/2
A	90.6	3.7	1.2	4.0	0.5
B	82.1	7.5	3.6	6.3	0.5
C	89.4	8.5	1.3	0.8	0.0
D	92.1	6.0	1.5	0.4	0.0
E	98.0	1.2	0.7	0.1	0.0
Median	94.8	3.6	1.1	0.5	0.0

Table II
Distributions of Individuals' Readings, by Distance from Median Reading (N = 1,168)

Reader	Number of Sub-Categories From the Median −3	−2	−1	0	+1	+2	≧+3
A	0.0	0.0	1.0	91.4	3.5	2.1	2.0
B	0.0	0.1	0.3	83.6	7.3	4.3	4.4
C	0.1	0.2	0.9	92.0	6.2	0.3	0.3
D	0.0	0.4	1.8	93.0	4.1	0.7	0.0
E	0.0	0.6	3.4	95.9	0.1	0.0	0.0

films more than one category above or below the median, we see that Readers A and B tended to read higher than the others. Readers C and D read on both sides of the median, with slightly greater readings above. Reader E read consistently lower than the others.

In order to assess the effect of adding two readers to an original three, all ten possible panels of three readers were considered. For each of these panels of three, the median reading for each film was recorded. Table III demonstrates, for each combination, the percentage of films that changed their classification when the medians were based on all five readers. Since a change of more than one category is considered important, the combinations of readers in Table III are ranked in descending order according to the percentage of films that changed more than one subcategory when two readers were added. In the worst case, adding two readers made any change in only 7.4% of the films (when A, B, and C are the original three), and a change greater than one category in only 1.6%. In the majority of combinations (70%), fewer than 0.5% changed by more than one category. The combinations that are affected the most by adding two readers are the ones that include Readers A and B, the two highest readers based on Table II. The addition of two more moderate readers will affect a greater proportion of film classifications. Nevertheless, even in these cases only 1.5% of the classifications changed by two or more categories, indicating that the addition of two readers had little effect.

The possible effects of age and smoking status on the classification of low-level opacities was investigated for each reader. Exposure information on the workers was not available at the time of analysis and was not included. Obviously, this very important explanatory variable should be considered when possible, since any detectable effects due to age and smoking alone could be confounded with an exposure effect. The limited attempt here is to see how often detection of the radiographic effects of age or smoking are changed by changing the size or composition of panels. Table IV presents the result of logistic regressions on age, smoking (ever versus never), pack years, and finally pack years after adjusting for age, for each reader. Readers A and E, high and low readers respectively, detected no effects (with the exception of an age effect for Reader E). Readers B, C, and D detected almost every effect. Therefore, no discernible relationship to over- or under-reading exists. Table V presents the result of logistic regressions for each three-reader panel and for the five-reader panel. Eight panels were sensitive to the radiographic effects of smoking, as shown by a significant relationship between small opacity profusion and either smoking category or pack-years. Three panels were similarly sensitive to the effects of age. The five-member panel was also sensitive to smoking, indicating that the addition of two readers is unlikely to eliminate this possible source of confounding with dust effects.

CONCLUSIONS

When using three experienced readers (the widely accepted minimum for epidemiologic research), the effect of including two additional readers seems to be neglible. Despite using readers with significant inter-observer variability, only a small proportion of films were changed by more than one category, after adding two readers.

Table III

Rate of Change in Median Profusion Category After Adding Two Readers, for Each Possible Combination of Three Readers

Readers	Percent Films Showing Any Change	Percent Films Changing More Than One Sub-Category
A B C	7.4	1.6
A B D	5.7	1.5
A B E	5.0	1.4
B D E	3.2	0.4
B C D	4.6	0.3
C D E	3.3	0.3
A C D	2.4	0.3
A D E	2.7	0.3
B C E	3.4	0.3
A C E	2.2	0.2

Table IV

Sensitivities of Individual Readers to Age and Smoking Effects on Small Opacity Profusion (Logistic Regression, N = 1,168)

Reader	% > 0/0	Age	Smoking	Pack-Years	Pack-Years/Age
A	9.4	NS	NS	NS	NS
B	17.9	**	**	**	*
C	10.6	NS	*	**	**
D	7.9	**	**	**	**
E	2.0	*	NS	NS	NS

*significant $p \leq 0.05$
**significant $p \leq 0.01$
NS = not significant

Table V

Sensitivities of All Three-Reader Panels to Age and Smoking Effects on Small Opacity Profusion

Readers	Age	Smoking	Pack-Years	Pack-Years/Age
A B C	NS	NS	*	NS
A B D	*	NS	*	NS
A B E	*	NS	NS	NS
B D E	*	*	**	*
B C D	NS	*	**	**
C D E	NS	**	**	**
A C D	NS	*	**	*
A D E	NS	*	NS	NS
B C E	NS	*	*	*
A C E	NS	NS	NS	NS
ABCDE	NS	*	NS	NS

*$p \leq 0.05$
**$p \leq 0.01$
NS = not significant

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ILO CLASSIFICATION OF THE STANDARD CHEST FILMS OF THE 1986 CHINESE ROENTGENO-DIAGNOSTIC CRITERIA OF PNEUMOCONIOSES

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ABSTRACT

As a preliminary step in joint Sino-American pneumoconiosis research efforts, the 32 standard chest films of the 1986 Chinese Roentgenodiagnostic Criteria of Pneumoconioses were interpreted according to the 1980 International Labour Office (ILO) Classification of the Pneumoconioses by three NIOSH-certified "B" reader radiologists. The Chinese interpretations on the films were obscured, and the films were read independently in random order. The median "B" reading was used in the analysis. The "B" readers' major category of profusion of small opacities agreed with the Chinese category in 27 of 34 cases. The Chinese category was included as either the major or alternative ILO profusion category in 32 of the 34 cases. The "B" readers' primary type of opacity agreed with the Chinese type in 24 of 32 cases, and agreed with regard to rounded or irregular lesions in all but one case. General agreement on zonal involvement and pleural plaques was also good. Four types of large opacities less than 1 × 2 cm (Chinese stage II+) were called either category "A" (3 cases) or coalescence of small pneumoconiotic opacities—"Ax" (1 case) by the "B" readers. Aspects of the Chinese classification without an ILO parallel include the concept of a bondary film, and the use of both profusion and zonal involvement to determine stage of disease. We conclude that, despite various differences, a clear correspondence can be made between the two pneumoconiosis classifications.

INTRODUCTION

A valid quantitative assessment of disease is a prerequisite to the development of appropriate dose-response relationships. The chest X-ray is the major tool in assessing the pneumoconioses, and in general has been found to be both valid and quantitatively accurate.[1-3] However, despite an international classification system for the pneumoconioses,[4] substantial differences in interpretation among X-ray readers in one country and among different countries are known to exist.[5-7] The differences between the Chinese and ILO classification systems pose another potential source of disagreement. Thus, before an effective exchange of epidemiologic pneumoconiosis data can take place, a clear correlation between the two classification systems is needed.

The 1986 Chinese Criteria is described in detail in another Proceedings paper (first authored by Lu Shixuan). In brief, the Criteria uses only a single (primary) type of small opacity (ILO letter system), the major category of small opacity profusion (ILO number system), a slightly modified large opacity classification, a simplified pleural disease evaluation, and similar "other symbols." In addition, the Chinese have stage symbols: 0, 0+, I, I+, II, II+, III, and III+, where 0 is normal and III represents large opacities (greater than 2 × 1 cm). The lower Chinese stages are determined by the number of lung zones involved as well as the profusion of small opacities. An abbreviated correspondence between the 1980 ILO and 1986 Chinese classifications is illustrated in Table I. For the first time, the Chinese Criteria in 1986 covers all pneumoconioses, and includes 32 standard films.

As a preliminary step in joint Sino-American pneumoconiosis research efforts, this study correlates the ILO and Chinese systems by evaluating 3 "B" readers' interpretations of the Chinese standard films.

METHODS

The 32 standard chest X-rays of the 1986 Chinese Roentgenodiagnostic Criteria of Pneumoconioses were interpreted according to the 1980 ILO Classification of the Pneumoconioses by three NIOSH -certified "B" reader radiologists. The Chinese interpretations on the films were obscured, and the X-rays were read independently in random order.

In the analysis the median "B" reading was used to compare to the Chinese interpretation. In a few cases, a simple median "B" reading of type of small opacity did not exist. In these cases the most frequent type (including primary and secondary) was selected. One Chinese film is divided into two sections and two into three sections; thus more than 32 comparisons are possible in some categories.

For profusion category, the kappa statistic[8] as well as the crude agreement value was calculated both between the Chinese and median "B" reading, and among the 3 "B"

Table I

Correspondence Between 1986 Chinese Criteria Stage and 1980 ILO Classifications of Pneumoconiosis

Chinese Stage	ILO Classification		
	Profusion of Small Opacities	Number of Zones	Comment
0	0/- ; 0/0	---	
0+	0/1	---	
I	1	2, 3, or 4	
I+	1	5 or 6	
	2	2, 3, or 4	
II	2	5 or 6	
	3	2, 3, or 4	
II+	3	5 or 6	
	--	---	Several types of large opacities < 2 X 1 cm
III	--	---	Large opacities > 2 X 1 cm but less than "C"
III+	--	---	"C" large opacity

readers. The statistic adjusts for the amount of chance agreement to be expected, and is expressed as:

$$\text{Kappa} = (PC—PE)/(1—PE)$$

where PC is the crude agreement (expressed as a proportion), and PE is the expected agreement. This is derived, as in a Chi-squared test of independence, from the expected numbers for the diagonal elements of the Table, which, in turn, are obtained using the products of the marginal totals. Kappa will equal zero if there is only chance agreement, and will be one with complete agreement.

RESULTS

The overall film quality was rated as quite good; all films having a median technical quality grade of 1 or 2.

Table II presents the reading data for the profusion of small opacities. The "B" readers' major category agreed with the Chinese category in 27 of 34 cases (79%). The kappa statistic, used to adjust the crude agreement, was 70%. By comparison, the average crude agreement among the three "B" readers was 61%, and the average kappa statistic 46%. The Chinese category was included as either the major or alternative ILO profusion category in 32 of the 34 cases. One of the remaining films, called 0/0 by median reading, was a "borderline" film in the Chinese classification. This film had profusion 1, but stage 0+ since the small opacities involved only one zone of the lung.

Table III presents the comparison of the type (size/shape) of small opacities. In all but one case, there was agreement with regard to rounded or irregular lesions. The "B" readers' primary type of opacity agreed precisely with the Chinese type in 24 of 32 cases. The only substantial disagreement was due to an apparent unwillingness of the "B" readers to report "t" opacities. In these 4 cases, however, the "t" opacity was recorded as the primary or secondary small opacity by either one (2 cases) or 2 (2 cases) radiologists. The comparison of zonal involvement is shown in Table IV. There was good general agreement, although it should be noted that over half of the cases had all 6 lung zones involved. All 4 examples of pleural disease were appropriately noted by the "B" readers.

The 1986 Chinese Standard Films contain examples of 4 types of large opacities (>1 cm) that are less than 2 × 1 cm. These abnormalities, all categorized as stage II+ are described as: 1. Aggregation of small opacities (analogous to the ILO "ax"); 2. Large opacities (which would be considered "A" lesions using the ILO scheme); 3. Definite shadows in appearance longitudinal, faint mottling in

Table II
Comparison of Small Opacity Profusion

Chinese Profusion Category	ILO Major Category				
	0	1	2	3	Totals
0	1				1
1	3	10	2		15
2		1	10		11
3		1		6	7
Totals	4	12	12	6	34

Table III
Comparison of Type of Small Opacities

Chinese Type	ILO Primary Type						
	P	Q	R	S	T	U	Totals
P	4	2		1			7
Q	1	5					6
R			6				6
S				5			5
T				4	1		5
U						3	3
Totals	5	7	6	10	1	3	32

Table IV
Comparison of Zonal Involvement

Chinese Standards	"B" Readers						
	1	2	3	4	5	6	Totals
1		1					1
2				1			1
3		1		1			2
4				6			6
5				1		1	2
6					1	14	15
Totals	0	2	0	9	1	15	27

peripheral parts of both upper zones; and 4. Homogeneous, hazy, and patchy shadows over both upper zones. The individual and median "B" readings for these films are presented in Table V. Abnormalities 1, 2, and 4 were graded as showing "A" size large opacities by the median "B" reading. Abnormalities 1 and 3 were marked "ax". There was agreement on the three other examples of large opacities.

DISCUSSION

The 1986 Chinese Roentgenodiagnostic Criteria of the Pneumoconioses represents a marriage between the older (1963) Chinese classification[9] and features of the 1980 ILO classification. The Chinese stage system is maintained since there is much experience in this format which is also related to compensation for pneumoconiosis in the People's Republic of China. Aspects of the ILO classification included in the 1986 Chinese Criteria enable researchers to make a clear correspondence between the two systems. From this small study, it appears that there is a good correlation between the type (size/shape) and profusion of small opacities between the Chinese and ILO classifications. The two classifications contain different standard films, and the Chinese standards represent boundary films as opposed to the mid-category standards of the ILO. In addition, the algorithm to determine the overall profusion category is slightly different. Thus it is not surprising that some small differences might exist.

In the important area of large opacities, the Chinese system makes several distinctions which do not exist in the ILO classification, particularly for what might be regarded as borderline large opacities. Although more readings are needed, it appears that the "B" readers also considered these abnormalities to be borderline or early large opacities (Table V). The other areas of comparison also showed good general agreement.

It should be emphasized that because of (sometimes substantial) variability among pneumoconiosis reading,[5,7] different results might be obtained with additional "B" readers. However, the overall conclusion is that despite various differences between the 1986 Chinese and 1980 ILO classification, a clear correspondence can be made.

Table V

"B" Reader Interpretation of Large Opacities Less Than 2 × 1 cm

Chinese Abnormality (all Stage II+)	"B" Reader Interpretation			
	Median	Reader #1	Reader #2	Reader #3
1. ax	ax, A	ax, A	ax, A	ax, A
2. A, < 2 X 1 cm	A	A	ax, A, R/O Ca	A, R/O Tb
3. Definite Shadows faint mottling	ax	ax	ax, A R/O Tb, Rp	0
4. Homogeneous, hazy & patchy	A	A	A, R/O Ca	B

R/O = Rule out; Ca = cancer; Tb = tuberculosis; Rp = Rheumatoid pneumoconiosis.

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AN ALGORITHM FOR THE DETECTION OF SMALL ROUNDED PNEUMOCONIOSIS OPACITIES IN CHEST X-RAYS AND ITS APPLICATION TO AUTOMATIC DIAGNOSIS

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INTRODUCTION

Computer diagnosis of pneumoconiosis has been studied by several groups since 1970's. Fundamental approaches for classification of profusion of pneumoconiosis opacities can be divided into two categories. One is based on texture analysis of density pattern of lung area, which has been adopted by a large majority of research groups.[1-8] The other is an approach trying to detect directly small opacities of pneumoconiosis. It may be superior to texture analytic approach because it is robust against fluctuations of film quality and individual differences of normal structural patterns in lung area. And, perhaps the latter approach can meet the requirement better according to the ILO classification system whose categorization is based on the density of pneumoconiosis opacities. Typical methods of detecting small rounded opacities have been developed.[9,10] However, category classification based on them has not been performed. Recently, two opacity detection methods have been proposed.[11,12] One is based on a contour line processing and the other adopts a matched filtering technique. Experiments of four major category classifications have been performed by those two methods, whose results show the usefulness of the opacity detection method. This paper presents a new method to identify small rounded opacities of pneumoconiosis and to classify the grade of their density.

DETECTION OF SMALL ROUNDED OPACITIES

The new method for detecting small rounded pneumoconiosis opacities in chest X-rays is based on the processing of local density pattern. The gray value in an opacity area is of the distribution like a local convex surface. Detection of such convex surfaces is performed by two processing steps. The first step is to locate local peaks, and the second one is to identify the shape and the size of them, which is the segmentation of the local convex surfaces from their neighboring area.

The First Step

Candidates of pneumoconiosis opacities are detected by this processing. Figure 1 shows a filter to detect convex surface. Detectors are arranged on three concentric circles. Each detector covers, in general, rectangular region, and its output is the mean pixel value in that region. The output of the filter, X, is given as follows.

$$X = \begin{cases} 3, & A>MAX3, \\ 2, & A>MAX2 \text{ and } A<MAX3, \\ 1, & A>MAX1 \text{ and } A<MAX2 \text{ and } A<MAX3, \\ 0, & \text{others} \end{cases}$$

where, MAXi (i=1,2,3) is the maximum of B_i, C_i, D_i, ...,I_i which are output values of detectors on the same circumference. Diameters of three concentric circles are 1.5, 2.0, and 3.0 mm. They are determined considering the sizes of pneumoconiosis opacities p, q and r. Filter outputs 1, 2, and 3 mean that local convex surfaces can be candidates of pneumoconiosis opacities whose sizes are p, q and r, respectively. Many false pneumoconiosis opacities are detected by the proposed filter. They are called noise opacities in the following and the following screening algorithm to exclude those noises is adopted. First, expansion and contraction processing is applied to merge candidates which are closely adjacent to each other. The next step is the noise reduction in which characteristics of each candidate are evaluated and those which satisfy the following conditions are excluded.

1. Area is less than a threshold h_s.
2. Film density is less than a threshold h_p.
3. The shape is long and slender.

The third condition is investigated as follows. Let us denote the area of a candidate, its widths in the directions of abscissa and the ordinate by s, l_x and l_y, respectively. If the shape of the candidate is a circle, its diameter l is given as:

$$l=2\sqrt{s/\pi},$$

which is equal to l_x and l_y. Considering this relationship, long and slender candidates can be detected as those which satisfy the following condition:

$$(l_x+l_y)/2 > 31.$$

The Second Step

The second processing step includes precise measurement of opacity area and a supplementary noise reduction.

Identification of the boundary of pneumoconiosis opacity is performed as follows. It is assumed that the gradient vector at any pixel which belongs to a pneumoconiosis opacity is directed to the top of its convex surface. And the pneumo-

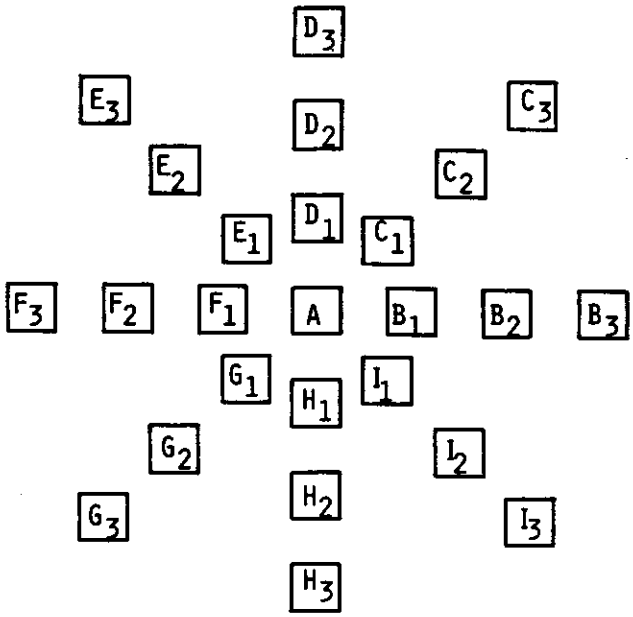

Figure 1. Pneumoconiosis opacity candidate detection filter.

coniosis opacity area defined in this paper is the union of the opacity candidate area and its neighborhood in which gradient vectors are directed to the opacity candidate area.

The second noise reduction algorithm is applied at this stage and the final result is obtained. Opacities which meet the following conditions are excluded.

1. The absolute value of a gradient vector in the opacity area is larger than a threshold h_d.
2. Those opacities which have large discrepancy between the output of the pneumoconiosis opacity candidate detection filter and the area measured in the second step.

EXPERIMENTS

Experimental Conditions

The films used in this study were 11 ILO 1980 standard films whose opacity shapes are rounded. Their classification is given in Table I. Each film was digitized by a drum scanner at a resolution of 5 pixels/mm with 12 bits accuracy and 3 partial zones with 350*200 pixels were extracted from each of the right and the left lung area. They correspond to the upper, the middle, and the lower lung zones. That is, 6 partial zones were extracted from one standard film. It is known that no pneumoconiosis opacities can be recognized in the lower lung area for two ILO standard films 1/1 q/q and 1/1 r/r, and four zonal images extracted from those areas were excluded from the experimental materials. Therefore, the number of zonal images used for automatic diagnosis was 62. Parameter values adopted in the following experiments were as follows.

h_s = 5 pixels,
h_p = 3200,
h_d = 500.

Verification of Opacity Detection Algorithm

Pneumoconiosis opacities identified by an expert reader and those detected by the proposed method were compared to each other. The test material was the upper half of the left lung area of the film 3/3 r/r. The number of pneumoconiosis opacities identified by an expert reader*) and that detected by the proposed method were 120 and 109, respectively. Among them, 66 opacities coincide with each other.

Classification Experiments

A. Features

In spite of the application of noise reduction in twice, noise opacities cannot be excluded completely. Therefore, it is necessary to extract information on the opacity density as much as possible, and the following 14 kinds of features were used for classification.

1. The numbers of opacities x_1, x_2, x_3 for which the convex surface detection filter outputs are 1, 2, and 3, respectively.
2. The numbers of opacities purged from x_1, x_2, and x_3 by the first noise reduction x_4, x_5 and x_6.
3. The sums of area for each opacity size x_7, x_8, x_9.
4. The number of opacities x_{10} and the total sum opacity area x_{11}.
5. The numbers of opacities for each size x_{12}, x_{13}, x_{14}.

The feature parameters x_{10},..., x_{14} can be derived from the other parameters. However, the use of these dependent features were useful for classification.

Table I
Experimental Materials

major category	ILO 1980 standard film
0	0/0×2
1	1/1 p/p, 1/1 q/q, 1/1 r/r
2	2/2 p/p, 2/2 q/q, 2/2 r/r
3	3/3 p/p, 3/3 q/q, 3/3 r/r

B. Classification Method

Defining fourteen-dimensional feature vector $x^t = (x_1, x_2, \ldots, x_{14})$, distance of an input image from a category k is defined as follows:

$$d(k) = \| x - r_k \|$$

where, r_k is the reference pattern vector of category k. It is defined as the mean of feature vectors of the category k. The computer diagnostic testing procedure was one-at-a-time removal test procedure. That is, it consisted of removing one sample from 62 partial zones, training on the remaining 61 samples, and resubmitting the withdrawn sample for reclassification.

C. Classification Results

Results for four major category classifications are given in Table II. Zonal correct classification rate is 69.4 percent. If we adopt a majority rule for overall film classification, it is perfect. Classification rates reported hitherto range between 50 and 80 percent, which have been attained all by texture analysis approaches.

Table II

Confusion Matrix for 4 Major Category Classifications

		assigned category			
		0	1	2	3
input category	0	6	1	3	2
	1	1	12	1	0
	2	0	2	14	2
	3	5	1	1	11

The second experiment is the classification of ILO substandard films. Seven substandard films were used, which consist of two normal, two 2/2 and three 3/2 films. Zonal images with the same size were used for classification. Reference patterns were defined by using all zonal images of ILO standard films. Normal/abnormal classification results is shown in Table III. Correct classification rate was 83 percent, which shows the effectiveness of the proposed method.

CONCLUSION

Identification method of pneumoconiosis opacities and classification based on it have been given. The proposed method is not sensitive to the changes of film quality, which is superior to texture analytic approaches. And the correct classification rate by the proposed method has been shown to be comparable to them. However, many false opacities are detected as pneumoconiosis opacities, and the further improvement of the method is necessary.

Table III

Confusion Matrix for Normal/Abnormal Classification

		assigned category	
		N	A
input category	N	6	6
	A	1	29

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APPLICATION OF COMPUTED RADIOGRAPHY FOR THE DIAGNOSIS OF PNEUOCONIOSES

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In 1982, Research Group for the Utilization of Image Processing for the Diagnosis of Pneumoconioses was organized in the Japan Industrial Safety and Health Association and by the three years' survey, image processing is found very useful for the diagnosis of pneumoconioses with small sized output films of Fuji Computed Radiography (FCR).[1] FCR is a computed radiographic system utilizing imaging plate of laser stimulated luminescence[2] and has linear response to the X-ray dose, resulting extraordinary wide latitude for the exposure. However the output film of this system is ½ size in length of the ordinary radiographic film, such as the ILO standard film of pneumoconioses.

The authors carried out five steps of experiments as shown in Figure 1 since 1982, although in 1985 the name of the research group was changed to the "Research Group for the Quantification of the Radiographs of the Pneumoconioses."

For the experiments 2 and 3 shown in Figure 1, the ILO standard films and test films selected from training films of pneumoconioses in U.S.A. were digitized by using a drum scanner. Digitized images were processed with the several contrast and spacial frequency characteristics which were similar to those employed in FCR system, and finally written optically onto X-ray film in reduced size using a drum scanner. From these experiments gamma 0.85 is found quite satisfactory for this reduced size of the picture, so at the latter stage of the experiments, only 0.85 of gamma curve was used.

For the experiment 5 shown in Figure 1, FCR films of pneumoconioses patients were used with the fixed contrast of 0.85 gamma with several spacial frequency characteristics of E,F,G and H shown in Figure 2. Image processing factors of F.G. and H are almost equally good as shown in Figure 3, but the best is probably G., i.e., slight enhancement at 0.17 cycles/mm.[3]

Magnetic tapes of the digitized images of ILO standard film and test films aforementioned and FCR were used for the study of the automatic determination of the size and profusion of small rounded opacities. Two methods were utilized for this purpose, one is direct detection method using difference linear filtering and the other is texture analysis method, details of these studies are reported respectively by J. Toriwaki and H. Kobatake in this International Conference, so I will not discuss these matters.

It seems rather easy to determine the size, p, q and r, while the automatic categorization of the profusion is not so easy

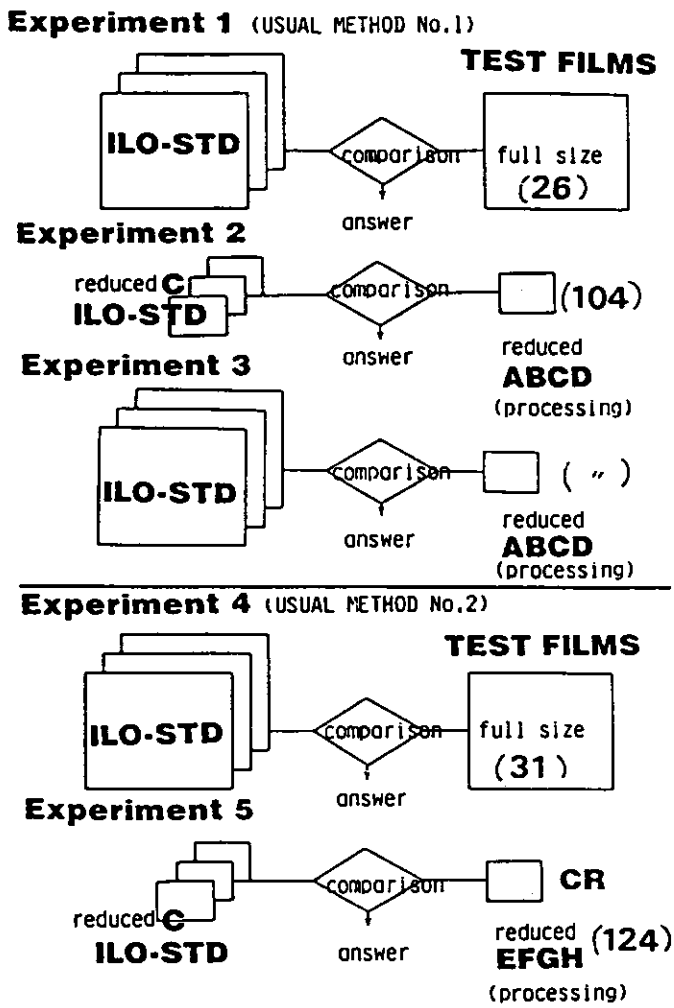

Figure 1. Reading experiments and their sequences.

FERQUENCY PROCESSING

PROCESSING	γ	RANK	BE	FRQ(cycle/mm)
A	0.85	-	-	-
B	0.85	4	0.50	(0.35)
C	0.85	2	0.25	(0.17)
D	0.85	4	0.30	(0.35)
E	0.85	-	-	-
F	0.85	0	0.30	(0.085)
G(=C)	0.85	2	0.30	(0.17)
H(=D)	0.85	4	0.30	(0.35)

GRADATION PRECESSING

BE : THE DEGREE OF SPATIAL FREQUENCY ENHANCEMENT

FRQ: THE CENTER OF ENHANCEMENT

Figure 2. Image processing factors.

for the low profusion groups, although various methods disclosed the accuracy of 45 to 71%, if majority rule is applied 82% was obtained by texture analysis. The result of the investigation is very promising for the future application of computer technique for the automatic diagnosis of pneumoconioses.

At present the authors are collecting more cases with FCR, for the preparation of excellent standard films of our country, and for the creation of better program of automatic diagnosis by computer.

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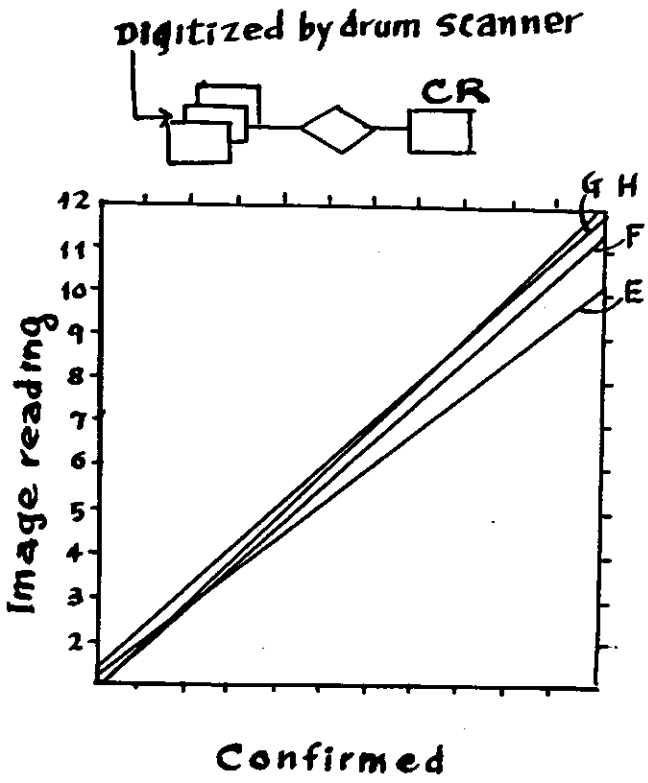

Figure 3. Accuracy of image reading.

3. Annual Report 1987, Research Group for the Quantification of the Radiographs of the Pneumoconioses. Japan Industrial Safety and Health Association Tokyo. (1988) (Japanese).

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THE POSSIBILITIES OF THE NEW THORACIC IMAGERY FOR EARLY DETECTION OF INTERSTITIAL SYNDROMES AND OF SILICOSIS

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In the study of Pneumoconioses, Tomodensitometry appears much more precise (high definition—separation power = 0.17 mm^2—interseptal interstitium = 100 µm) and objective (numerical image—unstacked millimetric cross sections of the thorax) than the standard plate. We have already observed the value of the tomodensitometry for the diffuse parenchymal pathology in general.

Our study covers 59 cases of Pneumoconiosis (20 cases of silicosis, 39 cases of asbetosis). The Pneumoconios diagnostic was made in the light of several elements (exposure time, clinical data, Table I, EFR—DLCO—scintigraphy—

Table I

New Thoracic Imaging, Insterstitial Syndromes, Pneumoconiose Early Detection—Pittsburgh 1988

DIAGNOSTICS PROCEDURES

- DURATION OF EXPOSURE
- CLINICAL EXAMINATION
- PULMONARY FONCTION TEST
- C O TRANSFERT
- B A L
- SCINTIGRAPHY
- MEDICAL IMAGERY
- PULMONARY BIOPSY

bronchiolo-alveolar flush—pulmonary imagery—pulmonary biopsy). Pulmonary imagery is not, indeed, the only method of diagnosis. It must be confronted with other non-morphological methods (for example, we carry out a prospective study on the respective contributions of tomodensitometry and of the other methods of diagnosis—DLCO—scintigraphy—LBA in early detection of the lung, of AIDS).

In our series of 50 Pneumoconiosis the pulmonary biopsy was only carried out 7 times; most of the diagnoses were made on epidemiological and clinical data, and on the results of bronchiolo-alveolar flush (28 cases).

All of these Tomodensitometric explorations were made with an apparatus from the "Compagnie Générale de Radiologie" (CGR) CE 1200. The realization protocol was as following (Table II):

Table II

New Thoracic Imaging, Instertitial Syndromes, Pneumoconiose Early Detection—Pittsburgh 1988

METHODS

- C.G. R. : C.E. 10 000 C.T.
- SECTION THICKNESSES : / 10 mm
- CONTIGUOUS SCANS
- "BONE" ALGORYTHM
- SUPINE OR PRONEPOSITION. IF NECESARY
- HIGHT RESOLUTION C.T. (HRCT)FOCALISED ON AREAS OF INTEREST.
  - edge to edge cross-sections of 1 cm.
  - focalized millimetric cross-sections using the high definition-algorithm for reconstruction of bone type. Table III-IV.
  - window systematically wide—250, 1800. This window gives the histologically most faithful image of the thorax (for example there are false thickenings of the bronchial walls when the so-called pulmonary window is used—700, 700). The other windows (mediastinal, parenchymal) were only used when needed (for example, in the search for calcifications).

The criteria of standard radiological interpretation were those recognized by the I.L.O. The standard plates were examined independently of the tomodensitometric documents.

Table III

New Thoracic Imaging, Interstitial Syndromes, Pneumoconiose Early Detection—Pittsburgh 1988
High Resolution C. T. Scan

TECHNICAL CONSIDERATIONS

- THIN SECTION C.T.SLICES (1 to 2 MM)
- LARGE WINDOW : (WIDTH OF 2000 UH)
  (LEVEL OF -750UH)
- HIGHEST SPATIAL FREQUENCY ALGORITHM OF RECONSTRUCTION ("BONE ALGORITHM" FOR EXAMPLE).
- MATRICE AND CIRCLES OF RECONSTRUCTION.

The criteria of tomodensitometric interpretation have previously been defined in the chapter on pulmonary parenchymal pathology. Let us remember that the semiology of the interstitial syndrome is made up of several stages and expressions (Figure 1): Table V.

1. Homogenous thickening of the interstitial sector parieto-alveolar septal and peri-broncho vascular and sub-pleural; this thickening gives rise to a sign which we have described as "trussed joint". Table VI.
2. Nodular thickening micro and macro-nodular septal or parieto-alveolar; the limit of separation in high tension is 0.17 mm^2; thus a very small nodule can theoretically be detected, nevertheless, this type of lesion is indiscernible from a pulmonary vessel. Table VII.
3. Mixed lesions of interstitial thickening and of pulmonary nodule.
4. "Honey comb" lung indicating an advanced parenchymal destruction.
5. In the case of asbestosis, the sub-pleural curvilineal opacity described by YOSHIMURA, corresponding to a peripheral atelectasis zone, can be bronchiolar and premonitory, in the asbetosis but also in other chronic interstitial pneumopathies, of an evolution towards the "honey comb" lung.

The results of this series are as follows:

29 silicosis were studied, divided into three categories according to the I.L.O. classification and each examined in thoracic tomodensitometry where a score of interstitial disease was given to them (light, moderate, severe disease).

Tomodensitometry shows the parenchymal lesions better than the standard plate (Table I). Thus out of 7 patients in category 1 of the I.L.O. classification, only one shows light disease with tomodensitometry. The six others have moderate disease. Out of 10 cases in category 2 I.L.O. 7 show severe disease with tomodensitometry, only 3 moderate disease. Table VIII.

The high resolution tomodensitometric semeiological study shows nodular disease for all cases, which concords well with the fundamental histological lesion (silicotic nodule), a diffuse disease of the interstitium often occurs also in 25 cases out of 29. The "honey comb" lung is clearly shown in 5 cases as compared to only 2 visible in standard radiography. With tomodensitometry accompanying lesions show up much better than with standard radiography (Table IX).

- 15 cases of emphysemias in smokers as against only 5 detectable with standard radiography.
- 14 cases of associated bronchiectasis invisible with standard radiography.

Table IV

New Thoracic Imaging, Interstitial Syndromes, Pneumoconiose Early Detection—Pittsburgh 1988
High Resolution C. T.

CIRCLE OF RECONSTRUCTION / MATRICE	525	393	262	131	87 H R
256/256	2 MM2	1,4 MM2	1 MM2	0,5 MM2	0,34 MM2
512/512	1 MM2	0,7 MM2	0,5 MM2	0,25MM2	0,17 MM2

Table V

New Thoracic Imaging, Interstitial Syndromes, Pneumoconiose Early Detection —Pittsburgh 1988, High Resolution C. T.

SEMEIOLOGY (INTERSTITIAL SYNDROME)
- HOMOGENEOUS THICKENING OF INTERSTITIUM
- NODULAR
- MIXED (THICKENING AND NODULAR)
- "HONEY COMBING" LUNG.

Table VI

New Thoracic Imaging, Interstitial Syndromes, Pneumoconiose Early Detection —Pittsburgh 1988, Semeiology Homogeneous Thickening

- INTERLOBULAR SEPTA
  - SHORT LINES - ASPECT OF "TRUSSED JOINT".
  - LONG LINES
  - MACRORETICULATION - DRAWNING OF SEPTA ARCHITECTURE.
- INTRALOBULAR LINES - MICRORETICULATION.
- BRONCHIAL VISIBLE MORE PERIPHERALLY WITH THICK IRREGULAR WALL
- HAZINESS OUTLINES OF THE VESSELS.
- VISCERAL PLEURAL THICK AND IRREGULAR

Table VII

New Thoracic Imaging Interstitial Syndromes, Pneumoconiose Early Detection—Pittsburgh 1988

SEMEIOLOGY

- NODULAR

- MACRO-NODULES :

  DIFFERENTIAL DIAGNOSIS : ALVEOLAR NODULES.

- MICRO-NODULES :

  DIFFERENTIAL DIAGNOSIS : NORMAL VESSELS.

Table VIII

New Thoracic Imaging, Interstitial Syndromes, Pneumoconiose
Early Detection—Pittsburgh 1988

SILICOSIS (N = 29)

COMPARAISON OF I L O / U C RADIOGRAPHIC WITH H R C T SCORE

I L O SCORE	NO OF SUBJECTS	H R C T SCORE		
		LIGHT	MODERATE	HIGHT
1	7	1	6	
2	10	0	7	3
3	12	0	0	12

Table IX

New Thoracic Imaging, Interstitial Syndromes, Pneumoconiose
Early Detection—Pittsburgh 1988

ABNORMALITIES ON H R C T IN SUJECTS WITH SILICOSIS (N = 29)

BRONCHO-PARENCYMAL FINDINGS	HRCT SCORE
- HOMOGENEOUS INTERSTITIAL THICKENING	25
- NODULAR INTERSTITIAL	29
- MIXED (THICKENING AND NODULAR)	16
- "HONEY COMBING"	5
- EMPHYSEMA	15
- BRONCHIECTASIS	14
- NEOPLASM	2 (WITH BIOPSY ON CT)

- 8 pseudo-tumoral masses, 4 of which were necrosed.
- 2 peripheral bronchio neoplasms, the histological diagnosis of which was carried out by puncture under tomodensitometric control.

30 cases of asbetoses were studied with the following final diagnosis (Table X):

- pleural disease alone: 11 cases.
- parenchymal disease alone: 1 case.
- associated pleural parenchymal disease: 18 cases.

Table X

New Thoracic Imaging, Interstitial Syndromes, Pneumoconiose Early Detection—Pittsburgh 1988

ABESTOSIS (N = 30)	
FINAL DIAGNOSIS	
– PLEURAL DISEASE ALONE	11
– PARENCHYMAL DISEASE ALONE	1
– PLEURO–PARENCHYMAL DISEASE	18

Where pleural disease is concerned (Table XI), the inadequacies of standard radiography as compared with tomodensitometry are obvious since 50% of the cases showing pleural disease (asbetiosic plaques and benign pleuresy) are retrospectively invisible in standard radiography and evident in tomodensitometry. The same applies for the pleural calcifications easily discerned with tomodensitometry.

In the case of associated parenchymal interstitium disease tomodensitometry has a higher score than standard radiography since it reveals, in 5 cases, a disease of the pulmonary parenchyma associated to a pleural disease whereas the standard plates showed a pleural disease alone (certain in 3 cases, uncertain in 2). In these 5 cases, showing up a pulmonary interstitial syndrome allowed for the diagnosis of associated parenchymal disease which was confirmed by the other methods of diagnosis (bronchiolo-alveolar flush in particular) and by pulmonary biopsy in one case. Table XII.

Interstitial disease of the pulmonary parenchyma in asbestosis shows up in our cases mainly through homogeneous thickening of the pulmonary interstitium of the diffuse alveolar fibrosis type whereas nodular disease is more scarce and more tardy. The curvilineal sub pleural line described by YOSHIMURA was observed in 4 cases, 2 of which "honey combed" towards the lung.

The account of these results caused much comment and questions from the audience. All of which may be resumed as follows:

1. Nobody doubts the superiority of Tomodensitometry over standard radiography in early detection of Pneumiconioses. This kind of exploration, however, must be carried out correctly (centimetrical edge to edge cross-sections then orientated usage of millimetric cross-sections and of high resolution). This superiority is clearly illustrated in Asbestosis (early detection of pleural plaques and of parenchymal disease). Other authors on important series (GISSEROT) underline, as we do, this interest of Tomodensitometry. By using Tomodensitometry the pre-radiological phase of the Pneumoconioses is reduced.

Table XI

New Thoracic Imaging, Interstitial Syndromes, Pneumoconiose Early Detection—Pittsburgh 1988, Asbestos (N = 30) Comparison of Pleuro-Parenchymal Involvement on Chest Radiographs and HRCT Scans

	C.R.	H R C T
PLEURAL INVOLVEMENT	15	30
PARENCHYMAL INVOLVEMENT	10	15

Table XII

New Thoracic Imaging, Interstitial Syndromes, Pneumoconiose
Early Detection—Pittsburgh 1988
Asbestosis (N = 30)

PLEURO–PARENCHYMAL ABNORMALITIES ON H R C T SCANS.

– PLEURAL		
BEGNIN	PLAQUES	29
	EFFUSION	6
	MESOTHELIOME	2
– PARENCHYMAL		
– THICKENING INTERSTITIUM		19
– NODULAR		7
– MIXED (THICKENING AND NODULAR)		5
– CURVULIGNE SUB PLEURAL LINES		4
– HONEY COMBING		3

2. As well as early detection, Tomodensitometry allows for a better morphological and topographical appreciation of the lesions (for example: pseudo mass—lesions of focalized fibroses or "honey combing" in general sub pleural postero-inferior latero-vertebrals), a better study of the associated lesions and of the complications (emphysemia, bronchial dilatation, bronchial or pleural neoplasm, secondary infection, tuberculosis). This morphological and topographical precision of the lesions will surely guide the pulmonary biopsy when necessary whether it be carried out by surgery or by puncture under tomodensitometry as was the case in 2 bronchial peripheral neoplasms in our series.

3. Tomodensitometry presents two disadvantages inherent to Medical Imagery in general:
   - The histological non specificity of the lesions. Numerous interstitial syndromes of various etiologies resemble each other even if that of silicosis is more nodular than that of asbestosis which is more linear. The finding of such lesions must therefore be confronted with the other methods of diagnosis (bronchiolo-alveolar flush and pulmonary biopsy if necessary). At the limit of high definition it is impossible to distinguish between a micro-nodule and an intra-lobular vessel. Other arguments must therefore be taken into account (the number of "vessels" per surface unit of the parenchyma for example). Nevertheless, allow us to point out that if the tomodensitometrical lesions are not very specific, those observed with standard radiography are even less so, harder to interpret in the face of artefacts linked to superpositions and to the technical realization of the plates.
   - The difficulty of quantifying the parenchymal disease. Interesting work is being done in this field (BERNADAC—GRENIER) using computerized mathematical analysis.

In conclusion, in the light of the various works, the possibilities which Tomodensitometry offers for the study of Pneumoconioses are far superior to that of the standard plate which, nevertheless, remains very useful for monitoring these lesions for example. The I.L.O. classification will certainly have to be revised or completed in the light of Tomodensitometry. In this type of pathology, the place of this examination is yet to be defined for, in spite of the present diffusion of the appliances, tomodensitometric exploration is still more expensive and harder to get than a simple standard plate.

INCREMENTAL EXERCISE TESTING IN PLEUROPULMONARY DISEASE DUE TO INHALATION OF INORGANIC DUSTS: PHYSIOLOGIC DEAD SPACE AS THE MOST SENSITIVE INDICATOR

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INTRODUCTION

Evaluation of dyspnea, and of respiratory impairment and disability, is of great social and economic importance, let alone physiologic and clinical interest, in patients thought to have pulmonary and/or pleural fibrosis secondary to inhalation of inorganic dusts.[1-7] The relationship of abnormalities on exercise to those in standard pulmonary function tests (performed at rest) is controversial. Cotes[2] has recently concluded that "loss of exercise capacity cannot be predicted with acceptable accuracy from the 4 commonly used lung function indices (FVC, FEV_1, FEV_1/FVC, D_LCO_{SB}) alone or in combination."

We have correlated FVC and D_LCO_{SB} (henceforth further abbreviated as D_L) with a number of exercise variables (both invasive and non-invasive) in 43 patients undergoing maximal incremental exercise to evaluate likely pulmonary and/or pleural fibrosis due to inhalation of inorganic dusts (in 35 patients, the dust was asbestos). Our results indicate that an abnormal D_L predicts excessive dead space ventilation often present at rest, and conversely, that this abnormality of gas exchange is frequently present even when D_L is normal.

METHODS

Standard pulmonary function tests were performed according to the recommendations of the American Thoracic Society.[8,9] Predicted values for spirometry were modified[10] from an earlier publication of Morris[11] and for D_L CO_{SB} and TLC_{SB} were those separately established by this laboratory[12] for current smokers, ex-smokers and nonsmokers.

Incremental exercise testing was performed using a model 2000 Medical Graphics, Inc., breath-by-breath system which employs a pneumotachygraph to obtain expiratory flows and volumes, an infra-red CO_2 analyzer, and a zirconium fuel cell O_2 analyzer. Exercise was performed on a bicycle ergometer which increments 5 to 25 watts per minute. The patient sat quietly on the bicycle while adjusting to the nose clip, mouthpiece, ear oximeter (Hewlett-Packard model 47201 A), electrocardiographic leads and radial artery catheter. Measurements were then made sitting, during unloaded cycling, during incremental cycling and several times following exercise. Exercise was terminated when the patient was unable to continue (usually limited by dyspnea) or if there were untoward changes in the electrocardiogram, blood pressure or O_2 saturation.

A microprocessor collected flow, F_ECO_2, and F_EO_2 data and computed O_2 consumption and CO_2 production for each breath. A separate computer (TEKTRONIX 4052 A) stored, analyzed and displayed data. Primary measurements included tidal volume, respiratory frequency, inspired and expired O_2 and CO_2 concentrations and heart rate (HR). These allow immediate calculation of such parameters as minute ventilation ($\dot{V}E$), O_2 consumption ($\dot{V}O_2$), CO_2 production ($\dot{V}CO_2$), respiratory equivalent (R; $\dot{V}CO_2/\dot{V}O_2$), $\dot{V}E/\dot{V}CO_2$, $\dot{V}E/\dot{V}O_2$, O_2 pulse ($\dot{V}O_2$/HR) etc. Arterial blood was blood sampled every one to two minutes. Samples were stored in ice and analyzed immediately after the test on a Radiometer model ABL30. Entry of these results permits the system to calculate and print values for dead space ventilation (as a percentage of tidal volume, V_D/V_T) and alveolar-arterial differences for PO_2 (A-aDO_2) during all phases of the test.

Ventilatory response was evaluated as the slope of $\dot{V}E$ vs. $\dot{V}O_2$ before ventilatory anaerobic threshold is reached; excessive values are ≥ 30.[13] Limit values for other tests are: FVC $<80\%$ of predicted, FEV_1/FVC <0.70 up to age 59 years and <0.65 beyond age 59, D_L $<75\%$ of predicted, $V_D/V_T \geq 0.35$ at rest and ≥ 0.25 on exercise ($\dot{V}O_2$ 1.0L)[14] and A-a DO_2 35 Torr during exercise.[4]

RESULTS

Of the 43 patients tested, 35 were studied because of occupational exposure to asbestos; several of these had normal chest radiographs and one-third had only pleural thickening. Of the remaining 8 patients, 6 were occupationally exposed to hard metal (half had normal chest radiographs) and 2 to beryllium (both had abnormal radiographs). D_L was not available on 4 patients. Dyspnea was equivocal in 9 patients, present in 29 and absent in 5. Because of the small number of patients without dyspnea, correlation with physiologic variables was not possible. It was noted that the 5 patients who did not complain of dyspnea had normal D_L (vs. 14 of the 26 with dyspnea) and 4 of the 5 had normal ventilatory responses (vs. 18 of 27 with dyspnea).

Mean values of the most important pulmonary function tests (FVC, D_L) and exercise variables ($\dot{V}E$ at $\dot{V}O_2$ 1.0L, V_D/V_T at $\dot{V}O_2$1.0L) and of V_D/V_T at rest are shown in Table I.

Table I
Mean Values of Pulmonary Function and Exercise Tests

Variable	Mean	SD
FVC (% pred)	80.2	18.2
D_L (% pred)	80.7	24.9
$\dot{V}E$ 1.0L (L/min)	30.2	9.73
V_D/V_T Rest (x 100)	35.9	8.6
V_D/V_T 1.0L (x 100)	28.8	9.9

Prevalence of Abnormal Test Results (Table II)

Of the patients studied, 18 (of 43) had a reduced FVC (42%), 15 (of 39) a reduced D_L (38%), 10 (of 41) increased ventilatory responses (24%) and 8 (of 41) an elevated A-a DO_2 (20%). The highest prevalence of abnormality was for V_D/V_T at rest and/or exercise (measured at a $\dot{V}O_2$ of 1.0L): 31 of 43 patients (72%). Of these 31, 19 were abnormal under both conditions, 5 at exercise only and 7 at rest only (4 of these did not have exercise values or did not reach a $\dot{V}O_2$ of 1.0L). Hence, 24 of 39 patients (62%) showed abnormal V_D/V_T at exercise and 26 of 43 (60%) did so at rest.

Correlations with D_L (Table III)

Of the 39 patients with D_L, 15 had abnormal values for this test (as stated above):

D_L (percent predicted) showed a moderate correlation with FVC (r=0.315, P 0.05) (Table III). Comparison of abnormal results for the two tests is shown in Table IV. 15 patients had abnormal values for FVC; 8 were abnormal for both tests, 17 normal for both, 7 abnormal only for D_L and 7 abnormal only for FVC.

D_L (percent predicted) correlated with V_D/V_T at rest (r= −0.274, p <0.1) and more strongly on exercise (r= −0.554, p 0.0005) (Table III). Comparison of abnormal results for D_L and for V_D/V_T is shown in Table V. 27 patients had abnormal values for V_D/V_T; 13 were abnormal for both, 10 normal for both, 14 abnormal for V_D/V_T alone and 2 abnormal for D_L alone. Thus, of the 15 patients with abnormal D_L, 13 (87%) had abnormal V_D/V_T yet 14 of the 24 (58%) with normal D_L still had abnormal V_D/V_T.

Only 8 patients had abnormal A-a DO_2 (Table VI); 6 were abnormal for both tests, 22 normal for both, 2 abnormal for A-a DO_2 alone and 8 abnormal for D_L alone. Of the 8 patients with abnormal A-a DO_2, only 2 had a normal D_L.

Only 9 of the 39 patients had abnormal $\Delta \dot{V}E/\Delta \dot{V}O_2$ (Table VII); 5 of the 9 had abnormal D_L.

Correlations with FVC (Table III)

FVC (percent predicted) correlated with V_D/V_T both at rest (r= −0.359, p 0.02) and on exercise (r= −0.436, p <0.006).

Correlations with Exercise $\dot{V}_E$ (Table III)

Exercise $\dot{V}_E$ (at a $\dot{V}O_2$ of 1.0 L^2 showed a weak correlation

Table II
Frequencies of Abnormal Test Results in 43 Patients with Suspect Pleuropulmonary Disease Due to Inorganic Dusts

FVC	42%	(18/43)
(FVC	38%)	(15/39)
D_L	38%	(15/39)
$\dot{V}O_2$ peak < 75% pred	28%	(12/43)
Δ VE/ Δ VO_2	24%	(10/41)
A-a DO2	20%	(8/41)
Resp. Rate > 50/min		0
Resp. Rate > 40/min	21%	(9/43)
V_D/V_T:		
Rest and/or 1.0L	72%	(31/43)
Rest	60%	(26/43)
1.0L	62%	(24/39)

Table III
Pearson Correlation Coefficients for Pulmonary Function and Exercise Tests

	$\dot{V}E$	FVC	D_L	V_D/V_T Rest	V_D/V_T 1.0L
$\dot{V}E$ 1.0L	1.00000	-0.22962	-0.41311*	0.38629*	0.48455*
FVC	-0.22962	1.00000	0.31537*	-0.36191*	-0.44035*
D_L	-0.41311*	0.31537*	1.00000	-0.27351	-0.55392*
V_D/V_T Rest	0.38629*	-0.36191*	-0.27351	1.00000	0.66262*
V_D/V_T 1.0L	0.48455*	-0.44035*	-0.55392*	0.66262	1.00000

* $p \leq 0.05$

Table IV
FVC vs. D_LCO_{SB}

	Abnormal FVC (15)	Normal FVC (24)
Abnormal D_L (15)	8	7
Normal D_L (24)	7	17
No D_L (4)	3	1

with FVC (r= −0.230, p 0.15), a strong correlation with D_L (r= −0.413, p 0.009) and strong correlations with V_D/V_T both at rest (r= 0.386, p 0.0115) and even more so on exercise (r= 0.485, p 0.0021).

$\dot{V}O_2$ Max

Of the 43 patients, 31 (72%) were able to reach a peak $\dot{V}O_2$ ≥75% of predicted. The 12 who were not able were more likely to manifest other abnormalities, e.g.; 10 had abnormal V_D/V_T (vs. 20 of the 31 with normal $\dot{V}O_2$ max) and 8 had abnormal FVC (vs. 7 of the 31 with normal $\dot{V}O_2$ max). Of the 10 with decreased $\dot{V}O_2$ max who performed D_L, 6 had abnormal D_L (vs. 9 of the 29 with normal $\dot{V}O_2$ max). Nevertheless, 12 of the 18 patients with abnormal V_D/V_T both at rest and on exercise were able to achieve a $\dot{V}O_2$ max ≥75% of predicted.

Respiratory Pattern

No patient reached a respiratory rate > 50 min; 9 (21%) reached a rate between 41 and 50. Nine patients achieved a V_T/VC ratio ≥0.70; 6 of these 9 had normal FVC. The 2 patients whose V_T/VC exceeded 0.80 both had reduced FVC.

DISCUSSION AND CONCLUSIONS

Our goals were to assess (1) "invasive" variables requiring sampling of arterial blood and (2) the responses to incremental exercise both non-invasive ($\dot{V}E$, $\Delta \dot{V}E/\Delta \dot{V}O_2$, respira-

Table V
V_D/V_T vs. D_LCO_{SB}

	Abnormal V_D/V_T (31)			Normal V_D/V_T at rest and at $\dot{V}O_2$ = 1.0L (12)
	At rest and at $\dot{V}O_2$ = 1.0L (19)	At rest only* (7)	At $\dot{V}O_2$ = 1.0L only (5)	
Abnormal D_L (15)	10	1	2	2
Normal D_L (24)	8	3	3	10
No D_L (4)	1	3	0	0

* Includes inability to reach $\dot{V}O_2$ = 1.0L or no sample obtained.

Table VI
A-a DO2 vs. D_LCO_{SB}

	Abnormal A-a DO2 (8)	Normal A-a DO2 (33)
Abnormal D_L (14)	6	8
Normal D_L (24)	2	22
No D_L (3)	0	3

tory rate and tidal volume) and invasive (V_D/V_T, A-a DO_2) compared with standard pulmonary function tests (FVC, D_L). Our patients demonstrated the full spectrum of disease from radiographically inapparent to minimal (1/0 irregular opacities and/or pleural thickening) to advanced diffuse pulmonary fibrosis. Most complained of dyspnea.

V_D/V_T was the most sensitive indicator of abnormality, being increased in 31 of 43 patients (72%), many of whom had normal FVC and/or D_L. The most useful comparison was with D_L; 13 of the 15 patients with abnormal D_L had abnormal V_D/V_T. It may, therefore, be said that a decreased D_L predicts abnormal V_D/V_T and that measuring the latter is then not required to detect disease. However, more than half the patients (58% or 14 of 24) with normal D_L still had abnormal V_D/V_T.

FVC was as likely to be abnormal as D_L (each was decreased in 15 of 39 patients who had both tests, or 38%). Abnormality of one was not very likely to predict abnormality of the other; roughly half the patients with an abnormal FVC had a normal D_L and vice-versa.

A-a DO2 and ventilatory response during exercise were least likely to be abnormal (in 20% and 24%, respectively). Widening of the A-a DO2 was associated with an abnormal D_L. No patient demonstrated a respiratory rate >50/min.

Table VII
$\Delta\dot{V}E/\Delta\dot{V}O_2$ vs. D_L

	Abnormal $\dot{V}E/\dot{V}O_2$ (10)	Normal Δ VE/ Δ VO_2 (31)
Abnormal D_L (15)	5	10
Normal D_L (24)	4	20
No D_L (2)	1	1

About three-quarters of the patients reached a $\dot{V}O_2 \geq 75\%$ of predicted maximum, demonstrating their motivation to perform. Many patients with manifest abnormalities achieved this level of work, e.g., two-thirds (12 of 18) of those with abnormal V_D/V_T both at rest and on exercise.

Of the 31 patients with abnormal V_D/V_T at rest or exercise, this was manifest in the majority (26 patients or 84%) at rest. It may thus be inferred that exercise is not usually necessary to demonstrate this derangement of gas exchange.

$\dot{V}_E$ at an exercise level corresponding to a $\dot{V}O_2$ of 1.0L/min has been advocated as a useful non-invasive measurement which additionally does not require maximal effort.[2] It was strongly correlated with D_L and with V_D/V_T both at rest and even more so at (the same level) exercise. An important consideration is whether anaerobic threshold (AT) has been reached before this level of exercise, which would increase $\dot{V}_E$ non-linearly; almost all our patients had a normal AT, beyond a $\dot{V}O_2$ of 1.0L.

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ROLE OF EXERCISE TESTS IN THE FUNCTIONAL EVALUATION OF SILICOTIC PATIENTS

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INTRODUCTION

Evaluation of labor capacity is frequently requested for patients with pneumoconioses. Spirometry and chest X-rays usually utilized in the diagnosis, have not been regarded as good predictors of pulmonary disability; and have poor correlation with the respiratory symptoms.[3,8,9]

Among the methods utilized in the functional evaluation of pneumoconioses, the exercise tests have emerged as useful, for evaluating the cardiorespiratory abnormalities, not present at rest.[1,2]

Although the exercise tests have been frequently utilized in the differential diagnosis of dyspnea,[4,10,12,13] in occupational medicine, the studies are scattered and utilized diverse methodology, making difficult the comparison of the results.[6,7,11]

Objectives

In this study, our purpose was to establish the role of the cardiorespiratory, metabolic and gas exchange analysis during exercise, in evaluationg ceramic workers with the diagnosis of silicosis; and to correlate these findings with the degree of dyspnea, the radiological alterations and the pulmonary function tests at rest.

METHODS

Casuistic

We have studied forty three ceramic workers with the diagnosis of silicosis based on the occupational history of silica dust exposure and on the radiographic features. They were separated in three groups, based in the ILO Classification, 1980 (Table I).[5]

The characteristics of the patients, the silica dust and the smoking exposure were not significantly different when compared to the three groups. However, group III subjects, were older than the ones of Group I.

Protocol

The patients were first submitted to a clinical evaluation and thereafter tested for spirometry, flow-volume curves and arterial blood gases at rest.

Secondly, they went to an incremental exercise test on a cycloergometer to the maximum tolerance, for cardiovascular, ventilatory and metabolic evaluation (n = 40).

Finally, after 30 min. of resting, the patients were submitted to a submaximal test corresponding to 50% of the maximum tolerance, for the analysis of the cardiorespiratory and metabolic responses and the arterial blood gases.

Table I
Classification of the Silicotic Patients, According to the ILO Classification, 1980[5]

GROUP	OPACITIES/PROFUSION	n
I	Small Opac. (up to 3mm) 1/0 to 1/2	21
II	Small Opac. (up to 3mm) 2/1 to 3/3	13
III	Large opac. (A, B or C)	9

RESULTS AND COMMENTS

Dyspnea was the most frequent symptom, being reported by 26 (61%) of the patients, with similar distribution and intensity in the three groups (Figure 1). Cough, sputum production and bronchospasm, also had similar incidency among the patients.

The spirometry was altered in 14 subjects (33%), also with similar distribution in the groups I, II and III. There was no predominant pattern of respiratory impairment (obstructive or restrictive) and most patients had slight to moderate abnormalities (Figures 2 and 3).

In the analysis of flow-volume curves (n = 41), the $\dot{V}$max 25% was the only variable that distinguished Group III from the other groups, being altered in 52% of subjects in Group I, 42% in Group II and 88% in Group III (Table III).

In the incremental exercise tests (n = 40), the patients of Group III had lower $\dot{V}O_2$max compared to Group I and II ($p < 0.05$—Gr. I vs. Gr. III) (Table IV). The symptoms reported at the interruption of exercise were mostly dyspnea and leg pain, with similar distribution and intensity in the three groups. A value of $\dot{V}O_2$max <70% Pred., indicating some degree of functional limitation was found in 14 patients, however with different distribution in the three groups: 3 of them were from Group I (16%), 4 from Group II (31%) and 7 (88%) were from Group III ($p < 0.05$—Group I + III vs. Group III) (Figure 4). This indicates an association between the more severe X-ray alterations and the lower working tolerance. However there were subjects of Group I, with reduced exercise capacity and conversely, subjects of Group III with normal exercise capacity (Figure 4).

No correlations were found between the exercise capacity

Table II
Characteristics of the Silicotic Patients

$\bar{X}$ GR.	n	AGE (yrs)	Wt (kg)	Ht (cm)	Silica Dust Exposition (yrs)	%	Smoking Pack/years
I	21	39.3	72,8	169	18.2	53	16.0
II	13	42.4	73.9	170	21.1	61	18.5
III	9	51.1*	65.4	165	22.6	33	29.0

* $p < 0.05$ - Gr. III > Gr. I. Kruskal-Wallis analysis of variance, and Dunn contrast test.
%: percent of smokers in each group.

Table III
Flow-Volume Curve Variables in Silicotic Patients of the Three Groups

$\bar{X}$		$\dot{V}$ max		$\dot{V}$ max 50%		$\dot{V}$ max 25%	
GR.	n	l/seg	% Pred	l/seg	% Pred	l/seg*	% Pred*
I	21	7.26	88	3.79	67	1.81	65
II	12	8.09	95	4.29	75	1.83	64
III	8	5.51	71	2.47	46	0.99	33

* $p < 0.05$ - I > III, II > III (l/seg); I > III (% Prev.) Kruskal-Wallis analysis of variance, and Dunn contrast test.

Table IV

Maximal Exercise Test Variables, Obtained in the Patients of the Three Groups

GROUP	n	WORK LOAD* (watts)	$\dot{V}O_2max$ § (l/min)	% Pred §	FCmax bpm	% Pred
I	19	191	2.32	86.5	150	83
II	13	189	2.35	89.2	149	82
III	8	103	1.24	55.1	128	75

$p < 0.05$ - *Gr. I and II > III; § Gr. I > III. Kruskal-Wallis analysis of variance and Dunn contrast test.

of the patients and the clinical symptoms or the pulmonary function tests at rest.

The arterial blood gases at rest and during exercise were similar to the three groups; and the percentual frequency of hypoxemia and of decrease in PaO_2 <5 mmHg (rest-exercise) was not significantly different when compared to the groups I, II and III. As the pulmonary function tests, the analysis of blood gases at rest and during exercise did not correlate with the exercise tolerance and the radiological changes of the patients (Figure 5).

Summarizing, the evaluation of the silicotic patients during an exercise test, revealed a certain number of incorrect prediction of working capacity, based on the resting data.

We concluded that the functional analysis during exercise can complete or modify the clinical, radiological and pulmonary function test analysis, in evaluating the impairment of patients with pneumoconioses.

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TIME DOMAIN SPIROGRAM INDICES OF SILICA EXPOSED WORKERS

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ABSTRACT

Time domain spirogram indices had been shown to be sensitive indicators of small airway function. The aim of this study is to assess the small airway function of 110 silica-exposed workers using these indices.

The workers were subdivided into high, moderate and low exposure groups, based on their occupational history. Their spirograms were digitized electronically and conventional indices as well as time domain indices (MTT—mean transit time, COVTT—coefficient of variation of transit time and IOSTT—index of skewness of transit time) were derived.

With adjustment for age, height and smoking status the FEV_1 and FVC did not differ significantly among the groups whereas all the time domain indices showed significant differences. $FEF_{75\%}$ and $FEF_{75\text{-}85\%}$ were also significantly lower in the high exposure group although the difference in $FEF_{75\%}$ in the moderate and high exposure groups was not statistically significant.

Separate analysis were performed for smokers and non-smokers, while excluding all those with FEV_1/FVC ratio of less than 0.75. Similar trend of greater small airways obstruction in the higher exposure groups was also seen. The most significant differences were seen with time domain indices, $FEF_{75\text{-}85\%}$ and $FEF_{75\%}$.

This preliminary study supports the presence of small airway dysfunction among silica exposed workers. Furthermore, time domain spirogram indices appear to be more sensitive to small airway dysfunction.

INTRODUCTION

Airway resistance of the lungs can be partitioned into central and peripheral components. The peripheral component is composed of the resistance from airways of less than 2mm in internal diameter down to the gas exchange areas. This region is commonly termed as the small airways. Since small airways resistance contribute only 10–15% of total airway resistance, it is possible for a subject to have significant diffuse obstruction in the small airways while the total airway resistance are essentially normal.[1,2] In normal individuals, maximum expiratory flow at large lung volumes like the peak flow and the forced expiratory volume in one second (FEV_1), depend mainly on flow in the larger airways whereas maximum flow at small lung volumes reflect predominantly the function of small airways.[3,4,5]

Several spirometric indices especially flow rates at low lung volumes may reflect the status of small airways. These would include forced expiratory flow at 50% and 75% of forced vital capacity ($FEF_{50\%}$ and $FEF_{75\%}$), forced expiratory flow between 25 and 75%, 75 and 85% of forced vital capacity ($FEF_{25\text{-}75\%}$, $FEF_{75\text{-}85\%}$).[6-8] Time domain indices by using moments analysis of the volume time spirogram have also been shown to be sensitive indicators of small airways obstruction.[4,9-15]

The mean transit time (MTT) is an index of the average rate of emptying of the vital capacity. It is influenced by all parts of the spirogram. Mathematically, this is the first moment about the origin (see appendix 1). The coefficient of variation of transit times (CoVTT), represents the amount of variation between the initial and the terminal slower portion of the VC. It is derived from the second moment about the mean. The index of skewness of transit times (IoSTT), is a measure of the 'slow finish' at the terminal end of the expiration. This is derived from the third moment about the mean. Some workers analyzed moments about the origin rather than moments about the mean.[9-11,16] As an index of dispersion, these authors used the moment ratio (MR).

There had been few studies utilizing time domain indices to assess the small airways function of dust exposed workers. In this study we have applied the various spirometric indices as well as time domain indices on a group of granite quarry workers to evaluate their small airways function in relation to their dust exposure.

METHODS

Subjects

The volume-time spirograms of 132 currently employed granite quarry workers were selected. Each spirogram had

at least 3 satisfactory tracings. The tracing with the highest FVC was digitized using an electronic digitizer. The digitized data is stored into a micro-computer and volume-time as well as flow-volume curves are plotted on the computer screen for visual checking. Flow was calculated by least square regression using pairs of volume-time data in an interval of 0.05 seconds on either side of a given time point. This method of digitizing volume-time tracings had been shown to be an accurate and useful way of deriving volume-time and flow-volume indices from volume-time tracings.[17,18] Early termination increases the error in indices at low lung volumes.[6] Early truncation increases the variability of time domain indices.[16,19] Hence only spirograms that had a flow rate of less than 0.05 l/s in the last 0.5 s were selected for further analysis.[20] Of the 132 spirograms, only 110 satisfy the above criteria. The FEV_1, FVC, $FEF_{50\%}$, $FEF_{75\%}$, $FEF_{25-75\%}$, $FEF_{75-85\%}$, MTT, CoVTT, IoSTT and MR were calculated.

Detailed information including age, height measurement, smoking habits and a lifetime history of occupational exposure to dust were recorded for each worker. The 110 workers were divided into three dust exposure groups based on occupational history and environmental assessment of personal dust exposure by job categories. The average quartz content in the respirable dust was 28%. The low exposure group comprised those who were in the administrative section all of their working life. The moderate exposure group consists of transport and maintenance workers. The high exposure group were those who were past or current drillers and crusher workers for most years of their working life. Recent full-sized chest radiographs taken of each worker had been read independently by three experienced readers according to the International Labour Organization Standard Classification of Radiographs of Pneumoconiosis. None of the 110 workers had radiological films with profusion of small opacities greater than 1/0.

Statistics

The data was processed on an IBM 3033 mainframe computer using statistical procedures from Statistical Analysis System (SAS). Adjustment for group differences in age, height and smoking was done using analysis of co-variance and separate analysis for smokers and non-smokers.

RESULTS

Description of Study Population

There were 50 non-smokers and 60 smokers in the study population. Non-smokers were younger (41.0 compared with 47.6 years for smokers). The mean height were similar (1.66 m for non-smokers and 1.64 m for smokers). 15 (25%) of the smokers have a FEV_1/FVC ratio of less than 0.75 whereas all the non-smokers have a ratio of greater than 0.75.

The mean age, height, duration of exposure as well as the proportion of smokers in the three exposure groups are significantly different (Table I). The high exposure group had the longest duration of employment while the low exposure group had the shortest. The high exposure group can therefore be expected to have the greatest dose of dust and the low exposure group, the lowest dose. Age and duration of employment was highly correlated ($r=0.78$ for non-smokers, $r=0.67$ for smokers).

Lung Function

With adjustment for age, height and smoking status the FEV_1 and FVC did not differ significantly among the groups whereas all the time domain indices showed significant differences (Table II). $FEF_{75\%}$ and $FEF_{75-85\%}$ were also significantly lower in the high exposure group although the difference in $FEF_{75\%}$ between the moderate and high exposure groups was not statistically significant.

Table I
General Characteristics of Study Population

	Exposure			
	Low	Moderate	High	p value
Number	26	39	45	
Age (years)	36.4	44.1	48.7	0.0001
Height (m)	1.67	1.64	1.63	0.0232
Duration of exposure (years)	7.9	13.2	15.9	0.0215
Smokers (%)	27	62	64	< 0.05

Table II

Age, Height and Smoking Status Adjusted Lung Function Parameters of the Three Exposure Groups*

PARAMETER	EXPOSURE GROUPS			p VALUES		
	L	M	H	L vs M	L vs H	M vs H
FEV1 (l/s)	2.77 (0.08)	2.69 (0.06)	2.65 (0.06)	0.3868	0.2607	0.7078
FVC (l)	3.16 (0.09)	3.23 (0.07)	3.26 (0.07)	0.5359	0.4301	0.8042
$FEF_{25-75\%}$ (l/s)	3.40 (0.17)	3.09 (0.13)	2.86 (0.13)	0.1582	0.0188	0.1995
$FEF_{75-85\%}$ (l/s)	1.35 (0.08)	0.93 (0.06)	0.75 (0.06)	0.0001	0.0001	0.0283
$FEF_{50\%}$ (l/s)	3.98 (0.21)	3.86 (0.16)	3.61 (0.15)	0.6475	0.1722	0.2423
$FEF_{75\%}$ (l/s)	1.88 (0.10)	1.35 (0.08)	1.14 (0.07)	0.0001	0.0001	0.0572
MTT (s)	0.51 (0.03)	0.63 (0.02)	0.71 (0.02)	0.0019	0.0001	0.0202
CoVTT	1.00 (0.04)	1.22 (0.03)	1.45 (0.03)	0.0001	0.0001	0.0001
IoSTT	0.88 (0.26)	1.58 (0.20)	3.21 (0.19)	0.0367	0.0001	0.0001
MR	1.42 (0.03)	1.59 (0.02)	1.77 (0.02)	0.0001	0.0001	0.0001

* Adjusted for age, height and smoking status using analysis of covariance

( ) - standard error of adjusted means

Exposure groups :
L - Low exposure
M - Moderate expsoure
H - High exposure

Separate analysis were performed for smokers and non-smokers, while excluding all those with FEV_1/FVC ratio of less than 0.75. Except for FEV_1 and FVC in the low exposure group, all the other parameters showed that the smokers have greater degree of airway obstruction than the non-smokers (Tables III and IV). Similar trend of greater small airways obstruction in the higher exposure groups was also seen. The most significant differences were seen with time domain indices, $FEF_{75-85\%}$ and $FEF_{75\%}$.

Table III

Age and Height Adjusted Lung Function Parameters of the Three Exposure Groups in Non-Smokers

PARAMETER	EXPOSURE GROUPS			p VALUES		
	L	M	H	L vs M	L vs H	M vs H
FEV1 (l/s)	2.81 (0.10)	2.93 (0.10)	2.79 (0.10)	0.4182	0.8522	0.3224
FVC (l)	3.15 (0.12)	3.38 (0.12)	3.32 (0.13)	0.1818	0.3347	0.7421
$FEF_{25-75\%}$ (l/s)	3.72 (0.20)	3.57 (0.22)	3.25 (0.22)	0.6301	0.1500	0.3062
$FEF_{75-85\%}$ (l/s)	1.49 (0.11)	1.19 (0.12)	0.87 (0.12)	0.0753	0.0007	0.0547
$FEF_{50\%}$ (l/s)	4.25 (0.25)	4.34 (0.26)	4.10 (0.27)	0.8192	0.7026	0.5356
$FEF_{75\%}$ (l/s)	2.11 (0.13)	1.65 (0.14)	1.28 (0.14)	0.0225	0.0002	0.0733
MTT (s)	0.46 (0.03)	0.56 (0.04)	0.63 (0.03)	0.0519	0.0022	0.1720
CoVTT	0.99 (0.04)	1.16 (0.05)	1.46 (0.05)	0.0135	0.0001	0.0001
IoSTT	0.51 (0.26)	1.15 (0.27)	2.44 (0.27)	0.1009	0.0001	0.0014
MR	1.42 (0.03)	1.54 (0.02)	1.78 (0.02)	0.0164	0.0001	0.0001

* Adjusted for age, height and smoking status using analysis of covariance

( ) - standard error of adjusted means

Exposure groups :
L - Low exposure
M - Moderate expsoure
H - High exposure

Table IV

Age and Height Adjusted Lung Function Parameters of the Three Exposure Groups in Smokers

PARAMETER	EXPOSURE GROUPS			p VALUES		
	L	M	H	L vs M	L vs H	M vs H
FEV1 (l/s)	3.00 (0.12)	2.61 (0.07)	2.74 (0.08)	0.0076	0.0794	0.2213
FVC (l)	3.38 (0.13)	3.15 (0.08)	3.33 (0.08)	0.1318	0.7207	0.1311
$FEF_{25-75\%}$ (l/s)	3.47 (0.29)	3.04 (0.17)	2.96 (0.19)	0.2146	0.1563	0.7500
$FEF_{75-85\%}$ (l/s)	1.32 (0.13)	0.82 (0.08)	0.74 (0.08)	0.0017	0.0006	0.4923
$FEF_{50\%}$ (l/s)	4.22 (0.34)	3.91 (0.20)	3.64 (0.21)	0.4321	0.1658	0.3766
$FEF_{75\%}$ (l/s)	1.75 (0.18)	1.23 (0.10)	1.18 (0.11)	0.0161	0.0109	0.7266
MTT (s)	0.48 (0.05)	0.64 (0.03)	0.67 (0.03)	0.0074	0.0018	0.3912
CoVTT	1.04 (0.06)	1.29 (0.04)	1.51 (0.04)	0.0015	0.0001	0.0003
IoSTT	0.68 (0.46)	1.82 (0.27)	3.04 (0.29)	0.0381	0.0001	0.0041
MR	1.45 (0.05)	1.64 (0.03)	1.81 (0.03)	0.0024	0.0001	0.0002

* Adjusted for age, height and smoking status using analysis of covariance

( ) - standard error of adjusted means

Exposure groups :
L - Low exposure
M - Moderate expsoure
H - High exposure

DISCUSSION

A few studies have reported evidence suggestive of small airways obstruction in occupationally exposed groups. In coal worker's pneumoconiosis without evidence of large airway obstruction, frequency dependence of compliance was demonstrated suggestive of small airways obstruction.[21] Evidence of small airways abnormalities were also seen among asbestos exposed workers[22,23] as well as mineral dust exposure[24] and hard rock miners.[25] Among gold miners, those with silicosis had lower $FEF_{25-75\%}$ suggestive of small airways obstruction attributable to silica exposure.[26]

Our present study suggests that small airway obstruction is present among silica exposed workers in the absence of radiological evidence of silicosis. There was also evidence of a trend of increasing small airways obstruction in higher dust exposure group. Wiles and Faure[27] demonstrated an

exposure-effect relationship between dust exposure and $FEF_{25-75\%}$.

Smoking is known to affect both the larger and smaller airways.[28] As expected, smokers showed greater evidence of small airways obstruction even after excluding those with evidence of significant airway obstruction ($FEV_1/FVC < 0.75$). The amount of cigarettes smoked (number of sticks per day × number of years smoked) was not significantly different in the three groups. Hence the trend of small airways obstruction in smokers is suggestive of the effect of silica exposure.

Our study also suggests that time domain indices are more sensitive to small airways obstruction. These indices give greater emphasis to the end of the forced expiratory manouvre and are hence more sensitive to events in the small airways.

The clinical and prognostic significance of early airways obstruction is still far from clear. Further studies would be required to evaluate its predictive value in identifying workers who will progress on to clinical airflow obstruction.

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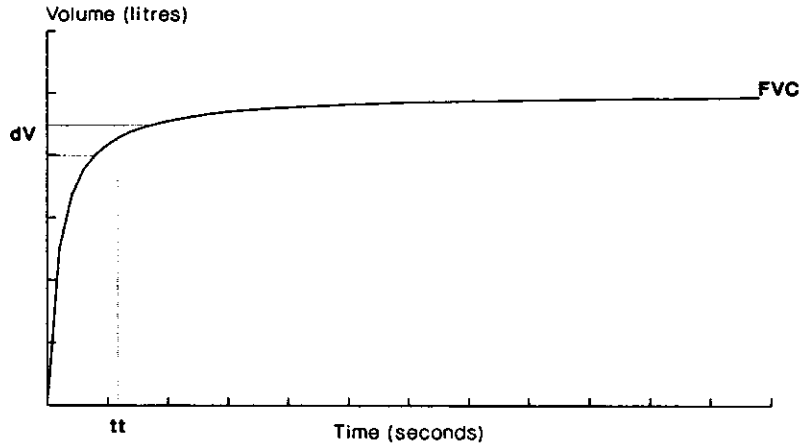
APPENDIX I



$$M_1 \text{ (MTT)} = \Sigma \frac{dV \times tt}{FVC}$$

$$M_2 = \Sigma \frac{(dV \times tt)^2}{FVC}$$

$$MR = M_1/M_2$$

$$SDTT = \left[\Sigma \frac{(tt - M_1)^2 \times dV}{FVC} \right]^{1/2}$$

$$SKEWTT = \left[\Sigma \frac{(tt - M_1)^3 \times dV}{FVC} \right]^{1/3}$$

$$CoVTT = SDTT/MTT$$

$$IoSTT = SKEWTT/(SDTT)^{3/2}$$

M_n : N^{th} moment about the origin

SDTT : Standard deviation of transit times

SKEWTT : Skewness of transit times

LUNG FUNCTION IN SILICA EXPOSED WORKERS

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INTRODUCTION

In long term silica-exposed workers, the attribution of changes in lung function to a direct effect of dust exposure or to the development of silicosis has been the subject of considerable debate in the literature and occupational lung conferences. The topic remains to this date a controversial issue, particularly in view of a recent pathological study which documented the presence at autopsy of fibrotic lesions and silicotic nodules in men who had normal pre-mortem chest radiographs.[7] Also, clinical studies[4-6] in silica exposed workers documented on lung lavage that a subclinical quartz-induced alveolitis may be present in silica-exposed workers with normal chest radiograph.

In that regard, we have documented that CT scan does not identify more patients with minimal parenchymal disease, although it images the disease more clearly in several cases with significantly higher CT scan score of disease. Also we have clearly demonstrated that CT scan identifies significantly more coalescence and/or large opacities in 33% of patients who were thought to have simple silicosis on the plain chest radiograph. To further investigate the clinical significance of these CT scan observations, we expanded our studied population to 94 long-term silica-exposed workers who were examined concomitantly by standard clinical, radiographic and pulmonary function tests.

SUBJECTS AND METHODS

Silica Exposed Workers

The 94 workers of this study had worked in either the granite or foundry industries or gold mines of Quebec for an average of 29 ± 3 years (range 14–42 years). Ninety percent were either current or former cigarette smokers and they had smoked on the average 21 ± 5 pack-years. Eighty of the 94 were granite workers, 10 were foundry workers and 4 were gold miners.

Pulmonary Function Tests

The lung volumes, pressure-volume curves, flow-volume curves and diffusing capacities were measured according to standard methods[1] as previously applied in our laboratory.[2]

Chest Radiograph

Standard high-kilovoltage posteroanterior, lateral, and oblique films were obtained at maximal inspiration. The radiograph was graded by three observers according to the International Labour Organization (ILO) 1980 classification.[8]

CT Scan of the Thorax

Eighty CT examinations were performed on a General Electric Model 8800 scanner in Sherbrooke (Canadian General Electric, Co., Montréal, Quebec) and 14 were done on a Picker 600 scanner (Picker, New York, N.Y.). For each patient, at least 10 slices of 1-cm thickness were obtained with wide windows, and 10 with narrow windows, for adequate assessment of pulmonary, chest wall, and pleural changes. CT scans were obtained within 48–72 hr of the plain chest film.

Subsets of Workers Based on Diagnostic Criteria and CT Scan

The 94 silica exposed workers were divided into 4 categories on the bases of evidence of silicosis and the findings of CT scan of the thorax. Group 1 consisted of 21 workers who did not meet the diagnostic criteria for silicosis.

Group 2 consisted of 28 workers with simple silicosis on chest radiograph and CT scan of the thorax.

Group 3 consisted of 18 workers with simple silicosis on chest radiograph but with coalescence and/or conglomeration on CT scan of the thorax.

Group 4 consisted of 27 workers with complicated silicosis on chest radiograph and CT scan of the thorax.

Statistical Analysis

All results are expressed as the mean ± standard error of measurement. The data were tested by the Student t-test or Mann-Whitney U test for differences between groups, by the Wilcoxon matched-pairs signed-rank test for differences between radiologic methods, and by Spearman's correlation procedure when appropriate.[9,10]

RESULTS

The lung volumes, compliance and change in vital capacity were within normal prediction in group 1. Subjects of group 2 had no significant change in lung volumes but lung compliance was significantly lower than that of group 1. In group 3, the silicotics with coalescence and/or large opacity on CT scan, we found significant reduction in vital capacity, lung compliance and an increased loss of vital capacity/year. The subjects of group 4 had lower total lung capacity, vital capacity, lung compliance and a significantly increased loss of vital capacity per year.

Diffusing capacity was normal in group 1 and decreased

gradually with increased disease severity. This was significant in groups 3 and 4. Exercise gas exchange parameters were also significantly reduced in groups 3 and 4. Group 2, patients with simple silicosis had gas exchange parameters between those without obvious disease, group 1, and patients with conglomerate disease, groups 3 and 4. These changes reached significance level for $\dot{V}_E/O_2$ ratio and exercise $\Delta(A\text{-}a)PO_2$.

In workers with radiographic silicosis, group 2, expiratory flow rates were lower than in group 1 and this reduction was more severe in groups 3 and 4, the workers with radiographic and/or CT scan coalescence/conglomeration. The lowest values were in group 4.

DISCUSSION

This study of lung function in long term silica exposed workers documents that the disease severity which is better defined radiographically by CT scan, is also reflected on lung function as restrictive changes. The disease severity also appears to be associated with excessive airflow limitation.

These data document that early coalescence/conglomeration in silicosis as seen often only on CT scan, is associated with worsened lung functions, a finding which strengthens our prior recommendation for the CT scan exam in radiographic simple silicosis.[3] These data also support the concept of a relationship of disease severity, loss of lung function and airflow limitation in silicosis.

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THE VALIDITY OF RADIOLOGICAL AND HISTOLOGICAL FINDINGS IN FORMER ASBESTOS WORKERS WITH LUNG CANCER

Die Validität der Röntgenologie und Histologie bei ehemals asbeststaub-gefährdeten Beschäftigten mit Lungenkrebs

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Einleitung und Fragestellung:

Der Nachweis der fibrogenen Asbesteinwirkung als Asbestose der Lunge oder der Pleura ist seit 1943 bzw. 1988 die entscheidende Voraussetzung für die Anerkennung auch der krebserzeugenden Wirkung von Asbest [11,7]. Demnach müssen im Röntgen-Toraxbild eine Strukturvermehrung des Parenchyms von ≥1/1 und/oder bestimmte ausgeprägte Veränderungen an der Pleura (≥2a) nach der ILO-Klassifikation [1,2,7,12] und/oder im histologischen Präparat des Lungengewebes eine Asbestose bzw. Minimalasbestose [12] für die Anerkennung einer Berufskrankheit in der Bundesrepublik Deutschland vorliegen. Wegen der erst kürzlich vorgenommenen Erweiterung des Begriffes "Asbestose" wurde in der Vergangenheit dem Pleura-Befund weder im Röntgenbild noch im histologischen Präparatügen gend Bedeutung beigemessen. Unter dieser Einschr nkung wurden Dignität und Validität der diagnostischen Verfahren bei Lungenkrebspatienten nach beruflicher Asbeststaub-Gefährdung untersucht.

Darüber hinaus stellt sich die Frage, insieweit die durch Asbest verursachte Fibrose weiterhin als pathogenetische Bedingung für den Lungenkrebs gelten kann?

Krankengut und Methodik

Es wurden 122 Patienten mit Lungenkrebs nach einer zurückliegenden, jeweils mehrjährigen bekannten Astbestfaserstaub-Gefährdung am Arbeitsplatz untersucht. Daz konnten u.a. das Alter bei Eintritt in die Gefährdung, die Expositionsdauer, nach grober Schätzung die kumulative Staubdosis sowie das Alter bei Diagnose bzw. Tod bestimmt werden. Dabei erfolgte die Unterscheidung nach Patienten *mit* und *ohne* Begleitasbestose sowie danach, ob sie in der Produktion oder im anwendenden Handwerk besch ftigt waren. Bei 76 Personen dieser Gruppe (62,3%) lag sowohl ein auswertbares Torax-Röntgenbild wie auch ein histopathologischer Befund vor. Eine Strukturver-mehrung von ≥1/1 im Röntgenbild [1,2] und der Nachweis einer histologischen Astbestose bzw. Minimalasbestose wurden als positiver Befund gewertet. Bei der Bestimmung der Validitätmaße der Sensitivität und Spezifität wurde einmal die Röntgenologie und zum anderen die Histologie als abhängige Variable verwendet.

Ergebnisse

1. Krankengut

   Tabelle I zeigt die verschiedenen Altersangaben. Auffallend dabei ist die Verschiebung von ca. 10 Jahren nach links bei den Personen *ohne* Begleitasbestose, die vorwiegend als Handwerker Asbeststaub ausgesetzt waren.

   In Tabelle II sind die "Asbestose-Parameter" aufgezeigt. Bei weitgehend gleicher Gefährdungsdauer von 20 Jahren und gleichlanger Latenzzeit von etwa 26 Jahren findet sich der Hauptunterschied in der kumulativen Dosis. Die Personen, die *keine* Begleitasbestose entwickelt hatten, weisen im Median 70 Faser-jahre (F . $10^6/m^3$. Jahre) weniger auf als die Patienten *mit* Begleitasbestose.

   Abb. 1 veranschaulicht in Teil A), daß selbst bei einer Dosis von unter 20 bzw. 50 Faserjahren noch histologisch erkennbare Fibrosen—hier meist Minimalasbestosen—auftreten. Im Teil B) erfolgt eine Unterscheidung nach den besonders gefährdenden Tätigkeiten. Unter den Anwendern ist nur in der Gruppe der Isolierer eine Fibrose gefunden worden.

2. Validitätsmße

   Röntgenbefunde des Torax

   In Abbildung 2 ist die Bewertung des Röntgenbildes der histopathologischen Diagnose gegenübergestellt. Das Verhältnis von negativen zu fraglichen, bis hin zu eindeutig positiven Befunden korreliert demnach gut. Unter den Lungenkrebspatienten mit einer histologisch eindeutigen Asbestose weisen zu Lebzeiten im Röntgenbild 40% (6:15) keinen positiven Beund auf. Unter den Patienten mit Minimalasbestose zeigen weniger als 1/4 (3:13) eine röntgenologisch eindeutige Asbestose.

   Histo-pathologische Diagnose

   Die histo-pathologischen Befundberichte aus Autopsie, Operation oder Endoskopie wurden in 30 verschiedenen Prosekturen erstellt. Mitunter ergaben sich divergierende Aussagen zum Vorliegen oder Fehlen einer Pneumokoniose, wenn zwei Posekturen zum gleichen Erkrankungsfall gehört wurden. Bei 44 der 76 hier besonders untersuchten Lungenkrebspatienten (58%) fand

Tabelle I

Altersangaben ab Eintritt in die Asbestfaserstaub-Gefährdung am Arbeitsplatz für 78 Lungenkrebspatienten, den Zeitpunkt der Diagnose Lungenkrebs sowie des Todes an Lungenkrebs in Abhängigkeit vom histologischen Nachweis einer Lungenasbestose. Entsprechende Angaben für 121 Lungenkrebspatienten in Abhängigkeit von den wichtigsten Tätigkeitsbereichen in der industriellen Herstellung und handwerklichen Anwendung von asbestprodukten.

LUNGENKREBS NACH ASBESTFASERSTAUB-GEFÄHRDUNG AM ARBEITSPLATZ: ALTERSANGABEN

	n	Median	Min. - Max.	n	Median	Min. - Max.	Median Diff.
Histologische Diagnose:	ASBESTOSE ODER MINIMAL-ASBESTOSE			KEINE ASBESTOSE			
Alter [Jahre] bei							
- Eintritt in die Gefährdung	28	32,0	14,0 - 53,0	50	23,0	14,0 - 52,0	+ 9,0
- Diagnose LUNGENKREBS	28	64,5	37,0 - 75,0	50	55,0	34,0 - 78,0	+ 9,5
- Tod (Stichtag)	28	66,0	38,0 - 76,0	50	56,0	36,0 - 79,0	+10,0
Tätigkeitsbereiche:	HERSTELLUNG VON ASBESTPRODUKTEN			ANWENDUNG VON ASBESTPRODUKTEN			
Alter [Jahre] bei							
- Eintritt in die Gefährdung	58	39,0	14,0 - 55,0	63	22,0	14,0 - 50,0	+17,0
- Diagnose LUNGENKREBS	58	64,0	34,0 - 80,0	64	54,5	36,0 - 78,0	+ 9,5
- Tod (Stichtag)	58	65,5	36,0 - 81,0	64	55,5	37,0 - 79,0	+10,0

zur Absicherung der histologischen Diagnose das lichtmikroskopische Zählergebnis von sogenannten "Asbestk rperchen" nach Lungengewebsveraschung Verwendung.

Validitätsmße

In Tabelle III sind die Validitätsmße für die geprüften diagnostischen Methoden gegenü bergestellt. Unter A wurde der Röntgenbefund (R) als Variable und die Histologie (H) als gesichertes diagnostisches Verfahren eingesetzt.

Im Röntgenbild beträgt die Rate der falsch-negativen Diagnosen 57%, während die Rate der falsch-positiven lediglich 2% ausmacht. Im Röntgenbild werden jedoch nur 43%, d.h. nur fast die Hälfte der Patienten als eindeutige Asbestose-Kranke erkannt.

Unter B gilt die Histologie als abhängige Methode. Dabei zeigt sich eine hohe diagnostische Sensitivität. Die Rate der falsch—positiven Diagnosen "Asbestose" liegt im Vergleich zum Röntgenbefund mit 25% jedoch revalit hoch. Die Rate der falsch-negativen Diagnosen beträgt knapp 8%.

Diskussion und Schlußfolgerungen

Als 1925 der Gesetzgeber das Recht für Arbeitsunfälle und Berufskrankheiten geschaffen hat, sollten den Arbeitnehmern, die einen beruflich verursachten Gesundheitsschaden erlitten hatten, als Ersatz für die verminderte Arbeitskraft eine Rente als Lohnersatz gezahlt werden. Mit diesem sozialen Gedanken sollte die moralische Verpflichtung des Arbeitgebers und der Gesellschaft umgesetzt werden, für beruflich verursachte Schäden aufzukommen und den Arbeiter und seine Familie vor wirtschaftlicher Not zu bewahren und dieses—wegen der Lohnersatzfunktion—möglichst zu seinen Lebzeiten.

Vor diesem Hintergrund und der Tatsache, daß die Überlebenszeit der Lungenskrebspatienten im Median 6 Monate beträgt [16] ist bei strenger Auslegung der Gesetze

Tabelle II

Kenngrößen der Asbestfaserstaub-Gefährdung am Albeitsplatz für 78 Lungenkrebspatienten nach Unterteilung in Gruppen mit oder ohne histologisch nachgewiesene Lungenasbestose einschießlich Minimalasbestose.

KENNGRÖSSEN DER ASBESTFASERSTAUB-GEFÄHRDUNG AM ARBEITSPLATZ FÜR LUNGENKREBSPATIENTEN MIT HISTOLOGISCHEN DIAGNOSEN (MEDIANWERTE)

Dosisäquivalente	Mit Asbestose und Minimal-Asbestose (n = 28)	Ohne Asbestose (n = 50)	Diff.
Kumulative Dosis [10^6 F/m^3 · Jahre]:	82,0	11,2	+ 70,8
Alter bei Eintritt in die Gefährdung [J.]:	32	23	+ 9
Gefährdungsdauer [J.]:	19,2	20,9	- 1,7
Latenzzeit (Tod bzw. Stichtag) [J.]:	27,2	26,8	+ 0,4

nicht gewollt, bis zum Tod des Erkrankten zu warten, um erst an der Leichenlunge festzustellen, ob der Beschäftgigte zu Lebzeiten eine Berufskrankheit erlitten hatte.

Das bedeutet, daß sich die medizinische Untersuchung zur Frage, ob der Asbeststaub eine Fibrose verursacht hat, auf das Röntgenbild stützen muß. Invasive Eingriffe sind im Unfallrecht nicht duldungspflichtig.

Die Untersuchung der 122 Patienten mit Lungenkrebs nach einer erwiesenen, teilweise relativ geringen Asbeststaubgefährdung hat jedoch gezeigt, daß eine Begleitfibrose nur dann auftritt, wenn die kumulative Dosis einen bestimmten Schwellenwert, der nach BERRY und FINKELSTEIN zwischen 35 und 50 Faserjahren liegt [6], überschritten hat. Für die karzinogene Wirkung von Asbestfasern gibt es aber keinen Schwellenwert. Das läßt die Schlußfolgerung zu, daß die Fibrose pathogenetisch keine Bedingung für die Entstehung eines Tumors der Lunge darstellt, wie es am Beispiel des Mesothelioms nach Asbestgefährdung bekannt ist [4].

Wie die Validitätsmaße in Tabelle III und die Abbildung 1 zeigen, kann auch durch die Einführung der Begriffe "Minimalasbestose" oder "Pleura-Asbestose" diese Schlußfolgerung nicht verdrängt weden. Darüber hinaus gibt es weder in der Bundesrepublik noch international eine einheitliche N'omenklatur zur Grenzziehung, was eben noch eine Asbestose ist und wann eben *keine* Asbestose—trotz beruflicher Asbestgefährdung— mehr vorliegt. Die nachfolgende Übersicht zeigt, in welchen Punkten eine einheitliche Normierung der Nomenklatur erforderlich erscheint:

VORSCHLÄGE ZUR DEFINITION UND DIAGNOSTIK DER "ASBESTOSE"

1. *Röntgenologische Diagnostik*
   - —Lungenasbestose (Streuung $\geq 1/0$) und/oder
   - —Pleuraasbestose als diffuse Verdickung und/oder hyaline oder verkalkte Pleuraplaques.
2. *Histologisch-pathologische Diagnostik*
   - —Lungenasbestose nach Febrosegrad[a)] und/oder
   - —Pleuraasbestose als dissufe Verdickung und/oder hyaline oder verkalkte Pleuraplaques.
3. *Faserstaubanalytische Diagnostik*
   - —Anzahl der Asbestkörperchen[a)] und/oder
   - —Anzahl der Asbestfasern[a)].

[a)] Konventionen nach Prüfung der methodischen Zuverlässigkeitskriterien erforderlich.

Darüber hinaus gibt es keinen erkennbaren wissenschaftlich begründbaren Ansatz, wie ein Lungenkrebs nach beruflicher Asbeststaub-Gefährdung *mit* oder *ohne* Begleitasbestose als asbestbedingt abgegrenzt werden kann. Demnach muß eine Konvention erarbeitet werden, unter welchen Randbedin-

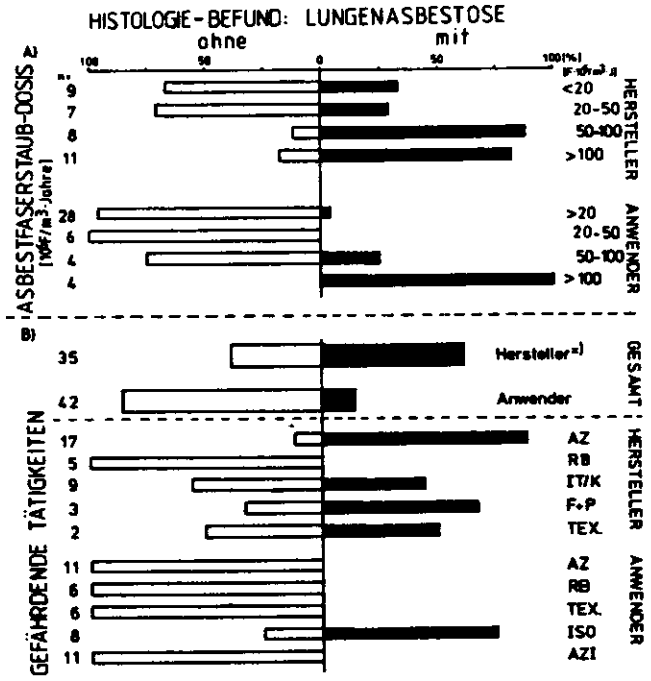

Abb. 1. Histologische Diagnose der Lungenasbestose (einschließlich Minimalasbestose) bei 77 Lungenkrebspatienten in Abhängigkeit von der über das Arbeitsleben kumuliert abgeschätzten Asbestfaserstaub-Dosis in 10^6 Asbestfasern einer Länge über 5 µm prom^3 Atemluft • Jahre (= Faserjahre), Teil A) bzw. B) unterteilt nach den wichtisgsten industriellen Herstellungs- und handwerklichen Anwendungsbereichen von Asbestprodukten. Abk. der Tätigkeitsbereiche:

AZ = Asbestzement, F + P = Filter + Pappen, RB = Reibbeläge, IT/K = Gummi-Asbest u. Kunst-stoffe, Tex = Textilien, ISO = Isolierer, AZI = Asbest zum Isolieren

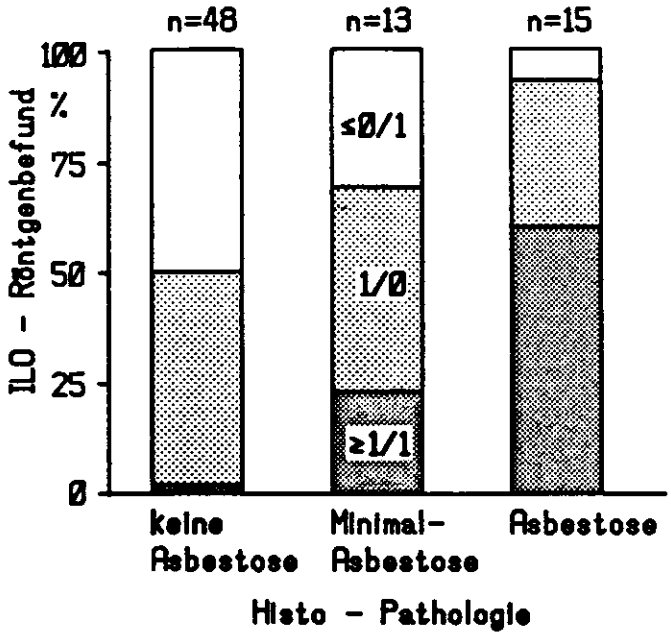

Abb. 2. Röntgenbefunde des Thorax im Hinblick auf eine Lungenasbestose in Abhängigkeit vom histopathologischen Befund bei 76 Patienten mit Lungenkrebs nach Asbestfaserstaub-Gefährdung am Arbeitsplatz.

Tabelle III

Vorschläge zur Definition und Diagnostik der Asbestose von Lunge und Pleura, einschließlich der Minimal-Asbestose und deren Faserstaub-analytischen Äquivalenten

Lungenkrebs nach Asbestfaserstaub-Gefährdung am Arbeitsplatz: Validitätsmaße der röntgenolgischen (R) und histologischen (H) Diagnostik der Lungenasbestose[1)]

	A) R : H		B) H : R	
	n	%	n	%
Sensitivitat	12 : 28	42,9	12 : 13	92,3
Rate der Falsch-Negativen	16 : 28	57,1	1 : 13	7,7
Spezifität	47 : 48	97,9	47 : 63	74,6
Rate der Falsch-Positiven	1 : 48	2,1	16 : 63	25,4
Prädiktiver Wert des				
- positiven Testes	12 : 13	92,3	12 : 28	42,9
- negativen Testes	47 : 63	74,6	47 : 48	97,9

[1)] Positive Befunde:
- Histologie: Asbestose oder Minimal-Asbestose
- Röntgenstruktur: ≥ 1/1 nach der ILO-Staublungen-klassifikation

gungen—sei es die Dosis, sei es die Dauer der Gefährdung—ein derartiger Lungenkrebs als beruflich verursacht anerkannt werden soll.

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MODERN WORK PROTECTION WITH THE SHOTCRETE CONSTRUCTION METHOD UNDER OVERPRESSURE

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The shotcreting method currently accounts for 90% of all urban traffic tunnels in the Federal Republic of Germany erected in the mining method of construction. Pressurized shotcreting has gained considerable importance in inner-urban tunnel construction during the past years. Examples in our country are encountered principally in the construction of the Munich subway system.

Driving underground cavities is accomplished under difficult working conditions and involves great health and accident hazards (Figure 1). The causes being:

- High dust development in shotcreting, rock excavating and conveying operations,
- poor air and visibility conditions,
- unfavourable climatic conditions,
- narrow, largely closed spaces,
- long handling distances for excavated and construction materials in long-extended, cramped spaces,
- frequently unforeseeable irregularities of the rock,
- piecework as well as schedule and cost pressure,
- parallelism of various operations performed in most closely restricted space.

The same health and accident hazards also apply for the workers engaged in shotcreting under overpressure.

The Compressed Air Ordinance stipulates that working chambers must be kept free from odours, as well as harmful gases, vapours and dusts (Figure 2).

Working methods involving intensive dust development, such as e.g. tunnelling with road headers without dust exhaust systems, are prohibited for work in compressed air just like the employment of internal combustion engines. Adherence to the maximum workplace concentration and technical standard concentration values for harmful substances in the breathing air must be assured. This can only be accomplished by means of constant control measurements of the inhaled air.

The technological problems had been solved. Concerning problems of labour medicine, studies were made to provide information on whether harmful mineral dust under overpressure constitutes a greater health hazard than atmospheric pressure.

The Medical Institute for Environmental Hygiene at the Düsseldorf University (Prof. Schlipköter) was thereupon commissioned by TBG to conduct appropriate animal experiments. In these preliminary studies it was found that the inhalation of dust containing quartz at an overpressure of 1.5 bar for a period of 6 months leads to increased typical quartz-induced lesions of mediastinal lymph nodes.

Further on it could be observed in the test of pulmonary function that for compressed air workers the flow-volume curve decreases significantly with increasing dust concentration:

> The test results indicate that with the measured high dust concentrations late damages to the respiratory tracts are possible.

More results on this deterioration of the pulmonary function tested after 1 working day and after 2 years will be published shortly in British JOURNAL OF OCCUPATIONAL HEALTH by Prof. Dr. Kessel, collaborator of Prof. Fruhmann, Munich University.

In view of these alarming findings, the following three institutions had been commissioned to perform further-going studies on primates under conditions similar to those prevailing at construction sites parallel to human medicine tests of compressed air workers at Munich subway construction sites:

- Med. Institute for Environmental Hygiene at the Düsseldorf University (Prof. Schlipköter)
- Institute for Surgical Research at the Munich University (Prof. Brendel)
- Institute and O.P.D. for Occupational Medicine of the Munich University (Prof. Fruhmann).

Interim results of these medical tests will be presented subsequently by Dr. Rosenbruch, Düsseldorf University and Dr. Krombach, Munich University. The Studiengesellschaft für unterirdische Verkehrsanlagen, STUVA, Köln, has assumed the technical management of the test programme and the medicine tests of compressed air workers were carried out by Munich University, Prof. Fruhmann.

Maximum workplace concentration values constitute a basis for assessing the questionableness or harmlessness of con-

No.	Work sector	Number of accidents	severe	fatal
1	Thrust-boring equipment	39	21	—
2+3	Tunnelling machines	17	6	1
4+5	Excavation work	8	3	—
6	Drilling and blasting	20	10	1
7	Falling stone, collapsing material	57	25	1
8	Sheeting, stabilization	27	13	—
9	Shotcreting work	76	10	—
10	Finishing (concrete + formwork)	32	13	—
11	Lining segments	11	6	—
12	Loading, mucking	16	8	—
13	(Underground) tracklaying	4	1	—
14	Materials handling	51	24	1
15	Welding + electr. work	11	3	—
16	Fitting	22	8	—
17	Toxic gases + vapours	7	5	—
18+19	Shaft construction + miscellaneous	31	14	1
	Total	425	173	5
	≙	(100 %)	(41 %)	(1.5%)

Figure 1. Accident analysis—tunneling, 2 years comparison.

centrations of noncarcinogenic working media appearing in the air at the workplace in the form of gas, vapour or suspended matter. Maximum workplace concentration values are scientifically founded, but apply only to pure substances. Since pollutant mixtures are the rule at the workplace, an orientation aid will be needed for the safety measures to be taken in modern work protection. This requires a pragmatic and generally applicable valuation concept. The Committee for Harmful Substances established by the Minister of Labour and Social Order in the Federal Republic of Germany has been engaged for some time in the valuation of pollutant mixtures in the air at the workplace with significant cooperation of the industrial insurance societies.

Re § 4 General requirements

1. Keep working chambers clean and free from odours as well as harmful gases, vapours and dusts

2. Ventilation

Supply 0.5 m^3/minute of fresh air per worker into the working chambers

Figure 2. Compressed air ordinance.

The valuation index of a substance mixture is the totalized value of pollutant indices J_i with the individual J_i being the quotient resulting from the concentration C_i established for the individual pollutant in the air at the workplace and the associated maximum workplace concentration (here MAK) value (Figure 3).

$$I = \frac{C_1}{MAK_1} + \frac{C_2}{MAK_2} + \ldots \frac{C_n}{MAK_n}$$

The valuation process is limited to those components of a substance mixture, for which parallel biological action can be supposed or not excluded with appropriate concentration in the breathing air. Since in compressed air work usually a lower air exchange and thus also a lower pollutant dilution occur than in tunnelling work under atmospheric pressure, particularly stringent requirements must be imposed on the quality of the breathing air. This is true all the more for pressurized shotcreting. Shotcrete dust normally must be classified under the category of siliciferous fine dust (Figure 4).

Therefore shotcrete dust is hazardous to health under two aspects:

- The dust may contain fine mineral dusts containing in some cases considerable amounts of quartz, which are added with the sand, the accelerating agents and the filler, and

$$I = \frac{C_1}{MAK_1} + \frac{C_2}{MAK_2} + \ldots \frac{C_n}{MAK_n}$$

$$= \sum_{i=1}^{n} \frac{C_i}{MAK_i} = \sum_{i=1} I_i$$

I ... Evaluation index

C... Average concentration

MAK .. Maximum workplace concentration

I ... Totalized value

I = 1 Limiting value for substance mixture

Figure 3. Evaluation of substance mixtures in the air at the workplace.

- due to their high alkalinity with a pH-value around 13, all accelerating agents must be regarded as caustic substances (Figure 5).

Additional dust sources, such as excavation and transportation e.g. contribute correspondingly to the silicon content of the total amount of fine dust.

The research project on shotcreting under overpressure is intended to clarify whether the current pollutant limits provide adequate health protection also for work under overpressure or whether more stringent requirements are necessary for the quality of the breathing air. We must make every effort to counter in time a silicosis hazard such as former generations experienced in mining, the consequences of which are still felt today.

As a rule following technical dust-combatting measures may contribute to the desired result (Figure 6).

1. Use of a liquid setting accelerator.
2. In case of powdered accelerators, selection of the one with the lowest possible respirable fine content and the lowest possible amount of quartz in the fine content. Accelerators without quartz are to be preferred.
3. Selection of sand without quartz, wherever possible, with a low respirable fine portion.
4. Fillers without quartz.
5. Addition and portioning of powdered accelerators in a closed system.
6. Addition of an adhesive to reduce dust.
7. For the shotcreting equipment:

Quartz content (% by weight)	Max. workplace concentration (mg/m^3)	Reference concentration
$Q < 1$	6.0	General dust limit (fine dust limit)
$1 \leq Q \leq 3.75$	4.0	Fine dust containing quartz
$Q > 3.75$	0.15	Fine quartz dust

Figure 4. Maximum workplace concentration limits for inert and siliciferous fine dust.

- selection of a low-dust shotcrete method
- lowest possible delivery lengths
- selection of the proper jet type, regular machine maintenance
- selection of a favourable hose diameter
- prewetting when adding adhesive
- proper inherent moisture of the design mix.

At some workplaces, such as e.g. the spray jet, technical dust protection measures alone will not be made available and also used.

The development of a dust protection helmet which combines protection of respiration, head, eye and face and also hearing was the result of a research project undertaken by the Tiefbau-Berufsgenosen-schaft.

Pressurized shotcreting is feasible only in combination with modern work protection.

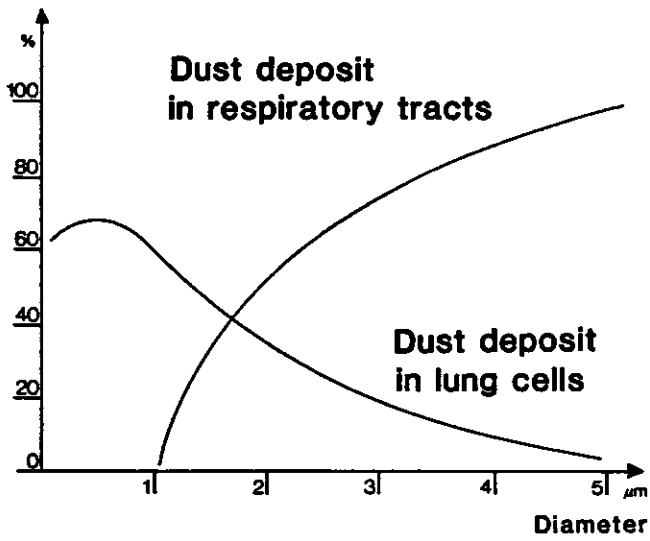

Figure 5. Schematic representation of dust deposit in the lung and in the respiratory tracts (acc. Winkler).

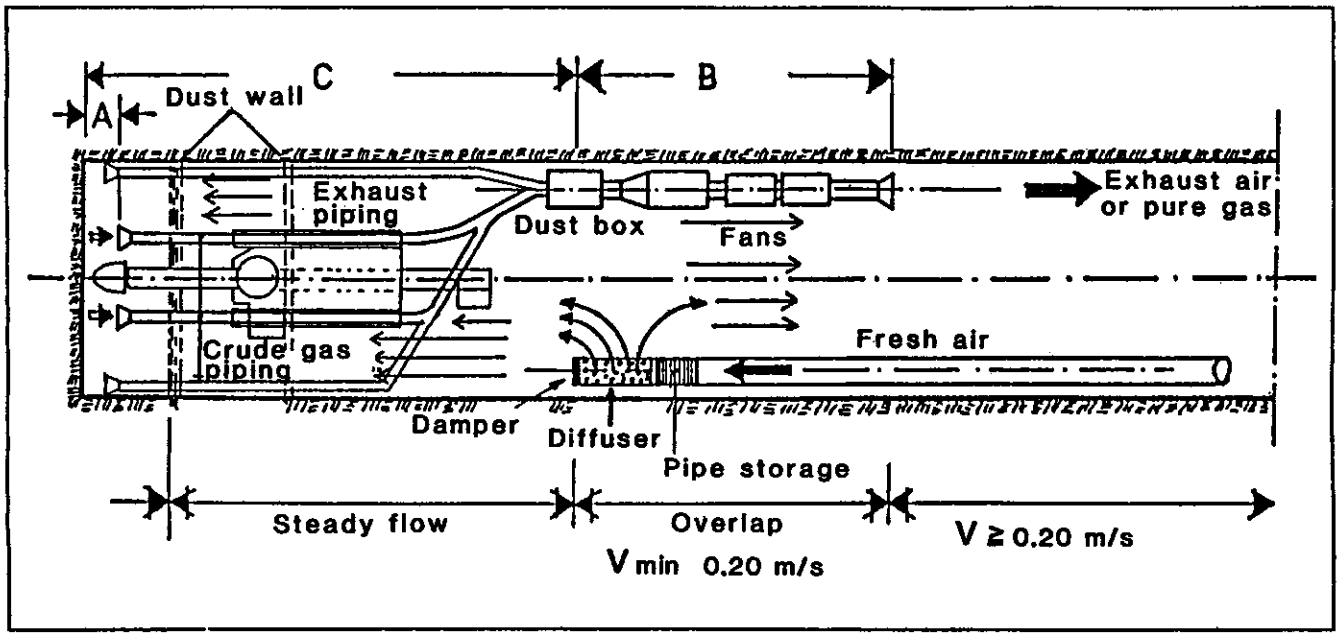

Figure 6. Principle of dust removal from a road header.

MORPHOLOGY AND MORPHOMETRY OF THE LUNG IN CYNOMOLGUS MONKEYS AFTER 2 YEARS INHALATION OF QUARTZ UNDER NORMAL AND EXCESS PRESSURE (*)

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INTRODUCTION

Modern tunnelling often includes working under excess pressure to protect buildings and the environment. Tunnel workers are exposed to different kinds of dust, arising from the underground rock or from material used for mixing the concrete. The dust exposure in tunnelling depends on the working station and the total dust concentration varies about 10 mg/m^3.[5]

In a multidisciplinary research project, the effects of "Shotcrete Tunnelling in Compressed Air" are investigated. This method is used more and more in tunnelling. Both, clinical investigations in tunnel workers and experimental studies in animals are conducted. The main inhalation experiment is carried out in monkeys with quartz dust and compressed air.[6]

This paper deals with morphological results of the experiment, especially regarding macromorphology and histopathology of the respiratory tract, preliminary morphometrical findings and some biochemical data of the lung collagen content.

MATERIAL AND METHODS

Final morphological and morphometrical evaluation as well as hydroxyproline determination was carried out on 21 cynomolgus monkeys (M. fascicularis) separated in 4 groups and kept for 26 months, 5 days per week and 8 hours per day under the following conditions:

Group I	(n=5)	normal atmospheric pressure (1.0 bar), without dust
Group II	(n=7)	quartz dust DQ-12 (5mg/m^3) and normal pressure (1.0 bar)
Group III	(n=4)	quartz dust DQ-12 (5mg/m^3) with 2.5 bar absolute pressure and
Group IV	(n=5)	2.5 bar absolute pressure, without dust

Evaluation of the experiment was done involving different disciplines. The results of BAL-cytology and CT-radiology are presented by Krombach et al. in another paper in the proceedings of this conference.

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After 12 and 18 months, open lung biopsies were taken using standard techniques, and studied morphologically (12 mo.: n = 25; 18 mo.: n = 24).

Immediately after the last radiological examination the animals were sacrificed. The lungs were fixed by instillation under controlled pressure (2.5% glutaraldehyde, pH 7.4; 20 cm H_2O). Additionally a retrograde perfusion via the abdominal aorta was carried out.

Tissue samples from six different locations were taken after 24 hours of fixation, corresponding to the levels of computed tomography.

After washing in phosphate-buffer, the specimens were embedded in paraffin and tissue slices (6 µm) were cut. Qualitative histomorphology was done on sections stained with Haematoxylin-Eosin (H&E), Giemsa and Azan.

Morphometric evaluation was done chequered on 6 H&E stained sections of each lung, using the 'Interactive Image Analysing System' (IBAS-2, Kontron). In this equipment the histologic structures of the lung tissue are transformed into evaluable black and white pictures. In a multistep semiautomatic morphometric programme of 90 single steps four different area parameters were determined: —air space,—total lung tissue,— lung tissue without blood vessels and bronchial airways, ('respiratory lung tissue') and—areas of cellular accumulations, corresponding to granulomatous reaction tissue.

The determination of hydroxyproline content of the lungs was performed on unselected, glutaraldehyde fixed lung tissue in a modified method according to Stegemann.[11]

For the statistical evaluation, the SAS-statistical system according to SAS—User's Guide (Statistics Version, 5. Ed., 1985) was applied.

RESULTS

Lung Biopsies

After 12 as well as after 18 months, reaction tissue can be detected in the lungs of all dust exposed animals. This granulomatous reaction tissue consists of inflammatory cells (macrophages, lymphocytes, polymorphonuclear granulocytes, mast cells), fibroblasts and collagenous fibers.

In the phagocytosing cells, quartz particles can be detected. Qualitatively, the degree of fibrosis is markedly higher in group II than in group III, especially after 12 months. But, after 18 months, the findings in group III increase comparatively.

Organ Weights

Weights of lung, mediastinal lymph nodes, heart, spleen, liver, and kidney were determined at necropsy. The weights of these organs, except the kidney, are increased in dust exposed groups (Figure 1). Due to intratracheal instillation, lung weights shown in Figure 1 do not give an exact information.

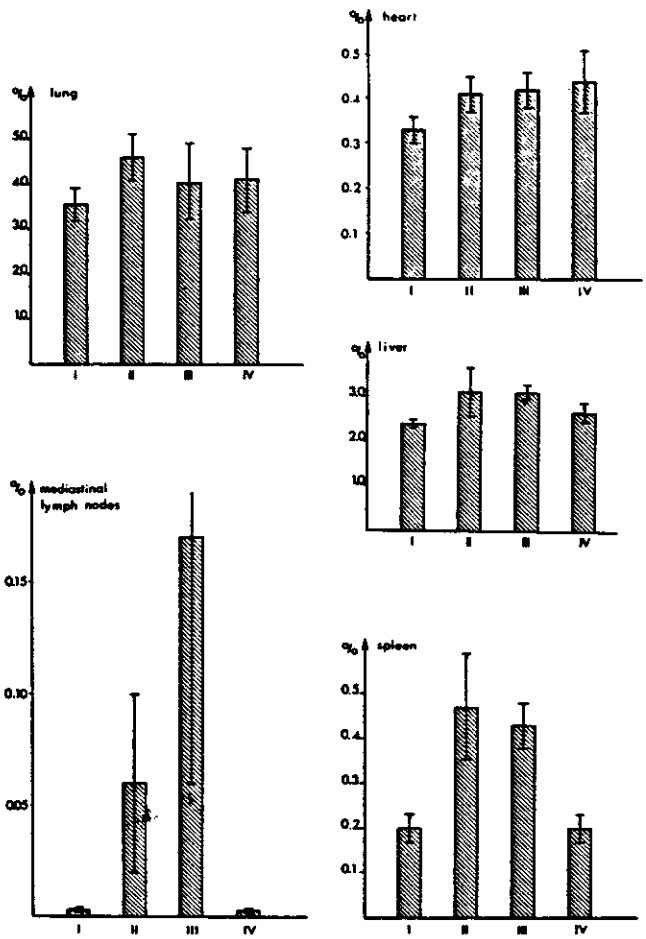

Figure 1. Relative organ weights of heart, lung, liver, spleen, and mediastinal lymph nodes, determined at necropsy, after intratracheal instillation and perfusion.

Macroscopy

Macroscopically, in control animals, the fixed lungs reveal a smooth surface, pale, red coloured and a soft elastic texture. Quartz exposed animals have more voluminous lungs with slightly rough surface, many whitish coloured nodules and a tight tissue texture. The mediastinal lymph nodes are extremely enlarged. In many cases, they are narrowing the lumen of the trachea and the main bronchi. In this way, they are hindering the respiration of the animals.

Histopathology

The qualitative morphologic evaluation of control lungs shows normal lung structure with thin alveolar septa (Figure 2a). Some macrophages and very few cellular accumulations are detectable. In dust exposed animals, the structure of lung tissue is totally altered. Extended areas of fibrosis (Figure 2b) with mast cells incorporated between fibroblasts, macrophages and collagenous fibers are visible in the animals of groups II and III. Fibrotic nodules often occur perivascularly. Due to intratracheal instillation, almost all intraalveolar cells are washed out. Many transformed alveolar pneumocytes II can be seen at the border of fibroses (Figure 3a). Using polarized light, bifringent phagocytosed quartz particles and collagenous fibers can be observed (Figure 3b). Furthermore, the quartz induced connective tissue is infiltrating those areas which do not reveal severe changes.

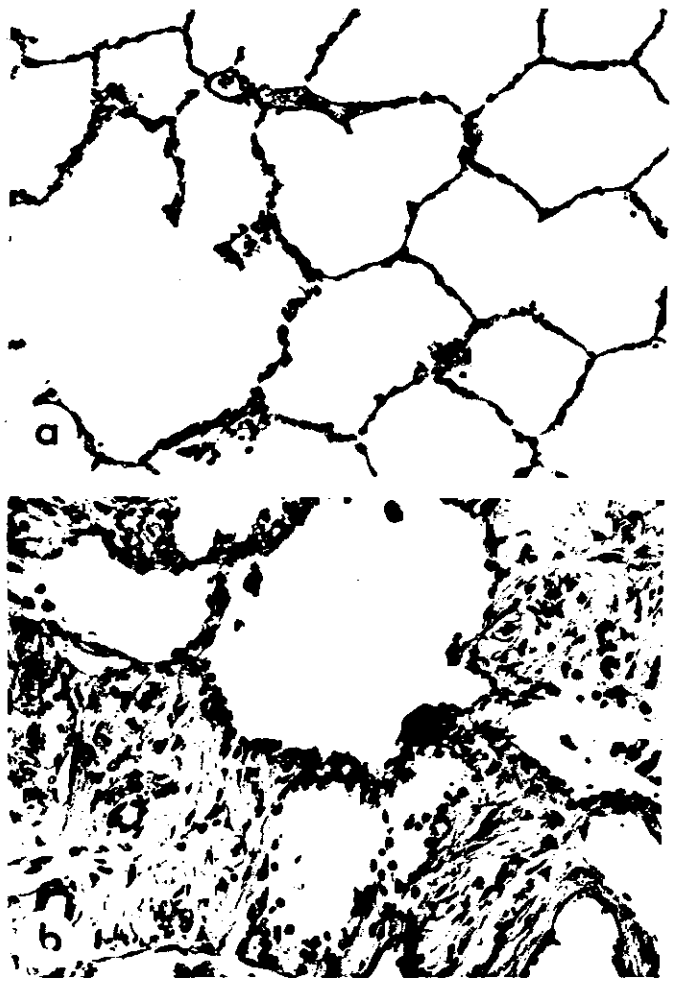

Figure 2. Lung histopathology after 26 months of inhalation:
a. Normal lung structure in a control animal (group I);
b. extended fibrosis in dust exposed animal (group II); H&E staining, obj. 10x.

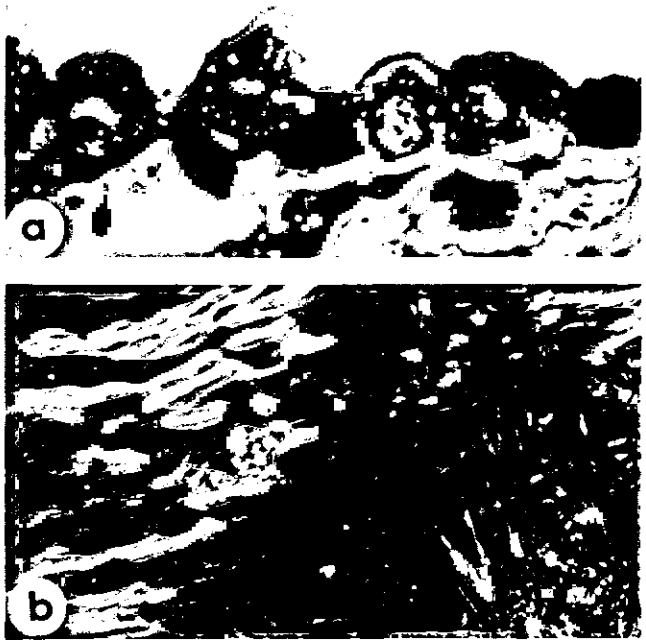

Figure 3. Detailed morphology of quartz induced lung alterations:
a. Pneumocytes typ II, with lamellar bodies in the cytoplasm, are lining alveolar surface; semithin section, methylene-bue staining, obj. 63x;
b. in polarized light, bifringent quartz particles as well as collagenous fibers are detectable; mast cells, as dark spots, included in the fibrosis; Giemsa staining, obj. 25x.

The lung structure of animals just exposed to compressed air (group IV) is not apparently altered compared with group I animals. In some areas alveolar septa seem to be slightly thickened. In all investigated locations of the lungs no morphological signs of any other pathological process or cancerogenic effect can be seen.

The mediastinal lymph nodes reveal severe fibrosis. They consist at almost 80% of collagenous fibers. Additionally, in the liver of all quartz exposed animals, a severe granulomatous reaction with quartz particles and marked fibrosis, so called "quartz induced nodules," is detectable. Quartz particles are also obvious in the spleen, mesenterial lymph nodes, but not in the kidney.

Morphometry

In lung biopsies, at both times the amount of reaction tissue is more extended in animals which inhaled quartz under normal pressure than under excess pressure. The number of reaction nodules decreases from 12 to 18 months, due to an enlargement of the nodules. The percentage amount of cellular accumulations is significantly increased in group II ($p < 0.01$) and only very slightly in group III (Figure 4).

The final morphometrical evaluation, however, shows a relative alignment between the two dust exposed groups

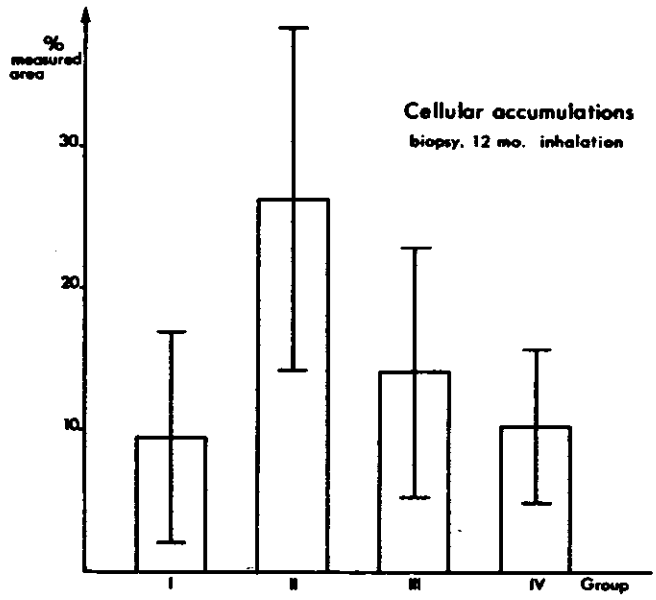

Figure 4. Percentage of cellular accumulations, corresponding to granulomas, in lung biopsies, taken after 12 months of inhalation; arithmetic mean and SEM.

(Figure 5). The significance values are group I/group II $p < 0.001$ and group I/group III $p < 0.05$. Marked differences between right and left lung, as well as between upper, middle and lower level could not be observed.

OH-proline

The hydroxyproline content of the lung, determined as 'mg per gram lung tissue,' shows a severe and significant increase in both dust exposed groups (I/II $p < 0.001$; I/III $p < 0.01$). In animals under excess pressure, however, this increase is somewhat lower than under normal baric conditions (Figure 6).

DISCUSSION

The comparison of findings in lung biopsies with final histomorphology indicates that a delay seems to exist in dust and excess pressure exposed animals, regarding the development of silica induced granulomas. The deposition of inhaled particles also depends on the animals breathing pattern.[3] As this breathing pattern may be changed under excess pressure, the delay may be due to another deposition of particles. But, the differences between groups II and III are almost equalized after 26 months. Therefore, group III animals eventually might have developed more extended granulomas, if the exposure time would have been longer.

And, further morphological and morphometrical studies have to be done on bronchial epithelia. A complete morphological characterization of the lung requires informations on the gas exchange tissue as well as on the airway tree.[12] Due to an eventually changed particle deposition, alterations possibly occur in the airway tree, too.

Recently, the dust content of the bronchial mucosa was discussed with regard to lung cancer.[2] Also because of this,

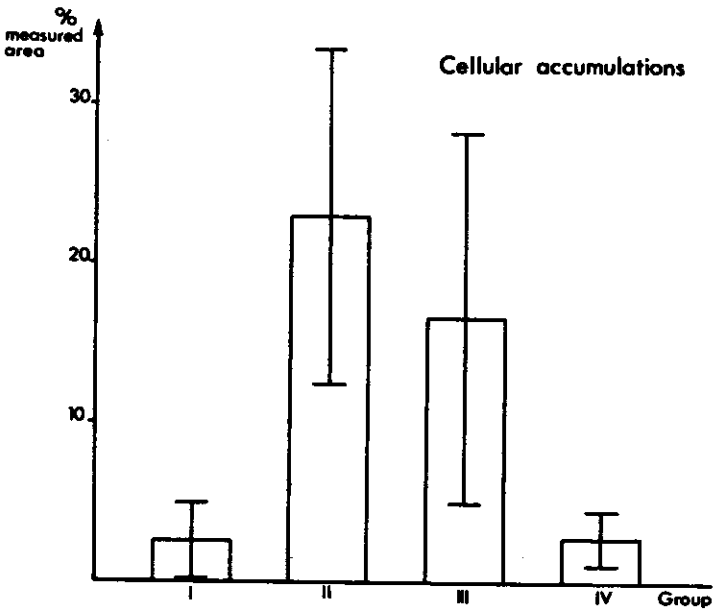

Figure 5. Percentage of cellular accumulations, corresponding to granulomas in the lungs, determined on 6 different locations after 26 months of inhalation; arithmetic mean and SEM.

studies on the morphology of the bronchi are necessary. But of course, because of the relatively short experimental period, our experiment cannot serve as a study on cancerogenicity of quartz dust.

The differences between the percentage amount in biopsy and necropsy cellular accumulations in control animals are caused by different kinds of tissue fixation, immersion and instillation, respectively.

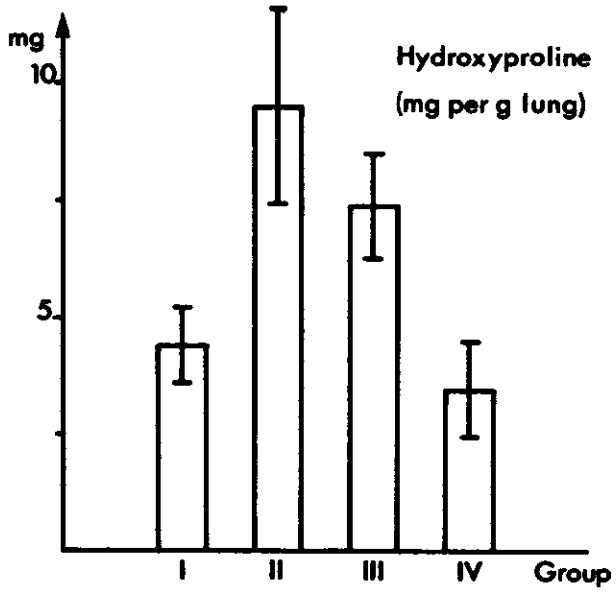

Figure 6. Hydroxyproline content of lung tissue.

A significantly increased lung hydroxyproline content could also be detected in monkeys after repeated paraquat treatment.[8] However, the absolute amount of hydroxyproline in those animals was lower than in our animals. This is probably due to different lung tissue treatment before the determination of hydroxyproline content. We used glutaraldehyde fixed samples, and in the other case[8] frozen lung tissue was taken.

Pathogenetically, the findings described develop in the following manner: the clearance of inhaled particles from the lung firstly takes place via bronchi and trachea and secondly via regional lymph nodes. The lymph nodes are overflowing and in this way macrophages with phagocytosed particles reach the blood and are deposited in other tissues, such as liver, spleen and mesenterial lymph nodes (Figure 7).

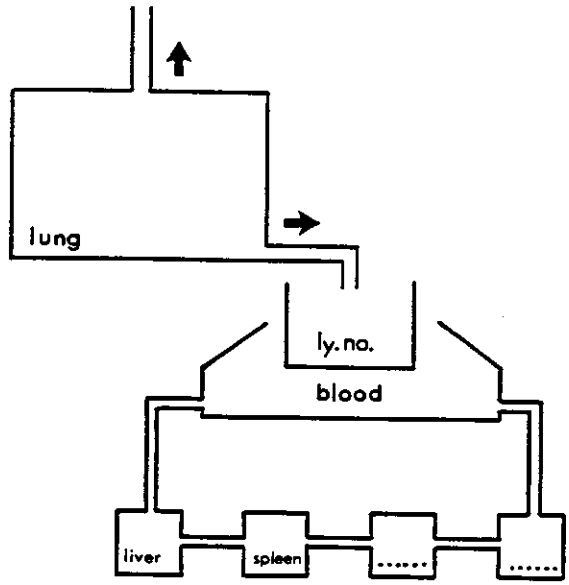

Figure 7. Pathogenesis of the lesions in various organs after inhalation of quartz dust.

Liver granulomas have been reported previously in rats, intravenously treated with silica[4] and as single case reports in humans due to inhalation of various dusts.[1,10] Because of this distinct cellular reaction the increase of the organ weight of the liver can be explained.

Interestingly the heart weights of group IV animals, just exposed to excess pressure, are increased compared with group I animals. This is an indication that just excess pressure causes effects on the respiratory and circulatory system. But, a direct effect of hyperbaric oxygen on the vascular wall has already been presumed elsewhere.[9]

Regarding morphometry, additional to the area measurements the evaluation of two 'mean chord lengths' will be carried out. These data are also known as 'mean linear intercept'.[7] Firstly, the chord lengths of the respiratory lung tissue will

provide informations concerning an interstitial fibrosis, and secondly, chord lengths of the alveolar diameter, to get an answer about any possible tendency of emphysema in the dust and/or excess pressure exposed animals. A more sophisticated discussion will be possible when these morphometric data are available.

Additional investigations shall be carried out in the same animals, using electron microscopy and enzyme histochemistry. This will provide more detailed morphological informations. And, furthermore some steps still have to be done:

1. The comparison of the results obtained with different morphological methods, such as cytology, radiology and pathomorphology, and

2. Morphological data have to be compared with lung function tests.

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CORRELATION OF BRONCHOALVEOLAR LAVAGE AND COMPUTED TOMOGRAPHY IN AN EXPERIMENTAL MODEL OF SILICOSIS*

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Modern tunnel construction involves health hazards such as quartz-dust and compressed air. Compressed air is used behind air-tight bulk-heads to control water seepage. Applying shotcrete lining methods, considerable amounts of quartz-containing respirable dust might be generated.[1] Thus shotcrete tunneling in a compressed air environment eventually exposes the underground workers to both silicogenic and hyperbaric conditions. In addition, exposure to compressed air always means exposure to hyperoxic conditions. Regarding the current concepts of the pathogenesis of silicosis,[2] the interactions between silica particles and alveolar macrophages might be altered by hyperoxia, finally leading to modifications in the development of silicotic lung fibrosis. Moreover, the deposition of respirable dust particles might be changed due to hyperbaric effects on lung function.[3]

The effects of short-term exposure on various parameters of lung function had been described in miners working with shotcrete in a compressed air environment.[4] Thus, the aim of our study was to investigate the individual and combined effects of long-term exposure to silica and compressed air in a non-human primate model. In a longitudinal study (26 months of exposure) we examined various parameters, using broncho-alveolar lavage (BAL) cytological and functional assessment of free lung cells, biochemical analyses of BAL fluid, lung function tests, radiological (X-ray, CT-scan) and pathohistological examinations as chief methods. This paper will focus on the correlation of cellular constituents of BAL and quantitative analysis of CT-scans of the lung.

METHODS

Animals

Thirteen months prior to the start of exposure, 28 cynomolgus monkeys (Macaca fascicularis; 4 male, 24 female) with a body weight of approximately 3–6 kg were separated into four groups. Previously, the animals had been kept in quarantine, dewormed, and tuberculin-tested. In exposure-free intervals, the animals were housed in spacious steel cages under natural daylight. A standard primate chop diet, additional fruit supplement, and tap water were supplied ad libitum.

*Supported in part by BMFT grant No. 01 VD 492/7.

Experimental Design

Following an acclimatization period of 6 months, control BAL was performed three times in each animal. After the start of exposure, BAL was carried out at intervals of 2 months. Open lung biopsies were taken 12 and 18 months after the start of exposure. After 26 months, the exposure was ceased. In the following two months, various lung function tests and radiological examinations (X-ray and CT-scan) were performed. Thereafter, the animals were sacrificed and the lungs were fixed by instillation of glutaraldehyde via the trachea under controlled hydrostatic pressure.[5]

Exposure Conditions

The four groups of animals received an intermittent inhalational exposure regimen of 8 hours/day and 5 days/week, except for public holidays and a 1-week rest following open lung biopsies. The animals were placed in open stainless steel cages, and the exposure took place in 7.5 m^3 capacity inhalational dust/pressure chambers. All test chambers featured controlled climatic conditions (25°C temperature, 70% relative humidity). One group of animals (quartz-exposed group) received a concentration of 5 mg/m^3 of DQ12 <5 µm (Dörentruper quartz) quartz-dust.[6] A second group (quartz/compressed air group) was exposed to a concentration of 5 mg/m^3 of DQ12 and additional hyperbaric conditions of 2.5 bar_a. A third group (compressed air group) was exposed to 2.5 bar_a only. A fourth group of animals (control group) was sham-exposed to clear normobaric air. The concentration of airborne respirable dust was measured with a TM digital µP photometer (OEB H. Hund GmbH, Wetzlar, FRG). The photometer reading was calibrated in terms of mass concentration of respirable dust by means of a gravimetric dust sampler.[7] In each test chamber, room temperature, humidity, pressure, and concentration of respirable dust were monitored and controlled continuously. Compression of the pressure chambers lasted 10–15 min. Decompression was initiated by a decompression step to 1.3 bar_a within 10 minutes, followed by decompression to 1.0 bar_a within 70 minutes.

Branchoalveolar Lavage

For BAL, the animals were anaesthetized with 15 mg/kg ketamine (Ketanest, Parke, Davis & Co., Munich, FRG) and

2 mg/kg xylacine (Rompun, Bayer, Leverkusen, FRG). With the animal in supine position, a flexible fiberoptic bronchoscope (BF P10, Olympus, Munich, FRG) was wedged into the main ronchus of the left lung. Following instillation of 100 ml of sterile 0.9% saline in aliquots of 20 ml, fluid was withdrawn, applying moderate suction. The lavage fluid was immediately filtered through sterile gauze, and the cells were pelleted at 300 g for 10 min. For some biochemical assays, the BAL supernate was examined in a fresh state. Otherwise, the supernate was aliquoted and stored at −70°C for further studies. In addition, possible bacterial contamination was assessed in each BAL sample. The BAL cells were washed twice and counted with a Coulter Counter. Cell viability was determined by the trypan blue exclusion technique. Cytocentrifuge smears served to identify the cellular populations stained with May-Grünwald-Giemsa, naphthyl acetate esterase and toluidine blue. Three hundred cells were counted, and the percentage of macrophages, lymphocytes, neutrophils, eosinophils and mast cells was determined.[8,9]

CT-Measurements

For CT-examinations, the animals were anaesthetized with 15 mg/kg ketamine and 2 mg/kg xylacine, and intubated. Immediately prior to each scan, the animals were hyperventilated to apnea and then scanned at a constant intratracheal pressure of 15 cm H_2O. CT-scans were performed in a Siemens Somatom DRH scanner (7s, 125 kV, 550 mAs). CT-sections were taken with a slice thickness of 1 mm at the level of the tracheal bifurcation, 5 cm cranially and 5 cm caudally, respectively. Lung areas of the thoracic scans were identified by using a modified ROI (region of interest)-method.[10] Starting from a manually specified line encircling each lung, contiguous pixels were analyzed. All pixels corresponding to chest wall, mediastinum and heart were eliminated based on their CT-numbers above −350 HU (Hounsfield units). Using histograms of CT-numbers, the mean CT-densities of both lungs were calculated in each animal.

Statistics

The results are expressed as means ± the standard error of the mean (x ± SEM). For data correlation, the Pearson correlation coefficient was calculated. The statistical comparison of group means was performed using One-Way Analysis of Variance and the Scheffé multiple comparison test. A p value <0.05 was considered to be statistically significant.

RESULTS

The exposure conditions were tolerated well by all animals. No signs of indisposition were observed during dust exposure, compression or decompression. The body weight of the animals kept stable and did not show any significant differences between the four test groups. However, during the entire observation period of 40 months, a total of seven animals was lost, due to severe fighting injuries or narcosis incidents respectively.

In all experimental groups, BAL cell viability and BAL fluid recovery did not change during the exposure period. However, total cell counts showed a bi-phasic profile, with a peak after 6 months followed by a decline and a final increase, starting after 18 months. The first peak of total cell counts was caused by increases of lymphocytes, macrophages, neutrophils and mast cells in that chronological order. In contrast, the final increase of total BAL cell counts was mainly due to a rise of neutrophils (Table I). Mean CT-densities were significantly ($p < 0.05$) augmented in both dust-exposed groups (Table II). There was perfect correlation of CT-densities, obtained after 27 months of exposure, and BAL total cell counts, obtained after 26 months ($r = 0.96$, $p < 0.001$).

DISCUSSION

The data obtained so far suggest that hyberbaric conditions do not accelerate or intensify the manifestation of silicosis dramatically. In contrary, particular data indicate some kind of a "protective" or delaying effect of long-term intermittent hyperbaric exposure. However, final conclusions may be drawn only when all measured parameters (cellular and biochemical BAL constituents, X-ray, CT-scan, various tests of lung mechanics and pulmonary gas exchange, morphometric pathohistology) will be evaluated and correlated. In our experimental model of silicosis, the serial BAL offered excellent insights into both the kinetics and function of free lung cells. In combination with biochemical factors of the BAL fluid (e.g., proteins, phospholipids, enzymes, immunological mediators, fibrogenic activity) more precise informations on the development of silicosis in a primate model will be available.

Under standardized conditions, the quantitative analysis of CT-scans proved to be a sensitive tool for the non-invasive assessment of structural pulmonary alterations. In addition, the perfect correlations of BAL-data and CT-data warrant more sophisticated analyses of CT-histograms as well as further studies on the validity of BAL in pneumoconioses.

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Table I

BAL Fluid Recovery, Total and Differential BAL Cell Counts Prior to and During Exposure

	months	control	quartz pressure	quartz	pressure
fluid recovery (%)	0	64.3 ± 3.9	65.4 ± 3.9	75.1 ± 1.6	74.4 ± 1.0
	6	70.5 ± 2.4	74.0 ± 1.8	74.1 ± 2.1	68.0 ± 3.0
	12	77.o ± 0.9	77.0 ± 1.1	75.7 ± 2.1	78.6 ± 1.0
	18	72.8 ± 5.6	76.6 ± 2.6	76.0 ± 0.9	77.7 ± 1.6
	24	79.4 ± 1.9	79.4 ± 1.4	80.5 ± 1.6	82.4 ± 2.3
total cell counts (x 10^6)	0	16.3 ± 2.2	15.1 ± 2.7	14.1 ± 2.9	14.1 ± 2.8
	6	19.9 ± 2.2	56.4 ± 8.6*	59.0 ± 5.0*	8.3 ± 1.2
	12	7.9 ± 1.1	26.2 ± 4.4*	37.7 ± 3.2*	5.5 ± 0.7
	18	9.6 ± 2.4	49.3 ± 6.2*	34.4 ± 4.0*	6.5 ± 1.4
	24	14.1 ± 3.5	82.6 ± 11.1*	56.0 ± 6.0*	4.2 ± 1.1
macrophages (%)	0	87.2 ± 3.2	84.0 ± 2.7	93.3 ± 1.9	88.7 ± 3.9
	6	84.0 ± 2.6	74.4 ± 4.2	76.1 ± 2.9	87.6 ± 3.6
	12	85.8 ± 3.0	74.3 ± 2.6	77.8 ± 2.8	82.7 ± 4.4
	18	85.6 ± 4.2	68.3 ± 1.3*	74.8 ± 3.9	85.2 ± 3.6
	24	82.6 ± 6.4	65.0 ± 3.3	65.8 ± 4.3	86.0 ± 3.3
lymphocytes (%)	0	6.3 ± 2.0	5.1 ± 0.6	2.7 ± 0.8	4.1 ± 0.9
	6	9.3 ± 1.8	9.6 ± 1.4	8.3 ± 0.9	5.0 ± 1.0
	12	6.2 ± 1.9	9.1 ± 1.8	4.5 ± 1.2	6.6 ± 1.7
	18	7.2 ± 2.4	7.4 ± 1.3	5.4 ± 0.5	5.7 ± 1.4
	24	8.4 ± 2.0	10.9 ± 1.4	11.8 ± 2.3	6.2 ± 1.4
neutrophils (%)	0	2.5 ± 1.1	4.0 ± 1.7	2.1 ± 1.7	1.0 ± 0.4
	6	1.3 ± 0.5	6.4 ± 1.1	8.3 ± 2.7	0.4 ± 0.3
	12	0.7 ± 0.5	7.7 ± 1.3	9.0 ± 3.9*	0.1 ± 0.1
	18	1.0 ± 0.5	11.3 ± 1.6*	11.1 ± 4.0*	0.3 ± 0.2
	24	2.6 ± 1.5	16.0 ± 3.1*	9.5 ± 1.6	0.2 ± 0.2
mast cells (%)	0	1.8 ± 0.9	1.3 ± 0.7	1.0 ± 0.7	1.3 ± 1.1
	6	2.8 ± 1.5	3.7 ± 1.7	5.6 ± 1.2	3.1 ± 1.8
	12	5.3 ± 1.9	6.6 ± 2.1	6.0 ± 1.7	4.9 ± 1.5
	18	4.0 ± 1.4	11.9 ± 1.6*	7.8 ± 2.0	4.0 ± 1.8
	24	5.4 ± 2.8	7.6 ± 2.3	11.8 ± 3.8	4.2 ± 1.2

Data expressed as mean ± SEM.
* $p < 0.05$ vs. control

Table II

BAL Fluid Recovery, Total and Differential BAL Cell Counts, and Mean CT-Densities after 26 Months of Exposure.

	control (n = 5)	quartz (n = 7)	quartz pressure (n = 4)	pressure (n = 5)
fluid recovery (%)	79.8 ± 1.8	80.7 ± 1.4	80.8 ± 2.3	80.2 ± 1.4
total cell counts (x 10^6)	7.0 ± 0.9	79.6 ± 20.3*	61.4 ± 2.3	5.1 ± 1.8§
macrophages (%)	87.4 ± 4.4	69.8 ± 5.7*	78.5 ± 2.2	88.0 ± 1.6§
lymphocytes (%)	4.2 ± 1.6	5.5 ± 1.3	3.8 ± 0.8	5.4 ± 1.7
neutrophils (%)	0.6 ± 0.4	19.5 ± 7.6*	10.5 ± 2.7	0.2 ± 0.2
mast cells (%)	4.6 ± 2.9	5.3 ± 1.9	7.3 ± 2.9	2.4 ± 1.4
mean CT-density (HU)	-892.3 ± 8.5	-734.6 ± 27.5*	-800.0 ± 7.5	-908.6 ± 7.8§$

Data expressed as mean ± SEM.
* $p < 0.05$ vs. control group
§ $p < 0.05$ vs. quartz-exposed group
$ $p < 0.05$ vs. quartz/pressure-exposed group

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CORRELATION OF CHEST FILM AND LUNG FUNCTION ANALYSIS IN PATIENTS WITH SILICOSIS

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INTRODUCTION

Numerous studies treating the subject on the correlation between X-rays of a patient with silicosis and a pulmonary function test can be found in today's literature. However, only a mere correlation between the two methods of examination could be demonstrated. The possible reason for this may be the inaccurate description of the X-rays which in all current publications was conducted using the ancient silicosis classification. For this reason we investigated a sizable patient collective with mixed dust silicosis for reasons of correlation and, in the process applied the new precise ILO-classification of 1980 in it's expanded version. In the course of this, the attempt was made to draw up a sum index which will register the crucial parameters of the chest X-ray, in order to establish the relation to the pulmonary function.

MATERIAL AND METHODS

Our material consisting of 283 miners was to be studied in a survey at our hospital. In addition to the clinical examinations, chest X-rays p.a. and lateral were made according to the technique suggested by the ILO. The coding was effected by two examiners employing the ILO-classification. In case of deviations a renewed classification was jointly carried out. The pulmonary function analysis involved the measurement of the vital capacity, the resistance, the intrathoracal gas volumina (ITGV) as well as the blood gas analysis.

The obtained data was statistically worked out applying the Chi-Square-Test and the regression analysis.

RESULTS

In Figure 1 it can be seen that 40% of the experimentees showed no signs of large opacity, in 20% an A-shadow, in 30% a B-shadow and in 10% a C-shadow was evident. The analysis indicating on which side the opacity was located revealed type A to always be single sided, type B to be mostly single sided and type C to be predominantly both sided ($p = 0.001$). Figure 2 demonstrates the distribution of the individual categories of profusion.

Sections S1 and S2 are predominant, thus groups 0/1 to 2/3. A similar distribution can be found in the size of the small rounded opacities, although hereby the categories p/p to p/q are dominant; 20% show larger spotty shadows. There was a correlation between the formation of small rounded opacities, inasmuch as large opacities turned up significantly more often when more formations of small rounded opacities were apparent in the pulmonary fields.

In the correlation of radio-morphological variation to the bronchial resistance, a significant augmentation in resistance was observed while the size of large opacities increased ($p = 0.05$). Most characteristic was the effect in B- and C-type shadows (Figure 4). At first, the number of large opacities, the size of small rounded opacities, the category of profusion as well as the distribution over the 6 pulmonary fields seemed to be of no importance. We then divided the patient collective into simple and complicated CWP. A positive correlation between the category of profusion and an increased bronchial resistance in patients without large opacities was found (Figure 5). Thus, the dominating factor influencing the resistance is to be found in the formation of large opacities.

There are many reasons for the lacking influence of the formation of small rounded opacities on the resistance. Following extensive epidemiological investigations Ulmer and Reichel have found the obstruction not to be an immediate result of pneumoconosis, but rather a result of the increased incidence of bronchial catarrhs in persons suffering from silicosis. An additional critical factor is the loss of elastic fibers which again will lead to small airways disease (Legg et al.). From a purely qualitative point of view, this lack of correlation between radiomorphologic and pneumofunctional analytical findings is clearly described in observations made by Marek. He conducted comparative examinations between miners, arc welders and persons exposed to asbestos and found concrete differences between size, form and number of pneumoconiotic small rounded opacities, however, there was no correlation between X-rays and progressive pneumofunctional disorders.

The vital capacity shows a clear and significant correlation to the size of the large opacity (Figure 6). In the same manner a statistically significant relationship to the number of large lesions was observed.

With increasing size of small rounded nodes, a statistically proven decrease in vital capacity was detected, while the number of small rounded opacities expressed in category of profusion showed no relation to the vital capacity, at most, a tremendous reduction of VC after an increasing category of profusion could be observed ($p = 0.073$). The influence of the vital capacity by the large opacity's size may at first be

explained by a decrease of intact tissue, on the other hand, however, the formation of an emphysema also plays a certain part. Yet, it must be considered that this fibrotic reaction in anthracosilicosis which leads to an increase of restrictive functional disorders occurs much less than in asbestosis (Ruckley). The lack of correlation to the formation of small rounded opacities could possibly be due to the fact that the small spotty shadows are often surrounded by an emphysema leading to a significant functional cut back, however, the X-ray picture will give cause for a much too low classification. At all events, the perinodular emphysema, however, shows no correlation to the silicosis degree (Hieber).

The comparison between type of lesion, the number of large opacities and the distribution over the pneumatic fields revealed no correlation whatsoever to the ITGV. Merely an increasing category of profusion indicated a trend towards an increase of ITGV ($p = 0.12$). This fact can be explained through observations made by Worth and Smidt, suggesting that already an early state of silicosis will lead to a significant bronchiolitis with bronchiolectasis as well as a dynamic bronchiolostenosis with a constructive formation of an emphysema. These alterations are radiomorphologically not ascertainable, yet they have an enormous influence on the pulmonary function and hereby especially on the ITGV. Furthermore, it should be considered, that an increase in the ITGV occurs with every chronic exposure to dust, thus making the disruption in pulmonary function silicosis unspecific (Ulmer).

The blood gas analyses exclusively demonstrate a dependency to the number of large opacities; an increase in number causes a statistically significant increase in the carbondioxide pressure as well as a decrease in the oxygen pressure, whereby the latter occurs only when there are bilateral lesions. The missing correlation to the formation of small rounded nodes may be due to the fact that in the case of an anthracosilcosis a fibrotic reaction happens only following an extended exposure, which then may lead to a disruption in the gaseous interchange.

We chose two of the 24 supplementary symbols available in the ILO-classification to investigate for a possible correlation to the pulmonary function. We selected the symbols em and tb to be the most profitable expecting a most likely relationship between morphology and function. The symbol em was coded in a total of 159 (56%) experimentees (Figure 7). The explanation for this large number is that the symbol em is not clearly explained in the ILO-classification and that the radiological definition is unclear seeing that no less than 36 radiologic symbols are described which are compatible with an empyhsema. Beyond this, the critical examination of the single symptoms is generally impossible since those structures of small rounded nodes and large opacities which are of interest are being superimposed. Nevertheless, in a medium or severe increase of ITGV a significantly more frequent coding of the symbol em was received.

The symbol tb was applied to 68 (24%) experimentees. No correlation to the pulmonary function analysis was evident in this group. The reason for this is the fact that a coding of the symbol tb happens most often when there are inactive apical localizations of pulmonary tuberculosis present which are of no importance to the pulmonary function.

In order to achieve an exact correlation of several radiological parameters with one single pulmonary functional analytical parameter each, a score for the radiological findings was introduced. The large opacities includinq their size, the small rounded opacities in size and distribution as well as the allocation over the pulmonary fields were given a value between 1 and 3, merely the location of large opacities received only half a point value, because no correlation could be obtained in previous single results. With an increasing sum index a significant boost in resistance ($p = 0.006$) as well as an important decrease in vital capacity was noted ($p = 0.0395$).

This result signifies that our originally stated assumption holds true, namely of a positive correlation between radiomorphologically comprehensible parameters, which can be metrically documented using symbols according to the ILO-classification. This conformity is of statistical significance in a large patient collective. Yet, the attempt to project the results on to the individual experiment turned out insufficient and uncertain because in the isolated case drawing to a safe conclusion from the X-rays to the anticipated pulmonary functions is impossible.

CONCLUSION

1. Severe silicosis with small rounded opacities having a category of profusion of 2/3–3/3 as well as large opacities of type B and C occure significantly more along with an increase of resistance. The number of lesions, as well as the size of small rounded opacities and their distribution over the six pulmonary fields have no influence on this functional parameter.

2. The size of large opacities and their number as well as the size of the formation of small rounded nodes significantly correlates with the vital capacity and vice versa.

3. An evaluation of the ITGV on the basis of radiologically comprehensible parameters is only possible in modestly severe and severe augmentations of the ITGV. Here the symbol em was coded much more frequently.

4. A correlation between X-rays and blood gas analysis exists only if several large opacities are apparent in both lungs and this holds true for hypercapnia as well as for a diminution in oxygen pressure.

5. By the establishment of a score, which takes into account all radioparameters including their various importance, a statistically significant correlation to resistance and vital capacity was found in the total collective. In the isolated case, however, the evaluation of the pulmonary function by means of radiological parameters is not reliable enough, thus making the use of such a score when applied to expert interrogations not sufficiently adequate.

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EVALUATION OF RESPIRATORY HAZARDS BY LUNG FUNCTION INVESTIGATIONS

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ABSTRACT

There are many different methods available for lung function measurements. In epidemiological studies and for the control of workers exposed to different hazards we compared the efficiency of the most available methods. The most useful method is the measurement of airway resistance and of thoracic gas volume by bodyplethysmography. This method is very sensitive and very specific. It does not depend on the cooperation of the measured persons. The predicted values are very precise and reliable. We also use for special questions the 1-concentration-metacholine-challenge-test. This test enables to differentiate between normal bronchoreagibility and hyperreabibility. After different short-term types of exposure, a hyperreagibility of the bronchial system could be detected. Early signs of changes will be found by these methods, and different exposure types results in typical functional changes.

No Paper provided.

SISTER CHROMATID EXCHANGE FREQUENCY AND CHROMOSOMAL ABERRATIONS IN ASBESTOS FACTORY WORKERS

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INTRODUCTION

Asbestos, belongs to a group of naturally occurring magnesium silicate fibrous substances. It has a wide variety of uses in modern society. It is considered to be a carcinogenic for several organ systems.[13] Past study reveals that asbestos exposed workers have an increased risk to develop mesothelioma, bronchogenic carcinoma and other cancers.[3,4] It has also been found to have mutagenic properties. Sincock and Seabright[14] first demonstrated that Chinese hamster ovary cells exposed to chrysotile and crocidolite asbestos showed the occurrence of chromatid and chromosomal changes. It has also been reported that chrysotile produced chromosomal aberrations in cultured Syrian hamster embryo cells in dose related manner.[8]

Chrysotile (UICC) variety has already been reported to induce chromosomal abnormalities in cultured human lymphocytes.[17] Rom et al.[12] found that asbestos workers had an elevated mean sister chromatid exchange (SCE) rate compared to that of controls. In another study slightly higher incidence of chromosomal aberrations in asbestos exposed factory workers was observed.[16]

An Indian variety of chrysotile asbestos has also been found to induce chromosomal aberrations and sister chromatid exchange in Chinese hamster ovarian cells in vitro.[1,2]

In India extensive use of asbestos in various occupations leading to an increased risk of asbestos exposure to workers demands a critical evaluation of asbestos dust. Therefore, present work was undertaken to evaluate the cytogenetic effects of asbestos dust on workers in an asbestos cement factory. This preliminary report may be helpful to determine genotoxic effects of asbestos dust exposure on human population.

MATERIALS AND METHODS

22 factory workers as well as 12 controls were studied to assess the frequency of sister chromatid exchange and the incidence of chromosomal aberrations. The controls were of similar age, sex, having similar habits and socio-economic status. All subjects were carefully examined and detailed clinical history was taken. No subject had taken any drug for at least two months prior the sampling of peripheral blood. All subjects were divided in four groups; asbestos exposed smokers, asbestos exposed non-smokers, control smokers and control non-smokers. The mean duration of exposure was 12.0 years.

From each subject, peripheral venous blood was collected in a heparinized tube under sterilized conditions. Whole blood lymphocyte culture was done in RPMI-1640 medium supplemented with fetal calf serum (20%), L-glutamine (0.03%), penicillin (100 I U/ml), Streptomycin (100 µg/ml), Phytohemagglutinin-M (3%), 5'-bromo-2'-deoxyuridine (5 µg/ml), and blood (0.3 ml). Culture vials were wrapped with aluminium foil and incubated at 37°C in 5% CO_2 atmosphere.

Cultures were harvested at 48 hours to study chromosomal aberrations and at 72 hours for SCE analysis. 3 hours prior to harvesting colchicine (0.1 µg/ml) treatment was given to arrest the cells in metaphase. Centrifugation of the culture was done at 1200 rpm for 10 minutes. Supernatant was discarded and pellets were resuspended in hypotonic solution (0.075 M KCl) and incubated at 37°C for 20 minutes. Again centrifugation of the material was done for 10 minutes at 1200 rpm, the supernatant was discarded and pellets were fixed in fresh and chilled fixative methanol and acetic acid (3:1). Slides were prepared by flame dry method. For differential staining slides were stained with Hoechst 33258 (50 µg/ml) for 15 minutes and then exposed to bright sunlight for 2 hours in the presence of 2 SSC followed by staining with Giemsa (4%) in phosphate buffer (pH 6.8). Coded slides were scored to avoid scoring bias. 100 well spread metaphases were scored for chromosomal aberrations and 50 well spread metaphases with good differentiation were scored for SCE analysis for each subject. Students' 't' test was used for statistical analysis.

RESULTS AND DISCUSSION

In the present study all the subjects were of similar age group. It is evident from Table I that the aberrant metaphase percentage was significantly higher ($p < 0.01$) in exposed smoker and exposed non-smoker groups in comparison to their respective control. Chromosomal aberrations were of chromatid gap and break type (Figure 1). Mitotic index was low in both the groups but not significantly. In both the exposed groups mean SCE/cell was elevated significantly ($p < 0.001$) without affecting mitotic index and cell cycle

Table I

Chromosomal Aberrations in Asbestos Factory Workers
The Values Represent Mean ± SD *(P / 0.01)

Subjects	Age (yr) Mean ± S.D.	Duration of exposure (yr) Mean±S.D.	Chromosomal aberrations				
			No. of cells scored	Mitotic index Mean±S.D.	Aberrant Metaphase (%) Mean±S.D.	Chromatid gap (%) Mean±S.D.	Chromatid break (%) Mean±S.D.
Exposed smokers (n=11)	34.1±2.4	12.0±0.3	1100	2.14±0.82	4.09±1.51*	2.05±1.20	2.04±1.21
Exposed non smokers (n=11)	34.0±2.3	12.0±0.4	1100	2.90±0.71	3.54±1.21*	1.76±1.00	1.78±0.9
Control smokers (n=6)	33.1±1.9	0	600	3.90±0.98	1.50±0.54	0.60±0.5	0.90±0.7
Control non smokers (n=6)	34.0±2.0	0	600	3.94±0.25	1.30±0.81	0.50±0.4	0.80±0.7

n = Number of subject

* p / 0.01

kinetics (Table II). It indicates that asbestos exposure may induce undesirable genetic damage in occupational populations.

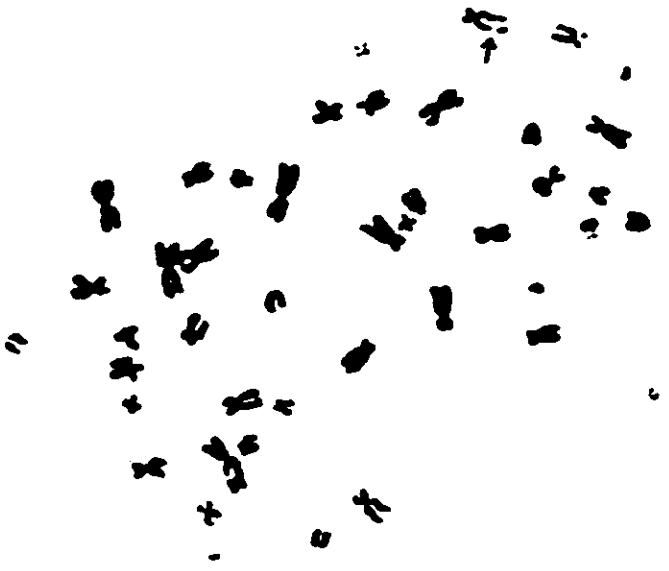

Figure 1. Cell with chromatid break in an exposed non-smoker subject.

The higher SCE/cell (Figure 2) in asbestos exposed smokers (8.16±0.45) in comparison to exposed non-smokers (6.63±0.50) (p / 0.001) may be due to synergistic action of asbestos and smoking (Table III). The results are in agreement with other workers.[6,12] The variation in the magnitude of chromosomal aberrations among both exposed smoker (4.09±1.51) and exposed non-smoker groups (3.54±1.21) was not significantly different. The elevation of SCE rate due to cigarette smoking is in accordance with the earlier reports.[7,10] The highest SCE frequency was observed in exposed smokers and lowest in control non-smokers. These results are analogous to lung cancer risk among insulators where the vast majority of cases occur in those insulators who smoke. The exact mechanism involved in the production of SCE is not well established. However, SCE analysis has been adopted as sensitive indicator of genetic damage.[11] The higher incidence of asbestosis in asbestos exposed smoker group (72.2%) in comparison to asbestos exposed non-smokers group (27.2%) (Table III) suggests that smoking may act synergistically to enhance asbestosis in the smoker group.

Marked variation in SCE frequencies have also been reported among individuals with several different types of cancer.[5,9,18] In addition, increase in SCE level has reportedly been found in cohort studies in those individuals who are at a higher risk of cancer due to occupational or environmental exposure to a wide variety of both mutagens as well as carcinogens.[15] We conclude that the evaluation of SCE per cell and higher chromosomal aberrations may point out the

Table II

Sister Chromatid Exchange Frequency in Asbestos Factory Workers
The values are expressed as mean ± SD *(P / 0.001).

Subjects	Age (yr) Mean ± S.D.	Duration of exposure(yr) Mean ± S.D.	Sister chromatid exchange						
			No.of cells Scored	Mitotic index Mean±S.D.	SCE/cell Mean±S.D.	SCE range	Cell cycle kinetics (%) Ist	IInd	IIIrd
Exposed smokers (n=11)	34.1±2.4	12.0±0.3	550	5.39± 0.72	8.16± 0.45*	3-16	30.39± 6.30	55.98± 5.53	12.50± 4.11
Exposed non smoker (n=11)	34.0±2.3	12.0±0.4	550	5.44± 0.60	6.63± 0.50*	3-12	29.20± 6.63	57.45± 9.62	10.15± 1.61
Control smokers (n=6)	33.1±1.9	0	300	5.80± 0.78	5.73± 0.16	3-9	33.64± 4.32	57.86± 3.34	8.74± 1.72
Control non smokers (n=6)	34.0±2.0	0	300	5.86± 0.80	3.61± 0.14	3-6	33.48± 5.18	56.44± 4.03	10.05± 3.47

n = Number of subject

* p / 0.001

Figure 2. Cell showing sister chromatid exchanges in an exposed smoker subject.

risk of developing cancer in asbestos exposed workers. However, further study is required to establish the fact that higher SCE and chromosomal aberrations are associated with development of lung cancer in asbestos exposed workers.

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Table III

Chromosomal Aberrations, Sister Chromatid Exchange, Frequency and Incidence of Asbestosis in Asbestos Factory Workers
The values represent mean ± SD *(P / 0.001).

	Exposed non smokers					Exposed smokers			
S.No.	Chromosomal aberration (%)	SCE/Cell mean±S.D.	Asbestosis	Incidence of asbestosis (%)	S.No.	Chromosomal aberration (%)	SCE/Cell mean±S.D.	Asbestosis	Incidence of asbestosis (%)
1.	2	5.88±2.13	A		1.	4	8.34±1.36	A	
2.	5	6.56±2.17	A		2.	3	8.10±1.57	P	
3.	4	7.26±1.73	P		3.	3	7.52±1.56	A	
4.	4	7.15±2.20	P		4.	5	8.38±2.15	P	
5.	3	6.08±1.95	A		5.	3	8,52±1.68	A	
6.	6	7.16±1.55	P	27.2	6.	2	8.66±1.93	P	72.7
7.	4	7.04±2.90	A		7.	3	8.12±2.42	P	
8.	3	6.10±2.30	A		8.	7	8.70±1.18	P	
9.	3	6.98±1.34	A		9.	5	7.58±1.67	P	
10.	3	6.40±1.62	A		10.	6	8.48±1.57	P	
11.	2	6.36±1.74	A		11.	4	7.46±2.40	P	
Mean± S.D.	3.54±1.21	6.63±0.50				4.09±1.51	8.16±0.45*		

P = Present
A = Absent
* = (P/ 0.001)

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THE DIFFERENT BIOLOGICAL EFFECTS OF DUSTS APPLICATED INTRATRACHEALLY SEPARATELY OR IN MIXTURES IN RATS

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An intraperitoneal injection of pure natural anhydrite has been shown to cause a mild fibrosis, which has been attributed to the content of quartz.[8] We postulated that anhydrite enhances the effect of the quartz. Cadmium sulfide also induces pulmonary fibrosis in our rat intratracheal test.[2] It is known, that polyvinylpyridine-N-oxide (PVNO) possesses an inhibitory action on quartz. However, we were able to show that CdS behaves differently in a mixture with PbS than with PVNO.[3]

In order to investigate the behaviour of dusts in mixtures, we used the rat intratracheal test to study anhydrite, cadmium sulfide and titanium dioxide dusts separately or in mixtures with Döorentruper quartz DQ 12 or polyvinylpyridine-N-oxide. The individual dusts and the artificial dust mixtures were initially made into suspensions, which were then physically characterized.[5] The results of this characterization are presented in the poster session.

A variety of dust samples were instilled in suspension in 0.5 ml of physiological saline solution into the trachea of female SPF Wistar rats (weight approximately 200 gr). The animals were sacrificed 3 months after instillation. The half of each left lung was hydrolyzed in sealed reagent tubes with 6 N.HCl for 16 to 18 hrs at 104°C. Following cooling and filtration the corresponding hydrolysate (0.1 to 0.5 ml) was neutralized with NaCl and the total hydroxyproline content determined.[7] The other half of each left lung was weighted, homogenized and extracted with chloroform-methanol (2:1). The total lipid content was then determined.[1] The corresponding right lungs of these animals and their regional lymph nodes were fixed in 4% formalin, dehydrated in graded alcohols and embedded in paraffin. Sections were stained with HE and EvG.

RESULTS

Those animals treated with anhydrite showed no increase in total lipid or hydroxyproline content in the lungs when compared with controls. After titanium dioxide these parameters were slightly raised. Treatment with PVNO or PVNO with CdS elicited only a mild increase in total lipid content compared with controls. Following separate instillation of quartz we found a dose-dependent increase in both total lipids and total hydroxyproline. Separate instillation of cadmium sulfide also caused significant elevation of both parameters (Table I).

Both successive and simultaneous instillation of anhydrite and quartz led to marked reduction in total lipid and hydroxyprolin content, compared with values obtained after separate quartz treatment. However, with decreasing quartz concentration or increasing anhydrite concentration an increase in lipid and hydroxyproline content was observed. Total lipids and hydroxyproline content in the lungs were also significantly elevated following a combination of titanium dioxide and quartz compared with values obtained with separate application of titanium dioxide.

The highest increase of total hydroxyproline content was established in animals which had been treated with quartz. The lowest level of hydroxyproline was achieved after simultaneous instillation of anhydrite with quartz. PVNO combined with quartz led to a clear reduction in hydroxyproline content, but significantly increased it when combined with CdS compared with that obtained after separate application of CdS.

Inflammatory changes in control lungs were not found. Following separate quartz treatment numerous disseminated histiocytic nodules with marked synthesis of collagenous connective tissue were seen both in the pulmonary tissue (Figure 1) and in the lymph nodes (Figure 2). The content of these changes was dose-dependent. In addition, in the lungs alveolar proteinosis was also observed.

After successive instillation of 35 mg anhydrite and 11 mg quartz a marked nodular histiocytic reaction without fibrosis was observed (Figure 3). In addition, simultaneous intratracheal instillation of 2 mg quartz with 35 mg anhydrite elicited in lymph nodes a minimal reaction with suggestion of nodule formation without fibrosis (Figure 4).

With increasing anhydrite dose the number of foam cells and foreign body giant cells decreased, whilst histiocytic nodules increased. In all anhydrite-quartz groups, independent of the anhydrite dose, merely numerous birefringent crystals were observed, without any increase in connective tissue component or alveolar proteinosis. In the swollen lymph nodes numerous partially confluent histiocytic nodules with a minimal collagenous reaction were found (Figure 5).

In the rat lung the separate intratracheal instillation of titanium dioxide failed to elicit a fibrous reaction. The foam

Table I

Means (x) and Standard Deviations (s) of Total Lipids and Total Hydroxyproline in Rat Lung 3 Months After Intratracheal Instillation

group (dust sample)	Total lipids/ lung mg		hydroxiproline/lung mg	
	x	s	x	s
35 mg anhydrite	43,47	5,06	3,40	0,52
2 mg DQ 12	122,80	49,19	4,94	1,12
5 mg DQ 12	191,95	49,93	5,85	0,67
7 mg DQ 12	202,94	45,48	8,20	1,33
11 mg DQ 12	207,13	58,46	8,22	1,29
20 mg PVNO	48,11	4,55	3,66	0,31
20 mg CdS	66,25	3,46	5,18	2,24
5 mg anhydrite + 11 mg DQ 12	156,96	13,37	3,81	0,70
20 mg anhydrite + 11 mg DQ 12	78,76	25,60	4,12	1,20
50 mg anhydrite + 11 mg DQ 12	78,83	13,04	3,73	0,92
35 mg anhydrite + 2 mg DQ 12	37,99	2,52	3,10	0,26
35 mg anhydrite + 5 mg DQ 12	40,34	3,42	3,22	0,14
35 mg anhydrite + 11 mg DQ 12	66,34	9,39	3,15	0,17
30 mg TiO_2	53,14	12,65	3,30	0,37
30 mg TiO_2 + 5 mg DQ 12	101,78	20,80	4,81	0,65
2 mg PVNO+11 mg DQ	55,53	5,97	3,47	1,21
11 mg PVNO+11 mg DQ	55,52	6,09	4,14	0,51
2 mg PVNO+20 mg CdS	58,55	3,87	5,72	0,70
11 mg PVNO+20 mg CdS	58,46	4,65	6,24	0,81
20 mg PVNO+20 mg CdS	59,76	5,22	6,50	0,84
control	44,17	5,00	3,26	1,03

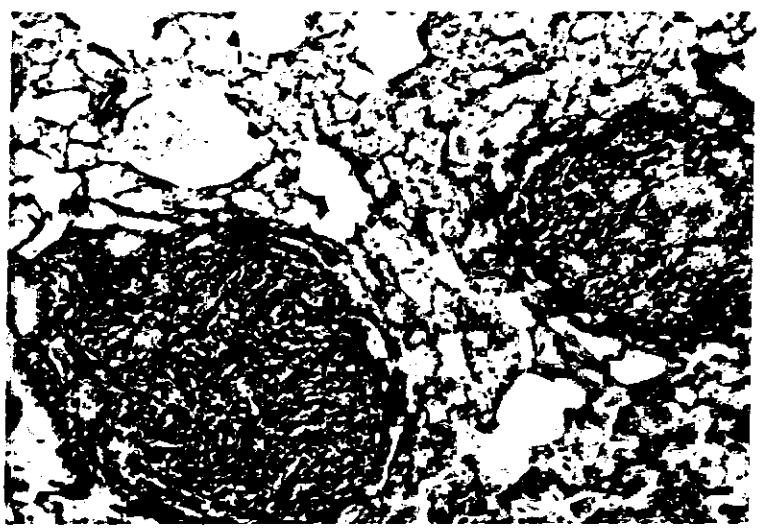

Figure 1. Rat lung with histiocytic nodules, a fresh formed collagen tissue and alveolar proteinosis 3 months after intratracheal instillation of 5 mg Dörentruper quartz.

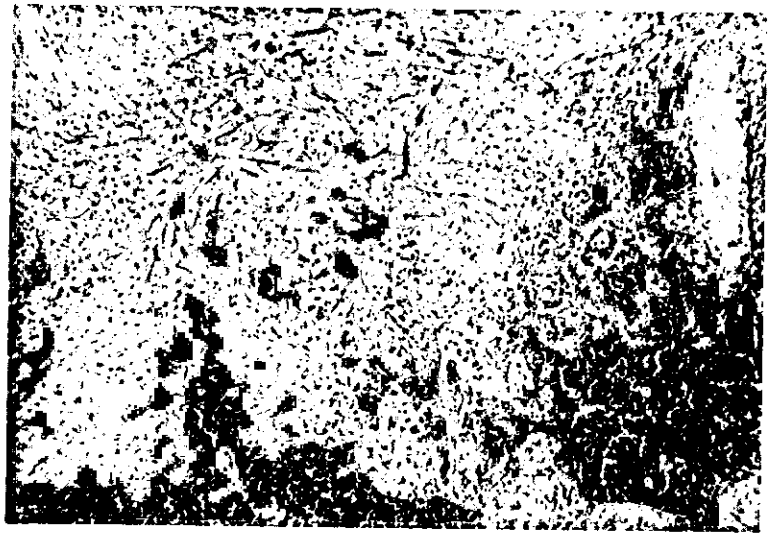

Figure 2. Partial compact fibrosis in the lymph nodes after intratracheal instillation of 5 mg Dörentruper quartz. EvG stain, magnification 50 fold.

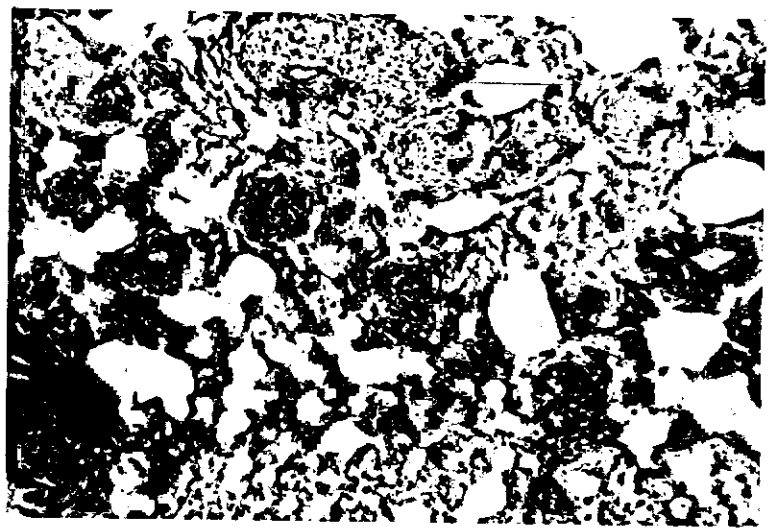

Figure 3. Rat lung with small histiocytic nodules without fibrosis after successive intratracheal instillation of 35 mg anhydrite and 11 mg Dörentruper quartz DQ 12. EvG stain, magnification 50 fold.

cell reaction in the lung after separate titanium dioxide instillation (Figure 6) was markedly enhanced following a combination of titanium dioxide and quartz (Figure 7). The alveolar septae beiing markedly thin and the alveolar epithelia much flattened. After combined treatment with titanium dioxide and quartz, the lymph nodes showed dense deposits of brown pigment and a focal histiocytosis.

After instillation of 20 mg PVNO there was no evidence of inflammation. Nodules of fibrosis did not occur.

After intratracheal instillation of 20 mg CdS, in the lungs, inflammation, moderate fibrosis within the nodular granulomata and single groups of foam cells were seen (Figure 8). Lymph nodes contained dense deposits of finally granular pigment but did not give evidence of fibrosis.

Figure 4. Rat lymph node with focuslike histiocytic reaction without fibrosis after simultaneous intratracheal instillation of 2 mg Dörentruper quartz with 35 mg anhydrite. EvG stain, magnification 50 fold.

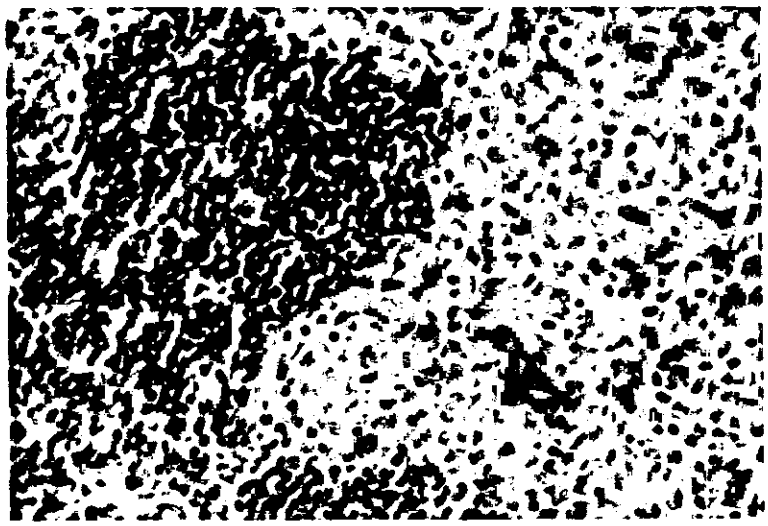

Figure 5. Rat lymph node with a slight fibrosis after simultaneous intratracheal instillation of 11 mg Dörentruper quartz with 35 mg anhydrite. EvG stain, magnification 50 fold.

With increasing PVNO dose at a constant level of CdS, the lungs revealed abundant granular material, which was not birefringent. An inflammatory reaction without nodule formation or foam cells were present. The inflammatory component in the lungs and the dust deposits in both lungs and lymph nodes increased with the total dose.

After the simultaneous instillation of 20 mg PVNO and 20 mg CdS a focal increase in connective tissue in the lung in the form of fibrosis (Figure 9) was observed. In the lymph nodes a focal fibrosis, occasionally, in the form of nodules was seen.

The simultaneous instillation of PVNO and quartz, neither in the lungs nor in the lymph nodes was there any fibrous reaction. Dust deposits could not be found in the lymph nodes.

Numerous nodular granulomata, pricipally histiocytosis with

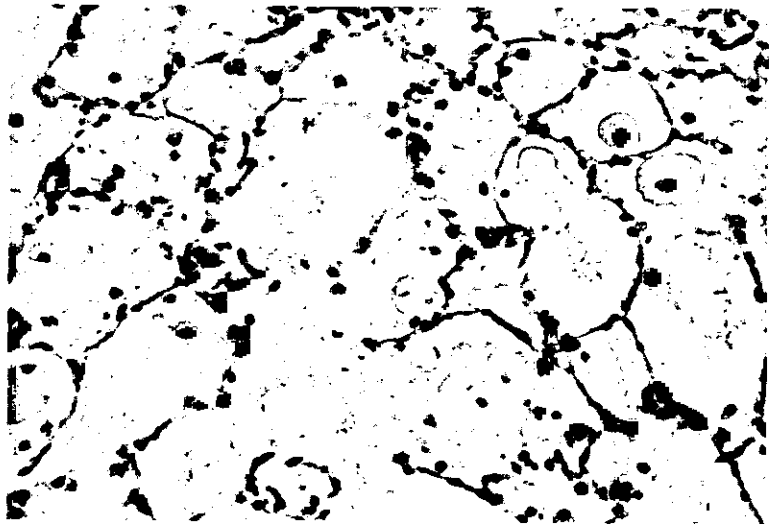

Figure 6. Rat lung, a slight foam cell reaction after intratracheal instillation of 30 mg titanium dioxide. EvG stain, mgnification 125 fold.

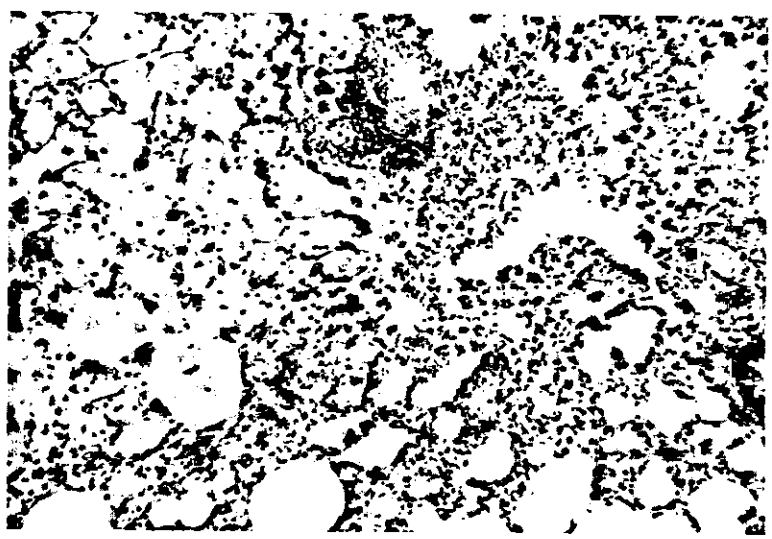

Figure 7. Rat lung, a intensifier foam cell reaction after intratracheal instillation of Dörentruper quartz with titanium dioxide. EvG stain, magnification 63 fold.

a tendency toward confluence, were not in evidence in the lung until 6 months following combined instillation of 2 mg PVNO and 11 mg Dörentruper quartz.

DISCUSSION

In the various mixtures PVNO showed variable behaviour, i.e. with quartz inhibitory, with CdS stimulatory. A similar behaviour was found with anhydrite: It acted inhibitory on quartz, whereas with the bounding catalyser, a mixture of iron and potassium sulfide, no inhibition could be found.[8]

Furthermore, the physical characteristics of the dust mixtures employed[6] indicates that the act of mixing imparts to the dusts properties which cannot be calculated on an additive basis. The mixture will thus react totally differently from the individual dusts applied separately. The observations lead us to the suggest that we may be dealing with a general principle, namely that each dust can demonstrate different behaviour in different dust mixtures.

Qualitative differences in histological appearance were estab-

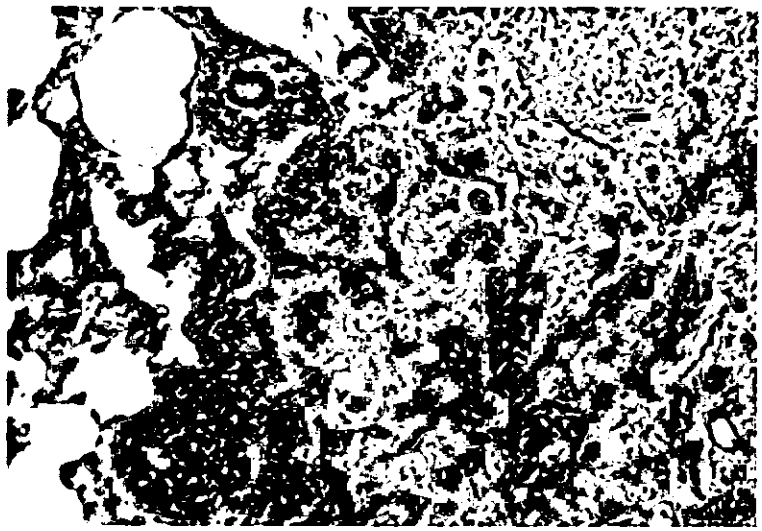

Figure 8. Rat lung, occasional foci of inflammation, moderate fibrosis within nodular granulomata after intratracheal instillation of 20 mg CdS. EvG stain.

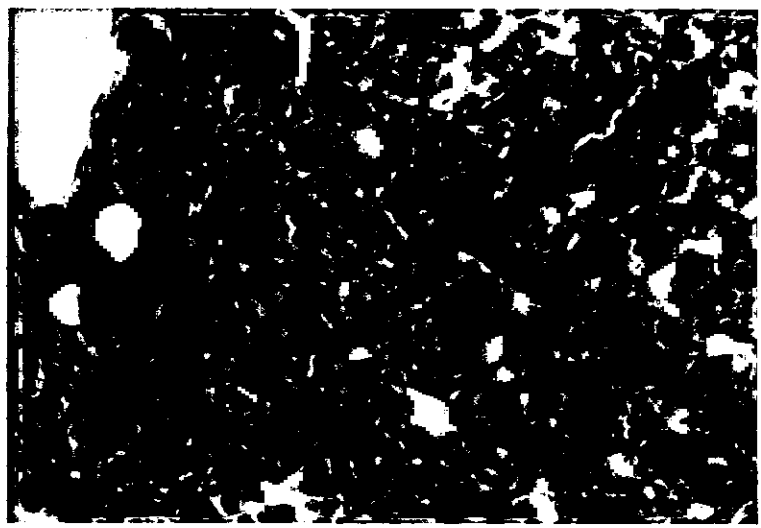

Figure 9. Rat lung, focal fibrosis after simultaneous intratracheal instillation of 20 mg Cds and 20 mg PVNO. EvG stain.

lished between the various experimental groups. The intratracheal instillation of CdS elicited a marked inflammatory reaction in the lungs. However, in contrast with the quartz effect, no sinus histiocytosis could be found in the lymph nodes. The addition of PVNO enhanced the effect of CdS by increasing the degree of penetration of the dust, resulting in fibrosis in the lymph nodes, too.

Increasing anhydrite dose in the dust mixture with quartz led to a decrease in form cell content but an increase in the number of histiocytotic nodules. By contrast, the combination of titanium dioxide with quartz not only enhanced the foam cell reaction but also caused flattering of the alveolar epithelium with the formation of thin alveolar septae. After the combined application of titanium dioxide and quartz the lymph nodes exhibited sinus histiocytosis with no evidence of fibrosis. Combining 35 mg anhydrite with 11 mg quartz elicited a minimal connective tissue reaction in the lymph nodes, but not in the lung.[4] The morphological differences correlated well with the alterations in the hydrogen concentration in suspensions of saturated solutions.[6]

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THE PROPORTION OF LONG FIBRES IN ATTAPULGITE AND SEPIOLITE CONTAINING ADSORPTION GRANULATES

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INTRODUCTION

In the Federal Republic of Germany every year more than one million tons of adsorption granulates are used by consumers as animal bedding, adsorption material for oil, or as additive in colours and glues. The majority of these granulates consists of the fibrous minerals attapulgite resp. palygorskite and sepiolite. Depending on the location of the mine, rather different lengths and compositions of the fibres can be found. It is suggestive that the content of fine fibres (D <0.1 µm) may have carcinogenic properties.[4] Intrapleurally and intraperitoneally injected attapulgite fibres of the long type caused cancer in rats whereas the short type was not effective.[3,4,5,6,7] In addition, Spanish sepiolite proved to be uneffective as revealed by intrapleural injection experiments.[6,7] Nevertheless, a Finnish sample of a remarkably long fibrous sepiolite, supposedly a rarity, was found to cause cancer in intraperitoneal injection experiments. (Pott et al. unpublished) Thus, the durability of the fibres in the lung has at least to be considered.

Morbidity and mortality studies on employees of American attapulgite mines and mills as well as X-ray examinations of workers in decomposition and processing factories of sepiolite in Turkey have been published.[1,8] However, even mortality studies, conducted during the processing of short fibrous attapulgite deposits in Georgia, distinctively neither excluded nor supported any tumour risk.[8]

Thus, carcinogenic properties of the minerals attapulgite and sepiolite can only be excluded by the use of injection experiments. Especially the content of long fibres in commercially available products has to be kept at least as small as in the tested samples. This communication describes the mineralogical composition and the content of fibres with a length of L $\geq$ 5 µm of adsorption granulates, used as animal bedding.

MATERIALS AND METHODS

Mineralogical Investigations

The mineralogical composition of 75 commercially available samples of adsorption granulates used as animal bedding was studied by means of:

- X-ray diffraction
- polarization—and phase contrast microscopy
- differential thermoanalysis.

Samples supposedly composed of fibrous components were subsequently classified according to number and length of fibres.

Scanning Electron Microscopy (SEM) Classification of Fibre Quality

Of each sample, by the use of sonication (30'), 5 mg were suspended in 50 ml distilled water. Aliquots were filtered with nucleporefilters (poresize 0.2 µm, previously sputtered with gold) to obtain a substrate density of 5 µg/cm^2. These specimens were analysed by SEM (13000x). In addition to the mineralogical study, the specimens were also investigated by energy dispersive X-ray analysis to obtain the elemental composition of each sample.

Qualification of Fibres by Scanning Transmission Electron Microscopy (STEM)

The concentration of fibres contained in 5 samples was revealed by the use of STEM. As described above, an aqueous suspension of the sample was prepared and filtered on an untreated nucleporefilter (poresize 0,2 µm). Subsequently, the specimen was sputtered with carbon, the filter material dissolved in a Jaffe washer, and the remaining transmission sample was analyzed at a magnification of 29000 times (STEM) for fibres of any length and at a magnification of 10000 times (TEM) for fibres with a length of L $\geq$ 5 µm.[4]

RESULTS

Attapulgite resp. palygorskite were characterized as main components in 7 samples and sepiolite in 19 samples, (Figure 1). In 9 other samples sepiolite was also found in minor quantities. These 35 products as well as 14 other samples containing various calciumsilicahydrates were analyzed for their fibrous components by the use of scanning electron microscopy. Twenty six products which were mainly composed of attapulgite and sepiolite proved to be aggregated of fine fibres. Although the overwhelming majority of these fibres did not exceed the length of L $\geq$ 5 µm, a smaller portion of the fibres was longer than 5 µm in all cases.

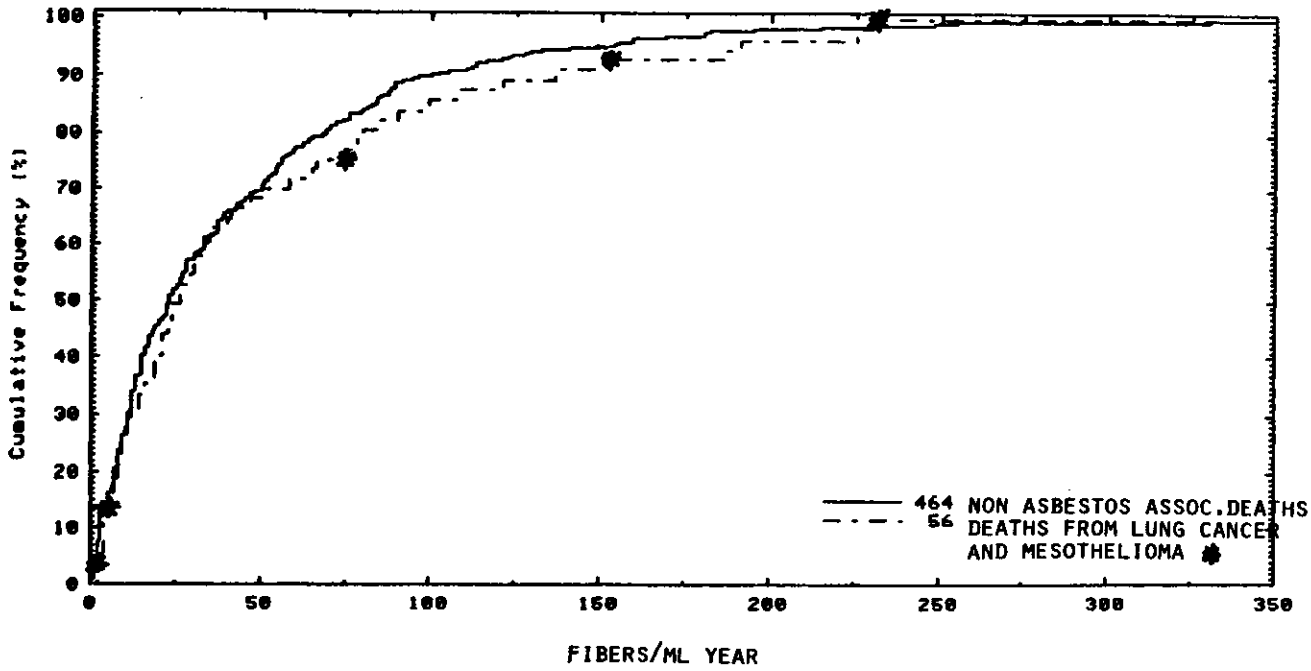

Figure 1. Cumulative doses of cases of lung cancer, mesothelioma and non-asbestos-associated deaths.

The results of X-ray diffraction and differential thermoanalysis studies were confirmed by the elemental analysis which showed a higher Al, Fe portion in attapulgite. However, the distinction between attapulgite and sepiolite with elemental analysis was not completely feasible.

Of the 26 products, 4 samples with relatively long and 1 sample with short fibres as revealed by qualitative fibre characterization were selected for a quantitative analysis by scanning transmission electron microscopy (STEM). The results are summarized in Table I. The median length of the fibres was measured as L = 0.7 to 1.3 µm, the median diameter as D = 0.03 to 0.05 µm and the ratio was calculated as L/D = 20 to 29. The remarkably constant number of all fibres was counted as 71 to 135 • 10^9 F/mg. Despite the generally short fibres, longer fibres (L ≥ 5 µm) were found in all samples. The concentration of fibres with a length of L ≥ 5 µm was found to be 1.8 and 26.4 • 10^6 F/mg for attapulgite and 12.2, 12.7, and 1240 • 10^6 F/mg, respectively, for sepiolite. The latter one was already found to consist of more long fibres than all other products by the use of SEM-analysis.

DISCUSSION AND CONCLUSION

The concentration of fibres longer than 5 µm in 5 adsorption granulates achieve a crucial importance if compared with results obtained from experimentally injected attapulgite and sepiolite in animals.[4] Figure 2 summarizes a comparison between the findings of both investigations. In 4 of the adsorption granulate samples the concentration of fibres longer than 5 µm was lower than the concentration yielding carcinogenic effects in the injection experiment. However, it

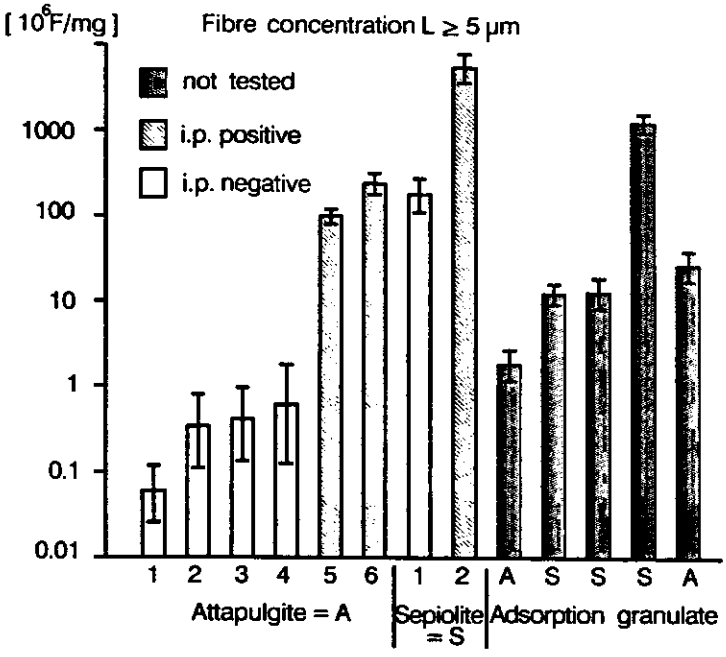

Figure 2. Number of fibres with a length of L ≥ 5 µm in 5 selected adsorption granulates as revealed by TEM at a magnification of 10,000x. Comparison of samples of attapulgite (Mormoiron 1, Lebria 2, Georgia 3, 4, Torrejon 5, Cacéres 6) and sepiolite (Spain 1, Finland 2) intraperitoneally or intrapleurally examined for carcinogenicity in rats, c.f.[4]

Table I

Causes of Death (ICD 9th Revision) 1950–1987

	Official diagnosis (best information)		Additional diagnosis
Malignant neoplasias			
Respiratory organs, intrathoracic organs (160–165)		59(58)	
lungs (162)	50(52)		
pleura (163)	7(4)		
larynx (161)	1(1)		
other (nose)	1(1)		
Organs of digestion, peritoneum (140–159)		58(59)	
stomach (151)	34(35)		1
intestine (152, 153)	3(4)		
rectum (154)	4(4)		
esophagus (150)	2(2)		
liver (155)	1(1)		
gallbladder (156)	3(3)		
pancreas (157)	4(5)		1
oral cavity and pharynx (140–149)	4(4)		
peritoneum (158)	3(1)		
Other		31(33)	
urinogenital organs (179–189)	14(14)		1
other locations	17(19)		
Primary location poorly designated		4(5)	
Neoplasias of unknown character (239)		1(0)	
Diseases of the respiratory organs (460–519)		32(33)	
chronic bronchitis (491)	4(5)		3
emphysema (492)	6(6)		4
asthma (493)	8(9)		2
tuberculosis (011, 012)	6(5)		-
pneumoconiosis (500–505)	1(2)		8
other chronic diseases	0(0)		2
pneumonia (480–486)	4(4)		11
other acute (infectious) diseases	3(3)		-
Diseases of the circulatory system (390–459)		203(201)	
myocardial infarction	61(62)		2
other ischemic heart diseases	31(31)		9
cor pulmonale	7(6)		3
other cardiac diseases	39(37)		13
diseases of cerebral vessels	40(40)		6
other circulatory diseases	25(25)		25
Diseases of the organs of digestion (520–579)		47(47)	
gastric and duodenal ulcer	7(7)		6
hepatic cirrhosis	29(29)		1
other	11(11)		-
Other diseases		27(25)	11
Accidents (E 800–949)		54(55)	2
Suicide and violent cause of death (E 950–999)		19(19)	-
Unknown causes of death		5(5)	

still higher than the concentration found to be uneffective. The concentration of fibres with a length of $L \geq 5$ µm was clearly raised in a fifth adsorption granulate sample of sepiolite. Sepiolite from Spain is reported to be non carcinogenic.[6,7] The authors state that in their investigated products no fibres longer than 5 µm were found.[7] Yet, in a suspension of this sepiolite which was prepared from respirable dust to perform intrapleural injections, the proportion of fibres with a length of $L \geq 4$ µm was found to be 10.5%. In contrast, a concentration of 5.5% of fibres with a length ≥ 4 µm was found in attapulgite from Torrejon which proved to cause mesotheliomas. In accordance with these findings, in Figure 2 the content of fibres with a length $L \geq 5$ µm in Spanish sepiolite tested by Wagner was rather high ($180 \cdot 10^6$ F/mg); whereas a Finnish sample containing $5500 \cdot 10^6$ fibres/mg longer than 5 µm and also anthophyllite was found to cause mesothelioma. (Pott et al., unpublished).

In summary, the concentration of fine fibres longer than 5 µm in adsorption granulates composed of attapulgite and/or sepiolite was lower with a factor of 4 to 100 in the majority of the samples than concentrations significantly carcinogenic in injection experiments. Only one animal experiment with a relatively high number of long sepiolite fibres shows a lower carcinogenic effect than experiments with long attapulgite fibres. However, the main component of adsorption granulates often resembles attapulgite as shown by analytical tests or it cannot be excluded as minor component or impurity. Thus, it is requested that the physical properties and biological effects of fibrous clays are investigated before deposits are handled.[7] In particular, the carcinogenic effects of the adsorption granulate of sepiolite with $1240 \cdot 10^6$ fibres per mg longer than 5 µm has to be tested in an animal experiment by intraperitoneal injection. Furthermore, the persistency of these long fibres has to be studied by intratracheal tests.[3]

Table II

Lung Cancer Mortality 1950–1986: Observed (O), Expected (E); Standardized Mortality Rate (SMR=O/E) with 95% Confidence Interval (95% c.i.)

Lung cancer (ICD 162)	O	E	SMR (95% c.i.)	p
Total	49	28,50	1,72 (1,21-2,57)	< 0,01
Total smoker-adjusted	49	47,04	1,04 (0,79-1,41)	n.s.
≤ 25 F/ml year	25	12,80	1,95 (1,17-3,74)	< 0,01
≤ 25 smoker-adjusted	25	19,91	1,26 (0,83-1,95)	n.s.
> 25 F/ml year	24	15,04	1,60 (1,01-2,96)	< 0,05
> 25 smoker-adjusted	24	26,16	0,96 (0,64-1,43)	n.s.

Table III

Crocidolite Exposure of 4 Mesotheliomas (verified by autopsy) and Controls Matched for Sex, Age and Time of First Employment and Duration of Employment

	high	high/medium	medium	negligible	unknown
mesothelioma	xx	x	x		
lung cancer (without asbestosis)		x	x	xx	
non-malignant respiratory disease		x		xx	x
cardiovascular disease	x		xx	x	
alive (1987)			x	xxx	

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CARCINOGENIC, MUTAGENIC AND FIBROGENIC EFFECTS OF FLY ASHES

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ABSTRACT

Studies of working environment in power plants and experimental studies aiming at the determination of the carcinogenic and fibrogenic effects of fly ashes produced during hard coal combustion, were carried on.

Total dusts concentration at workplaces varied between 0.5 and 32 mg/m^3 and respirable fraction concentrations ranged from 0.3 to 0.9 mg/m^3.

The dust contained quartz and mullite, radioactive elements K^{40}, Ra^{226}, Th^{228} trace elements / mainly Ba, Cr, Pb and Zn/, polycyclic aromatic hydrocarbons—benzene—soluble fraction /0.002 μg/mg. Free crystalline silica content was 9.6% and the content of fibrous dusts reached 50 × 10^3 fb/mg. In about 43% of rats, after intraperitoneal administration of 20 mg of dust, cancers, including 2 cases of mesothelioma malignum peritoneum, developed. Statistically significant increase of sister chromatide exchange frequency when compared with the control group, was found by means of SCE test /in vitro/ in human blood lymphocytes, already after the administration of 10 μg/ml of dust.

Fibrogenic effect indices, lung weight and hydroxyproline in lungs were significantly higher than in the control group.

The results obtained indicate that exposure to fly dusts may be associated with the risk of cancer and pneumoconiosis development.

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THE DEPENDENCE OF THE BIOLOGICAL EFFECTS IN RATS ON THE PHYSICAL CHARACTERISTIC VALUES OF INTRATRACHEALLY TESTED DUSTS

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To study the effect of the physical properties of the coal mine dusts on their specific harmfulness, four fractions of different size distributions (B, C, D, E) from four total airborne coal mine dusts (TF 1, TF 3, TF 4 and TF 5) sampled on filters[1] were characterized by means of physical methods in their dispersed state.[2]

Due to the discrepancy of sizes of coal and the different minerals, the composition of the fractions sometimes deviates considerably between each other. For the same dust, the proportion of coal generally tends to increase with particle size while the proportion of ash diminishes. By contrast, particularly in dusts high in minerals the quartz percentage rises with the coarseness of the dust.[1]

50 mg of each dust sample were applicated intratracheally in rats by a single instillation as a suspension in 0.5 ml of saline solution. 12 months after instillation the rats were killed and the total amount of hydroxyproline[3] and lipids[4] as well as the dust mass in lungs and lymph nodes[5] were determined and compared with the physically determined values (Table I).

Table I

Results of the Mineral, Physical and Biochemical Analysis of the Tested Airborne Coal Dust Samples

		1	2	3	4	5	6	7	8	9
TF 1	B	90,8	24,6	1,31	0,50	14,36	10,59	102,22	56	0,4
	C	92,3	19,0	1,70	0,64	17,80	10,49	93,97	49	1,0
	D	91,8	19,4	2,24	0,85	13,70	9,86	90,90	50	1,8
	E	92,6	11,6	3,18	1,21	15,03	9,76	75,86	49	7,9
TF 3	B	23,3	2,4	0,98	0,63	3,72	8,29	86,51	63	0,5
	C	27,8	2,6	1,46	0,92	4,70	8,15	65,56	62	1,3
	D	30,8	2,8	1,81	1,12	4,12	9,15	74,37	51	1,9
TF 4	B	72,1	20,0	1,13	0,53	14,32	8,97	87,34	70	0,4
	C	74,8	19,3	1,38	0,63	12,14	9,71	101,53	58	1,3
	D	77,8	18,3	1,80	0,80	11,31	9,95	98,72	52	2,1
	E	82,8	13,2	2,12	0,91	14,35	9,34	70,47	55	6,4
TF 5	B	81,4	28,9	0,89	0,35	20,11	9,74	102,50	58	1,0
	C	84,2	28,9	1,32	0,56	13,34	9,08	87,32	60	1,6
	D	86,2	25,9	1,87	0,77	10,43	8,74	77,07	48	2,5
	E	89,1	15,4	2,72	1,11	10,70	8,57	61,70	50	7,5

1 = ash content (wt-%), results of IR-spectroscopy (1)
2 = quartz content (wt-%), results of IR spectroscopy (1)
3 = minimum outer surface per volume (m^2/cm^3)
4 = minimum outer surface per mass (m^2/g)
5 = surface structure number
6 = total hydroxiproline (mg/lung)
7 = total lipids (mg/lung)
8 = dust mass in lungs (% of dose)
9 = dust mass in the lymph nodes (% of dose)

The fibrogenity of the applied dusts was dependent only on their surface properties, i.e., on the surface structure number (r_s = 0.66— Figure 1), the total lipids correlated with the minimal outer surface area per mass (r_s = −0.76— Figure 2), the elimination of applicated dust from the lung, and the penetration of dust in the lymph nodes respectivelly were dependent on their minimal outer surface area per volume (r_s = −0.78—Figure 3 and r_s = 0.88—Figure 4).

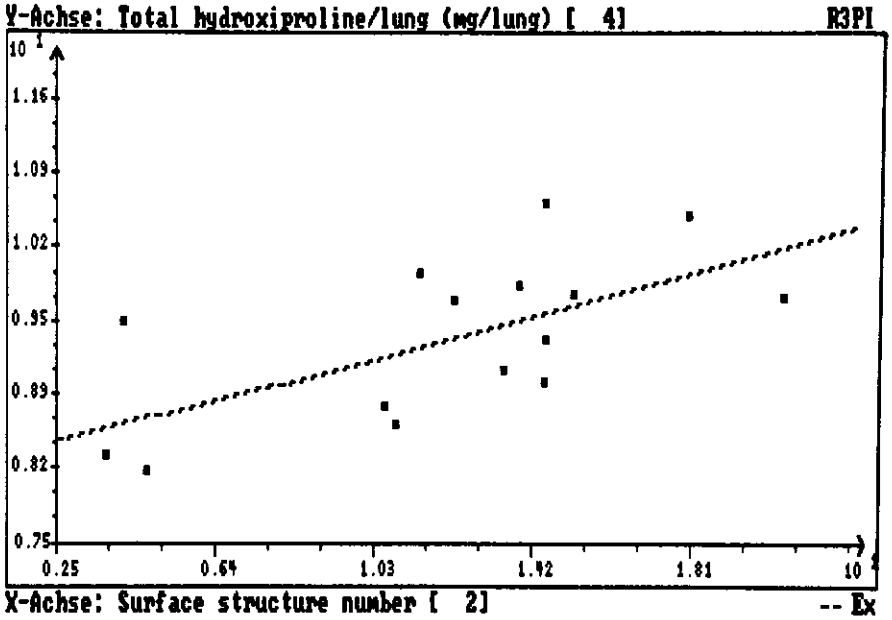

Figure 1. Relationship between the surface structure number and total hydroxyproline (mg/lung).

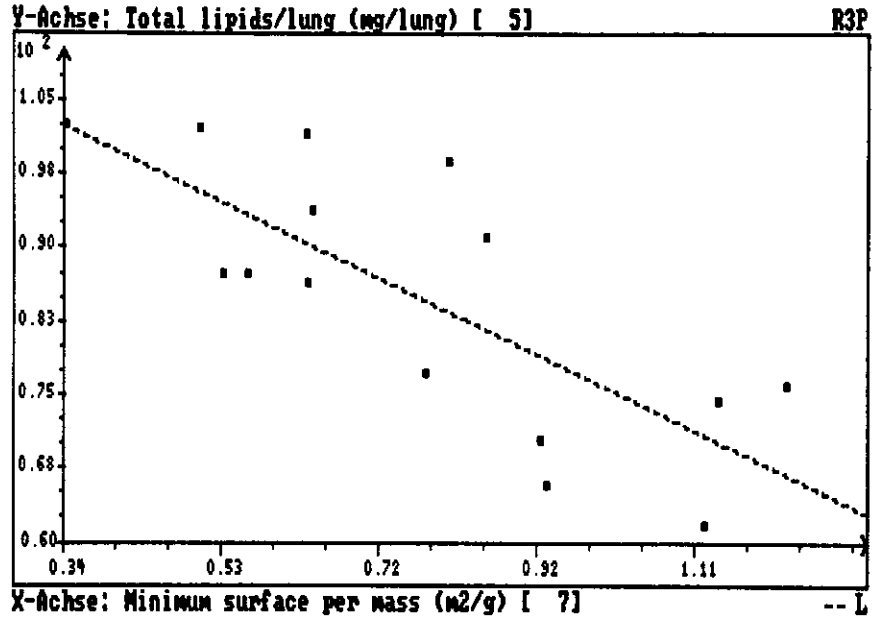

Figure 2. Relationship between the external minimum outer surface per mass (m^2/g) and total lipids (mg/lung).

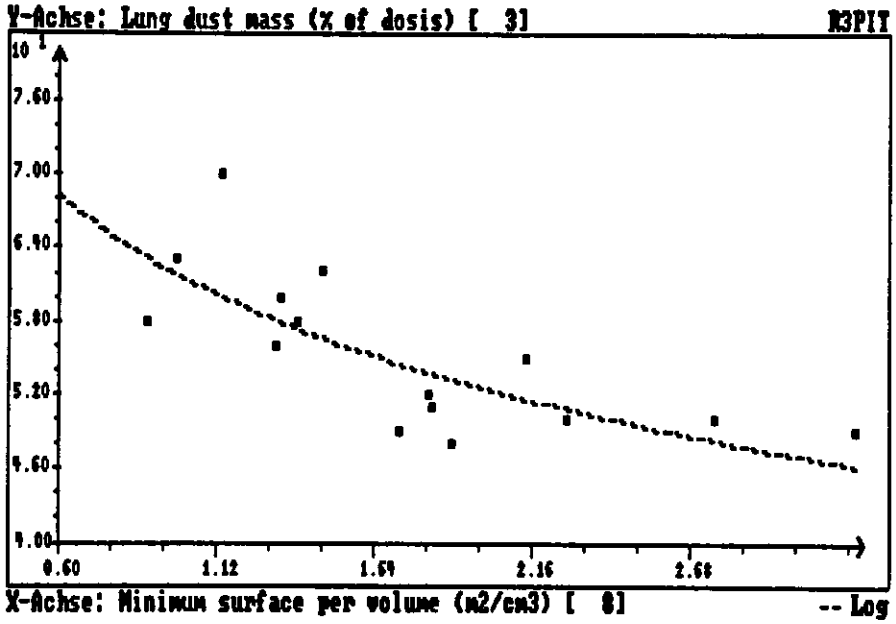

Figure 3. Relationship between external minimum surface per volume (m^2/cm^3) and the dust mass in the lung (% of dose).

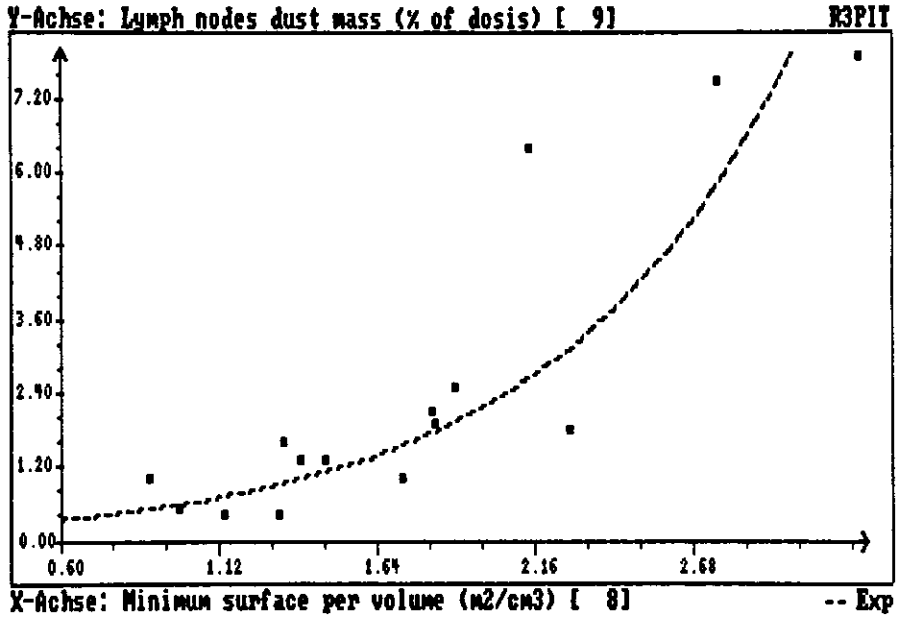

Figure 4. Relationship between external minimum surface per volume (m^2/cm^3) and the dust mass in the lymph nodes (% of dose).

According to the epidemiological studies, the results show that the activity of the surface gives a better indication of the fibrogenity of coal mine dust than the quartz content.

The different penetration rate of airborne coal mine dusts correlated not only with their minimum surface per volume but also with their cytotoxicity.[6] The results demonstrate that the cell cytotoxicity of coal mine dusts does not reflect the fibrogenity of these dusts.

On the other hand, the relationship between the physically determined parameters of tested dusts in their suspended states[7] and the corresponding biological effects were studied in Dörentruper quartz (DQ 12), natural anhydrite, titanium dioxide, McIntyre aluminium, polyvinylpyridine-N-oxide and cadmium sulphide instillated intratracheally separately or in mixture in rats (Table II). 3 months after intratracheally instillations the rats were killed, total hydroxyproline and total lipids were determined (Table II) and compared with the physically determined values in the dispersed states of the tested dusts.

The total hydroxiproline correlated again with the surface properties (i.e. with the coefficient of permeability) of the applicated dusts ($r_s = 0.79$—Figure 5), the total lipids in the lungs with the surface tension of the tested solution ($r_s = -0.87$—Figure 6).

The surface structure number as well as the coefficient of permeability represent the surface quality. The surface structure number represents the activity of the surface between the solid and the gas phase, the coefficient of permeability reflects the state of the surface between the suspension and the gas phase.

The total lipids were dependent on the hypothetical minimum surface per mass and were reflected by the different surface tension of the tested solution respectively. According to the thermodynamic low the surface tension tends to stop the surface of the phase (mass) in minimum it's energetic state and this tendency can be compared with the extrapolation to the minimum value of the surface in the solid matter. Therefore, the lipid effect of the tested dusts was produced by their influence on the surfactant system of the lungs and did not reflect the fibrogenity of dusts.

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Table II

Results of Physical and Biochemical Analysis of the Tested Dust Samples

	1	2	3	4
35 mg anhydrite	5,52	3,4	65	65,2
30 mg titanium dioxide	5,19	3,3	73	59,2
30 mg TiO_2 + 5 mg quartz	5,64	4,8	101	58,2
35 mg anhydrite + 5 mg quartz	5,09	3,3	93	55,2
5 mg Dörentruper quartz	8,78	5,9	192	53,2
2 mg Al + 11 mg quartz	4,20	3,4	115	65,5
11 mg Al + 11 mg quartz	3,95	3,7	152	59,5
20 mg Al + 11 mg quartz	4,40	4,5	178	57,0
50 mg Al + 11 mg quartz	4,35	5,7	153	60,0
2 mg PVNO + 11 mg quartz	3,30	3,5	56	69,5
11 mg PVNO + 11 mg quartz	3,90	4,1	56	70,0
2 mg PVNO + 20 mg CdS	5,50	5,7	59	70,0
11 mg PVNO + 20 mg CdS	5,55	6,2	59	69,0
20 mg PVNO + 20 mg CdS	5,70	6,5	60	69,5
control		3,3	41	71,2

1 = coefficient of permeability (joule/cm^2sec.10^{-6})
2 = total hydroxiproline (mg/lung)
3 = total lipids (mg/lung)
4 = surface tension (erg/cm^2)

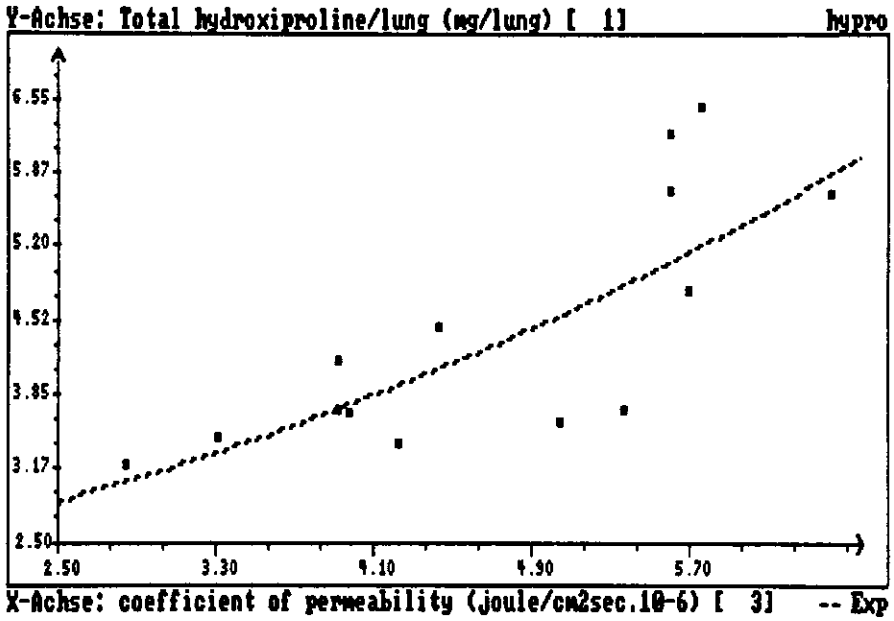

Figure 5. Relationship between the coefficient of permeability (joule/cm^2 sec • 10^{-6}) and total hydroxiproline (mg/lung).

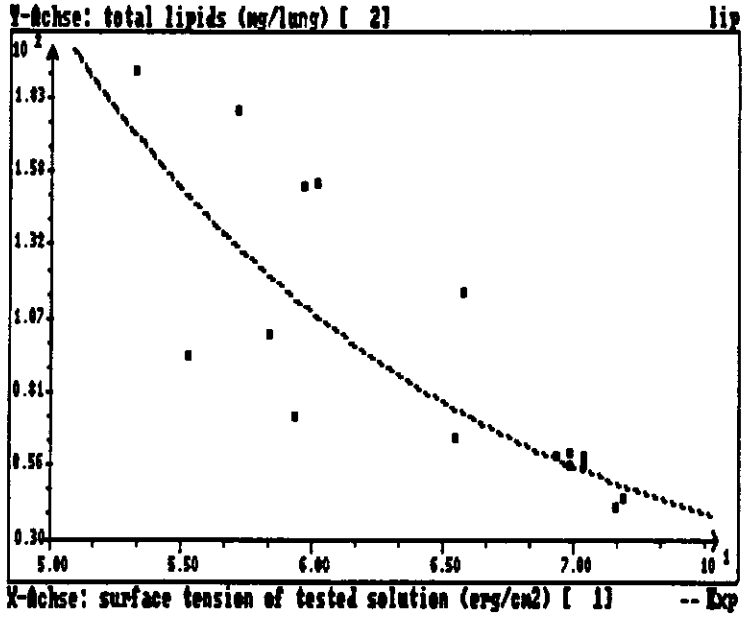

Figure 6. Relationship between the surface tension of tested solution (erg/cm^2) and total lipids (mg/lung).

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A STUDY ON CHANGE OF TYPE I AND III COLLAGEN DURING FIBROSIS INDUCED BY SILICA AND WELDING FUME DUST

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ABSTRACT

ELISA method was used to study the quantity and distribution of type I and III collagen in lungs of rats induced by silica and welding fume dust. The ratio of I/III collagen was obtained and tested for evaluation of the degree of fibrosis. On the 10th day after instillation of silica, I/III collagen ratio was lower than normal. After 20 days, it increased significantly and stayed at constant level since then. Similar type change of collagen was also observed from histological specimens. Increase of Type III collagen appeared in the early stage of fibrosis and Type I collagen increased more rapidly in the later stage.

In lungs of rats instilled with welding fume dust, Type III collagen increased predominantly until 180 days after instillation, while significant increase of Type I collagen was observed not until after 180 days. It induced a slower and milder fibrosis in the lung. Ratio of Type I/III collagen contents can be used to evaluate the degree of fibrosis.

INTRODUCTION

The main characteristic of lung fibrosis is massive increase of interstitial collagen in the lung. The study of type change of lung collagen may be helpful to understand the process of fibrosis. In this study, ELISA method was applied to determine the contents and distribution of Type I and III collagen. The ratio of these two kinds of collagen was tested for evaluation of degree of fibrosis induced by silica and welding fume dust.

MATERIALS AND METHODS

1. Rats

   Female Wistar rats were used. Body weights were about 200 g.

2. Dusts

   a. Quartz 95% of quartz with particle sizes smaller than 5 μm. Free silica content was about 97%. 50 mg of quartz were instilled to each rat intratracheally.
   b. Welding fume dust (Ji-507) 95% of the welding fume dust particles were smaller than 5 μm. Dosage of dust for each rat was 50 mg.

3. Preparation of Type I and III collagen and their antibodies. The procedures were the same as described in Reference 1.

4. Method for determination of Type I and III collagen content in the lung. Rat lungs were dipped in acetone for 2 days, then dried and pulverized. To 25 mg of the dried lung powder, 5 ml of 0.5 mol acetic acid containing 5 ml of pepsin solution (2 mg/ml) were added and collagens were extracted for 24 hrs. The supernatants obtained after centrifugation were used for determination of Type I or III collagen contents with ELISA method.

5. Histological study of distribution of Type I and III collagen in the lung. Lung tissue slices were soaked in 1% peroxidate solution to inhibit the intrinsic peroxidase activity. After rinsing with saline, they were covered with collagen antiserum (Type I or III) and incubated at 37°C for 1 hr. Rinsed with phosphate buffered saline (PBS). The slices were then covered with hydrogen peroxidase labelled IgG at 37°C for 30 min. Washed with PBS again. The slices were dried, dehydrated and fixed and then were observed under the microscope to study the distribution of Type I and III collagen and their relative contents were determined by microscopic specrophotometric analysis.

RESULTS

1. Changes of Type I and III collagen in silicotic rat lung.

   The contents of Type I and III collagen in silicotic rat lung were both increased continuously as the time prolonged after dusting. At 10 days after dusting the ratio was about 2 and kept at constant level until 90 days after dusting (Figure 1, Table I). Histological study of collagen fibers in the slices showed that after dusting, the alveolar septa and lung interstitial were all expanded and accumulated with Type I and III collagen. At 10 days after dusting with silica, there was mainly Type III collagen appearing in the lung, while at 20 days, there was mainly type I collagen present in the lung (Figure 1). This indicated that Type III collagen increased predominantly at early stage of silicosis and Type I collagen increased predominantly at later stage of silicosis.

Table I
Change of Type I and III Collagen Contents in Lungs of Silicotic Rats

Group	Days after dusting	Collagen content (mg/g protein)		I/III Ratio
		Type I	TypeIII	
Normal	-- (6)	38.9 + 6.2	28.2 + 4.6	1.38
Silicotic	10 (6)	48.4 + 10.3	54.6 + 2.7**	0.89
	20 (6)	172.6 + 66.7**	67.6 + 22.5*	2.55
	30 (6)	239.5 + 109.7*	113.8 + 26.8**	2.10
	60 (6)	291.0 + 92.1**	145.1 + 54.3**	2.10
	90 (6)	353.8 + 111.4**	177.6 + 29.4**	1.99

* $P < 0.01$, compared with the normal control
** $P < 0.001$, compared with the normal control
( ) Number of rats indicated in the parenthesis

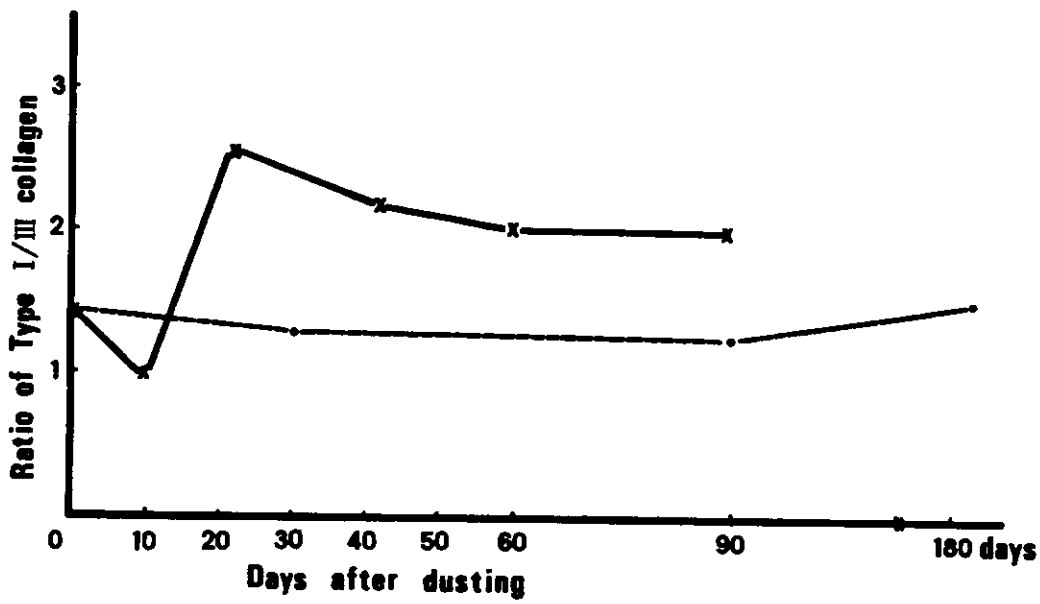

Figure 1. Ratio of Type I/III collagen in rat lung after dusting.
——— Silica
------ Welding fume dust

2. Change of Type I and III collagen in lungs of rats instilled with welding fume dust.

   At 30 days after installation with welding fume dust, the content of Type III collagen increased significantly, but significant increase of Type I collagen was not observed until 180 days after dusting (Table II). The ratios of I/III collagen in the lung decreased gradually within 90 days and were raised to nearly normal level at 180 days (Figure 1). The results showed that this kind of welding fume dust induced a slower and milder lung fibrosis as compared to silicosis. Histological observation confirmed this results (Figure 3).

DISCUSSION

The increase of lung collagen was usually expressed by increase of hydroxyproline. In this paper, we used ELISA method to determine both Type I and Type III collagen. The privilege of this method is that collagen contents and change of type of collagen in the fibrotic process can be determined directly. Through comparison of Type I/III collagen ratio, the fibrogenic ability of various dusts can be demonstrated. By ELISA staining method the distribution of Type I or III collagen in the lung can be observed, while all other methods do not differentiate the collage types.

Table II

Change of Type I and III Collagen Contents in Rats Lung Instilled with Welding Fume Dust

Group	Days after dusting	Collagen content (mg/g protein)		I/III Ratio
		Type I	Type III	
Normal	-- (6)	38.9 + 6.2	28.1 + 4.63	1.38
Silicotic	30 (6)	48.1 + 6.6	38.4 + 5.4 **	1.25
	90 (6)	40.0 + 2.7	35.2 + 2.6 *	1.13
	180 (6)	69.0 + 21.5 *	48.9 + 8.2 **	1.41

* $P < 0.05$, compared with the normal control

** $P < 0.01$, compared with the normal control

( ) Number of rats indicated in the parenthesis

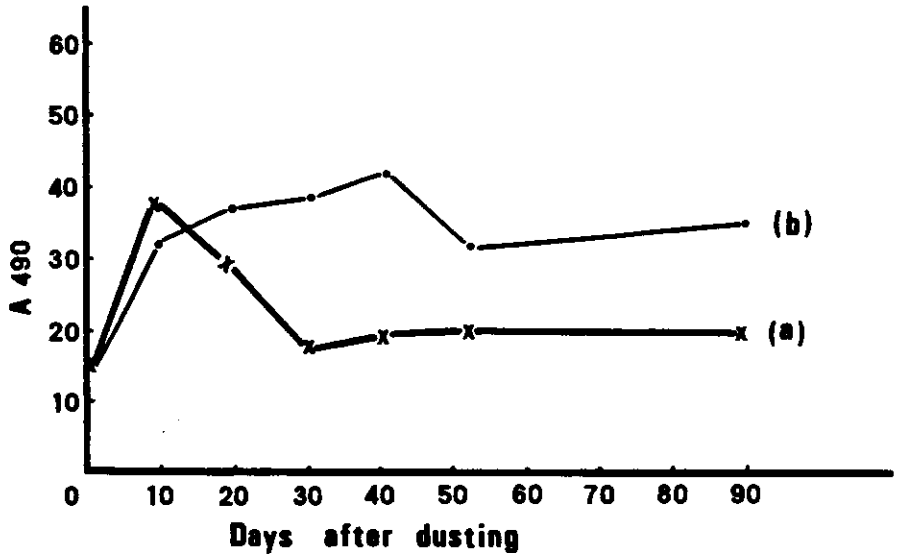

Figure 2. Microscopic spectrophotometric analysis of silicotic lung slices stained with ELISA method.
a. Type III collagen, b. Type I collagen

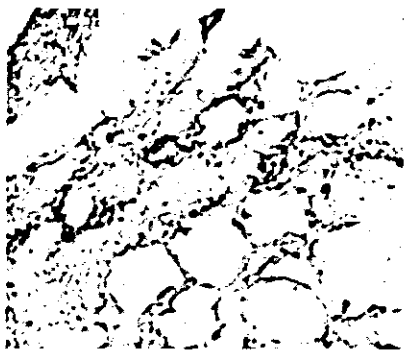

Figure 3. ELISA staining of normal lung (collagen Type I).

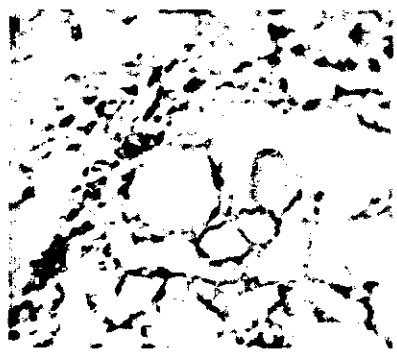

Figure 4. ELISA staining of normal lung (collagen Type III).

Figure 5. ELISA staining of SiO_2 dusting lung (1 month, collagen Type I).

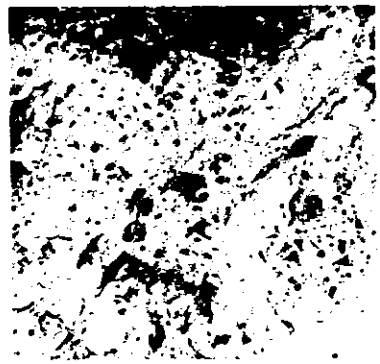

Figure 7. Welding fume dust lung specimen (ELISA staining, 3 month, collagen Type I).

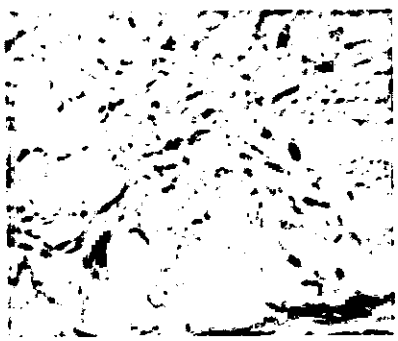

Figure 6. ELISA staining of SiO_2 dusting lung (1 month, collagen Type III).

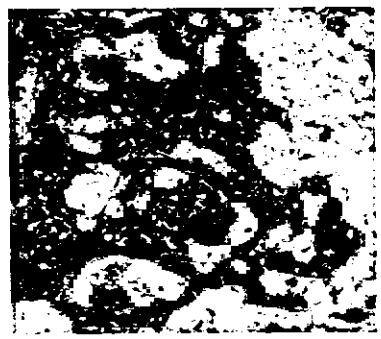

Figure 8. Welding fume dust lung specimen (ELISA staining, 3 month, collagen Type III).

Reiser[2] in his study reported that I/III ratio was constant during silicosis, but in our study, a sharp decrease of I/III ratio on 10th day after dusting and an obvious increase on the 20th day were observed which indicated that Type III collagen increased predominantly in the early stage of fibrosis. This fact is similar to those reported by Ganesh[3] in the study of adult respiratory distress syndrome.

Comparison of I/III ratio between rat lung dusted with silica and welding fume dust showed that the difference was significant. The ratio of I/III for welding fume dust was lower, the type change was not so obvious as those in silicotic fibrosis. It proved that I/III ratio can be used for evaluation of fibrogenicity of dusts.

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THE DEPOSITION OF FIBERS AND SPHERES AT THE CARINA IN EXCISED LUNGS

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INTRODUCTION

The deposition of dusts in a respiratory system is a function of the airflow characteristics and the aerodynamic behavior of the particles within the system. The deposition of spheres in the human respiratory track has been studied both empirically and theoretically.[1] Thus, several models exists for the deposition of compact particles in regions of the respiratory system. However, the information on the deposition of fibers is relatively lacking. The correspondence of the mathematical models available to predict the deposition of fibers in the human respiratory tract to the deposition models for compact particles suffer due to the limited empirical knowledge of fiber deposition available. Studying the comparative deposition of fibers and spheres at the carina can provide valuable insight into the deposition of fibers in the tracheo bronchial system. The aim of this study was to investigate the comparative deposition of fibers and spheres at the carina experimentally.

EXPERIMENTAL METHODS

The basic principle of the experimental method is the assimilation of the natural breathing in an excised calf lung. To accomplish this end, the excised lungs were caused to inspire and expire by varying the pressure around them by placing them into a variable pressure apparatus consisting of a sealed chamber connected to a respiration pump. The pump controlled both the breathing rate and the tidal volume by systematically withdrawing and replacing air from the chamber housing. On inspiration the resultant decrease in pressure around the lung caused it to expand until the intra alveolar pressure equilibrated with the new pressure in the chamber. The pumps full cycle was complete when the withdrawn air was replaced returning the chamber to its original atmospheric pressure. Every experiment utilized 15 respirations per minute. Typically, the tidal volumes generated were between 400–500 cc.

Nearly monodisperse, size classified glass spheres and glass fibers prepared by using the method described by Esmen et al.[2] were used as the deposition material. The dust generator used in this experiment consisted of a dust reservoir, a clapper, and tubular delivery system. Before reaching the trachea air the stream was split in two by a copper bifurcation to provide for a sampling port. The sampling port was used to measure the airborne concentration of the particles during each experiment. This sampling rate was equal to the lung's tidal volume and was drawn simultaneously with lung inspiration.

The 29 pneumonia free calf lungs used in this experiment were obtained at the time of slaughter. After carefully excising the lung carcass, the surrounding tissues and organs were removed. The lung surface was rinsed and inspected for cuts and rips and the lungs were kept moist until the end of the experiment. In the final preparation, the trachea was cut about 18 cm above the carina and two ring clamps were placed on the trachea just above the right apical bronchi. An artificial tracheal extension was inserted into the trachea and secured by the ring clamps. The entire preparation was seated inside the variable pressure unit with the artificial trachea passing through a hole in the top of the chamber connected a leg of copper bifurcation. The lung, inspiring and expiring with the changes in chamber pressure was connected to a spirometer. The tidal volume was monitored for 3–5 minutes. The tidal volume usually stabilized within 1–2 minutes. The dust generator was started and synchronized such that a clap on the dust reservoir occurred simultaneously with the onset of inspiration. The exposure was about 20 minutes.

The experimental section was separated from the rest of the lung by carefully cutting away the surrounding parenchymal tissues and then cutting the bronchi about one inch distal to the carina. This portion was carefully cleaned of adhering fat and parenchymal tissue and frozen. In order to minimize particle translocation, all subsequent cutting was performed on the frozen tissue. The trachea was sliced into two sections for analysis of deposited particles. The first slice was made just under the right apical bronchi. The second section which included the carina was taken after slicing 1.5 cm posterior to the carinal plane. The removal of the particles from the tissue was achieved by sonication and subsequent ashing. The ashed material was redeposited on a filter for analysis. The filters were viewed under cross polarization. If the total number of spheres or fibers deposited on the filter was less than about 2000, then the entire filter was viewed and all particles counted. Generally, an analysis of 1 cm^2 was sufficient. Some of the particles were lost during the transfer and processing operations. A calibration was performed to delineate the lost fraction.

RESULTS AND DISCUSSION

A list of the experimental parameters are presented in Table

Table I

The Experimental Conditions and Parameters

Lung	Size			Tidal Volume	Tracheal Velocity	Stokes' Number(*)	
	Sphere Dia.	Fiber Dia.	Length				
	um	um	um	liter	cm/sec	Sphere	Fiber
12	24.5	10.9	50	0.330	34	0.126	0.054
13	24.5	10.9	50	0.355	36	0.133	0.057
15	24.5	10.9	50	0.355	55	0.232	0.104
16	24.5	10.9	50	0.330	77	0.396	0.185
17	24.5	10.9	50	0.380	55	0.243	0.104
18	24.5	10.9	50	0.430	68	0.315	0.134
19	24.5	10.9	50	0.330	93	0.574	0.245
21	24.5	10.9	50	0.380	45	0.181	0.082
22	24.5	10.9	50	0.430	72	0.333	0.146
30	12.5	6.4	48	0.400	58	0.063	0.051
32	12.5	6.4	48	0.475	134	0.202	0.164
34	12.5	6.4	48	0.550	103	0.124	0.101
36	12.5	6.4	48	0.575	87	0.095	0.078
38	12.5	6.4	48	0.500	98	0.124	0.101
39	12.5	6.4	48	0.525	111	0.141	0.115
40	12.5	6.4	48	0.475	65	0.068	0.055
41	17.2	9.1	50	0.505	85	0.199	0.143
42	17.2	9.1	50	0.565	111	0.282	0.202
43	17.2	9.1	50	0.485	58	0.110	0.079
44	17.2	9.1	50	0.500	69	0.143	0.103
45	17.2	9.1	50	0.505	82	0.187	0.134
46	17.2	9.1	50	0.525	70	0.128	0.092
47	17.2	9.1	50	0.555	88	0.183	0.131
48	17.2	9.1	50	0.570	101	0.243	0.174
49	17.2	9.1	50	0.525	81	0.176	0.126
50	17.2	9.1	50	0.525	92	0.210	0.151
51	17.2	9.1	50	0.515	86	0.196	0.141
55	12.5	6.4	48	0.560	123	0.165	0.134
56	12.5	6.4	48	0.575	96	0.119	0.097

(*) The Stokes' numbers for the fiber diameters Df and aspect ratio B is calculated by the use of impactive diameter Di using the formula (3):

$$Di = Df\,(1+0.013(\ln B)^3\,(0.71 + 0.91 \ln B)^{1/2}$$

calculated using impaction diameter formulation developed by Burke and Esmen.[3] The graphical representation of the deposition efficiency as a function of tracheal velocity for the lowest group of Stokes' number particles is shown in Figure 1. These results indicate that a consistent deposition occurs at low velocities; seemingly independent of the velocity. This may be explained by theory developed by Harris,[4] who predicted such an effect would occur due to interception. As the tracheal velocity increases, the slope of the curve changes rapidly, indicating that a critical point was reached permitting the impaction to facilitate deposition rapidly.

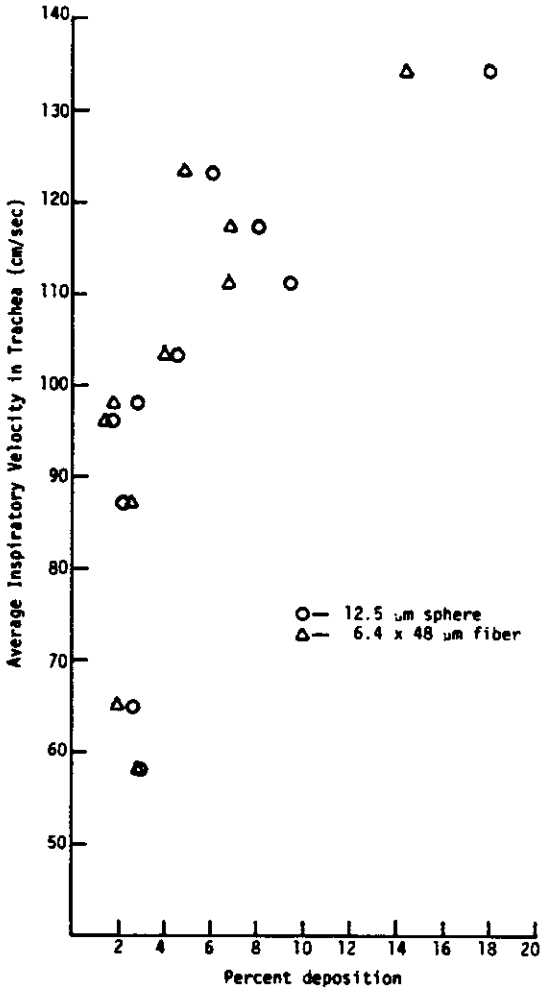

Figure 1. Deposition of fibers and spheres as influenced by inspiratory velocity.

The critical point was investigated by incorporating the air flow characteristics with particle physical parameters and observing the depositional efficiencies as a function of Stokes number. Such a graph of all results is provided in Figure 2. In this figure, data of impactive deposition as observed by Johnston and Muir[5] and Landahl and Herrmann[6] are also included.

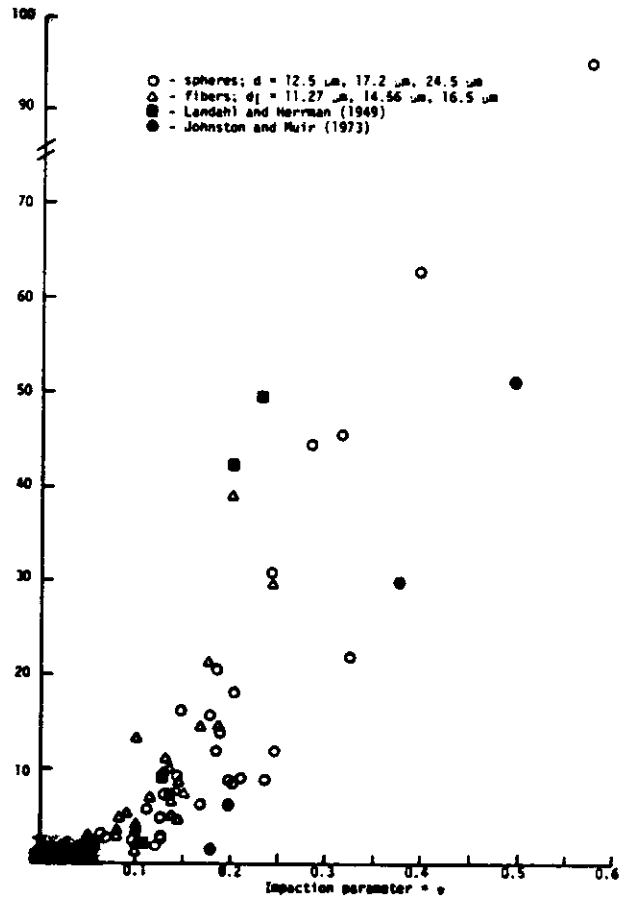

Figure 2. Deposition of fibers and spheres as a function of Stokes' number.

Clearly, during the experiments, impaction was occurring simultaneously with particle removal by other mechanisms. By the use of current theories, estimates of depositional efficiency due to the other mechanisms may be made. Harris noted that interception is an effective removal mechanism in the tracheobronchial region for fibers as small as 10 μm in length. If interception were significant in these experiments then one would expect a uniform shift to the left on the deposition curve (Figures 1 and 2); because, the amount removed would be independent of all parameters except airway and particle size. The results shown in Figure 1 suggests that the interception would account for 2–4 percent deposition.

Similarly, if sedimentation were a significant mode of particle removal the shift would not be uniform. Rather it would be biased in favor of those experiments involving large particle sizes and low average tracheal velocities. Review of the data does not provide any evidence of such bias. Harris' equation for settling in turbulent flow suggests that only 2 percent of the largest fibers which experienced the lowest average tracheal velocity would settle at the carina.[4]

If the impaction efficiency for round jets impinging upon an impaction surface perpendicular to the flow axis is taken to be 0.5 for Stokes' number about 0.25,[7] then the results suggest that the impaction efficiency observed is significantly less than what would be expected. In fact a recent theoretical work on impactive deposition of fibers this deviation was also noted.[8] There is strong evidence indicating that interception, and sedimentation may be augmented by secondary flow patterns that develop downstream from a bifurcation. Schroter and Sudlow[9] identified these flows as occurring both on inspiration and expiration. On inspiration a pair of vortices develop in each daughter branch. They are strong enough to complete one helical cycle within three diameters downstream. Under this condition, by the rotation of the fibers, the impaction efficiency is expected to drop significantly. In the experiments reported here, the enhancement of interception and sedimentation is not expected to play an important role, since the contribution of these mechanisms to deposition is relatively low. In contrast any change in the impaction efficiency would be fully reflected on the observations. In addition to the secondary flows developed during inhalation, on expiration a set of four vortices are generated in the parent airway ahead of the bifurcation. The effect of this air pattern on deposition has not been investigated. However, it is reasonable to assume that, using the rationale suggested for the secondary airflow patterns which develop on inspiration, deposition would be further enhanced by interception and sedimentation, and further diminished by impaction. It should be noted that no attempt was made to control the branching angle of the bronchi in this study. The angle is fixed by the rigid cartilaginous structure for the first 0.5–1.0 cm from the carinal ridge. Estimates of the branching angle in these calf lungs appeared to correlate well with reported branching angles in the human lung. Thus the use of the Stokes' number for fibers and compact particles in the estimation of impactive deposition in the human lung should be reasonable.

CONCLUSIONS

Mathematical modeling, animal exposure, airway simulator and human exposure experiments have been employed to predict the deposition of compact particles in the human respiratory system. The depositional probabilities of spheres is modeled by relation to an associated aerodynamic equivalent diameter with reasonable accuracy. In the estimation of impaction potential fibers, Figure 3 suggests that there is no discernible difference in the deposition of fibers and spheres as a function of Stokes number when the actual diameter is employed for the spheres and the empirical impaction diameter is employed for the fibers.

This implies that not only can the impaction diameter be employed as a viable predictor of impaction, but one may estimate the series of fiber parameters that comprise the smallest fibers removable in the lung by this mechanism. That is to say that for every fiber diameter there will correspond a length that will represent the smallest fiber of that diameter that will be removed by impaction early on.

Weibel[10] has provided an exhaustive description of lung architecture developed from airway casts. Using his information and assuming that given a particle size, shape and density impaction is governed only by the airway radius and average conveyance velocity, an impaction index may be calculated as a ratio of the average velocity to airway radius. Such an impaction index for the first ten generations of human respiratory tract with liter/sec airflow is given in Table II. Clearly this potential reaches its maximum in the third through sixth generation with the fifth generation theoretically possessing the largest capability. We may visualize the first five generations as successive impaction stages, each stage being capable of removing successively smaller particle sizes. The lower limit of removal by this mechanism is then related to the 5 characteristics of the final stage. For instance, a unit density fiber 4.4 μm in diameter

Table II

Impaction Index for the First Ten Generations in the Human Lung

Generation	Velocity	Radius	Impaction Index
	cm/sec	cm	1/sec
0 (trachea)	393	0.900	437
1	427	0.610	700
2	462	0.415	1113
3	507	0.280	1810
4	392	0.225	1742
5	325	0.175	1857
6	254	0.140	1814
7	188	0.115	1634
8	144	0.093	1548
9	105	0.077	1364
10	74	0.065	1138

would have to be almost 90 μm long to afford complete removal. The fiber size parameters decrease with an increase in the tidal volume. Thus, at a 1450 cc tidal volume, the fiber would only have to possess an impaction diameter of 10.2 μm. This criteria would be satisfied by a unit density fiber 4.1 μm in diameter and 82 μm in length. If we further assume a fiber to have a density equal to 2.5 gm/cc (asbestos or fiberglass), the lower size limit for impaction in the lung (T.V. = 1450 cc) becomes a 3.6 × 29 μm fiber. Gross et al.[11] has observed that fibers present in the lungs of fibrous glass workers at autopsy are rarely in excess of 3.5 μm in diameter with an average length of 27 μm. This suggests that impaction initially prescreens those fiber sizes within the first six or so generations effectively and those fibers which pass this prescreening are then available for removal by sedimentation, diffusion and interception in the finer airways.

The method presented for studying particle deposition at the carina in excised lungs can be utilized to investigate the influence of sedimentation, interception and diffusion on fiber removal. Altering the physical properties of the particles and/or the tracheal velocities should provide suitable conditions to derive empirical relationships defining the interplay of particle and airflow characteristics and removal efficiencies via these other deposition mechanisms. For example, by choosing several large fiber sizes of equal impactive potential but of dramatically different length, the deposition enhancement by interception may be investigated.

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THE PULMONARY TOXICITY OF MIXED DUST IS NOT ONLY RELATED TO ITS MINERALOGICAL COMPOSITION

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INTRODUCTION

Studying the relationships between the physico-chemical characteristics of some dust particles and the activity that these particles may exhibit when in contact with various biological systems is a fascinating area of research. Our understanding of the question, however, is quite limited. We know that exposure to asbestos dust may lead to asbestosis, free silica to silicosis and coal mine dust to coal worker pneumoconiosis. But we do not know which parameter at the level of the particles will trigger the relevant biological mechanisms. Several hypotheses have been made, but no satisfactory theory has emerged from the many studies on the subject.

The problem is even more complicated when dealing with mixed dust, such as coal mine dust. In addition to coal from various rank, coal mine dust generally contains free silica and clay minerals. Each component may play a role in the pathogenesis of the disease. For example, studies in rats by inhalation and intratracheal injection revealed that quartz in coal mine dust exhibited less activity than expected.[8] This phenomenon was attributed to the release of aluminum from clay minerals present, especially from illite.[6] It led to the hypothesis that the biological activity of quartz in mixed dust was depending to the ability for accompanying minerals to mask the potential toxicity of quartz.[6,7,10] The toxicity of coal mine dust would more depend on the overall mineralogical composition rather than on the quartz content alone.[12,9]

In order to explore this hypothesis, we tested in the rat two samples of coal dust having the same bulk mineralogical composition in terms of coal, quartz, illite and kaolin. They did not exhibit the same pulmonary activity.

METHODS

Sample #1 was obtained by finely grinding some coal materials extracted from the Aumance coal mine in France. The final product contained 35% coal, 17% quartz, 31% illite and 17% kaolin. Mineralogical determinations were made using a combination of X-ray diffraction and infrared spectroscopy. Sample #2 was a reconstituted mixture of fine particles of "pure" coal and minerals from other origin (illite from Le Puy, kaolin from Cornwall and quartz from Madagascar). The two samples had the same final mineralogical composition by weight. Particles in each sample were examined by Analytical Transmission Electron Microscopy (ATEM) and their number size distributions were established.

Three groups of 40 female Wistar rats were used for this study. Each animal in the exposed groups received a single intratracheal injection of 60 mg of fine particles suspended in 1 ml of saline. Some animals were killed 12 and 24 months later.

The lungs and the tracheobronchial lymph nodes were removed and weighed. Left lobes were used for histopathological examination and ATEM analysis of retained dust particles. Left lobes were perfused under 25 cm H_2O pressure and fixed in 10% neutral buffered formalin. Sections stained by hematoxylin eosine and Picrosirius were examined at three different locations under crossed polaroid filters.[5] The intensity and profusion of the lesions were scored, each on a 0–4 scale. Criteria used for intensity grading are indicated in Table I. A final histopathological score was obtained by multiplying the intensity score and the profusion score.[1] Lung tissue was then extracted from the remaining block by dewaxing in hot toluene. After digestion of the tissue in sodium hypochlorite, retained particles were concentrated by filtration on Polycarbonate membrane and analysed by ATEM.

For each group, right lungs and remaining tissue fragments not used for histology were dried and pooled. The pool was analysed for collagen by the method of Stegeman,[13] for total dust by the formamide method of Thomas,[14] for quartz by X-ray diffraction and for total Al in dust by X-ray fluorescence.

Similar methods were used to prepare and analyse lymph nodes.

RESULTS

For exposed animals, mean weight of fresh lung and mean collagen content of the lung were both above corresponding control values (Table II). The highest figures were measured at month 24 in the group of animals injected with the reconstituted mixture. In particular, the collagen content of the lung was more than three times higher with the reconstituted mixture than with the Aumance coal dust.

No histological changes were noticed in the lung of control animals, but lesions were present in the lung of exposed animals. Histopathological scores are presented in Figure 2.

Table I

Criteria Used for Scoring Intensity of Lung Lesions

Grade 0	Normal histology.
Grade 1	Focal accumulation of dust-laden macrophages without any fibrotic organisation.
Grade 2	Early fibrotic organisation with few thin collagen III fibers peripheraly to the granulomas, or intersperced throughout (green color with Picrosirius stain under cross polaroid filters).
Grade 3	Fibrotic organisation of the granulomas, with thick bundles of collagen I, in addition to collagen III (yellow orange or red color with Picrosirius stain).
Grade 4	Massive fibrotic reaction located around the main bronchus and vessels.

Table II

Weight of Fresh Lung, Weight of Lymph Nodes and Pulmonary Collagen

Month 12			Month 24		
Controls	Aumance	Mixture	Controls	Aumance	Mixture
Mean weight of fresh lungs (g/rat)					
1.3	1.8	1.8	1.3	2.1	3.6
Mean weight of lymph nodes (mg)					
--	0.08	0.28	--	0.36	1.1
Mean collagen content of the lung (mg/rat)					
29.4	47.5	52.8	31.3	52.5	167.3

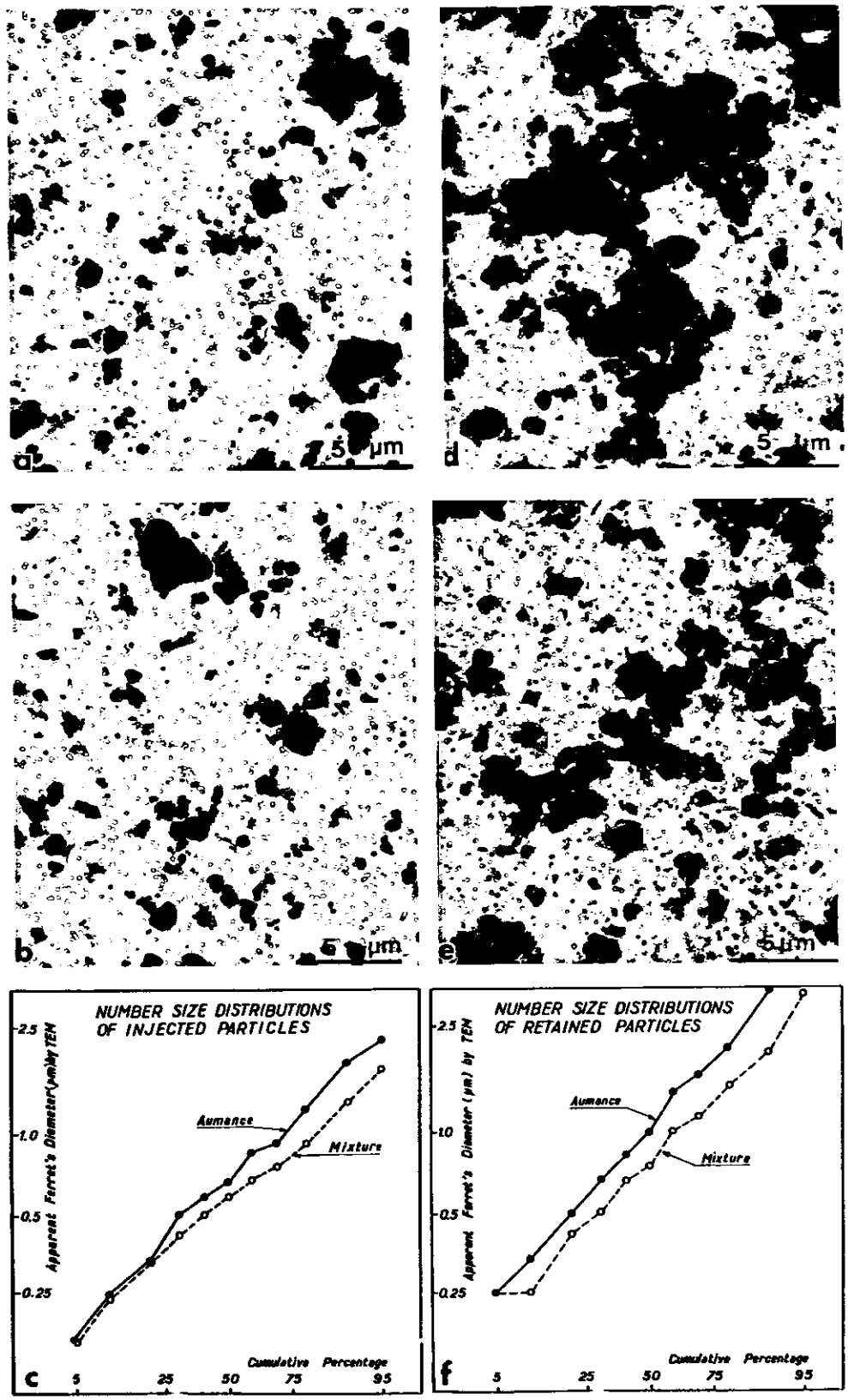

Figure 1. Analysis by transmission electron microscopy of dust particles injected, and extracted from the lung at month 24.

a. Aumance, particles injected
b. Mixture, particles injected
c. Number size distribution of injected particles
d. Aumance, particles retained in the lung
e. Mixture, particles retained in the lung
f. Number size distribution of particles retained in the lungs

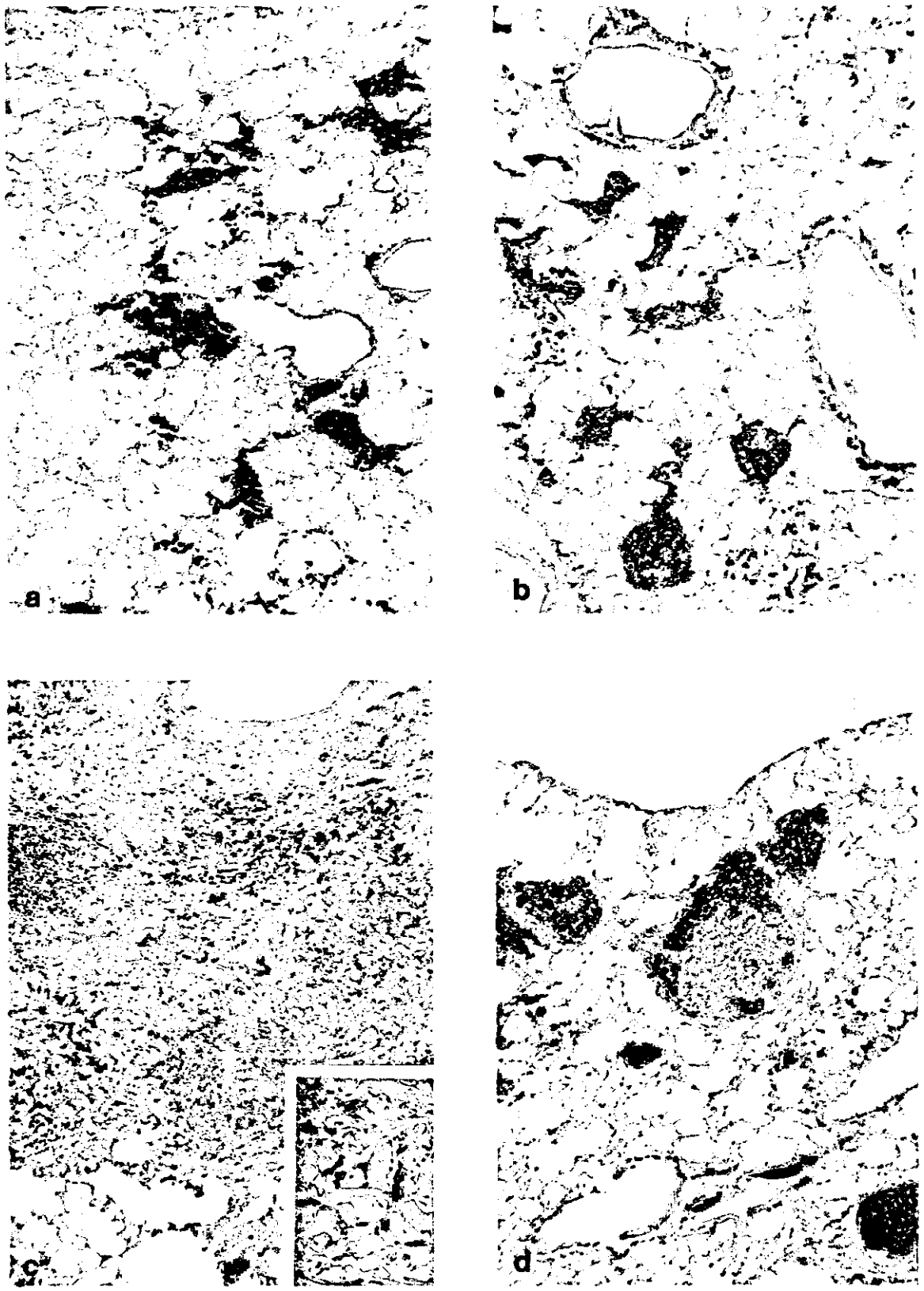

Figure 2. Histological changes of the lungs (HEX50). Note the slight progressive fibrotic reaction between 12 (a) and 24 months (b) for Aumance. Exposure to reconstituted mixture yielded at month 24 fibrotic nodules sparse in the lung (c) and massive fibrotic reaction (see collagen bundles in insert) around the main bronchus and vessels (d).

In each exposed group, the mean score was significantly higher at month 24. At this date, histopathological changes were significantly more pronounced with the reconstituted mixture. At month 12, pulmonary lesions were quite similar in the two groups but the fibrotic reaction of the tracheobronchial lymph nodes was much more intense with the mixture.

Mineral contents of the pooled lung tissue and lymph nodes are reported in Table III. A very high proportion of the injected dust was still present in the lung at month 12 and at month 24. Figures for total dust, quartz and Aluminum were systematically higher in the Aumance group. Quartz accounted for 17% of the injected dust, but overall, the proportions of quartz in the lung dust were less. At month 12, proportions of quartz and proportions of Aluminum in the lung dusts did not differ between the two exposure groups. The lung dusts were richer in quartz at month 24. The quartz contents of tracheobronchial lymph nodes were quite similar in both groups (Table III).

ATEM analysis of dust used for injection indicated the presence of very fine particles in both samples. Most of the particles observed by ATEM were less than 2.5 μm in apparent Ferret's diameter. The number size distributions were similar in the two samples, although the particles were somewhat finer in the mixture (Figure 1). Particles extracted from the lung at month 24 were either isolated or grouped into large agglomerates. Such agglomerates were not detected in the injected dust.

Detailed mineralogical analysis of the lung dust by ATEM is still in progress. Preliminary observations suggest that the clay contents of the lung were different for the two groups, with apparently more illite retained at month 24 by animals exposed to the Aumance dust.

DISCUSSION

The model used was able to produce a fibrotic reaction progressing over the two years of the experiment, and to document different activities of the two dust samples tested.

These experiments illustrate once more how complex are the mechanisms of biological action of mixed dust. The two mixed dust samples with the same bulk mineralogical composition yielded different fibrotic pulmonary responses.

Table III

Mineral Content of the Lung and of the Tracheobronchial Lymph Nodes

Month 12		Month 24	
Aumance	Mixture	Aumance	Mixture
Total mineral dust in the lung (mg/rat)			
47.8	35.5	41.7	35.5
Quartz in the lung (mg/rat)			
5.6	4.2	7.4	4.9
Percentage of quartz in lung dust			
11.7	11.8	17.7	13.8
Aluminum in lung dust (mg/rat)			
1.8	1.3	2.5	1.1
Percentage of Aluminum in lung dust			
3.7	3.7	5.9	3.1
Quartz in the lymph nodes (mg)			
1.0	1.4	1.5	1.5

The bulk analysis of lung dust did not provide any convincing explanation for this difference. May be that the microscopical analysis in progress will bring interesting information. It is conceivable that the particles be differently assembled in the natural and in the reconstituted dust. Preliminary observations of clays in lung dust do support this hypothesis. Surface analysis of injected and retained dust may also be informative.[3]

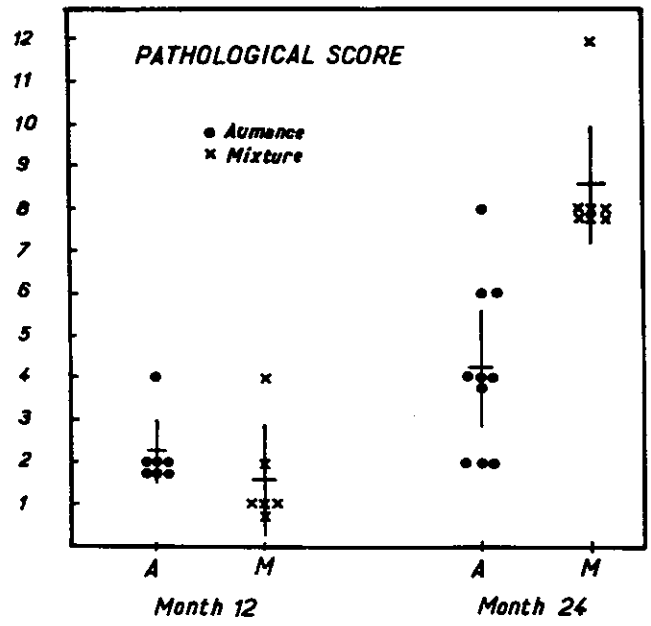

Figure 3. Pathological scores (see text for explanation) at month 12 and month 24 for the two groups of exposed animals.

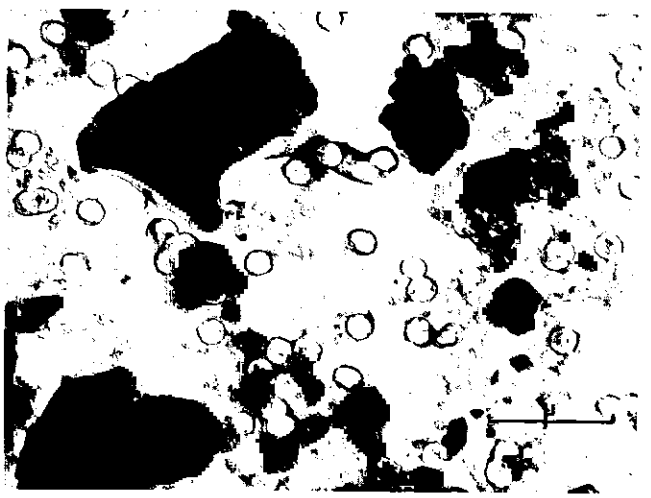

Figure 4. Morphological features of dust extracted from animals exposed to the Aumance coal dust. Note the presence of disolving illite particles.

Whatever the explanation may be, it is clear from these and other data,[2,4,9,11] that the toxicity of coal mine dust and probably of other mixed dust is not only related to its mineralogical composition (as usually determined). More subtle properties of the dust particles may also play a role. This put into question the usefulness of incorporating expensive mineralogical analyses in routine dust measuring programs.

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EFFECTS OF ANTIOXIDANTS ON EXPERIMENTAL SILICOSIS

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Our previous studies,[15,16,17,18] documented also by other authors,[4,5,9,21,23,34] provided support for the assumption that lipid peroxidation may be one of quartz dust cytotoxic mechanisms in cells and lung tissue. Also, a continuously growing body of evidence indicate that antioxidants as selenium, zinc, vitamins A, E, and C are either incorporated in the biological membranes or/and influence their stability through the antioxidative systems, and, thus can provide line of defense against peroxidative damage.[6,7,11,24,25,30,33] The involvement of lipid peroxidation in lung tissue and macrophage damaging processes promoted by quartz dust justify the use of various antioxidants and free radical scavengers.[2,19,20,22,27]

The present study was conducted to gain some insight into the protective effects of antioxidant agents on experimentally induced by quartz lung changes.

MATERIAL AND METHODS

Male rats with body weights about 180–200 g were used in three experimental series.

Experiment 1. Rats were divided into the following six groups: 1) Control, intratracheally instilled with 1 ml saline; 2) Silicotic rats (DQ12), intratracheally instilled with a single dose of 30 mg DQ12 standard quartz dust, particle size 5 μ (kindly supplied by Prof. K. Robock, Bergbau-Forschung, GmbH in Essen, West Germany); 3) Selenium-supplemented (Se) 1 ppm; 4) Selenium-supplemented (Se) 4 ppm; 5) Se 1 ppm + DQ12; 6) Se 4 ppm + DQ12.

Experiment 2. Designed to investigate the effects of adding Vitamin A (20 mg/kg b.w.), or Vitamin E (40 mg/kg b.w.) to 1 ppm selenium, was performed on the following animal groups: 1) Control; 2) DQ12; 3) Se + Vitamin A; 4) Se + Vitamin A + DQ12; 5) Se + Vitamin E; 6) Se + Vitamin E + DQ12.

Experiment 3. Aimed at evaluating the effectiveness of zinc supplementation (18.5 ppm), and of the concurrent administration of zinc and selenium (1 ppm), used also six animal groups; 1) Control; 2) DQ12; 3) Zn; 4) Zn + Se; 5) Zn + DQ12; 6) Zn + Se + DQ12. The antioxidants were given orally in the drinking water. Rats were maintained on antioxidant supplement for 1 month prior to the dust instillation and 2 months before sacrifice. By the 2 months all the animal groups were killed. The lungs and the tracheal lymph nodes were removed and weighed. The lungs were examined for fibrogenesis development and for peroxidative damage (experiments 2 and 3). In order to evaluate the severity of fibrogenesis the following biochemical parameters were used: lipid,[13,28] phospholipid,[31] and hydroxyproline[29] content of the lungs. The degree of lung peroxidative damage was evaluated by measurements of malondialdehyde formation, as an index of lipid peroxidation release, with thiobarbituric acid (TBA)-test,[32] glutathione peroxidase, GSH-Px,[14] and glucoso-6-phosphate dehydrogenase, G6P-DH,[3] activities.

The data are presented as percent of control and of DQ12-instilled rats. Statistical intergroup significance were performed by using Student's t-test.

RESULTS AND DISCUSSION

Experiment 1. Figure 1 shows that under 1 ppm and 4 ppm selenium treatment no additional benefit was found in the increased by 2 months final lung and lymph node weights of silicotic rats. No significant differences were observed between the DQ12-instilled and supplemented with selenium, and the non-supplemented silicotic groups, except for 1 ppm selenium which diminished lymph node weights, but only at marginal statistical significance ($p < 0.05$).

In contrast, both selenium doses markedly reduced ($p < 0.001$) lung lipids and phospholipids induced by quartz (Figure 2). Selenium supplements exerted the same decrease rate ($p < 0.001$) of lung hydroxyproline in silicotic rats (Figure 3).

Experiment 2. Feeding selenium 1 ppm in combination with vitamin A and E did not modify the increased lung weights induced by quartz, but significantly reduced ($p < 0.01$) the lymph node weights compared to non-supplemented silicotic rats (Figure 4).

Co-administration of selenium with both vitamins was equally effective in decreasing biochemical parameters of lung fibrosis,—lipid, phospholipid and hydroxyproline content (Figures 5 and 6). However, none of the used antioxidant supplements returned the observed changes to control values.

The TBA levels reported in Figure 7 show a significant higher lipid peroxidation in the DQ12-instilled rats. Supplemental to selenium vitamin A and E tended to reduce lipid peroxide release, but the decrease was not significant as against the silicotic rats.

GSH-Px activity depicted in the Figure 8 was found to be increased in silicotic rat lungs, but no significant response was observed compared to control group. The enhanced activity suggests an adaptative reaction and may indicate an

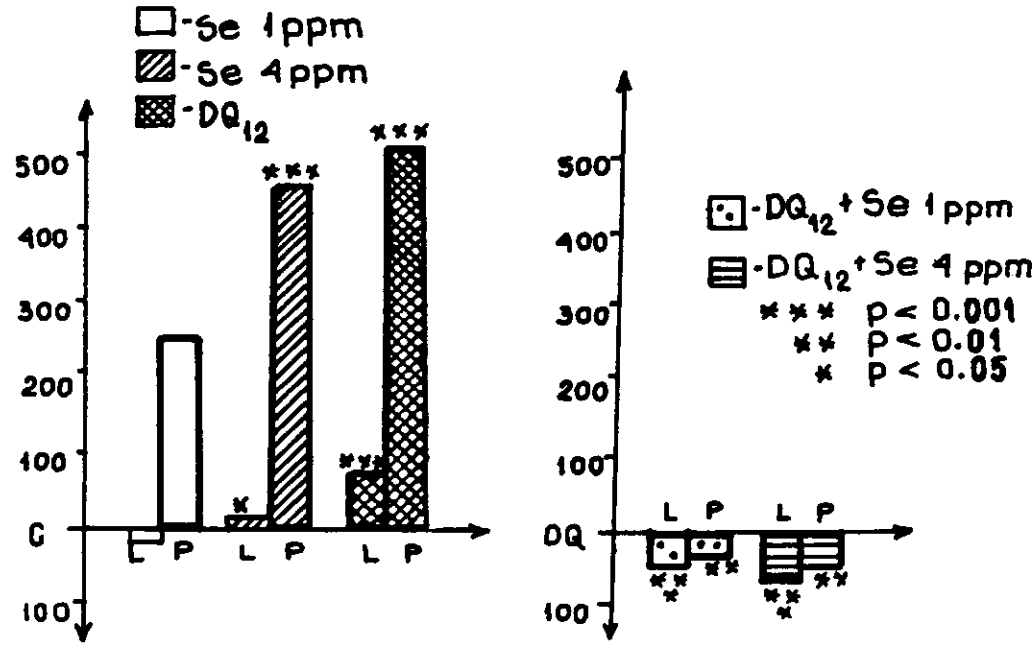

Figure 1. Lung and tracheal lymph node weights of quartz-treated and Se-supplemented silicotic rats.

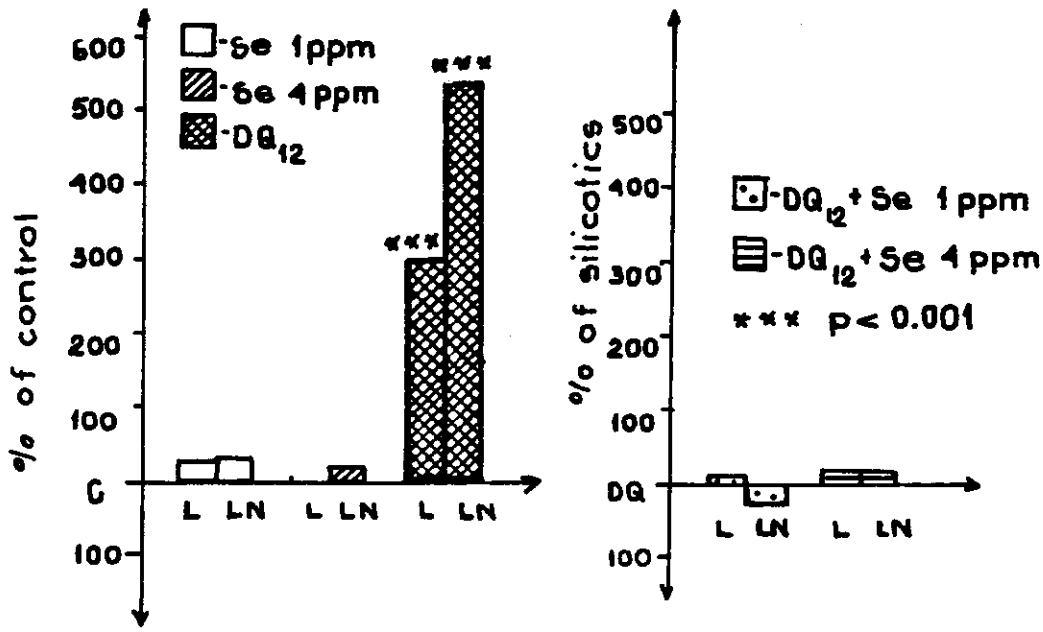

Figure 2. Lung lipids and phospholipids of quartz-treated and Se-supplemented silicotic rats.

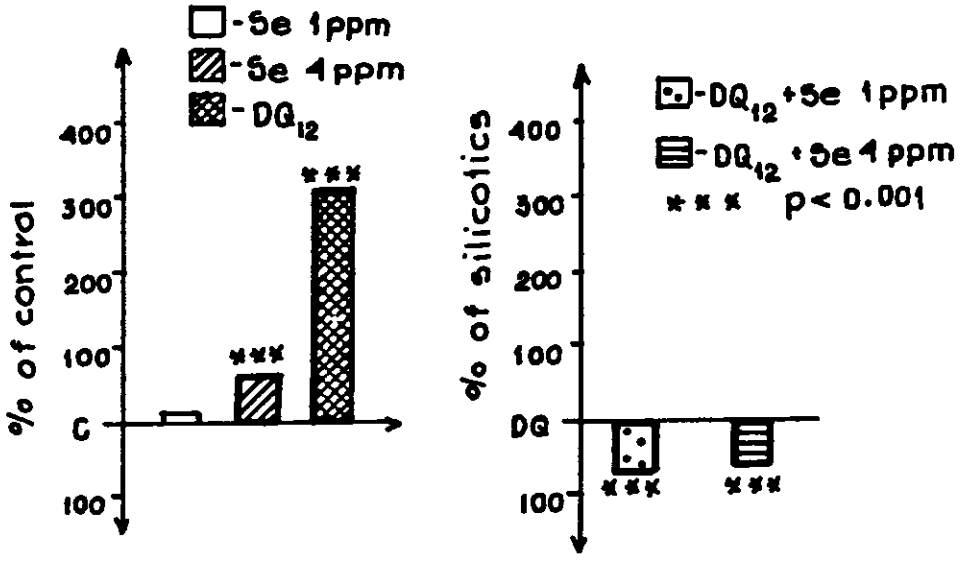

Figure 3. Lung HYPRO of quartz-treated and Se-supplemented silicotic rats.

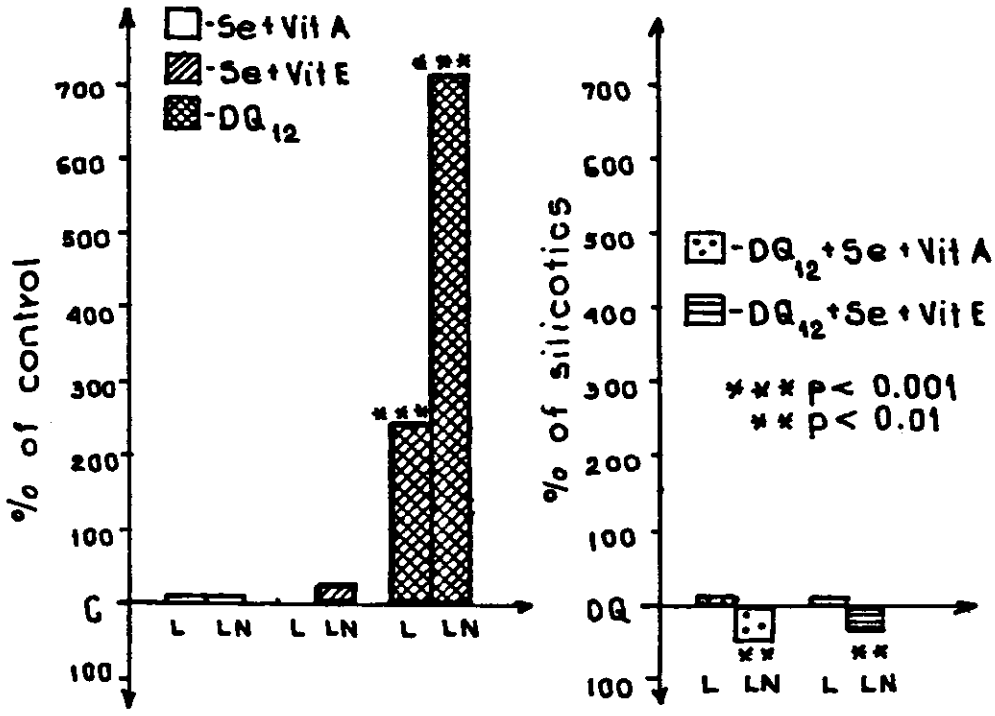

Figure 4. Lung and tracheal lymph node weights of quartz-treated, Se+vitamin A, and Se+vitamin E-supplemented silicotic rats.

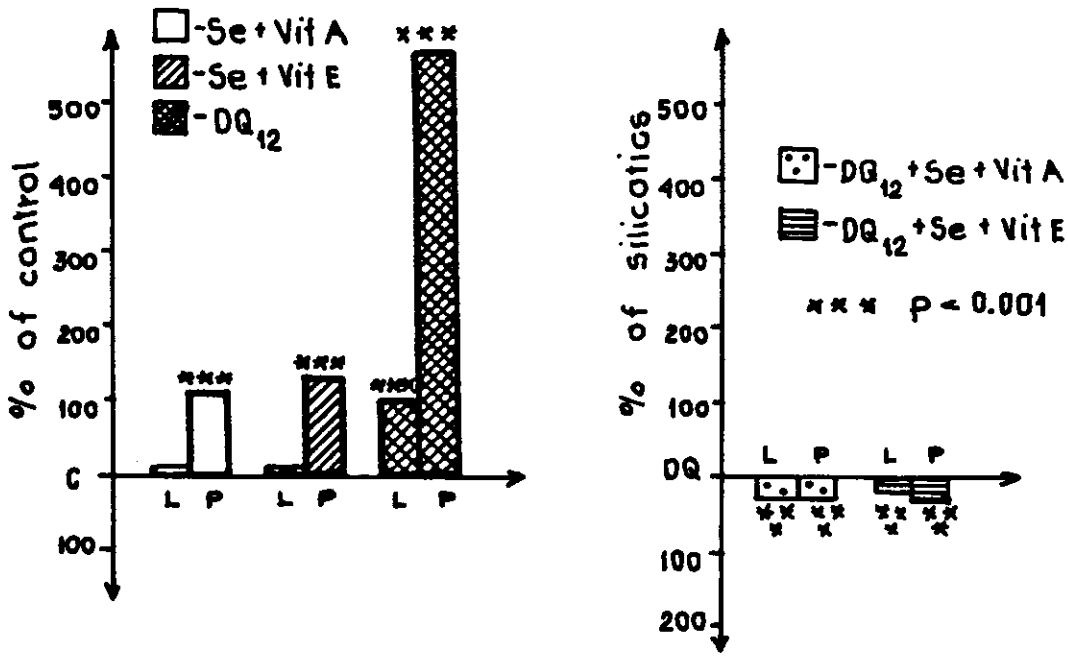

Figure 5. Lung lipids and phospholipids of quartz-treated, Se+vitamin A, and Se+vitamin E-supplemented silicotic rats.

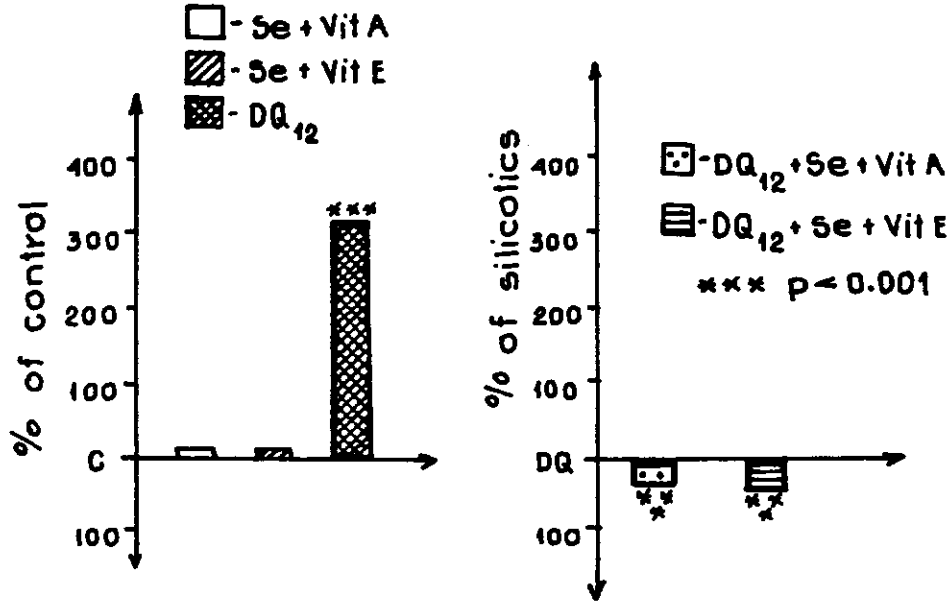

Figure 6. Lung HYPRO of quartz-treated, Se+vitamin A and Se+vitamin E-supplemented silicotic rats.

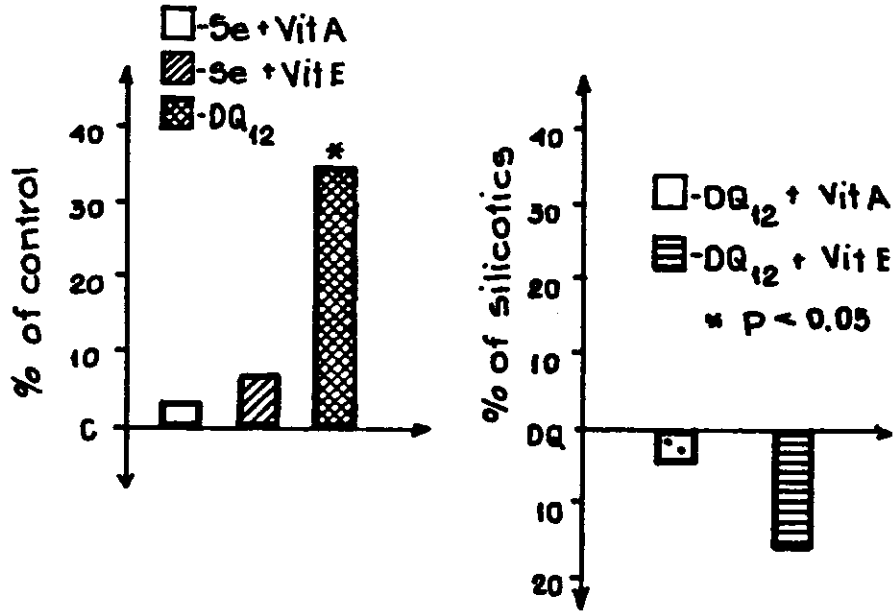

Figure 7. Lung LIPID PEROXIDES of quartz-treated, Se+vitamin A, and Se+vitamin E-supplemented silicotic rats.

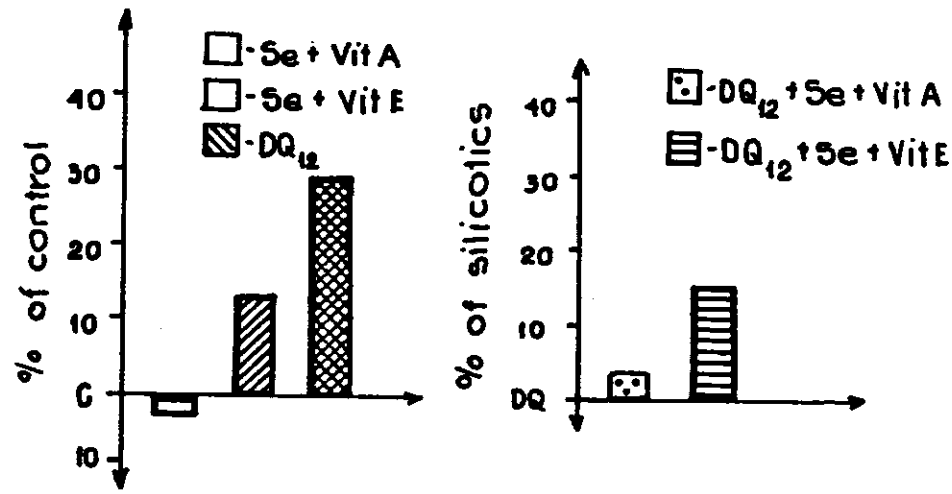

Figure 8. Lung GSH-Px of quartz-treated, Se+vitamin A, and Se+vitamin E-supplemented silicotic rats.

increased demand of the enzymatic activity to cope with tissue peroxidative damage. An inverse relationship between lung GSH-Px activity and lipid peroxidation in selenium + vitamin A and E-supplemented silicotic rats was observed. However, this effect was not significant compared to DQ12-instilled rats. G6P-DH exhibited a significantly higher ($p < 0.001$) activity in the silicotic rat lungs versus of the control group. Addition of both vitamin combinations significantly lowered the enzyme activity by the 2 months when compared to non-supplemented silicotic rats (Figure 9). The reason of the increased enzyme activity in silicosis might be due to the stimulation of the pentoso-phosphate pathway by supplying NADPH for "de novo" lipid biosynthesis and for glutathione redox cycle. Antioxidants exerted a beneficial effect on this metabolic point as demonstrated by the previous Figure 5 showing a reduced rate of lung lipids in antioxidant supplemented silicotic rats.

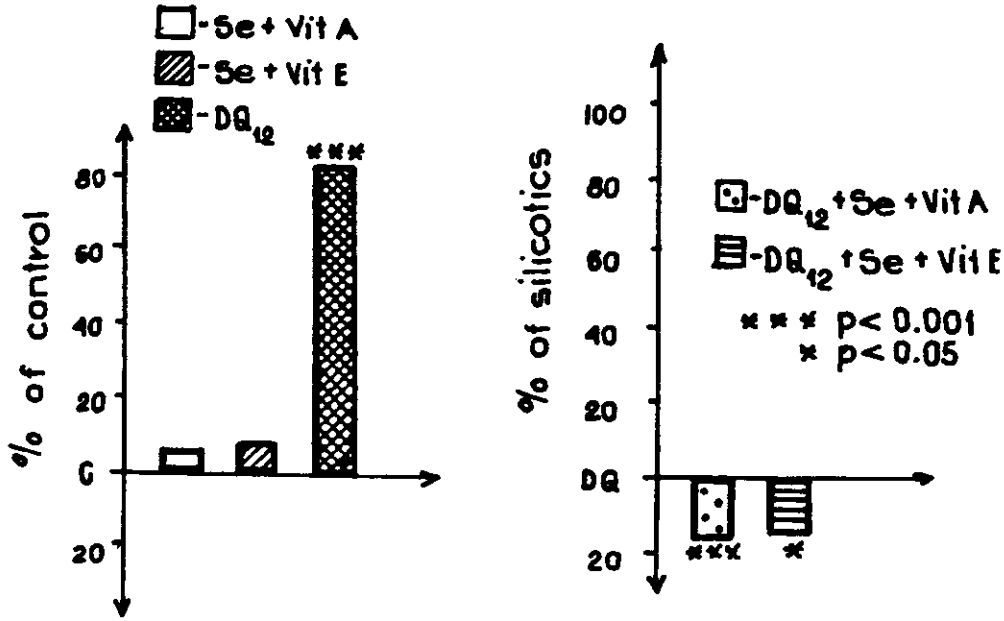

Figure 9. Lung G6P-DH of quartz-treated, Se+vitamin A, and Se+vitamin E-supplemented silicotic rats.

Experiment 3. No response in case of treatment with zinc and zinc + selenium was noted in lung weights of silicotic rats; however, the lymph node weights were found to be increased (Figure 10). In terms of biochemical lesions, zinc supplementation resulted in a significant decrease of lung lipid, phospholipid and hydroxyproline content (Figure 11 and 12). Concurrent administration of zinc and selenium showed the same pattern, except for lung lipids whose values did not differ from those of silicotic non-supplemented group.

Lung lipid peroxides of silicotics were significantly increased ($p < 0.01$) when zinc was supplemented, while zinc + selenium combination alleviated this effect. The failure of zinc to decrease lipid peroxidation induced by quartz dust might be explained by the reported bimodal response of this element in vivo: low doses inhibit, but higher doses enhance lipid peroxidation.[8,26] Most probably, the applied dose of 18.5 ppm zinc, though is considered to be physiological and non-toxic, under our experimental conditions was high enough to increase lipid peroxidation compared to control and silicotic rats.

Lung GSH-Px activity of silicotic rats kept on zinc showed a slight non-significant increment running in parallel with the observed lipid peroxide excess. Adding selenium to zinc resulted in an unexpected decline of this selenium-dependent enzyme at the borderline significance ($p < 0.05$).

Enhanced G6P-DH activity observed in silicotic rats was decreased by zinc supplementation to values significantly lower ($p < 0.001$) when compared to non-treated DQ12-instilled animals. Co-administered selenium to zinc failed to exhibit synergistic effect, the enzyme activity being reduced with a lower significance rate ($p < 0.01$). It is worth mentioning that the less pronounced effect of selenium in the presence of zinc supports the opinion that the biological role of the former might be diminished by its direct binding to the ionized zinc.[12] Consequently, a decreased availability of selenium to antioxidant enzyme systems occurs.

The design of our experiments does not allow a detailed discussion on the mechanisms of the antioxidant effects on silicosis. We can only speculate that selenium, vitamin A and vitamin E as well as their combinations act mainly on the course of inflammatory events preceding fibrosis, by trapping the formed free radicals, and, thus, preventing lipid peroxidation. Zinc, element with a broad range of biologic activity, though is a co-factor of the scavenging free radical metallo-enzyme superoxide dismutase, impairs mainly collagen synthesis and processing.

Our results confirm the reported previously protective effect of zinc with respect to induced by quartz lung collagen accumulation. The beneficial effect of zinc was explained by the interference with macrophage functions, having no direct effect on collagen deposition.[10] Recent evidence, however, indicates that zinc has a direct and selective preventive effect on rat lung collagen accumulation by inhibiting procollagen hydroxylation.[1]

In conclusion, our results give support to the hypothesis that the peroxidative damage plays an important additional role in the fibrotic action of quartz dust. One of the most significant findings in this study is that under antioxidant treatment silicotic fibrosis was diminished. Therefore, given correct concentrations, these antioxidants appear to be beneficial, as prophylactic and therapeutic agents in silicosis. Since the

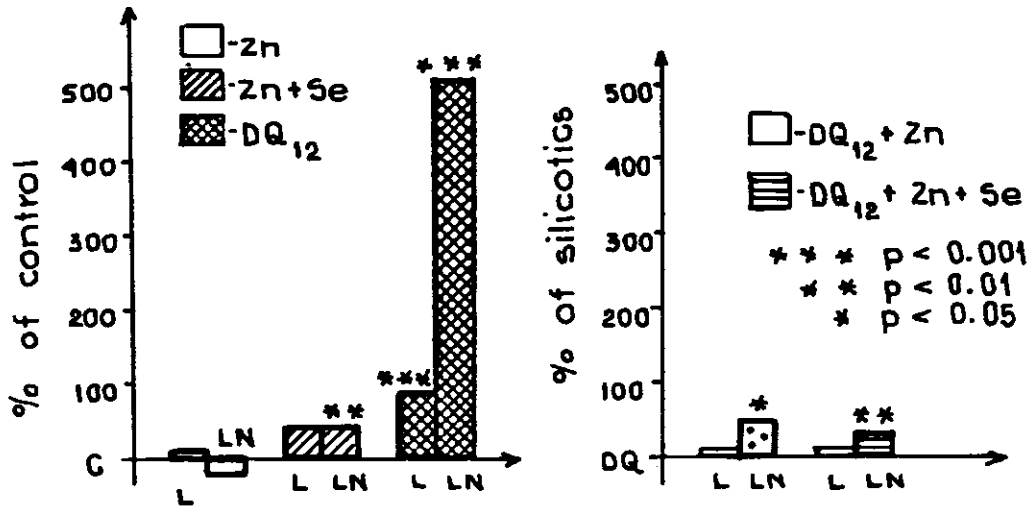

Figure 10. Lung and tracheal lymph node weights of quartz-treated, Zn and Zn+Se-supplemented silicotic rats.

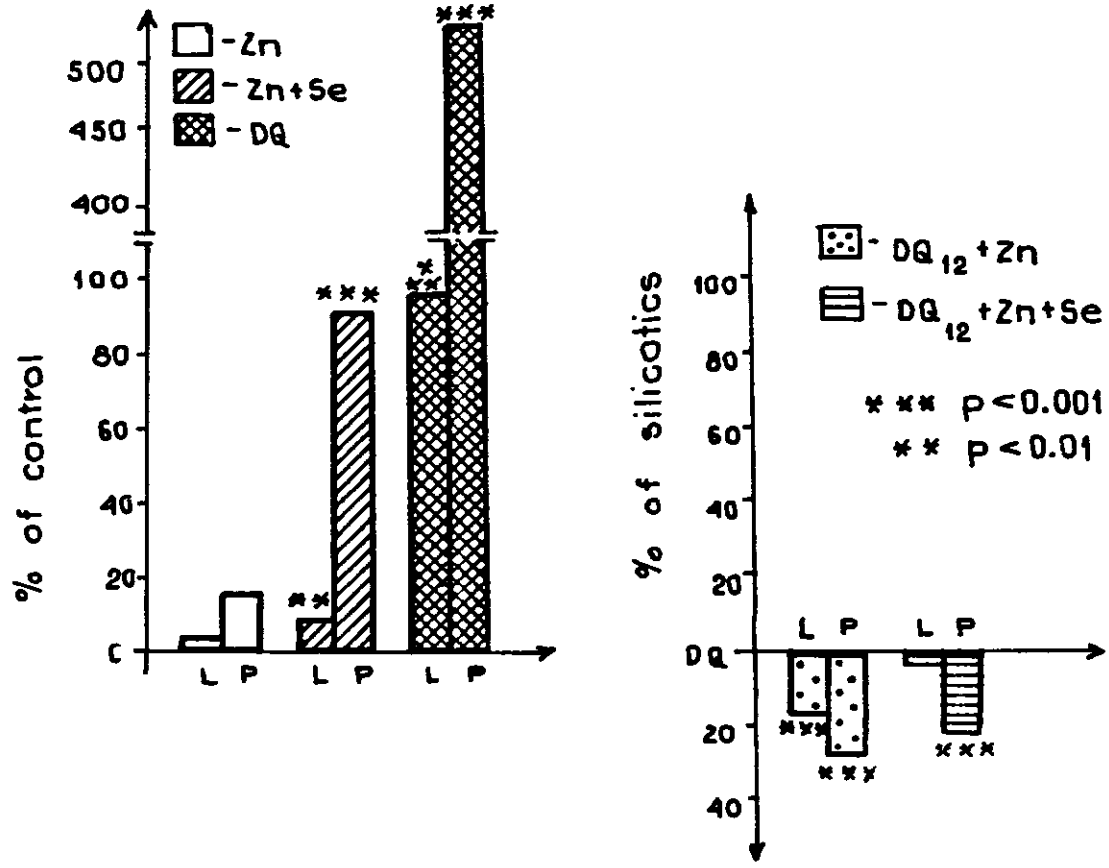

Figure 11. Lung LIPIDS and PHOSPHOLIPIDS of quartz-treated, Zn and Zn+Se-supplemented silicotic rats.

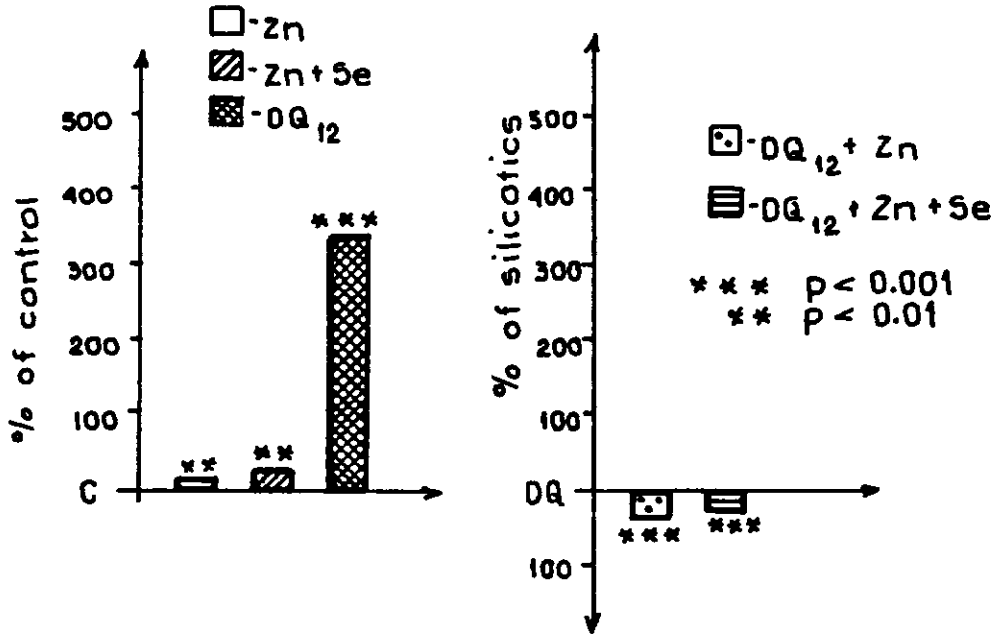

Figure 12. Lung HYPRO of quartz-treated, Zn and Zn+Se-supplemented silicotic rats.

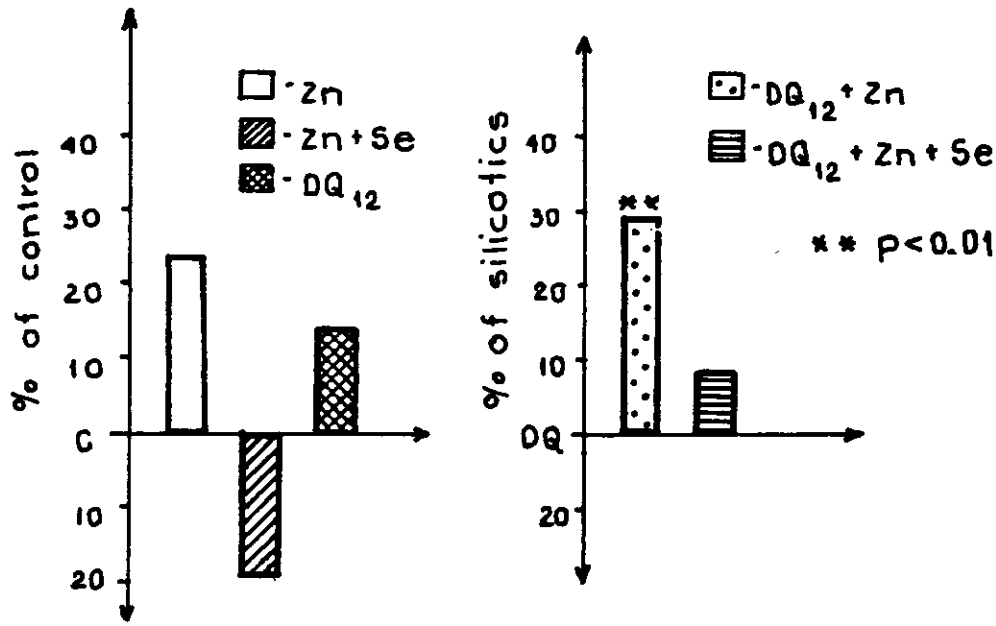

Figure 13. Lung LIPID PEROXIDES of quartz-treated, Zn and Zn+Se-supplemented silicotic rats.

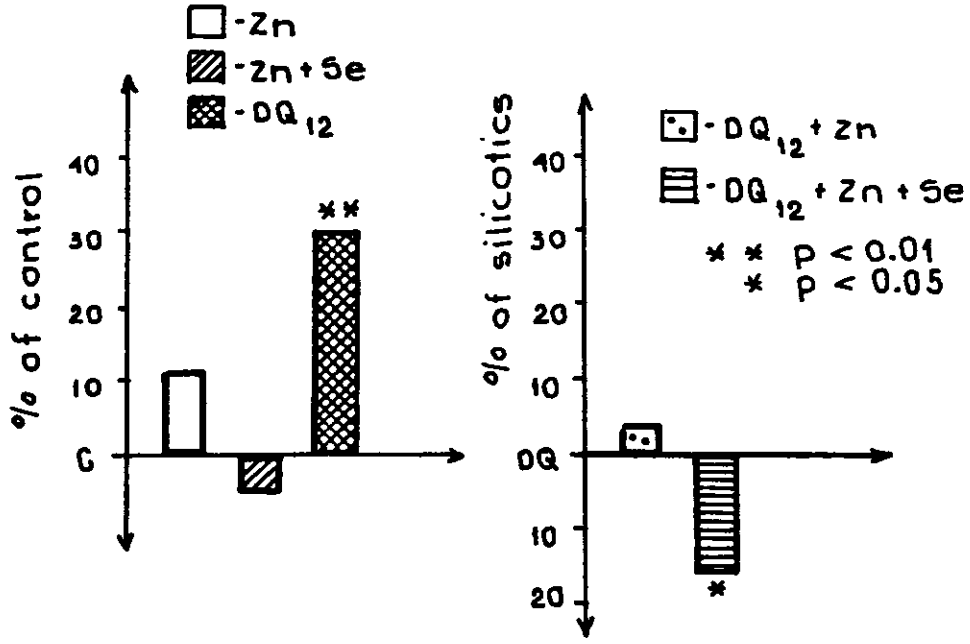

Figure 14. Lung GSH-Px of quartz-treated, Zn and Zn+Se-supplemented silicotic rats.

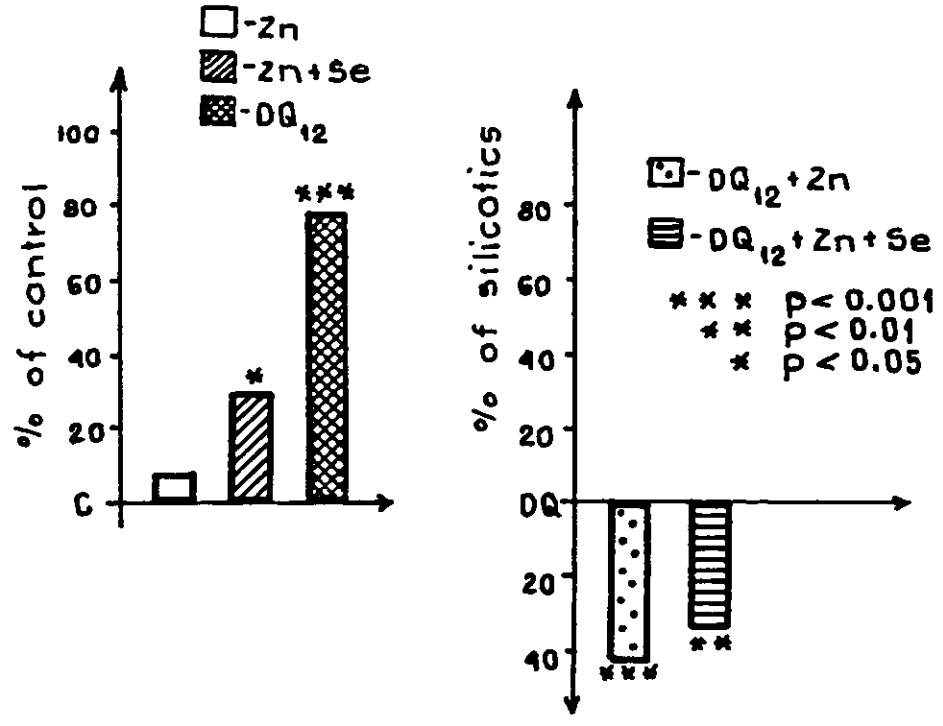

Figure 15. Lung G6P-DH of quartz-treated, Zn and Zn+Se-supplemented silicotic rats.

applicability of our findings to humans can only be speculated upon at this time, it is suggested that a clinical trial with antioxidant supplements to silicotic patients will have a similar effect.

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ALTERATIONS IN PULMONARY RESPONSE AND BRONCHOALVEOLAR LAVAGE CONSTITUENTS IN RATS CO-EXPOSED TO QUARTZ AND COAL FLY ASH

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ABSTRACT

Coal fly ash is the major particulate pollutant present in the effluent stream of thermal power stations where coal is burnt for generation of electricity. Co-exposure to fly ash and dusts rich in free silica occur in and around industrial settings, particularly in developing countries, among stone cutters and workers engaged in and around road and building construction.

The effect of coal fly ash on lungs and its potential to modify pathogenesis of pulmonary silicosis was investigated in rats. Exposure to coal fly ash alone resulted in concentration of the particulates within hyperplastic alveolar macrophages, situated in the various compartments of the pulmonary parenchyma and the draining lymph node. In spite of its long residence in lungs, fly ash elicited only a meagre fibrotic reaction. Quartz exposed rats developed nodular silicotic reaction, comprised predominantly of reticulin and collagen fibers. In silicotic animals exposed to fly ash the increase in lung weight, hydroxyproline contents and laying down of collagen was less than in silicotic animals not exposed to fly ash. The elevated levels of soluble proteins, content of lysosomal enzymes and the cellular constituents of the bronchoalveolar lavage were similarly less in fly ash-quartz exposed rats than in those exposed to quartz alone.

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INTERACTION OF MINERAL FIBRES WITH EXTRACELLULAR MATRIX AND MESOTHELIUM AFTER INTRAPERITONEAL INJECTION IN RATS

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INTRODUCTION

Serosal tests have proven as appropriate methods for detecting the neoplastic potency and fibrogenicity of asbestos fibres and man-made mineral fibres.[4,7,15,24,28,29] The results have strongly supported the hypothesis, that besides the elongated shape of the fibrous particles (lengths and diameter) their dose, durability and possibly also their surface properties may be the cause of their pathogenic effects.[5,6,16,22] The correlation between fibre-induced fibrosis and the development of mesotheliomas had been discussed contradictory and not yet been fully understood.[8,9,14,18,19,23,25,26] The mainly commercially used kinds of asbestos crocidolite and chrysotile obviously possess different fibrotic and neoplastic potency in man.[1,2,3,12,13,17,20,21,27] Because of this fact our studies on rat omentum aimed first for the presentation of differences in the composition of the extracellular matrix components collagen types I and III, laminin and fibronectin in crocidolite and chrysotile-induced granulomatous lesions. In addition we have examined in which way these fibrous natural dusts with very different physico-chemical properties lead to malignant transformation of the mesothelium. We have wondered, if these mechanisms were the same, which account for the tumour-inducing effect of some man-made mineral fibres.

Material and Methods

Our investigations were carried out on omentums of altogether 64 female Sprague-Dawley rats which had been sacrificed under narcotization 8 hours to 15 months after intraperitoneal injection of 1.5 or 15 mg crocidolite (South Africa, like UICC reference sample but fibre lengths greater) and chrysotile B (UICC reference sample) either. The omentums were divided into several parts and their preparation and fixation in formaldehyde, cold phosphate-buffered (0,5 M, ph 7,4) 2,25% glutaraldehyde and 1,3% osmium tetroxide for the light microscopical and the electron microscopical examination were done in normal manner. Sections were stained with HE chromo-trope-aniline blue, Prussian blue or Toluidin blue and Uranyl acetate. Cryostat sections for the immunofluorescence microscopical investigations were incubated with specific antibodies against collagens types I and III, the multifunctional glycoprotein fibronectin and the basement membrane glycoprotein laminin or with non-immune-serum as described elsewhere.[11] We further have examined specimens of the omentums from long term carcinogenicity studies on natural and man-made mineral fibres which were already referred in detail.[24] In these intraperitoneal tests very low doses between 0.05 and 0.5 mg asbestos, for example, have led to tumour incidences of about 20 to 80%. Only those animals have been chosen for our light microscopical investigations, however, which had been sacrificed in a bad health condition not earlier than two years after the intraperitoneal injection of different fibrous dusts. They have macroscopically shown no tumour growth. Doses of all intraperitoneally applied dusts and the life-spans of the animals after injection are listed in Table I.

Results

Focal granulomatous lesions of the omentum have been found only in those animals, which had been intraperitoneally injected with more than 1 mg of either natural or man-made mineral fibres in 1 ml physiological saline solution. Already 3 days after crocidolite administration the fibres have accumulated within the area of the "milk spots" of the omentum. These are circumscribed deposits of cells belonging to the monocyte macrophage system especially in the area of vascular branching. The granulomatous foreign body reactions characteristically have had a large number of mononuclear macrophages and multinucleated giant cells not only within the first week but also in the end of the investigation period. The crocidolite fibres are spread over the entire area of the granulomatous lesions and they are deposited especially at the surface of multinucleated giant cells in form of larger accumulations (Figure 1B). Shorter fibres can also be seen under the electron microscope within the cytoplasm of macrophages. New collagen, especially type III, can be demonstrated with the immunofluorescence microscope already after 3 days. At that time you can electron microscopically identify mainly macrophages and some lymphocytes in perivascular and submesothelial position. Fibroblasts and myofibroblasts are nearly absent (Figure 2A). There was a steady increase of fibrillogenesis throughout the 6 months studied immunofluorescence microscopically and during this time the collagen fibres were distributed symmetrically between the macrophages all over the lesions (Figure 1A).

On the other hand in chrysotile-induced lesions collagen types I and III synthesis was limited on the periphery of the granulomas (Figure 1C). Different to earlier reports chrysotile fibre bundles could be shown in the center using light microscopy (phase contrast or differential interference

contrast) even up to six months (Figure 1D).[28] They seem to possess collagenolytic activity. The cellular debris lying between them can only be detected with the transmission electron microscope (Figure 2B).

Table I
Intraperitoneally Applied Natural Mineral Fibres (a) and Man-made Mineral Fibres (b)

	Dosis i.p. (mg)	Microscopically investigated omentums (n)	Life-span after i.p. injection (months)
a)			
Crocidolite (S.Africa)	1-15	32	<1-15
Chrysotile	1-15	32	<1-15
	0,05	7	24-27
Actinolite	0,01	6	24-28
	0,05	8	25-28
	0,25	4	25-28
	0,25 + PVNO	7	24-26
Erionite, Oregon	2,00	3	28
Wollastonite	100	5	26-28
b)			
Glass fibres JM 104/475	5	6	27-28
Polypropylene fibres	50	3	28
Kevlar fibres	20	2	27

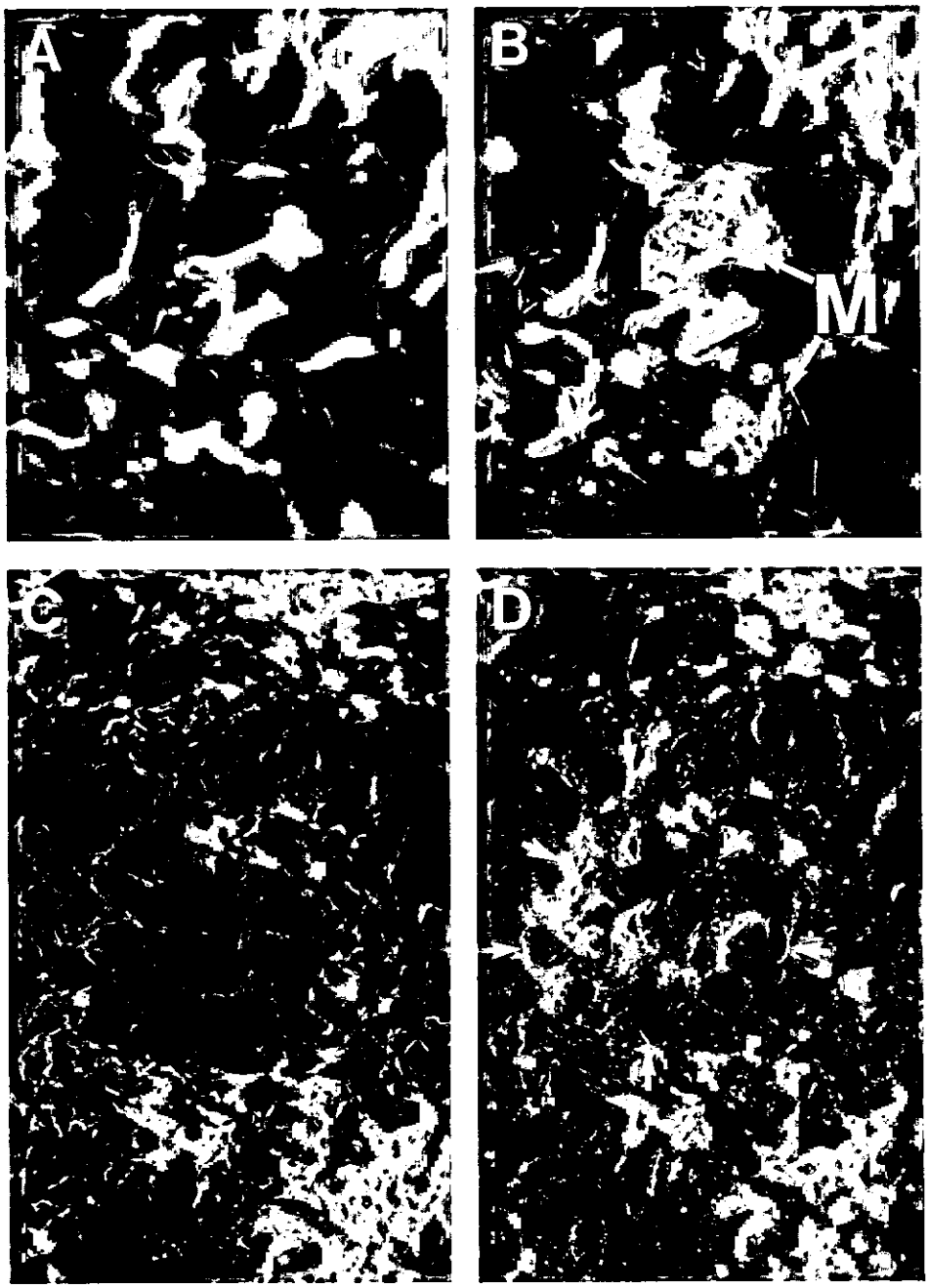

Figure 1. Asbestos induced fibrosis in the rat omentum 1–2 weeks after the i.p. injection of the dusts.
(A) and (B) Intact pericellular network of collagen type III in crocidolite containing granulation tissue.
((A) Immunofluorenscence microscopy 460 X;
(B) The same section as in (A) with light from the bottom and phase-contrast 460 X)
M: Multinuclear giant cells containing crocidolite fibres.
(C) and (D) Dissolution of collagen fibres (type III) and necrotic macrophages in the center of chrysotile containing granulomas.
((C) Immunofluorescence microscopy 290 X;
(D) the same section as in (C) with light from the bottom and phase-contrast 290 X)
➡ Chrysotile fibres

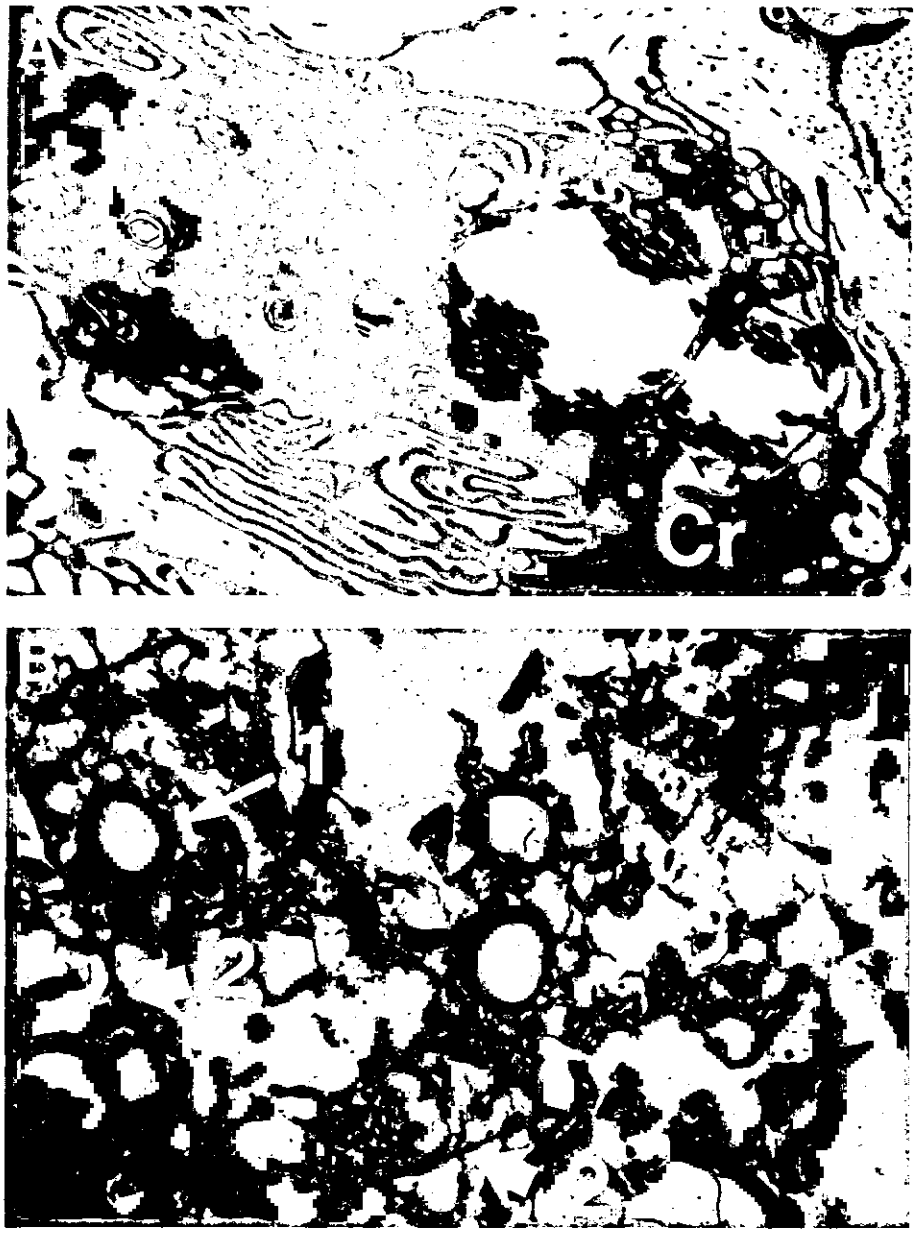

Figure 2. (A) 3–7 days after i.p. injection of crocidolite the granulomatous lesions in the rat omentum are dominated by macrophages. Fibroblasts and myofibroblasts are nearly absent. (EM 55.500X) Cr: Crocidolite.
(B) Cellular debris and chrysotile fibres in the center of granulomas six months after i.p. injection of 15 mg/ml saline solution. (EM 7.000X).
1. Fatvacuoles
2. Chrysotile fibres

As we have reported elsewhere the glycoprotein fibronectin can be found between and at the surface of macrophages in crocidolite induced inflammatory infiltrates and especially accumulates at the surface of very long crocidolite fibre bundles.[10] Therefore we have discussed the importance of its opsonic activity in case of asbestos induced fibrosis. Also, chrysotile fibres and clustered cellular debris were coated with fibronectin (Figure 3). In this way delayed scarring of the inflammatory reactions induced by chrysotile depositions in the fat tissue of the omentum might be promoted too. The scarring has not been finished 6 months after chrysotile application. Until this moment also the remarkable differences in the vascularization of chrysotile and crocidolite induced lesions continue (Figure 4). The surface properties of chryso-

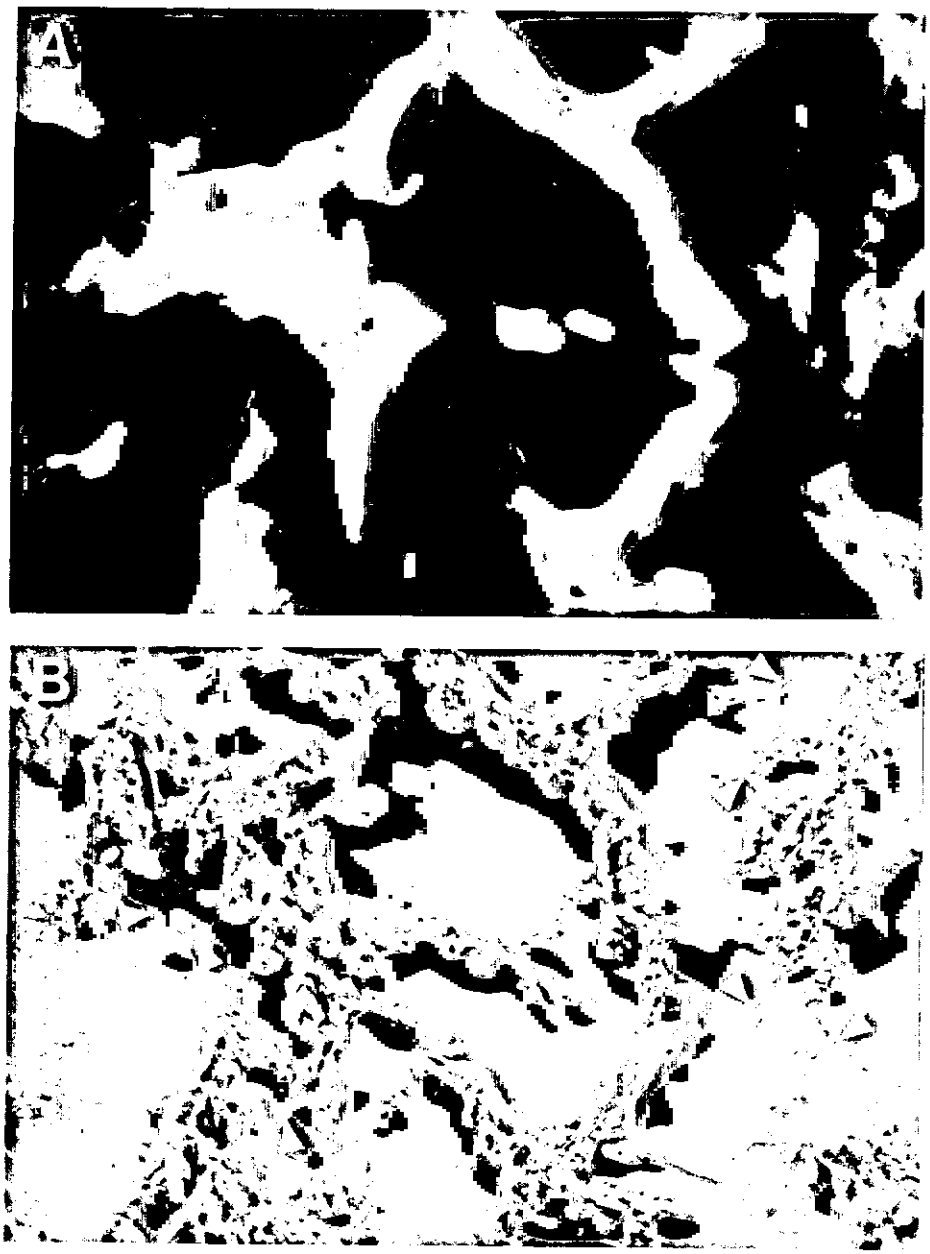

Figure 3. Immunofluoroscence microscopical demonstration of fibronectin (A) at the surface of chrysotile fibres and clustered cell detritus (B) in the center of a foreign-body granuloma in the rat omentum 2 months after i.p. injection of the fibrous dust.
((A) Immunofluorescence microscopy 460X;
(B) The same section as in (A) with light from the bottom, polarization and phase-contrast 460X)
➡ Chrysotile fibres

tile fibres seem not only to counteract the chemotactic and opsonic activity of fibronectin but also a vascular sprouting.

In combination the reaction patterns of extracellular matrix components, crocidolite induces a well vasculated granulation tissue and after 6 months much more fibrosis than chrysotile (Figure 5 left on top). Around the latter foreign-body-granulomas were formed with central necrosis and collagenous connective tissue only in the periphery (Figure 5 at the bottom). Fibres containing granulation tissue and granulomas, both however, are no obligatory conditions for mesothelial proliferation (Figure 5, right).

On the contrary even without contact to the focal dust containing lesions we have found narrow connective tissue

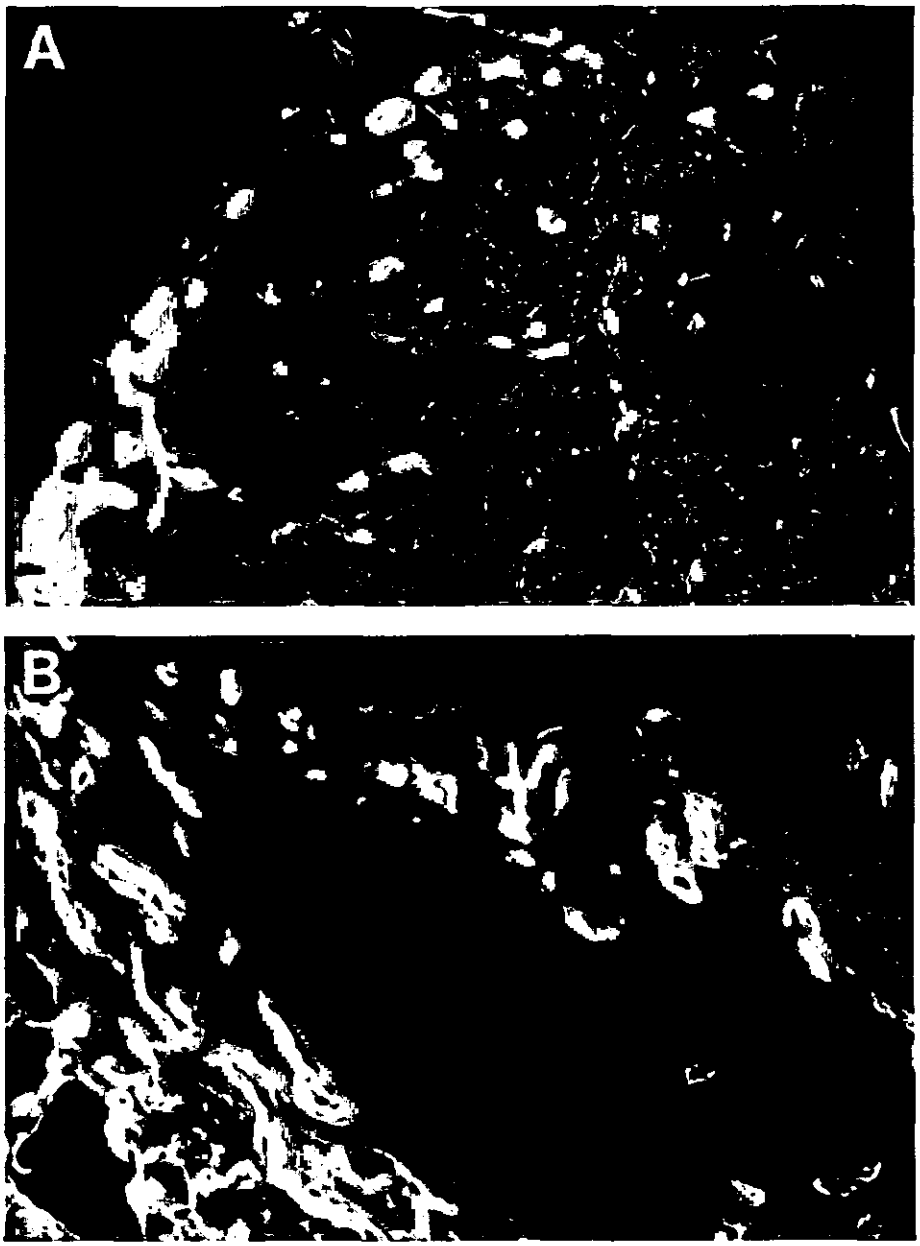

Figure 4. Dense vascularization of the granulation tissue induced by crocidolite fibres (A) and only in the periphery of a chrysotile containing granuloma (B).
((A) and (B) Immunofluorescence microscopy with an antibody against the basement-membrane glycoprotein laminin; (A) 190X, (B) 300X)

strands directly beneath the mesothelium already 7 days after intraperitoneal injection of 15 mg crocidolite, for example (Figure 6A). The covering cells were rounded, enlarged and often multinuclear. They have never stored asbestos fibres. In our opinion these changes can be conceived as a repairing process of the submesothelial mesenchyme. They are not only present in the fat areas of the omentum but also in the normally very thin mesothelial duplicatures spread between them (Figure 6B). The latter are the preferred localization of the generally less intensive chrysotile induced submesothelial fibrosis which also last for months and years after fibre administration. Even 28 months following the intraperitoneal injection of not more than 0.05 mg chrysotile/ml fibrotic thickening of the mesothelial duplicatures of the omentum could be observed.

Although macroscopically the omentums from long term carcinogenicity studies showed no tumour growth we microscopically have often found focal mesothelial proliferations associated with submesothelial fibrosis. In some ani-

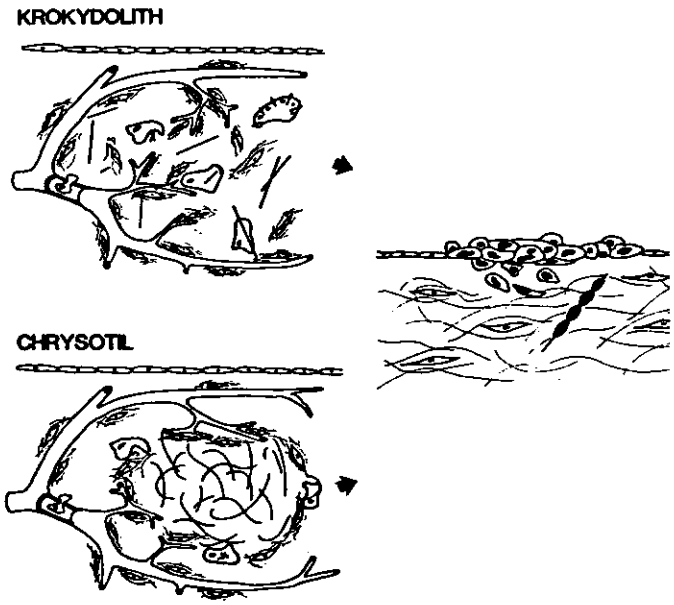

Figure 5. Crocidolite containing granulation tissue (left side on top) and chrysotile-induced granulomas (left side on the bottom) in the rat omentum as non obligatory precondition of mesothelial proliferation (right side).

mals mesothelial proliferation has reached the intensity of early mesotheliomas infiltrating the underlying connective tissue (Figure 7B). The activation of the submesothelial mesenchyme and the mesothelial proliferation, both proved to be a rather unspecific answer to injuries of the mesothelium by fibrous dusts provided that the single particles were only long and fine enough. These changes could be observed in a similar way 28 months after intraperitoneal deposition of the natural mineral fibres, type actinolite, and of man-made mineral fibres as glass microfibres and Kevlar (Figure 7A). They seem to depend in the quantity on fibre type only.

CONCLUSIONS

1. Phagocytosis of asbestos fibres is obviously mediated by fibronectin and in early fibrosis macrophages may be one place of collagen synthesis.
2. There are remarkable differences in the intensity of collagen synthesis in crocidolite induced granulation tissue with a symmetrical fibrillogenesis and in chrysotile induced granulomas with central necrosis and newly formed collagen fibres only in the periphery.
3. Natural mineral fibres and man-made mineral fibres tested intraperitoneally induce lesions of the serosal surfaces which are followed by submesothelial fibrosis and mesothelial proliferations up to the development of malignant mesotheliomas. These changes seem to depend in the quantity on fibre type only.

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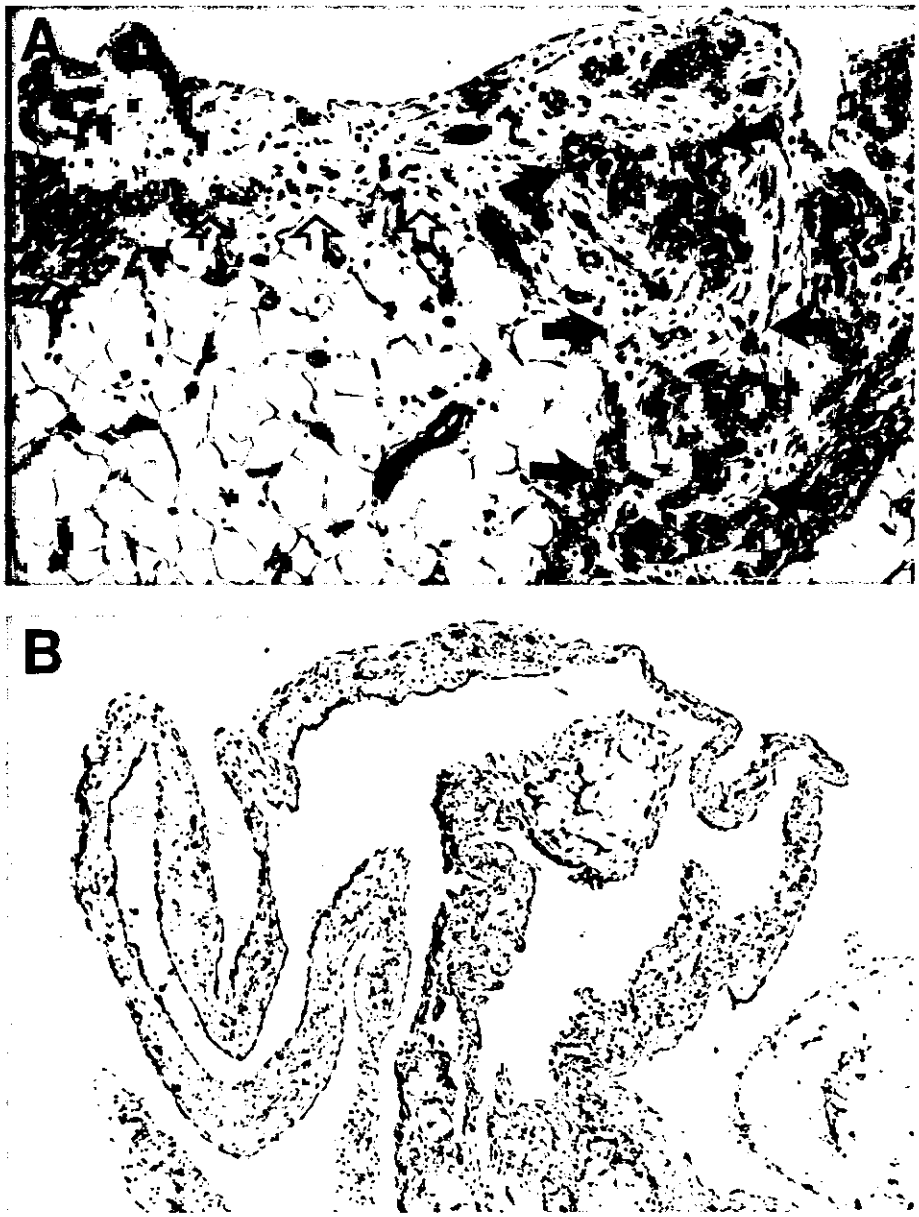

Figure 6. (A) Submesothelial fibrosis without crocidolite fibres visible with the light microscope (➡) and adjacent proliferating mesothelial cells without close connection to the foreign-body granuloma (➡) on the right side of the figure, 7 days following crocidolite administration.
(B) Cross section of mesothelial duplicatures of rat omentum. 3 weeks after crocidolite application the fibrotic thickening is remarkable.
((A) HE 74 X; (B): HE 60 X)

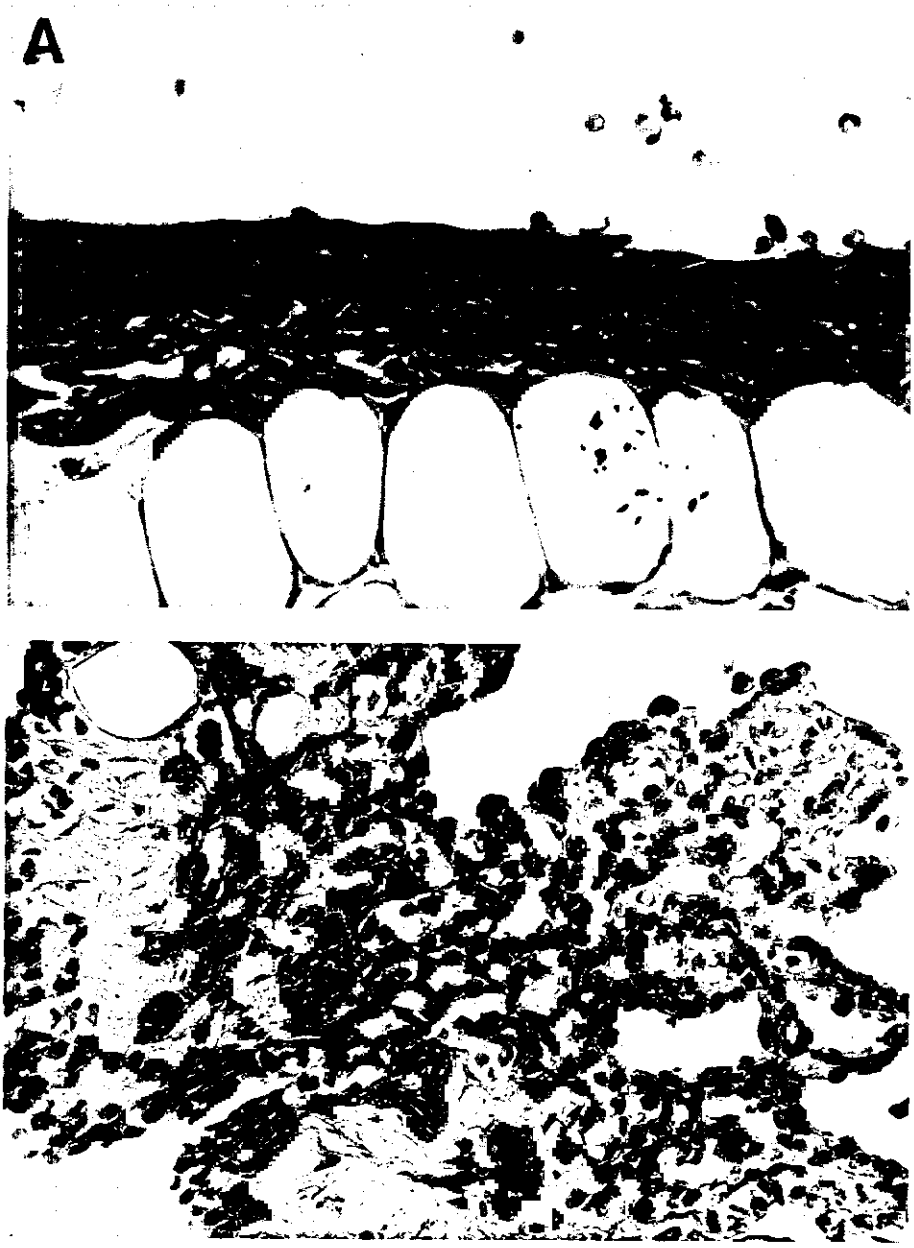

Figure 7. (A) Proliferation of probably preneoplastic cells in the submesothelial tissue 28 months after glass micro-fibre-induced injury of the mesothelial lining. (HE 400 X)
(B) Early mesothelioma of the mesothelial duplicature of rat omentum 21 months after exposure to actinolite. (HE 360 X)

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IN VITRO INJURY TO ELEMENTS OF THE ALVEOLAR SEPTUM CAUSED BY LEUKOCYTES FROM THE BRONCHOALVEOLAR REGION OF RATS EXPOSED TO SILICA

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INTRODUCTION

Quartz exposure is associated with lung fibrosis (silicosis) and Type II alveolar epithelial cell hyperplasia is also commonly present.[1] Bronchoalveolar lavage studies using rats in our own laboratories,[2] and in humans,[3] have demonstrated that there is leukocyte recruitment into the lungs following inhalation exposure to silica. Studies on other fibrotic lung diseases have stressed the importance of the leukocytes of the alveolitis in the progression of disease via release of important mediators.[4] We have therefore set out to examine the ability of bronchoalveolar leukocytes from rats exposed to silica by a single intratracheal instillation, to cause injury to the extracellular matrix and cellular elements of the alveolar septum *in vitro*. Leukocytes from rats exposed to two other inflammogenic particulates—a heat killed bacterial preparation and a yeast cell wall preparation (zymosan)—were similarly assessed, for comparison with quartz.

MATERIALS AND METHODS

Animal Model of Silicosis

Syngeneic PVG rats, SPF bred, were exposed by intratracheal instillation to 1 mg of DQ_{12} standard quartz. As controls, the heat killed bacterial preparation *Corynebacterium parvum* was also injected as was the yeast cell wall preparation zymosan; both of these particulates are known to cause inflammation. Bronchoalveolar leukocytes were obtained by lavage as described in detail elsewhere[5] at various time points after injection. In this model quartz exposure causes fibrosis, Type II epithelial cell hyperplasia and alveolar lipoproteinosis beyond 1 month exposure which are evident in histological sections of exposed lung.

Assay of Leukocyte-Mediated Type II Alveolar Epithelial Cell Injury

This assay is described in detail elsewhere[6] and involves labelling of Type II alveolar cell line (A549) with ^{51}Cr. Bronchoalveolar leukocytes are then added to the labelled cells in microtitre wells and co-cultured for 4 hours; the ability of the leukocytes to cause lysis or detachment of the epithelial cells is assessed.

Assay of Leukocyte-Mediated Proteolysis of Fibronectin

Leukocyte-mediated proteolysis of fibronectin was assessed using a solid phase assay of ^{125}I-labelled fibronectin in microtitre plate wells. This assay has been described in detail elsewhere[7] and measures protease-mediated injury. The leukocyte-mediated proteolyic activity shown here against fibronectin is also active against ^{125}I-labelled collagen and laminin. Leukocytes are cultured on the solid phase of ^{125}I-labelled fibronectin and allowed to degrade the matrix for 4 hours; products of proteolysis of fibronectin are measured as free counts in the supernatant.

Leukocyte Separation

Whole inflammatory bronchoalveolar leukocyte populations from quartz-exposed rats were separated by centrifugation through Sepra-Cell medium into macrophage and neutrophil-enriched fractions.

Statistical Analyses

Results were analysed by analysis of variance and differences in treatments compared for significance using a 't' test.

RESULTS

Inflammation Caused by a Single Injection of Silica, *C. parvum* or zymosan

Figures 1 and 2 show the total number of bronchoalveolar leukocytes and percentage neutrophils lavaged from rats injected intratracheally with quartz, *C. parvum* or zymosan. All three particles caused initial burst of inflammation characterized by recruitment of large numbers of leukocytes containing high proportions of neutrophils. In the case of *C. parvum* and zymosan this initial alveolitis was followed by a return to the normal situation where no neutrophils were present although the numbers of macrophages remained raised indicating a mild macrophage alveolitis. In the case of quartz, however, an intense macrophage/neutrophil alveolitis persisted until at least one month. Previous studies have shown that this alveolitis persists for up to three months.[8]

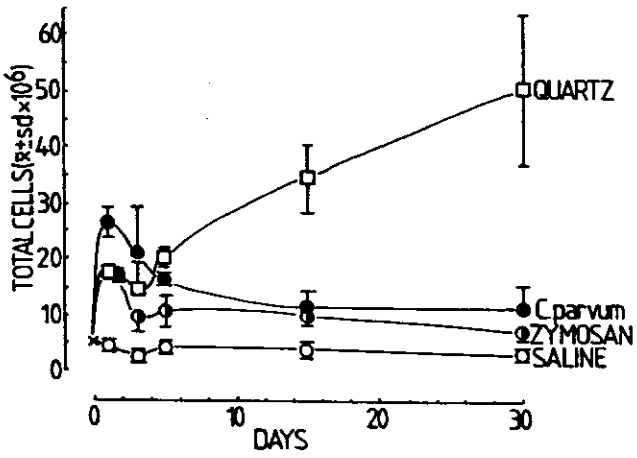

Figure 1. Total leukocytes in bronchoalveolar lavage up to 30 days after instillation of saline, quartz, *C. parvum* or zymosan into the lungs of rats. Data is mean ± standard deviation from 3 rats. Significant ($P<0.01$–0.001) increases with all particulates compared to saline.

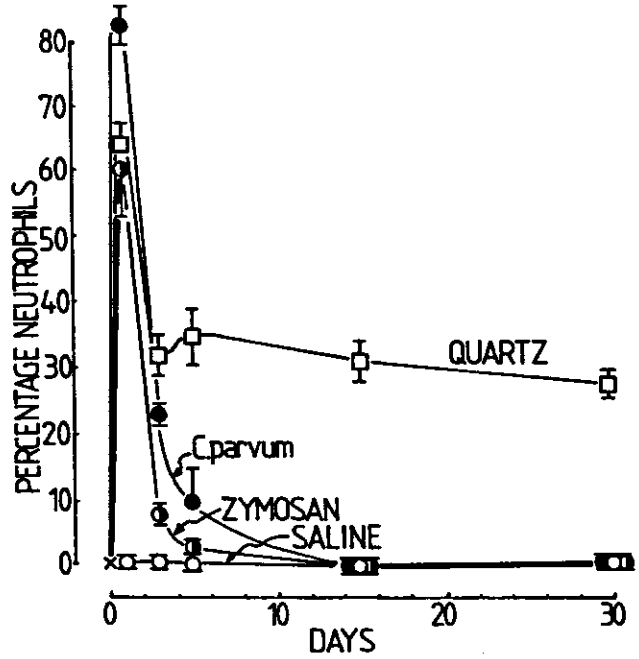

Figure 2. Percentage neutrophils in bronchoalveolar lavage up to 30 days after instillation of saline, quartz *C. parvum* or zymosan. Data derived as in legend to Figure 1. Significant ($P<0.01$–0.001) increases in percentage neutrophils, compared to saline, for quartz at all time points and for *C. parvum* and zymosan at 1, 3 and 5 days.

Activity of Bronchoalveolar Leukocytes in Breaking Down Fibronectin

As shown in Figure 3 the bronchoalveolar leukocytes obtained from the lungs following injection of different particles showed varying abilities to break down fibronectin. During the acute inflammatory phase the leukocytes from lung exposed to all three particulates were capable of breaking down fibronectin. However, only quartz was capable of eliciting a sustained high level of proteolysis, in keeping with the persistence of the inflammation in quartz-exposed lung. It was notable that the ability to break down fibronectin correlated strongly with the presence of neutrophils.

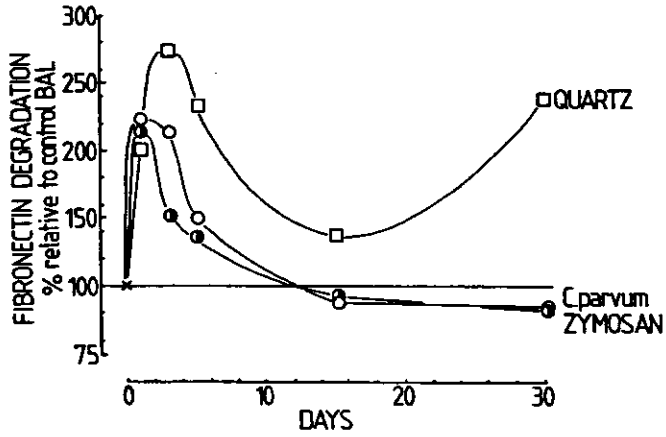

Figure 3. Proteolytic activity against fibronectin shown by bronchoalveolar leukocytes from rats injected with the indicated particulates. Data expressed as a percentage of the activity shown by control bronchoalveolar leukocytes.

Injury to Alveolar Epithelial Cells Caused by Bronchoalveolar Leukocytes

Bronchoalveolar leukocyte populations elicited with quartz or C. parvum were tested for their ability to cause injury to cells of an alveolar epithelial cell line *in vitro*. Both *C. parvum*-elicited bronchoalveolar lavage cells obtained after one day (70–90% PMN) and 5-day quartz leukocytes (50% macrophages/50% neutrophils) were capable of causing the target cells to detach from the sub-stratum (Figure 4). There was no lytic injury to the target cells and the detachment injury could be completely inhibited by protease inhibitors such as alpha 1-protease inhibitor.[6]

We have also examined the ability of leukocytes from the lungs of rats chronically inhaling coalmine dust to mediate injury. This showed that rats exposed, by inhalation, for 48 days to coalmine dust collected from the air of a British colliery[5] also caused epithelial injury and degradation of fibronectin (Figure 5).

Cellular Origin of Epithelial Cell Detaching Injury in Quartz-Elicited Bronchoalveolar Leukocyte Populations

As shown above, high proportions of neutrophils seem to accompany fibronectin-degrading and epithelial-injuring activity in the inflammatory leukocyte populations which we have examined. To determine whether the macrophages could also be producing proteolyic activity against fibro-

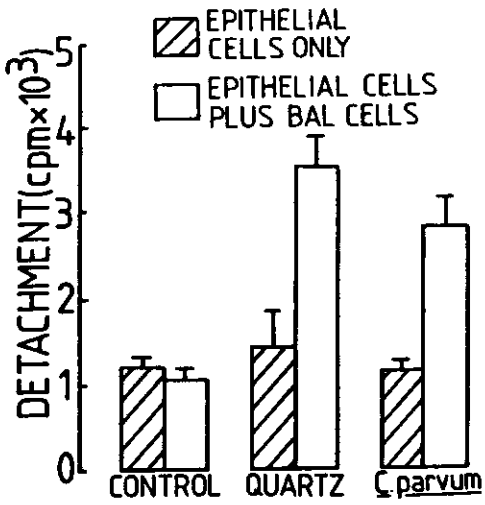

Figure 4. Detachment injury caused to alveolar epithelial cells *in vitro* by co-culture with control, quartz or *C. parvum* elicited bronchoalveolar leukocytes. All data given as mean + SEM of triplicate cells in 3 separate experiments. Significantly increased detachment caused by quartz and *C. parvum* treatment ($p<0.001$).

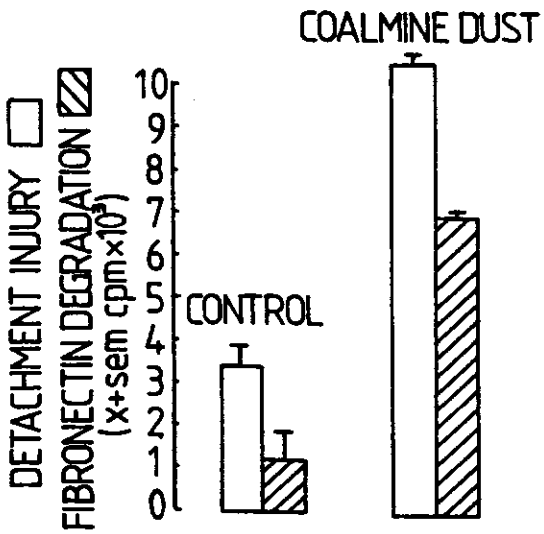

Figure 5. Detachment injury and fibronectin degradation caused by control bronchoalveolar leukocytes and bronchoalveolar leukocytes from rats inhaling coalmine dust for 45 days. Significant increases ($P<0.001$) in both parameters with coalmine dust exposed bronchoalveolar leukocytes compared to controls.

nectin, and causing detachment injury, the 5 day quartz bronchoalveolar leukocytes were separated into macrophage-enriched and neutrophil-enriched populations. These were then tested for their ability to cause epithelial cell detachment injury. Figure 6 demonstrates that separation of the mixed population into the enriched populations resulted in very high levels of epithelial injury being caused by the neutrophil-enriched fraction. However, despite the macrophage-enriched fraction containing only 5% PMNs, this population caused 5-fold more detachment injury than control alveolar macrophages.

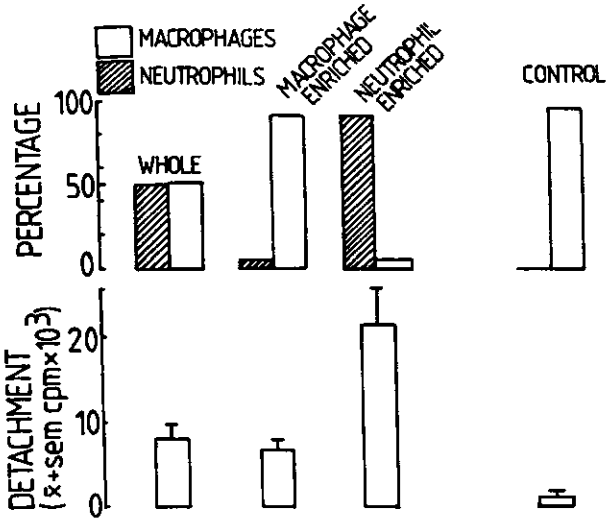

Figure 6. Cellular composition (upper panel) of, and detachment injury (lower panel) caused by, whole quartz-elicited bronchoalveolar leukocytes and both macrophage-enriched and neutrophil-enriched fractions obtained from it. Proportions of neutrophils and macrophages shown as mean percentage. Detachment injury shown as mean + SEM of cpm in detached cells.

DISCUSSION

This study has shown that a single injection of silica into the rat lung causes a long-term alveolitis. The alveolitis is characterized by a 3–12 fold increase in bronchoalveolar leukocytes comprising 30–40% neutrophils. Intratracheal instillation of a heat-killed bacterial preparation (*C. parvum*) or yeast cell walls (zymosan) also caused large scale burst of inflammation immediately following injection but these resolved quickly, returning to near normal levels by 15 days. Thus the initial severity of the alveolitis is not the main factor determining the persistence of silicotic inflammation in the intratracheal model.

The exact events which engender persistent inflammation with silica are speculative but cytoxicity of quartz towards alveolar macrophages might be central. The consequence of silica-induced alveolitis is likely to be fibrosis since the ability of inflammatory leukocytes to mediate further damage and pathological change in the lung is well established for a range of aetiologic agents.[4] In an attempt to understand which leukocyte-derived injurious factors might be important in the development of quartz-related pathology we examined the ability of the leukocytes from quartz-exposed lung to break down fibronectin. During the acute inflammation engendered

by *C. parvum* and zymosan there were high levels of proteolyic activity present; the levels of protease however returned to normal within 15 days. An examination of the proteolytic activity of quartz-elicited leukocytes showed that this proteolytic activity, capable of breaking down fibronectin and other connective tissue elements[7] and so generating chemotaxin[10] and causing epithelial injury and basement membrane damage,[6] was 4, present persistently, and in increased quantities, for up to 1 month following quartz instillation; previous studies suggest that this inflammation and hence the increased protease burden persist for up to 3 months and possibly longer. The total proteolyic burden of the lung is not reflected adequately as the increase, on a per cell basis, in dust-elicited bronchoalveolar leukocytes since the total number of leukocytes is also increased. If the increase in cell numbers is taken into consideration (a 16-fold increase on day 30) this produces a greater than 30-fold increase in the total protease burden of the lung following silica exposure for 30 days. Although the present study has utilized intratracheal instillation we have found that inhalation exposure to a pneumoconiotic dust (coalmine dust containing quartz) also caused an alveolitis producing greatly enhanced lung burdens of fibronectin-degrading activity.[11]

The ability of inflammatory bronchoalveolar lavage leukocytes to injure epithelial cells correlates with proteolyic activity[6] and so we examined this aspect of injury production by quartz bronchoalveolar leukocytes. The quartz bronchoalveolar leukocytes caused detachment injury which appeared to be mediated by both macrophages and neutrophils as shown by separation studies where the different leukocyte types were obtained in enriched form. It is therefore possible to conclude that the bronchoalveolar macrophages from quartz-exposed lung are activated with regard to proteolyic activity. The time course studies with *C. parvum* revealed a modest macrophage alveolitis present beyond 15 days but this population was not activated with regard to protease production. The fact that the cell numbers were increased compared to controls argues for the fact that this did indeed represent an inflammatory population albeit one which was not characterized by increases in neutrophils. It is possible therefore that only inflammatory macrophages from mixed populations, where neutrophils are also present, show increased proteolytic activity. A likely explanation for this is that the alveolar macrophages from such populations have internalized neutrophil elastase as has been previously reported.[12] It was noteable that the neutrophil-enriched fraction had twice the proportion of neutrophils found in the whole population but produced a 3-fold increase in detaching activity. This suggests that either the separation procedure caused activation of neutrophils or that macrophages suppressed neutrophil proteolytic activity in the mixed population.

This study has shown that a single deposition of 1 mg of quartz in the rat lung causes a prolonged and intense alveolitis characterized by increased proteolytic activity of bronchoalveolar leukocytes, capable of causing injury to the epithelial and matrix elements of the alveolar septum. The results strongly suggest that leukocytes from rats exposed by inhalation to pneumoconiosis-producing dust also have these properties and that both macrophages and neutrophils express this injurious proteolytic activity, although in the case of macrophages this may be due to sequestered neutrophil elastase.

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THE EFFECT OF TACHYKININ DEPLETION ON HYDROGEN SULPHIDE TOXICITY IN RATS

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INTRODUCTION

Hydrogen sulphide (H_2S) toxicity is one of the leading causes of sudden death in the work place. Hydrogen sulphide occurs naturally in coal, oil and natural gas deposits, and is also produced by anaerobic decomposition of sulphur containing organic matter. it is used extensively in industry and more than 70 occupations are potentially exposed to H_2S.[9] The problem of H_2S toxicity is particularly acute in Alberta; approximately one in six gas wells emit sour (H_2S) gas, and the major emphasis of sulphur containing energy resources in the province has increased the risk of exposure for workers in the petro-chemical industries and the general public.[5]

H_2S is both an irritant and asphyxiant gas which exerts its primary toxic effects on the respiratory and neurologic systems.[4] Fatal cases almost invariably exhibit fulminant hermorrhagic pulmonary edema as well as cerebral edema and severe damage to the conjunctiva, olfactory nasal mucosa and upper respiratory tract.[1,5] Similar findings are observed in experimental animals.[4,14,15,16]

The mechanism for H_2S induced pulmonary edema is not understood. H_2S induced paralysis of the respiratory control centre and/or stimulation of carotid body receptors, may be involved.[4,3,9] There is also evidence that H_2S is directly toxic to the lungs. H_2S is only moderately soluble, and is able to penetrate to the lung periphery. Injury to the alveolar/capillary membrane would result in increased vascular permeability and edema.[10] The high protein and cellular content in the alveolar fluid in experimental H_2S exposure support the latter possibility.[14] A direct toxic effect on the respiratory system is also indicated by the observation that pulmonary edema occurs at exposure levels below those associated with severe central nervous system depression.

A further possible mechanism for H_2S induced pulmonary edema might involve stimulation and release of vasoactive neuropeptides from vagal nerve fibres. Unmyelinated postganglionic nerves of the C-fibre group contained in the vagus nerve, are important mediators of neurogenic inflammatory responses in the lung. This response is mediated by a specific neurotransmitter known as substance P which, in part, is responsible for increased vascular permeability and edema occurring during the acute stages of lung inflammation.[18,19,11,6] In addition to modulating vascular permeability in the respiratory tract, substance P is a potent constrictor of bronchial smooth muscle, stimulates mucociliary activity and promotes mucous secretion in the airways.[23,26,28] Immunohistochemical studies have revealed a rich plexus of substance P containing nerve fibres within and beneath airway epithelium, and around blood vessels and seromucous glands.[20,21] Capsaicin, the main pungent ingredient of hot peppers, is a vanilly/amide derivative that produces selective depletion of tachykinins, including substance P, in C-afferent fibres.[12]

In view of the important role of substance P in airway inflammatory responses, we decided to study the effects of hydrogen sulphide in animals previously depleted of substance P. This report will focus on the pathophysiology of the airway lesions. The vascular and edemogenic component will be published in detail elsewhere. In addition, the histological changes induced in the lungs of animals exposed to H_2S were compared with those observed in the lungs of human cases of fatal hydrogen sulphide exposure.

REVIEW OF WORKPLACE EXPOSURES IN ALBERTA, 1977–1986

One hundred and sixty two lost-time workman's compensation cases were recorded in Alberta in the decade 1977–1986.[2] The majority of these (68%) involved exposures in the oil and gas industry. 79% were aged 34 or less. There were 21 fatalities; most of these occurred in facilities where the dangers were known and protective equipment was available. Eight fatalities were a direct result of failure to follow correct safety practices. 87% of all workers exposed to H_2S developed respiratory system symptoms. In all cases where H_2S intoxication was the primary cause of death, autopsy revealed pulmonary edema. (Figure 1)

ANIMAL STUDIES

Materials and Methods

Thirty-six male, Fischer-344 (CDF24Cr1BR), eight week old rats (Charles River, Inc., Quebec) were obtained for this study and acclimatized for ten days under carefully controlled conditions.[24] The guidelines provided by the Canadian Council of Animal Care, were followed throughout all phases of the study.[7] At the time of exposure, the rats weighed

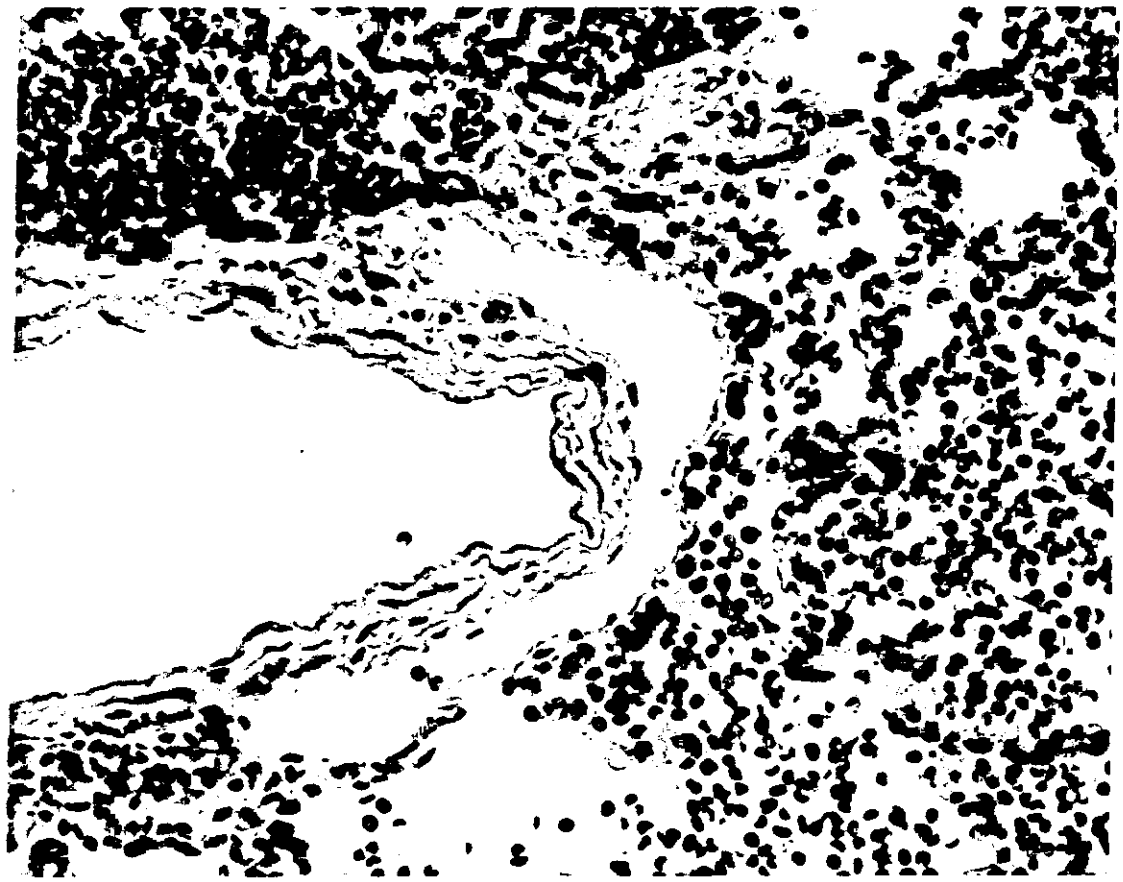


Figure 1. Microscopic appearance of lungs from human fatal case of acute H_2S intoxication. A. The alveoli are flooded with hemorrhagic edema fluid. Polymorphonuclear cells are noted in the alveoli and marginating along vessels in the alveolar interstitium. (Hematoxylin and eosin x 150)

138.4±4.8 gms. Rats were assigned to one of four different groups using a randomized model (Table I). Within one hour of termination of exposure, rats were anesthetized with Halothane (5%) and exsanguinated by incising the abdominal aorta.

Depletion of Substance P

Capsaicin (Rotichrome[R] Carl Roth) was dissolved in 10% alcohol and 10% tween 80. In the treated group, capsaicin was administered to a total dose of 150 mg/kg subcutaneously, in eight divided doses over a period of two days. The acute effects of capsaicin were reduced by pretreatment with aminophylline 10 mg/kg IP. Rats of the control group received physiologic saline and aminophylline.

Hydrogen Sulphide Exposures

Fourteen days after the last injection of capsaicin or saline, rats were divided into four groups and exposed for four consecutive hours to either air or H_2S. The concentration of gas in the two H_2S chambers is shown in Table I. The H_2S exposure system has been described in detail elsewhere.[24] A schematic diagram of the exposure system is shown in Figure 2. The chamber atmosphere was sampled every two minutes and analyzed by gas chromatography (Model 5790A, Hewlett Packard[R]).

Bronchoalveolar Lavage and Protein Determination

The left lung was cannulated and three consecutive bronchoalveolar lavages performed. The protein concentration (g/l) in the lavage fluid supernatant was determined using methods previously reported.[14]

Light and Electron Microscopy

The tracheas of subgroups of rats were cannulated and the lungs inflated with 2.5% glutaraldehyde (320 M Osmol) at a constant pressure of 20 cm of water for 30 minutes in situ. They were then removed from the thoracic cavity and allowed to fix for twenty-four hours. Following fixation, blocks were processed for routine light microscopy and 5 μ sections were mounted on glass slides and stained with hematoxylin-eosin.[17]

For scanning electron microscopy and morphometry, the intrapulmonary portion of the left main bronchus was excised with adjacent lung and dehydrated in graded concentrations

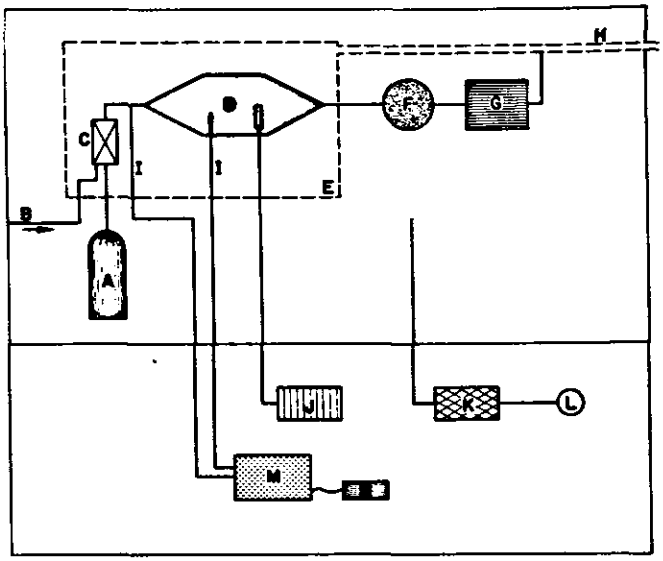
Figure 1. Microscopic appearance of lungs from human fatal case of acute H_2S intoxication. B. Section of main bronchus showing ciliated epithelial cell exfoliation and mucosal edema. (Hematoxylin and eosin x 400)

Table I
Experimental Design

Treatment	Hydrogen sulphide (mg m^3)		
	0	H_2S (1)	H_2S (2)
Capsaicin	6*	6*	6**
Saline	6*	6*	6**

Total number of rats = 36

(1) actual concentration 559 ± 144 mg m^3
(2) actual concentration 525 ± 87 mg m^3
* for bronchoalveolar lavage
** for histopathology



LEGEND

A - GAS CYLINDER
B - AIR
C - FLOW CONTROLLERS
D - EXPOSURE CHAMBER
E - FUME HOOD
F - VACUUM PUMP
G - SCRUBBER
H - EXHAUST TO OUTSIDE
I - SAMPLE LINE
J - RELATIVE HUMIDITY & TEMPERATURE MONITOR
K - H_2S MONITOR
L - ALARM
M - GAS CHROMATOGRAPH
N - COMPUTER

Figure 2. Diagram of the H_2S exposure system.
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of ethyl alcohol, critical point dried and coated with gold/palladium. The specimens were examined in a Hitachi S-450 scanning electron microscope. Five approximately equally spaced photographs were obtained of the proximal 3 mm of the left intrapulmonary bronchus at 1000 x magnification and constant working distance. The density of ciliated and nonciliated epithelial cells, expressed as a percent of the total area, was determined for each photograph using a Dapple[R] image analysis system.

Detection of Substance P

Substance P was detected in tissues using an indirect immunofluoresence technique[27] and examined using a Reichert-Jung Polyvar microscope, equipped with filter system Bl (excitation wavelength 450-495 nm).

Statistical Analysis

The effect of capsaicin and/or H_2S on mortality was tested by the Fischer Exact Test. The effects of capsaicin and H_2S on airway epithelial cells was tested by analysis of variance.[25]

RESULTS

Sections of lung and trachea stained by immunofluorescence for substance P, showed staining of nerve fibres in the mucosa of the trachea and within the walls of small airways and around blood vessels in the lung.The density of fibres was greatest in the trachea and least in the peripheral lung. Animals treated with capsaicin showed almost complete depletion of substance P containing nerve fibres.

Animals pretreated with capsaicin showed normal weight gain and exhibited no signs of toxicity or mortality prior to exposure. Exposure to H_2S for four hours, produced 100% mortality in the capsaicin treated animals and 20% mortality in the saline treated controls. (Table II) At postmortem examination, frothy blood-stained fluid was noted to exit from the mouths and noses of all animals dying from hydrogen sulphide exposure. The lungs of these animals were deeply congested and failed to collapse when the thorax was opened. Histological examination of the affected lungs revealed large quantities of hemorrhagic and highly proteinaceous fluid within the alveolar spaces. Edema fluid was also noted in perivascular and interstitial locations.

Animals exposed to H_2S alone, showed significantly more protein in bronchoalveolar lavage fluid than was seen in air exposed saline or capsaicin pretreated animals. This effect was even greater in animals pretreated with capsaicin and then exposed to H_2S. Animals pretreated with saline and exposed to H_2S, showed a significant increase in lung wet weights. This effect was even greater in animals pretreated with capsaicin.

Table II

Mortality (%), and Substance P in Rats Pretreated with Saline Solution or Capsaicin and Exposed to Hydrogen Sulphide

Variable	Air		H_2S	
	Saline	Capsaicin	Saline	Capsaicin
Substance P	+	-		
Mortality (%)	0	0	20	100*

* $P<0.05$

Examination of large and small conducting airways by light and scanning electron microscopy revealed evidence of severe mucosal damage following H_2S exposure. The changes were most marked proximally and occasional areas of ulceration were noted in the mucosa of the trachea but not in the major bronchi. (Figure 3) The primary finding in the major conducting airways was wide-spread exfoliation of epithelial cells with lateral spreading of basal and intermediate cells. (Figure 4) The bronchioles were relatively spared of toxic effects. The effects noted above were much more severe in animals pretreated with capsaicin and subsequently exposed to H_2S. (Figure 5) The results of morphometric eval-

Figure 3. Scanning electron micrograph of area of ulceration in trachea from saline pretreated rats exposed to H_2S for 4 hours. (x 2000)

uation of the extent of loss of ciliated epithelial cells in the left main bronchus, are shown in Figure 6. There is evidence of an additive effect attributable to capsaicin alone p=0.0003 and an additive effect attributable to hydrogen sulphide p=0.003. There was no evidence that the effect of capsaicin depended on the presence or absence of hydrogen sulphide p=0.61.

Figure 4. Scanning electron micrograph of left main bronchus from saline pretreated rat exposed to 559 mg M^3 H_2S for 4 hours. There is exfoliation of ciliated epithelial cells with lateral spreading of basal and intermediate cells. (x 2000)

DISCUSSION

These experiments confirm the previously reported findings concerning the toxic effects of H_2S on the lungs. Animals exposed to H_2S without capsaicin pretreatment, had a 20% mortality at an average concentration of 542 mg M^3. These results are similar to those previously reported from this laboratory with this strain of rat where the LC50 and LC10 values for four hours of exposure were 701 and 591 mg per m^3, respectively.[24] The exposure concentration was selected such that there would not be significant mortality in normal

Figure 5. Scanning electron micrograph of left main bronchus from: (A) air-exposed, saline pretreated rat. Approximately 50% of the mucosal surface is ciliated.

rats. Animals pretreated with capsaicin and exposed to the same concentration of hydrogen sulphide, showed 100% mortality. In addition, the animals died at an earlier time during exposure than animals pretreated with saline and then exposed to H_2S. Animals pretreated with capsaicin and subsequently exposed to H_2S, also had more severe pulmonary edema with greater concentrations of protein in the lavage fluid and heavier lungs postmortem. Although to

Figure 5. Scanning electron micrograph of left main bronchus from: (B) saline pretreated H_2S exposed rat showing loss of ciliated epithelium.

some extent these changes could reflect transudation of fluid into the lungs postmortem, we consider this unlikely in view of the magnitude of the effect.

The airway lesions noted in the H_2S exposed rats are similar to those reported for sulphur dioxide.[22] The lesions were most severe in the proximal airways with relative sparing

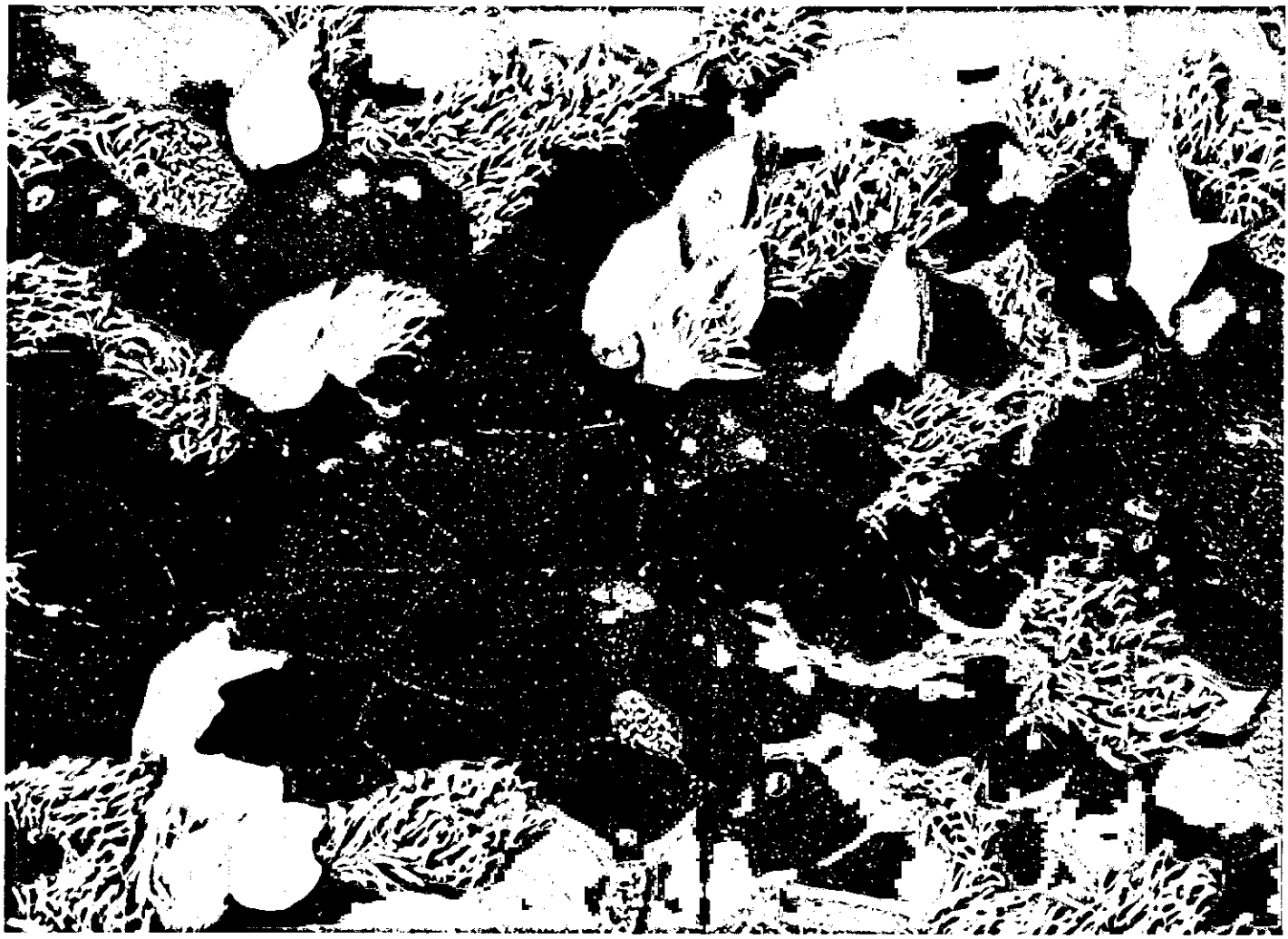

Figure 5. Scanning electron micrograph of left main bronchus from: (C) capsaicin pretreated H_2S exposed rat showing greater loss than is seen in B. (x 1000)

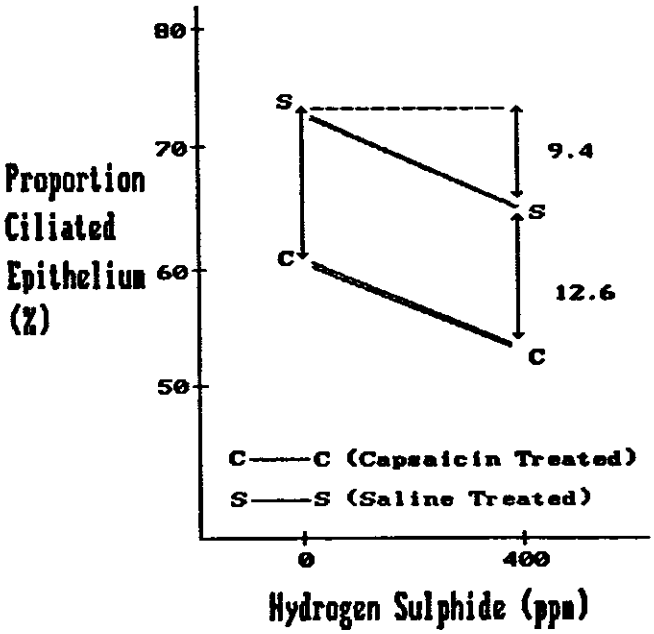

Figure 6. Proportion of airway mucosa occupied by ciliated epithelium by group. H_2S exposure alone and capsaicin pretreatment alone result in loss of ciliated epithelium. Capsaicin plus H_2S has an additive effect.

of the bronchioles and alveolar ducts. Previous studies have shown that the respiratory and olfactory epithelial cells of the nasal mucosa are also very sensitive to H_2S induced injury.[15] This pattern of injury is consistent with the moderate solubility of H_2S in water. Scrubbing of H_2S (as H_2SO_3) in the nasal passages and upper airways should result in maximal concentrations of gas proximally with greatest injury to this site.

The mechanism of irritant and oxidant gas injury of the upper airway has been extensively studied. (reviewed in 22) Ciliated epithelial cells appear to be more susceptible to injury than non-ciliated cells. This is true for SO_2, O_3 and NO_2[22,13] and based on this study, appears to be also true for H_2S induced injury. Lipid peroxidation is probably the primary biochemical mechanism for cell injury due to oxidant gases. The mechanism of cellular toxicity due to H_2S is likely to be different. H_2S is toxic to a number of cellular systems and biochemical pathways,[3,4] however the ability of H_2S to react with metal ion-containing proteins is probably of primary importance. H_2S is able to reduce one of the hemes of the intracellular mitochondrial enzyme cytochrome C oxidase, thus interfering with oxidative metabolism. (reviewed in 3) H_2S is reported to be a more potent inhibitor of cytochrome oxidase than hydrogen cyanide.[8] H_2S also interacts with succinic dehydrogenase, catalase and peroxidase and these interactions may also be important in promoting epithelial injury.

Injury of airway epithelium results in cytoskeletal abnormalities and disruption of the tight junctions between the epithelial cells. This leads to an increase in paracellular permeability and exfoliation of the ciliated cells. (reviewed in 22) The repair process is initiated immediately as the remaining viable non-ciliated epithelial cells spread laterally to maintain the epithelial barrier. The data presented in this paper indicate that a similar sequence of events occurs following H_2S injury.

An unexpected finding in this study was the demonstration of a potentiating effect of neuropeptide depletion on H_2S induced airway injury. Thompson *et al.*[29] have demonstrated that airway responsiveness to toluene diisocyanate in guinea pigs is mediated by capsaicin sensitive afferent nerves. These findings indicate a role for tachykinins in pulmonary defense mechanisms against inhaled toxic agents and in the maintenance of structural integrity of the airway mucosa. Studies are underway to fully characterize this phenomenon and elucidate the mechanisms.

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JOINT EUROPEAN INVESTGATIONS OF NEW GENERATIONS OF DUST SAMPLING INSTRUMENT

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INTRODUCTION

Considerable success has been achieved in understanding the predominant relationships between the risk of coalworkers' pneumoconiosis and exposure to fine particles of airborne coalmine dust. This has led to the setting of meaningful standards and, in turn, substantial reductions in the incidence of disease by improved dust suppression. However there is still the need for further improvement to deal with a number of important dust-related health problems which remain. In order to make progress in these areas, new research questions are posed requiring more detailed information about the properties of the airborne dust which cannot be obtained just by the use of instruments like those employed in much of the previous research. A need is therefore identified for a new generation of dust sampling instrument. Various new instruments have emerged in recent years, and it is timely to critically assess some of them in relation to the current research needs. To this end a Joint Project, involving six laboratories from five European Member States, has been carried out under the auspices of the Commission of European Communities (CEC). The participating laboratories were:

- Bergbau-Forschunginstitut GbmH, Essen, West Germany (BF)
- Silikose-Forschunginstitut, Bochum, West Germany (SF)
- Centre d'Etudes et Recherche des Charbonnages de France, Verneuil en Halatte, France (CERCHAR)
- Institut d'Hygiene des Mines, Hasselt, Belgium (IHM)
- Instituto di Medicina del Lavoro, Milan, Italy (IML)
- Institute of Occupational Medicine, Edinburgh, UK (IOM)

This paper describes the project coordinator's preliminary assessment of what was achieved.

RATIONALE

The new generation of dust sampling instrument includes a range of particle size-selective devices from which information about health-related fractions of airborne dust may be obtained. The rationale against which to compare and evaluate these instruments was based primarily on the 1983 recommendations of the International Standards Organization (ISO),[1] updated where appropriate in the light of more recent experimental evidence. The dust fractions in question are inspirable (the fraction that enters through the nose and/or mouth during breathing), thoracic (that penetrates below the larynx) and respirable (that penetrates to the alveoli). Of these, it is the inspirable fraction which, when it is referred to below, has been updated from the 1983 version, thus bringing it in to line with the definition contained in the 1985 recommendations of the American Conference of Governmental Industrial Hygienists (ACGIH).[2] In addition, since it forms the basis of present sampling in some European countries, an alveolar fraction was also included, describing a fine fraction which takes account of the fact that—in actual human exposure—the finest inhaled particles remain airborne for long enough to be exhaled during the exhalation phase of the breathing cycle.[3] The important philosophy embodied in the ISO recommendations is that all the dust fractions which deposit in the regions of the respiratory tract are subfractions of the inspirable fraction. This is consistent with what happens during actual human exposure. Ideally, it should also be reflected in sampler performance; namely that the efficiency with which particles enter the sampler in the first place should match the inspirable fraction.

The information provided by the various instruments includes details not only about airborne mass concentrations within defined fractions but also about mineralogical composition (and, possibly, physical properties such as particle shape). The instruments themselves fall into two categories. In the first, dedicated instruments sample to a given, single criterion (e.g., respirable dust), although some can also provide information about 'total' dust. In the second, more versatile instruments—broadly referred to as spectrometers—can provide a wider range of information. These operate on the principle that, if a defined fraction of airborne dust can be aspirated and its particle aerodynamic size distribution subsequently obtained, then all the information is available to allow determination of the particle aerodynamic size distribution and airborne mass concentration of any health-related subfraction which can be defined numerically. If the dust thus classified can be recovered in sufficient quantities for analysis, then the mineralogical composition of such subfractions can also be determined.

THE INSTRUMENTS

During a Workshop which took place in Edinburgh early on in the project, involving all the participants, the following instruments were identified for inclusion in the study:

- The French 10 l/min CIP10 personal sampler for respirable dust, also capable of providing a measure of 'total' dust. Its pre-selector operates on the principle of filtration by porous foam filtration media.
- The Italian 2 l/min modified-Zurlo (M-Z) personal sampler for respirable dust. Its pre-selector operates on the principle of virtual impaction.
- The Italian 3.5 l/min personal sampler for 'total' dust (TD)
- The British 3 l/min static inspirable dust sampler (IOMID).
- The Italian 0.4 l/min static dust spectrometer (INSPEC). It operates on the principle of inertial classification.
- The Italian 2 l/min personal dust spectrometer (PERSPEC). This too operates on the principle of inertial classification.
- The German 40 l/min static dust spectrometer (PCI). It operates on the cascade impactor principle.
- The British 10 l/min static inspirable dust spectrometer (SIDS), also operating on the cascade impactor principle.
- The British 2 l/min personal inspirable dust spectrometer (PIDS), also operating on the cascade impactor principle.

In addition to these, various instruments from the previous generation were also included for the purpose of comparison. These were:

- The German 50 l/min cyclone-based static sampler for alveolar dust (TBF50), also capable of providing a measure of 'total' dust.
- The German 46 l/min horizontal elutriator-based static sampler for respirable dust (MPGII).
- The Italian 2.4 l/min cyclone-based personal sampler for respirable dust (CYCLO).
- The French 50 l/min cyclone-based static sampler for alveolar dust (CPM3).
- The British 2.5 l/min horizontal elutriator-based static sampler for respirable dust (MRE).
- The British 1.9 l/min cyclone-based personal sampler for respirable dust (SIMPEDS).
- The Belgian 17 l/min static sampler for total dust (STASER).

The mean features of the above instruments are summarized in Table I.

THE PROGRAMME OF WORK

The research was carried out during the 3-year period 1985 to 1988. During the Edinburgh Workshop, it was agreed that, as far as possible, each of the principal instruments identified for inclusion in the trial should be evaluated by more than one laboratory and that each laboratory should evaluate more than one instrument. Thus assessment of a given instrument is less likely to be biased by the findings of, say, just one laboratory. In addition, it was agreed that two of the instruments—namely the CIP10 and PCI—would be evaluated by all six participating laboratories.

The project called for a programme of comparative trials both in the laboratory and underground in mines (pyrites for Italy, coal everywhere else). Each laboratory developed its own experimental strategy, determined by the resources and expertise at its disposal. Thus the emphasis varied considerably between laboratories. At IOM, for example, the main emphasis was placed on the laboratory aspect, based on the extensive facilities available (notably the large wind tunnel) and associated expertise. Elsewhere, greater importance was given to the underground trials. In some, greater stress was placed on the abilities of the instruments to provide information about mineralogical composition; and, in others, on the basic performance characteristics (notably with respect to particle size-selectivity) of the individual devices. The net effect of all the complementary contributions has been to provide an overall, balanced programme of work, as summarized in Table II.

The experimental inquiry fell into three broad areas:

- Experiments to assess basic performance characteristics (e.g., aspiration efficiency, particle size selectivity).
- Measurements of concentrations of health-related dust fractions and subfractions.
- Measurements of mineralogical composition.

RESULTS

In this paper, only concise, largely qualitative summaries of the results available at the time of writing are given. Whilst most are based on information obtained directly during the Joint Project itself, some information obtained during other studies has also been taken into account in some cases. The full experimental and statistical details of the individual studies are given in the final reports of the six individual component projects, while the combined analysis and overall conclusions will appear in the synthesis report which is still in preparation.

Basic Performance Characteristics

This aspect of the work was conducted in the laboratory. One area of interest is the efficiency with which particles enter the sampler initially. For ideal health-related sampling, this should match the inspirable fraction, since any samplers for which this is true are consistent with the ISO rationale referred to above. Experiments to assess entry efficiency were performed with this in mind, mostly in the large wind tunnel at IOM. All devices intended for use as personal samplers were tested in that mode, mounted on the torso of a tailor's mannequin which, during sampling, was rotated step-wise through 360 degrees (to eliminate preferred-orientation effects). In the case of the CIP10, it was also tested as a static sampler (since it is used by some workers in this mode). The results are summarized in Table III where, here and in the following tables, the quantitative experimental information reported in the original investigations has been reduced to the qualitative form shown. At this stage, until further analysis of the data is carried out, it is possible only to place the instruments into arbitrarily-chosen broad performance categories, without reflecting the degree to which each either conforms or fails to conform. In Table III, therefore, 'YES' indicates acceptance, with more than 50% of the available data points falling within $\pm$ 10 percentage points of the definition in question (inspirable or true total dust). 'NO' indicates non-acceptance, with less than 50% of the available data points lying within the same band. In certain cases, the

Table I
The Instruments Tested and Their Main Features

Sampler	Type	Flowrate l/min	Principle of size selection	Nominal fraction	Other fractions
CIP10	Dedicated	10	Porous foam filtration	Respirable/ alveolar	'Total'
M-Z	Dedicated	2	Virtual impaction	Respirable	-
TD	Dedicated	3.5	Aspiration	'Total'	-
IOMID	Dedicated	3	Aspiration	Inspirable	-
INSPEC	Spectrometer	0.4	Inertial separation	-	-
PERSPEC	Spectrometer	2	Inertial separation	-	-
PCI	Spectrometer	40	Cascade impactor	True total + subfractions	-
SIDS	Spectrometer	10	Cascade impactor	Inspirable + subfractions	-
PIDS	Spectrometer	2	Cascade impactor	Inspirable + subfractions	-
TBF50	Dedicated	50	Cyclone	Alveolar / respirable	'Total'
MPGII	Dedicated	46	Horizontal elutriator	Respirable	-
CYCLO	Dedicated	2.4	Cyclone	Respirable	'Total'
CPM3	Dedicated	50	Cyclone	Alveolar/ respirable	-
MRE	Dedicated	2.5	Horizontal elutriator	Respirable	'Total'
SIMPEDS	Dedicated	1.9	Cyclone	Respirable	'Total'
STASER	Dedicated	17	Aspiration	True total	-

judgement may be influenced also by any obvious contradictory trends present in the data. The table shows that the PCI provides a fair sample of true total dust (not surprisingly, since sampling with this instrument is arranged to take place almost isokinetically by virtue of the choice of number of entry nozzles). So too (for similar reasons) should the STASER (although this has not been investigated experimentally). The M-Z, IOMID, SIDS and PIDS all match the inspirability criterion quite well. So too does the CIP10 in its personal mode, but *not* as a static sampler.

The basic selectivities of the two new samplers dedicated (nominally) to the respirable dust fraction (CIP10 and M-Z respectively) were also assessed at some laboratories. For the CIP10, selectivity matches the BMRC-definition (as a subfraction of the inspirable fraction) quite well except at small particle sizes where the finest particles are not collected by the porous foam final collection stage of the instrument and so are lost. However, it is noted that the proportion of the mass carried by particles lost in this way may be expected always to be very small in most practical situations. In any case, it may be argued that the dust which is lost in this way is roughly equivalent to that which is exhaled. Therefore the CIP10 selection curve has features in common with both the BMRC respirable dust definition and that for the alveolar fraction (although it matches neither perfectly). For the M-Z, agreement with the BMRC-definition is fair. For the earlier-generation instruments, selectivity is available from previously published information. For these devices, it is worth noting that the TBF50 and the CPM3 both exhibit selection characteristics which more closely reflect true alveolar deposition. The MPGII and MRE both conform closely to the BMRC-definition.

The INSPEC and PERSPEC require special comment. The performance of the first was found to exhibit effects associated in part with its low sampling flowrate; namely, biased entry characteristics (depending on the type of entry piece attached), high particle losses between the entry and the sensing region, and collected mass too small to allow gravimetric assessment. The first two effects are more pronounced the larger the particle size. Furthermore, in its present mains-powered version, INSPEC does not satisfy intrinsic safety criteria which would allow its use underground

Table II
Outline of Programme of Work Carried Out

Sampler	LABORATORY					
	BF	SF	CERCHAR	IHM	IML	IOM
CIPIO	P	L,U	L,U,P,M	U,M	. .	L,P
M-Z	. .	. .	. .	. .	U,P	L,P
TD	. .	. .	. .	. .	U	L,P
IOMID	. .	. .	. .	. .	. .	U,P
INSPEC	. .	. .	. .	. .	. .	P
PERSPEC	. .	. .	. .	. .	. .	P
PCI	U,M	L,U	L	U,P,M	. .	L,U,P
SIDS	. .	. .	. .	. .	. .	L,U,P
PIDS	. .	. .	L	U,M	U	L,P
TBF50	U	U	. .	. .	. .	L,U,P
MPGII	U	U	. .	. .	. .	-
CYCLO	. .	. .	. .	. .	U,P	L,P
CPM3	. .	. .	L,U	U,M	. .	-
MRE	. .	. .	. .	. .	. .	L,U
SIMPEDS	. .	. .	. .	. .	. .	L
STASER	. .	. .	. .	U,M	. .	-

L = Comparative trials in the laboratory
U = Comparative trials underground
P = Evaluation of basic performance characteristics
M = Evaluation of instrument's ability to provide mineralogical data

in coalmines. In its present form, this instrument would seem to be more suited to fine-particle aerosol studies in the laboratory or in less ardous workplace conditions. PERSPEC, with its higher sampling flowrate does permit the collection of larger dust deposits. However the recovery of fractions classified according to particle size is difficult in present versions of the instrument since it requires precise dissection of the collection filter. For such reasons, these two instruments did not feature significantly in the comparative studies that subsequently formed the bulk of the project. It is understood that both are undergoing further development to improve performance and practical applicability.

Comparative Performances in Relation to Health-Related Dust Fractions

Large numbers of comparative trials were carried out, both in the laboratory and underground in mines. In each individual run, an instrument was identified which provided a reference for the fraction of interest. For example, for true total dust the reference was usually a thin-walled probe facing into the wind and aspirating isokinetically. For the inspirable fraction, it was the IOMID, SIDS or PIDS. For respirable dust, it was the MRE (or an equivalent horizontal elutriator-based sampler such as the MPGII), and for the alveolar fraction the TBF50 (or CPM3). For the thoracic fraction, no suitable reference sampler was available. For this, therefore, it was decided to use the thoracic sample obtained from the PCI.

For the dust spectrometers (i.e., PCI, SIDS, PIDS), the determination of the dust concentration in each fraction was carried out by first determining the particle aerodynamic size distribution for the sampled dust, and then numerically cal-

Table III

Summary of the Entry Characteristics of the Instruments Tested

Sampler	Entry efficiency	
	True total	Inspirable
CIP10 (personal)	NO	YES
CIP10 (static)	NO	NO
M-Z	NO	YES
TD	NO	NO
IOMID	NO	YES
INSPEC	NO	NO
PERSPEC	NO	YES
PCI	YES	NO
SIDS	NO	YES
PIDS	NO	YES
TBF50	NO	NO
MPGII	*	*
CYCLO	*	*
CPM3	NO	NO
MRE	NO	NO
SIMPEDS	*	*
STASER	YES	*

YES - unqualified acceptance NO - not appropriate
* - no information

culating the size (frequency) distribution of the fraction of interest. The area under this new curve gives the mass sampled in the fraction of interest, and hence its airborne concentration.

From the large body of data available from all the trials that were carried out, Table IV summarizes qualitatively how well the various instruments provide information relevant to the various health-related dust fractions. Here, as in the previous table, a fairly bland assessment of the relative performance is given. It is based on examination of combinations of the various instrument comparisons against suitable reference samplers and information about their selection characteristics. Where there are inconsistencies, the judgement is made by inspecting the total information available and, where appropriate, a qualified acceptance ('OK') is indicated. It should be noted that although the first two columns appear to be the same as those in Table III, the ratings now take into account the accessibility of the sampled dust in those fractions. Hence, for example, although the CIP10 actually aspirates the inspirable fraction quite satisfactorily, it is not so easy to recover it for gravimetric assessment. Therefore a 'YES' in Table III becomes 'OK' in Table IV.

Later, when all the results have been combined and analyzed in greater detail and have been discussed by all the participants in the Joint Project, a more detailed picture will become available.

Mineralogical Assessment of Sampled Dust

One important aspect of sampler performance is the ability to collect dust samples within desired fractions or classified size ranges in a form (i.e., quantity, accessibility) suitable for mineralogical assessment. This was studied, again both in the laboratory and in the field trials. The conclusions are summarized in Table V for typical coalmine dusts. In these studies, the main emphasis was placed on the quartz content—reflecting the general interest in health-effects associated with quartz-containing dusts.

The methods which were used for mineralogical assessment included infrared spectrophotometry and X-ray diffractometry. For both, the greater the amount of dust which is available for the assay, the better. Obviously, however, the minimum amount of dust required to carry out a satisfactory analysis depends greatly on the particular analytical instrumentation available. Within the laboratories participating in the Joint Project, such capability varied appreciably. For present purposes, the simple 'rule-of-thumb' was adopted that a minimum mass of 0.1 mg of mixed mine dust should be available in order to enable assessment for quartz content. Table V therefore indicates judgements made on the basis of estimates of amounts collected—in the various parts of each instrument as appropriate—for typical dust concentrations over typical (up to 8-hour) sampling shifts. Of the spectrometers, the 40 l/min PCI comes out particularly well since amounts of dust are provided at each of the impactor stages more than adequate for determination of the mineralogical content of the dust throughout the particle aerodynamic size distribution. The same can be achieved using the lower-flowrate SIDS and PIDS but with less sensitivity due to the smaller amounts of dust available for analysis.

CONCLUDING REMARKS

In general, the dedicated samplers were found to be generally easier and more convenient to use. Some of the ones intended for respirable (or alveolar) dust may also provide—with some additional effort—a reasonable measure of 'total' (or, in some case, inspirable) dust. By contrast, the spectrometer-type devices require more skill on the part of the operator. This is the price of the greater versatility required in some of the expected research applications.

During the Joint Project which has been described, a number of dust samplers, originating from a number of European countries, have been tested and their performances compared. From the results, it should be possible to judge the relative strengths and weaknesses of each in relation to each proposed new application and to choose the instrument appropriate to the task accordingly. Although there is no single instrument which emerges as the universal 'best', it is clear that certain of the instruments are not appropriate for certain tasks. It is recommended that, in designing new studies to further understanding of the health-related properties of airborne dusts in mines, sampling instrumentation should be chosen after careful consideration of the results of this Joint Project.

Table IV

Summary of the Performances of the Instruments Tested in Relation to the Various Health-Related Dust Fractions

Sampler	Fraction				
	True total	Inspirable	Thoracic	Respirable	Alveolar
CIPI0 (personal)	NO	OK	NO	OK	OK
CIPI0 (static)	NO	NO	NO	OK	OK
M-Z	NO	OK	NO	OK	NO
TD	NO	NO	NO	NO	NO
IOMID	NO	YES	NO	NO	NO
INSPEC	NO	NO	*	*	*
PERSPEC	NO	YES	OK	OK	OK
PCI	YES	YES	YES	YES	YES
SIDS	NO	YES	YES	YES	YES
PIDS	NO	YES	YES	YES	YES
TBF50	NO	NO	NO	NO	YES
MPGII	*	*	NO	YES	NO
CYCLO	*	*	NO	OK	NO
CPM3	NO	NO	NO	OK	YES
MRE	NO	NO	NO	YES	NO
SIMPEDS	*	*	NO	YES	NO
STASER	YES	*	NO	NO	NO

YES - unqualified acceptance
OK - qualified acceptance
NO - not appropriate
* - no information

Table V

Summary of the Performance Characteristics of the Instruments Tested in Relation to Their Abilities to Provide Information About Mineralogical Content of the Dust During a Typical Sampling Shift in a Mine

Sampler	Coarse fractions		Fine fractions	
	Dust accessible for analysis?	Sufficient dust for analysis?	Dust accessible for analysis?	Sufficient dust for analysis?
CIPI0	OK	YES	OK	YES
M-Z	OK	YES	YES	YES
TD	YES	YES	NO	NO
IOMID	YES	YES	NO	NO
INSPEC	OK	NO	YES	NO
PERSPEC	OK	YES	YES	YES
PCI	YES	YES	YES	YES
SIDS	OK	YES	OK	YES
PIDS	OK	YES	OK	OK
TBF50	OK	YES	YES	YES
MPGII	★	★	YES	YES
CYCLO	★	★	YES	YES
CPM3	OK	YES	OK	YES
MRE	OK	YES	YES	YES
SIMPEDS	OK	YES	YES	YES
STASER	YES	YES	NO	NO

YES - unqualified acceptance
OK - qualified acceptance
NO - not appropriate
★ - no information

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COMPARATIVE MEASUREMENTS WITH VARIOUS INSTRUMENTS: PROBLEMS IN THE EVALUATION OF DUST EXPOSURES IN THE HARD COAL MINING INDUSTRY

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Dust measurements with the tyndalloscope for the evaluation of dust exposure in the mining industry were performed from the middle of the fifties until 1973. Threshold values based on this measuring procedure. For the introduction of measurements, the tyndalloscope was at first the suitable device since it obtains data per minute about time-referred concentrations. Measuring values could therefore be allocated to a defined working process, thus indicating priorities of dust development and introducing measures of dust suppression. The disadvantages of the tyndalloscope were the dependence of scattering light intensity not only on concentration but also on particle size.

Realizing that the evaluation of dust conditions according to mass concentrations of fine dust results in a more suitable risk evaluation than other measuring parameters had, in connection with the establishment of mass-referred maximum workplace values for the whole mining industry, the consequence of converting the whole measuring and evaluating system. Thus the tyndalloscope was no longer suitable for the general occupational medical assessment of workplaces since the allocation of intensity values could not be realized in individual cases (Figure 1). Due to conversion to gravimetry, partly very different, evaluations of dust conditions in comparison with tyndalloscope assessments could be observed. Including tyndalloscope measuring data in epidemiological studies raised therefore many uncertainties about earlier critical dust conditions.

In the FRG, maximum workplace concentrations are derived from the Johannesburg Convention fine dust definition. The MPG II equipped with a horizontal elutriator (Figure 2) theoretically meets this defined fractionation. In the following time, it served as reference instrument in the German mining industry. When using devices with other separating functions comparative measurements with the MPG II are obligatory to determine whether conversion relations with a sufficient statistical significance are present. The TBF 50 (Figure 3), a double-cyclone instrument, used in routine measurements without follow-up filter behind the second cyclone, was tested in 180 comparative measurements. Concentration levels are compared in Figure 4. Because of the formerly supposed global connection between ash proportion and dust particle size, a correction of TBF 50 values with regard to ash proportion was tried. Based on these calculations, a corrective diagram was made (Figure 5) which was referred to for the indication of concentration-equivalent values for the MPG II. Obviously, alterations of mining and support techniques as well as of mine layout have increasingly blurred the connection between ash proportion and dust particle size. Thus, a correction via ash proportion is questionable at present. According to recent research findings, the conversion factor between these two instruments is independent of this parameter (Figure 6). The individual registered measuring positions represent mean values of 3 to 4 measurements at the same positions over a whole shift. Any position reflects various faces with different coal types and different mining techniques.

Relating the results obtained by the TBF 50 instrument with and without filter, a dependency of dust retained in the second cyclone on dust particle size is still present (Figure 7). However, distributions are also enormous when referring to dust particle size so that further influences are supposed to play a role. They might occur due to concentrations considering that cyclone efficiencies in addition to the particle size of dust to be collected also depend on concentrations. Furthermore, aggregates of suspended dust may be destroyed in cyclones. This factor has also an effect on dust masses separated in individual stages, thus being able to falsify the reference to primary conditions of airborne suspended dust. Dust may show various aggregation degrees which could not be correlated to defined workplace atmosphere parameters up to now.

The dependence of cyclone efficiencies on suspended dust uptake is also revealed in a comparison with the personal dust sampler Simpeds 70 MK II. In case of high concentrations, the throughput decreased which had the consequence that less dust was separated on the follow-up fine dust filter (Figure 8). In addition, varying flow velocities had a substantial effect on the collecting capacity of the intake. When performing alternating measurements with both instrument types, these parameters should be considered for concentration determinations.

Different conversion factors had to be taken into account, too, in a comparative test using the French device CIP 10 (Figure 9). Applied at the same position and at the same time hitherto obtained test results of instruments show a de-

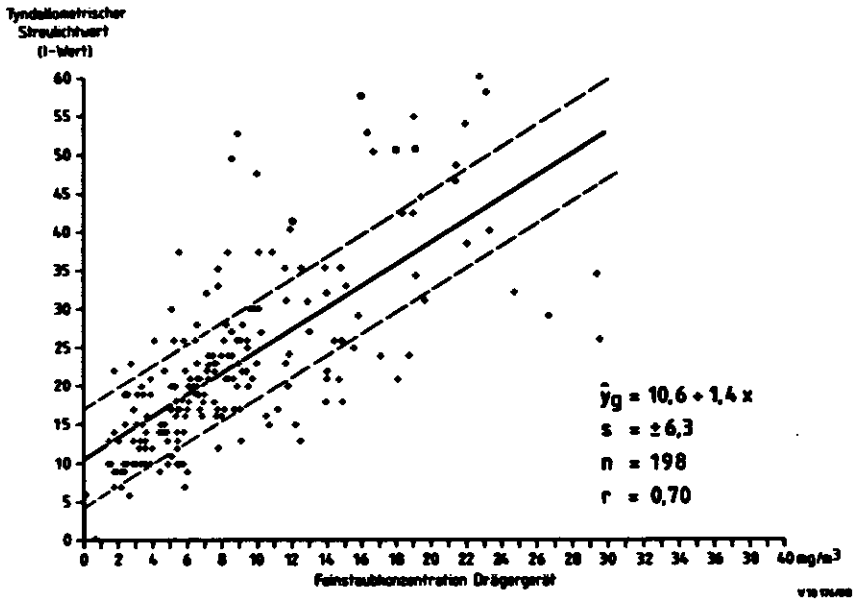


Figure 1. Comparison between tyndalloscopic and gravimetric measuring values.

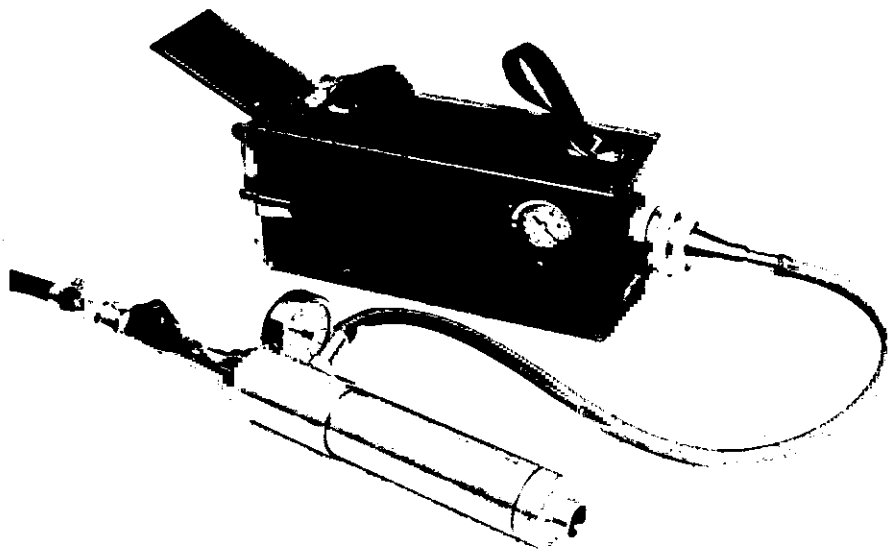


Figure 2. MPG II.

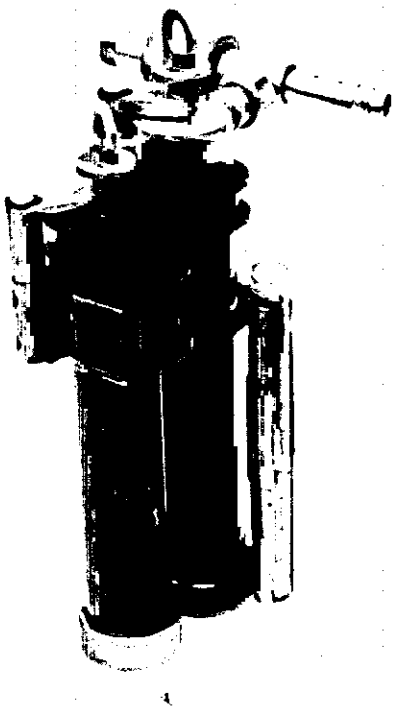


Figure 3. TBF 50

pendency of the conversion factor level on mined coal type as well as on mining method (Figure 10).

Outgoing from gas-flame coal, a low rank coal, and ending with high rank coal, the conversion factor increases, especially for plough mining. This tendency is less distinct when mining is performed with shearer-loaders. For this type of mining, uncorrected results of almost equal concentrations for MPG II and CIP 10 instruments can be based in general. The different reaction of both types during dust measurements in various mines applying different mining methods and the mining of coal with varying ranks is the result of different coarse dust pre-extraction in connection with varying particle size distributions of suspended dust. In one case for example, a change of mining methods from stripping to cutting resulted in the reduction of average particle size diameters by about 26 per cent. Likewise decreased the conversion factor from 1,4 to 1,1.

The outcome of these comparative measurements indicates the difficulty to use instruments with a deviating fractionation when referring threshold limits to a specific fine dust definition. Usually, general conversion factors cannot be applied; allocation has to be face-specific.

Due to the conversion to gravimetric methods, it is nearly impossible to recognize individual emitters and to proportionate them according to mining methods. Therefore, a new handy instrument, measuring on tyndallometric basis, was

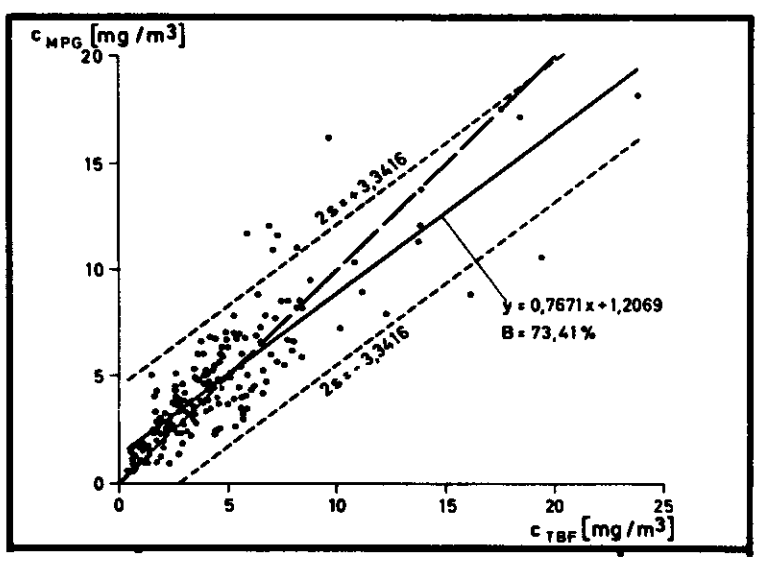


Figure 4. Concentration comparison between C_{TBF} and C_{MPG}.

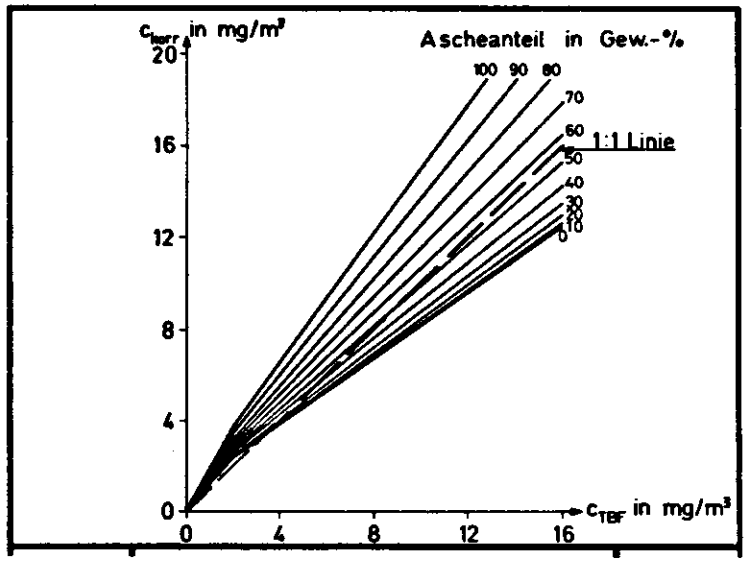


Figure 5. Conversion C_{TBF} into C_{corr}.

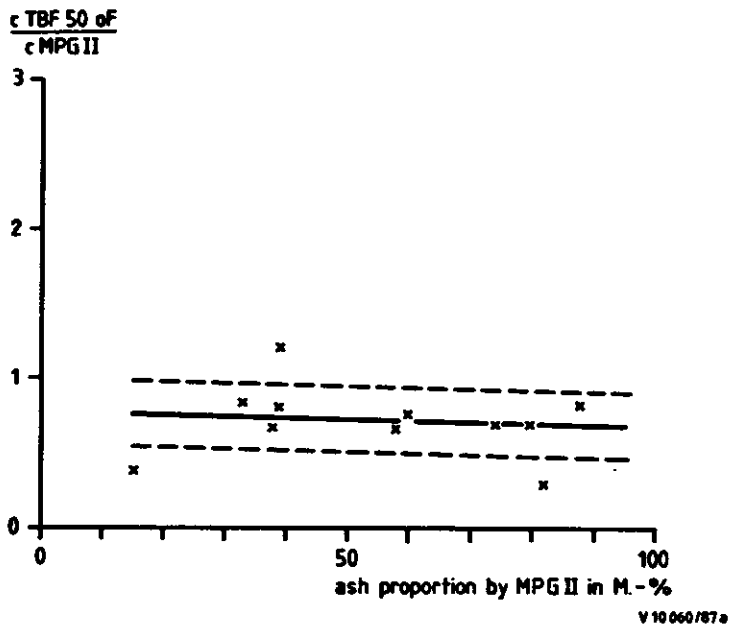


Figure 6. Ash proportion obtained by MPG II in mass %.

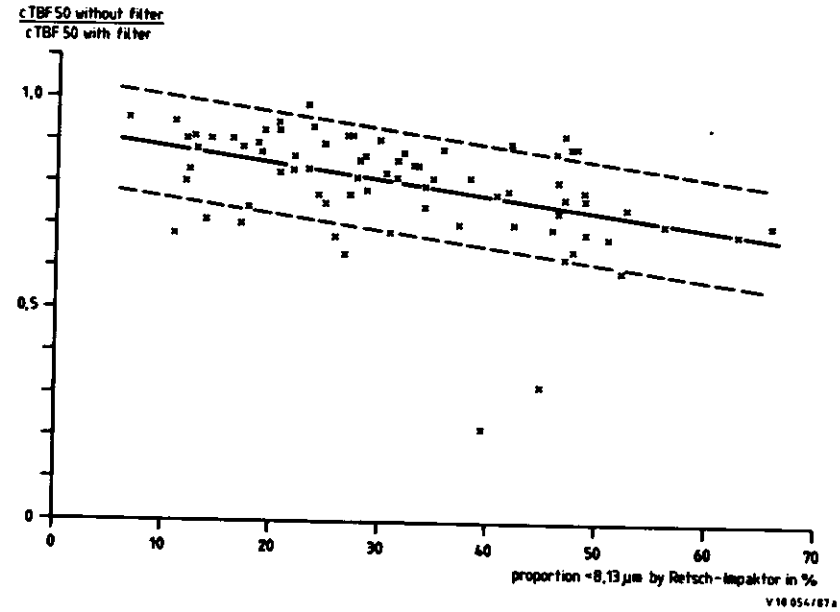


Figure 7. Conversion factors for TBF 50 with and without filter.

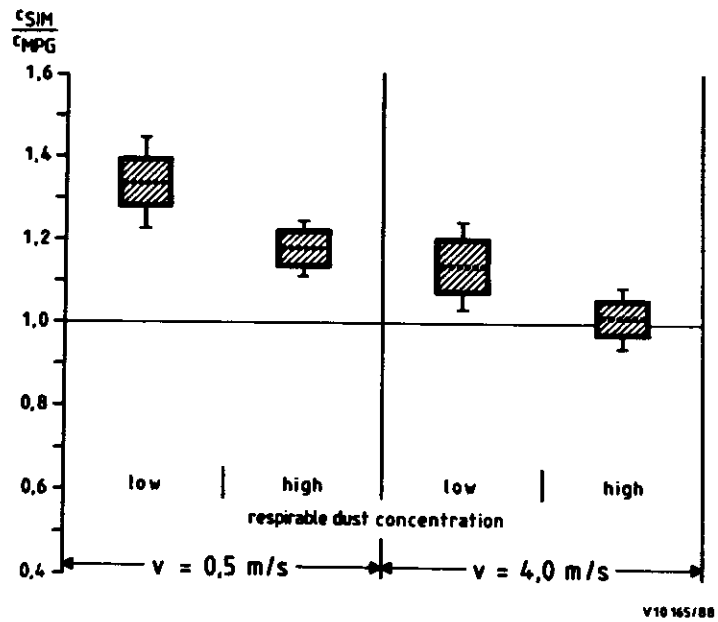


Figure 8. Conversion factors for Simpeds and MPG II.

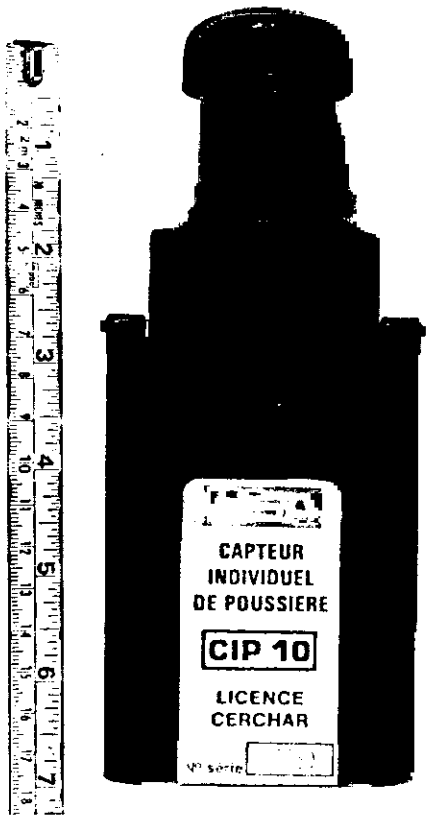


Figure 9. CIP 10.

developed: the TM digital μP which indicates single and average values for random measuring periods (Figure 11). Measuring sensibility due to particle size was diminished in this equipment. The advantages were mainly attained by measuring scattered light at an angle of 70° compared to 30° for the former tyndalloscope, and using monochromatic primary light of a wave length of 0,94 μm instead of visible light. Although the primary objective for using the TM digital μP was dust measurement for technical purposes it was also designed as supplementary or auxiliary device for occupational medical surveillance under specific operational conditions. At first, comparative measurements with the MPG II did not yield encouraging perspectives (Figure 12). The wide distribution of comparative values seemed to exclude an acceptable allocation of scattering light values to gravimetric concentrations. Classifying values according to specific characteristics of mining did not result in a substantial improvement, either. However, face-referred evaluations and limitation to areas of low exposures obtained good correlations between MPG II and tyndallometer (Figure 13). It is true that conversion factors vary widely from face to face; a linear relationship to comparative values is obtained, however, if a specific face is referred to.

At first, this assessment had the only objective to find out which tyndallometric measuring values have to be determined for the "worst case" in an area of low dust make and thus a low health risk in order to abstain from time-consuming gravimetric measurements. The linear correlations shown in figure 13, however. To prove this, comparative measurements during about 100 subsequent shifts were performed

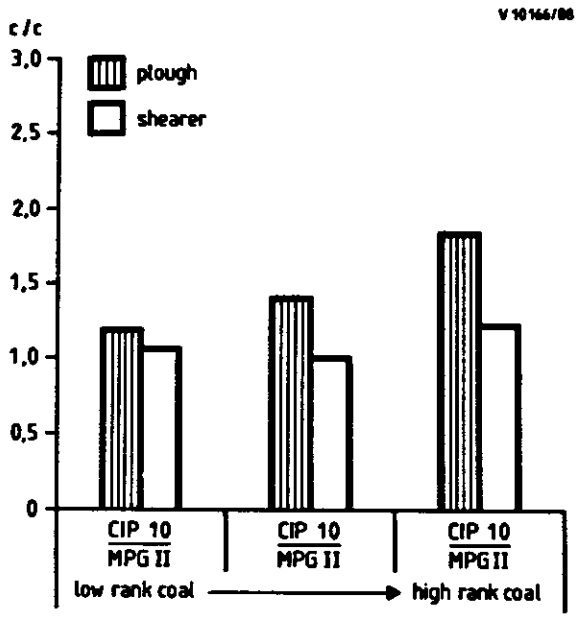


Figure 10. Conversion factors CIP : MPG II.

Figure 11. TM dig. μP.

in various mines with the TM digital μP, the MPG II, the TBF 50 and with a fine dust measuring device developed for permanent measurements with remote transmission of values on the basis of the tyndallometer digital μP. These devices were placed in a frame to maintain the same arrangement of instruments even when positions in mines changed (Figure 14).

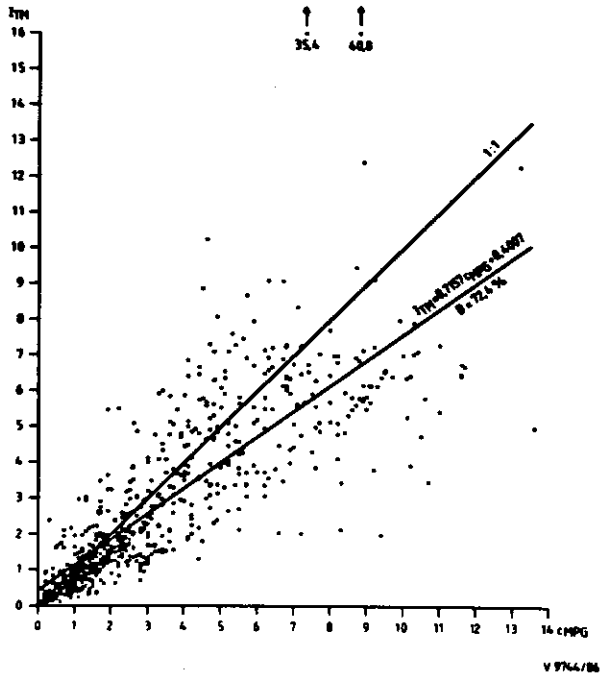


Figure 12. Relation between gravimetric and tyndallometric intensity values of respirable dust concentrations.

To avoid dust deposits in the measuring chamber of the tyndallometric dust measuring device, clean air flows through a small fan at the inside of the measuring chamber. Speed

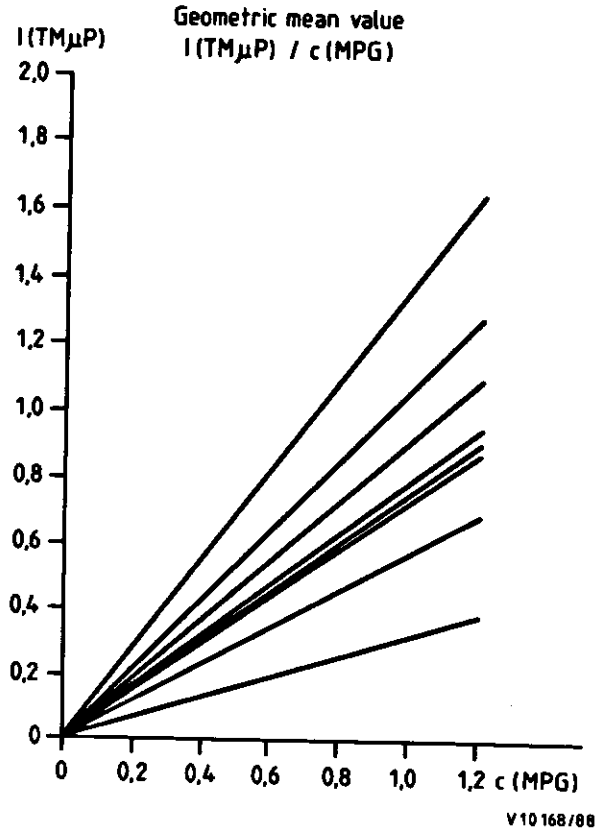
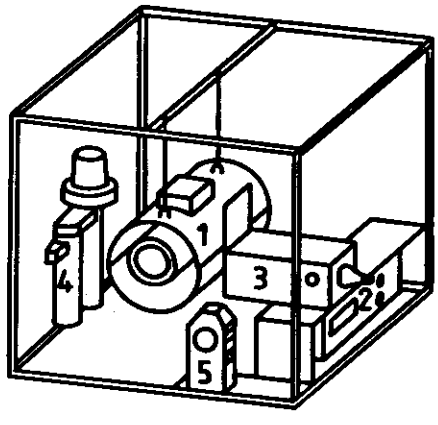


Figure 13. Conversion relation for different faces (low concentrations).



1 FMA (measuring head)
2 FMA (electronic element)
3 MPG II
4 TBF 50
5 TM digital μP

Arrangement of dust measuring instruments in comparative measurements

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Figure 14. Arrangement of dust measuring instruments in comparative measurements.

can be adapted to environmental velocity. In order to illustrate the comparison of results achieved by the tyndallometric fine dust measuring instruments with those of other instruments a field test typical for instrument reaction is described. The comparison with the MPG II showed a linear correlation over the whole sphere of concentrations (Figure 15). This also includes the other field tests which show in some cases a varying increase of the balancing straight line. However, the positions of balancing straight lines are typical for each face. Their rise remains nearly unchanged during varying operational processes in the same face. Thus, a face-specific allocation to the MPG II is feasible but also necessary. In this case, the conversion factor is not only valid for short-term but also for long term periods.

Regarding the TBF 50, correlations are less distinct (Figure 16). The distribution is higher. In another case, an allocation was even impossible (Figure 17). Since measuring values of the tyndallometer can be face-specifically allocated to gravimetric measuring values of the MPG II as the basic instrument, the following consequences can be drawn:

1. It is suitable to give a review on dust conditions between two gravimetric measurements.
2. It can help to decide for which shifts of operational procedures gravimetric measurements are required and for which shifts separate measurements should be carried out.
3. It is apt to indicate whether normal dust conditions were prevailing in the time of gravimetric measurements in order to exclude positive or negative extreme situations which may influence long-term classifications of the face.
4. In particular cases, the interval between two gravimetric measurements could be extended under the condition that the frequency of tyndallometric measurements increases in the meantime or a permanent tyndallometric surveillance is provided.
5. Basically, tyndallometric measuring instruments offer the possibility to allocate short-term concentration changes to specific operational procedures, to introduce dust suppression measures and to check the efficiency of them.

However, the tyndallometric measurement will not be able to replace the gravimetric measurement. As far as test methods for the direct determination of specific fibrogeneity of a dust collective are not at disposal substance quantities obtained by gravimetric samplers will have to be classified more extensively than hitherto to acquire a better knowledge on changing proportions of individual components, their particle size distributions and information about their potential interactions in dust mixtures with regard to fibrogenic tissue reactions. Primarily, single particle analyses on homogeneous and heterogeneous compositions including element analyses by electron microscopy and Lamma spectrometry are required.

As in many other countries, the evaluation of quartz-including fine dust mixtures in the FRG is carried out according to total fine dust concentration considering the quartz proportion of this dust mixture. Quartz as individual mineral serves as reference value (Figure 18, middle-line). Thus, the approved fine dust concentration in case of quartz quantities $< 100\%$ is an operand only. In the FRG, however, this method is not consequently applied in cases of low quartz

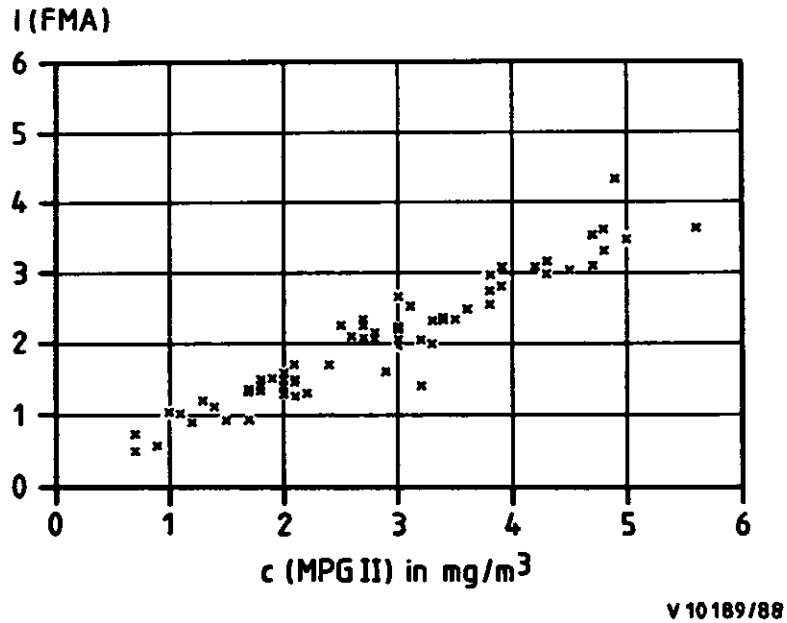


Figure 15. Comparison tyndallometer (FMA) and MPG II.

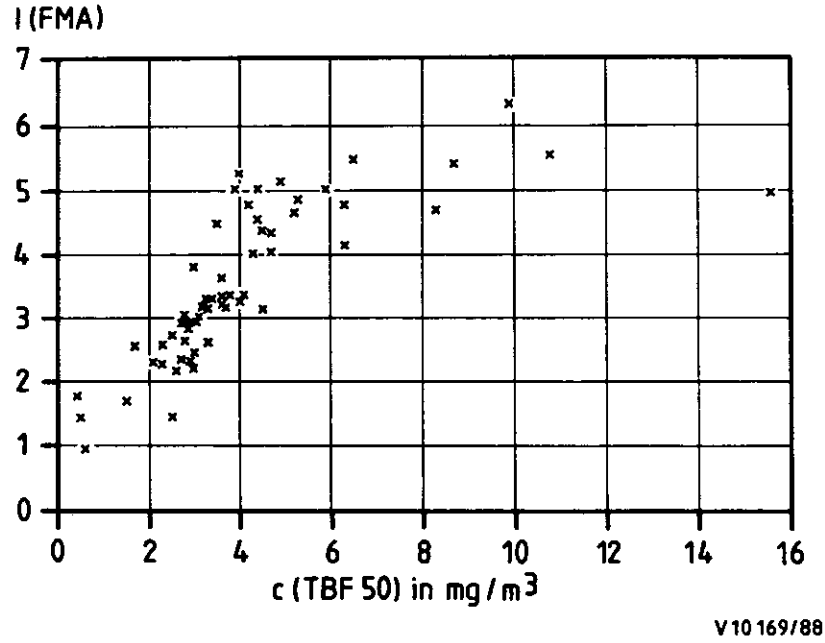


Figure 16. Comparison tyndallometer (FMA) and TBF 50.

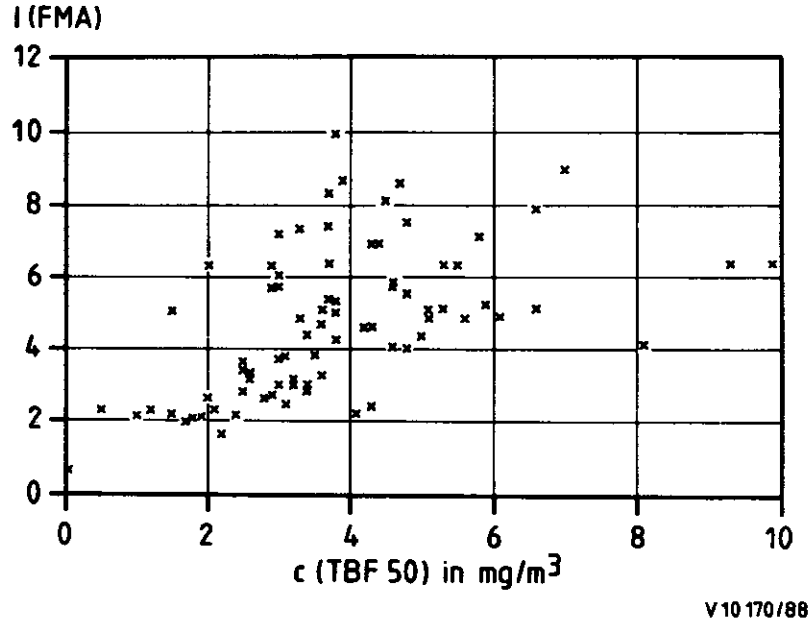
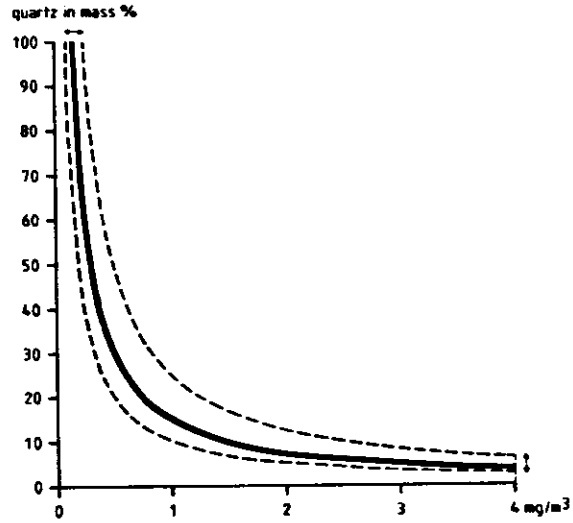


Figure 17. Comparison tyndallometer (FMA) and TBF 50.



Scheme of bands for quartz concentrations in case of modified quartz evaluation

Figure 18. Scheme of bands for quartz concentrations in case of modified quartz evaluation.

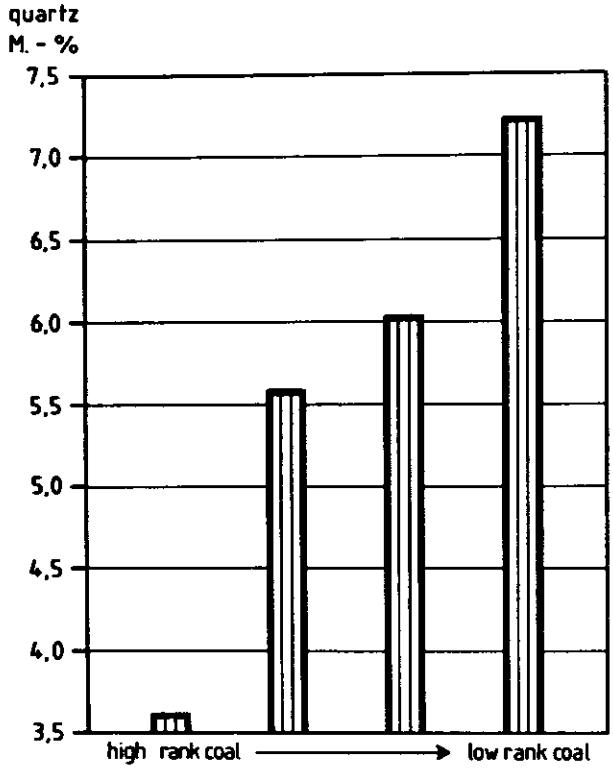


Figure 19. Quartz contents in respirable dust (measurement results obtained between 1980 and 1988).

proportions. In the presence of low quartz proportions, a defined fine dust threshold value was established which is not to be exceeded during a long-term assessment period. In case of small proportions, quartz is believed not to be the decisive biological parameter. At least in the hard coal mining industry it is doubted that quartz has the same fibrogenic power under any petrographic condition. Due to different developments, quartz as single component might show varying activities, or, referring to its harmfulness, it could be modified on account of interaction with other mineral components during or after deposit formation. For example, in spite of high quartz dust concentrations in a mine of a sedimentary hydroxide iron ore over a long-term exposure period did not provoke lung damages in exposed miners. At that time, this outcome was attributed to insoluble quartz surface masking.

In other hard coal mines, too, the risk to disease obviously cannot be directly and generally related to quartz fine dust concentrations. For example: the quartz proportion of dust originating from high rank coal is essentially lower than that of younger strata (Figure 19). The number of diseases is contrasting, however. These hints and findings raise two questions

1. Can occupational medical evaluation be based on a standardized quartz definition?

   When referring to pure quartz wouldn't it be preferrable to make modifications considering the different fibrogeneity and to fix specific limit values?

2. Is it justified to restrict approved total fine dust concentration mathematically only by taking into account the respective quartz proportion without considering the components in the dust mixture interacting with quartz?

Several countries might have based their limit values on reference values for quartz of different origin which have different effects, therefore. This could explain the partly widely varying approved mass concentrations. A well-known fact is that free crystalline silica has not only structural differences but also varying biological effects. The results of animal experiments after using quartz of different genesis but also with cristobalite, tridymite, coesite, stishovite as well as amorphous silica confirm these findings. This means that the conditions of quartz formation and of the growth of quartz crystals in the plutonic development from early release out of liquid magma up to the telethermal phase in the hydrothermal sphere can vary widely. Therefore, deviant effective potentials of the mineral which is generally regarded as quartz should be taken into account. The SiO_4 tetrahedron arrangement determining SiO_2 modifications does not seem to be decisive, but rather the undisturbed or disturbed formation of individual tetrahedrons, for example substitution of Si ions by aluminium or phosphor.

Under the condition that a specific limit concentration of for example 4 mg/m³ for respirable dust including quartz must not be exceeded the curve progression of the approved fine dust concentration considering the proportion of the modified

quartz component would change (Figure 20). However, the potentially inhibitory effect of substances in the dust mixtures would not be taken into account when applying this purely mathematical procedure. A more reliable assessment might be possible if chemical, physical and mineralogical characteristics could be determined for the specific nocuousness of a total respirable dust collective. This assessment cannot be realized yet for the hard-coal mining industry. Subject of present discussions is a model to better adapt the occupational medical assessment of dust uptake in workplace atmospheres in case of exposure to dust originating from various stratigraphic horizons by means of correction factors. In case of an uncorrected reference to the quartz proportion, this mineral component in the dust of seams with low rank coal was the decisive parameter of the approved total fine dust concentration since the limit of 5 mass per cent was essentially exceeded in general. However, disease frequency in the presence of seams with high rank coal and substantially lower quartz components was much higher.

These different findings are intended to be harmonized by correction factors for exposure evaluation. This means that the quartz proportion in mass percent of seam strata with low rank coal has to be converted into an "effective quartz proportion" referring to the conditions in layers with a higher rank coal. Irrespective of this parameter, the fine dust concentration of 4 mg/m³ represents the maximum limit concentration in an assessed period (Figure 21). In the practice, the consequences would be as follows: Applying factor 1, valid for seam strata with high rank coal, quartz evaluation would continue to begin for a quartz proportion of 5 mass percent in the German hard-coal mining industry. The further progression of approved respirable dust concentrations will ensue from the orientation to the pure respirable quartz dust concentration of 0.2 mg/m³. Using factor 0.5, quartz evaluation would start for a quartz proportion of 10 mass percent only, i.e., that the calculated respirable quartz fine dust concentration of 0.4 mg/m³ analytically determined via the quartz proportion in mass per cent would be converted into an effective concentration of 0.2 mg/m³. It is certainly not yet justified to provide as many categories for seam strata as shown in figure 21. A relatively rough differentiation into 2 or 3 groups of factors would be preferrable. In our opinion, the observed risk variations could be better taken into account by such a procedure, even when evaluating dust uptake in various stratigraphic horizons. Such a convention demands that the adaptation to an evaluation is restricted to modified factors of the quartz component until general systems to evaluate the specific nocuousness of the whole dust collective will be developed.

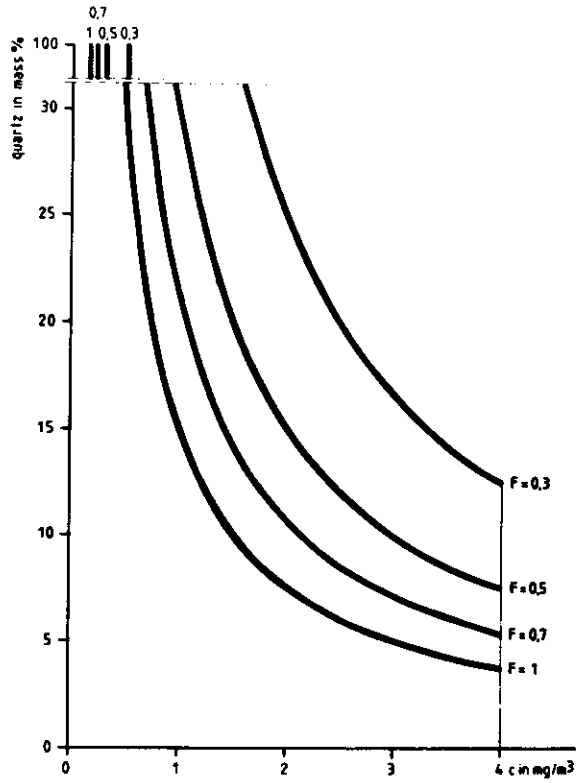
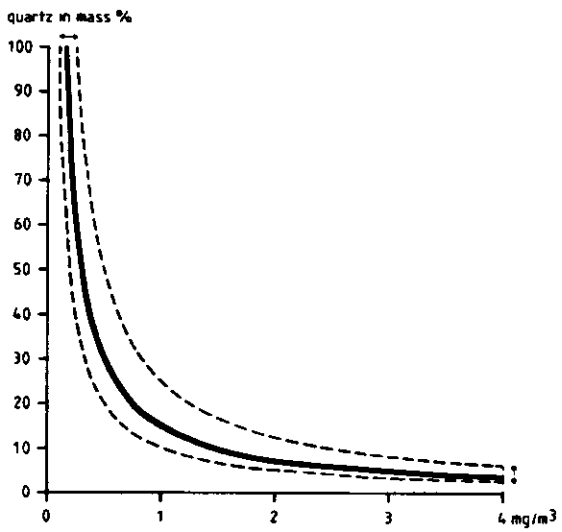


Figure 21. Approved respirable dust concentration in dependence on quartz proportion and the application of correction factors.



Scheme of bands for quartz concentrations in case of modified quartz evaluation

Figure 20. Scheme of bands for quartz concentrations in case of modified quartz evaluation.

MEETING DUST ASSESSMENT NEEDS OF AN AUTOMATED MINING INDUSTRY

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INTRODUCTION

The Bureau of Mines is vigorously conducting research to automate mining processes in an effort to keep U.S. coal mining competitive in the world market. However, just as the industrial revolution and its aggressive push for productivity exposed increased numbers of workers to serious injury, will "high-tech" mining also mean high-risk mining? The answer is "no," or at least "not necessarily." In fact, one potential benefit of automation is to remove humans from the most hazardous underground tasks. This concept is certainly not new. Tethered or radio-operated remote control miners signaled the very beginnings of automation. Miner operators could now work under well-supported roof, away from potential methane ignitions and high dust levels in the face area.

The Bureau is now conducting the next logical step in automation research. A continuous miner has already been outfitted with a suite of sensors and a computer to interpret sensor data and control movement of the machine. With the push of a button, the mining machine can execute a complete sump-shear-load cycle with the machine head position controlled to within 1 cm. Navigation research is well underway, so eventually the miner will be able to mine coal within the seam with very little human intervention. Several schemes to detect the interface between the coal and surrounding strata are being researched. Sophisticated laser, acoustic, inertial, and magnetic guidance systems will soon become feasible. The ultimate goal, of course, is completely automated operation that requires no human involvement.

Does this mean that our worries about pneumoconiosis, silicosis, and related dust-induced diseases are over? Not for many years. While the objectives of automation and robotics are admirable, humans will still be going underground well into the next century. Individual exposure to dust may be reduced in many cases, but certainly not eliminated. For the foreseeable future, robotic miners will require human supervision; and like today's technologically advanced automobiles, tomorrow's mining systems will still require maintenance. Maintenance will be a service that highly trained humans will continue to provide, and those humans will be exposed to dust. Machines designed to mine more coal will likely liberate more dust, unless dust control research keeps pace. In addition to health concerns, increased dust levels may pose problems for optical or laser guidance systems and other types of sensors, as well as increase the requirement for rock dusting to prevent dust explosions.

A critical element of any control system is monitoring. Information about the contaminant must be gathered so control efforts can be assessed and adjusted as required. This paper provides a brief overview of a Bureau project that addresses improved monitoring and analysis of hazardous coal mine dusts. Since the project is a recent initiative, the intent of the paper is not to provide extensive technical detail, but only to introduce the reader to the work being conducted.

REAL-TIME DUST LEVEL ASSESSMENT

Since the respirable coal mine dust exposure standard in the United States is expressed as a mass concentration (2 mg/m^3), gravimetric dust sampling techniques are appropriate and acceptable for compliance monitoring if conducted properly. The Bureau recognized several years ago, however, that a real-time method for assessing dust levels was needed to locate dust sources and evaluate dust control systems efficiently. The long sampling time required to collect filter samples and the delay involved in weighing the filter make gravimetric techniques too time-consuming and labor-intensive for such purposes. This realization brought about the development of several light-scattering dust monitors, including the widely used RAM-I[1] and the more recent MINIRAM. Other private sector instruments were developed without Bureau sponsorship. The advantages of these devices are almost instantaneous indication of dust levels, portability made possible by small size and battery-powered operation, and relative mechanical simplicity.

Many researchers have evaluated the performance of these and other light-scattering dust monitors. The conclusion common to almost all of these works is that the response of photometers is *not* directly related to the mass concentration of the dust. Particle characteristics such as size, index of refraction, and shape all affect the response. A special concern when sampling near water sprays used for dust abatement is that water droplets entering the instrument sensing chamber can scatter light and cause falsely high readings. The water droplet problem is minimized with instruments like the RAM-1 that use a cyclone preseparator. In that case, the cyclone captures most droplets larger than a few micrometers. In passive, open-chamber instruments like the MINIRAM, however, the problem can be severe unless a

cyclone adaptor is used. Such uncertainty in light-scattering measurements makes them unsuitable for compliance measurements, but is generally acceptable for relative "before-and-after" measurements associated with evaluation of control systems. Even here, however, results can be very misleading if the size distribution of the dust cloud is dramatically altered by the dust control system.

The Bureau is conducting basic research to develop a light-scattering dust monitor that accurately measures the mass concentration of dust, even in the presence of water droplets. The Mie theory of scattering of electromagnetic radiation is often applicable to the scattering of light by respirable dust particles. The detailed mathematics are quite complex, but in general, the intensity of light scattered by a particle is a function of detection angle, intensity and wavelength of the source light, and particle size, index of refraction, shape, and surface properties. The Bureau is using computer models of Mie scattering to study the implications of varying instrument configurations and particle characteristics. The theory and computer models deal with ideal spherical particles. Although particle irregularity will introduce unknown changes into the model predictions, the model can still provide general guidance regarding the selection of important instrument parameters.

As an example, Figure 1 shows a two-dimensional diagram of the intensity of light scattered by a spherical particle as a function of angle for a given set of conditions. The value α, called the particle size parameter, is the ratio of the particle diameter to the source light wavelength. Figure 2 shows an intensity diagram for a somewhat larger particle, all other parameters remaining the same. This analysis indicates that each particle will have a scattering signature that may be unique to its physical characteristics. A novel experimental apparatus, called DAWN-A, has been obtained by the Bureau's Pittsburgh Research Center that will allow direct three-dimensional measurement of the intensity of light scattered by a particle as a function of angle. As shown in Figure 3, the device consists of a sphere upon which are mounted several photodetectors. As a particle passes through the sphere, laser light is scattered to the detectors in a pattern associated with that particle. Intensity information is processed by a computer. Research during the remainder of the project will examine the scattering signatures for a wide variety of particles likely to be found in coal mines. Once these signatures are known, a photometer may be designed that uses only those parts of the scattering signature needed to discriminate between liquid and solid particles, and to compensate for particle size, shape, and index of refraction effects. The eventual design might need to include more than one source and detector in order to gather enough information to complete the analysis. Long-term research might even lead to limited dust component analysis using the scattered-light signature.

The anticipated result of the research will be a dust monitor that can continuously and accurately measure the real-time mass concentration of dust particles in a coal mine. A monitor with such capabilities will find applications in dust control research, and perhaps even in compliance monitoring. The real value of such a device, however, lies in automated dust

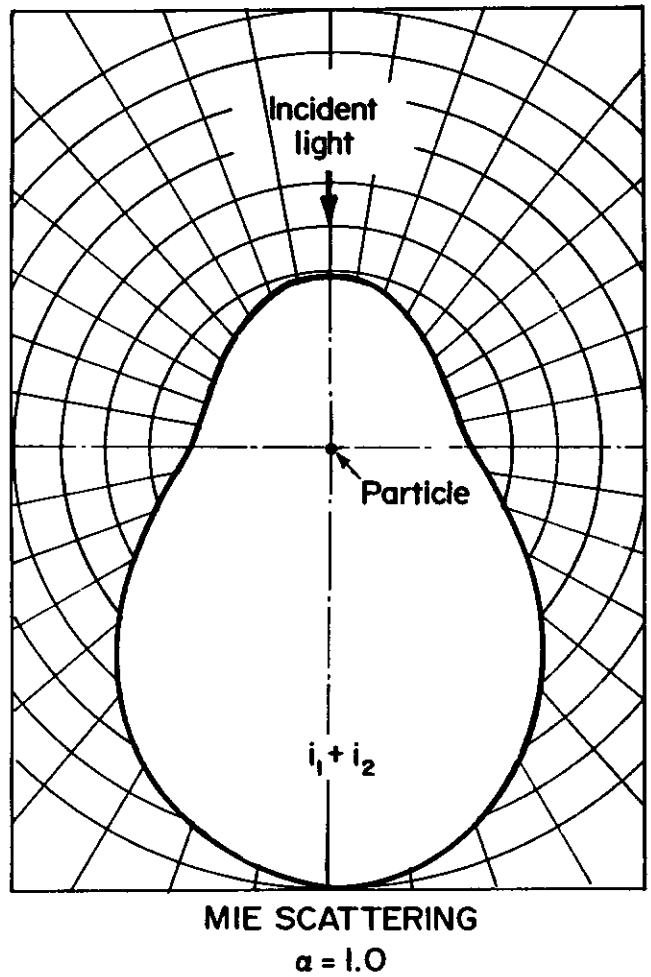

Figure 1. Scattered light intensity as a function of angle $\alpha = 1$.

control systems. Dust control research has identified many viable methods to control respirable dust, but operating parameters must often be adjusted to fit the situation at hand. Water spray pressure or ventilation rate may need to be changed, for example. To automate the adjustment of dust control parameters requires that information about dust levels be fed back to a control unit that can decide what change to make in the operating parameters. The improved photometer could serve as that critical feedback mechanism.

Requiring worker presence to adjust dust control system operating parameters manually would largely defeat one purpose of automated mining, that is, to remove personnel from hazardous areas. Automated dust controls would greatly reduce the need for human presence.

In addition, they would address the other main reason for automated mining, competitiveness. Controlling dust is not free. Power for fans, scrubbers, and water pumps is an expense that must ultimately be reflected in the cost of coal. Along with reducing labor costs to monitor and adjust dust

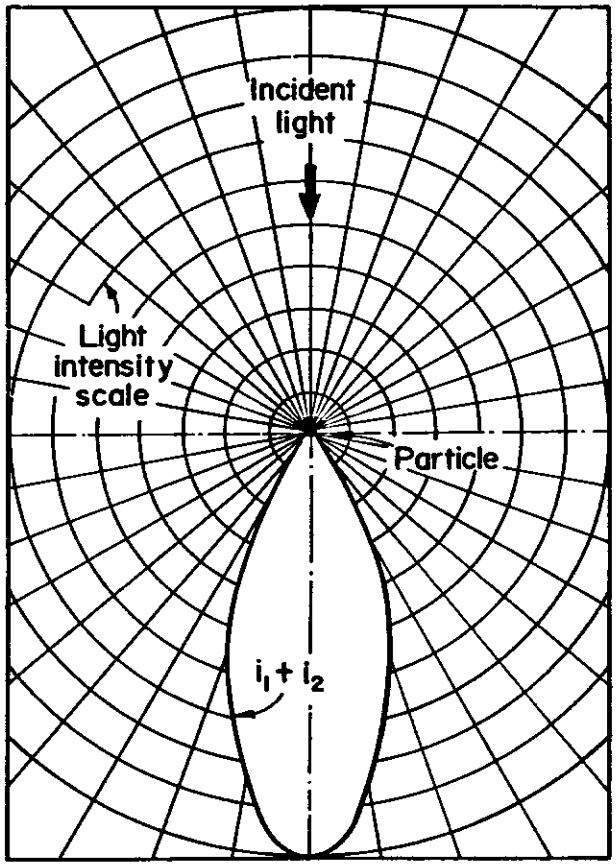

Figure 2. Scattered light intensity as a function of angle $\alpha = 4$.

control operating parameters, automated systems could prevent unnecessary costs incurred by using overly restrictive dust control methods.

DUST COMPONENT ANALYSIS

While real-time knowledge of airborne mass concentrations of respirable coal mine dust is important for control purposes, health specialists know that lung diseases, especially silicosis, are not correlated simply to levels of coal mine dust. The individual components of the dust have an important bearing on the likelihood of contracting disease. This realization is reflected in the practice of reducing exposure standards in coal mines when quartz levels exceed 5 pct. Some European data suggest that silicosis is not directly related to the percentage of quartz alone. Other minerals such as kaolin and mica have some fibrogenic capacity of their own. On the other hand, minerals such as feldspar, calcite, calcium sulphate, siderite, hematite, pyrites, etc., exist in high quantities in coal mine dust samples and may reduce the toxicity of the quartz present. All of this research points to the importance of being able to determine the amount of quartz and other components in respirable coal mine dust samples accurately.

Real-time, in situ component analysis of airborne coal mine dust remains a researcher's dream, but significant progress has been made in spectroscopic analysis techniques. The Bureau has purchased a Fourier transform infrared (FTIR) spectrometer to assess its capabilities. Already, the instrument has demonstrated an order of magnitude greater sensitivity to quartz than dispersive infrared techniques. These results were obtained by the manufacturer during courtesy analyses of Bureau-prepared filter samples.

Dispersive infrared spectroscopy has served as a mainstay analysis technique for quartz for many years. It has a working measurement range of 25 to 250 µg of quartz with a precision of 13 to 22 pct. Figure 4 is a diagram depicting the operation of a typical dispersive infrared spectrometer. By a system of mirrors and lenses, the source beam is split and follows two separate paths to the detector. Synchronized beam choppers (C_1 and C_2) allow the beams to alternately pass through a sample and a reference cell to the detector. The reference cell measurement allows compensation for such things as variation in source light intensity, temperature, pressure, etc. Infrared light from the source is viewed in discrete wavelength intervals throughout the range of interest, and the transmitted intensity is measured at the detector at each wavelength interval. These wavelength intervals can be referred to as "resolution elements." According to Skoog and West,[1] "The quality of the spectrum—that is, the amount of spectral detail—increases as the number of resolution elements become larger or as the frequency intervals between measurements become smaller." For dispersive infrared spectroscopy, then, increased spectral quality involves two costs. The first is the increased time required to measure transmittance at a greater number of resolution elements. The second is diminished sensitivity. This results because as the resolution interval gets smaller, the signal available to the detector is smaller.

Figure 5 is a diagram of a typical FTIR spectrometer. Here as well, the beam is split, but there are no choppers to alternate beam paths. Half the beam is reflected from a fixed mirror, through the sample to the detector. The other half of the beam is reflected from a mirror that moves at a well-defined rate, changing the path length of half the beam. The recombination of the two beams results in an optical interference that strengthens or diminishes the signal at the detector. In fact, the rate of change of signal strength is directly proportional to the movement of the oscillating mirror. By applying a mathematical Fourier transform to the function that describes the detected signal intensity as a function of mirror position in time, a function describing the intensity as a function of wavelength, that is, the absorption spectrum, can be obtained. The advantage of the FTIR is that all resolution elements for a spectrum are measured simultaneously. Separate measurements need not be taken for each wavelength as is the case in the dispersive infrared system.

Since quartz is recognized as a major health hazard and receives special emphasis under the respirable coal mine dust

Figure 3. DAWN-A

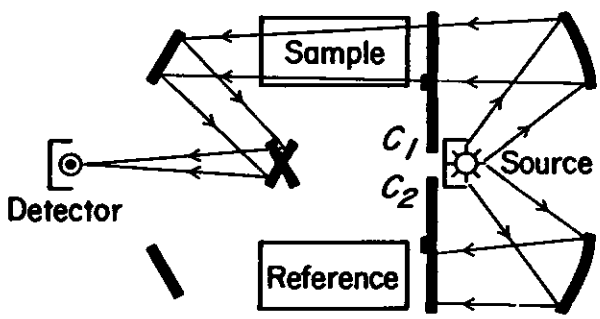

Figure 4. Typical dispersive infrared spectrometer.

exposure standard, the project is directing substantial effort to improving the analysis methods for quartz. The Mine Safety and Health Administration (MSHA) is already considering the use of an FTIR in its Method P7 for routine coal mine dust sample analysis. Although users will enjoy the benefits of improved sensitivity, they must conduct the somewhat laborious sample preparation required by Method P7. Preparations include low-temperature ashing and sample redeposition. One objective of the Bureau project is to develop a valid, convenient method for direct on-filter FTIR analysis for quartz.

As discussed above, other minerals appear to either enhance or diminish the toxicity of quartz, or even cause damage

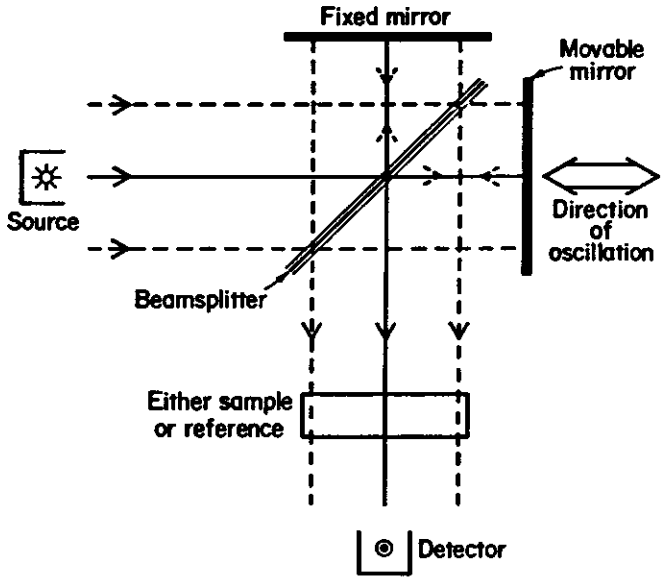

Figure 5. Typical FTIR spectrometer.

on their own. Thus, to understand completely occupationally related lung diseases, the capability of measuring the other components in the dust sample will be essential. Multicomponent analysis of dust samples is, therefore, another of the many long-range objectives of the project.

SUMMARY

The project reviewed in this report has two primary goals. The first is to provide accurate real-time measurement of the mass concentration of airborne respirable coal mine dust. Such capability is needed to provide feedback regarding dust levels to future automated dust control systems. The DAWN-A, a unique experimental apparatus for studying light scattered by dust particles, will be used to design an improved photometer. The second goal is to provide improved capabilities for respirable dust sample component analysis. Such information will be needed to understand occupational lung disease and to better assess the hazards of workplaces. Fourier transform infrared spectroscopy has been selected as a promising technique to accomplish that goal. Just as the Bureau of Mines is applying high technology solutions to problems of production and competitiveness in the international mineral industry market, it is also applying state-of-the-art technology to the measurement and analysis of respirable dust. The project tasks are in their early stages, but initial work points to an exciting and fruitful future.

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[1] Use of trade names is for identification only and does not imply endorsement by the Bureau of Mines.

ASSESSMENT OF PERSONAL DUST EXPOSURE WITH THE CIP10 FOR A BETTER MEDICAL MANAGEMENT OF THE PNEUMOCONIOSIS RISK IN COAL WORKERS

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ABSTRACT

According to French regulations, level of coal dust exposure in each underground working must be measured by static sampling. In collieries of Lorraine a single sampling site, in the return air, is selected for each working. Each miner is assigned to one working in accordance with his fitness for work as determined by the occupational physician.

A new individual dust sampler (CIP 10) developed by the *CERCHAR* has been used in a national survey in which more than 5000 measurements in 194 jobs were carried out. That sampler is now at the occupational physician's disposal for a better prevention of pneumoconiosis.

So far it has been possible to:

- look after the placement of pneumoconiotic miners still occupied underground. A survey (207 measurements) showed that those workers were in average exposed to 0,64 mg/m^3 respirable dust TWA;
- check dust exposure of miners with a profusion of 0/1 level (263 measurements, mean = 0,89 mg/m^3);
- document the exposures associated to some job suspected by the physician to be specially at risk.

Some over exposure situations have been already detected. They offer a possible explanation for recent cases of particular pneumoconiosis.

A strategy for the use of CIP 10 is proposed, based on 5 successive days of measurements, eventually repeated following the results dispersion and their extreme values.

See Table of Contents, Part II, for Paper.

CORRELATION OF TESTS FOR MATERIAL DUSTINESS WITH WORKER EXPOSURE FROM THE BAGGING OF POWDERS

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INTRODUCTION

Laboratory dustiness tests have been devised[1] to provide a quick and convenient means of estimating a material's relative dustiness. These tests are empirical in that they do not measure a fundamental property or response of the material being tested. In using these dustiness tests, one assumes that the dust generation in the test simulates the dust generation in an actual powder handling operation. In order to be useful, the results of these tests must be correlated with personal dust exposures. Because this correlation has not been evaluated, NIOSH researchers conducted a study to evaluate the correlation between worker dust exposure and the results of two dustiness tests. The two dustiness test devices are the Heubach Dust Measurement Appliance and the Midwest Research Institute (MRI) tester.[1,2]

This study was conducted in the packaging room for a powdered acrylic resin production line. The plant produced a variety of resins which differ in bulk density, particle size, moisture content, and observed dustiness. The resin powders were auger fed into tuck-in valve bags. The bags were filled with 50 pounds of powder, they were sealed and dropped onto a conveyor belt which transported the bags to a palletizing operation. The operator tended a number of bag packing machines. Several workers rotated between the bagging equipment and the palletizing equipment in an adjacent storage area.

EXPERIMENTAL PROCEDURES

For six different resins, the workers' dust exposures were measured and dustiness tests were conducted on bulk samples of the material to determine if the dust exposures and the dustiness test results were correlated. For each material packaged, exposures to total dust were measured using NIOSH Method 0500.[3] Air samples were collected using personal pumps operated at 3.7 liters per minute. Separate sets of measurements were taken for different workers who rotated through the bagging machine operations. Usually, 4–6 measurements were taken for each powder.

The Heubach unit, depicted in Figure 1, consists of a horizontal rotating drum with internal baffles that produces a repeated dust fall through a regulated airstream. Airborne dust from the drum enters a settling chamber and is then collected on a preweighed glass fiber filter (50 mm, Schleicher and Schull GmbH). The test parameters (mass of material, airflow rate, and total flow) for the Heubach dustiness tester are not unique; they are set for each type of powder tested so that a desirable quantity of dust is collected on the filter. A sample of about 20 grams, a flow rate of 4 liters/minute and a sampling time of 5 minutes were selected as appropriate test conditions for this study site.

In the MRI tester shown in Figure 2, powder is poured out of a metal beaker in an enclosed space and the resulting air-

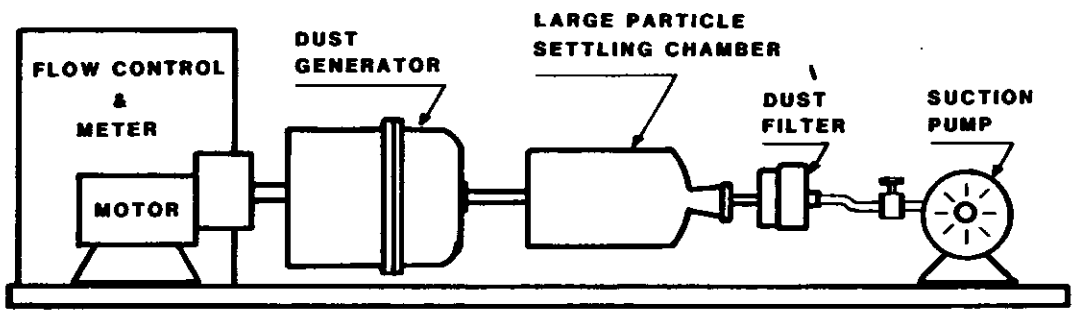

Figure 1. Heubach dustiness tester.

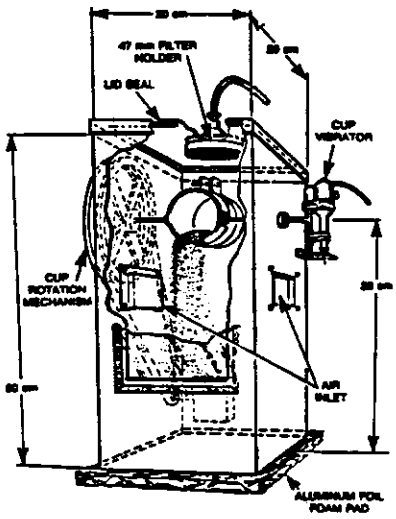

Figure 2. MRI dustiness tester.

borne dust is collected on a preweighed filter (47 mm glass fiber Gelman type AE) at a rate of 10.8 liters per minute. The cup was rotated at a constant speed to dump the powder. A vibrator mounted to the cup shaft helps to dislodge the dust. The sample pump was run for 10 minutes after the rotation of the cup was initiated. The MRI dustiness index was computed from the following formula: Dustiness Index = Dust collected (mg)/((Sample Weight [Kg])(Flow rate [1 pm])).

RESULTS

The personal dust exposure data and the dustiness test indices were fit to a regression model of the following form: in (X) = a + b (Y). In this model, the terms "a" and "b" are the regression coefficients, the term "X" is the individual dust exposure, and the term "Y" is the average dustiness index for a material. For both the MRI and Heubach dustiness test indices, a significant correlation was found between MRI and Heubach dustiness test results and worker dust exposures. Statistical results for the analyses are listed in Table I. In Figures 3 and 4, the exposure data, the predicted worker dust exposure, and the 95% prediction intervals for individual dust exposures are plotted as a function of dustiness test results. The prediction intervals include 95% of the exposures which would be predicted from the regression model.[4] The prediction interval width is proportional to the standard error of estimate (S_e), which is essentially the standard deviation about the regression line. It is the result of two sources of error: (1) the lack of fit of the model to the data; and (2) the sampling error in measuring the dust exposure. The significance of the lst source of error was evaluated using the method described by Mendenhall.[4] This method tests whether the error caused by the lack of fit is larger than the sampling error. The significance of this difference is stated as "the-significance level for lack of fit" in Table I. This indicates that the correlation between the MRI dustiness test and the worker dust exposure involves a significant lack of fit. Apparently, this source of error causes the wider prediction intervals for the MRI dustiness tester. For the Heubach dustiness test, the lack of fit was not significant. This means that the width of the prediction interval is caused by the variability in the workers' exposure data. Thus, the prediction intervals in Figure 3 cannot become much smaller.

DISCUSSION AND CONCLUSION

The preceding regression analysis shows that dustiness test results were correlated with worker dust exposure and can be used to predict worker dust exposure to within an order of magnitude. The width of the prediction interval about the regression lines was largely caused by the variability in the worker dust exposures and the width of this prediction cannot become much smaller. The correlations between worker dust exposure and dustiness test results are totally empirical and the results of the regression analysis must be used care-

Table I
Evaluation of Exposure Models

Statistical terms	Heubach	MRI
intercept (a)	-0.5	-0.1
slope (b)	10	0.09
Probability of a larger F	<0.0001	<0.0001
R^2	0.59	0.45
s_e	0.75	0.86
significance level for lack of fit test (Probability of a larger F)	0.28	0.013

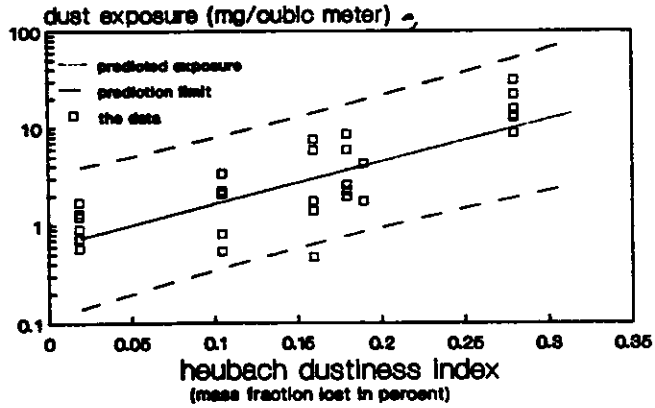

Figure 3. Predicted dust exposure, and prediction intervals plotted as a function of weight % lost, Heubach test.

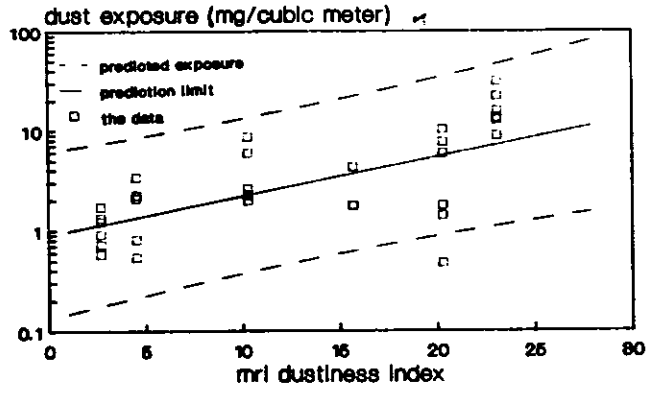

Figure 4. Predicted dust exposure, and prediction intervals as a function of MRI Dustiness Index.

fully. The regression equations present in this paper are useful only to the extent that conditions at this plant at the time of this study are duplicated. If conditions at the plant change, the correlation will change.

The fact that a significant correlation between dust exposures and dustiness test results was observed in an actual plant shows that addressing material dustiness is important in predicting and controlling worker dust exposure. It also suggests that significant correlations may be present at other plants and other processes. As a result of this, dustiness testers can presently be used to do predictive industrial hygiene (the estimation of exposures before they occur). For example, suppose a new product is being considered for production in a process or an operation where two or more different materials are being used. For this process or operation, one can develop a correlation between dustiness tester results and dust exposure. The correlation and dustiness test results from a small sample of this new material could be used to predict the dust exposures to within an order of magnitude. This could allow one to make dust control recommendations before the new product is produced or used on an industrial scale.

Presently, dustiness testers are empirical tests which are used to simulate the formation of airborne dust during powder handling operations. Unfortunately, the mechanism of aerosol generation during operations such as bag dumping is not well understood in terms of the identity and magnitude of the forces which affect dust generation. An improved fundamental understanding of airborne dust generation by powder handling operations would allow one to select and devise dustiness tests which closely simulate the actual process which generates the airborne dust.

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Note: A more complete version of this paper has been submitted to *Applied Industrial Hygiene.*

MEASUREMENT OF COAL DUST AND DIESEL EXHAUST AEROSOLS IN UNDERGROUND MINES

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ABSTRACT

In a cooperative study by the University of Minnesota and the U.S. Bureau of Mines, diesel exhaust and mineral dust concentrations have been measured for aerosols generated in the laboratory and in five underground coal mines. Three mines utilized diesel-powered haulage equipment and two used all-electric equipment. Two source apportionment techniques have been applied to differentiate between the mineral dust and diesel exhaust aerosol concentrations measured. The first technique, using a micro-orifice, uniform deposit impactor (MOUDI) for size selective sampling, is based on modeling aerosol size and the premise that the diesel exhaust portion of the aerosol is predominantly submicron and the mineral dust portion is mostly greater that one micrometer in size. The second technique, Chemical Mass Balance (CMB) modeling, was used to referee the analysis of diesel exhaust and mineral dust aerosol concentrations from the size selective sampling results.

The MOUDI size distribution data were modeled to obtain parameters describing the fine and course fractions of the sampled aerosol and to estimate the contributions to each mode from both mineral dust and diesel exhaust aerosol sources. The results showed the size distribution of the mixed aerosols exhibited two definite modes with the minimum between the modes occurring at 0.8 μm. Less than 5 pct of the coal mine diesel aerosol was found in the coarse size fraction. CMB analysis confirms the original premise for using aerosol size to separate diesel exhaust and mineral dust aerosol during sampling.

Based on the results from the size selective sampling, a personal diesel aerosol sampler has been developed for measuring diesel aerosol mass concentrations. This sampler uses an inertial impactor to size separate the respirable aerosol at 0.8 μm. All material less than 0.8 μm is collected on an afterfilter for subsequent gravimetric analysis.

INTRODUCTION

Measurement of the contribution of diesel exhaust to respirable aerosol in mine environments has become increasingly important because of recent research which suggests that exposure to diesel exhaust particulate matter may have adverse occupational health effects. To support these efforts, the U.S. Bureau of Mines is developing and evaluating new sampling methods for the measurement of diesel aerosol in underground coal mines.

Two of these techniques are size selective sampling and chemical mass balance modeling (CMB). Size selective sampling, is being adapted for diesel aerosol sampling by the Particle Technology Laboratory (PTL) of the University of Minnesota under sponsorship by the.[1] It is based on the premise that diesel and mineral dust aerosol can be physically separated by size and collected during sampling using inertial impaction.

The second technique, CMB, is an alternative measurement technique used to referee the results obtained using size selective sampling.[2] It compares elemental 'finger prints' of the aerosol sources with similar profiles measured for mine aerosol samples. From this the portions of the sample contributed by each source can be determined.

The Bureau and the PTL have conducted a study in five coal mines using both size selective sampling and the CMB techniques. This study was undertaken as a follow-on to the laboratory study of size selective sampling applied to the measurement of diesel aerosol.[1] The results from the laboratory and field studies are summarized in this paper. The design of a prototype personal diesel aerosol sampler, based on the size selective results, is also presented.

LABORATORY EXPERIMENT

Laboratory experiments were conducted to investigate the

feasibility of using the Micro-Orifice, Uniform Deposit Impactor (MOUDI) to measure the size distribution of aerosols containing various mixtures of coal dust and diesel exhaust aerosols.[1] The objective of the work was to determine the mass concentration of diesel exhaust aerosol in an airborne mixture of coal dust and diesel exhaust aerosol from the size distribution of the mixed aerosol. A prototype seven stage MOUDI with cut sizes ranging from 0.1 to 10 μm was used.[3]

The experiment successfully demonstrated that coal dust and diesel exhaust aerosol can be separated and measured on the basis of size. Data from the tests, typified in Figure 1, show that the overall diesel exhaust/coal aerosol size distribution is bimodal with the diesel exhaust (accumulation) mode aerosol having a mass median aerodynamic diameter (MMD) of approximately 0.15 μm. The coal (coarse particle) mode has a MMD in the 3 to 10 μm size range. A clear separation between the two modes exists in the 0.7 to 1.0 μm size range with the minimum near 0.8 μm. Analysis of a combined size distribution permits a quantitative determination of the diesel aerosol contribution to within 15%.

FIELD STUDIES

The five mines visited during the field study are summarized in Table I. The table indicates each mine's geographical region, coal type being mined, and type of haulage equipment used. Three of the mines, A, B, and H were equipped with diesel haulage equipment and C and G had all electric equipment. The electric equipped coal mines were used to generate comparison samples for a mine environment without diesel aerosol.

Measurements consisted of collecting size differentiated aerosol samples at four locations in longwall development sections employing a continuous miner: in the air intake entry, conveyor beltway entry, air return entry, and haulage way. A ten stage MOUDI was used for most of the field size distribution measurements and a dichotomous sampler was used to collect aerosol for the elemental analysis used in the CMB model calculations. The samplers and CMB analysis are described elsewhere.[2,4] Both samplers were operated at a flow rate of 30 lpm.

Aerosol samples were collected at the intake and haulage or beltway locations periodically during each mine work shift. Sampling at the return location was usually conducted only once during the shift, while the continuous miner was in operation. Samples of primary interest were those collected at the conveyor belt or in the haulage way since they are from areas where workers are exposed. These were collected only when the breaker was on and diesel haulage equipment was in use. As a result, no attempt was made during the field experiments to take representative exposure samples for the work shift. The focus of the study was on developing a method for measuring the diesel component of a mine aerosol containing a mixture of both diesel exhaust particulate and mineral dust.

Trace element profiles of mine aerosol sources used in the CMB analysis were obtained from samples of the material from which the diesel or mineral dust aerosols originate.

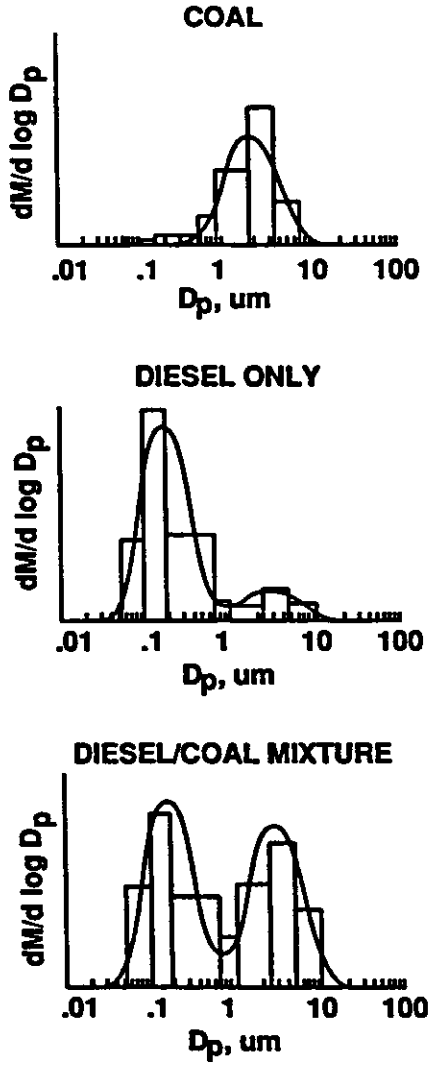


Figure 1. Laboratory diesel/coal dust size distributions.

Bulk material samples were collected of coal and the rock dust used in the mine as an explosion and fire retardant. For the diesel equipped mines visited, exhaust source aerosol samples were collected from the tailpipes of the haulage vehicles operating in the mine. In each case, the assumption is made that the profiles thus obtained are representative of the aerosols originating from these sources.

Where collection of diesel tailpipe aerosol samples was not feasible, diesel fuel and diesel lubricating oil were collected to use as a surrogate for the diesel exhaust aerosol source.[5] To enhance the use of diesel fuel as a surrogate for diesel aerosol emissions, a tracer material, a nominal 10 parts per billion of Indium as Indium 2,4 pentanedionate in xylene, was added to the fuel supply for the vehicles operating in the test section of the mines. The trace element analysis technique used Instrumental Neutron Activation Analysis (INAA), was performed by the University of Rhode Island.[6]

FIELD MEASUREMENT RESULTS

Average aerosol size distributions measured in the haulage

Table I
Mine Data for Operations Visited FY 85-87

Mine	Region	Haulage	Coal Rank
A	West	Diesel	HVB* C[1]
B	West	Diesel	HVB C[2]
C	East	Electric	HVB B[1]
G	East	Electric	HVB A[3]
H	Midwest	Diesel	HVB B[3]

* HVB - High Volatile Bituminous

Sources
1 Based on ASTM Standards.
2 Company information
3 1987 Keystone Coal Industry Manual. McGraw-Hill, Inc., New York, 1987, 1244 pp.

way of the diesel equipped and all-electric coal mines are shown in Figures 2 and 3. The MOUDI separates and collects the sampled aerosol in several size intervals by aerodynamic diameter. The number of size intervals provides enough differential size resolution to model the measured aerosol size distributions with empirical functions. This analysis, termed modal analysis, uses a sum of two log-normal functions to fit the data.[7] Each function represents one of the maxima or modes evident in the data. The log-normal distribution parameters, given in Table II for the average distributions, are the mass mean diameter (MMD), geometric standard deviation (σg) and mode concentrations.

Each mode can be identified with the aerosol contributed by a primary aerosol source; diesel exhaust aerosol for the submicron mode and mineral dust for the coarse particle mode. Under this assumption, the separate contributions from these sources to the total aerosol concentration can be determined using modal analysis. Treating each mode as a source connected entity, also permits the determination of that portion of the coarse particle mode that encroaches on a sample of submicron mode aerosol as it might be collected by a size selective sampler. This is done by integrating the distribution function for the coarse particle mode over the range of sizes for which the submicron mode aerosol is collected. An illustration of such modal overlap for the average diesel/coal size distribution of Figure 2 is given in Figure 4. The range of integration is 0.001 to 0.8 μm. Shaded areas indicate the portion of the submicron and coarse aerosol that will contribute to a sub-0.8 μm sample.

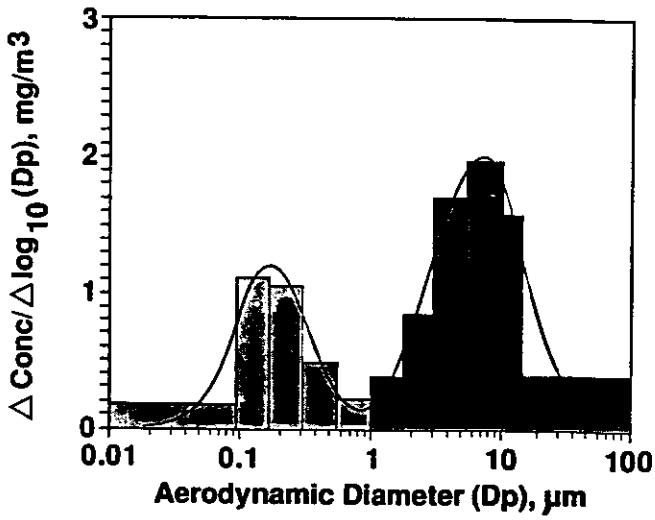


Figure 2. Average mass size distribution measured in the haulage entries of diesel equipped coal mines.

A comparison between modal and CMB analysis results is given in Table III. Values from the modal analysis for the fraction of sub-0.7 μm aerosol contributed by the coarse particle mode are 7±5% for mine A, 15±7% mine B, and less than 2% for mine H. Results for mine A and H are well within each others stated variability. There is a barely resolvable difference between the two analysis results for

Table II

Summary of Log-normal Size Distribution Parameters for Average Aerosol Distributions Measured in Haulage Entries of Diesel Equipped and All-electric Coal Mines

Mine Type	Submicron Mass Mean Dia.[1] um	Submicron Geometric Std. Dev.[2]	Submicron Mode[3] Conc. mg/m³	Coarse Mass Mean Dia. um	Coarse Geometric Std. Dev.	Coarse Mode Conc. mg/m³
Diesel	0.17±0.04	2.0±0.3	0.88±0.52	6.8±1.6	2.3±0.3	1.8±0.8
Electric	0.46±0.10	2.6±0.9	0.06±0.04	7.2±2.0	2.0±0.3	1.2±0.8

[1] Mass Mean Diameter (MMD)
[2] Geometric Standard Deviation (σ_g)
[3] Mode Concentration

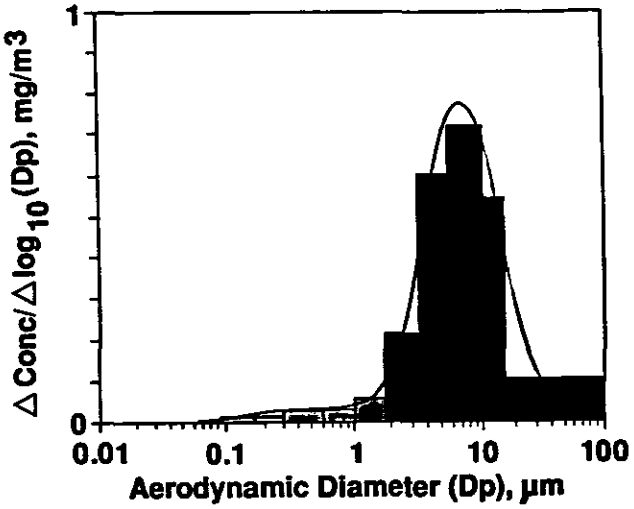


Figure 3. Average mass size distribution measured in the haulage entries of all-electric equipped coal mines.

mine B. This difference may be due to the limited number of samples analyzed.

Using the results of the limited CMB analysis, two key points can be made concerning the contribution of the various diesel mine sources to fine and coarse aerosols in the mine environment. These are:

1. Diesel emissions aerosol is the dominant component of the submicron mode aerosol measured in the diesel mines. From 75 to 90% of the measured aerosol concentration is contributed from diesel sources.

2. Coal is the primary component of the coarse aerosol, as much as 92%.

Table III

Average Coarse Particle Contamination of Sub-0.7 µm Samples for Mines A, B and H

Mine	Analysis Modal %	Analysis CMB %
A	7±5	<8
B	15±7	25±4
H	<0.2	<4

These points confirm the basic assumptions advanced to justify the use of the MOUDI or other size selective sampler to separate and measure diesel and mineral dust aerosol in the mine environment. Separate confirmation for the assumption that the mineral aerosol contributes predominantly in the coarse aerosol size range is found in the average size distribution measurement results for the all-electric equipped coal mines in Figure 3.

The optimum particle size for the separation of diesel from mineral dust aerosol was determined from the average size distribution measured in the haulage entries of the three mines using diesel equipment. This analysis treated the submicron mode as entirely diesel aerosol and the coarse particle mode as entirely mineral. Integrating the log-normal functions that describe the size distribution modes from zero up to a given size, as illustrated in Figure 4, the aerosol mass that would be collected by a sampler with that separation size was determined. Using these results, the gravimetric error made by assigning the aerosol mass collected by the sampler to diesel aerosol alone was calculated as a function of separation size. The least error, ±7%, occurs for size separation at 0.8 µm.

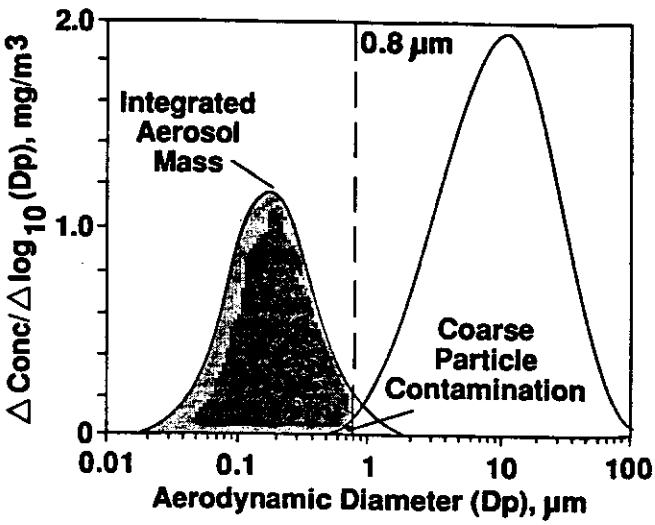
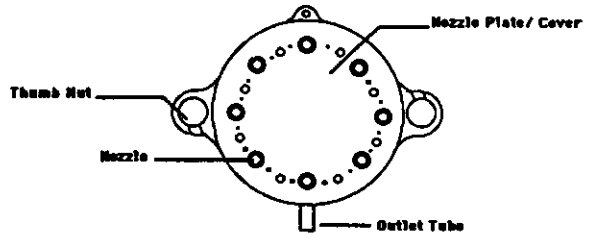


Figure 4. Illustration of the integration of aerosol mode functions to calculate aerosol mass less than 0.8 µm.

PERSONAL DIESEL AEROSOL SAMPLER

A prototype personal diesel exhaust aerosol sampler has been designed for underground coal mines. The sampler was designed on the premise that size selective sampling techniques can be used to separate diesel exhaust aerosol, which is predominantly submicron in size, from coal dust aerosol, which is mostly greater than a micron in size. The sampler has three stages and employs inertial impaction for particle separation. The first, sample inlet/preclassifier, stage is a composite impactor with an aerosol penetration efficiency that conforms to either the American Conference of industrial Hygienists (ACGIH) or the British Medical Research Council (BMRC) respirable dust sampling criteria. This first stage serves as a preclassifier to select the respirable portion of the sample aerosol and prevent overloading of the second stage. The second stage is an multiple-orifice impactor with a sharp separation or cut size that passes only aerosol smaller than 0.8 µm. The respirable aerosol larger than 0.8 µm is deposited on an impaction plate. The third stage, which is a filter, collects all aerosol less than 0.8 µm aerodynamic diameter. This instrument is a research prototype and the design permits the second stage impaction substrate to be removed for gravimetric and chemical analysis. To increase the amount of sample for such analysis, the sample flow rate for the prototype will be 4 lpm. The sampler can be modified for the DORR-OLIVER 10 mm cyclone preclassifier and a flow rate of 2 lpm.

A schematic diagram of the sampler is presented in Figure 5. The sampler inlet is a 2.5 cm. ring of nozzles in the sampler cover. These nozzles are part of a preclassifier/impactor with an aerosol collection efficiency that can approximate either the ACGIH or the BMRC respirable dust sampling criteria.[8] The impaction surface for this first section is a porous plate impregnated with oil to reduce particle bounce and blow off. A sample stream next passes to a multiple-orifice impactor with a cutpoint of 0.8 µm. The impaction plate for this stage is a removable aluminum foil coated with silicone oil. The sample stream then passes through a filter which removes the remaining aerosol. Sampler height is 2.5 cm. The sampler divides the respirable aerosol into two size fractions, greater and less than 0.8 m m. These samples can be used to measure the concentrations of the diesel and mineral dust portions of respirable coal mine aerosol.



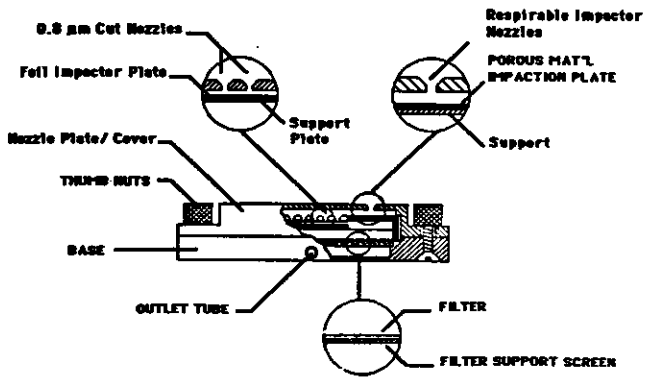


Figure 5. Schematic diagram of personal respirable/diesel aerosol impactor sampler.

The primary limitations on a personal diesel sampler based on size selective sampling are diesel aerosol loss from the sample, contamination by coarse particle mode aerosol, and resolution of the gravimetric analysis performed on the sample. Of secondary importance is the presence of background aerosol in the sample. The latter is due to external diesel, atmospheric, or nondiesel sources of submicron aerosol. The final sample contains most of the diesel particulate material present in the mine air plus a small amount of mineral dust, usually less than 10%. If a sample flow rate of 2 lpm is used and gravimetric analysis is to within 0.1 mg, a sub-0.8 µm aerosol concentration should have a limit of detection of 0.3 mg/m^3.

CONCLUSIONS

The primary result from this study is that size selective sampling can be effective as a technique for measuring diesel aerosol concentrations in underground coal mines. The MOUDI size distribution data were modeled to obtain parameters describing the fine and course fractions of the sampled aerosol and to estimate the contributions to each mode from both mineral dust and diesel exhaust aerosol

sources. The results showed the size distribution of the mixed aerosols exhibited two definite modes with the minimum between the modes occurring at 0.8 μm. CMB analysis confirms the original premise for using aerosol size to separate diesel exhaust and mineral dust aerosol during sampling.

A personal diesel aerosol sampler has been developed for measuring the diesel aerosol concentration in underground coal mines. This device consists of three sequential stages. The first stage classifies aerosol in the sample stream according to the BMRC respirable efficiency curve. The second stage separates the resulting respirable aerosol into two parts by aerodynamic diameter using a single stage impactor with a cutpoint of 0.8 μm. The third stage collects the <0.8 μm diameter aerosol on a media that is suitable for gravimetric analysis.

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MINERAL DUST AND DIESEL EXHAUST AEROSOL MEASUREMENTS IN UNDERGROUND METAL AND NONMETAL MINES

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INTRODUCTION

Measurement of the contribution of diesel exhaust to respirable aerosol in mine environments has become increasingly important because of current concerns over the occupational health effects resulting from exposure to diesel emissions. In response to this, the U.S. Bureau of Mines is developing and evaluating new sampling methods for measuring diesel aerosol in underground mines. Two such techniques are being studied by the Bureau, size selective sampling and Chemical Mass Balance (CMB) modeling. These techniques use measurable physical or chemical characteristics of a mine aerosol sample to infer the amount of diesel particulate material contained in the sample.

Size selective sampling is being adapted for measurement of diesel aerosol by the Particle Technology Laboratory (PTL) of the University of Minnesota under sponsorship by the Bureau.[1] It is based on the premise that diesel and mineral dust aerosol can be physically separated by size and collected during sampling using inertial impaction. An independent effort by the National Institute for Occupational Safety and Health to develop a size selective sampling technique was also sponsored by the Bureau.[2]

The second technique, CMB modeling, is being developed by the Bureau as an alternative measurement technique to referee the results obtained using size selective sampling.[3] It compares measured trace element "finger prints" of aerosol sources with similar profiles of mine aerosol samples. From these, the portions of the sample contributed by each source can be determined. Results of these investigations in underground coal mines have confirmed that diesel and coal dust aerosol are of different size and can be measured separately using size selective sampling techniques.[4]

A major difference in diesel usage among underground mines is the requirement for exhaust gas cooling systems in coal and gassy noncoal mines. Nongassy mines usually employ limited exhaust conditioning in the form of catalytic converters, which have limited effect on primary exhaust particulate. The cooling system in most general use in gassy mines is the water scrubber. This device has little effect on most of the gases but removes particulate material from the exhaust.[5] Because of this, exhaust aerosol characteristics in nongassy mines are expected to be different. To see if size selective sampling techniques can be used in such mines, the Bureau and the University of Minnesota conducted a second study in three metal and nonmetal mines, two nongassy and one rated as gassy.

FIELD STUDIES

The field study conducted in metal and nonmetal mines is summarized in Table I. The table indicates each mine's geographical region, the material being mined, and the type of haulage equipment used. The studies consisted of collecting size-differentiated aerosol samples at four locations in a working section employing diesel haulage equipment: the air intake entry (I), beltway entry—where applicable (B), air return entry (R), and haulage way (H). These locations are illustrated in Figure 1 for the soda ash mine.

Aerosol samples were collected using Micro-Orifice, Uniform Deposit Impactor (MOUDI) and respirable dichotomous samplers.[4] The MOUDI, used for size distribution measurements, is a 10-stage cascade impactor with particle separation sizes at 15, 10, 5.62, 3.16, 1.78, 1.0, 0.562, 0.316, 0.178, and 0.1 μm plus an after-filter. The dichotomous sampler was used to collect aerosol for the elemental analysis used in the CMB model calculations. It consists of an impaction-type inlet designed to pass sample aerosol with an efficiency approximating the American Conference of Governmental Industrial Hygienists (ACGIH) respirable dust sampling criteria, followed by two MOUDI impaction stages, both with 0.7-μm separation sizes, plus an after-filter.[6] Configured in this way, the dichotomous sampler provides a partition of the collected respirable aerosol sample into two size fractions, greater and less than 0.7 μm in size. This partition was selected because it was close to the size found to separate diesel exhaust and coal dust aerosol components in laboratory studies and the impactor stages were available.[1] Both samplers operate with a 30 lpm sample flow rate.

Trace element profiles of mine aerosol sources used in the CMB analysis were obtained from samples of the material from which the diesel or mineral dust aerosols originate. Exhaust source aerosol samples were collected from the tailpipes of the haulage vehicles operating in the mine. Bulk material samples were collected of the mineral being mined. In each

Table I
Mine Data for Metal/Nonmetal Mines Visited 1985–1987

Mine	Region	Haulage	Type of Material
D	Midwest	Diesel	Shale
E	West	Diesel*	Soda Ash
F	West	Diesel	Quartzite

*Gassy mine, water scrubbers used on diesel equipment.

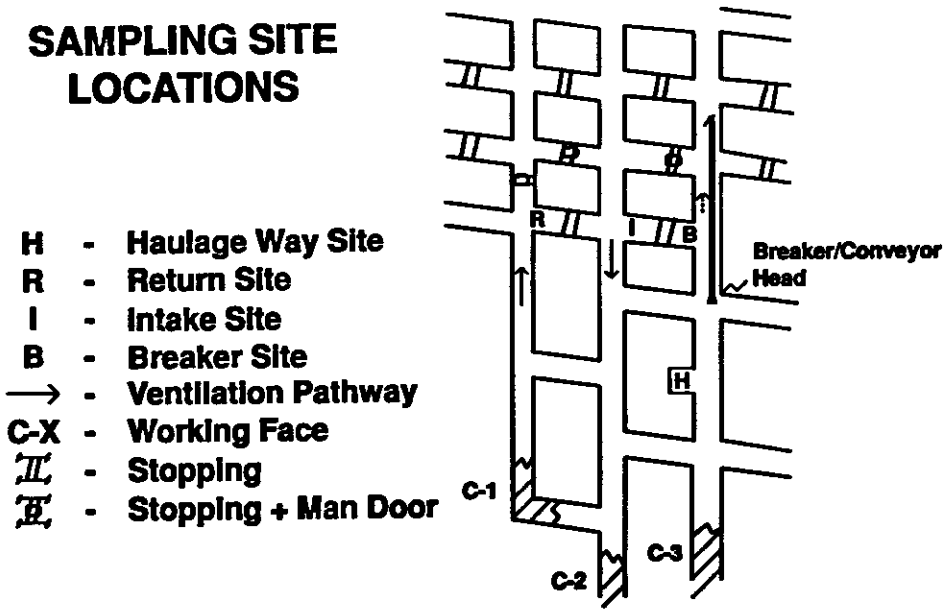

Figure 1. Sampling site locations used for in-mine sampling experiments are indicated together with ventilation vectors.

case, the profiles obtained are assumed to be representative of the aerosols originating from these sources.

To enhance the diesel tailpipe samples, a tracer material, a nominal 10 parts per billion of indium as indium 2,4 pentanedionate in xylene, was added to the fuel supply for the vehicles operating in the test section of the mines. The trace element analysis technique used, instrumental neutron activation analysis (INAA), is very sensitive to indium, which is rarely found in nature.[7]

Aerosol samples at haulage way or beltway locations were collected periodically during the entire mine work shift. Since they were collected in areas where workers are exposed, they are the samples of primary interest. Sample collection was only done when the conveyor belt was on and diesel haulage equipment was in use. The samples collected are therefore biased toward high concentrations of both diesel and mineral aerosol and are not representative personal exposure samples for the work shift. Although not analyzed for the study, sampling at the return location was conducted once during the shift, while the continuous miner was in operation.

Measurement and Analysis Techniques

Only two measurement techniques were used in the field study. These were gravimetric analysis of the impaction substrates and after-filters from both the MOUDI and dichotomous samplers and elemental analysis of the dichotomous samples using INAA.[3]

INAA was performed at the University of Rhode Island.[8] Analyses were performed on dichotomous substrates and after-filter pairs containing sufficient aerosol mass for irradiation (1 mg or more), quality control blanks of both substrate and after-filter, and samples of the aerosol source materials. The source materials were analyzed in triplicate, and average values for the resulting element concentrations were used in the CMB analysis.

Modal Analysis

Average aerosol size distributions measured in the haulage way of the diesel-equipped mines visited are shown in Figure 2. The measured aerosol size distributions were modeled using a sum of two log-normal functions to fit the data.[9] Each

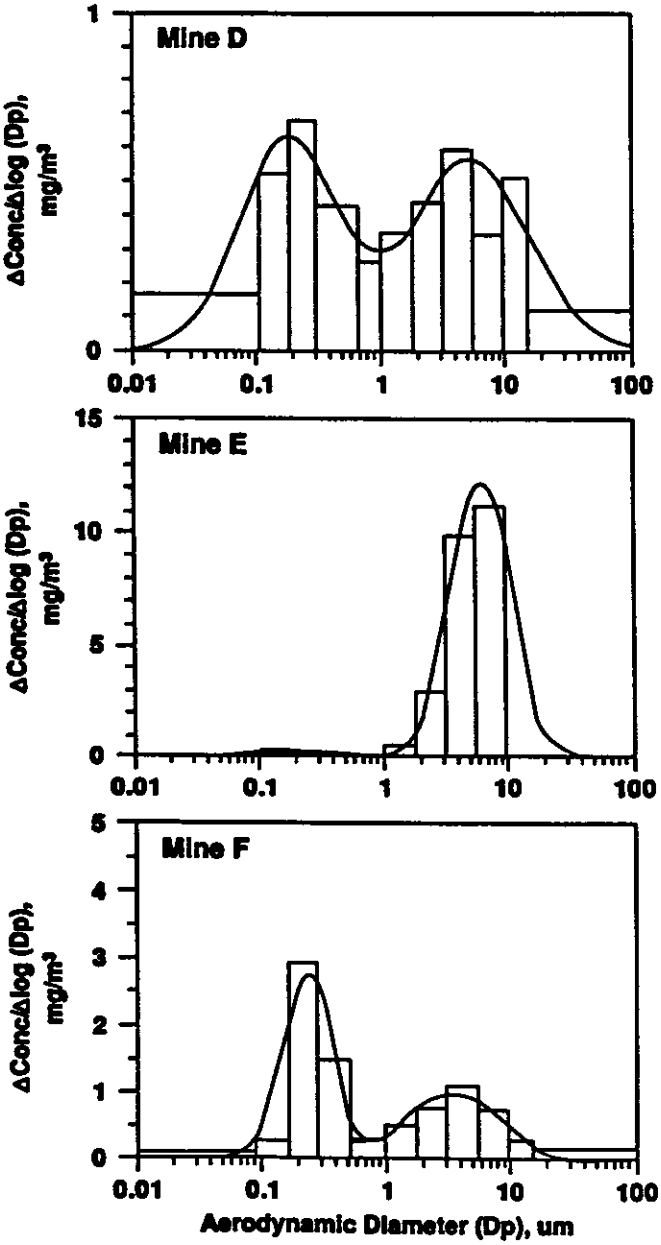

Figure 2. Average mass size distribution measured in the haulage entries of mines D, E, and F.

function represents one of the maxima, or modes, evident in the data. The log-normal distribution parameters, given in Table II for the average distributions, are the mass mean diameter (MMD), geometric standard deviation (σg), and mode concentrations.

For coal mines, each mode was identified with the aerosol contributed by a primary aerosol source diesel exhaust aerosol for the submicron mode and mineral dust for the coarse particle mode.[3] Under this assumption, the separate contributions from these sources to the total aerosol concentration can be determined using modal analysis. For these noncoal mines, the results of the size measurements are very similar. Two well-separated aerosol modes are evident for each of the mines. It remains for the CMB analysis to determine whether the same interpretation can be made.

CMB Model Analysis

CMB model analysis permits the relating of elements or chemical components in an aerosol sample collected at a given location to those same components in the sources of the aerosol.[10,11] The model is expressed as:

$$C_i = \sum_{j=1}^{P} a_{ij} S_j \qquad (1)$$

Here, p is the number of aerosol sources, C_i is the mass concentration of the ith elemental component of the sample in μg/m³, a_{ij} is the fractional amount of component i in emissions from source j, and S_j is the amount of the aerosol mass concentration attributable to source j. S_j/(total sample mass concentration) is termed the source apportionment fraction. Apportionment of the source is achieved by measuring trace element component profiles of the aerosol sources, thus obtaining values for a_{ij}, analyzing the aerosol in the collected aerosol sample for the same components, and determining S_j using a least squares analysis of the overdetermined system of equations expressed by equation 1.

The CMB analysis used for the work employs effective variance weighing for the least squares calculation of the source apportionment terms S_j in equation 1.[3,11] In this analysis the S_j are determined by minimizing the following chi-square (X^2 function:

$$X^2 = \sum_i \frac{(C_i - \sum_j a_{ij} S_j)^2}{\sigma_c^2 + \sum_j \sigma_{a_{ij}}^2 S_j^2} \qquad (2)$$

Here σ_c is the standard error in C_i, and σ_a is the standard error in a_{ij}. The minimization was carried out using a direct search technique rather than matrix inversion calculations.

RESULTS

Average values for the CMB source apportionments are given for mines E, F, and G in Table III for the fine, sub-0.7 μm, and coarse, super-0.7 μm, portions of the dichotomous samples. Errors quoted in the table are more indicative of the variability of the results from sample to sample than of the true statistical errors. In each case diesel exhaust is the dominant component of the submicron aerosol, greater than 92%. These apportionments deviate from those of the coal

Table II

Summary of Log-normal Size Distribution Parameters for Average Aerosol Distributions Measured in Haulage Entries of Diesel Equipped Metal and Nonmetal Mines

Mine	Submicron			Coarse		
	Mass mean dia.[1] μm	Geometric std. dev[2] σg	Mode[3] conc. mg/m³	Mass mean dia.[1] μm	Geometric std. dev[2] σg	Mode conc. mg/m³
D	0.18 ± 0.03	2.5 ± 0.2	0.6 ± 0.2	5.1 ± 1.0	3.1 ± 0.3	0.7 ± 0.2
E	0.16 ± 0.13	2.4 ± 0.7	0.20 ± 0.06	6.1 ± 3.3	1.8 ± 0.3	7.5 ± 4.0
F	0.26 ± 0.04	1.6 ± 0.1	1.4 ± 0.3	3.8 ± 0.7	2.4 ± 0.3	1.1 ± 0.8

[1] Mass Mean Diameter (MMD)
[2] Geometric Standard Deviation (σg)
[3] Mode concentration

Table III

CMB Source Apportionment Results for Mines E, F, and G

Mine	Source	RESPIRABLE SIZE FRACTION, %	
		SUB-0.7 μm	SUPER-0.7 μm
D	Diesel	94 ± 12	25 ± 20
	Ore	5.6 ± 0.8	75 ± 13
E[1]	Diesel	95 ± 7	<20
	Ore	4.9 ± 4.8	81 ± 7
F	Diesel	92 ± 12	40 ± 5
	Ore	<12	60 ± 5

[1] Gassy mine, wet scrubber used.

mine samples in that a significant fraction of the respirable coarse aerosol in the mines where diesel equipment does not use a wet scrubber is diesel—up to 40% for Mine F.[3] This translates to approximately 20% of the total diesel aerosol being greater than 0.7 μm in size.

Applying modal analysis to concurrent size distribution samples permits a comparison with the CMB analysis results. Table IV gives this comparison for coarse particle contamination of the sub-0.7 μm aerosol in the three diesel equipped metal and nonmetal mines. The two analyses give the same result, within the quoted errors.

Table IV

Average Coarse Particle Contamination of Sub-0.7 μm Samples for Mines E, F, and G

Mine	Analysis	
	Modal %	CMB %
D	4 ± 2	5.6 ± 0.8
E	<2	4.9 ± 4.8
F	2± 1	<12

CONCLUSION

Using the results of the limited CMB analysis, two points can be made concerning the contribution of the various diesel mine sources to both fine and coarse fractions of the respirable aerosol concentrations in the metal and nonmetal mine environment:

1. Diesel exhaust aerosols are the dominant component of the submicron mode aerosol measured in the diesel mines. More than 90% of the measured aerosols is contributed from diesel sources.
2. As much as 20% of the diesel exhaust aerosol contributes directly to the coarse part of respirable aerosol in the mine atmosphere.

It is not clear that the size selective technique used in the measurement of coal mine diesel aerosol can be extended to diesel-equipped metal and nonmetal mines. That technique depends on separating the collected aerosol sample into two size fractions at 0.8 μm.[4] In metal and nonmetal mines the substantial contribution to the respirable coarse fraction made by diesel exhaust aerosol compromises the use of size selective sampling, reducing the accuracy to less than 80%. As a result, alternate, carbon-specific, methods for determining diesel aerosol concentrations should be used in such mines if higher accuracy is desired. One such method is thermal-evolved gas analysis.[12] This technique permits analysis of the volatile, carbonate, and elemental carbon fractions of an aerosol sample. It should permit an unambiguous analysis of elemental carbon (soot) in a mine aerosol sample.

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MEASUREMENT OF AIRBORNE DIESEL PARTICULATE IN A COAL MINE USING LASER RAMAN SPECTROSCOPY

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INTRODUCTION

The goal of this research has been to develop the Laser Raman Quantitative Analysis (LRQA) method to measure the composition of respirable particulate, i.e. the fractions of coal and of diesel particulate, in the mine ambient air. In earlier Bureau of Mines sponsored research, we successfully demonstrated that the LRQA method could be used to measure the fraction of Diesel Particulate Matter (DPM) in coal/diesel particulate mixtures which were prepared in the laboratory.[1] The immediate objective was to test and refine this LRQA method on samples collected in a diesel underground coal mine.

Specific objectives required to meet this goal include:

1. Develop in-mine sample collection methods which will insure sufficient particulate loading on filters for LRQA.
2. Develop methodology for in-mine collection of reference samples ("coal-only" and "diesel-only" filters) which are required for quantitative LRQA.
3. Analyze precision and accuracy of the LRQA method.
4. Compare composition measurements with another analytical method, i.e. the University of Minnesota /Bureau of Mines size-selective sampling Micro-Orifice Uniform Deposit Impactor (MOUDI) method.

An advantage of the LRQA method is that it allows analysis of filters which have been collected by a method similar to that used to determine the respirable dust concentration in US underground coal mines. No new sampling instruments and techniques are required. Transfer of sample from collection substrate to analysis substrate is not necessary. Furthermore, other analyses can be made on the same sample since the technique is nondestructive.

The health effects of diesel exhaust, especially particulate, are a concern in the underground workplace. The constituents of DPM include insoluble carbonaceous particle agglomerates, adsorbed or condensed soluble organic compounds, trace metals, and low level sulfates. Many of the organic compounds are mutagenic and some are known carcinogens.[2,3]

Measurements made in underground mines with diesel equipment have shown that DPM may contribute as much as 60 % of the 2.0 mg/m^3 respirable coal mine dust standard.[4] While coal dust has been an important health concern for a number of years, the concern about DPM is more recent.[5]

Measurement of pollutant concentrations is prerequisite to engineering control of the airborne particulate and gaseous pollutants to which a miner is exposed in a diesel underground coal mine. At the present time, there is no fully-proven quantitative analysis method which can distinguish between diesel and coal particulate.

EXPERIMENTAL

The mine air particulate samples were collected in a manner similar to that used for gravimetric respirable dust sampling in underground coal mines. Respirable dust was sampled using a personal sampler which draws mine air at 2 L/min through a 10 mm nylon preseparator and then through a filter at 2 L/min. Diesel/coal samples were collected in triplicate (collection times varied from 2.95 to 7.27 hr). Smaller Gelman A/E glass fiber particulate collection filters (25 mm filters instead of the normal 37 mm diameter) were used to assure filter loadings close to 0.10 mg/cm^2 and preferably 0.15 mg/cm^2. This 0.1 mg/cm^2 nominal level was determined by LRQA of various filter loadings above and below this level in previous studies. Only 8% of the samples fell below 0.07 mg/cm^2 with the majority falling in the 0.1 to 0.4 mg/cm^2 range (72%). Three locations were sampled for the diesel/coal mixtures each day: near the feeder-breaker, in the return, and on the ram car within 2 feet of the operator (as designated in Figure 1.

As part of a systematic approach to monitoring diesel emissions for control of mine air quality, we also measure ambient air pollutants and CO_2 concentrations.[6] This approach, developed at Michigan Technological University (MTU), provides a means to relate air quality measurements to engineering controls. The CO_2 concentration, which is related to the fuel consumption and airflow per unit of diesel power used, is related to the DPM fraction. A typical value of 13 mg/m^3 /%CO_2, determined from previous sampling in a number of metal mines, was used to calculate this CO_2—derived DPM value. The DPM concentration estimated using the % CO_2 does not compare well with LRQA values; % CO_2—is expected to be a rough indicator only.

Four "diesel-only" tailpipe particulate matter samples were collected from each of 3 Ram Cars using the portable Emissions Measurement Apparatus (EMA). The EMA, developed at MTU, is illustrated in Figure 2.[1] The EMA is a tailpipe apparatus designed to instantaneously and dynamically dilute the exhaust to a dilution ratio of about 20:1. A 63 mm

diameter Pallflex T60A20 filter was used to collect particulate (ca. 1.5 min sampling time).

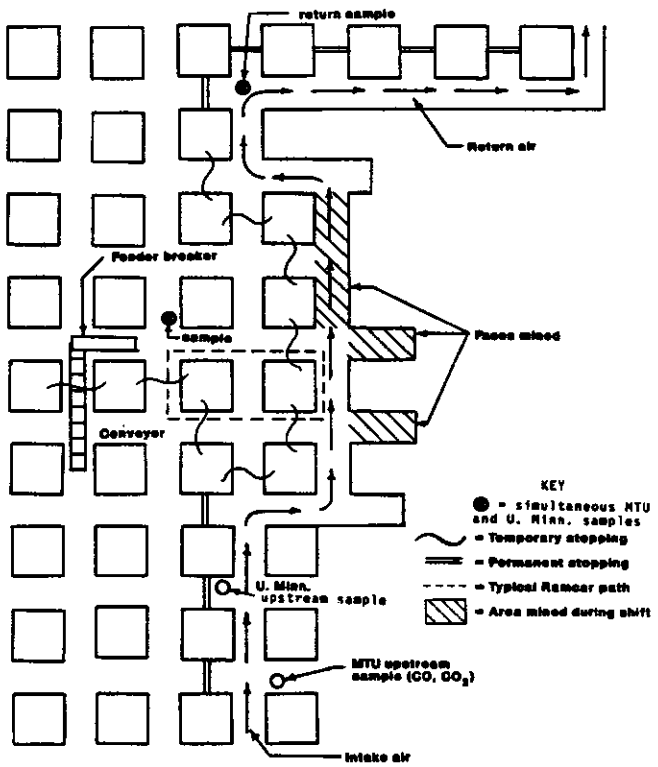

Figure 1. Schematic of coal mine section defining sampling locations.

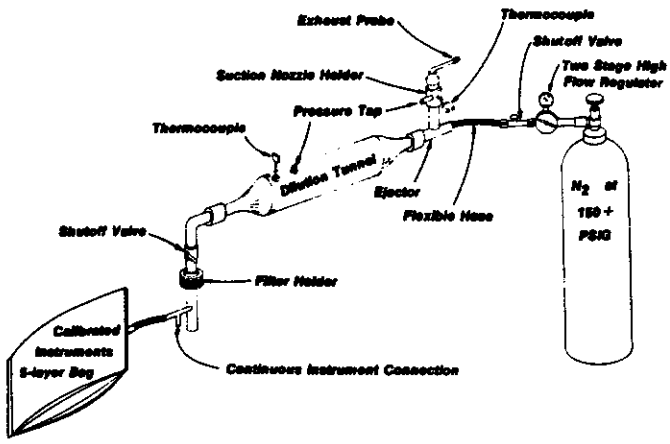

Figure 2. Schematic of emissions measurement apparatus (EMA-2) which is used to collect diesel-only tailpipe samples.

apparatus designed to instantaneously and dynamically dilute the exhaust to a dilution ratio of about 20:1. A 63 mm diameter Pallflex T60A20 filter was used to collect particulate (ca. 1.5 min sampling time).

"Coal-only" particulate reference samples were taken daily for 4 days next to the continuous miner (CM) scrubber (Figure 3). The collection procedure was similar to that used for the diesel/coal mixture samples. With the high dust concentrations between the cutter and scrubber, respirable coal dust can be collected in 15 minutes or less.

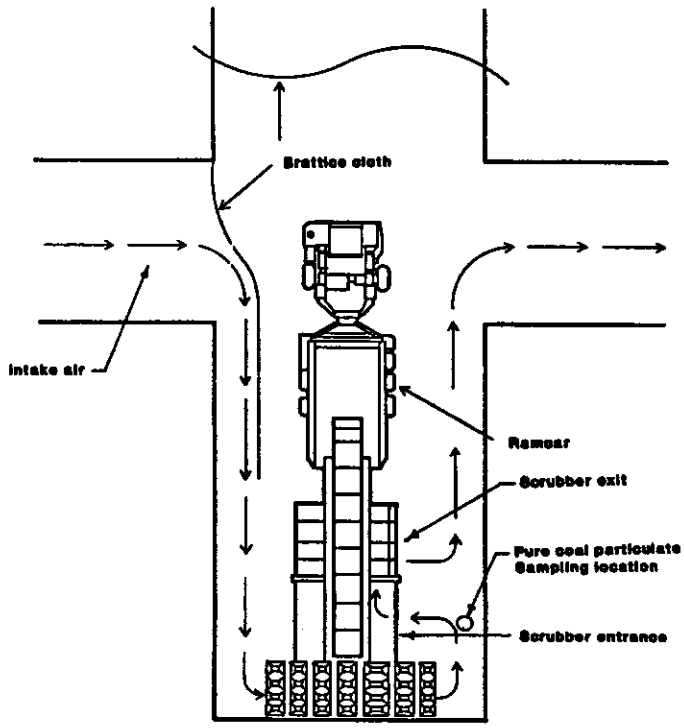

Figure 3. Illustration showing location of coal-only particulate sample collection.

After weighing to determine the respirable dust concentration, the filter is mounted on a sample spinner and analyzed by LRQA. No transfer of the particulate to a different filter is required. Samples are rotated to prevent decomposition in the laser beam.[1] The schematic in Figure 4 depicts the LRQA instrumentation.

The LRQA spectral scan procedures have been designed to test for sampling inconsistencies which might arise from sample decomposition in the laser beam. Four spectra are collected, a pair at each of two different radii on the spinning filter. The individual spectra are designated as "1x spectra." The sum of the two spectra at one radius is designated as a "2x spectrum." Any decomposition in the laser beam will

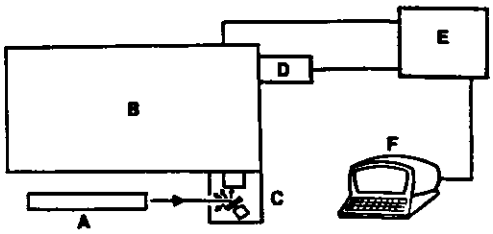

Figure 4. Schematic diagram of Raman instrumentation used to collect coal/diesel particulate spectra.
A) Argon-ion laser
B) Spectrometer (double monochromator)
C) Sample chamber with spinning sample holder
D) Photomultiplier tube
E) Interface between spectrometer and computer
F) Computer used to control spectrometer and to analyze spectra

be apparent upon comparison of two 1x spectra. Comparison of two 2x spectra will indicate radial inhomogeneity. This procedure also allowed detection of radial sampling inhomogeneities on a filter which are caused by particle size segregation. The sum of all four 1x spectra is designated as a "4x spectrum," and is representative of a given filter.

LRQA samples have been collected simultaneously with the size-selective sampling method being developed at the Twin Cities Research Center (TCRC) and the University of Minnesota.[4,7] The latter samples were collected by University of Minnesota personnel. MOUDI samplers, used for this purpose, separate the particles into size fractions on the basis of their aerodynamic diameters and densities.[7] This side by side collection allows direct comparison of the fractions of diesel and coal in the mine air measured by the two methods. All samples were collected during one week of underground air sampling during August, 1987, in the Kerr McGee Galatia Mine.

RESULTS AND DISCUSSION

Coal-only and Diesel-only Measurements and Use

A well defined relationship (equation 1) exists between the diesel/coal composition (y) and the intensity ratio (M) of two bands in the Raman spectrum of a mixture.[1] Figure 5 graphically depicts this relationship. Raman spectra of coal-only and diesel-only samples are shown in Figure 6.

$$1/y = (g'/g)\ \{(r'-M)/(M-r)\} + 1 \qquad (1)$$

y is the percent diesel particulate matter, %DPM, in a coal/DPM mixture. g represents the coal-only intensity and g' represents the DPM-only intensity. The slope in equation 1, g'/g, is the intensity ratio of the two samples and must be obtained when the two components are identically aligned. The coal-only intensity ratio (r) and the DPM-only ratio (r') must be determined to allow quantitative analysis of the mixtures.

The ratio for coal-only filters (r) was determined for 6 filters which were collected on three different days. The 1x, 2x and

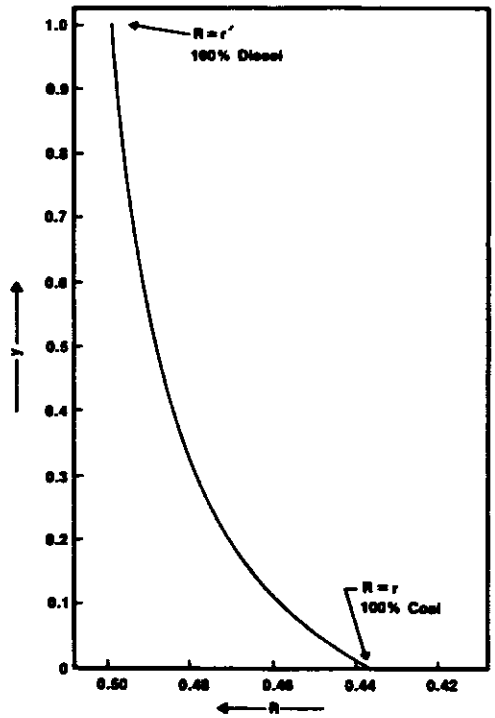

Figure 5. A graphical representation of the dependence of composition, i.e., %DPM (y), upon the experimental intensity ratio (R).

4x spectra demonstrate good reproducibility. This consistency shows that the samples are not decomposing in the laser beam. The mean and standard deviation (SDEV) for the coal-only samples are 0.522 and 0.022, respectively (C.V.=4.3%). This precision is comparable to that expected theoretically for these scan times.[1] The overall accuracy of mixture composition analysis depends on precise measurement of the coal-only intensity ratio (r) and the DPM-only ratio (r').

Spectral ratios have been determined for four DPM-only filters (after-scrubber), collected from two different ram cars. A mean r' value has been calculated by averaging the ratios measured for the four filters (a pair collected from each ram car). Reproducibilities for these are reasonable with an average r' of 0.958 and with a SDEV of 0.089 (C.V.= 9.3%.

Spectral Analysis and Reproducibility

The calculated %DPM values are analyzed statistically to demonstrate spectral reproducibility for a triplicate set of filters. Table I summarizes the %DPM values for one set of diesel/coal mixture filters collected at the feeder-breaker. The %DPM for each filter in column B of Table I are each an arithmetic mean of four 1x spectra. Column C gives the corresponding standard deviations. At the bottom of this table the overall arithmetic mean and standard deviation for the 12 spectra are given. Column D presents the %DPM measured on the summed (4x) spectra, with the mean and

Table I
Statistical Analysis of %DPM for a Triplicate Set of Filters
Collected at the Feeder-Breaker (on 8/10/87)

Column:	B	C	D	F	G
	% DPM for four 1x spectra		% DPM for one 4x spectrum	% DPM for the 2x spectra	
Filter	Mean	SDEV		Inner	Outer
3393	60.4	9.3	65.9	55.6	70.9
4730	61.9	8.7	67.6	62.5	68.9
6337	67.7	8.4	61.7	57.1	65.9
Values for twelve 1x spectra:	63.3	8.8	Values for three 2x spectra, mean:	58.4	68.6
Values for three 4x spectra:	64.9	3.0	and SDEV:	3.6	2.5

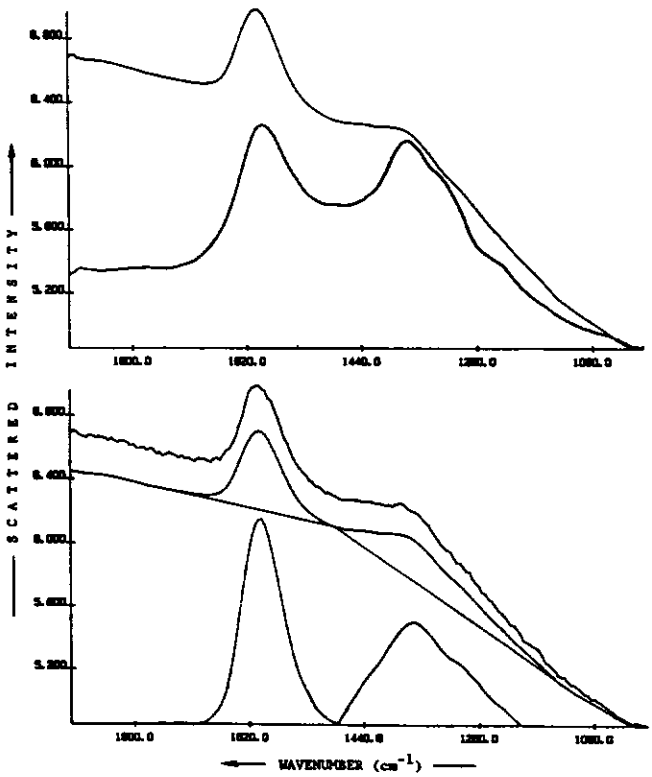

Figure 6. Raman spectra of coal-only and DPM-only filters (top), and baseline subtraction procedure for measurement of the intensity ratio (bottom).

standard deviation for the set of three at the bottom. Note that the standard deviation for the 4x spectra is smaller than for the 1x spectra because of the increased S/N ratio in each summed spectrum. The inter-filter mean composition is 64.9% DPM.

The intra-filter reproducibility is measured by the standard deviation of the %DPM (in column C of Table I) for each filter. The 4x %DPM for each filter (column D) must be consistent with the 1x average (column B), and they are in each case. These results indicate that the samples have not changed during the time of measurement in the laser beam.

Table I also compares %DPM values for 2x spectra (each a sum of two 1x spectra) collected at two different radii (columns F and G). This comparison shows whether or not the sample is radially homogeneous.

The inter-filter reproducibility is demonstrated by the standard deviation for the three filters (bottom of Table I, column C). In particular, the values in column D provide a measure of the inter-sample precision which can be attained for three filters collected simultaneously. The SDEV of 3.0% DPM demonstrates the high precision attainable. It is comparable to the uncertainty predicted theoretically upon consideration of standard counting statistics and the count time per data point. SDEV values that are higher than this will be found when real sampling differences occur.

Composition Measurements at the Feeder Breaker Ram Car, and Returns

Table II summarizes the DPM compositions at the various mine locations. While we have observed some inconsistencies for some filters, DPM compositions between 60 and 83% (SDEV < 10.5) have been measured with good precision. Samples with compositions outside this range exhibit inconsistencies among the multiple 1x spectra. Their origin is under further study.

In some filters the compositions measured at the two different radial positions differ substantially, as indicated by a t-test on the difference of the means (see Table II). Table III presents an example calculation. The null hypothesis that the two sets of data are equal can be rejected at the 95% confidence level if the t-value is greater than 2.9. We can reject the null hypothesis since the observed t-value is 6.4. This result indicates that the compositions measured at these two radii are statistically different. The inner radius has a higher coal content.

Five out of eleven of the filter sets listed in Table II show significant differences between the means for the 2x spectra at the inner and outer radii. These results indicate inhomogeneous deposition which changes the measured coal/diesel ratio. Visual observation also reveals the inhomogeneous particulate deposition on some filters. Therefore steps must be taken to insure uniform deposition.

Table II

Summary of %DPM and Statistical Results to Determine if Inner Radius and Outer Radius Analyses Differ

Sample Location	Date taken	No.*	% DPM Mean**	% DPM SDEV**	C.V. %	Calc. t	t at 0.05	Inhomogeneous at 95% conf.	% DPM*** est. from CO_2 conc.
Feeder	8/10	3	64.9	3.0	4.6	3.8	2.9	yes	ND
	8/11	2	65.1	10.5	16.1	5.9	6.3	-	ND
	8/12	3	47.4	16.4	34.6	7.1	6.3	yes	68.8
	8/13	2	47.9	30.3	63.1	3.6	6.3	-	93.6
Ram Car	8/11	3	48.4	13.4	27.8	6.4	2.9	yes	47.2
	8/12	2	68.2	6.3	9.2	8.1	6.3	yes	65.1
	8/13	2	70.0	10.0	14.2	2.0	6.3	-	54.8
Return	8/10	2	77.9	0.6	0.7	2.0	6.3	-	78.9
	8/11	3	83.1	7.5	9.1	2.7	2.9	-	57.7
	8/12	2	82.4	7.9	9.6	3.0	6.3	-	49.9
	8/13	3	60.7	11.1	18.2	4.1	2.9	yes	59.7

* Number of samples analyzed per set.
** Mean and standard deviation for two or three 4x scans.
*** %DPM estimated from CO_2 concentration in mine.

Table III

Statistical Analysis of %DPM for a Triplicate Set of Filters with Radial Inhomogeneity; Ram Car (8/11/87)

Column:	B	C	D	F	G	H
	% DPM for four 1x scans		% DPM for one 4x scan	% DPM for two 2x scans		Delta
Filter	Mean	SDEV	Mean	Inner	Outer	F-G
2022	68.0	14.1	63.2	39.4	72.7	33.3
2431	51.8	30.3	45.1	20.8	75.6	54.8
6541	20.2	30.8	36.9	00.0	56.8	56.8
Total number of spectra analyzed:	12		3	3	3	3
Mean:	46.7		48.4	20.1	68.4	48.3
SDEV:		31.5	13.4	19.7	10.2	13.0
t :						6.4

Segregation by particle size can cause such inhomogeneity, with the larger particle size coal particulate concentrated toward the center. This natural tendency for nonuniform deposition of particulate on the filter surface has been observed with asbestos fiber collection. Size-selective sampling research has indicated that coal dust tends to exhibit a particle size distribution above +0.7 micrometer with diesel particulate below 0.7 micrometer.[4,7] Improved uniformity of particulate deposition has been achieved for asbestos fiber collection by using a cassette with a cylindrical "extension cowl." It should be pointed out that the observation of radial inhomogeneity demonstrates the sensitivity of the LRQA technique.

Comparison of Compositions as Measured by Different Methods

For two of three simultaneously collected samples there is excellent agreement between the MOUDI and the LRQA results (see 8/12 and 8/13 results in Table IV). The MOUDI gives %DPM values of 46.2% and 62.1%, while the LRQA gives values of 47.4% and 60.7% DPM, respectively. For these two pairs, the overall time spans for collection were comparable and no sampling irregularities occurred. It is important to note that the Raman triplicate filters are collected at the same time and for the whole period (ca. 5 to 6 hr.), whereas the MOUDI samples are collected in sequence. Each MOUDI filter is collected over a 1 to 2.5 hr period. Thus the arithmetic mean %DPM values calculated by the two methods may differ because of the differences in times sampled. For the third measurement (on 8/11), the two methods do not exhibit such agreement. The mean values differ by 25%. During the last hour of sample collection on 8/11, the dust from the mine face did not pass by the samplers. This occurred when the continuous miner broke through the mine face into the adjacent drift, drastically changing the air flow pattern.

The S/N ratio based upon the counting statistics for the scan time used in this study indicates that precision is not limited

by the scan time. (A longer scan time will, of course, improve the S/N ratio.) Radial inhomogeneity reduces interfilter reproducibility. Empirical variables can be controlled to improve precision. These are being optimized in our continuing work.

CONCLUSIONS

The LRQA method has been tested and refined on samples collected in a diesel underground coal mine. The amounts of DPM found at the feeder-breaker, on the ram car or at the returns, are in the range from 37 to 83% DPM. Total respirable DPM ranges from 0.18 to 1.61 mg/m^3 (Table V). Sampling reproducibility (precision) has been confirmed by statistical analysis of results for triplicate filters. Standard deviations below ± 10 % DPM are attainable. This precision is that expected for the scan conditions used. Reproducibility can be improved with longer scan times.

Table IV

Comparison of Compositions Measured by LRQA with those Measured by MOUDI and Those Estimated from %CO_2

Date/ Location	Sample No.	TIME start	TIME stop	TIME diff.	%DPM Est. from CO_2 conc.	MOUDI %DPM	MOUDI Mean	MOUDI SDEV	LRQA % DPM	LRQA Mean	LRQA SDEV
8/11/87 Return	GNA-1	10:19	11:19	60 min.*		47.1					
	GNA-2	11:41	12:41	60 min.+		51.7	57.9	14.84			
	GNA-3	13:01	14:01	60 min.++		74.8					
	20	8:20	14:00	5.76hr.	56.7				77.8		
	21	"	"	"	57.2				79.7	83.1	7.5
	22	"	"	"	59.2				91.7		
8/12/87 Feeder	GNA-4	8:38	11:08	150 min.**		51.7					
	GNA-5	11:29	13:59	150 min.**		40.7	46.2	7.78			
	30	8:35	13:45	5.17 hr.	-				40.9		
	31	"	"	"	59.5				35.2	47.4	16.4
	32	"	"	"	78.1				66.0		
8/13/87 Return	GNA-6	9:45	11:45	120 min.*		64.9					
	GNA-7	12:00	12:49	158 min.*		59.2	62.1	4.03			
		15:34	17:23								
	44	9:36***	17:15	4.87h	53.4				55.3		
	45	"	"	"	60.0				55.3	60.7	11.1
	47	"	"	"	65.7				73.4		

\+ some mining, moving mine roof bolting
++ dust from face not passing samplers
* mining
** hauling
*** pump off 12:51-15:38

Table V

Summary of LRQA %DPM, Total Respirable Dust and Airborne Diesel Particulate Matter

Sample Location	Date Taken	No.**	LRQA % DPM Mean*	Total Respirable Dust, mg/m^3	DPM mg/m^3
Feeder	8/10	3	65.1	0.915	0.596
	8/11	2	65.1	0.582	0.379
	8/12	2	47.4	0.596	0.283
	8/13	2	47.9	0.373	0.179
Ram Car	8/11	3	48.4	1.523	0.737
	8/12	2	68.2	1.158	0.790
	8/13	2	70.0	1.074	0.752
Return	8/10	2	77.9	1.073	0.836
	8/11	3	83.1	1.690	1.404
	8/12	2	82.4	1.957	1.613
	8/13	3	60.7	0.987	0.599

* Mean for two or three 4x scans.
** Number of samples analyzed per set.

Composition measurements for samples collected simultaneously and analyzed by the LRQA and size-selective methods have been compared. The %DPM values obtained for this limited set of samples at two locations are in reasonable agreement. Two out of three %DPM comparisons agree very well, the third does not.

Sampling objectives were attained which make quantitative Raman analysis possible. First, in-mine collection methods have been shown to provide satisfactory particulate loading on filters. Secondly, methods to provide the diesel-only and coal-only reference samples were developed.

We have demonstrated that sample homogeneity on the filter surface can be confirmed by scanning at two different radii. Filter "extension cowls" are expected to remove radial inhomogeneities, and these will be tested in up-coming work.

These results indicate the importance of DPM-monitoring techniques. Optimization of the LRQA procedures will allow increased precision and accuracy. Further comparison of the size-selective and the LRQA methods is needed. Improved monitoring methods that are able to quantify the diesel and coal fractions are prerequisite to the development of adequate control technology.

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EXPERIMENTAL AND THEORETICAL MEASUREMENT OF THE AERODYNAMIC DIAMETER OF IRREGULAR SHAPED PARTICLES

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ABSTRACT

A theoretical technique has been developed and verified experimentally for determining the aerodynamic diameter of irregular shaped particles. The aerodynamic diameter of a particle is a very important parameter for determining where that particle deposits in the respiratory tract. Many instruments, such as impactors and cyclones, will determine the aerodynamic size distributions of aerosol particles but few analyze the particles individually. The theoretical approach of our technique is to solve, by use of high speed computers, the three-dimensional Navier-Stokes equations to obtain the flow field around an irregular shaped particle of any contour. The computer program will then determine the drag on the particle, and thus the aerodynamic diameter of the particle can be calculated. The experimental approach has been to pass the particles through a centrifuge and collect the particles upon a collection foil. The position of a particle on the foil is an indication of its aerodynamic diameter. These particles were then shadowed in two orthogonal directions and inspected under an scanning electron microscope (SEM). The top view of the particle in the SEM plus the views of the two orthogonal shadows allows one to determine the three-dimensional shape of the particle. Studies have been performed on silica, coal and talc particles with aerodynamic diameters in the 1 to 4 μm size range. The three-dimensional shape, as is determined from SEM analysis, was used in the theoretical computer program and the results compared. It was found that in most cases the agreement between the experimentally and theoretically determined aerodynamic diameters was within 5%.

INTRODUCTION

The equivalent aerodynamic diameter (EAD) of a particle, defined as the diameter of a unit density sphere with the same falling speed as the particle in question, is an important size measurement of the particle. This is especially true when attempting to predict where particles may deposit in the respirator tract. Therefore, EAD is an important parameter when considering respiratory diseases caused by particles, such as coal workers pneumoconiosis (CWP).

Many instruments will measure the EAD size distribution of the aerosol particles, but few analyze the particles individually. Impactors, cyclones and virtual impactors normally collect particles upon substrates or filters which are then analyzed gravimetrically to determine the mass concentration of the particles in that size classification. The EAD of particles can be measured on an individual basis with centrifuges, inertial spectrometers and the TSI Aerodynamic Particle Sizer (APS). Centrifuges are most ideally applicable for studying individual particles as the particles are deposited, on long removable foils, at locations dependent upon their EAD.

The theoretical approach to determining the EAD of a particle has been primarily limited to regular shaped particles of symmetry to which analytical solutions of the flow field equations for air flowing around the particles can be applied. However, if the particle is irregular in shape, these analytical approaches do not apply and the EAD is very difficult to calculate. One technique that can be applied to determine the flow field around an irregular shaped particle is the numerical solution of the Navier-Stokes equations. In aerosol technology applications, this technique has been primarily used to determine the flow field through instruments. In most of these problems, the Navier-Stokes equations have only been expressed in two dimensions. However, to be able to describe the flow around any arbitrary irregular shaped particle, the Navier-Stokes equations must be solved in three dimensions.

The object of this paper is to apply the numerical solution of the three-dimensional Navier-Stokes equations to the flow around any irregular shaped particle and demonstrate that the aerodynamic diameter, so calculated, agrees with that determined experimentally in a centrifuge. Studies have been performed on silica, coal and talc particles with aerodynamic diameters in the 1 to 4 μm size range.

The shape of the particles used in the numerical solution of the flow field are defined by scanning electron microscopic (SEM) analysis of the particles collected on the foil in the centrifuge. An important discovery was made in the process of determining the three-dimensional shape of a particle in the SEM. It was found that the two-dimensional view of a particle is not sufficient to fully describe the shape of the

particle. To fully describe the particle, it is necessary to shadow the particle with a film in two orthogonal directions. These two shadows, along with the plane view of the particle, can then provide a reasonable indication of the particle shape.

NUMERICAL ANALYSIS TECHNIQUE

Numerical analysis of the Navier-Stokes equations has been used extensively in our laboratory to obtain information on flow fields through aerosol analyzing instruments.[1-3] Although several techniques have been used to solve the Navier-Stokes equations, they are all basically the same in that the finite difference form of the equation is expressed in terms of the stream function and vorticity, or in terms of the velocity vector components and the pressure. A grid is placed over the area of interest and the finite difference equations are solved at the node points (intersection of the grid lines) of the grid. The solution is achieved by an iterative relaxation procedure that determines the value of the stream function and vorticity or the velocity vector components and the pressure at each node point. Since numerical solution techniques have been used extensively and many cases reported in the literature,[4,5] the techniques will not be described in detail here.

The particular numerical solution technique used in the work described here is that described by Patankar.[4] The reader is referred to his textbook for details of the technique. This technique solves for the velocity vector components and the pressure at the node points rather than the stream function and vorticity. However, once the velocity vectors and pressure are known, the stream function and vorticity can be calculated, if desired. The stream function is often calculated so that the stream lines (lines of constant stream function) can be shown to provide a clearer understanding of the nature of the flow fields.

Most of the work utilizing finite difference solutions to the Navier-Stokes equations has been in two dimensions. However, three-dimensional solutions can be obtained[6] and must be used when analyzing the flow around random irregular shaped particles. The solution technique is exactly as has been described by the two-dimensional analysis of Patankar, with the addition of the third direction. However, the computer program is substantially larger and the solution time much longer.

The fluid drag acting on the particle and the EAD can be computed from the numerically determined flow field surrounding the particle. Based on the calculated flow field, the fluid drag on the particle surface can be calculated by integrating the fluid stresses over the surface of the particle. The drag force on a particle will be the sum of both the pressure forces on the particle and the shear forces resulting from the fluid flowing past the surface of the particle. Once the drag force is equated to the gravitational force acting on a particle, the EAD is computed based on its basic definition. Since the aerodynamic diameter is defined as the diameter of a unit density sphere which falls at the same speed as the particle in question, the problem reduces to one of determining the falling speed of a particle. This problem further reduces to one of determining at what speed the drag force is equal to the gravitational force on particle, for these are the conditions which must exist when the particle is falling in equilibrium at its terminal settling speed.

Verification of Numerical Technique on Regular Shaped Particles

Since two-and three-dimensional computer algorithms had not previously been applied to determining the flow around particles, the first step was to verify the programs on regular shaped particles where analytical solutions for the flow fields exist. The algorithms were therefore applied to particles that are symmetric in shape such as spheres, cylinders and disks. Due to symmetry, the drag acting on these types of particles can be computed as either two- or three-dimensional problems.

The two-dimensional program was verified by studying spheres, cylinders and disks.[7] The two-dimensional analysis has been applied to single spherical particles, cylinders in cross flow, disk shape particles and spherical particles connected in chains. In all cases the shapes were selected because there was a prior determination of the drag force on the particle, either by analytical or experimental methods, and reported by other investigators, since it was the object of this portion of the project to gain confidence in a numerical technique. For the single spherical particle, the drag force from the numerical solution was compared to the drag force predicted by Stokes law. The results of this analysis for particle diameters of 2, 5 and 10 μm show that the calculation of the drag force on a particle agreed within 4% of that determined by Stokes law. For the case of cylinder in cross flow, which utilized rectangular coordinates, only one case was analyzed (10 μm diameter) and compared to the analytical solution. The difference was only approximately 2.5%. The disk in cross flow was studied utilizing cylindrical coordinates. The results of this test were compared to that of Oseen's solution. In the case of the disk, the analysis was run for several values of the Reynolds Number. The error in the drag forces increased with decreasing Reynolds Number from approximately 1 1/2% at a Reynolds Number of 0.13 to about 6% at a Reynolds Number of .00326.

Upon verification, the computational method was optimized and the technique expanded to include the three-dimensional case. For the three-dimensional case, test runs were performed on spherical and cubical particles. The numerically determined drag force on spheres was within 4.5% of the analytically determined value. For cubes, the values were within 5% of the experimental values reported in the literature.

Verification of Three-Dimensional Algorithms on Irregular Shaped Particles

The verification of the three-dimensional algorithm on regular shaped particles was encouraging. However, we felt that in the development of any numerical technique of this complexity, it is also important to compare the numerical results to experimental results, preferably obtained with a proven, standard method. For this reason a spiral duct centrifuge, which can provide information on the EAD of either regular or irregular shaped particles, was used to collect particles of several types. This instrument has been developed

and used successfully for many years by investigators to determine the EAD of agglomerates of spheres and chain aerosols as well as irregular shaped particles.[8,9] In the centrifuge, particles are introduced into the center of a rotating spiral channel in which aerosol and clean sheath air are flowing. Particles introduced into the inner edge of the spiral channel are collected upon a foil attached to the outer edge of this channel. The distance from the introduction point to where the particles strike the foil is a function of their EAD, with the larger EAD particles being collected closest to the inlet.

The centrifuge used in this project was the Lovelace Aerosol Particle Separator (LAPS) which is used extensively by Lovelace Inhalation Toxicology Research Institute (ITRI). With the aid of ITRI personnel, several runs were made with coal, silica, and talc particles. This provided a variety of shapes for which the numerical technique could be applied. Sections from the centrifuge foils were removed at locations corresponding to aerodynamic diameters from 1 to 4 μm and the particles subjected to SEM analysis.

EXPERIMENTAL DETERMINATION OF PARTICLE SHAPE

The three-dimensional shape of an irregular shaped particle must be known in order to determine the EAD of the particle with the numerical computer program. However, inspection of the particles with the SEM only provides two-dimensional views of the particles. In our initial attempts to determine the three-dimensional shape of the particles, the shape and size of the particles in the third dimension were inferred from their two-dimensional shapes. This required that assumptions be made about the symmetry and regularity of the particles based on one two-dimensional view. It was realized that these assumptions could be erroneous. To eliminate the need for the assumptions in the third dimension, the particles were shadowed with a gold film in two orthogonal directions at an angle of 15° and then the particles and their shadows inspected with the SEM. The shadows were successful in providing views of the third dimension of the particles. This technique was very informative, in that the third dimensions of the particles were often drastically different than what we would have inferred from their two-dimensional shape. For example, a particle that looks like a sphere could in actually be a particle shaped like a disk or a spear.

Photomicrographs of four particles inspected in this manner are shown in Figure 1. These are three coal particles of various shapes and a talc particle. The particles in Figures 1a and 1b have projections protruding from the top of the particle. These projections would not have been suspected.

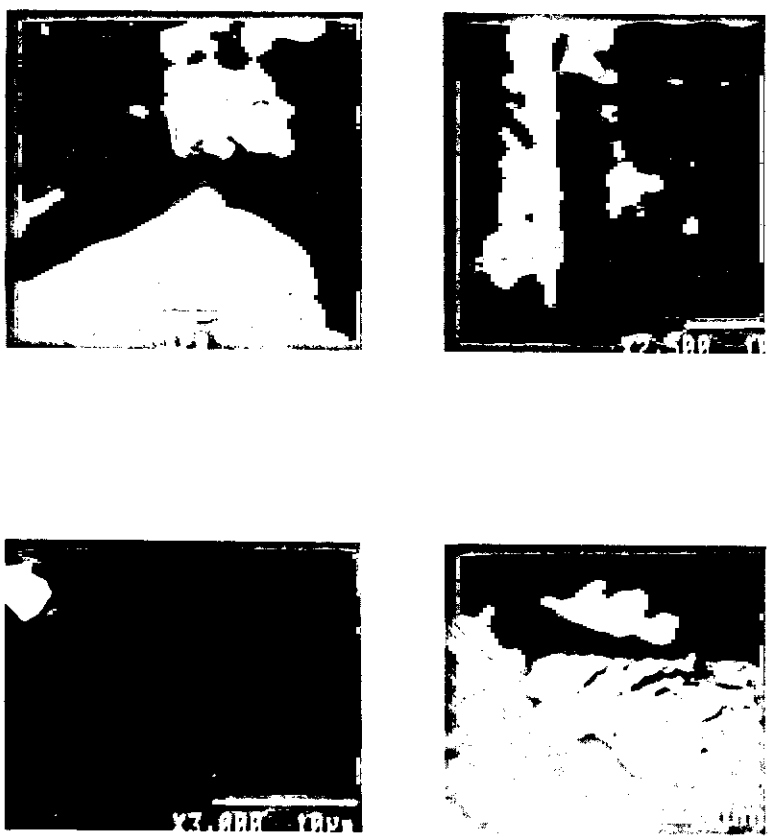


Figure 1. Photomicrographs of coal and talc particles shadowed in two orthogonal directions.

In some cases, the particles have multiple projections as shown in Figure 1c. The talc particle is a flakelike particle with a diameter approximately 10 times its thickness.

APPLICATION OF NUMERICAL TECHNIQUE TO CALCULATE AERODYNAMIC DIAMETER

The first step, in applying the numerical technique to determine the aerodynamic diameter of irregular shaped particles, such as shown in Figure 1, is to approximate the shape of the particles by a series of blocks as shown in Figure 2. The reason for approximating the particles as a series of blocks is that the numerical program is in rectangular coordinates and each cube in the three-dimensional array must represent either a portion of the particles or the space around the particles.

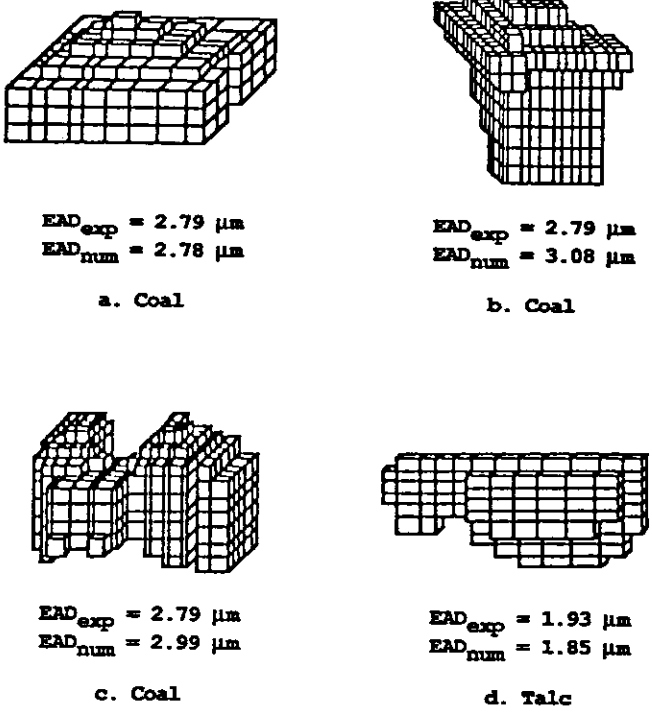
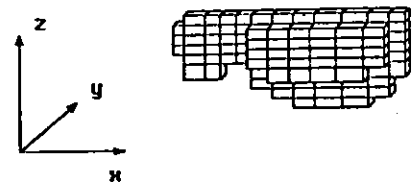


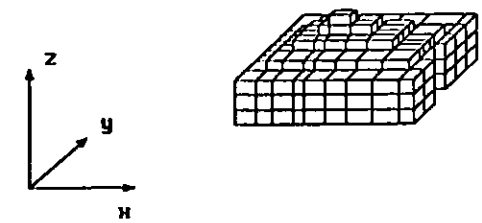
Figure 2. Digitized three-dimensional representations of particles in Figure 1 and a comparison of the numerically and experimentally determined EAD's.

Once the cubes within the three-dimensional array which represent a particle are identified, the viscosity in these cubes is set at a very high value. Therefore, when the flow field equations are solved over the entire domain (the domain of the particle plus the surrounding volume of approximately 10 times the particle diameter), the volume defined by the large viscosity will be considered as a solid within the domain and will not flow, while the volume around the particle will have the viscosity of air and will define the flow field around the particle. After the flow field has been determined, the drag on the particle can be calculated and, thus, its EAD determined. For each particle shown in Figure 2, the experimentally determined EAD from the centrifuge is compared to the numerical results. In most cases the agreement is quite good, especially since the orientation of the particle as it passes from the inlet to the foil in the centrifuge is not known. The aerodynamic diameter of the particle will be a function of its orientation as it moves toward the foil.

To determine the sensitivity of a particle's aerodynamic diameter to its orientation, the aerodynamic diameter in three orthogonal directions were determined numerically for two particles shown in Figure 3. The table associated with each particle indicate that the aerodynamic diameter is a function of its orientation. Note that the variation is only about 17% from their smallest to largest value of EAD's. Also, indicated



Direction of the flow	EAD, μm Numerical	EAD, μm Experimental
x	2.17	----
y*	1.85	1.93
z	2.10	----



Direction of the flow	EAD, μm Numerical	EAD, μm Experimental
x	2.89	----
y	2.92	----
z*	2.78	2.79

* Direction of the particle settling

Figure 3. Comparison of the numerically determined EAD's for three orthogonal orientations of a talc and coal particle.

in the table is the experimentally determined EAD corresponding to the direction that the particle was found on the foil. The agreement between these experimental values of the EAD's and the theoretical EAD's for the same orientation is very good.

CONCLUSIONS

A powerful tool has been developed for determining the EAD of an irregular shaped particle in any orientation. This technique utilizes the numerical solution of the Navier-Stokes equations in three dimensions and provides detail for the features of the flow around the particle, which leads to the calculations of the drag coefficient and EAD of the particle. The experimental verification of the theoretical technique has been quite satisfactory in that the aerodynamic diameter determined experimentally agreed with the theoretically determined values.

In the process of determining the three-dimensional shape of a particle in an SEM, it was found that the shadowing of the particle in two orthogonal directions was necessary. This shadowing revealed that inferring the three-dimensional shape of a particle from its two-dimensional projection is not satisfactory and that the shadowing is absolutely necessary if detailed information of the particle shape and size is to be obtained.

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CHEMICAL SPECIATION AND MORPHOLOGICAL ANALYSIS OF RESPIRABLE DUST IN FOUNDRIES

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Various studies have related dust exposure of foundry workers to mixed-dust fibrosis,[1-4] bronchial obstruction,[5] and lung cancer.[6] The relationship between silicosis and pulmonary cancer has been constantly mentioned in the last ten years[7-9] leading to the inclusion of silica in the IARC list of compounds which should be regarded as probably carcinogenic to humans.[10] However, many of the epidemiological studies[6-8,11,12] have indicated the almost impossible task of establishing a dose-effect relationship in foundries because of the complexity of workers' exposure, and the lack of data on cumulative exposure to etiologic agents.

The aim of this work was thus to selectively collect foundry dust with granulometric fractions of biological significance and to carry out a comprehensive analysis of these fractions.

Methods

Dust samples were collected at fixed stations with cascade impactors, cyclones and closed cassettes in three ferrous foundries, one aluminum foundry and one copper smelter.

Dust characterizations were performed by scanning and transmission electron microscopes fitted with energy dispersive X-ray analyzers (EDXA); X-ray photoelectron spectroscopy (ESCA), secondary ion mass spectrometry (SIMS), X-ray diffractometry, infrared spectrophotometry and atomic absorption spectroscopy.

Results

The melting technique, size of the industry, variety of compositions and whether the installation has dust control equipment are obviously highly related to the observed changes in dust composition. However, in this short presentation, results that are thought to be relevant to the toxicity of these dusts will be emphasized.

Ferrous foundries

The three ferrous foundries (A, B and C) cast ductile iron and gray brass in various types of sand moulds without any organic resins. Figure 1 gives a representative example of

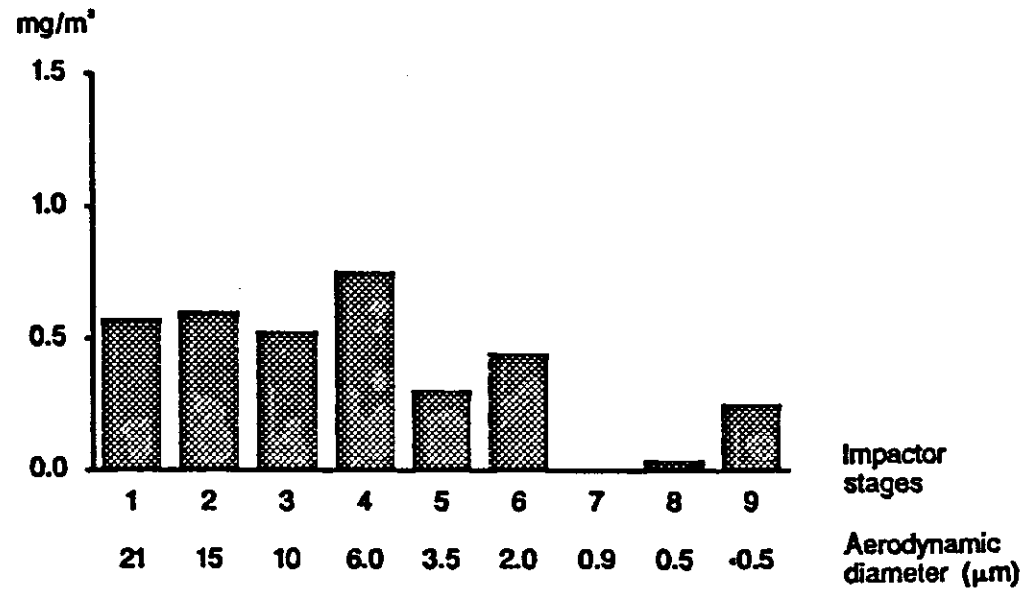

Figure 1. Example of the bimodal distribution of foundry dust as collected with a Sierra Cascade Impactor.

the bimodal distribution of foundry dust as particulate dust (> 2 μm) and fumes (< 0,5 μm) as observed by Dams and Zhang.[13-14]

In this instance, the dust concentration results as sampled with the cascade impactors in the general environment of the casting facility of each foundry can be conveniently separated into three fractions, each fraction being the sum of three successive impactor stages. The average dust concentrations can then be summarized as being 1.7, 1.5 and 1.6 mg/m^3 for particles having aerodynamic diameters larger than 10 μm; 1.3, 2.5 and 0.8 mg/m^3 for particles between 1–10 μg; and 0.3, 2.9 and 0.1 for particles smaller than 1 μm which we will describe as fumes. The striking feature of these results is the comparability of large-particle dust concentrations in the three foundries as compared to the variability of respirable dust and fume concentrations.

The determination of the quartz content of these foundries dusts gives a partial evaluation of their pulmonary toxicity. However, it was observed that the airborne quartz concentrations as sampled with the cascade impactor were 0.08, 0.10 and 0.08 mg/m^3 for particles in the 1–10 μm range, as compared to results of 0.04, 0.05 and 0.01 mg/m^3 as sampled with a standard cyclone for respirable dust. These results can be explained by the absence of quartz in the fume fraction or by the widening of the quartz diffraction line with the decrease in particle size which makes quartz unobservable.

The metallic elements detected in the airborne dust from ferrous foundries are given in Table I in decreasing order of intensity for particles larger or smaller than 1 μm. It is easily seen that the composition of particulates larger than 1 μm is much simpler than that of the fume portion of the aerosol. In contrast to the two other foundries, in foundry B there are significant proportions of lead in the portion of the aerosol composed of particles smaller than 1 μm. Foundry B was the only one melting untreated iron scrap. Elevated lead levels in the blood of scrap metal shop workers have been reported.[14]

Al foundry

The concentrations of dust particles at the Al foundry ranged from 0.6 (>10 μm), 0.4 (1–10 μm) and 0.5 (<1 μm) mg/m^3. The sampling of total inspirable dust with a closed 35 mm—cassette gave an average of 2.6 ± 0.9 mg/m^3 s while respirable dust sampling with a cyclone gave an average of 1.1 ± 0.3 mg/m^3. The analysis of these samples by SIMS, EDXA and ESCA showed a preponderance of NaF on all granulometric fractions with Cl and traces of Zn, and of Mn in particles smaller than 1 μm. Sodium fluoride is a respiratory tract irritant and a cause of fluorosis. The time weighted average concentration for worker exposure has been fixed at 2.5 mg/m^3 as F in the United States.

Cu smelter

Dust concentrations at the reactor and the converter stages of the smelting process were determined. Cascade impactors gave 1.0, 0.3 and 0.45 mg/m^3 for the three same fractions of large particles (> 10 μm), respirable particles (1–10 μm) and fumes (< 1 μm). For comparison purposes, inspirable dust as sampled with 35 mm closed cassette showed an average concentration of 2.6 mg/m^3 and respirable dust sampled with a cyclone was 1.0 mg/m^3.

Quartz, As, Pb and Cu concentrations were compared to TLV^R values to infer a preliminary evaluation of the pulmonary agressivity of these samples. Thus, the As, Pb and Cu concentrations of inhalable dusts were respectively 0.02, 0.23 and 0.26 as compared to the accepted TLV^R of 0.05, 0.15 and 1.0 (fumes: 0.2) mg/m^3.

After extensive characterization by X-ray diffractometry and infrared spectroscopy, it was concluded that most of the lead was present as lead sulphate. The quartz concentration in respirable dust was around 5% as opposed to the 20–30% found in the flux.

In this industry, Fe, Cu and Zn are in general important and constant constituents of all particulate sizes, with lead being

Table I

Principal Elements in Foundry Dust as Measured by Secondary Ion Mass Spectrometry and Photoelectron Spectrosopy

Foundries	Particle size um	Elements (Decreasing order of intensity)
A and C	> 1	Ca, Fe, Zr, F, Zn
	< 1	Mn, Fe, Zn, Cu, Pb, Co, Cr, As, V
B	> 1	Ca, Fe, F, Zn
	< 1	Pb, Fe, Mn, Cu, Zn

Traces of Co, Cr, As, V.

Table II

Principal Elements in Dust from a Cu Smelter as Measured by Secondary Ion Mass Spectrometry (SIMS) and Photoelectron Spectroscopy (ESCA)

Instruments	Particle size um	Elements (Decreasing order of intensity)
Both	> 1	Fe, Cu, Zn (Pb)
Both	< 1	Pb, Fe, Cu, Zn, S, Sn
SIMS	< 1	Br, Ba, In, Sr
ESCA	< 1	Cd, Se

present in particles smaller than 1 μm. The presence of lead in the fume portion of the dust was similarly noted in ferrous foundries. In, Cd, Se and of Sn are also observed in fume particles as well as traces of Ni, V, Cr and As.

Conclusion

A first step has been made in the comprehensive analysis of dust in foundries indicating the following trend: foundry dust can be conveniently separated into three fractions of particles sizes closely associated with inhalable particles (> 10 μm) respirable dust (1–10 μm) and fumes (< 1 μm). The present of lead compounds is largely concentrated in the fume fractions. The presence of quartz is detected in the inhalable and respirable fractions.

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AQUEOUS SEDIMENTATION AND GLOVE BOX AEROSOL DETERMINATION OF POTENTIAL RESPIRABLE FIBERS FROM SAND SAMPLES USING SCANNING ELECTRON MICROSCOPY

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ABSTRACT

There is no established method which allows simple prediction of the aerosolized respirable particulate concentration from a compact sample such as sand, soil, crushed stone, etc. In response to a problem requiring such information, we have developed a simple method which we propose for further testing.

Ten grams of sample is suspended in 60 ml of filtered water in a 100 ml graduated cylinder, mixed by repeated inversion for 1 minute, and allowed to settle. Small (50–400 µl) micropipette aliquots from a constant distance (0.5 cm) below the surface are taken at 2, 5, 15, 30 and 60 min and filtered onto 0.2 m pore membrane filters. The filters are attached to carbon and carbon coated, followed by standard quantitative analysis of fibers (and non-fibers, if indicated) using scanning electron microscopy (SEM) and energy dispersive X-ray analysis (EDXA). For correlation, aerosol filter samples are taken in a glove box during or after pouring or mixing the sample. Results are expressed as fibers/gm of initial sample, or as fibers/ml in aerosol samples. As an example, sand samples tested contained 10^8 to 10^9 total particles/gm, 10^5 to 10^6 fibers >5 µm length/gm and 0.3 to 6 fibers/ml in aerosols. In the glove box conditions, the fraction actually aerosolized is approximately 1% of the total possible. Aerosol concentrations in rooms of varying volume can be predicted.

No Paper provided.

DUST EXPOSURE INDICES AT THE EARLIEST APPEARANCE OF PNEUMOCONIOSIS

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INTRODUCTION

In 1981 a number of workers with a radiologic appearance compatible with pneumoconiosis were identified in a cross-sectional survey of an iron ore mine and beneficiation plant in Labrador West, designated as the Labrador West Dust Study (LWDS).[1] In some, pneumoconiosis had been diagnosed in the years preceding the survey but in the case of others, the LWDS marked the first appearance of radiologic abnormality. Various indices for exposure to dust have been calculated for each of these workers at the point in time when pneumoconiosis was first suspected or diagnosed from their periodic surveillance chest radiographs. These indices were compared for their power to predict pneumoconiosis (ILO category ≥ 1), using workers placed in ILO category 0 in the LWDS as a comparison group. One of the indices, cumulative quartz, has been used to assess the validity of ACGIH recommendations for exposure to silica.[2]

METHODS

Case Selection

One thousand nine hundred and fifty workers (1950) completed all phases of the LWDS. Forty-four (44) qualified for inclusion in category 1 or higher in the ILO classification (1980) of radiographs for pneumoconiosis by the method described elsewhere.[1,3]

Exclusions

1. For workers in all ILO categories.
   a. Exposure to rock dust at previous places of employment in excess of 25% of employment with present company.
   b. Location in administrative or "not dusty" jobs as defined elsewhere.[1]
2. For workers scoring $\geq$ ILO category 1 LWDS.
   a. Presence of confounding factors in radiographic interpretation.
   b. Absence of antecedent normal chest radiographs.

The 36 workers remaining in ILO category ≥ 1 comprised two groups. The first Group A—were workers where the LWDS confirmed a diagnosis of pneumoconiosis made for the first time between 1972–79. The second Group B, were workers where the diagnosis was made for the first time in the LWDS (1981). In both groups periodic surveillance chest films had been read by a single observer without reference to the ILO classification. Consequently, in Group A the earliest appearance of pneumoconiosis has been defined as the first mention of radiographic changes compatible with or suspicious of this diagnosis. In Group B however, the first manifestation of changes suggestive of pneumoconiosis occurred in the LWDS film which had been read to the ILO classification. For this group the earliest appearance of pneumoconiosis refers to a score of 1/0 or higher on the ILO scale.

Exposure Indices

Five exposure indices were created for each worker as described elsewhere.[4,5] In brief, they were years of exposure to detectable amounts of dust and four quantitative dust exposure indices. The latter were functions of years of exposure and dust concentrations (based on Harvard nylon cyclone measurements) at all the locations where a worker had been employed. The four measurements were cumulative and "peak" respirable dust and quartz indices. "Peak" indices, were devised to take account of periods in a worker's dust concentration-time profile when dust levels were much higher than usual. These elevations would receive no special weighting in calculating cumulative indices. Hence these special "peak" parameters were computed to assess their importance.

For each index of exposure, the 1709 workers were analyzed and the observed prevalence values i.e. (number of diagnosed cases)/(number in workforce) were calculated and tabulated for a set of sub-intervals appropriate to each index of exposure. Multivariate logistic regression analysis was performed on all of the five indices to give predicted prevalence figures.

RESULTS AND ANALYSIS

The characteristics of the workers scoring ILO category 1 or higher in the LWDS, and who were included in this analysis, are listed in Table I by group. In the combined groups, when radiologic abnormality was first noted, the mean months of exposure at the present company of employ-

Table I
Worker Characteristics at Appearance of Radiologic Abnormality

	Max	Min	Mean	Median
Months of Exposure Present Company				
Group A	224	85	135	135.5
Group B	211	61	150	156.0
Group A & B	224	61	147	138.5
Months Since Previous Normal X-ray				
Group A	26	2	13	12.0
Group B	96	5	33	15.5
Group A & B	96	2	23	12.5
Age				
Group A	52	27	38	35.5
Group B	61	24	40	37.0
Group A & B	61	24	39	36.0

LWDS ILO Classification (1981)

	Subcategory (n)	Shape	n	%
Group A	1/0 (4); 1/1 (5); 1/2 (4); 2/1 (2); 2/2 (5); 2/3 (2); 3/3 (2)	Round	17	71
Group B	1/0 (11); 1/1 (1)	Round	4	33
Group A & B	1/0 (15); 1/1 (6); 1/2 (4); 2/1 (2); 2/2 (5); 2/3 (2); 3/3 (2)	Round	21	58

Group A: Diagnosed as pneumoconiosis prior to LWDS n = 24

Group B: Diagnosed as pneumoconiosis at LWDS n = 12

Group A & B: n = 36

ment was 147 months with a maximum of 224 and a minimum of 61 months. The mean of the interval between the normal and the abnormal chest radiographs was 23 months with a maximum of 96 and a minimum of 2 months. The explanation for this wide spread was that five workers, all in Group B, had moved from "dusty" jobs where surveillance films are customary to locations where they are not. At the time of the LWDS, the profusion of the small opacities ranged from 1/0 to 3/3 and the shape of the primary small opacities was described as round in 58% of the 36 diagnosed cases.

A stepwise multivariate logistic regression analysis was performed on the five exposure indices. This gives the logistic response function which is the probability that an employee is in ILO category ≥ 1. The most important variable chosen by the regression analysis was "peak" quartz (PQ)—in fact, this was the only variable chosen if a p-value of 5% is kept as the criterion for the 'improvement chi-square'. This gave the function:

$$\text{Probability (Category} \geq 1) = \frac{\exp[-5.12 + 0.00343(PQ)]}{1 + \exp[-5.12 + 0.00343(PQ)]}$$

The observed and predicted values for this function are shown in Table II. If the 5% value is relaxed to 6%, then cumulative quartz (CQ) and years of exposure (YRS) are included as the next variables in the response function.

$$\text{Probability (Category} \geq 1) = \frac{\exp[-4.87 + 0.003(PQ) + 0.18(CQ) - 0.11(YRS)]}{1 + \exp[-4.87 + 0.003(PQ) + 0.18(CQ) - 0.11(YRS)]}$$

However, further analysis does not allow the inclusion of the remaining two indices—cumulative and "peak" respirable dust—for an acceptable response function. This is in accord with our Case-Control Study where quartz was identified as the dominant differentiating mineral index for exposure between category 0 and categories 1, 2 and 3.[4]

The rest of this present analysis concerns only the three significant indices; viz, years of exposure, cumulative quartz and "peak" quartz. Figures 1–3 show the distributions for the healthy workers as opposed to the "cases' for each of the three indices. These figures along with the median values in Table III show that "peak" quartz is the index which distinguishes best between the distributions of the 'healthy' worker and the 'cases'.

Values for the ratio: (number of cases)/(number of total workers) for sub-intervals of the three significant exposure indices are shown in Figures 4–6. The ratios rise with increasing exposure, but for reasons which are not apparent, this rise was not sustained in years of exposure after 12 years.

DISCUSSION

The workers scoring ILO category 1 or higher in the LWDS comprised two groups—one diagnosed prior to, and the other during the LWDS. The groups differed in the method used for determining the earliest manifestation of pneumoconiosis; the significance of this is being examined.

Table II
Observed and Predicted Values for Logistic Response Function

PQ	200	400	600	800	1000	1200	1400
Obs%:	0.5	4.0	7.5	8.5	20.0	15.1	38.1
Pred%:	1.1	2.0	4.0	7.8	14.3	24.5	38.8

PQ: "Peak" Quartz; $(mg/m^3)^3.yr$

Table III
Median Values for Exposure Indices for 'Healthy' Workers and 'Cases'

	Years of Exposure	CQ	PQ
Healthy Workers n = 1673	5.9	1.8	34.2
Cases n = 36	11.4	7.6	912.0

CQ: Cumulative Quartz; mg/m^3yr

PQ: "Peak" Quartz; $(mg/m^3)^3.yr$

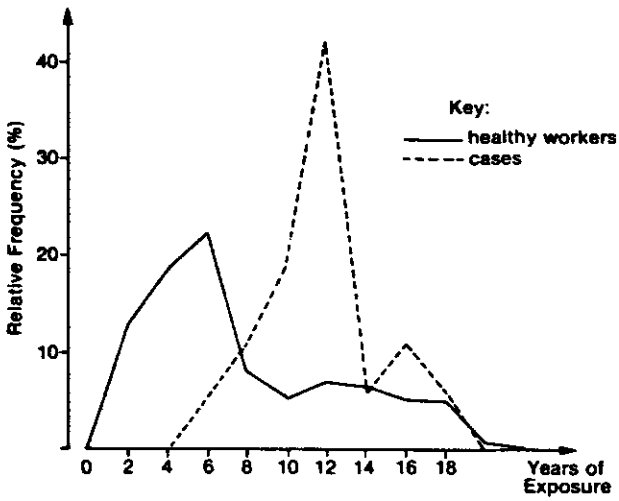

Figure 1. Relative frequency polygons for healthy workers and cases—years of exposure.

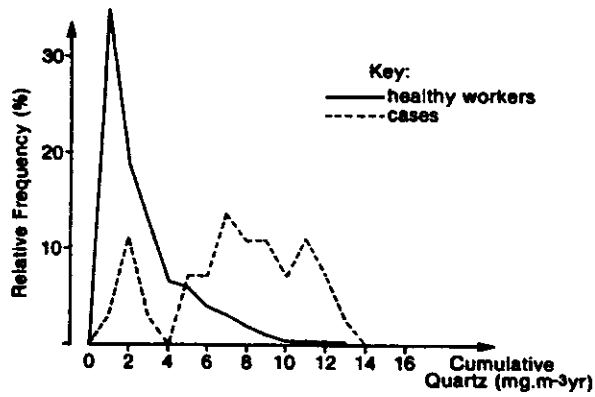

Figure 2. Relative frequency polygons for healthy workers and cases—cumulative quartz.

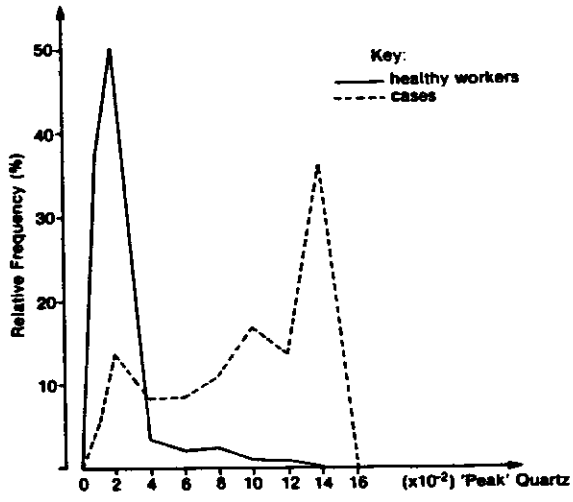

Figure 3. Relative frequency polygons for healthy workers and cases—"Peak" quartz.

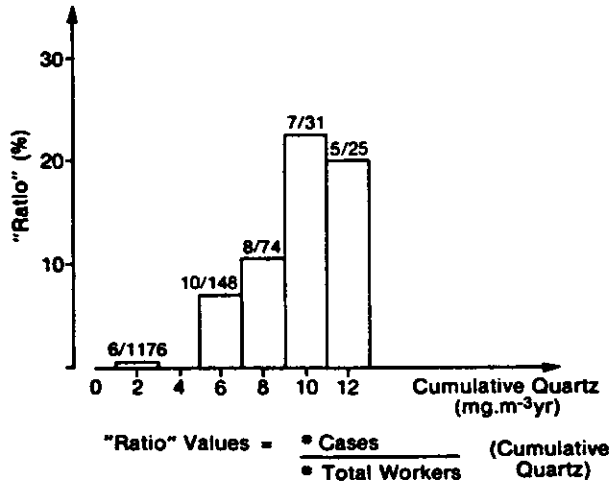

Figure 5. Ratio values for cumulative quartz.

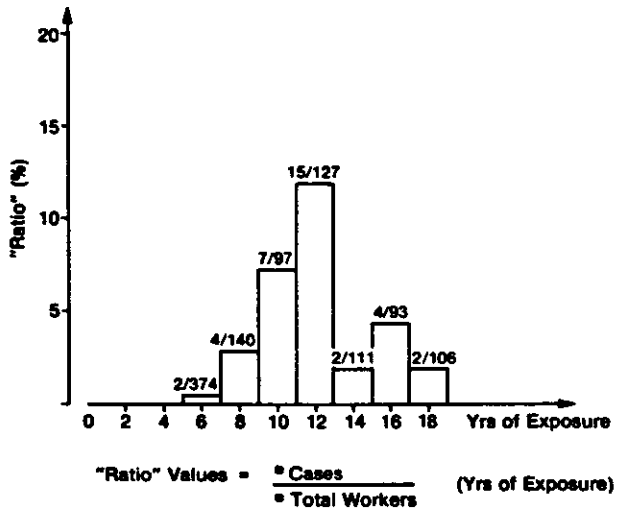

Figure 4. Ratio values for years of exposure.

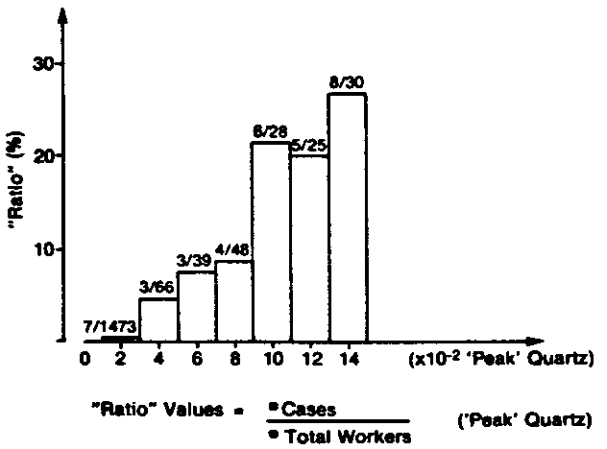

Figure 6. Ratio values for "Peak" quartz.

Dividing the workforce into two populations—those with pneumoconiosis (cases) and those without pneumoconiosis (healthy workers)—"peak" respirable quartz is the index which most clearly separates the two (Figure 3). This is substantiated by the logistic regression which singles out only this same index for prediction purposes at the 5% level. Thus the "peak" exposure index is a better predictor for pneumoconiosis than the cumulative exposure index evaluated on the same dust concentration time profile. This result is further confirmation of our previous observation that short lasting periods or "peaks" when dust levels are much higher than usual, contribute significantly to the development of pneumoconiosis.[4]

"Threshold limit values ... represent conditions under which it is believed that *nearly all* (our emphasis) workers may be repeatedly exposed day after day without adverse effect."[2] The ACGIH Threshold Limit Value—Time Weighted Average (TLV—TWA) for exposure to silica is 0.1 mg/m^3. Assuming that a worker is exposed to this TLV-TWA for say forty years, about the maximum duration of employment that could be expected for such workers, then his cumulative quartz index would be $40 \times 0.1 = 4$ mg/m^3 yr. In our study, for workers with cumulative quartz indices of 4 mg/m^3 yr or less, the average number of years of exposure was 7 years and as Figure 5 shows, the prevalence of pneumoconiosis was 6/1176 cases or 0.5%. Thus, to date, in the conditions prevailing at this mining complex, 99.5% of those workers who have been exposed to silica concentrations resulting in a cumulative quartz index of ≥ 4 mg/m^3 yr, appear to have suffered no adverse respirable effects.

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SILICA DUST, RESPIRATORY DISEASE AND LUNG CANCER —RESULTS OF A PROSPECTIVE STUDY

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INTRODUCTION

Mineral particles are not generally considered to be carcinogenic, except for a few specific species such as asbestos, and the carcinogenicity of crystalline silica to humans has been a matter of controversy[2,4] since results of retrospective studies and results on persons selected for silicosis have been questioned.[6] Our investigation was initiated by the hypothesis that chronic irritation of the bronchial mucosa by inspirable particles increases lung cancer incidence. Meanwhile other and more detailed pathogenetic mechanisms have been discussed in this context, considering respiratory clearance, carrier effects and other combined effects.[2] Our contribution will be new results on the first cohort of dust exposed workers which has been followed prospectively from a preventive checkup in the 1950s, during the second part of life up to death (and in about 50% up to autopsy). Details of the source population,[10] setting up of cohorts[5] and first results of follow-up[8,9] have been given earlier.

METHODS

A mobile team of the occupational health care unit started screening examinations in 1950 which included an occupational and a smoking history.[10] All persons with a history of dust exposure were chest X-rayed and are the source of our exposed cohort. 1630 men given the first chest X-ray in 1950–1960 because of silica and/or heavy "inert" dust exposure were born before 1911 and resident in Vienna. An equal number of Viennese men without occupational dust exposure was selected from the occupational health care examination files by matching year of birth, year of first examination and smoking.[5] At a later control of exposure histories at the pension insurance board 5 men were found not to meet the eligibility criteria and were therefore eliminated from the study together with their matched counterparts (dustworkers: 1 because of confounding asbestos exposure, 1 because of lack of dust exposure, 1 because of being born 1911; references: 2 because of dust exposure). Thus we followed 1925 workers exposed to non fibrous dust in the metal, glass, ceramics, stone, construction, cleaning agent and a few other industries and 1625 non-dust-exposed workers from a great variety of branches (publishing and printing, chemical, construction, textile, leather, food, electrical industry, etc.).

Diagnoses at death were traced and encoded without knowledgement of the exposure. Death certificates in Vienna are based on autopsy in more than 50%,[3] but a small proportion of diagnoses had to be clarified with the reporting hospital or physician. The best available informations were used for comparison on dust and non-dust-exposed. The official diagnosis was used for comparison with the general population of Vienna, which gives conservative estimates of standard mortality ratios (SMR), because mortality (especially cancer mortality) is higher in Vienna than in Austria, and some of the cohort members moved to rural districts after retirement.

RESULTS

1621 dust-exposed (DUST) and 1621 reference subjects (NO DUST) = 99,8% could be traced up to the end of 1986. 1442 DUST (89%) and 1384 (NO DUST) (85,4%) died. The underlying cause of death is given in Table I for 1439 (99,8%) DUST and 1379 (99,6%) NO DUST. Observed cases (0) in DUST divided by expected cases in NO DUST are given under Relative Risk (RR). This age-adjusted relative risk of DUST was significantly raised ($p < 0,001$, Poisson, two-sided) for lung cancer, stomach cancer, chronic obstructive lung disease (emphysema, bronchitis, asthma) and silicosis/fibrosis/tuberculosis of the lung. Gastrointestinal diseases (mainly liver cirrhosis) were found more frequent, too ($p < 0,05$).

Respiratory diseases were also found increased in OUST as secondary cause on death and additional diagnoses on death certificates (mainly silicosis and chronic obstuctive lung disease, but also pneumonias).

Table II shows official diagnoses of underlying cause of death and standard mortality ratios. In DUST overall mortality, lung cancer, stomach cancer, chronic obstructive lung disease, silicosis/fibrosis/tuberculosis and acute/infectious respiratory diseases was found higher ($p < 0,001$, Poisson, two-sided) than expected in Viennese men of same age. In NO DUST overall mortality was the same as in the general population; silicosis/fibrosis/tuberculosis, cardiovascular diseases and accidents were lower than expected and lung cancer was slightly higher ($p < 0,05$).

For 775 foundry workers, 475 grinders and other metal workers, 191 glass and ceramic workers, 87 stone cutters and construction workers and 65 other dust-exposed workers observed lung cancers and stomach cancers are given in Table III (32 workers could not be included in this stratification because the main branch of occupational dust exposure was

Table I
Main Causes of Death: Dust Exposed Compared to Reference Cohort

Best available diagnose	DUST 0	NO DUST 0	RR
cancer of lung	183	142	146***
" other respirat.o.	4	4	114
" stomach	80	48	190***
" intestine	37	50	88
" other digestive o.	50	45	125
" other sites	67	84	92
" not localised	1	2	
chron. obst. lung dis.	83	47	202***
tuberculosis, silicosis	78	15	513***
acut, infect. respir.d.	50	55	110
heart disease	362	404	106
cerebrovascular dis.	125	157	97
other vascular dis.	132	145	107
gastrointestinal dis.	93	84	127*
accidents, suicide	41	39	109
other disease	55	58	112
unknown, ill-defined	3	5	111

* $p < 0,05$, ** $p < 0,01$, *** $p < 0,001$

ill-defined on entry file). Table III shows increased lung cancer mortality in all subgroups of DUST with the highest SMR in stone and glass/ceramics ($p < 0, 001$). The SMR for stomach cancer was above 100 in all strata, but significantly only in those employed in foundries and other metal industries.

Life table analyses showed reduced survival of DUST not before 7 years of observation and 58 years of age (Figure 1). At the median the survival difference between DUST and NO DUST was 3 years. Survival probability from lung cancer at age 70 was 91,4% in DUST (95% confidence interval: 89,9–92,9) and 71,7% in NO DUST (95% confidence interval: 93,2–95,6) which is significant (Figure 2).

DISCUSSION

In Viennese workers we found a relation between exposure to respirable particulates and mortality from lung cancer and chronic diseases of the lung. The rate of chronic obstructive lung deseases was 2-times higher and the rate of lung cancer was 1,5-times higher than in non-dust-exposed workers with comparable smoking habits. The 17% lung cancer increase in

Table II

Main Causes of Death: Dust Exposed and Reference Cohort Compared to General Population

OFFICIAL DIAGNOSE (ICD, 9.REV.)	DUST		NO DUST	
	O	SMR	O	SMR
CANCER OF LUNGS (162)	180	168***	142	117*
" OTHER RESPIRATORY O.(161, ETC.)	4	67	4	60
" STOMACH (151)	78	167***	47	89
" INTESTINE (152-154)	36	84	50	100
" OTHER DIGESTIVE (140-150, 155-159)	48	115	44	92
" OTHER	70	92	85	95
CHRON.OBSTR.LUNG DIS. (490-493)	77	205***	45	101
TUBERCULOSIS, SILICOSIS, FIBROSIS (011, 502, ETC.)	75	299***	17	63*
ACUTE, INFECT.RESPIRAT.D.(460-487)	52	135*	55	120
CARDIOVASCULAR D. (390-459)	628	97	707	92*
GASTROINTESTINAL D. (520-579)	95	109	85	87
ACCIDENTS, SUICIDE (800-999)	42	86	42	76*
ALL CAUSES	1442	123***	1384	100

+ $P<0,05$, ** $P<0,01$, *** $P<0,001$

Table III

Lung and Stomach Cancer in Dust Exposed Industries Compared to General Population

CANCER DEATHS	FOUNDRY		METAL		GLASS/CERAMICS		STONE		OTHER	
	O	SMR	O	SMR	O	SMR	O	SMR	O	SMR
LUNG	85	163***	44	135*	28	236***	15	293***	6	153
STOMACH	40	176***	21	149*	6	116	4	173	3	172

* $P<0.05$, ** $P<0.01$, *** $P<0.001$

non-dust-exposed workers compared to the general population could be due to smoking and occupational exposures (vapours etc.) except dust. In dust-exposed the increased lung cancer rate was found in all subgroups, which have very different confounding exposures (e.g. polycyclic aromatic hydrocarbons in foundries, possibly arsenic in glass industry, nitrosamines in some metal grinders, etc.). We discussed elsewhere[8,9] the minor importance of confounding exposures for our study, such as the very limited use of asbestos in Vienna and its metal industry (no signs of asbestos exposure were found on chest X-rays of dust-exposed and no mesotheliomas occurred), the lack of sources of radiation in the plants investigated (only in a few stone- and tunnel-workers radiation might have been a co-factor) and the negligible use of carcinogenic metals and compounds in iron foundries at the time of the cohort recruitment. Confounding exposures after registration seem to be of minor importance, too, because work histories obtained in 1982 from the national pension insurance board showed a low inter-industry and interplant mobility of dust-exposed (because of registration after age 40) and no second jobs with exposure to accepted carcinogens (one lung cancer case was exposed to glass wool as an insulator and a few other cases with suspected confounding exposure such as a sepiolite grinder are still alive or died from nonmalignant diseases).

Most earlier studies on lung cancer in dust workers have been biased by selection and competing causes of death (silicosis). In coal workers a protective effect of coal dust has been discussed.[7] The seemingly conflicting results on lung cancer in silica and "inert" dust-exposures could perhaps be explained by a multistage model of carcinogenesis: Genotoxic substances (from tobacco smoke as well as from foundry air or other sources) could function as initiators and particles as adsorbens and promotors. In this case it would not be surprising if lung cancer increases with total dust load and not necessarily e.g. with PAH-concentrations, even though both might be involved. From available measurements in our study[8] we cannot decide whether silica or total respirable or inspirable dust was responsible for the increase of lung cancer, but we suspect that also "inert" dust exposure (if heavy and long lasting) can promote chronic obstuctive lung diseases and lung cancer. Bombardment of airways by dust particles, even "inert" ones, could eventually sustain high levels of polymorphonuclear recruitment, alveolar macrophage activation and finally result in a disturbed balance of protease and antiprotease activity.[1]

From the age in which we observed excess lung cancer deaths (Figure 2) we conclude that screening examinations should be continued after retirement from a job with heavy dust exposure. Screening for chronic obstructive lung disease must begin much earlier. Most important, however, is primary prevention by reduction of dust exposures, even "inert" ones.

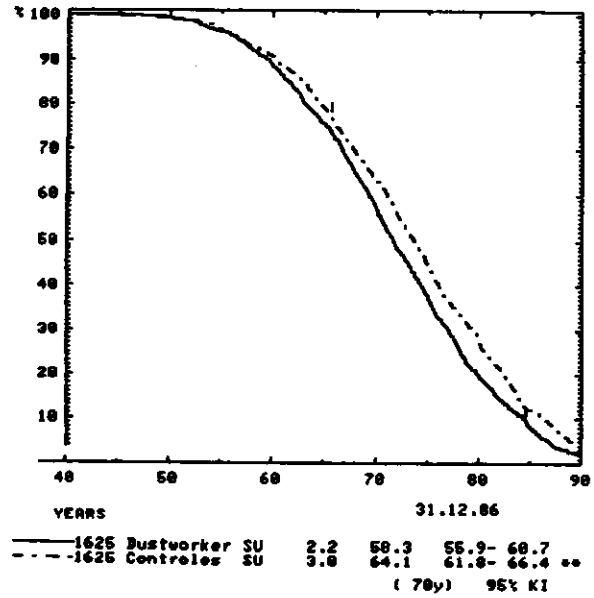

Figure 1. Survival of dust-exposed (solid line) and reference subjects (dashed line).

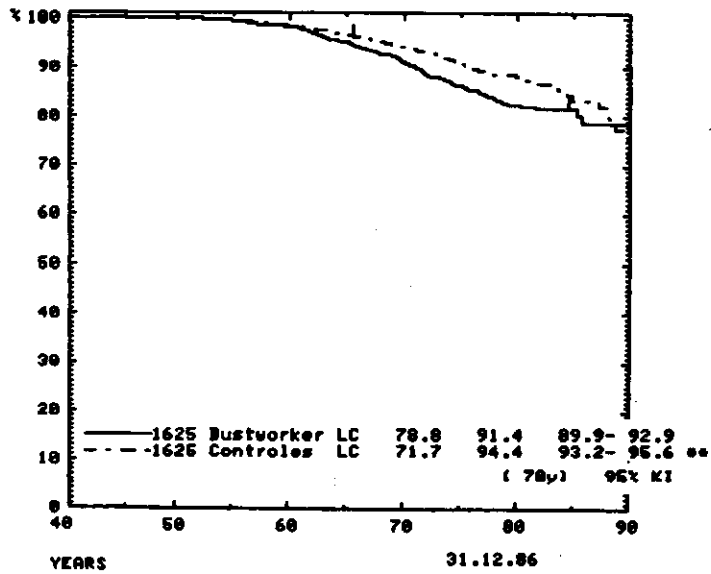

Figure 2. Survival from lung cancer (dust-exposed: solid line, reference subjects: dashed line).

SUMMARY

From 1625 men examined in 1950–1960 with a history of occupational exposure to silica and other non-fibrous particulates in foundries, other metal, glass, ceramic, brick, stone and some other dusty industries 1621 were traced up to 1986, 1442 died, 183 from lung cancer (SMR 168), 80 from stomach cancer (SMR 167), 83 from chronic obstructive lung disease (SMR 205) and 78 from silicosis/fibrosis /tuberculosis (SMR 299).

From 1625 non-dust-exposed workers from the same source population, matched in 1950–1960 to dust exposed workers for age, smoking and begin of observation, 1621 were traced, 1384 died, 142 from lung cancer (SMR 117), 48 from stomach cancer (SMR 89), 47 from chronic obstuctive lung disease (SMR 101) and 15 from tuberculosis/fibrosis (SMR

63). Life table estimates show that primary and secondary prevention should not be focused on pneumoconioses alone.

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EPIDEMIOLOGIA DE LA SILICO-TUBERCULOSIS EN MINEROS ASTURIANOS: TASA DE NUEVOS CASOS BACTERIOLOGICAMENTE POSITIVOS. PERIODO 1971-1985.

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ABSTRACT

La población diana la forman 50.470 ± 7.454 mineros—del carbón de Asturias. La muestra estudiada prospectivamente abarca a 3.612.2 ± 1.779 primeras visitas que son estudiados en el Instituto Nacional de Silicosis cada año. A todo sospechoso de tuberculosis se le practica sistematicamente: 4 extensiones de esputo (Método Ziehl-Nielsen) y 3 cultivos (Medio de Lowenstein) y si precisan, otros tests diagnósticos más invasivos. Durante el periodo 1971-1985, 1.136 pacientes fueron diagnosticados de tuberculosis por presentar positivos los tests bacteriológicos. Durante los 7 primeros años de observación, entre los 508 tuberculosos, la distribución de la categoria de neumoconiosis (ILO 1971) y edades era 7.8% tenian Categoria 0 y 51.1 ± 13.6 años; 9.8% con Categorias 1,2,3 y 54.3 ± 13.3 años; 82.3% con Fibrosis Masiva Progesiva y 53.5 ± 10.6 años. Entre 1978-85, la distribución de neumoconiosis y edades eran respectivamente: 33.3% y 48.7 ± 14.7 años; 14.1% y 55.5 ± 10.5 años; 62.6% y 58.4 ± 10.2 años. La tasa de nuevos casos bacteriologicamente positovos fué de 150.1 ± 30.9 por 10^5 mineros y año, no modificándose significativamente a lo largo de los 15 años, a pesar de la eficacia de los tratamientos. Esta tasa es 3 veces superior a la de la población no minera de la zona, pero no es diferente a la encontrada en otras poblaciones ocupacionales similares.

INTRODUCCION

La Tuberculosis Pulmonar es responsable en en nuestra región de la evolución de las categorias simples de neumoconiosis (1,2,3) a Fibrosis Masiva Progresiva (FMP) en el 9.7% de los casos.[1] Por ello el control de la Silicotuberculosis reduciria la morbilidad y mortalidad que condiciona la FMP.

METODOS

El periodo de estudio comprende desde el 1 de Enero de 1971 hasta el 31 de Diciembre de 1985, dividido en dos periodos 1971-1977 y 1978-1985.

La población diana, objeto de este estudio, es la población minera de Asturias. Esta región, localizada en el Norte de España tiene yacimientos de hulla y antracita. La cuantia media anual, con una desviación standard (±1SD), de esta población se compone, a lo largo de estos años de 50.470 ± 7.454 mineros.

La población muestreada anualmente (±1SD) asciende a 3.612.2 ± 1.779.1 mineros.

Los diagnósticos de neumoconiosis se realizaba en base a exposición laboral y presencia de opacidades redondas de profusión igual o mayor a P 1/1 (Clasificación ILO 1970).[2] La lectura radiológica se efectuó por 3 lectores con experiencia en neumoconiosis, usando la escala de profusiones ampliada.[3] Las discrepancias de lecturas eran promediadas.

El diagnóstico de tuberculosis pleuro-pulmonar se hacia al observar cuadro clinico-radiológico compatible y presencia de material alcohol-acido resistente con el método de ziehl Nielsen y/o identificación del Mycobacterium Tuberculosis en medio de Lowenstein-Jensen. A todo sospechoso de tuberculosis se le practicaba sistematicamente 4 extensiones de esputo con el método Ziehl y 3 cultivos sucesivos en medio de Lowenstein; si era preciso, el paciente era sometido a otros métodos diagnósticos, (broncoscopia, punción transpulmonar, etc.).

A efectos epidemiológicos eran excluidos los casos en que el diagnóstico se sustentaba solo por métodos histológicos.

Las resistencias "in vitro" del Mycobacterium Tuberculosis eran estudiadas mediante el método de Canetti, modificado.[4,5]

Todos los pacientes tuberculosos eran seguidos por una sección especifica de Neumologia del INS, que los trataba y controlaba su evolución. Durante el periodo 1971-1977, el tratamiento antituberculoso era el "standard" de 18 meses, con seguimiento, clinico, radiológico y bacteriológico cada 3 meses hasta 2 años después de finalizado el tratamiento Desde 1978 a 1985 los tratamientos usados fueron 2 regimenes de curso corto; a) Hidracida (I) 300 mg./dia, Rifampicina (R) 600 mg./dia, Etambutol (E), 1200 mg/dia, durante 9 mg./dia, Rifampicina 600 mg./dia y Pirazinamida (Z) 1500 mg./dia, durante 2 meses, seguido de Hidracida y Etambutol durante 7 meses más. (SIZR)2, (IE)7. (6). Se practicó el mismo tipo de seguimiento pero a intervalos de

1 mes. También durante este periodo se hizo chequeo de contactos intimos.

En caso de retratamientos en enfermos tuberculosos, se usaba el régimen standard de 18–24 meses, intentando que la combinación de drogas útiles, conocidas por antibiograma, sumase 1.5. Esto se hacia adjudicando valor 1 a I,R y 0.5 a Z y aminoglicosidos.[7]

La cuantificación de la enfermedad tuberculosa, se hacia midiendo la tasa anual de los nuevos casos bacteriológicamente positivos. Esta se obtenia refiriendo el número de nuevos enfermos, hallados por cultivo y/o estensión, a la población diana que existia a 31 de Diciembre del año correspondiente.

RESULTADOS

1.136 pacientes fueron diagnosticados de tuberculosis pulmonar después de excluir 2 casos en que creció una Mycobacteria no tuberculosa.

Durante 1971–77, entre los 507 tuberculosos la distribución de las categorias de neumoconiosis y edades eran: 7.8% tenian categoria 0 y 51.1 ± 13.6 años; 9.8% con categorias 1,2 y 3 y 54.3 ± 13.3 años; 82.3% con FMP y 53.5 ± 10.6 años. Entre 1978-85, la distribución de neumoconiosis y edades eran respectivamente de 33.3% y 48.7 ± 14.7 años para la categoria 0, 14.1% y 55.5 ± 10.5 años para las neumoconiosis simples y 62.6% y 58.4 ± 10.2 años para la FMP.

La tasa de resistencias primarias a las drogas antituberculosa fueron para los mineros sin neumoconiosis (categoria 0) del 12.9% y 11.9% para las categorias 1,2 y 3.

Las cifras de curación para los pacientes que completan los tratamientos, al finalizar los mismos eran:

a) Tratamiento standard 121/123 (90.9%).
b) Tratamiento curso corto (EIRZ)2 (IE)7 26/27 (96.2%).
c) Tratamiento curso corto (IRE)9 39/40 (97.5%).
d) Retratamiento con "standard" en pacientes sin resistencias: 48/49 (97.9%).
e) Retratamiento con "standard" en pacientes con resistencias a 1 droga: 25/28 (89.2%).
f) Retratamiento con "standard" en pacientes con resistencias a 2 drogas 14/17 (82.3%).
g) Retratamientos con "standard" en pacientes con resistencias a multiples drogas 9/10 (90.0%).

DISCUSION

La tasa de neuvos casos bacteriologicamente positivos se ha mantenido estable a lo largo del periodo de observación, con un valor medio (± 1SD) de 150.1 ± 30.9 por 10^5 mineros y año. Esta cifra triplica a la de la población no minera de la zona. Las tasas registradas en otras poblaciones mineras han variado desde cifras de 49.6 × 10^5 y año[8] hasta las encontradas por Popovac et al[9] que alcanzan valores de 8000 × 10^5 y año. Nuestros resultados son casi coincidentes con la cifra de 146 × 10^5 y año encontrada por Lander en Dinamarca.[10] La persistencia de la tuberculosis ocurre a pesar de la alta eficacia de los tratamientos y la no excesiva alta prevalencia de resistencias primarias.

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EPIDEMIOLOGICAL STUDY OF SILICOSIS IN HARDROCK MINERS IN ONTARIO

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ABSTRACT

An epidemiological survey of silicosis in hardrock miners in Ontario was undertaken. Radiographs had been taken annually, and these were classified by 5 readers for silicosis. The point in time at which miner's radiographs were considered to have passed the 1/1 category for small round opacities was taken as identifying the onset of silicosis. A side-by-side comparison of konimeter and gravimetric dust sampling was carried out in both gold and uranium mines, the resulting relationship being used to convert historical konimeter data from the mines to equivalent respirable quartz concentrations. By using work records, a cumulative respirable quartz exposure index was calculated for each miner. A Kaplan-Meir survival curve analysis was used to derive risk estimates for the development of silicosis in relation to cumulative respirable quartz exposure.

No Paper provided.

RADIOGRAPHIC ABNORMALITIES IN VERMONT GRANITE WORKERS EXPOSED TO LOW LEVELS OF QUARTZ

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ABSTRACT

Whether exposure to levels of granite dust below the current OSHA limits leads to radiographic abnormalities after a lifetime of exposure has not been settled. In 1953, we carried out an X-ray survey of the Vermont granite industry. Quarry and stone shed workers who had been exposed to the low dust levels prevailing in the Industry since 1940 were offered chest X-rays. Films were read by three "B" readers, and were considered abnormal if 2 or 3 of the readers assigned a profusion score of 1/0 or greater. 976 workers out of a total of approximately 1400 participated. 65 (6.9%) of the films were judged abnormal, but the profusion scores were low, only 4 of the films being assigned scores of 6/1 or greater. Only 7 (0.7%) had "pqr" or rounded opacities as the major abnormality. The remaining 61 had irregular opacities, largely lower lobe in location, which are of doubtful significance, but may be related to smoking and aging. In addition, total dust concentrations were measured using personal samplers; dust levels were similar to previous measurements. Mean concentrations were 601 ± 365 micrograms/cuhic meter. Using previously estimated values for percentage quartz of 10%, the mean quartz concentration was below the current OSHA standard of 100 micrograms/cubic meter, although 11% of the samples were above this value. If exposure levels have remained approximately the same over the past 45 years, we conclude that current dust controls, which conform to OSHA standards, have essentially eliminated silicosis.

BACKGROUND

Studies of workers' health in the Vermont granite industry have provided a great deal of information on the health effects of quartz dust inhalation since 1969, when the first comprehensive study of the industry was published.[4] Based on a high incidence of silicotuberculosis, control measures which reduced granite dust levels below 10 million parts per cubic foot (mppcf) were accomplished between 1935 and 1940. At that time, the Vermont Division of Industrial Hygiene (DIH) began annual radiographic surveys to assess the effect of dust reduction on the prevalence of silicosis. Subsequent studies showed that as workers with established silicosis retired or left the industry because of illness, and as new workers were hired, the percentage of the work force with radiographic abnormalities declined.[1,3] In 1964, it was stated that no new cases of silicosis had been detected in workers exposed only to the lower dust levels prevailing after 1940.

In 1974, a study analyzing the results of the DIH radiographic survey of 1970–1 suggested that radiographic abnormalities were present in approximately 30% of the workforce.[7] Most of these were of low grades of profusion and comprised both irregular and rounded shadows. However, 67 films (5% of the total) were assigned profusion scores of 6 or 3, which was believed to be consistent with definite silicosis.

Three possible criticisms might he made of this study. First, the films were interpreted only by a single non-certified reader. Second, workers who were exposed only to the low dust levels prevailing after 1940 were not analyzed as a separate group. It was therefore not possible to know whether levels less than 10 mppcf had eliminated silicosis, or were, on the contrary responsible for some of the radiographic abnormalities. Finally, a certain percentage of the films were interpreted as showing opacities in workers with zero dust years of exposure.

The present study attempts to clarify the issue whether the dust levels present in the industry since 1940 have caused radiographic abnormalities, and if so, of what type and extent. We present the results of an industry-wide radiographic survey done in 1953, which includes only workers exposed to granite dust after the institution of dust controls in 1935. Results of dust sampling for total respirable dust will also be mentioned briefly.

METHODS

All workers employed in 1953, including quarry and stone shed workers, were offered 14×17 chest radiographs taken in a mobile van provided by the Appalachian Laboratory for Occupational Safety and Health (ALOSH). Work histories were recorded or updated on all participants, including oc-

cupational category, the shed where employed, duration of employment and smoking histories. Forced spirometries were also carried out. The chest radiographs were interpreted by three "B" readers using the ILO format (1980). The definition of an abnormal film was that either 2 or 3 of the readers assigned a profusion scores of 1/0 or greater, either of the rounded (pqr) or irregular (stu) type. One worker with definite silicosis was excluded because his major work experience occurred in Canada. Gravimetric dust sampling of respirable size particles were collected using personal breathing zone samplers at flow rates of 6 liters/minute.

RESULTS

972 workers out of a total work force of approximately 1400 were x-rayed. Of those workers not having X-rays, 102 were absent on the day of the survey and the remainder (326 or 23% of the work-force) refused. Only 28 (2.88%) of those x-rayed were interpreted by 2 or 3 of the three readers as showing abnormalities consistent with pneumoconiosis. In only 7 films did all 3 readers agree that an abnormality was present. 21 of the 28 films judged abnormal had as the primary abnormality an irregular or stu type of opacity; this was true of the secondary readings as well. Only 7 (0.7% of the total cohort) showed rounded opacities (pqr) of the type typically seen in early silicosis. The grades of profusion were extremely low, only four films being judged as have profusion scores of 2/1 or higher and these films showed irregular (stu) types of opacities. The location of the stu changes, even at low grades of profusion, tended to be in the lower lung zones. No large opacities or egg shell calcifications were observed.

Comparison of the workers with abnormal radiographs compared to the remainder of the workforce showed that the former were older on average (53.6 yrs vs. 41.5 yrs.), and spent longer in granite (30.9 yrs vs. 17.5 yrs.), had smoked longer (27.9 yrs. vs. 19.2 yrs.), and more heavily (32.3 yrs. vs 26.99 yrs.) P values for the first three variables show significant differences at the .001 level. Several of the workers with abnormal films had notably low exposures to dust: one was a lumper for 6 years, and for the remainder of his 37 years had been a draftsman with little exposure. Another had worked exclusively in an office as a draftsman without any exposure.

Average dust concentrations of 417 samples was 601 $\pm$ 368 micrograms/cubic meter, which is similar to values observed by previous workers.[5]

DISCUSSION

These results indicate that radiographic abnormalities consistent with silicosis have occurred at a very low level (0.7% of cohort) at quartz exposures which are in conformance with the current OSHA limit of 100 micrograms/cubic meter.,This is particularly surprising inasmuch as approximately 10% of the samples, using the 10% quartz value of previous workers, were over 100 micrograms/cubic meter. Further, the changes observed tend to be a very low grades of profusion. The predominant type of opacities judged to be present were of the stu or irregular type, seen in 21 of the 28 workers judged to have abnormal films. The significance of these changes is uncertain, but may be associated with peribronchial fibrosis associated with pathological changes of chronic bronchitis which has been described in older, heavily smoking patients.[6]

In summary, this study provides an overview of the prevalence and type of radiographic abnormalities which have developed in Vermont granite workers over a 45 year period of observation, when dust controls were effectively maintained. This essential elimination of radiographic silicosis has occurred at quartz levels which are in conformance with current OSHA standard.

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A STUDY OF SILICOTIC CHINESE GRANITE QUARRY WORKERS IN SINGAPORE

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SYNOPSIS

Although silicosis is less prevalent today than in the past owing to better dust control at workplaces, cases still occur in a number of countries. In Singapore, the greatest hazard of silicosis is in the granite quarries.

In 93 Chinese granite quarry workers diagnosed as having silicosis and followed up, there was an increased prevalence of chest X-rays with large opacities for category 3 profusion compared to category 1 although this was not statistically significant. The duration of exposure to silica dust did not seem to affect the extent of opacities in the chest X-rays as workers with more than 20 years exposure in the quarries did not have a higher category of profusion of opacities on chest X-ray than those with shorter exposure. There was no statistical significance in the difference in prevalence of cyanosis, clubbing and crepitations among the 3 profusion categories of chest X-ray. Although nearly 25% of the cases had pulmonary tuberculosis, this did not seem to be related to the profusion category on chest X-ray. 58% of the cases had FVC results which were less than 80% of the predicted values, including all the 6 cases with category 3 profusion on chest X-ray, compared with about 52% of those in category 1. This was statistically significant ($p = 0.002$).

INTRODUCTION

It is well-established that occupational exposure to silica dust can cause silicosis.[1] Although the disease is less prevalent today than in the past owing to better dust control at workplaces, new cases still occur in a number of countries.[2]

This paper describes the radiological, clinical and ventilatory function findings in silicotic workers on followup in Singapore.

MATERIALS AND METHODS

Silicosis is a notifiable and compensable occupational disease in Singapore. Confirmation of the diagnosis is made by the Department of Industrial Health, Ministry of Labour, after due investigation. The diagnosis is made mainly on:

a) a confirmed history of occupational exposure to dust containing free silica

b) a chest X-ray picture consistent with silicosis, with a grading of at least category 1/1 of the ILO international classification

c) a clinical picture consistent with the disease, and exclusion of other similar diseases.

Silicosis cases are followed up 3 yearly by the Department of Industrial Health. A clinical examination, full size postero-anterior chest X-ray and ventilatory function tests (FEV_1 and FVC) are done. The ventilatory function tests are done on the Autospiror HI-498. The best of 3 readings is taken and corrected to BTPS. Each reading is compared to the predicted value for the local population, specific for ethnic group, sex, age and height of the subject.[3]

The chest X-rays were read by one of the authors together with a consultant radiologist. The films were compared to the standard ILO films and graded according to the ILO international classification of radiographs of pneumoconioses.[4] Although the workers were asked for respiratory symptoms (cough, breathlessness, sputum), this study has excluded them because the authors felt that the replies might be too subjective for reliable analysis. Instead, this study has included the objective clinical findings of cyanosis, clubbing and crepitations.

All cases were asked for a history of pulmonary tuberculosis. This was then checked with the tuberculosis registry of the National Tuberculosis Control Unit to confirm the history.

The period of 1984 to 1986 was taken. As the silicosis cases are followed up 3 yearly, this period would cover all the cases on followup. New cases during this period were also included. However, the final number included in this study has excluded 82 who had died, and 63 others who were unable to come for examination, were unable to cooperate sufficiently for the FEV_1 and FVC tests, and those who were lost to followup. Four of the cases whose latest chest X-rays were graded as category 0 were also excluded. Thus a total of 140 were included in this study.

In the analysis of the data, Pearson chi-square test was used, with the significance level set at 0.05. Fisher's Exact Test was used where cell values were less than 5.

RESULTS

A total of 140 cases were followed up in the period 1984 to 1986. Most of them were men. Chinese male workers

comprised by far the largest single group (Table I). Of the 115 Chinese men, 93 were granite quarry workers, 22 of whom were still working in the quarries at the time of the follow-up. Seventeen had been exposed to a powder containing a high percentage of free silica which was used as a "filler" in the milling of rubber (Table II). Two of the workers worked in a quarry where such powder was obtained; the others worked in rubber factories which used the powder.

Since the vast majority of the cases were Chinese men who had worked or were still working in the granite quarries, it was decided to study them as a fairly homogeneous group. Table III shows that their mean exposure duration as at the date of follow-up was 22.8 years, with a standard deviation of 9.9 years. Their average age was 59.1 years with a S D of 10.2 years.

In nearly 68% of this group, the profusion grading of opaci-

Table I
Distribution of Silicotic Workers Followed-Up 1984–86, by Ethnic Group and Sex

Ethnic Group	Male	Female	Total
Chinese	115	15	130
Malay	7	-	7
Indian	3	-	3
Total	125	15	140

Table II
Distribution of Chinese Male Silicotic Workers by Type of Exposure

Type of Silica Exposure	Still Exposed	Ceased Exposure	Total
Granite quarry	22	71	93
Rubber filler	2	15	17
Others	1	4	5
Total	25	90	115

ties on their chest X-rays was category 1, with only 6 out of 93 with category 3 (Table IV). The average age of the workers in the 3 categories was similar. Workers with more than 20 years of dust exposure did not have a higher category of profusion of opacities than those with shorter exposures (Table V).

Table III
Duration of Exposure of Chinese Male Silicotic Granite Quarry Workers

Duration of exposure* (years)	No.
1 -	5
6 -	6
11 -	7
16 -	23
21 +	52
Total	93
$\bar{x}$	22.8 yrs
SD	9.9 yrs

(*as at date of followup)

Table IV
Chest X-ray Category and Age of the Chinese Male Quarry Workers

Chest X-ray Profusion	n	Age (years)	
		$\bar{x}$	SD
Category 1	63	59.6	10.2
Category 2	24	58.0	11.0
Category 3	6	58.2	7.8
Total	93	59.1	10.2

A total of 11 out of the 93 cases showed large opacities on their followup chest X-ray films (Table VI). There was an increasing prevalence of chest X-rays with large opacities from the category 1 profusion group to category 3. However this was not statistically significant at the 0.05 level. As the symptoms of cough and dyspnoea were subjective, we analyzed for the more objective signs of cyanosis, clubbing of nails, and crepitations on clinical examination. There was no statistical difference in the prevalence of these signs among the 3 profusion categories of chest X-ray (Table VII).

Table VIII shows an apparent increasing prevalence of past occurrence of pulmonary tuberculosis with profusion category. But this was not statistically significant at the 0.05 level. There was no statistical significance in the prevalence of "abnormal" FEV_1[5] results among the 3 chest X-ray categories (Table IX). But the difference in the prevalence of "abnormal" FVC[5] results was significant between categories 1 and 3 ($p = 0.002$). All the 6 workers with category 3 chest X-rays had FVC values which were less than 80% of those predicted for their age and height.

Table V
Duration of Exposure in Quarries and Chest X-ray Category

Chest X-ray Profusion	Exposure in Quarries		
	< 20 years	> 20 years	Total
Category 1	26	37	63
Category 2	13	11	24
Category 3	2	4	6
Total	41	52	93

Table VI
Prevalence of Large Opacities on Chest X-ray

Chest X-ray Profusion	No.	With large opacities	
		n	%
Category 1	63	5	7.9
Category 2	24	4	16.7
Category 3	6	2	33.3
Total	93	11	11.8

Table VII
Clinical Signs and Chest X-ray Category

Chest X-ray Profusion	No.	Clinical signs		
		Cyanosis	Clubbing	Crepitations
Category 1	63	2	6	10
Category 2	24	1	5	2
Category 3	6	0	0	1
Total	93	3	11	13

Table VIII
History of Pulmonary Tuberculosis and Chest X-ray Category

Chest X-ray Profusion	No.	Pulmonary tuberculosis	
		No.	%
Category 1	63	12	19
Category 2	24	8	33.3
Category 3	6	3	50
Total	93	23	24.7

All the 6 persons in category 3 had stopped smoking compared with 9 out of 20 smokers in category 2, and 15 out of 52 smokers in category 1.

DISCUSSION

In Singapore, the greatest hazard of silicosis is in the granite quarries where the blasting and crushing of granite are very dusty operations. The second commonest type of exposure was to powder containing a high percentage of free silica which was used in the milling of rubber. Such exposure is much less common now.

Of the 93 Chinese granite quarry workers with silicosis followed up, 68% had a chest X-ray profusion grading of category 1, with only 6 in category 3. Eleven showed large opacities. This compares with the 9 out of the 144 silicotics who had large opacities in the followup study reported by Koskinen.[6] There was an increasing prevalence of chest X-rays with large opacities from the category 1 profusion group to category 3 but this was not statistically significant.

Theriault et al.[7] were able to obtain a dose-response curve of granite dust on roentgenograms by plotting the percentage of people with opacities on their chest X-rays against an increasing exposure expressed in dust-years. In our study, the duration of exposure to silica dust did not seem to affect the extent of opacities in the chest X-ray. Workers with more than 20 years exposure in the quarries did not have a higher category of profusion of opacities on chest X-ray than those with shorter exposure.

The pathogenesis of silicosis involves the interaction between

Table IX

FEV_1 and FVC Results, and Chest X-ray Category

Chest X-ray Profusion	No.	FEV_1		FVC	
		normal*	abnormal**	normal*	abnormal**
Category 1	63	22	41	30	33
Category 2	24	7	17	9	15
Category 3	6	1	5	0	6
Total	93	30	63	39	54

* normal is ≥ 80% of the predicted value.

** abnormal is < 80% of the predicted value.

silica dust and pulmonary macrophages. Inflammatory and fibrotic reactions involved in cell-mediated and humoral immune responses also participate in the pathogenesis.[8] The immunological basis for the development of silicosis, which would have contributed to our findings, could also explain the well-documented wide variation among individuals in the way workers respond to the same exposure to silica dust.[9]

As the symptoms of cough and dyspnoea were largely subjective, we analyzed for the more objective signs of cyanosis, clubbing and crepitations on clinical examination. There was no statistical significance in the prevalence of these signs among the 3 profusion categories of chest X-ray. This could be because the physical signs associated with generalized pulmonary fibrosis, including asbestosis, i.e. clubbing of nails and basal inspiratory crepitations, are less frequent findings in silicosis.[10]

Twenty three (or nearly 25%) of the 93 cases had pulmonary tuberculosis. This compares with 23 (16%) of 144 cases in the series reported by Koskinen.[6] However, tuberculosis is endemic in Singapore. It has been said that the risk of contracting tuberculosis increases with the severity of silicosis, and that previous tuberculosis, whether treated or not, probably increases the risk and severity of silicosis.[11] But although our cases showed an apparent increasing prevalence of past occurrence of pulmonary tuberculosis with profusion category on chest X-ray, this was not statistically significant at the 0.05 level.

Ventilatory function may be affected in silicosis. This is mainly restrictive in nature, and is indicated by a FVC reading which is less than 80% of the predicted value for the age and height.[6] Fifty-four or about 58% of our cases had FVC readings which were less than 80% of the predicted values (Table 10). In the series reported by Koskinen, 46% of 144 followup cases were in this category.[6] The decrease in lung function may be greater with the coalescence of shadows on the chest X-ray.[11] In our series, those with category 3 profusion on chest X-ray all had abnormal FVC readings, compared with about 52; of those in category 1. This was statistically significant ($p = 0.002$). Smoking could be a potential confounder although it is less likely to affect the FVC results. Category 3 chest X-rays also showed more large opacities than category 1.

It was interesting to note that all the 6 persons in category 3 had stopped smoking on followup, compared with only 15 of the 52 smokers in category 1, although their mean ages were similar. This might have been partly due to the increasing respiratory difficulty experienced by those in category 3.

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REVISED ESTIMATES OF PULMONARY FUNCTION LOSS IN VERMONT GRANITE WORKERS: RESULTS OF A LONGITUDINAL STUDY

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ABSTRACT

Previous studies have suggested that excessive losses of FVC and $FEV_{1.0}$ were occurring in Vermont granite workers despite the fact that quartz levels existing in the industry were below the current OSHA standards. We re-examined these losses in granite workers over an eight year period, testing the workforce from 1979 to 1987 on alternate years. All workers including stone shed, quarry and office were offered forced spirometry using a 10 L. Collins water-sealed spirometer. In the peak year of participation (1983), 887 workers out of a total of approximately 1400 were tested. Estimates of longitudinal loss were based on 711 workers who participated in at least 3 of the semi-annual surveys. The mean age of this group was 42.9 years, and the mean years employed was 19.3 yrs. 21.4% were non-smokers (NS), 34.2% ex-smokers (ES) and 44.4% current smokers (CS). Average annual losses of FVC were .025 ± .055 L. (CS: .032 L.; NS: .014 L.; ES: .024 L.). Average annual losses of $FEV_{1.0}$ were .036 ± .040 L. (CS: .044 L.; NS: .027 L.; ES: .033 L.). Analysis of covariance indicated that losses were related to the initial values for FVC or $FEV_{1.0}$, height, age, and smoking history. The losses of both FVC and $FEV_{1.0}$ were not correlated with years employed in the granite industry. The losses of pulmonary function were significantly smaller than those estimated previously, e.g., .070–.080 L. in FVC, and .050–.070 L. in $FEV_{1.0}$. We conclude that current dust levels in the Vermont granite industry do not accelerate pulmonary function loss.

See Table of Contents, Part II, for Paper.

LUNG FUNCTION WITH ASBESTOS-RELATED CIRCUMSCRIBED PLAQUES

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Early studies of asbestosis made no mention of plaques, and pleural calcifications were not identified with asbestos exposure until 1955.[10,12,22] In 1965 Selikoff[36] found a long latent period of 20 years and a high prevalence of 44%. Thereafter, pathologic studies showed no difference between plaques with and without calcification, and often plaques were found without microscopic asbestosis.[20,23] Radiographs showed plaques in only a small proportion of cases who had such lesion at autopsy.[20,37] Epidemiologically, it emerged that plaques can be caused by relatively slight household and neighborhood exposure.[8] Clinically, plaques early on were described as "harmlos-skurriler Schönheitsfehler," that is, a harmless beauty mark,[5] since they were neither precancerous lesions nor caused symptoms or loss of function.[5,7,23]

A number of studies since 1968[24] have dealt with the functional consequences of asbestos-related pleural disease but most often no clear distinction was made between circumscribed plaques and diffuse pleural thickening. Because fibrothorax of whatever cause may have serious physiologic consequences,[13,16,27,29,38] in this study we made a strict distinction between plaques and diffuse thickening. Also, we addressed the confounding effect of smoking; and for controls we used both normal subjects studied by the same protocol and employees matched for age and years of employment but without plaques.

METHODS

Clinical Material

We studied 1,764 persons during annual industrial surveys between 1966 and 1988 at two large shipyards, three papermills and one asbestos plant. Details of employment and type of exposure have been described elsewhere.[9,15,27]

Control subjects included two groups: *100 Normal unexposed males (group I)* 40 years or older without discernable lung disease and without prior asbestos exposure, who presented for pre-employment examination (Table I). The second group consisted of *154 persons exposed for 15 or more years* (group II) who had normal roentgenograms and who were selected from our survey group by matching for age and years since first exposure with group III which had plaques only and no diffuse thickening or asbestosis.

Survey Studies

On-site examination included a medical and detailed occupational history, a physician-administered respiratory questionnaire and chest physical examination.

Lung function studies included forced vital capacity (FVC), the forced expiratory volume in one second (FEV_1) and other flow derivatives, and the single breath diffusing capacity (D_L) with alveolar volume (VA) calculated from single-breath helium dilution. Instrumentation, unchanged over the years, has been described in detail.[17] FVC and FEV_1 were selected from the best of 3 efforts[2] and DL values were accepted if VA (BTPS) was at least 90% of FVC (BTPS). Predicted values were calculated from Morris et al.,[31] and for D_L from our own data.[18]

Chest roentgenograms, PA, lateral, and on at least one occasion oblique views, were obtained within one week of examination. Reading was according to the 1980 ILO scheme[21] by two "B" readers, one of whom was unaware of the nature and type of exposure. Films were read prospectively without recourse to other films ("apart reading"), and were reviewed later by display of the entire series of each case in order of date ("side-by-side" reading).

Definitions for this Study

Excluded were persons with significant non-asbestos intrathoracic disease, most often chest surgery, trauma, extensive pleural and parenchymal scarring from tuberculosis or residuals from infarction or pneumonia. Persons with heart disease we excluded only with marked cardiomegaly and/or evidence of chronic passive congestion.

Chronic obstructive lung disease (COLD) was diagnosed for this study only when the ratio of FEV_1 /FVC was more than 2 SD below the normal predicted.[1] We ignored lesser degrees of COLD and evidence of "small airways disease" which was observed in virtually all smokers and ex-smokers.

Circumscribed plagues were distinguished from *diffuse thickening* by detailed study of routine and oblique films aided by review of history, outside records, and CT scans in some cases.[27] Descriptions of Fletcher and Edge[11] were useful, but the ILO Film was of no help because we believe that the single example of "diffuse thickening" also represents a circumscribed plaque.[21] *Large plaques* were bilateral with width "b" and extent "2" or larger. *Large diffuse thickening* could be unilateral but had to be of width and extent 2b or larger. Asbestosis was graded according ILO major categories 0,1,2 and 3.[21] *Years since first exposure* included prior asbestos exposure. *Nonsmokers* had

Table I
Clinical Material for Plaque Study

Group	Definition	No COLD	Also COLD	Also Diffuse
I	Normal Unexposed, age over 40	100	0	0
II	Exposed > 15 Yrs, Normal X-ray (Matched For Age & Exposure With Group III)	129	25	0
III	Circumscribed Plaques Only	197	21	12
IV-VI	Plaques and Asbestosis 1,2 or 3	151	25	50

smoked less than 2 pack-years and had stopped at least 20 years earlier.

RESULTS

Among 1,764 persons in the survey we found 218 (12.3%) with circumscribed pleural plaques as the only abnormality (Group III), and there were 176 (10.0%) who had plaques and asbestosis (Groups IV–VI) (Table I). Additionally, 158 exposed persons with normal roentgenograms were matched for age and years since first exposure with the group with plaques (Tables I, II). COLD was found in 16.2% of those with normal X-rays, 9.6% with plaques only, and 14.2% among those with plaques and asbestosis. For some comparisons with normal unexposed persons the COLD group was excluded (Tables I–III, Figure 2). Mean age was similar for all exposed groups, but the 100 unexposed controls were 3 years younger. First exposure was 27 years ago for groups II–VI, and in this study this figure was virtually the same as total years exposed.

Lung function tests for the 100 controls were about 4% lower than predicted (Table II) because the Morris equations are for nonsmokers.[31] For the 40 nonsmokers in this group all function tests averaged almost exactly 100% (Table III). Mean values for the exposed controls (Group II) were slightly lower ($p < .05$).

With circumscribed plaques as the only abnormality (Group III) all three screening tests actually were slightly higher than the normal subjects ($p < .05$) or exposed persons without plaques ($p < .01$) (Table II). With progressing asbestosis there was the predictable precipitous decline, with D_L most severely affected. Inclusion of persons with COLD reduced mean function by only 2%–3% (Table II) because there were few such persons (Table I) and usually their obstructive disease was slight. COLD was no more common among persons with plaques than those without them (Table I). However, among all smokers and ex-smokers, including "normal" controls, both FEV_1 and D_L were significantly worse ($p < .01$) than among nonsmokers (Table III).

The fact that circumscribed plaques have no measurable effect on function was further documented by separation according to width and extent. Table IV and Figure 2 indicate no functional difference between large and small plaques.

Calcified plaques were seen in 80 persons (17.5%). This group was older and had longer employment by about 4 years. Nevertheless, the screening tests were virtually identical compared to the group with uncalcified plaques.

Diffuse pleural thickening initially was recorded from apart readings in 158 cases (Table V). Subsequent detailed study led to exclusion of 96 cases. Among these, subpleural fat pads were recognized more often following publication of the beautiful illustrations by Sargent et al.[35] Among the included 62 cases (3.5%) diffuse thickening was most often the residue of a benign effusion (Table V).

Diffuse thickening, unlike plaques, caused a significant loss of lung function and, unlike plaques, this loss was strongly related to extent and thickness, with bilateral cases most markedly impaired (Figure 2). Lung volume (FVC) was most severely affected, and D_L/VA often was larger than predicted as has been noted by others.[26,29,38]

DISCUSSION

The prevalence of asbestosis is declining rapidly, and most of the 254 cases (14.4%) in this series were the result of first exposure more than 38 years ago.[15] Circumscribed pleural plaques were more frequent (23.6%), and many were recognized among persons first exposed less than 38 years ago. This was, in part, because plaques can arise from lesser exposure and, in part, because of improved recognition of early lesions. Therefore, clinical and functional implications of plaques have become of increasing interest.

Published material does not provide a good overview of the physiologic effects of circumscribed plaques because, initially, attention was focused on calcifications,[24] and later the effect of plaques was obscured by inclusion of diffuse pleural thickening under the general term of "pleural changes."[3,6] This is not surprising because neither the 1958 nor the 1971 ILO schemes provided for separate quantification of these pleural reactions.[27].

Initial physiologic and pathologic studies of benign asbestos effusion showed that these often bilateral and often recurring bloody effusions frequently result in marked functional impairment and fibrothorax, sometimes so severe as to require decortication.[16,29] An epidemiologic study of effusions showed persisting radiographic changes: Among 34 persons there remained a blunted costophrenic angle in 91.4% and measurable diffuse thickening in 54.3%.[9] The serious con-

sequences of imprisoned lung, so well described in the days of tuberculosis and empyema,[13] have now been rediscovered in the asbestos-exposed under such fancy terms as "lung en currasse," "lung entrapment,"[29] "pleural hyalinosis complicata,"[32] or "squashed lung."[38] However, unlike pleural thickening after empyema or trauma, in asbestos cases the cortex may increase over the years,[28,38] probably from recurring subclinical effusions. Rounded atelectasis from effusion is also described in the asbestos exposed[4,30] and also may be associated with functional impairment. In all of these cases there was marked dyspnea, severe reduction of all lung volumes and D_L, and sometimes ventilatory failure. However, in contrast to pulmonary fibrosis, D_L/VA (sometimes called KCO) was normal, indi-

Table II

Pleural Plaques: Age, Years Since First Employment and Lung Function

Group	No.	Age	Years Since First Empl.	FVC % Predicted	FEV_1 % Predicted	D_L % Predicted
Excluding Obstruction, and Excluding Diffuse Thickening						
I	100	51.8 ± 10.7	0	94.5 ± 12.6	96.9 ± 13.3	95.3 ± 17.4
II	129	55.3 ± 8.1	27.9 ± 7.5	91.0 ± 13.6	97.3 ± 13.3	93.8 ± 17.9
III	197	53.8 ± 7.6	27.4 ± 5.9	96.1 ± 11.4	101.8 ± 13.6	101.6 ± 13.9
IV	112	56.1 ± 7.6	27.4 ± 6.1	82.3 ± 11.3	87.5 ± 12.5	80.2 ± 16.5
V	31	59.5 ± 8.1	29.0 ± 7.0	73.6 ± 16.7	77.6 ± 17.7	58.1 ± 13.6
VI	8	56.8 ± 6.6	23.4 ± 7.9	53.9 ± 16.8	58.7 ± 20.1	45.8 ± 11.1
Including Obstruction, Excluding Diffuse Thickening						
I	100	51.8 ± 10.7	0	94.5 ± 12.6	96.9 ± 13.3	95.3 ± 17.4
II	154	55.5 ± 7.7	28.3 ± 7.4	90.5 ± 14.3	93.6 ± 17.2	91.0 ± 19.1
III	218	54.0 ± 7.5	27.4 ± 6.3	94.5 ± 12.7	98.7 ± 16.8	100.4 ± 14.7
IV	128	56.3 ± 7.3	27.4 ± 6.8	81.6 ± 12.5	84.9 ± 15.4	78.4 ± 17.0
V	40	59.5 ± 7.3	28.9 ± 7.1	74.4 ± 17.1	75.2 ± 19.1	58.4 ± 14.0
VI	8	56.8 ± 6.6	23.4 ± 7.9	53.9 ± 16.8	58.7 ± 16.8	45.8 ± 11.1

Table III

Pleural Plaques: Effect of Smoking

Excluding Diffuse Thickening, Including Obstruction

Group		No.	Smokers	No.	Nonsmokers
I	FVC %	60	92.4	40	97.8
II		110	90.5	44	90.5
III		163	93.8	55	96.8
IV		107	82.4	20	77.6
V		36	75.6	4	63.8
VI		7	55.3	1	44.0
I	FEV_1 %	60	93.4	39	102.4
II		110	91.1	44	99.7
III		163	97.4	55	102.6
IV		107	84.9	20	84.6
V		36	75.4	4	73.0
VI		7	60.1	1	49.0
I	D_L %	60	91.6	39	101.0
II		110	86.5	44	102.2
III		163	98.8	55	105.0
IV		107	77.3	20	86.3
V		36	57.8	4	64.1
VI		7	47.7	1	32.4

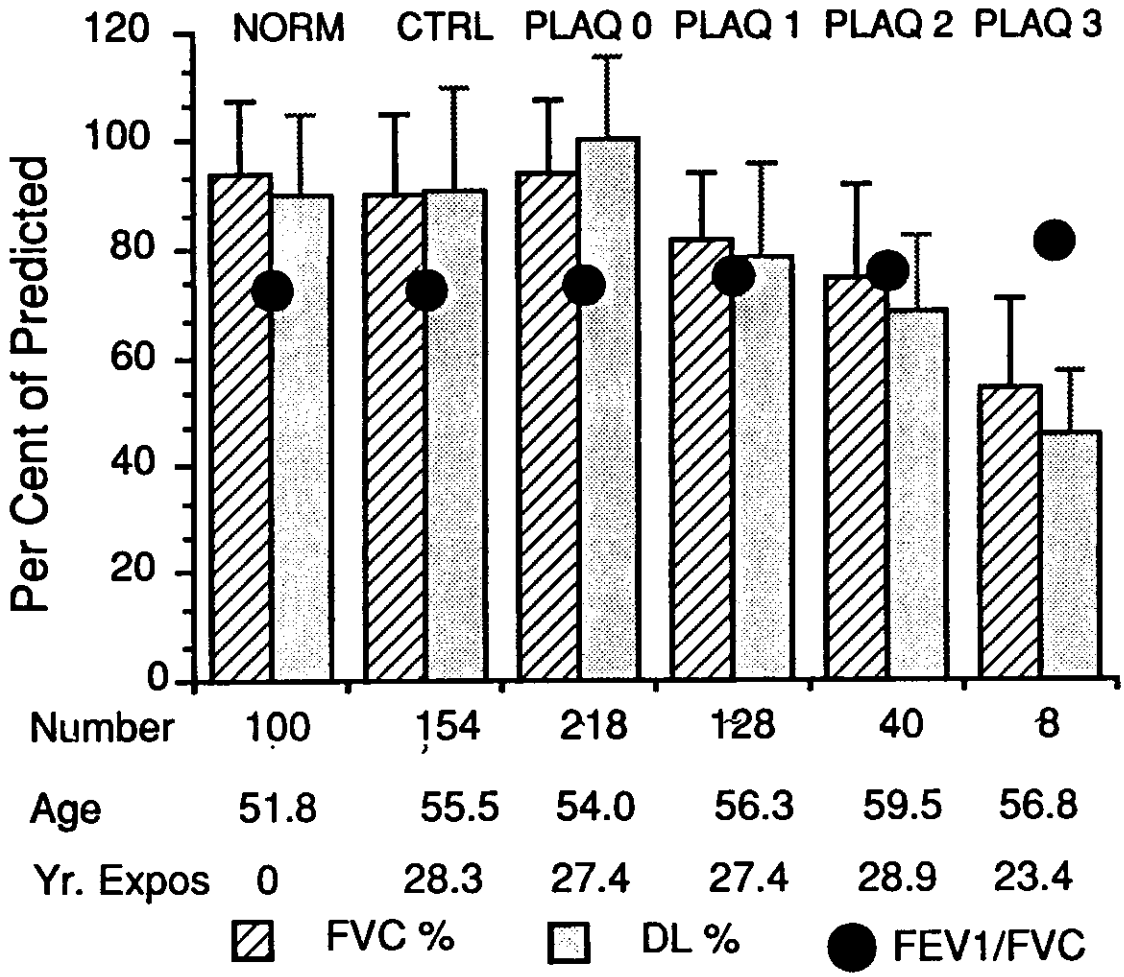

Figure 1. Lung function with plaques and asbestosis. Forced vital capacity (FVC) and diffusing capacity (D_L) as percent of predicted, and the FEV_1/FVC ratio of 100 normal unexposed males over age 40 (NORM), exposed males with normal roentgenograms matched for age and years since first exposure (CTRL), 218 males with circumscribed hyaline pleural plaques only (PLAQ 0), and 176 persons with plaques and varying degrees of asbestosis (PLAQ 1,2,3). This representation includes persons with chronic obstructive lung disease while persons with diffuse pleural thickening have been excluded.

cating that reduced D_L was the result of reduced lung volume and not of impaired respiratory gas exchange. From the foregoing it is evident that inclusion of but a single case of this nature in a group largely with circumscribed plaques would have a significant effect on average values of lung function.

A larger series of diffuse thickening was reported by McGavin and Sheers.[26] They, like Britton[6] before them, devised a grading scheme to measure radiographic extent of diffuse thickening and found impairment of FVC and D_L closely related to severity score. Calcifications alone had no significant effect on function.[24,25]

SUMMARY AND CONCLUSIONS

In 218 persons with circumscribed pleural plaques, but without diffuse thickening or apparent asbestosis, we found lung function with respect to volume, flow and gas exchange no different than that of 154 persons matched for age and years since first exposure who had no visible plaques, and no different than that of 100 unexposed normal subjects. Inclusion of persons with chronic obstructive lung disease in the exposed groups did not alter results significantly. There was no difference among persons with and without calcification of plaques, and no difference between large and small plaques. With plaques and increasingly severe asbestosis there was the predictable progressive functional impairment.

Diffuse pleural thickening, unlike plaques, caused significant functional loss, especially with regard to lung volumes. This is because pleural plaques involve only the parietal pleura, do not cause adhesive pleuritis, and are patchy and interrupted structures that do not interfere with thoracic motion. Diffuse thickening, on the contrary, involves both visceral and parietal pleurae forming an uninterrupted fibrous peal with granulation tissue that extends to involve cortical interlobar septa, and seriously interferes with motion of both

Table IV

Circumscribed Plaques: Effect of Size and Extent (Cases with Diffuse Thickening or Obstruction Excluded)

Group	No.	Age	Years Since First Empl.	FVC % Predicted	FEV_1 % Predicted	D_L % Predicted
Small Plaques (< 2b)						
III	100	53 6 ± 6.9	27.5 ± 5.5	96.0 ± 11.6	102.5 ± 13.1	101.0 ± 14.4
IV	27	55.9 ± 7.5	28.5 ± 7.2	81.3 ± 9.0	89.4 ± 8.8	75.1 ± 17.8
V	7	62.4 ± 6.8	31.4 ± 6.9	74.7 ± 23.2	74.3 ± 16.7	58.8 ± 9.5
VI	4	59.3 ± 5.1	26.5 ± 8.5	58.8 ± 18.7	65.8 ± 22.6	47.5 ± 10.7
Large Plaques (≥ 2b)						
III	97	54.0 ± 8.3	27.4 ± 6.4	96.3 ± 11.1	101.2 ± 14.1	102.2 ± 13.4
IV	35	56.4 ± 5.9	27.9 ± 5.3	80.3 ± 10.6	86.5 ± 12.0	84.7 ± 17.2
V	11	58.4 ± 9.5	29.5 ± 7.0	71.4 ± 19.3	76.0 ± 19.3	49.2 ± 12.1
VI	4	54.3 ± 7.7	20.2 ± 6.9	49.0 ± 15.7	51.8 ± 17.2	44.0 ± 13.0

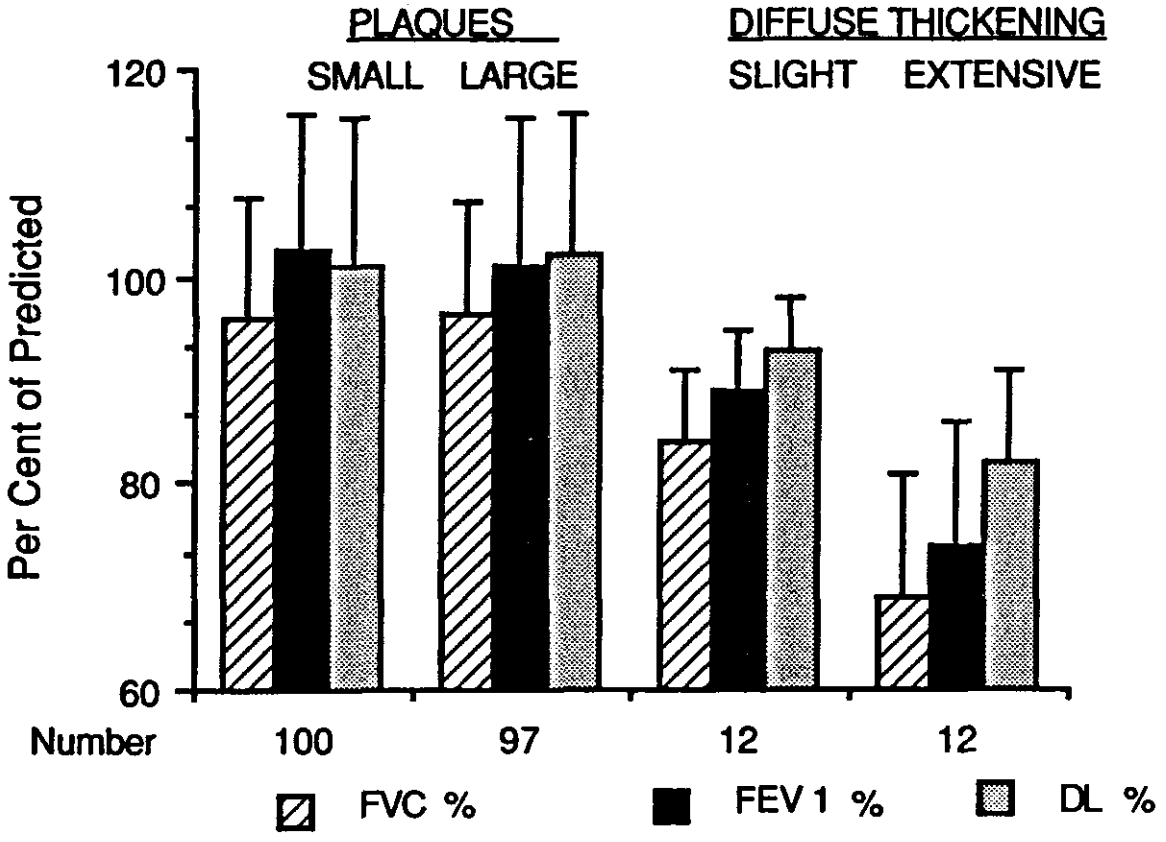

Figure 2. Lung function: plaques and diffuse thickening. The effect on lung function of asbestos-related pleural disease. Forced vital capacity (FVC), forced expiratory volume in one second (FEV_1) and diffusing capacity (D_L) were all in the normal range for persons with circumscribed plaques, and there was no difference between small plaques (<2b) and large plaques (>2b). Persons with diffuse pleural thickening had a significant functional deficit, and this was greater with extensive diffuse pleural disease.

Table V
Causes of Diffuse Thickening

Initial Coding from Apart Readings	158
Excluded After Further Study	96
Actually Confluent Plaques	40
Malignancy	5
Infection, Trauma, Surgery	22
Subpleural Fat Pads	18
Included as Diffuse Thickening	62
After Benign Effusion	41
Related to Asbestosis	15
Unexplained	6

lungs and thorax. The cause of diffuse thickening in most cases could be traced to one or more episodes of benign asbestos effusion. Our studies confirm the old dictum of Bohlig et al[5] that plaques are an epidemiologic leading fossil for asbestos exposure, but otherwise are merely a beauty mark and without functional consequences. We also agree with McGavin and Sheers[26] that diffuse thickening at times may lead to significant pulmonary insufficiency and then represents an industrial injury even when there is no asbestosis.

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PREDICTIVE SIGNIFICANCE OF LESSER DEGREES OF PARENCHYMAL AND PLEURAL FIBROSIS. PROSPECTIVE STUDY OF 1,117 ASBESTOS INSULATION WORKERS, JANUARY 1, 1963–JANUARY 1, 1988. MORTALITY EXPERIENCE

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ABSTRACT

In 1963, 1,117 asbestos insulation workers were examined. X-ray findings were categorized according to the Saupe classification and reported. Subsequently, the films were recategorized when the International Labour Office Classification was introduced, using the 1980 Classification. The entire cohort has been maintained under observation. We have investigated all deaths that have occurred in the 25 years and will present the mortality experience of this group in relation to the radiological findings in 1963, with particular reference to 0/0, 1/0, 0/1, 1/1 interstitial, as well as the presence or absence of pleural fibrosis.

No Paper provided.

SPIROMETRIC ABNORMALITIES IN 2573 ASBESTOS INSULATORS WITH LONG TERM EXPOSURE: EFFECTS OF SMOKING HISTORY AND RADIOGRAPHIC ABNORMALITIES

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INTRODUCTION

The 2573 insulators who are the subjects of this report comprise one of the largest reported populations occupationally exposed to asbestos. They were selected on the basis of a long duration from onset of exposure (DURON; 87% were ≥ 30 years) in order to provide sufficient time for evolution of disease, whether it be pleuropulmonary fibrosis caused by asbestos or chronic airways obstruction attributable to smoking and perhaps to occupational dusts. This population is therefore well suited to provide information concerning:

1. The prevalence of the various pulmonary function impairments in a large well defined group occupationally exposed to asbestos.
2. The effect of such influences as radiographic abnormalities, DURON and smoking on pulmonary function. In this regard, the large number of lifetime nonsmokers (n = 506) allows characterization of the effects on pulmonary function of asbestos inhalation alone, unconfounded by cigarette smoking.

METHODS

Details concerning subject selection, medical evaluation and radiographic reading are given in a companion paper.[1] Subjects were studied in 19 cities in North America over a two year interval. Spirometric tests adhered to current guidelines;[2] at least 3 acceptable efforts were obtained on each subject, who was standing and wore a noseclip. A computerized rolling seal spirometer was used; efforts were monitored by maximum expiratory flow-volume curves recorded in real time and all data, including the flow volume arrays, were stored on digital tape.

Predicted values were those published by this laboratory using the same equipment in a random sample of the population of a large industrial state, adjusted for the effects of smoking in current smokers (which were significant on all tests except FVC).[3]

"Nonsmokers" (NS) smoked less than one cigarette a day, had smoked ≤ ten cigarettes a day for ≤ six months or smoked only cigars and pipes, which are not inhaled. Current smoker (SM) exceeded these limits. "Ex-smokers" (XS) exceeded these limits and had discontinued smoking ≥ two years previously.

Impairments were defined as follows:

Normal (Nl): Nl. FVC, FEV_1/FVC and MMF;

Restrictive (Rest): FVC <95% lower confidence interval (CI)

Restrictive (Rest): FVC <95% lower confidence interval (CI), ↓FEV_1/FVC nl (≥0.65 age ≥60, ≥0.70 age 30–59);

Overt Obstructive (Obs): FVC nl, FEV_1/FVC below limits defined above;

Small Airways Dysfunction (SAD): FVC nl, FEV_1 /FVC normal, $FET_{25-75\%}$ (also called mid-expiratory time) ≥0.78 sec;[5]

Combined, primarily restrictive (Comb Rest): Both FVC and FEV_1/FVC ↓ ; ↓ FVC ≥ ↓ FEV_1/FVC;

Combined, primarily obstructive (Comb Obs): ↓ FEV_1/FVC > ↓ FVC.

RESULTS

Mean Values

Table I shows mean demographic, exposure and pulmonary function variables for NS and those with a smoking history. There is no difference in age, DURON or years exposed. FVC and FEV_1 are reduced in the NS, but not FEV_1/FVC or the flows $FEF_{25-75\%}$ or $FEF_{75\%}$. FVC and FEV_1 are reduced to a greater extent in the smokers but FEV_1 /FVC and flows are only minimally reduced using smoking specific predicted values.

Prevalences of Functional Impairment

By Smoking History (Table II):

Of the 2573 workers studied, 506 (19.7%) were NS, 861 (33.5%) SM and 1206 (46.9%), XS. This last group, which includes only those who have discontinued smoking for at least 2 years, reflects the effect of educational efforts to discontinue smoking among asbestos workers.

Table I

Demographic, Exposure and Pulmonary Function Variables by Smoking History (Mean and SD)

	Nonsmokers (n = 506)	Current and Ex-Smokers (n = 2067)
Age (yrs)	58.6 (8.6)	57.3 (8.0)
Height (cm)	173.2 (6.9)	174.0 (6.6)
Duron (yrs)	36.3 (7.6)	34.9 (7.0)
Yrs exposed	32.0 (8.3)	31.6 (7.5)
Dur smoking (yrs)	0	31.6 (12.0)
Pack years	0	40.6 (26.1)
FVC (% pred)	86.5 (16.6)	82.0 (17.3)
FEV_1 (% pred)	85.5 (17.4)	82.3 (20.6)
$FEF_{25-75\%}$ (% pred)	96.6 (36.2)	86.6 (40.1)
$FEF_{75\%}$ (% pred)	101.2 (45.5)	97.7 (49.3)
FEV_1/FVC x 100	79.2 (7.6)	73.4 (10.5)
FEV_1/FVC (% pred)	100.6 (9.5)	97.1 (13.5)

Table II

Spirometric Impairments in 2573 Asbestos Insulators ≥20 Years from Onset of Exposure (by Smoking History)

	NS (19.7%)*	SM (33.5%)	XS (46.9%)	All Smoking Categories
Normal pf	222 (43.9)*	146 (17.0)	376 (31.2)	744 (28.9)
Restrictive	156 (30.8)	270 (31.4)	413 (34.2)	839 (32.6)
Obstructive	17 (3.4)	144 (16.7)	92 (7.6)	253 (9.8)
Small Airways	98 (19.4)	145 (16.8)	204 (16.9)	447 (17.4)
Combined	13 (2.6)	156 (18.1)	121 (10.0)	290 (11.3)
Combined, rest	11 (2.2)	110 (12.8)	92 (7.6)	213 (8.3)
Combined, obst.	2 (0.4)	46 (5.3)	29 (2.4)	77 (3.0)
All Impairments	506	861	1206	2573

* Percentages are shown in parentheses. Percentages after each smoking category are of the total population (e.g., 19.7% of the population were NS). Percentages within each smoking category are of each impairment within that smoking category (e.g., 43.9% of NS had nl pf).

The prevalence of several impairments varies by smoking history. Normal pulmonary function was most likely in NS (43.9%) and least in SM (17.0%); XS were intermediate (31.2%). Overt obstruction was most likely in SM (16.7%) and least in NS (3.4%). While restrictive impairment by itself did not vary in frequency by smoking category, combined impairment was far more common in SM (18.1%), again with XS intermediate. Frequency of small airways dysfunction was similar in all smoking categories.

By radiographic abnormality (Table III):

Normal pulmonary function was most likely (43.4%) when the chest radiograph was normal and least likely (21.2%) when both parenchymal and pleural disease was present. While frequencies of small airways dysfunction did not vary by radiographic abnormality, restrictive and combined impairments were most common when parenchyma and pleura were both abnormal and obstruction was more likely when only the parenchyma was abnormal. Interestingly, when frequency of restriction was compared in *isolated parenchymal* vs. *isolated pleural* disease, it was greater in the latter (34.4% vs. 22.3%).

Despite the greater frequency of normal function when the radiograph was normal (43.3%), 21.3% of those with a normal film had restriction and 7.7% had combined impairment, meaning that 29% had a reduced FVC. Similarly, while a normal film was more likely when pulmonary function was normal (25.1%), 10.4 percent of workers with restriction had a normal film.

Table III

Spirometric Impairments in 2573 Asbestos Insulators ≥20 Years from Onset of Exposure (by Radiographic Abnormality)

	"Normal" (16%)*	Parenchymal Only (11.7%)	Both (Parpleu) (48.2%)	Pleural Only (24.1%)	All Radiograph Categories
Normal pf	187 (43.3)*	105 (34.9)	263 (21.2)	189 (30.5)	744 (28.9)
Restrictive	88 (21.3)	67 (22.3)	471 (38.0)	213 (34.4)	839 (32.6)
Obstructive	36 (8.7)	37 (12.3)	121 (9.8)	59 (9.5)	253 (9.8)
Small Airway	77 (18.6)	64 (21.3	202 (16.3)	104 (16.8)	447 (17.4)
Combined	25 (7.7)	28 (9.3)	182 (14.7)	55 (8.9)	290 (11.3)
All Impairments	413	301	1239	620	2573

* Percentages are shown in parentheses. Percentages after each radiographic abnormality are of the total population (e.g., 16% of the population had normal films). Percentages within each radiographic abnormality are of each impairment within that radiographic abnormality (e.g., 43.3% of subjects with normal films had normal pulmonary function).

The percentage of NS was relatively greater in subjects with normal pulmonary function no matter in which radiographic category they fell whereas the percentage of SM was increased in those with obstructive or combined impairments within each radiographic category.

By Duration from Onset of Exposure (Table IV): Frequency of normal pulmonary function fell with increased duration of exposure while frequency of restriction and of combined impairment increased. Small airways dysfunction did not change and obstruction actually decreased.

Regression Analysis of Pulmonary Function

FVC (analyzed as percent predicted, to adjust for age and height) and the actual ratio FEV_1/FVC were analyzed for the contributions of such independent variables as radiographic category (any par, any pleu and parpleu interaction), DURON and pack years (Table V). Parenchymal involvement was not significant for FVC, although pleural and combined parenchymal-pleural involvements were. Pleural involvement (alone or combined) was not significant for FEV_1/FVC: The predominant influence on FEV_1/FVC was pack years, each pack year diminishing the FEV_1/FVC (x 100) by 0.11 so that 41 pack years (the mean of all subjects with a positive smoking history) would diminish the FEV_1/FVC (x 100) by 4.5. By contrast, DURON 35 years (the mean of all subjects in the study) would diminish FEV_1/FVC (x 100) by two-thirds of the smoking effect (2.9) and the presence of parenchymal disease on chest film would diminish the ratio negligibly (0.013).

Each year from onset diminished the FVC by 0.436 percent of predicted, so that DURON 35 years would diminish FVC by 15.3 percent of predicted, whereas each pack year diminished FVC by 0.096 percent of predicted. Cumulative decrement for 41 pack years was 3.9 per cent of predicted or 25% of the effect of DURON. The presence of pleural involvement on radiography diminished the value by 4.7 percent of predicted and the presence of parenchymal plus pleural involvement diminished the value by 7.8 percent of predicted.

DISCUSSION

The 2573 asbestos insulators are a large enough group to allow analysis of the effects on lung function of such independent variables as years from onset of exposure, cigarette smoking (pack years) and radiographic abnormalities. We used percent predicted FVC, the most easily and universally measured single test of pulmonary function, as our index of restrictive impairment. The largest effect was that of DURON, followed by combined pleuropulmonary involvement, smoking and isolated pleural involvement. As expected, smoking was the predominant influence on FEV_1/FVC, used as an index of airways obstruction. The effect of DURON is probably attributable to aging (which obviously parallels duration) since the FEV_1/FVC ratio is not adjusted for age as is percent predicted FVC.

In computing the prevalence of impaired pulmonary function, common practice has been to use as the numerator the number of subjects with abnormal values for *any* of the major pulmonary function parameters, e.g., FVC or FEV_1. This tends to obscure differences in the types of impairments and the relationship of these impairments to various exposures, e.g., asbestos vs. cigarette smoking. A reduced FVC is not necessarily indicative of restriction (airways obstruction with air trapping and an elevated RV may reduce

Table IV

Spirometric Impairments in 2573 Asbestos Insulators ≥20 Years from Onset of Exposure (by Duration from Onset of Exposure)

	≤ 29 Yrs. n = 331 (12.9%)	30-39 Yrs. n = 1593 (61.9%)	≥ 40 Yrs. n = 649 (25.2%)
Normal	127 (38.4)	470 (29.5)	147 (22.7)
Restrictive	84 (25.4)	487 (30.6)	268 (40.3)
Obstructive	39 (11.8)	171 (10.7)	43 (6.6)
Small Airways	56 (16.9)	287 (18.0)	104 (16.0)
Combined	25 (7.6)	178 (11.2)	87 (13.4)

Table VA

Regression Analysis of Percent Predicted FVC
Percent Predicted FVC (n = 2667)

Intercept	106.19
Duron	-0.436 (p0.0001, F 92.4)
Pack Yrs.	-0.096 (p0.0001, F 74.2)
Any pleu	-4.676 (p0.0001, F 28.1)
Parpleu interact	-3.091 (p0.0001, F 14.8)
Any par	NS
R^2	11.7

Table VB

Regression Analysis of FEV_1/FVC
$FEV_1/FVC \times 100$ (n = 2573)

Intercept	81.949
Pack Yr.	-0.111 (p0.0001, F 265.8)
Any par	-0.013 (p0.0018, F 9.73)
Duron	-0.084 (p0.002, F 9.56)
Any pleu	NS
Parpleu interact	NS
R^2	11.1

the FVC as well) nor are reduced FEV_1 and flow rates specific for obstruction (restrictive disease will generally result in a reduction in FEV_1 and flow rates proportional to the reduction in FVC).

Instead, a mutually exclusive classification of impairments based on a *combination* of spirometric measurements, including the FEV_1/FVC ratio, was employed. We have published the prevalence of these impairments in 351 patients with chronic pulmonary sarcoidosis.[4] Preliminary results from our sampling of the population of the state of Michigan[5] show far lesser frequencies of restriction (7% NS, 9% XS, 12% CS) and combined impairment (0% NS, 5% XS, 5% CS) but similar or greater frequencies of obstruction (13% NS, 17% XS, 21% CS).

Not surprisingly, normal pulmonary function was most likely in NS (44%) and least likely in SM (17%) while obstruction was most likely in SM (17%) and least in NS (3%). FREQUENCY OF RESTRICTIVE IMPAIRMENT DID NOT VARY BY SMOKING HISTORY, consistent with the predominant effects on FVC of asbestos exposure (measured as years from onset) and radiographic evidence of pleuropulmonary or pleural fibrosis. However, combined impairment was far more frequent in SM (18%) than NS (2.6%), with XS intermediate. This pattern results from the addition of obstruction (attributable to smoking) to the restriction of pleuropulmonary fibrosis. Such combined impairment is frequently seen in advanced sarcoidosis, bronchiectasis, cystic fibrosis or silicosis (progressive massive fibrosis).[6,7]

It is of interest that the most common impairment in both SM and XS (as well as NS) was restriction. It is recognized that what we call combined impairment can also result from reduction in FVC secondary to air trapping in severe obstruction. True combined impairment and air trapping can be distinguished only by full lung volumes. These obviously cannot be measured using physiologic methods on such large numbers of subjects under survey conditions. (We hope to measure full lung volumes using a planimetric method[8] on the posteroanterior and lateral chest films of these workers). We attempted to separate combined impairments into "predominant restrictive," and "predominant obstructive" by the relative decreases in FVC vs. FEV_1/FVC.

RESTRICTION WAS IDENTIFIED AS THE PREDOMINANT ELEMENT IN THE COMBINED IMPAIRMENT IN ALL SMOKING CATEGORIES (Table II)

The large number of NS in our study permits us to characterize the pulmonary function patterns attributable to inhalation of asbestos fibers alone. The 3 percent prevalences each of overt obstruction and of combined impairment do not provide strong evidence for obstructive impairment resulting from such inhalation (Table II). Half of the patients with these impairments (14 of 30) did not show radiographic evidence of pulmonary fibrosis. These 30 (of 506) NS may well have an independent cause of obstruction (e.g., asthma).

The decrease in frequency of obstruction with increasing

duration of exposure is the reciprocal of the increase in combined impairment, resulting from the superimposition of restriction in subjects with obstruction.

The greater contribution of radiographically identified pleural fibrosis (by itself) than of interstitial fibrosis (by itself) to restrictive impairment is seen in the regression analysis (Table V) and in the higher frequency of restrictive and combined impairments in those with isolated pleural vs. isolated parenchymal involvement (Table III). These findings concerning pulmonary function are similar to those concerning dyspnea in this population[1,9] and demonstrate the important effect of pleural fibrosis on lung function. These conclusions concerning pleural vs. parenchymal fibrosis may not be generalizable to other exposed populations for the following reasons:

1. This population was selected for long duration from onset and for heavy occupational exposure.
2. It is to a certain extent a survivor population in which those with the most severe interstitial fibrosis may have died (either of respiratory insufficiency or of bronchogenic carcinoma).
3. The largest proportion of subjects (48.2% of all subjects and 52.4% of those with abnormal films) had pleuropulmonary disease.

However, pleural disease is more prominent than interstitial fibrosis in many occupations with less intense exposure, and in family exposures. The important effect of pleural disease on lung function may be relevant to these groups.

Pulmonary function tests are used not only to *quantify* and *characterize* impairment in asbestos-related disease but to *detect* evidence of disease which is not apparent clinically or radiologically. In this regard, it is noteworthy that 21.3% of those with a normal film had restriction and an additional 7.7% had combined impairment and that of those with only pleural disease, 34.4% had restriction and an additional 8.9% had combined impairment. Further testing, especially of gas exchange (D_L, V_D/V_T) would undoubtedly uncover additional individuals with intrinsic lung disease despite normal lung fields on chest radiograph.

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MORTALITY AND CANCER INCIDENCE AMONG SWEDISH CERAMIC WORKERS WITH SILICOSIS

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The question whether quartz exposure increases the risk for lung cancer was raised 50 years ago by Anderson & Dible.[1] More recently two literature reviews considering both animal experiments and epidemiological investigations have been published, one talking for[3] and the other against[4] such an association. In most published epidemiological investigations the subjects have, beside quartz, been exposed to known lung carcinogens such as polycyclic aromatic hydrocarbons in the foundry industry and ionizing radiation in mining, which make the interpretation difficult.[5] This investigation, which has become a part of a multicenter initiative by IARC, was undertaken in order to study the risk for lung cancer in the Swedish ceramic industry, where no confounding lung carcinogens are known to occur.

MATERIAL AND METHODS

The Swedish Pneumoconiosis Registry has compiled case notifications from 1931 and onwards. The study population consists of those 314 males from the ceramic industry who had been accepted as compensated cases of silicosis. Since there were only 36 females they were excluded from analysis.

The vital status of the study persons was established by linking the ten-digit identification number based on time of birth for each person with the census register for all living persons in Sweden, the death register of all deceased persons in Sweden, and the emigration register. By these procedures all but one of the persons could be identified as alive or deceased during the study period.

During the study period (1951–1985) for the mortality analysis the study population has accumulated 5695 person-years. Cause of death from the death certificates was recorded on all deceased persons in the study population.

The Swedish Cancer Registry was established in 1958 and receives notifications on more than 95% of all malignancies. During the study period (1958–1983) for the cancer incidence calculations the study population had accumulated 4247 person-years. The cancer morbidity was established by linking the identification numbers of the individuals in the study population with the National Cancer Register.

The expected number of deaths and malignancies was calculated by multiplying person-years of observation within five-year age categories during each year of the study periods by site- and gender-specific national rates. The calculations of standardized mortality/morbidity rates (SMR) with 95% confidence intervals (CI) based on a Poisson distribution was performed by a computer program developed at the University of Linköping (EPILIN program package).

RESULTS

The overall mortality in the study population was increased (SMR=138; CI 120–157) due to an excess in mortality from respiratory tuberculosis (SMR=1932; CI 1144–3054) and other non-malignant respiratory diseases (SMR=746; CI 577–947).

There was no overall increased incidence of malignant diseases in the study population (SMR=94; CI 67–126). However, nine cases of lung cancer were observed vs. 4.8 expected (SMR=188; CI 85–356). With a latency time requirement of 10 years from discovery of silicosis SMR was 236 (CI 107–448), and with a latency time of 20 years there was a further increase (SMR=267; CI 98–582). Lung cancer was diagnosed 36–72 years after first quartz exposure and 11–32 years after that silicosis had been detected.

DISCUSSION

The results from this study on Swedish ceramic workers with silicosis demonstrate an increased mortality in non-malignant, but not in malignant, respiratory diseases. However, the lung cancer incidence was doubled.

The size of the cohort is small, and we have no data on smoking habits in the study population. The results are, however, in accordance with other studies on silicotics from the ceramic industry. An increased risk among pottery workers of dying from lung cancer has been reported, especially if they had been exposed to talc,[7-9] but also in individuals with no talc exposure.[8] Talc was, however, only used in four of the 19 factories in our study, and the lung cancer cases were not accumulated to these factories. A recent Italian case-referent study among ceramic workers controlling for age, period of death and smoking did also show an increased lung cancer risk, especially among individuals with silicosis.[2]

The mechanism for a carcinogenic effect of quartz is not clear. A direct carcinogenic effect is supported by the cytotoxic effect of quartz *in vitro*.[6] It has been shown

among ceramic workers that silicotics have a greater risk for lung cancer than non-silicotics.[2] This could be due to a higher quartz exposure, but a causal relationship between the silicotic lesions and the cancer should be considered. Fibrotic lesions in the lung might impair the pulmonary clearance mechanisms for various carcinogenic substances, and a high incidence of bronchial carcinoma has been reported among individuals with various fibrotic lung diseases without relationship to dust exposure.[10]

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PATHOLOGY CLASSIFICATION AND GRADING SCHEMATA FOR SILICOSIS

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ABSTRACT

In 1985, the National Institute for Occupational Safety and Health established a committee to review the pathology of silicosis and the silicate-associated lung diseases, and to develop a classification and pathology grading system for epidemiological studies. The committee considered a number of different schemata developed in the USA and abroad. However, we were unsuccessful in devising a satisfactory approach which would permit pathology grading for correlative studies. An outline of the various proposed grading systems will be presented, and the shortcoming and problems in their utilization and broad application will be discussed.

No Paper provided.

MICROBIAL CONTAMINANTS OF STORED TIMBER AS POTENTIAL RESPIRATORY HAZARDS FOR SAWMILL WORKERS

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INTRODUCTION

Occupational exposure to wood dust may be a cause of respiratory diseases such as hypersensitivity pneumonitis (allergic alveolitis),[7,12,23,26] asthma[8] and chronic obstructive lung disease (COLD).[2] The etiology of these diseases is not fully known and both the allergenic and/or toxic constituents of wood tissue itself and the substances produced by microorganisms developing in wood have been suggested as potential agents.[8,10,22,27] Many species of allergenic and/or toxic molds developing on wood (*Alternaria tenuis, Aspergillus fumigatus, Cryptostroma corticale, Mucor spp., Paecilomyces spp., Penicillium spp., Rhizopus spp.)* have been described as causative agents of pulmonary diseases in woodworkers.[6,7,8,12,23,24,25,26] The role of bacterial factors in wood-associated diseases was studied to a lesser extent.[10,22] It has been reported that woodworkers may be exposed to notable amounts of gram-negative bacteria and endotoxin.[1,4,25]

The aim of this study was to extend the knowledge of the potential respiratory risk of woodworkers to wood-inhabiting microorganisms by quantitative and qualitative determination of the microflora of stored timber logs scheduled for processing in a sawmill.

MATERIAL AND METHODS

Two series of microbiological wood samples were taken in August and October of the year 1987 from timber logs stored on the lumber yard at a sawmill in Kingwood, West Virginia. The logs had been stored for a period of 4–6 weeks and did not show any apparent signs of decay. At each sampling time, samples were taken from a log of each of the following species: American basswood (*Tilia americana L.*), black cherry (Prunus serotina Ehrh.), black locust (*Robinia pseudoaccacia L.*), red oak (*Quercus coccinea Muenchh.*), soft maple (*Acer saccharinum L.*) and white poplar (Populus alba L.). From each log, one sample was taken from the heartwood (by boring from the transverse section), one from the sapwood (by boring from the transverse section) and one from the bark (by centripetal boring).

The wood samples were collected with a novel "drill and collect" device (model #2) for quantification of microorganisms in wood.[5] This is a manually operated drilling device in which a combined action of a twist boring bit and a spring-containing mobile ring collects the pulverized wood into a sterile flask attached beneath the bit in a one-step sterile process. The wood surface to be sampled was first sterilized by wiping with 70% propanol and "Clorox" (a commercial 5.25% sodium hypochlorite solution) and then an average sample was taken by multiple boring (5–7 times) in a circle up to 3 cm in diameter.

The concentrations of bacteria and fungi in the wood samples were determined by dilution plating. Aliquots of 200 mg of each sample were suspended in 20 ml of sterile phosphate buffered saline (Sigma Chemical Co., St. Louis, MO) containing 0.1% (v/v) Tween 80 (Fisher Scientific Co., Fair Lawn, NJ) and, after vigorous shaking, serial 10-fold dilutions were made up to 10^{-6}. The 0.1 ml aliquots of each dilution were spread on duplicate sets of the following agar media: (i) sheep blood agar for total aerobic bacteria, (ii) eosin methylene blue agar (EMB agar; Difco Lab., Detroit, MI) for gram-negative bacteria, (iii) half-strength tryptic soya agar (Difco) for thermophilic actinomycetes, (iv) rose bengal streptomycin agar (RBS) for total fungi, and (v) yeast malt agar for yeasts. The blood agar and EMB plates were incubated for 48 hrs at 35°C, the tryptic soya plates for 120 hrs at 55°C, and the RBS and yeast malt plates for 96 hrs at 28°C.

Following incubation, bacterial colonies were counted and differentiated on the basis of colony morphology, Gram reaction, and biochemical reactions. The gram-positive isolates were identified according to Bergey's Manual.[21] The gram-negative isolates were identified with the API^{R} Systems 20 E (for enterobacteria) and NFT (for non-fermenting bacteria) (API Analytab Products, Plainview, NY), using supplementary biochemical tests selected according to Bergey's Manual[14] and API^{R} Systems recommendations. Mold colonies were counted and differentiated on the basis of morphological properties. Representative yeast colonies were isolated and differentiated on the basis of morphological and biochemical properties.[13] Final results for microbial concentrations were reported in terms of the colony forming units (cfu) in one gram of ground wood.

For endotoxin determination, 100 mg portions of the wood samples were extracted with 5 ml of sterile non-pyrogenic water (Travenol Laboratories Inc., Deerfield, IL) by rocking for 60 min. at room temperature. The suspension was centrifuged at 1000 g for 10 minutes to remove particulate debris, and the supernatant fluid was separated for further

analysis. Quantification of gram-negative bacterial endotoxin content was performed in duplicate by a quantitative chromogenic modification of the Limulus amebocyte lysate test (QCL-1000; Whittaker Bioproducts, Walkersville, MA). Results were reported in terms of Endotoxin Units (EU) in one gram of ground wood.

The Students' t-test for matched pairs, test for linear regression and chi-square test were used for statistical evaluation of the results.

RESULTS

The concentration of microorganisms and endotoxin varied significantly with the kind of wood examined ($P<0.001$). As shown in Figures 1–6, the highest levels of bacteria, fungi and endotoxin were found in the wood samples from logs of American basswood and black locust (10^3–10^8 cfu/gm, 10^2–10^7 cfu/gm and 10^4–10^6 EU/gm, respectively). The levels were lower in the logs of soft maple and black cherry (0–10^6 cfu/gm, 0–10^7 cfu/gm and 10^1–10^4 EU/gm, respectively) and lowest in the logs of white poplar and red oak (0–10^4 cfu/gm, 0–10^5 cfu/gm and 10^0–10^5 EU/gm, respectively).

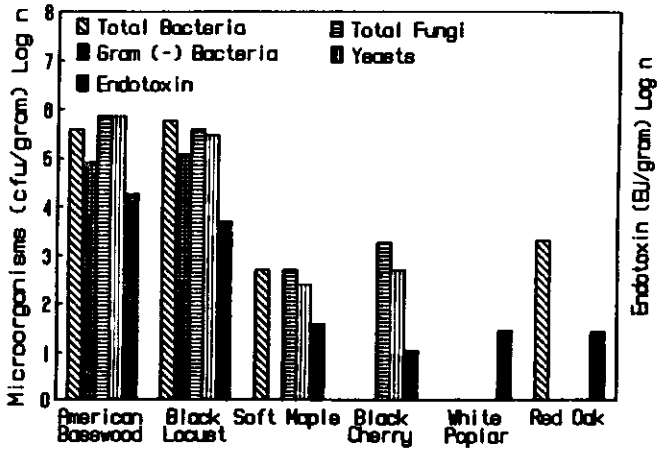

Figure 1. Concentrations of bacteria, fungi and endotoxin in the samples of heartwood collected in August, 1987.

High concentrations of bacteria, fungi and endotoxin were found in all the examined kinds of wood tissue: heartwood (Figures 1–2), sapwood (Figures 3–4) and bark (Figures 5–6). No significant differences were noted between the contamination rates in August and October ($P>0.05$).

In most of the samples of heartwood and sapwood, gram-negative bacteria dominated the total bacteria flora. Except for two cases (Figure 5), this was not observed in the bark samples. In bark samples taken in October, viable gram-negative bacteria were absent completely and the very high level of bacteria found in the bark of the black locust was due to the presence of large numbers of spore-forming bacilli (Figure 6). For each kind of wood tissue (heartwood, sapwood and bark) a significant correlation has been found between the concentrations of gram-negative bacteria and endotoxin ($P<0.05$). No thermophilic actinomycetes were found in the examined wood samples.

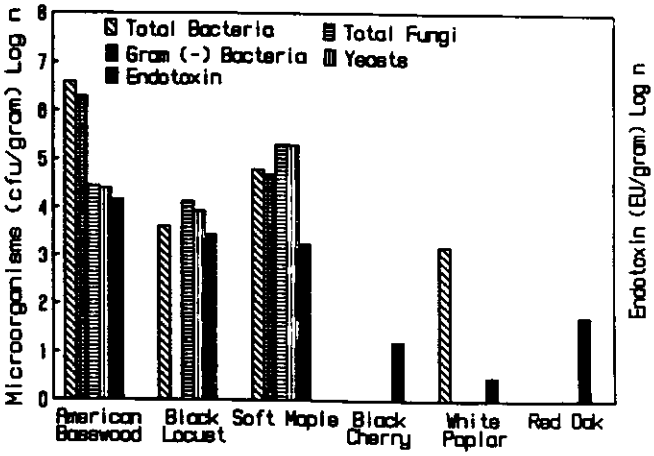

Figure 2. Concentrations of bacteria, fungi and endotoxin in the samples of heartwood collected in October, 1987.

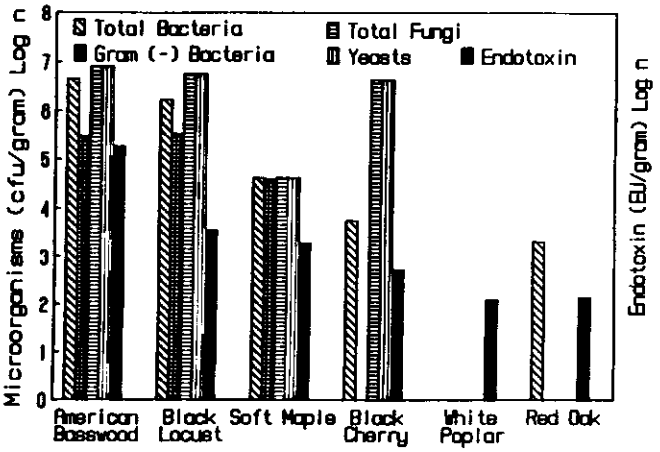

Figure 3. Concentrations of bacteria, fungi and endotoxin in the samples of sapwood collected in August, 1987.

Twelve species and/or genera of gram-negative bacteria and seven genera of gram-positive bacteria were found in the wood samples (Table I). The gram-negative flora comprised five fermentative species (belonging to the *Enterobacteriaceae* family) which, in most cases, were associated with the sapwood and seven non-fermentative species (mostly of the genus *Pseudomonas)* which were mostly associated with the heartwood. Among the gram-positive bacteria, the most common organisms were endospore-forming bacteria of the genus *Bacillus* and coryneform bacteria belonging to the genera *Arthrobacter, Brevibacterium, Corynebacterium* and *Microbacterium.*

In all kinds of wood samples examined, yeasts were the predominant fungi observed (Figures 1–6, Table II) and the

Table I

Species of Bacteria Occurring in Wood Samples

Name of the species	Heartwood	Sapwood	Bark	Maximal concentration (X 10^5 cfu/gram)
GRAM-NEGATIVE BACTERIA				
Fermentative				
Citrobacter freundii	+ (B, M)	++ (B), + (M)		0.10 (Sapwood, B)
Enterobacter agglomerans	++ (B), + (M)	+++ (B), + (M)	++ (B, L)	3.00 (Sapwood, B)
Enterobacter cloacae		++ (M)		0.38 (Sapwood, M)
Klebsiella sp.		+++ (B), + (M)		1.45 (Sapwood, B)
Serratia rubidaea	++ (L)	++ (L)		0.41 (Sapwood, L)
Non-fermentative				
Acinetobacter calcoaceticus	+ (M)		+++ (L)	30.50 (Bark, L)
Agrobacterium radiobacter	+++ (L)	+++ (L)		2.64 (Sapwood, L)
Pseudomonas fluorescens	+ (M)			0.07 (Heartwood, M)
Pseudomonas maltophilia	+ (M)			0.02 (Heartwood, M)
Pseudomonas oryzihabitans	+++ (B)			15.10 (Heartwood, B)
Pseudomonas putida	+++ (B), ++ (M)	+ (B)		3.84 (Heartwood, B)
Pseudomonas stutzeri	++ (B), + (M)	+ (M)		0.45 (Heartwood, B)
GRAM-POSITIVE BACTERIA				
Bacillus spp.	+++ (B), ++ (L), + (M)	+++ (L), + (B, M)	+++ (L, M), ++ (B), + (C, O, P)	154.00 (Bark, L)
Coryneform bacteria*	+++ (B, L), + (P)	+++ (B, L) + (C, M, O)	+++ (L), ++ (B, M), + (C, P)	20.30 (Heartwood, B)
Staphylococcus spp.	+ (M, O, P)	+++ (L), + (O)	+ (P)	5.00 (Sapwood, L)
Streptomyces spp.		+++ (L)	++ (L), + (B)	2.51 (Sapwood, L)

B = American Basswood M = Soft Maple + = occurred in concentration below 1 x 10^4 cfu/gram *Comprise: *Arthrobacter spp.*, *Brevibacterium spp.* *Corynebacterium spp.*.

C = Black Cherry O = Red Oak ++ = occurred in concentration 1 x10^4 - 1 x 10^5 cfu/gram

L = Black Locust P = White Poplar +++ = occurred in concentration over 10^5 cfu/gram

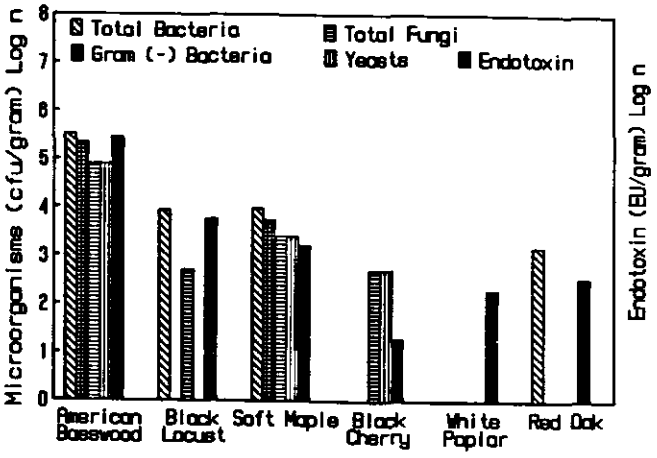

Figure 4. Concentrations of bacteria, fungi and endotoxin in the samples of sapwood collected in October, 1987.

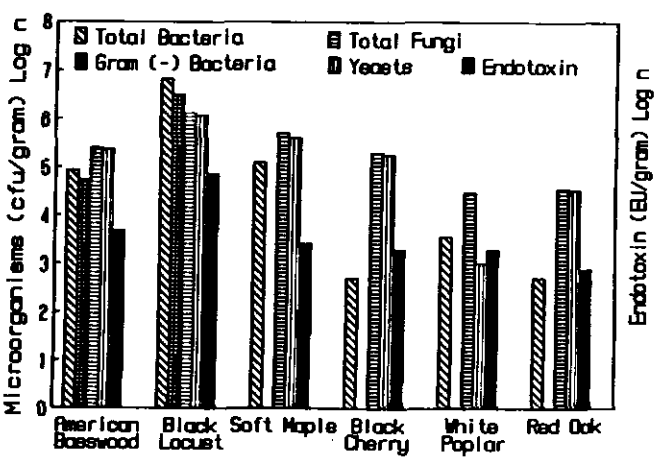

Figure 5. Concentrations of bacteria, fungi and endotoxin in the samples of bark collected in August, 1987.

Table II
Fungi Occurring in Wood Samples

Organism	Heartwood	Sapwood	Bark	Maximal concentration (X 10^5 cfu/gram)
DBB- yeasts[a]	+++ (B,L), ++ (M) + (C)	+++ (B,C,L), ++(M)	+++ (B,L,M), ++ (C,O), + (P)	78.35 (Sapwood, B)
DBB+ yeasts[b]	++ (B,L,M)	+++ (B), ++ (C,L)	++ (B,C,L,O)	1.45 (Sapwood, B)
Acremonium sp.	++ (L), + (B)	++ (L)	+++ (M), + (B,P)	14.00 (Bark, M)
Oidiodendron sp.			++ (C,M)	0.79 (Bark, M)
Penicillium sp.	++ (L)	++ (B,L)	++ (L,P), + (B,C,O)	0.72 (Bark, L)
Trichoderma sp.		++ (C)	++ (B,L)	0.49 (Bark, L)
Nonsporulating	+ (B,C,M)		++ (L,M), + (B,O,P)	0.26 (Bark, M)

[a]Negative reaction with Diazonium Blue B (DBB); presumptive Ascomycetes and their anamorphs (includes Candida zeylanoides, other undetermined Candida spp., and Hansenula silvicola.

[b]Positive reaction with DBB; presumptive Basidiomycetes and their anamorphs (includes undetermined Candida spp., Cryptococcus laurentii, and Rhodotorula glutinis).

B = American Basswood M = Soft Maple + = occurred in concentration below 1 x 10^4 cfu/gram

C = Black Cherry O = Red Oak ++ = occurred in concentration 1 x 10^4 - 1 x 10^5 cfu/gram

L = Black Locust P = White Poplar +++ = occurred in concentration over 10^5 cfu/gram

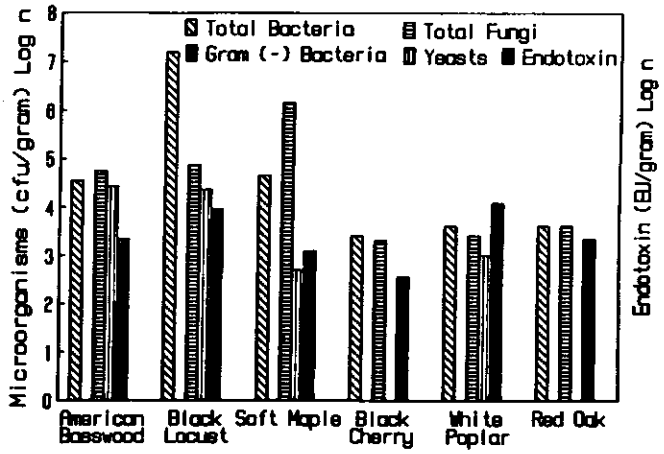

Figure 6. Concentrations of bacteria, fungi and endotoxin in the samples of bark collected in October, 1987.

most numerous among them were presumptive Ascomycetes and their anamorphs, i.e., they gave a negative reaction with Diazonium Blue B (DBB).[13] Yeast fungi tended to be found in the greatest numbers in the sapwood. Species of yeast isolated include undetermined *Candida spp.* (include both DBB+ and DBB− species), *Candida zeylanoides, Cryptococcus laurentii, Hansenula silvicola and Rhodotorula glutinis*.

Molds found in these samples included *Acremonium (Cephalosporium sp., Alternaria sp., Aspergillus fumigatus, Aureobasidium pullulans, Bispora sp., Cladosporium sp., Mortierella sp.,* and *Trichoderma sp.* as well a number of fungi that could not be identified because of their failure to sporulate. The molds that occurred in the greatest numbers were *Acremonium sp., Oidiodendron sp., Penicillium sp.,* and *Trichoderma sp.*. The highest numbers of molds were found in the bark.

DISCUSSION

The levels of microorganisms and endotoxin in timber logs showed notable variation depending on the species of the tree. The concentrations of bacteria and fungi in the most contaminated wood species (basswood, locust) exceeded the level of 10^6 cfu/gm, and were comparable to the values reported for certain organic dusts related to harmful respiratory effects in workers.[3]

The concentration of endotoxin in the wood reached, in many cases, a level of 10^5–10^6 EU/gm which corresponds to the values found in organic materials (grain, silage, mushroom farm pre-flush) associated with the cases of respiratory disorders in exposed workers.[17] This finding is in agreement with the fact that some of the wood samples contained high concentrations of gram-negative bacteria. Among these bacteria were the species *(Enterobacter agglomerans, Klebsiella spp., Pseudomonas putida)* which are known producers of biologically active endotoxin that can cause pulmonary

injury through non-specific stimulation of alveolar macrophages.[19]

The occurrence of high concentrations of fungi in the wood presents another factor of potential respiratory risk for sawmill workers. The *Penicillium* species that were frequently isolated in this study have been reported as a source of the pathogenic respiratory allergens.[6,24] Another potentially pathogenic species are *Aspergillus fumigatus* and *Aureobasidium pullulans*.[8,10,22]

The data conform to some earlier reports on the occurrence of bacteria and fungi in the wood[9,15,16,18] The composition of the microflora of examined logs, characterized by the prevalence of yeasts and gram-negative bacteria indicates that it was in the stage of "pioneer colonization" which precedes the stage of wood decay by brown rot and white rot fungi.[11,20]

The main conclusion from this preliminary study is that some kinds of apparently not decayed timber stored for processing in sawmill contain very high concentrations of "pioneer" microorganisms and their toxins. These organisms may cause respiratory disorders in the woodworkers if inhaled with the sawdust. Although not defined by the current study, the potential problems associated with microbiologically contaminated woods are intriguing and require further research.

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Mention of company names or products does not constitute endorsement by the National Institute for Occupational Safety and Health.

MICROBE EXPOSURE AND THE OCCURRENCE OF ANTIBODIES AGAINST THE EXPOSING MICROBES AMONG WOOD WORKERS IN CELLULOSE INDUSTRY

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ABSTRACT

Exposure to airborne fungal spores and bacteria, and occurrence of antibodies against the most common fungal[14] and bacterial[3] species in sera of the 11 workers were studied in a cellulose factory. Air samples for microbiological analysis were taken by a six-stage Andersen impactor in barking department and on wood chip piles out-of-doors. Barking workers were exposed mainly to bacteria (geometric mean of bacterial concentration 46.3×10^3 cfu/m^3) and to lesser extent to fungal spores (5.9×10^3 cfu/m^3) in contrast to catepillar drivers on wood chip piles (1.5×10^3 cfu/m^3 and 45.5×10^3 cfu/m^3 respectively). Rhodotorula glutinis was the dominating fungal species in the barking department and Aspergillus fumigatus and Penicillium brevicompactum on wood chip piles.

Enzyme-linked immunosorbent assay (ELISA) found differences in IgG-antibody levels between different microbial species as also between different work environments. Highest antibody levels were found against Paecilomyces variotii, Sporobolomyces salmonicolor and Aspergillus niger while lowest levels were found against Rhizopus nigricans, Humicola grisea and Streptomyces albus. Generally, the levels of antibodies against fungal species were 2–5 times higher in the wood chip workers than those in the barking workers. Although the amount of the bacteria in the barking department was about 30 times higher than that on the wood chip piles, no differences in the levels of bacterial antibodies were found between the two groups.

Probably the dry microbial material such as that in wood chip work penetrates into the lower parts of the respiratory tracts and initiates the formation of antibodies more easily than the moist aerosols.

INTRODUCTION

In pulp production wood used as raw material is cutted after barking into chips and stored outdoors in huge piles, where chips are transferred by caterpillars. Chips are stored approximately a couple of months before taking in to the production. During the storage microbiological changes occur in the piles (Bergman and Nilsson 1979, Pellikka and Kotimaa 1983). Some cases of allergic alveolitis have been described among wood workers after exposure to fungal spores (van Assendelft et al. 1985, Lundgren and Rosenhall 1979, Jorgensen and Fjellheim 1982). Wood is barked in big barking drums, where water is used in the process. Water is circulated and becomes contaminated by bacteria and fungi. Process is mostly open and water becomes easily aerosolized. Microbial aerosols from humidifiers may cause so-called humidifier fever (Rylander et al. 1978, Marinkovich and Norey 1983). Because of respiratory symptoms among wood workers in a cellulose factory in central Finland, microbe exposure and the antibodies against 17 most common exposing microbes were investigated.

MATERIALS AND METHODS

Subjects and Serum Samples

Serum samples from six catepillar drivers on wood chip piles and four workers in the barking department were taken within two weeks after air sampling. All the examined workers had work-related symptoms suggesting allergic background with microbial etiology (Table I).

Air Sampling for Estimating the Microbe Exposure

Air samples for microbiological analysis were collected by a six-stage fractionating impactor (model 10-800, Andersen Inc., Georgia, USA) (Andersen 1958). Three sets of media were used in successive samplings on each sampling site: Hagen-medium (incubated at 20°C) was used for mesophilic fungi, the same medium incubated at 40°C was used for thermotolerant fungi and plate count agar was used for total count of mesophilic bacteria. 10 air samples for each microbe group were collected both on wood chip piles and in the barking

Table I

Workers' Age, Type of Work, the Duration of Exposure, Symptoms, and the Clinical Findings

ID.CODE	AGE (YRS)	WORK	DUR.OF EXPOSURE (YRS)	SYMPTOMS R E C F M D	CL. FINDINGS PEF	ESR
VA 1	55	CD	25	- - - F M -	NORMAL	12
SA 2	38	CD	8	R - C - - -	NORMAL	2
LA 3	56	CD	14	- - C F M -	NORMAL	12
LI 4	39	CD	14	- - C F - -	NORMAL	5
KU 5	46	CD	26	R - - F - -	LOWERED	17
TO 6	36	WO/S	7/4	R - - - - D	NORMAL	4
KA 7	47	WO/B	4/3	R E - F M -	NORMAL	7
KA 8	37	B	17	R - C - - -	NORMAL	2
MA 9	37	B	15	- - C - - -	NORMAL	2
HA 10	47	B	17	- - C - - -	NORMAL	5

CD = CATERPILLAR DRIVER
WO = WOOD WORKER OUTDOORS
S = SLASHER
B = BARKING WORKER

R = RHINITIS
E = EYE IRRITATION
C = COUGH
F = FEVER
M = MUSCLE PAIN
D = DYSPNEA

ESR = ERYTHROCYTE SEDIMENTATION RATE

department. After incubation the number of colonies was counted, and the positive hole correction method was performed to calculate the concentrations of viable airborne microbes.

Antigens

For antigen preparation 14 fungal end 3 bacterial strains were subcultured from original cultivation plates in nutrient broth containing 5 g/l peptone (Difco Laboratories, Detroit, Mich., USA) and 3 g/l beef extract (Difco) at optimal temperature for each species. Bacterial growth was harvested by centrifugation and fungal growth by filtering, and washed three times by distilled water. Microbial pellets were disrupted mechanically (Ultra Turrax, Janke and Kunkel, Staufen i Breisgan, FRG) and then by ultrasonic disintegrator (Soniprep 150, MSE, Crawley, U.K.). The supernatants after a centrifugation at 40,000 g for 30 min were used as ELISA antigens.

Antibody Determination

IgG-antibodies were determinated by enzyme-linked immunosorbent assay (ELISA) carried out on disposable polystyrene microtiter plates (Immumoplate I, Nunc, Denmark). Microbial sonicates were used as antigen and alkaline phosphatase-labelled swine anti-human IgG (Orion Diagnostica, Espoo, Finland) was used as conjugate. Antibody levels were given as ELISA absorbance at a serum dilution of 1:100, read at 405 nm by a Titertek Multiskan (Eflab, Helsinki, Finland).

RESULTS

Microbe Exposure

Marked qualitative differences were found in the microbial exposure of caterpillar drivers and barking workers. Barking workers were exposed mainly to bacteria (geometric mean of bacterial concentration 46.3×10^3 cfu/m^3) and to lesser extent to fungal spores (5.9×10^3 cfu/m^3) in contrast to caterpillar drivers on wood chip piles and 1.5×10^3 cfu/m^3 and 4.5×10^3 cfu/m^3 respectively) (Table II). Rhodotorula glutinis was the dominating fungal species in the barking department, and Aspergillus fumigatus and Penicillium brevicompactum on wood chip piles (Table III).

Antibodies

Differences in antibody levels between different microbial species as also between different work environments were found by ELISA (Table IV). Highest antibody levels were found against Paecilomyces variotii, Sporobolomyces

Table II

Total Concentrations of Airborne Bacteria and Fungi (cfu/m^3) in the Barking Department and on Wood Chip Piles Outdoors ($\bar{x}$ = geometric mean)

	BARKING DEPARTMENT (n=10)		ON WOOD CHIP PILES (n=10)	
MICROBE GROUP	$\bar{x}$	RANGE	$\bar{x}$	RANGE
BACTERIA	46000	9200-230000	1500	770-35000
FUNGI	5900	1400-70000	45000	1000-200000

Table III

Concentrations of Airborne Microbes (cfu/m^3) in the Barking Department and on the Wood Chip Piles Outdoors ($\bar{x}$ = geometric mean)

	BARKING DEPARTMENT (n=10)		ON WOOD CHIP PILES (n=10)	
	$\bar{x}$	RANGE	$\bar{x}$	RANGE
Aspergillus fumigatus	28	0-740	40000	880-200000
Aspergillus niger	2	0-62	9	0-190
Humicola grisea	0	-	9	0-48
Paecilomyces variotii	2	0-41	6	0-110
Penicillium brevicompactum	500	41-3400	6000	12-88000
Rhizopus nigricans	2	0-33	3	0-71
Streptomyces albus	2	0-80	7	0-170
Trichoderma viride	110	17-490	5	0-24
Aureobasidium pullulans	5	0-44	2	0-24
Cephalosporium curtipes	0	-	0	-
Cladosporium cladosporioides	52	0-180	9	0-570
Geotrichum candidum	2	0-21	7	0-150
Phialophora bubakii	0	-	0	-
Rhodotorula glutinis	3900	510-65000	54	0-560
Sporobolomyces salmonicolor	1	0-10	8	0-150
Bacterium 1	930	180-4700	5	0-120
Bacterium 2	33000	8300-210000	9	0-800

Table IV

Antibody Levels ($\bar{x}$ + S.E.) Against the Microbes Found in the Working Environment in Barking Workers and in Wood Chip Workers

MICROBE	BARKING WOS (N=4) $\bar{X}$ + S.E.		WOOD CHIP WOS (N=6) $\bar{X}$ + S.E.	
ASP. FUMIGATUS	0.248	0.057	1.080	0.210
ASP. NIGER	0.477	0.120	1.362	0.242
HUM. GRISEA	0.074	0.011	0.136	0.015
PAEC. VARIOTII	0.408	0.082	1.528	0.103
PENIC. BREVICOMPACTUM	0.157	0.070	1.145	0.201
RHIZ. NIGRICANS	0.115	0.039	0.128	0.033
STR. ALBUS	0.087	0.014	0.172	0.029
TRICH. VIRIDE	0.443	0.107	0.810	0.194
AUR. PULLULANS	0.297	0.074	0.594	0.065
CEPH. CURTIPES	0.683	0.162	1.085	0.094
CLAD. CLADOSPORIOIDES	0.262	0.092	0.853	0.137
GEOTR. CANDIDUM	0.302	0.066	0.469	0.095
PHIL. BUBAKII	0.107	0.029	0.420	0.112
RHODOT. GLUTINIS	0.408	0.040	0.967	0.128
SPOROB. SALMONICOLOR	0.392	0.059	1.377	0.230
BACTERIUM 1	0.425	0.075	0.498	0.066
BACTERIUM 2	0.810	0.254	0.812	0.122

salmonicolor and Aspergillus niger while lowest were found against Rhizopus nigricans, Humicola grisea and Streptomyces albus. Generally, the levels of antibodies against fungal species were 2–5 times higher in the wood chip workers than those in the barking workers. No differences in the levels of bacterial antibodies were found between the two groups.

DISCUSSION

In the cellulose factory, the concentrations of airborne microbes except for bacteria were significantly higher on dusty wood chip piles than in the barking department, and correspondingly, the levels of antibodies against fungal species were higher in the wood chip workers than in the barking workers. Highest antibody levels were found against Paecilomyces variotii, Sporobolomyces salmonicolor, and Aspergillus niger and lowest antibody levels were found against Streptomyces albus, Humicola grisea and Rhizopus nigricans reflecting differences in capability of the species to stimulate a formation of antibodies. Although the amount of the bacteria in the barking department was about 30 times higher because of aerosolized processing water than that on the wood chip piles, no differences in the levels of antibodies against bacteria were found between the caterpillar drivers and the barking workers. Probably the dry microbial material such as that in wood chip penetrates into the lower parts of the respiratory tracts and initiates the formation of antibodies more easily than the moist aerosols.

Fever and muscle pain as work-related symptoms in wood chip workers suggest the diagnosis of allergic alveolitis, which is supported also by high antibody levels in this group (Terho 1982), whereas rhinitis and cough found mostly in barking workers with low antibody levels seem not to be IgG-mediated reactions.

The comparison of antibody findings in the cellulose factory with those in office workers gave a surprising result. The barking workers' antibody levels were not at all higher than those in bank clerks with minimal exposure to airborne microbes (unpubl. data). The dry microbial material occurring in wood chip work and in office work penetrates probably easily into the alveoli and initiates the formation of antibodies more effectively than the moist aerosols irrespective of the amount of antigen.

These results suggest that in addition to microbial concentration the physical nature of aerosols should be considered for evaluating the health risks caused by airborne microbes. On the other hand, the immunization against occupationally exposing microbes could be diminished by controlled air-humidifying to prevent allergic respiratory diseases.

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ETIOLOGICAL INVESTIGATION OF FARMER'S LUNG —SEROLOGICAL STUDY

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SUMMARY

The reactions of precipitins in serum against the antigens from two strains of T. vulgaris were shown in 46.7 and 66.7% in 30 patients with farmer's lung, significantly higher than those in the control groups, while the reactions against M. faeni and A. fumigatus were low in the patients' group and not significantly higher than those in two control groups. The results indicated that the main etiological agents of farmer's lung were some strains of T. vulgaris in the patients.

INTRODUCTION

From 1980 through 1981, an epidemiological survey was conducted among 1054 hay grinders in Dafeng County, Jiangsu Province. 120 of them had history of farmer's lung disease. During follow-up study of these 120 grinders, acute episodes of farmer's lung after exposure to mouldy hay dust were seen in 67 of them.[1] Meanwhile, a microbiological study of sputum of these patients and mouldy hay samples from their workplaces was performed. 80 strains of thermophilic actinomycetes were isolated from these samples, 61.2% of them being T. vulgaris.[2] In order to confirm whether T. vulgaris was the main etiological agent of farmer's lung in that county, we studied the precipitins in serum from the patients using serological method.

MATERIALS AND METHODS

Antigens

Six strains of Thermoactinomycetes, including 4 strains of T. vulgaris called 801, 806, 816, 832 and 2 strains of Thermophilic nocadia called 835 and 836, which were isolated from mouldy hay collected from the workplaces of the patients with farmer's lung, were selected and then, antigens were prepared by using a modified Salvaggio's method.[3] Meanwhile, the strains of M. faeni 1., T. vulgaris 2. and T. candidus, one of each, provided by Dr. V. P. Kurup (Medical College of Wisconsin) were also selected to prepare antigens. The antigens were diluted to 30 or 40 mg per ml of normal saline, when they were used. In addition, other antigens including those form M. faeni 2., T. vulgaris 1. provided by Dr. J. H. Edwards (MRC Pneumoconiosis Unit) and A. fumigatus provided by Dr. J. Marx, JR (Marshfield Medical Foundation) were also used for detecting precipitins in serological test. Besides, the extracts from mouldy hay was prepared by using a modified Williams' method and diluted to 12 mg per ml of normal saline, also employed in the serological test.

Serum Samples

Serum samples from 30 of these 67 patients were collected just one month after they ground mouldy hay. 30 serum samples from healthy people with no history of exposure to mouldy hay in the same area matched with the patients in sex and age were selected as control group A. Another 29 serum samples were collected from the healthy students in Shanghai Medical University as the control group B.

Serological Test

The presence of precipitins against the antigens was tested by using modified Ouchterlony's agar-gel double-diffusion assay.[5]

RESULTS

It was shown that the reactions against two strains of T. vulgaris 1. and 2. were 46.7 and 66.7% in the patients' group, significantly higher than those in the control groups, whereas the reaction against T. candidus was 80% higher than that in group B, and it had not much difference with the control group A. Besides, the reactions against M. faeni 1. and 2. and A. fumigatus were rather low (16.7, 3.3 and 9.1%) in the patients' group and not significantly higher than those in the two control groups.

The reactions against six strains of thermophilic actinomycetes named T. vulgaris 801, 806, 816 and 832 and Thermophilic nocardia 835 and 836 ranged from 13.3 to 80.0% in the patients' group. The reactions against T. vulgaris 816 was 36.7% in the patients' group, significantly higher than that in the two control groups, and those against T. vulgaris 806 and 832 were 80.0 and 33.3% in the patients' group, significantly higher than those in the group B, but not in the group A. Besides, reactions against T. vulgaris 801, Thermophilic nocardia 835 and 836 and the extracts of mouldy hay in the patients' group were not significantly higher than those in the control group.

DISCUSSION

The precipitin test against farmer's lung antigens has been widely used in clinical diagnosis and epidemiological survey of the farmer's lung disease. The positive reactions against these antigens always indicate that the people have the history of exposure to them. Based on these reactions, the etiological agents of farmer's lung could be determined.[6] In our study, the precipitins against a variety of farmer's lung antigens in sera from the patients with farmer's lung in Dafeng County, Jiangsu Province were tested and it was found that the percentages of positive reaction against three strains of T. vulgaris 1., 2. and 816 were 46.7, 66.7 and 36.7% in the patients with farmer's lung, respectively, which were significantly higher than those in the two control groups. The results might indicate that the main causative agents were some strains of T. vulgaris. The microbiological study of the mouldy hay from that county and sputum from the patients had also indicated that T. vulgaris was the dominant thermophilic actinomyces in the samples, while M. faeni was not found in them[2] So, the findings of our serological study and the microbiological study were consistent with each other.

Pepys had reported that the percentage of positive reaction against M. faeni in the patients with farmer's lung was as high as 85% in Britain.[7] So, the main causative agent of the disease was M. faeni in Britain. But in Finland, Terho found that the main etiological antigen of farmer's lung was from T. vulgaris.[8] Perhaps the difference might be referred to the different way of preparing and storing hay, perhaps also climatic differences and differences in crop types. In Dafeng County as well as other area in east part of China, hay before stocking would be sun-dried as much as it could be and then stocked outdoors. In this instance, the weather is rather humid and warm in these regions, but the time is not long enough for M. Faeni to grow in the stacks, which might be the reason why the percentage of positive serological reaction against M. faeni was very low in the patients in that county.

It was reported that the reactions against different strains of T. vulgaris in the same group of patients with farmer's lung might be significantly different from each other, and similar results could be found from different strains of T. candidus.[8,9,10] In our study, it was also found that the reactions against six strains of T. vulgaris in the patients with farmer's lung ranged widely from 13.3 to 80.0%. These findings may indicate that different strains of T. vulgaris could have different antigens. Therefore, a variety of strains of T. vulgaris should be used to test precipitins in serum from the patients with farmer's lung.

In addition, the reactions against the extracts from Thermophilic nocardia and mouldy hay in the patients was found not significant in this study.

In conclusion, it may be said that the etiological agents of farmer's lung in Dafeng County were mainly from some strains of T. vulgaris, but not M. faeni, and different strains of T. vulgaris should be applied to detect precipitins in serum diagnosis of farmer's lung.

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IN SITU QUANTITATION OF NON-FIBROUS INORGANIC PARTICLE BURDEN IN LUNG TISSUE USING SCANNING ELECTRON MICROSCOPY AND ENERGY DISPERSIVE X-RAY ANALYSIS

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ABSTRACT

To investigate the interaction of inhaled inorganic particulates with the lung one needs quantitative information on the particulate burden of lung tissue. The vast majority of tissue samples (biopsies and autopsies) are fixed with formaldehyde and embedded in paraffin wax. Over the past 16 years, I have attempted to obtain maximal analytical use of such tissue. Standard paraffin sections of tissue are analyzed in the scanning electron microscope (SEM) using secondary electron and backscatter electron imaging (BEI). Inorganic material is detected in the BEI and is analyzed using Energy Dispersive X-ray Analysis (EDXA). Quantitation of the tissue particulate burden is readily accomplished using a point-counting, morphometric approach.

I have collected quantitative data from analyses of particulates in over 400 lung samples. The data includes numerous comparative digestion analyses. The results from this *in situ* method correlate well with other analytic methods, and with comparison of results from other laboratories using similar or other techniques—with the exception of submicrometer metal particles which are better represented in the *in situ* analyses, as they may be lost during digestion and filtration. Currently, of over 30,000 particles in the data base, major non-fibrous particles are comprised of 13.8% silica, 47.7% silicates and 38.6% metals. These data, plus data on medical and occupational histories, smoking, age, sex, pathologic diagnoses, etc. are being queried regarding normal and diseased lungs.

No Paper provided.

PULMONARY FIBROSIS ASSOCIATED WITH SMOKING IN MEN RESIDING IN A CLEAN-AIR ENVIRONMENT

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ABSTRACT

The role of cigarette smoking in the pathogenesis of pulmonary fibrosis has not been defined. This question is important to pathologists concerned with pneumoconiosis since many inhalant-related lesions result in fibrosis in the smaller airways. Using Gough-Wentworth slices and microscope tissue sections, we analyzed lungs of Vermont males over a range of ages who died suddenly and unexpectedly and were autopsied. Gough sections were analyzed by the method of Thurlbeck and by planimetry. Microscopical tissue was evaluated by the method of Hogg, et al. (Med. J. Aust. 142:605, 1985). Postmortem interviews with next-of-kin were conducted by trained nurse epidemiologists to determine cigarette use and possible occupational exposures.

Overall, enphysematous changes were not striking, but there was a gradual increase in scores with advancing age in both smokers and nonsmokers using both techniques of analysis. In microscopic sections, inflammation reflected by cellular infiltration in the walls of bronchioles and the presence of intraluminal macrophages was most prominent in younger smokers, whereas fibrosis of the walls of the bronchioles increased with age among smokers. Inflammation and the lung fibrosis indices in smokers and nonsmokers differed significantly. This study provided an opportunity to evaluate pulmonary changes associated with smoking among men living in a clean air environment, and not employed in dusty trades. In addition, it excludes possible terminal effects on the tissue morphology. A significant association of smoking with fibrosis of the membranous and respiratory bronchioles was found. The data suggest that respiratory bronchiolitis may be a contributory pathogenetic factor.

No Paper provided.

ACCUMULATION AND COMPOSITION OF INHALED PARTICULATES IN HUMAN LUNGS

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SUMMARY

The black particulate matters deposited and accumulated in the autopsied human lung of deceased residents of the Tokyo Metropolitan area with no history of lung disease were separated, and their composing elements and substances were identified using several analytical techniques. The origin of lung contamination was examined. The carbon free radicals detected from human lungs were an original finding. Alpha-quartz was identified, carbon element, minerals and trace elements were determined, asbestos fibers were found and a result of the mutagenicity test on deposits was positive. The results observed in most cases were almost identical to the composition of an urban atmosphere. As for the exogenous factors related to the formation of pulmonary lesions, the effect of tobacco smoking cannot be ignored. In our pathohistological study, the observations of pulmonary lesions were found to be related to smoking. In view of the high concentration of element observed therein, it is considered that multiple factors participate in the development of exogenous pulmonary disease due to substances in the environment. These findings may be important in elucidating factors involved in the development of the lung disease due to particle deposition.

INTRODUCTION

The pulmonary anthracosis which has generally been assumed to have little pathological significance has been used as a simple indicator for estimating exogenous lung contamination. In studing the effects of suspended particulate matters in the atmospheric environment, it should be noted that the amount of black dusts deposited in a life time in human lungs depend upon various factors such as age, place of residence, smoking habits, and occupation. Published research reports pertain to anthracosis in the lung of such animals as dog, monkey, pigeon and autopsied human tissues.[1,2,3] These studies were conducted from the pathological standpoint. However, there has been a need to chemically analyze the composition of black deposits only, because it has been thought that black deposits are mainly composed of inhaled suspended particulate matters in the atmosphere. In a report published[4] in which Ohta was a co-author, multiple elements analysis was first conducted on anthracosis using spark source mass spectrometry. The ongoing studies[5,6,7] have concentrated on the establishment of a relatively large base of data obtained by analyzing particulate matters isolated from autopsied lungs not only for element but also for accumulated toxic materials using several analytical techniques.

MATERIALS AND METHODS

Lung Specimens and Pathohistological Findings

The autopsied lung samples used for this study were taken exclusively from people living in the Tokyo Metropolitan area with no history of lung disease. The age of 108 cases ranged from the second decade to the ninth decade. A defined site of the left upper autopsied lung lobes of these cases was employed, and pathohistological observations were examined.

Separation of Black Deposits from the Lung Tissue

The lung tissue was dissolved in alkaline solution. First, a test was made to determine whether 0.5N NaOH or 0.5N KOH would be satisfactory. Results by these solutions were not so different in regard to dissolve the lung tissue. After weighing the lung tissue which was kept in room temperature after removal from storage at −80°C, they were cut into small pieces and placed in polyethylene bottles with demineralized water to eliminate blood. After repeating this procedure for a few times using high speed centrifugation, 0.5N NaOH which was used for many samples were poured into the bottles. By repeated ultrahigh speed centrifugations at 12,000 rpm and 30,000 rpm, the solid residue was retained. The final residue was then washed using water, ethanol, acetone and finally dried. These black powders were used as samples for analysis.

Deposition Rate and Observation of Particulates Using Scanning Electron Microanalyzer (SEM-EDAX)

Elementary Analysis

1. Determination of elementary content using SEM-EDAX for obtaining general survey of the particulate components
2. Quantitative analysis by neutron activation

The analysis of Mn, V, Al and Ti in 92 samples was completed, and other selected 13 samples were analyzed into trace elements. The samples were irradiated for 30 sec. for short halflife nuclides and for 5 hours for long half life nuclides at 1.5×10^{12} n/cm^2 • sec.

3. Determination of carbon content using CHO Elemental Analyzer

   In the analysis of total carbon content, CHO Elemental Analyzer was used. A sample measured precisely to 0.3 mg or 1.2 mg was placed in a sample container. Elemental carbon content was measured by combustion at 300°C for 30 min. The volatilized carbon was calculated by subtracting the weight of residue carbon from the total carbon.

Detection of Free Radicals in the Black Particulate Deposited in Lungs Using Electron Spin Resonance (ESR)

Soot, tobacco, other kinds of smoke and products of combustion are serious sources of harmful particulates. Samples of black deposits from the lung which were removed with tweezers without any chemical treatment were lyophilized and approximately 20 mg of each sample was subjected to ESR analysis at room temperature. Solid DPPH was used as standard for the g factor and its benezene solutions was used for the estimation of radical concentration.

Mutagenicity Test for Black Deposits in the Lung

A mutagenicity test for black deposits isolated directly from the lung tissue was examined by the Ames Test. The strain used for this test was Salmonella typhimurium TA98 and TA100.

Identification of Crystallized Materials in Deposited Dust

The crystallized material in the black dust which was treated with alkaline solution was identified using X-ray diffraction for 50 cases.

Detection of Asbestos

The asbestos fibers were detected and identified using a transmission electron microscope (TEM) coupled with X-ray microanalyzer for selected samples.

RESULTS AND DISCUSSION

Pathohistological Findings

Some of 108 cases were detected to have pathohistological findings. The main observed findings were chronic bronchiolitis, emphysema and pavement epithelium metaplasia. These cases were found in relating to smoking considerable amount of cigarettes. This is especially true of 9 cases found in this study.

Deposition Rate and Observation of Deposited Particulates

The deposition rate of inhaled dust was positively correlated with age. Correlation factor (r) was 0.65 ($n=95$, $p<0.001$). The particle size and shape of collected dust particles from human lungs were observed that an individual particulate was approximately 0.1 micron in diameter, and many particles had aggregated into clumps.

Elementary Composition of Deposited Particulates and their Accumulation in the Lung

Usually Mg, Al, Si, P, S, K, Ca, Ti and Fe were detected in almost all samples, while Cl and Zn were detected in many samples, those contents were represented in weight percent (wt%). The concentration of Hg, Cr, Fe, Zn, Co, Ag, Sb, Cd and As in 13 specimen's samples were determined by neutron activation analysis. In case of chromium worker, Cr concentration was very high because of exposure to hexavalent chromium. V and Mn in the particulate are considered to originate from artificial sources, such as fuel or combustion, Al and Ti are assumed coming from soil or sand in the natural environmental sources. The concentration of these elements were determined. We attempted to correlate the concentration of element to age. The correlation factor (r) of Al was $r=0.48$ ($n=92$, ***), that of V, $r=0.40$ ($n=91$, ***), that of Si, $r=0.46$ ($n=95$, ***), that of Fe, $r=0.34$ ($n=95$, ***). These elements showed a positive correlation to age, that is, they were accumulated in the lung according to increase in age. However, Mn and Ti were not correlated to age. And furthermore, Ca concentration showed a negative correlation to age ($r=-0.56$, $n=72$,***). The average total carbon content was 55 wt% ($n=77$). The data comparing the total carbon content between smokers and nonsmokers were not discriminating. The average content of elemental carbon was 39 wt% ($n=39$). The volatilized carbon was considered to be organic carbon.

Determination of Free Radicals in Black Deposits

Carbon-centered free radicals were detected in all 21 specimens. Figure 1-a shows an ESR spectrum from specimen A who was 81 year-old woman, where a narrow singlet is seen with a width of 2.7G and a factor of 2.0025. This spectral component is designated R_1. This is more evident in the spectrum obtained with a wider field sweep in Figure 1-b. Such a broad signal apparently arises from inorganic magnetic species in the black deposits. Carbon-centered free radicals are not among those substances commonly expected to be contained in the air dust. Thermolysis or combustion of hydrocarbons is essentially a free radical process accompanying bond cleavage. As a simple comparison, tar and ash from Japanese cigarettes were collected and measured. The observed spectra were the same as that shown in Figure 1. The intensity of R_1 component in each specimen measured by the height of the derivative peaks was obtained.

Mutagenicity Test for Black Deposits

A mutagenicity test which is called the Ames Test was used to determine the black deposits, which were isolated directly from lung tissues, and a small amount of them was used in this test. They were set in the center of an agar plate, the so-called spot test. The strains used for mutagenesis testing were salmonella typhimurium TA98 and TA100, S-9(−) and S-9(+). some inhibition was observed, however, His^+ revertants were not more than the numbers of spontaneous revertants both in S-9(−) and in S-9(+). The result was that one sample was positive in both of TA98 and TA100 to

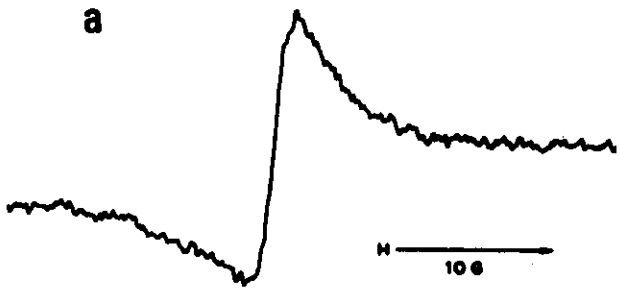

Figure 1-a. ESR spectrum of carbon free radical signal of specimen A who lived in the center of Tokyo for 60 years. Age: 81, Tobacco (−). The signal consists primary of R_1 type radical case. Gain = 4×10^4. Modulation width = 1G at g = 2.00.

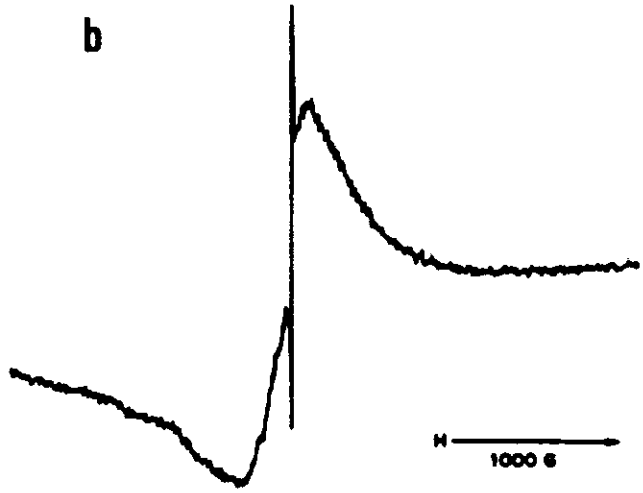

Figure 1-b. The whole ESR spectrum of the same specimen taken with a wide magnetic field sweep. Besides R_1 radical (the sharp signal in the center), a very broad absorption due to inorganic magnetic species is observed. Gain = 1×10^4. Modulation width = 10G.

S-9(−) and S-9(+), 3 samples were probably positive in TA98 only.

Identification of Crystal Structure in the Deposited Particulates

Alpha quartz was detected in 55 samples and crystallized stearate calcium was also detected. In a few samples, talc and ferric hydroxide were detected. Alpha quartz ($\alpha-SiO_2$) is a natural mineral, originating from soil and rock. They were blown up in the atmosphere. The stearate calcium detected in the lung deposit was produced by chemical procedures with alkaline solution at 40°C for several days.

Detection of Asbestos Fibers in the Black Deposits

Asbestos fibers were detected in three cases among the 10 samples. We studied them using a TEM-XMA to identify asbestos fibers in the lung deposits. Chrysotile fibers were found in specimen B who was 78 year-old medical doctor, tremolite fibers and crocidolite fibers were detected in specimen C who was 65 year-old man. These fibers were qualitatively examined. However, other samples were not detected asbestos fibers.

CONCLUSION

The black dust deposited and accumulated in the human lung were separated and through the identification of their composed elements, crystallized materials, carbon free radicals, asbestos fibers and the mutagenicity test, the origin of lung contamination was examined. The results observed in most cases were identical to the composition of an urban atmosphere except for several cases, which were depended on their profession. The one case was a hexavalent chromium worker, and others were laborers worked at a industrial factory, public engineering works, construction industry etc. As for the exogenous factors related to the formation of pulmonary lesions, the effect of smoking cannot be ignored. We have detected free radicals in the human lung deposits as an original finding related to smoking and soot. A mutagenicity test for black deposits also was examined and a few cases were positive. Some of these data provide a large information base for future work and will be useful for making a risk evaluation for lung contamination by low exposure to toxic substances.

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CARCINOMA OF THE LUNG AND SILICOSIS: PATHOLOGICAL STUDY

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INTRODUCTION

The relationship between silicosis and lung carcinoma can be approached from both epidemiologic and morphologic viewpoints. The majority of epidemiologic studies indicate that lung carcinoma occurs less frequently in coal miners than in comparable populations. However, excess lung carcinoma has been reported among metal miners, pottery workers, foundry workers and silicotic patients.

To our knowledge, detailed morphologic studies of lung carcinoma in silicotic patients have not been reported.

This is a report on pathologic evaluation of lung carcinoma associated with silicosis which was reviewed between 1960 and 1986 at our Laboratory.

MATERIALS AND METHODS

Between 1960 and 1986, the authors evaluated about 450 autopsies of silicosis. Of these, 140 were our own consecutive autopsies in our Laboratory and remaining 310 were kindly provided to us from other hospitals in Japan. Carcinoma of the lung was seen in 48 of the autopsies.

Pathological studies, including cell types, cancer sites, severity of silicosis, were performed in the 48 cases of lung carcinoma associated with silicosis.

Severity of silicosis was determined by extent of progressive massive fibrosis as follows; (1) mild silicosis; silicosis without PMF (simple silicosis); (2) medium silicosis: silicosis with small PMF that were formed within lung segment; (3) severe silicosis: silicosis with large PMF including some segments.

RESULTS

Carcinoma of the lung was seen in 25 of our own consecutive autopsies, an incidence of 19.9%. The incidence of lung carcinoma was definitely elevated among mild silicosis and lowered among severe silicosis (Table I).

Table II shows the distribution of lung carcinomas by histologic cell type in all 48 lung carcinomas.

Over all, the predominant cancer was squamous cell carcinoma (54.2%) followed by small-cell carcinoma (22.9%) and adenocarcinoma (14.6%). There was a clear trend of squamous cell carcinomas arising in the larger airways, whereas the adenocarcinoma was found only in peripheral lung tissue.

More tumors were observed in the right lung, but the difference was not observed between upper and lower lobes (Table III). In case of mild silicosis, the majority of tumors arose in the right, upper and larger airways. On the other hand, in case of medium and severe silicosis, more tumors arose in the left, lower and peripheral lung tissues.

The distribution of primary focus in the large bronchi are illustrated in Figure 1. In case of mild silicosis, many tumors arose in stem and lobar bronchi, whereas many tumors arose in segmental bronchi in case of medium and severe silicosis.

In case of silicosis with PMF, the majority of tumors arose in the segmental bronchi leading to PMF. (Figure 2 shows the typical case of such cases.)

The primary foci of tumors arising in peripheral lung tissues were illustrated in Figure 3. Almost all the tumors in periph-

Table I

Incidence of Lung Carcinomoma Among Our Autopsy Cases

Severity of Pn.	Number of Cases	Lung Carcinoma	%
Mild	40	13	32.5
Medium	51	10	19.6
Severe	49	2	4.1
Total	140	25	17.9

Table II

Distribution of Lung Carcinoma Associated with Pneumoconiosis Cases by Histologic Type

	Central Type	Peripheral Type	Unknown	Total	%
Squamous Cell Ca.	15	10	1	26	54.2
Adenocarcinoma	0	6	1	7	14.6
Small-Cell Ca.	6	4	1	11	22.9
Large-Cell Ca.	2	1	1	4	8.3
Total	23	21	4	48	100.0

Table III

Location in Lung of Tumors by Site of Origin

	Mild Pn.	Medium Pn.	Severe Pn.	Medium+Sever	Total
Right:Left	16: 7	7: 7	4: 3	11: 10	27: 17
Upper:Middle:Lower	14: 0: 9	5: 1: 8	4: 0: 3	9: 1: 11	23: 1: 20
Central:Peripheral	14: 9	7: 7	2: 5	9: 12	23: 21
Total	23	14	7	21	44

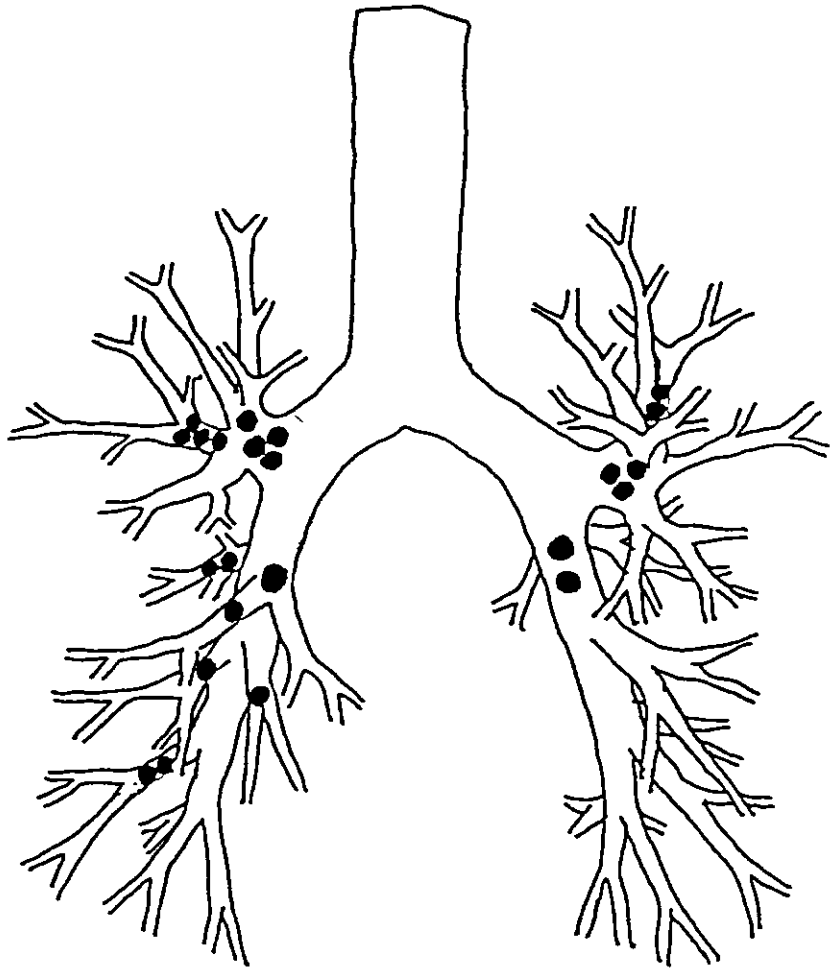
eral lung tissues arose in S_2, S_3, S_6, S_9 where PMF were usually formed.

The majority of the tumors in peripheral lung tissues were centered on closely adjacent to PMF or originated on the basis of pathologic course to PMF. In these cases, there were three cases of scar cancer arising in scar tissues of PMF (Figure 4 and Figure 5).

Diffuse interstitial fibrosis of the lung was often associated with silicosis. Five cases of carcinoma of lung were found in these cases (Figure 6).

SUMMARY

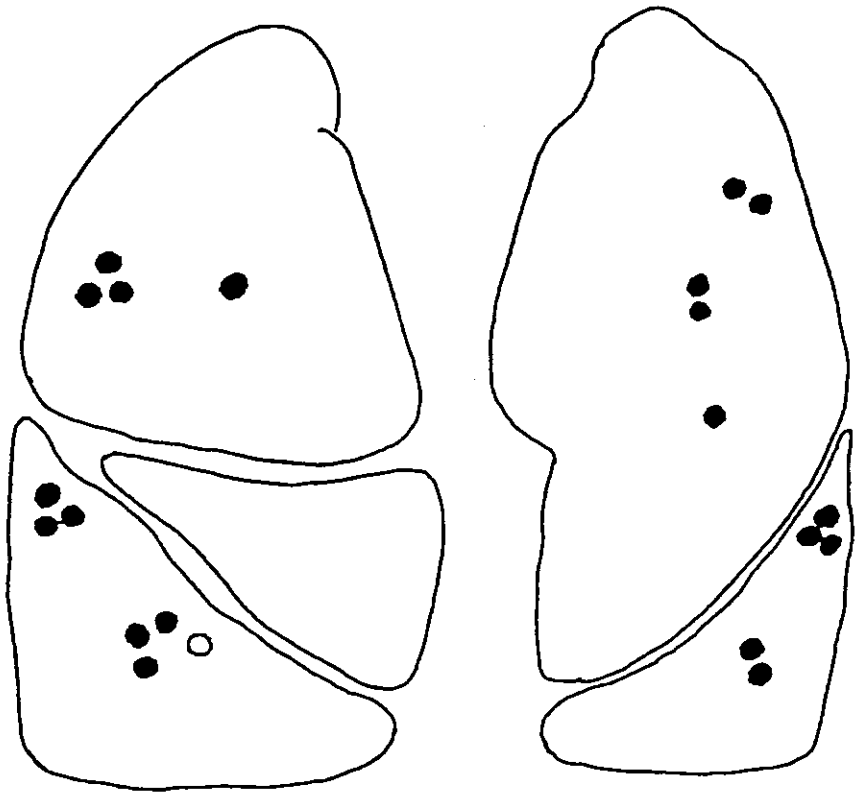
The data indicate the close relationship between pathological, changes of lung tissues by dust exposure and carcinoma of the lung.



	Right Lung	Left Lung
Upper Lobe Bronchus	4	3
Lower Lobe Bronchus	1	2
B_2 (B_{1+2})	4	2
B_4	1	0
B_6	2	0
B_7	1	0
B_8	1	0
B_9	2	0
Total	16	7

Figure 1. Location in bronchial trees of central type of tumors by site of origin.

Figure 2. Squamous cell carcinoma originated from bronchus leading to progressive massive fibrosis.



	Right Lung	Left Lung
S_2 (S_{1+2})	3	2
S_3	1	2
S_4	0	1
S_6	3	3
S_7	1	—
S_8	3	2
Total	11	10

Figure 3. Location in lung of peripheral type of tumors by site of origin.

Figure 4. Scar cancer originated from anterior portion of progressive massive fibrosis.

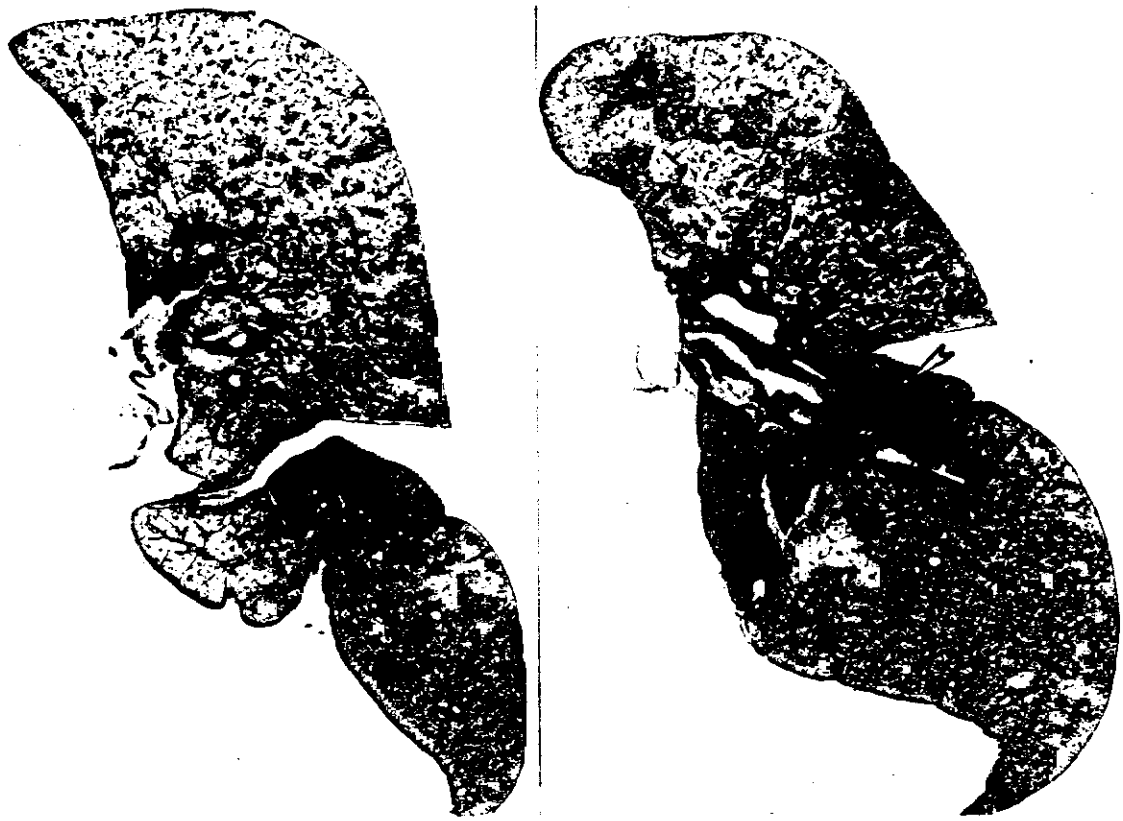


Figure 5. Scar cancer originated on the basis of pathologic course to progressive massive fibrosis.

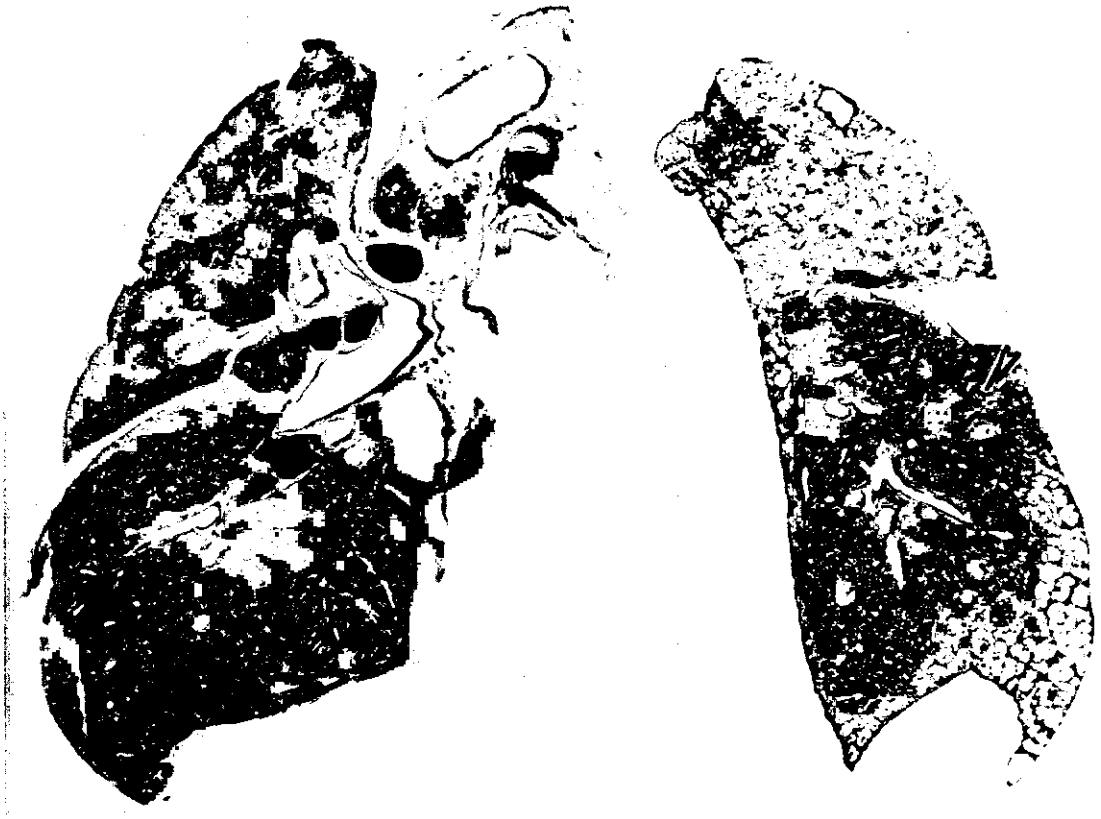


Figure 6. Adenocarcinoma associated with mild pneumoconiosis and diffuse interstitial fibrosis.

STUDY ON DUST PARTICLE SIZE IN AUTOPSIED LUNGS OF UNDERGROUND COALMINERS

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INTRODUCTION

Some scholars suggested that particle less than 5 μ m was most harmful. Others thought that particle less than 5–7 μm had the selective effect on the lungs. Some countries adopted the respirable dust concentration as dust standard.[1] But both the measurement of particle size distribution of dust after death from the lungs of coalminers and the experimental study on dust retained in the respirable organ of animals failed to reach a consensus about hygienic evaluation of different fractions of particle sizes. Dust 40–60 μm in diameter were found at autopsy.[2] Professor Chen Hongquan[3] observed particle size distribution of dust at autopsy, using biological microscope and scanning electron microscope and suggested that the particles with dia. below 2, 5 and 10 μm made up 65.2, 88.4 and 95% of total number. Author[4] thought that dust more than 5–7 μm must be considered when working out limit standard of dust and monitoring dust in production environment.

In this paper, our results of study on particle size distribution of dust in underground coalminers' lungs were reported.

MATERIALS AND METHODS

Subjects

120 histological sections were at random sampled from the lung sections of 60 autopsies (2 sections per case), who had been exposed to coal dust or with Coal Workers' Pneumoconiosis for this study, most of them had been coal mining workers and the few had been rock drifting workers. In view of the difference of physical and chemical properties of coal mineral dusts, 120 sections were divided into two dust groups which were treated with digestion and microincineration, respectively.

Hydrogen Peroxide Digestion

The specimen were digested in 70 ± 5 centigrade temperature H_2O_2 for 3 hrs and treated with concentrated HCl and observed by polarizing microscope.

Microincineration

Thin sections with their waxembedding material were moved by washing in xylene, dried and microincinerated in a muffle furnace at 540 centigrade temperature for 4 hrs, treated with concentrated HCl.

Size-Groups by Particle Size

Dusts were divided into down to 2, 2–5, 5–7, 7–10 and over 10 μm size-groups by geometric projection diameter. Fractions of particle numbers and masses of dust were calculated.

RESULTS

Number Distribution of Particle Sizes of Dust in lungs

The observations of the treated specimens which were divided into many parts equally were performed using the X 400 light microscope and Polarizing microscope. 500 particles were measured per section. Results were in Table I. The % of particle numbers was similar in the small particles of two dust-groups, significantly different in two dust-groups of particle 7–10 μm and over 10 μm in dia.($t > t_{0.01}$ $P < 0.01$). In mineral dust-group, numbers of particle 7–10 μm in dia. made up 7.7 % of all mineral particle numbers. In coal dust-group, number of particle in 7–10 μm dia. only constituted 4.4 % of all coal particle numbers, number of dust >10 μm covered 0.4% and 0.2% respectively in mineral dust-group and in coal dust-group. It was clear that large particle mineral dust predominated over that of coal dust.

To account of different definitions of the respirable dust in the inspirable dust curve recommended by some countries and organisms[5] Table I was changed into Table II. Grain size distribution >7 μm fraction had significant difference in mineral dust-group and coal dust group ($t > t_{0.01}$, $P < 0.01$).

Mass Distribution of Dust Particle Size in Lungs

Accumulative distribution derived from number distribution of particle size was plotted on logarithmic normal log-probability graph paper so as to attain number distribution N(D) which was necessary to account and more minute than the measuring of groups by means of geometric projection using microscope. Total mass of particles with dia. ranging from D_1 to D_2 is given by

$$m_{1,2} = \int_{D_1}^{D_2} \rho \, \alpha_v \, D^3 \, N(D) \, dD$$

Table I
Number Distribution of Particle Sizes of Two Dust-Groups

Types of Dusts	Number of Samples	% of Number Distribution of Particle Sizes (μm)				
		<2	2-5	>5	7-10	>10
Mineral	53	55.6	25.8	10.5	7.7	0.4
Coal	57	57.6	26.5	11.2	4.4	0.2

Table II
Numbers of Particle Sizes of Two Dust-Groups

Types of Dusts	Number of Samples	% of Particle Sizes (μm)			
		<5	5-7	7-10	>10
Mineral	53	72.9	18.6	8.1	0.4
Coal	57	79.1	15.9	4.7	0.3
Mean		76.0	17.2	6.4	0.4

Here: ρ: Particle Density
α_v: Volume Shape Factor of Particle
D: Geometrical Projective Diameter of Particle.

If composition of particles and mechanism of producing particle are same, ρ and α_v are not related to particle size, so the formula above is changed into:

$$m_{1,2} = \rho \alpha_v \int_{D_1}^{D_2} D^3 N(D)\, dD$$

But relation between N(D) and D measured really showed that distributions of N(D) was different within the range of particle sizes considered. For the sake of convenience, integral method of numerical value was used. So:

$$m_{1,2} = \rho \alpha_v \sum_{D_i=D_1}^{D_2} D_i^3 N(D_i)$$

Within the given range of Particle size ($D_1 - D_2$), the per cent of particle mass in total particle mass is:

$$F_{1,2} = \frac{m_{1,2}}{m_t} = \frac{\rho \alpha_v \sum_{D_i=D_1}^{D_2} D_i^3 N(D_i)}{\rho \alpha_v \sum_{D_i=D_{min}}^{D_{max}} N(D_i) D_i^3} = \frac{\sum_{D_i=D_1}^{D_2} D_i^3 N(D_i)}{\sum_{D_i=D_{min}}^{D_{max}} D_i^3 N(D_i)}$$

Where D_{min} and D_{max} are the smallest and largest particle diameters. M_t is total mass. The calculated results were shown in Table III and Figure 1. It was seen in Table III that masses of Particle greater than 5, 7 or 10 μm in size made up respectively 83.7 ± 3.3, 66.3 ± 6.1 and 14.2 ± 7.7

Table III
Mass Percent of Particle Sizes in Two Dust-Groups

Types of Coal	Number of Samples	% Mass of Particle Sizes (μm) <5	5-7	7-10	>10
Mineral	53	16.3	17.4	52.1	14.2
Coal	57	22.5	11.3	55.5	12.5
Mean		19.4	14.3	53.8	12.5

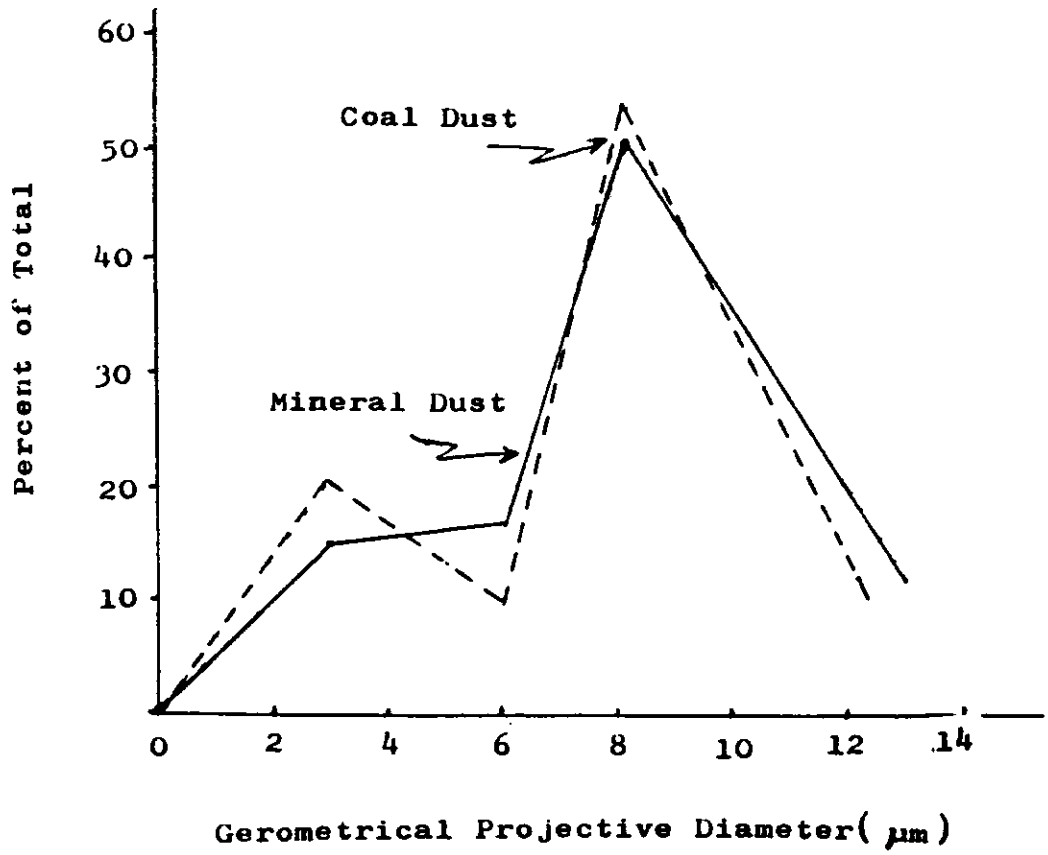

Figure 1. Mass percent of particle sizes of two types of dusts.

percent of the total mass in mineral dust in autopsic lung tissue and in coal dust in lung, masses of particle with more than 5, 7 or 10 μm in dia. accounted for 77.6 ± 7.2, 45.3 ± 10.4 and 10.8 ± 8.4 % of total mass, respectively. Significance tests showed that particle fractions over 5 μm and 7 μm of two types of dusts were significantly different ($t > t_{0.01}$, $P < 0.05$)and that fractions >10 μm of two types of dust had statistical significance($t > t\ 0.05$, $P < 0.05$).

Relationship between the Mass and the Number Distribution of Dust Particle Sizes in Autopsic Lungs

The mass and the number distributions of dust particle sizes in the lung tissue were studied. (Figure 2). Figure 2 illustrated that number of dust < 5 μm amounted to 76.0% of total number, but its mass was only 19.4%, of total mass; that number of dust >5 μm made up only 24.0% , but its mass accounted for 80.6% of total mass and that number of dust † 7 μm was 6.8% total number, its mass was 66.3% total mass and that number of dust >10 μm was 0.4% of total number, its mass constituted 12.5%, total mass.

Some scholars had observed 37297 airborne particles of samples from the gold mine and come to the conclusion that number of particle <1 μm made up 92/% of total number and its mass only 10.5% weight of sample, which was correspondence with our results.

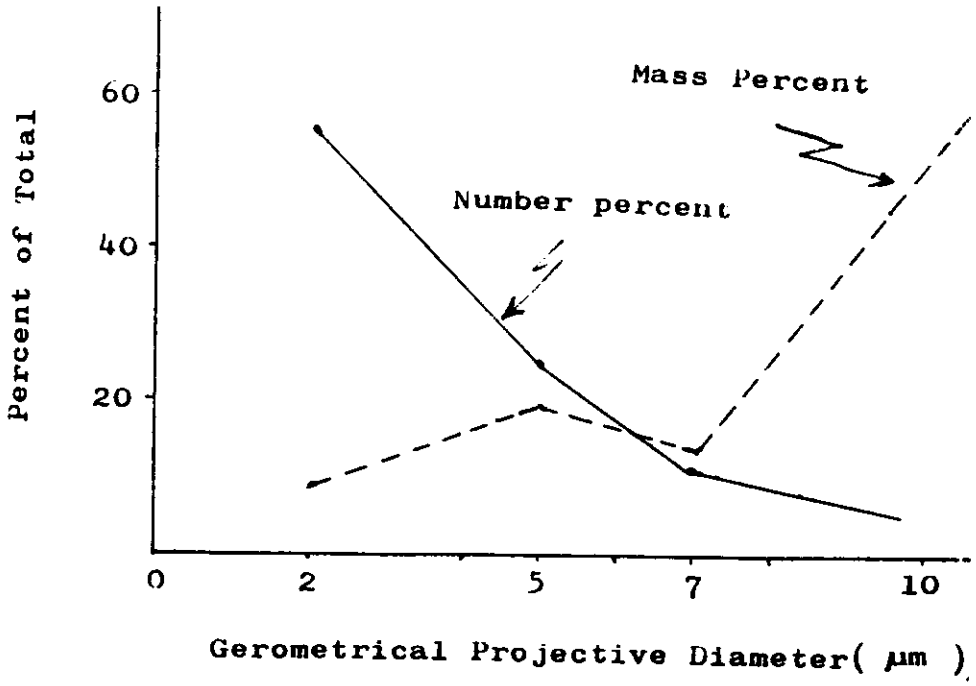

Figure 2. Comparison of percent content of particle sizes of dusts in autopsic lungs.

DISCUSSION

Some scholars[2] had injected the same weight of quartz 0.8–2.0μm and 5–10 μm in dia. into two groups of rats (A group and B group), respectively and observed 19 small dust focuses and 3 large dust focuses in A group and 47 small dust focuses and 15 large dust focuses in B group. It may be seen that quartz 5–7 μm.in dia. caused the more and the larger dust focus than quartz 0.8–2.0 μm in dia.. Hence, the respirable dust concentration was only part of dust concentration.

Other articles[6,7,8] and our study confirmed that the level of pathological change and categories by X-ray were closely relative to mass and content of dust retained in lungs. Such research has shown that CWP is related to exposure to respirable dust, partially dust 2 μm or larger in size, is the most important factor associated with CWP. So we think that when drawing up the dust hygiene standard and monitoring dust concentration, we considered not only the respirable dust concentration but also the total dust concentration.

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THE EFFECT OF ALUMINIUM CITRATE ON ELECTROKINETIC POTENTIAL ON THE SURFACE OF QUARTZ AND TITANIUM DIOXIDE PARTICLES

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ABSTRACT

The electrophoretic mobility of quartz and titanium dioxide particles and the Al content and electrokinetic potential on their surface were measured. The effects of aluminium citrate (Al citrate) and AlCl3 on them were also examined. The results show that both these particles are negatively charged, but the surface charge density of quartz is higher than titanium dioxide. Moreover, it was found that a certain amount of Al can be firmly bound on quartz surface under the pretreatment with Al citrate or AlCl3 resulting in the decrease of their electrokinetic potential. In contrast, the significant changes of the Al content and electrokinetic potential on the surface of titanium dioxide particles pretreated by the same way could not be detected.

The present investigation provides further evidence for explaining the mechanisms of membrane damage caused by quartz and the antagonistic effect of Al citrate. Also, the probability of Al as a preventive measurement for silicosis in worksite was discussed in this paper.

INTRODUCTION

It has been demonstrated In Vitro that cytotoxic effect and membrane damage by quartz were much higher than by titanium dioxide under the same conditions of their dose and particle size. Al citrate can exert an antagonism against the toxicity of quartz by a possible mechanism of its action on the particle surface, but the effects of titanium dioxide on membranes were not affected by Al citrate, which may be attributed to the differences of both these particles it their surface structure and properties and the mechanisms involved in their interactions with cells.[1-4]

To evidence the hypothesis, the Al content, charge density and electrokinetic potential (−potential) on the surface of quartz and titanium dioxide particles were detected using the techniques of fluorescence and microelectrophoresis. The effects of Al citrate and AlCl3 on them were also examined in the present study.

MATERIALS AND METHODS

Chemicals and Preparation

Quartz (99% pure) was supplied by Hygiene Institute of Chinese Prophylactic Medical Center. Particle diameter was all less than 5 μm, among which 89.3% was less than 2 μm and its specific surface was 4.59 m^2/g. The suspension was prepared at the concentration of 1 mg quartz/ml with deionized water. Al citrate with Al of 9.26% was supplied by Pharmaceutical Factory of Beijing Medical University and its solution was prepared at the concentration of 1 mg Al/ml with deionized water. The suspension of quartz plus Al citrate was prepared by Al citrate with 1 mg Al dissolved in 1 ml quartz suspension mentioned above. Quartz particles were pretreated with a same Al amount contained in Al citrate or AlCl3 solution. So called pretreatment, quartz or titanium dioxide particles were mixed proportionally with a certain Al amount contained in Al citrate or AlCl3 solution. The suspension was centrifuged repeatedly, and washed with deionized water until Al in the last supernatant was not detected and then the precipitated particles were stoved.[1] Titanium dioxide with a similar pure and size was obtained from Beijing Chemical Factory and its preparation was also as same as quartz. Fluorescence probe morin was purchased from Merck, Germany. The concentration of its stocked solution and applied solution were 500 μm/ml ethanol and 50 μm/ml ethanol, respectively.

Instrument and Conditions

Viscosimeter Model E (Japan), 25°C, shear transformation velocity 100 S-1.

Cell electrophoresis Autotimer Model Sx-2 (China), 25°C, voltage 40 V, electrode distance 5 cm, e.g. electric field intensity 8 v/cm.

Formulation (5): particle electrophoretic mobility (V)=L/E

L: mobility distance (μm) of particle in unit time (sec);

E: electric field intensity

The charged property of colloidal particle is expressed usually by its surface −potential as following:

$$\zeta = 6\ \pi\eta\ L/DE.f(Kr) \quad (6)$$

D: dielectric constant of water, 78.54 at 25°C;
η: medium viscosity (P);
f(Kr): coeffient related to size and shape of the determined particle, taken 1 usually in small spherical particle

Statistical Methods

F test

RESULTS AND DISCUSSION

The Determinations of Surface-Bound Al of Quartz and Titanium Dioxide Particles.

As shown in Figure 1 and 2, fluorescence excitation and emission peak position of Al citrate after the addition of morin shift all about 5 nm towards high frequency as compared to AlCl3. However, Figure 3 and 4 illustrate that the difference disappears under the pretreatment of quartz particles with Al citrate or AlCl3, and their excitation and emission are 440 nm and 515 nm, respectively, suggesting that ions such as Cl-, citrate radical which may interfere with the determination have been washed out after the pretreatment and only Al remains to be bound on the surface of quartz particles. While fluorescence intensity of titanium dioxide pretreated with Al citrate is not only very low, but also its excitation and emission peak position exhibit blue shift about 15 nm and 10 nm, respectively. On the other hand, no Al can be detected on the surface of quartz or titanium dioxide particles without the pretreatment, indicating a little of their inherent Al. Policard et al has determined the surface-bound Al of quartz by X-diffraction.[6] It is obvious that fluorescence label technique utilized in the present study is simple and sensitive and is used to do quantitative analysis.

The data listed in Table I show that: a) surface-bound Al of the pretreated quartz particles was increased with increasing Al dose to a certain extent, but not by proportion. It was also found that about 1:2 ratio of Al to quartz dose can prevent effectively the cytotoxicity or membrane damage from quartz in our other studies; b) the amount of surface-bound Al of quartz particles pretreated with a same Al dose is similar between Al citrate and AlCl3; c) the pretreated quartz under the washing with HCl led their surface-bound Al not to be detected, then the antagonistic effect of Al disappeared and the toxicity of quartz recovered;([1-2] d) the amount of surface-bound Al of titanium dioxide pretreated with a same Al dose of Al citrate is still very low, which is consistent with the finding that its effect on cells or membranes was unable to be affected by Al citrate.[2-4]

The Determinations of Surface 2 ζ −potential of Quartz and Titanium Dioxide Particles and the Effects of Al Citrate or AlCl3

We began with the examination of medium viscosity due to its effect on electrophoretic mobility and surface ζ −potential of particles. From Table II, viscosity of Al citrate solution and the addition of quartz or titanium dioxide is higher, but medium viscosity was not influenced by the pretreatment with Al citrate or AlCl3, suggesting that only free ions such as Al3+ presented in solution may affect medium viscosiy.

It is seen from Table III, both quartz and titanium dioxide particles charge negatively but surface charge density of quartz is much higher than titanium dioxide ($P<0.01$), resulting in its higher electrophoretic mobility and surface −potential, for instance, its ζ −potential value is 34.5% higher than titanium dioxide. Why quartz can interact with the choline groups charged positively in membranes leading

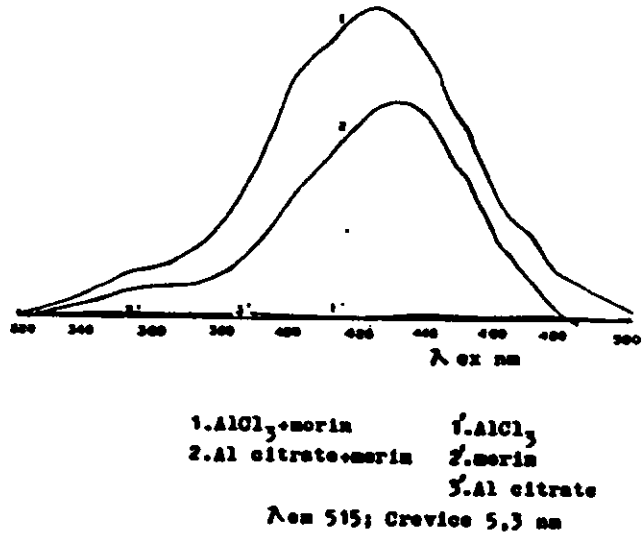

Figure 1. Fluorescence excitation spectra.

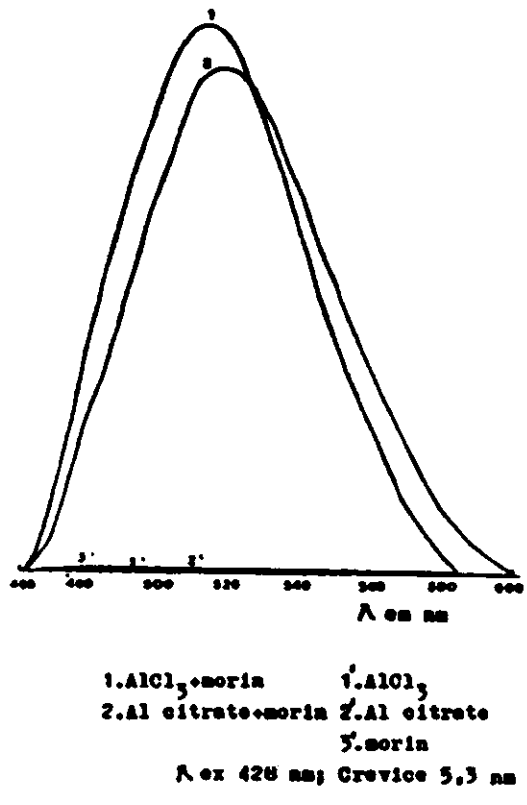

Figure 2. Fluorescence emission spectra.

Table I

Surface-bound Al of Quartz and Titanium Dioxide Particles Pretreated with Al Citrate or $AlCl_3$

Al dose	quartz		titanium	HCl washing
(μg)	μgAl/mg	nM Al/cm	μg Al/mg	
31.3	1.82	1.47	----	----
62.5	2.58	2.08	----	----
125.0	3.22	2.60	0.32	undetected
125.0*	2.99	2.41	----	undetected
250.0	3.12	2.52	----	----
500.0	3.16	2.55	----	----

The doses of quartz and titanium are all 300 μg. *$AlCl_3$

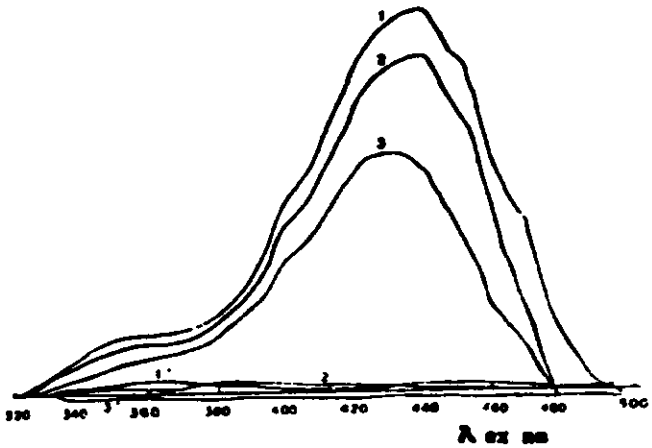

Figure 3. Fluorescence excitation spectra.

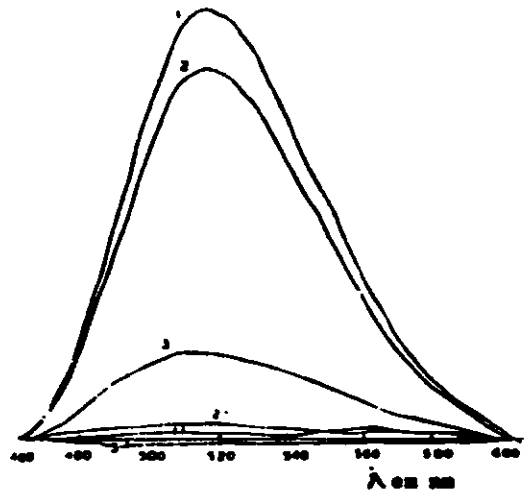

Figure 4. Fluorescence emission spectra.

the increase of the negative charge density on the surface of macrophages may be just due to its larger inherent negative charge density and its higher affinity for $-N+(CH3)3$. As pointed out by Nolan, the more the negative charge is imparted by ionized silanol groups on quartz surface the stronger its haemolysis is.[7]

It is interesting to find the amount of surface-bound Al of quartz particles pretreated with Al citrate or AlCl3 were not only increased significantly, but also their electrophoretic mobility and surface ζ −potential were lowered markedly. Although the decrease of ζ −potential is less in the pretreatment than in quartz plus Al citrate without the washing, surface-bound Al of the pretreated particles is very firm, and plays an important role in pharmacology. The combination of quartz with Al by Si-0- Al bond can block the direct in

Table II
Medium Viscosity (η)

medium	η (cp)
Water	1.008
Solution of Al citrate	1.089
Suspension of quartz	0.996
Suspension of titanium dioxide	0.990
Suspension of quartz+Al citrate	1.071
Suspension of titanium dioxide+Al citrate	1.056
Suspension of quartz pretreated with Al citrate	1.002
Suspension of titanium dioxide pretreated with Al citrate	0.990

Table III
Electrophoretic Mobility (V) and Surface Electro Kinetic Potential (ζ −potential) of Quartz and Titanium Dioxide Particles and the Effects of Al Citrate on Them

Groups	V (μm/sec/ v/ cm)	ζ-potential (mv)	
	$\bar{X}$ ± SE	$\bar{X}$±SE	%
Quartz	4.051±0.075	87.5±1.6	100.0
Titanium dioxide	2.654±0.081	57.3±1.8	65.5
Quartz pretreated with $AlCl_3$	3.426±0.112	74.0±2.4	84.6
Quartz pretreated with Al citrate	3.381±0.118	73.1±2.5	83.5
Titanium dioxide pretreated with Al citrate	2.568±0.032	55.5±0.7	63.4
Quartz+Al citrate	2.296±0.062	54.0±1.5	61.7
	----	(49.6±1.4)	(56.7)
Titanium dioxide+Al citrate	2.173±0.048	51.4±1.1	58.7
	----	(46.9±1.1)	(53.8)

The values in brackets are theoretical values calculated except the effect of medium viscosity.

teraction of quartz with choline groups of membranes, so that the order structure and stability of membranes were maintained.

As compared with quartz, no significant decrease of surface ζ −potential of the particles was found after the addition of Al citrate to titanium dioxide suspension, a difference of ζ −potential occurred only between the theoretical value calculated except the effect of medium viscosity and the determined value of titanium dioxide itself ($P < 0.01$). However, there is no significant difference in ζ −potential between under the pretreatment with Al citrate and without the pretreatment ($P > 0.05$) (Table III). This fact indicates that surface-bound Al of titanium dioxide is very little and is unable to change the structure and property of the particles and explains why its effect on cells or membranes can not be affected by Al citrate.

In deed, surface-bound cations like A13+ of quartz will increase its nonpoisonous surface area resulting in the reduction of its toxicity, which will provide a clue for screening new drugs for silicosis. In addition, according to theory of electric double layer, whether collosol is stable in a certain condition will depend on the gravitational force and electrostatic repulsion among these particles. They will become easy to coacervate and sedimentate due to the reduction of their repellent potential energy and stability, if ζ −potential and charge of the colloidal particles are decreased. The

coacervation and sedimentation of these particles are not only beneficial in discharging from lung, but also in precipitation from the air. Therefore, it will be more efficient to prevent silicosis through the way changes the physical and chemical properties of the particles, so that their toxicity themselves will be lowered and their fall will be increased. It should be considered that a potential role of such cations as A13+ plays in wet clearing dust, for example wet drilling.

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RELATIVE TOXICITIES OF PHLOGOPITE, BARITE AND QUARTZ

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ABSTRACT

Phlogopite is a silicate mineral belonging to the biotite mica group. Apatite mine deposits of eastern Finland contain 65% phlogopite, 14% calcite, 4% dolomite, 10% apatite, and 5% richterite. Phlogopite is used in many industrial applications including paints and fillers. Although mica is considered as a non-toxic mineral, recent toxicity studies in our laboratories and sporadic case reports have indicated a potential for lung damage. This investigation evaluated the *in vitro* effects of respirable phlogopite using conventional toxicity bioassays. The results were then compared with positive (quartz) and negative (barite) controls to assess relative toxicities. Cytotoxicity of minerals were compared by measuring their effects on sheep erythrocyte hemolysis, lactate dehydrogenase, β-glucuronidase, β-N-acetyl glucosaminidase release from alveolar macrophages (AM) and hydrogen peroxide and superoxide secretions from AM. Results of hemolysis studies indicated that phlogopite mineral is non-toxic to erythrocyte cell membranes at a dust concentration as high as 10 mg/ml. Data on the AM enzyme studies have, however, shown considerably greater levels of enzyme release and secretions of superoxide and hydrogen peroxide from AM by phlogopite. These results suggest that phlogopite mineral in respirable fraction is cytotoxic, and further studies are warranted to evaluate the fibrogenic potential.

No Paper provided.

EFFECTS OF MINERAL DUSTS ON ULTRASTRUCTURE AND FUNCTION OF ALVEOLAR MACROPHAGES

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ABSTRACT

The effects of mineral dust on biomembrane and organelle in alveolar machrophages in vitro were studied. The results suggest:

1. When the mineral dusts were concentrated at the secondary lysosome in the alveolar macrophages in vitro it indicates that the structure of cytoplasma is always normal. Swelling and degenerative mitochondria, abnormal structure cytoplasma and separated karyolemma were observed when silicon dust spread in cytoplasma.
2. The investigation of the effects of dusts of quartz, asbestos, graphite, TiO_2, Be, Sb etc. on biomembrane of alveolar macrophages in vitro indicated that they differed greatly at the same concentration.
3. It is postulated that stress should be put on choice of drugs with protection effect on cytomembrane. Such as VitE, SOD, PVPNO and piperaquie in order to prevent cell damage.
4. The study on effects of the four kinds of mineral dusts on protein synthesis in alveolar macrophages was carried out by incorporation of ^{5}H-Leu.

INTRODUCTION

Alveolar macrophages play an important role in the onset and development of the diseases in the lung, especially during the process of pulmonary fibrosis in pneumoconiosis.[1-2]

Scientists in various country have paid special attention to the investigation of the relation between macrophages and the factors which cause diseases. In this investigation the electron microscopy had been applied to study the effects of different dusts on the morphorological changes of cell membrane and organellae and to observe the protective effects of several kinds of drugs to cell membrane. Radioactive isotope tracer technique has been used to determine the synthesis of protein to illustrate the toxicity of alternative way.

MATERIAL AND METHOD

Dusts

The content of free SiO_2 in quartz is 99%. All asbestos are UICC product produced in Germany. The Particles of Sb_2O_3 dust are less than 1 μm. No free SiO_2 was found in it. The purity of TiO_2 was more than 99%. All the dust particles were less than 5 μm. the particles of graphite and Be dust were less than 5 μm. There was no SiO_2 to be found. All of the dust was steriled by autoclaving and a 1 mg/ml solution was prepared with medium. Before using mixer. It was stirred thoroughly with a magnetic.

^{5}H-Leucine

The activity of the solution was 3.7×10^5. Bq/ml(100μ Ci/ml)

Drug

VitE was in capsules. SOD was obtained from the laboratory of Suzhou Medical College. Piperaquine and P_{204} were unprocessed powder.

Alveolar Macrophage (AM)

AM were obtained by pulmonary lavage of guinea pigs using RPMR-1640 at sterile condition. Lhe cell suspensions were cultured with quartz and TiO_2 dust at different concentrations. Control cultures were treated similarly except that the dusts were omitted. After 6 and 15 hr incubation respectively the AM were collected by centrifugation. The precipitates were fixed. The samples were examined in transmission EM. 0.5 ml cell suspension was transferred into culture bottle with a sterile cover glass slip. After 2 hr incubation the cover glass slips were taken out. Then the cover glass slips were placed in the bottles with 199 medium 100 μg of quartz, asbestos, Sb, Be, graphite and TiO_2 dust were added respectively with the exception of the control. After incubation, the samples were taken out at different intervals.

The experiment of protein synthesis in vitro was carried out

in Hank's solution.[3] One milliliter of AM suspension at a concentration of 1×10^6/ml was put in centrifuge tubes and the dust of quartz, asbestos, graphite or TiO_2 was added to make the final concentration at 100 mg/ml. All tubes and the control were incubated at 37°C for 2 hr. After incubation 7.4×10^4 BQ(2 μCi) labeled leucine was added to each aliquot and incubated for another 3 hr. The same amount of labeled leucine was added to the control after incubation. The protein was collected and the activity was counted by liquid scintillation counter.

RESULTS

Effect of SiO_2 on Damage of Organella

Under the TEM one can find that pseudopodia disappeared, lysome disrupted Si particles existed in cytoplasm freely, mitochondria expanded pyknosis, necrosis of some cells appeared losing normal cytostracture with vacuolar changes of matrix, presence of spare cytoplasm, nuclei were expanded to become round or oval, matrix vacuolar change in nuclei, heterochromatin condensed under the nuclear envelope, expending or nuclear envelope disrupting were observed. In some cases the content of nuclei became homogeneous and showed a medium electron density. It was completely impossible to distinguish euchromatin, heterochromatin and nucleolus. The boundary of cells became indistinct. Cells were disrupted finally.

Damage to cells caused by TiO_2 was less than that caused by SiO_2. In this case the majority of cells are in stress shown by expanding of cell volume, increasing of pseudopodia, phagosome and rough surfaced endoplasmic reticulum. No necrosis cells were observed in the control.

The Effect of Quartz and Other Dusts on Cell Membrane

The investigation of the effects of quartz, asbestos, graphite, TiO_2, Sb, Be on the biological membranes has demonstrated that AM be different in response to different kinds of dusts. Among them the damage effect of quartz to membrane is the most obvious one. No abnormal changes of cell membrane were observed in the control in which cells had been cultured for different periods of time. The majority of these cultured adhesive AM cells in vitro coming from healthy rabbits were round, oval and astroid. There were evenly spreading ruffles at the cell membrane with irregular margin. Long or short filopodia, finger-like and pseudopodia were observed at cell membrane (Figure 1). The static pseudopodia were less and the active pseudopodia were more. When the pseudopodia accept a stimulating information it stretched itself to the foreign body and the cell at the opposite side then the cell moved to the foreign body (Figure 2).

The response of AM cultured in medium to Si dust was active. The change of membrane was characterized by the following features: (1) uneven ruffles were present first then disappear gradually and the cell membrane becomes homogeneous and smooth (Figure 3); (2) vacuoles were present at the surface of cell (Figure 4); (3) various size of holes were present at cell membrane (Figure 5); (4) pseudopodia and microvilli disappeared.

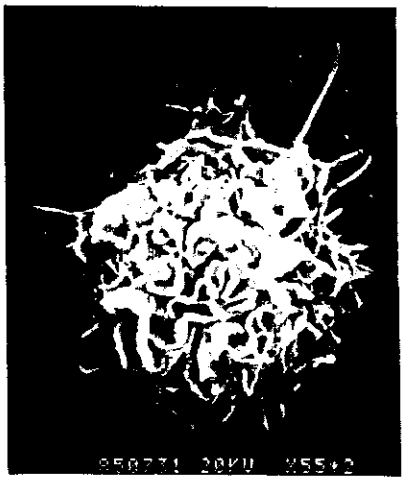


Figure 1. Control M ×5500.

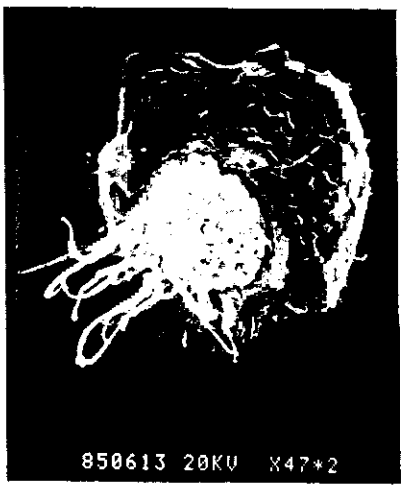
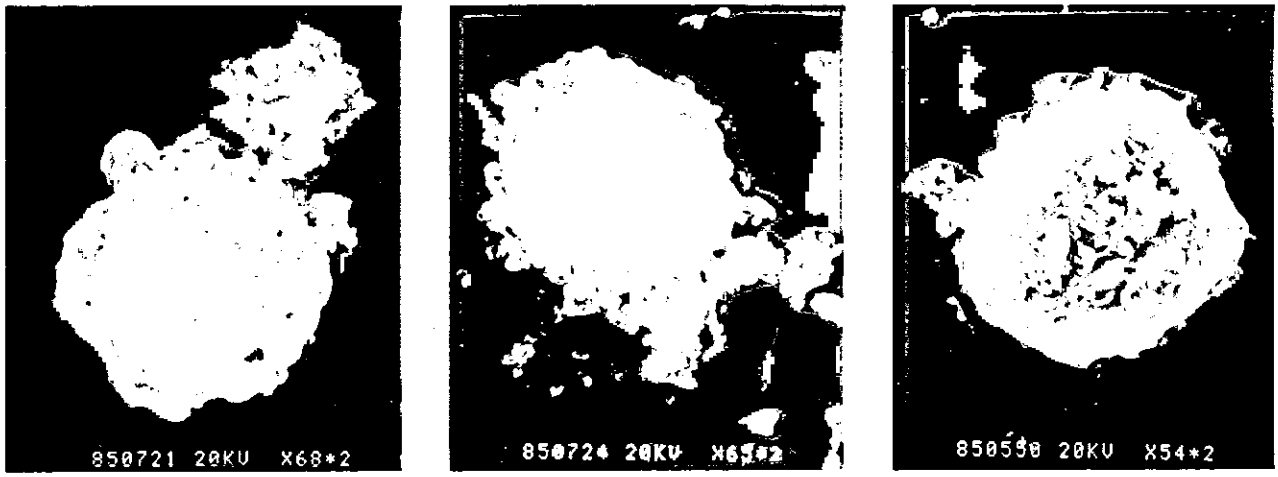


Figure 2. Pseudopodia and skirt margin ×4700.

In the AM cultured with asbestos fibers attachment was observed in the samples taken at the 5 min after the adding of the dust. The response of AM to different length of asbestos fibers was different. The short asbestos fibers were absorbed locally and were phagocytosed in situ. In this case the response was not obvious and the change of cell membrane was less. As the long asbestos fibers were concerned, the cells were phagocytosed in a sleeve-like fashion or phagocytosed the dust from the near end of the asbestos fibers by stretching numerous small pseudopodia at the surface of the cells. Some macrophages could phagocytose a large amount of asbestos (Figure 6). Such kinds of cell were more often to be observed at the interval of 18 hr and 24 hr samples cultured and structure of cell membrane and its morphology were normal. The phaocytosis in the cells cultured with Si dust was different from that in the cells cultured with



Figures 3–5. After adding SiO_2 and incubated at 37°C for 30 min. Ruffles are uneven and pseudopodia disappear, ×5400. The vacuole structure is present at the surface of membrane. The membrane is even, ×6500. Various sizes of holes are present at the pyknosis membrame, ×6800.

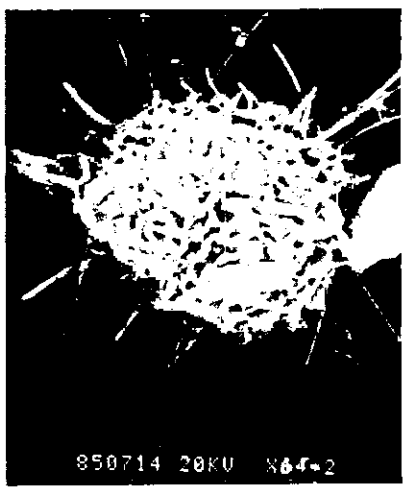


Figure 6. After adding asbestos fibers and incubating at 37°C for 10 hrs randomly fibers are present. ×6400

asbestos. In the latter case the cells aggregation should be observed on the cover glass slips and more cells phagocytosed a bundle of asbestos in common. As the culture time prolonged the dying cells increased gradually. The cell membrane interrupts before dying, the membrane ruffles disappeared and membrane dissolved locally. Comparing with that in Si group the dying of cell delays.

When Sb, Be, Graphite and TiO_2 dusts were added into the medium with AM and incubated for 5 hr the difference of cell membrane was very significant. In the group of Sb dust filopodia stretched themselves to various directions, and disorder of ruffles observed. The reaction of cells were very strong (Figure 7). In the group of Be dust straw-hat-like changes were observed in the majority of cells (Figure 8). In the group of graphite no obvious changes in the cell membrane were observed. In the group of TiO_2, large amount of absorbed TiO_2 particles which were phagocytosed in situ were observed. Some dust particles were taken by the flattened pseudopodia and there were partially morphorological changes of cell membrane. Ruffles at cell membrane could still be observed. It seems that TiO_2 has less effect on membrane structure.

Protection Effect of Drugs on AM Cell Membrane

SiO_2 was used as a cell damage agent. Cells were cultured in vitro and SiO_2, VitE, SOD, 4% P_{204}, and piperaquine were added to the cell suspension to make the final concentration to be 100 μg/ml, 40 μl/ml, 40 μl/ml, 100 μg/ml respectively. The samples for SEM were prepared at the 5 hr and 10 hr interval after the addition of drugs. All of the 4 drugs have protective effect on cell membrane. After the addition of these drugs AM were very active and the activity of pseudopodia was very frequent. Among them the effect of Vit E and SOD were more obvious.[4] Incorporation of H-Leucine in Cultured Cells

The effect of 4 kinds of dusts on protein synthesis in AM were shown that suppressive effects on protein synthesis the asbestos dust is the most significant one. The ratio to control counterparts for protein synthesis was 54.6%. The effect of graphite was the minimum.[4] (Table I)

DISCUSSION

AM is one of the most effective cells for phagocytosis. It plays an important role in removing foreign bodies in lung.

Figure 7. After adding Sb dust and incubating at 37°C for 5 hrs. filopodia are present, ×3300.

Figure 8. After adding Sb dust and incubating at 37°C for 5 hrs straw-hat like margin is present, ×4900.

Table I
Effects of 4 Kinds of Dusts on Protein Synthesis in AM

Sample	No	Viability %	Counts cpm/10^5 AM	Correcting to living cells	Ratio to the control
Control	7	96	26346	27443	100
Quartz	13	85	15838	18629	67.9
Asbestos	9	90	13478	14975	54.6
Graphite	8	89	22313	24792	91.2
TiO_2	10	87	17825	19375	74.7
*Blank			1221		

*^{3}H-Leu was addid at the end of incu bation in blank.

Recent investigations demonstrate that the function of AM have close relation with various pulmonary diseases e.g., infection, tumor and pulmonary fibrosis. Great attention has been paid to the investigation of morphorology, function and metabolism of AM and its interrelation to other kinds of pulmonary cells. Phagocytosis to 15 kinds of dust in AM in vitro has been investigated by successive photography by Diavert revert phase contrast microscope.[5] During the process of phagocytosis the change of cell membrane and response of cells were obvious. In order to know the mechanism of phagocytosis the effect of quartz dust etc. on organellae has been investigated. The results obtained demonstrate that the toxic effect of SiO_2 on lysosome is present most early. The toxicity of quartz is closely related to its concentration and the duration of action.

The response of cell membrane to different kinds of dust or different length of fiber dust particles of the same dust was different.[6] Brains[7] has reported that when the cells contact with foreign body, absorption occurs first and the change of the absorption depends on the chemical and physical properties of the dust particles. During phagocytosis, the increasing of the cell volume, energy metabolism and membrane receptors were observed. In this investigation the holes of cell membrane at the site of absorption and formation of phagocytosis vacuoles to quartz were observed in the process of AM.

The way of short asbestos fiber phagocytosis is the same to that of SiO_2. But the phagocytosis was slow and only a slight change of cell membrane was observed; while the long

asbestos fiber can be phagocytosed by one or more than one cell which caused aggregation of cells. The ability of phagocytosis of AM to dusts of quartz and asbestos may be related to C_3 receptor and Ig G receptor.[8-10] Sb dust caused the formation of a large amount of filopodia, intensive cell response and obvious morphological changes of cell membrane. Be dust caused the formation of more straw-hat-like cells which will be studied further.

In the aspect of morphological change of the cells the membrane change caused by SiO_2 was the fastest one and damage was obvious. Asbestos had less effect on AM. After phagocytosis of a large amount of fibers only less changes of cell membrane were observed until 24 hr after addition of dusts of asbestos. During the process of examination of AM cells in vitro by successive photography we found that cells can still move in peristalsis way and trasmigrate. There are some reports on interaction between mineral dusts and the membrane. The common viewpoint is that the change of membrane is concerned with the electronic structure at the surface of the mineral particle.

Both VitE and SOD are removing agents of free radicals. The picture of SEM demonstrates that they can protect the membrane from being damage. Schlipköter has demonstrated that P_{204} can form hydrogen bonds with SiO_2 in priority competitively to protect cell membrane piperaquie can make the membrane of lysosome stable. In the investigation of the effect of quartz and coal on phagocytosis, Comolli et al[11] found that labeled leucine tracer technique was the most sensitive one for the determination of protein synthesis. After addition of dusts, protein synthesis was observed 2 hr later. The effect of asbestos dust on protein synthesis was the most obvious one while the effect of quartz dust came the second. The mechanism of suppression of protein synthesis is waiting for further study.

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SUPPRESSION OF QUARTZ CYTOTOXICITY BY PULMONARY SURFACTANT—ELECTRICAL EFFECTS

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ABSTRACT

It is known that respirable native quartz particles are cytotoxic to erythrocytes. Coating the quartz particles with lecithin, a major component of pulmonary surfactant, reduces hemolysis significantly. The zeta potential of lecithin coated quartz, in physiological saline, is significantly less than that of native quartz. A biophysical model for erythrocyte cell—quartz particle interactions, in physiological conditions, has been developed. The model predicts that native quartz particles, approaching an erythrocyte to distances below 10 nm, induce, in the erythrocyte cell membrane, large electrical fields (400 kV/m to 600 kV/m), sufficient to rupture the cell membrane and cause hemolysis. Because of their low zeta potential, lecithin coated quartz particles, on the other hand, do not induce large membrane electrical field strengths. This result adds to the evidence supporting the electrical nature of the mechanism of hemolysis by mineral dusts.

No Paper provided.

PHYSICOCHEMICAL CHARACTERISTICS OF QUARTZ DUST WHICH CONTROLS ITS BIOLOGICAL ACTIVITY

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ABSTRACT

The biological activity of quartz is controlled by specific and defined characteristics of its respirable dust. Virtually the totality of the evidence concerning the fibrogenic activity of quartz dust shows that it is dependent on particle-size distribution, surface properties of the constituent particles and dose delivered to pulmonary tissues. All of these characteristics have been tested *in vivo* and *in vitro*, and have been demonstrated to be the most important variables which control biological activity. The progression of human lung pathology, and fibrosis, are strongly dependent upon the intensity of exposure and these physicochemical characteristics.

Although historically considered a fibrogenic agent, recent reports have suggested that quartz, as well as other forms of crystalline silica, may be an animal carcinogen. Some citations have extended this so that quartz and other silica polymorphs are considered possible human carcinogens. The properties of quartz found to be important in fibrogenesis will be reviewed and extended to include its proposed carcinogenicity.

No Paper provided.

ALTERATION OF RESPIRABLE QUARTZ PARTICLE CYTOTOXICITY BY THERMAL TREATMENT IN AQUEOUS MEDIA

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ABSTRACT

Respirable quartz cytotoxicity, as measured by erythrocyte hemolysis and pulmonary macrophage release of lactate dehydrogenase *in vitro,* is neutralized by boiling in water in glass test tubes for 10 to 40 minutes. The cytotoxicity is reduced to near zero by boiling 1 to 10 mg quartz per milliliter water. For greater concentrations of quartz in water the hemolytic potential after 40 minutes of boiling approaches that of native quartz. Replacing the medium with fresh water midway through boiling results in full detoxification through 20 mg quartz per milliliter water. Pre-boiling the medium with silica reduces the detoxification effect. Detoxification persists after mild drying at 110°C for 8 hours, and persists after three days of resuspension in water at room temperature.

INTRODUCTION

Reasearch underway to determine interactions of quartz and other mineral dust surfaces with pulmonary fluids and alveolar macrophages in culture led to the observation that when dusts were autoclaved in aqueous suspension, their cytotoxic effects on macrophages were suppressed, in some cases fully and even after several days incubation with the cells. This finding was in direct contradiction to earlier results from both short term macrophage lysosmal enzyme release assays, as well as longer term cytotoxicity assays from macrophages in culture; in those studies, dusts were steam autoclaved at 121°C with no liquid water but with steam present.[1,2] However detoxification under boiling conditions has been reported in other research.[3] It was decided to use the hemolysis assay to further investigate these findings, because of its sensitivity, simplicity and cost.

RESULTS AND DISCUSSION

Respirable quartz dust used in this study was taken from a stock of crystalline silica, Min-U-Sil, obtained from Pennsylvania Sand Glass Corporation, fractionated in air with a particle classifier. The small size fraction retained for use was 80% less than 5 micrometer particle diameter, with an area equivalent median diameter of 1.24 micrometers as estimated by automated image analysis. The silica was at least 98.5 mass percent silica as determined by X-ray energy spectrometric analysis; and the crystalline form was alpha-quartz as determined by X-ray diffraction. It's specific surface area was 3.97 square meters per gram as determined by nitrogen adsorption isotherm methods.[1]

To measure the erythrocyte hemolytic potential of treated and untreated dusts we use the method of Harington et al,[4] with minor modification.[1] Briefly, dusts suspended in buffer are mixed with an equal volume of 4% sheep red blood cells, and incubated 60 min. at 37°C with periodic mixing. Next the cells are spun down, and the absorbance of the released hemoglobin from any lysed cells read at 540 nm. Absorbance values are compared to positive controls (100% lysed cells) and negative controls (cells in buffer only).

Initial experiments involved bringing deionized water to a boil, adding the dry dust (12 mg), vortexing, and boiling for periods up to 60 min., without stirring. This was done in flint glass tubes for samples with dust concentrations of greater than 1 mg/ml, and in polycarbonate tubes for lower concentrations. After the boiling period was completed, sample tubes were spun down for 60 sec., the supernatant discarded, and the dust resuspended in phosphate buffered saline (PBS) and run in the hemolysis assay. Results indicated that the toxicity was reduced almost to zero at 1 mg/ml, and increased in a roughly linear fashion to approximately full (native dust) toxicity at 20 mg/ml dust concentration during boiling. (Figure 1).

When individual magnetic stirrers were used in each sample, results were similar, except the toxicity was reduced to virtually zero at concentrations to 10 mg/ml, and then increased in a linear fashion. Samples were also boiled for half the specified times, centrifuged, the medium changed to fresh water, and boiling continued for the rest of the period. The toxicity was reduced to very low levels through the highest

concentration tested. (Figure 2) As also shown, pre-boiling the water with a separate quartz sample before using the still hot supernatant to boil the test sample, somewhat diminished the detoxification phenonenon. We observed this diminution also in the case of pre-boiling the water with silica gel.

Experiments involving various boiling times showed a weak dependence of detoxification with time, except at 1 mg/ml, where detoxification progressed with boiling time. (Figure 3)

Limited tests of the persistance of the detoxification have been made and are continuing. One question was whether or not the passivation effect was due to some gel or other coating which might not withstand drying and resuspension. Samples were vacuum dried after boiling, and assayed the following day. Fully detoxified samples remained the same, and partially detoxified samples had slightly less toxicity after drying than replicate samples promptly assayed. (Figure 4) Fully detoxified samples boiled at 1 and 10 mg/ml which were decanted and placed in fresh distilled water or PBS did not retoxify over a 3 day period. (Figure 5) Other samples were left standing after boiling in the supernatant from the boiling water at room temperature. Fully detoxified samples boiled at 1 mg/ml remained at zero toxicity after 4 days. Samples at higher concentrations showed some increase with time; the sample boiled at 10 mg/ml was essentially fully retoxified. (Figure 6)

Certain samples in the assay yielded consistently anomolous results, and were difficult to reconcile with any simple physical model; specifically, samples boiled at 0.5 mg/ml were not detoxified. The only experimental difference in these samples was that they were boiled in plastic (polycarbonate) centrifuge tubes, since glass tubes were not available in an appropriate size. When quartz was boiled in flint glass, polycarbonate, and Tefzel tubes, only partial detoxification was seen. When boiled in polycarbonate tubes using water that had been boiled only in polycarbonate, no detoxification was seen at any concentration. (Figure 7)

Since the effect seemed clearly to be an effect of the glass containers, additional experiments were done to clarify the finding. Quartz dusts were boiled in water in polycarbonate tubes with varying amounts of 3 mm soda-lime glass beads. (Figure 8) There is a roughly proportional dependence of detoxification on the number of glass beads, and thus the glass surface area present. The effect was investigated also by using shards of glass cover slips in polycarbonate tubes during boiling. In general detoxification occurs with increasing glass content, but with a lessening of the effect seen at the highest glass content level. (Figure 9) The converse of this hypothesis, that polycarbonate somehow supressed the detoxification of quartz, was tested by boiling quartz in flint glass tubes with polycarbonate pieces in suspension; no significant effect of the polycarbonate was seen. (Figure 10)

An additional anomolous result occured when there was a failure in the reverse osmosis water purification cartridge in our laboratory building distilled water system, resulting in a higher impurity level than that present in tap water. Toxicity was partially supressed in all samples, even those boiled in polycarbonate; but detoxification was not complete for any treatment, even using flint glass tubes. (Figure 11) When the water system was restored to proper operation, the results

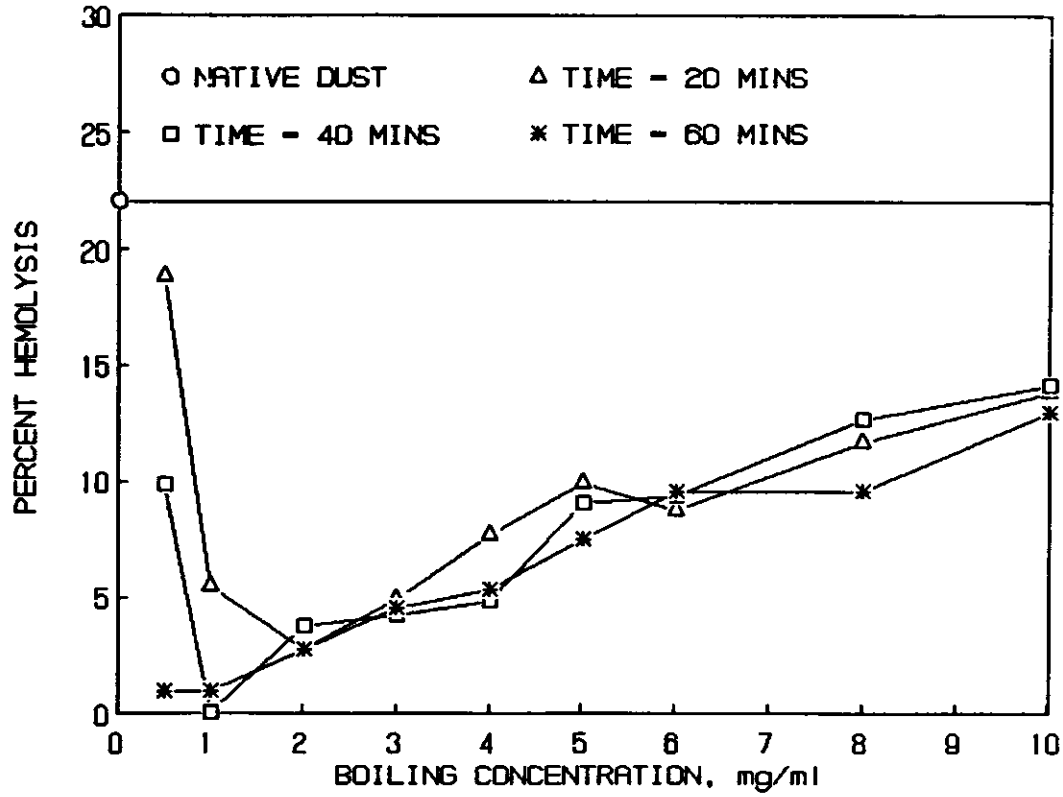

Figure 1. Silica cytotoxicity with boiling.

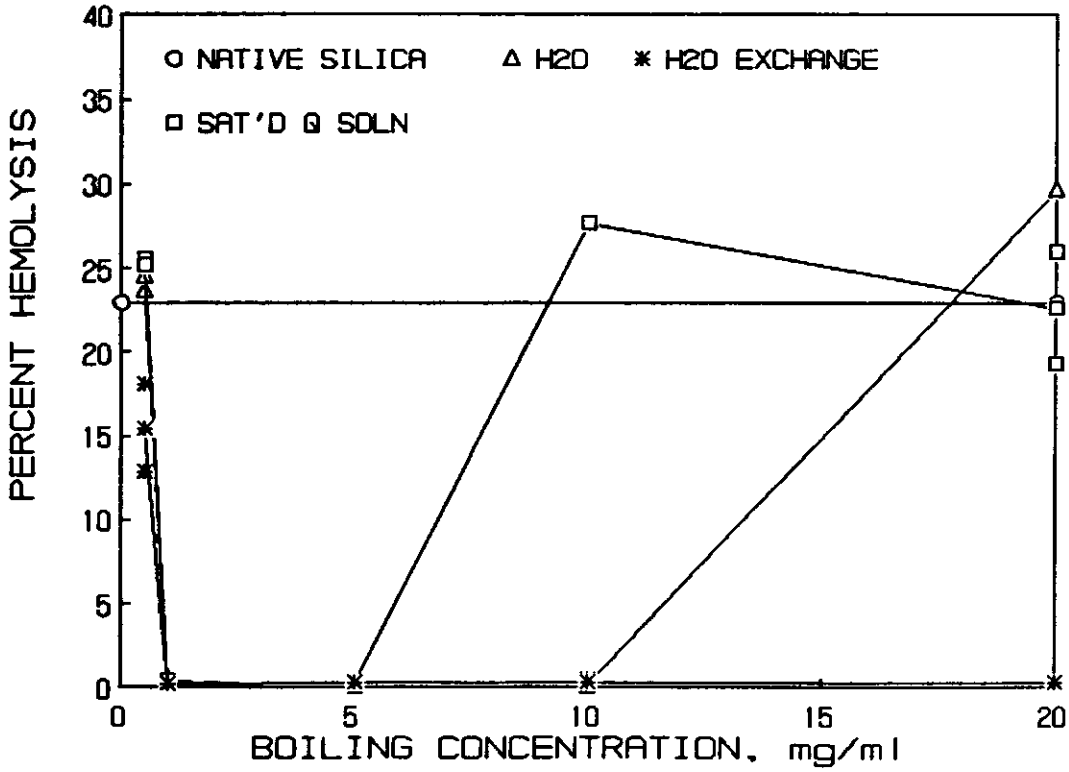

Figure 2. Quartz boiled 40° in various solutions.

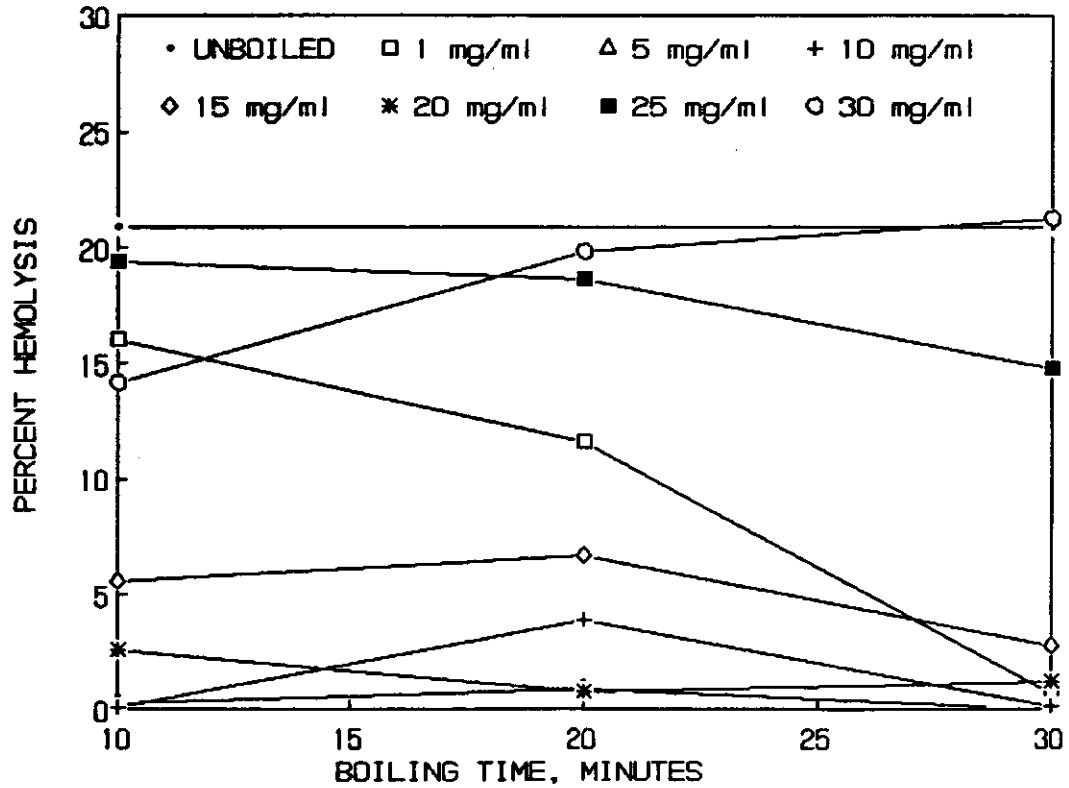

Figure 3. Hemolysis vs. boiling time.

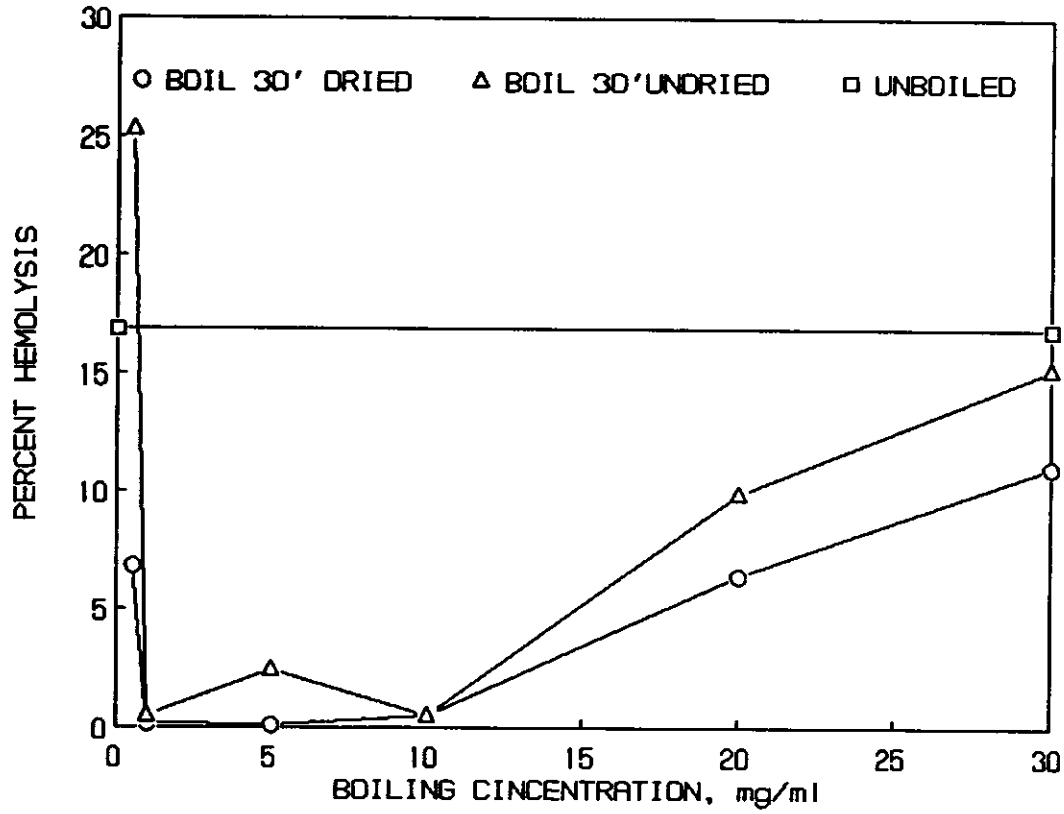

Figure 4. Hemolysis vs. post-boiling drying.

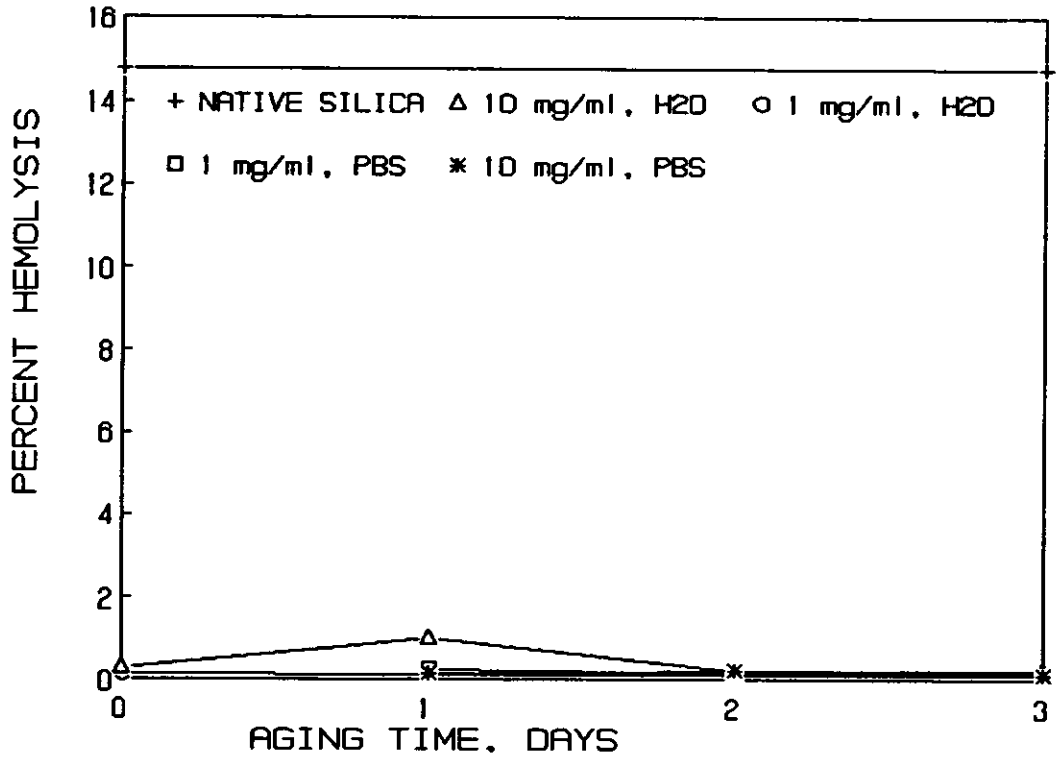

Figure 5. Quartz aged in H_2O and PBS.

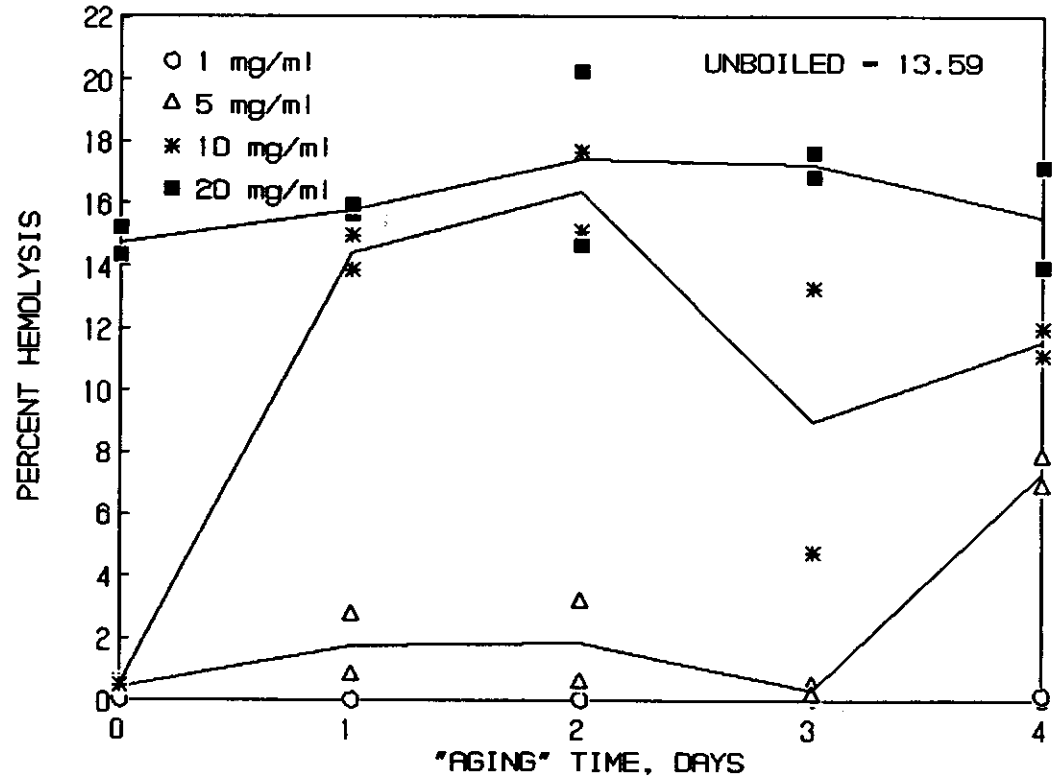

Figure 6. Hemolysis vs. time in supernatant after boiling.

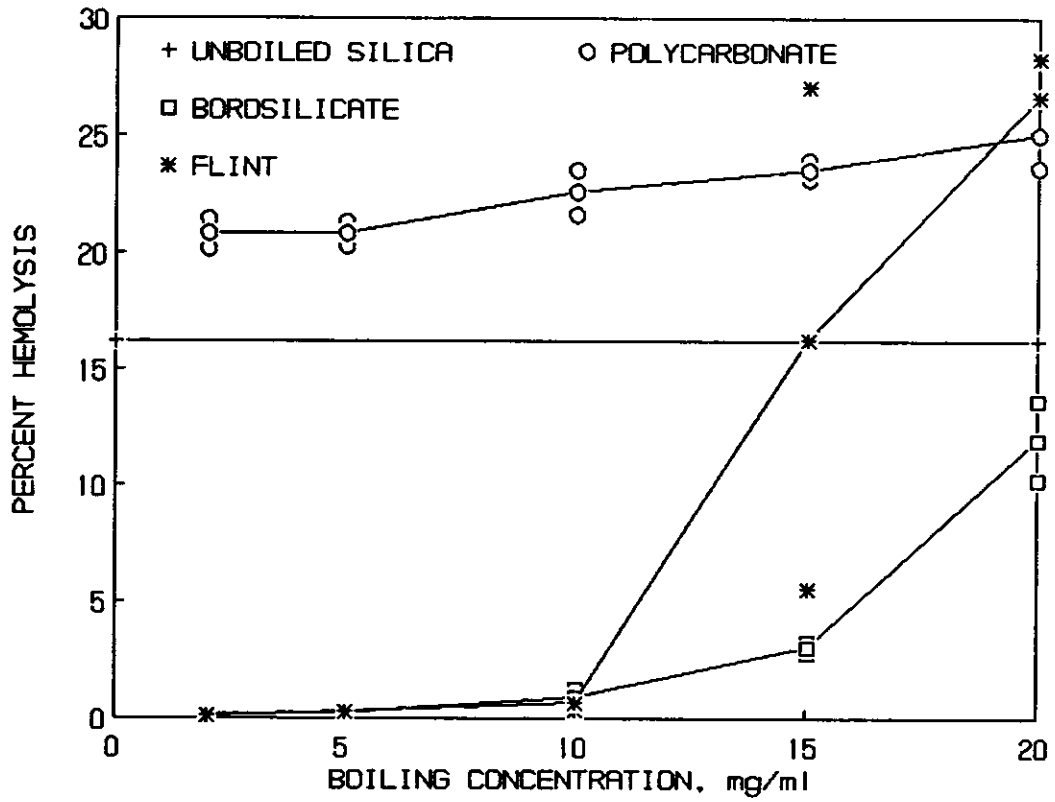

Figure 7. Hemolysis: quartz boiled in various tubes.

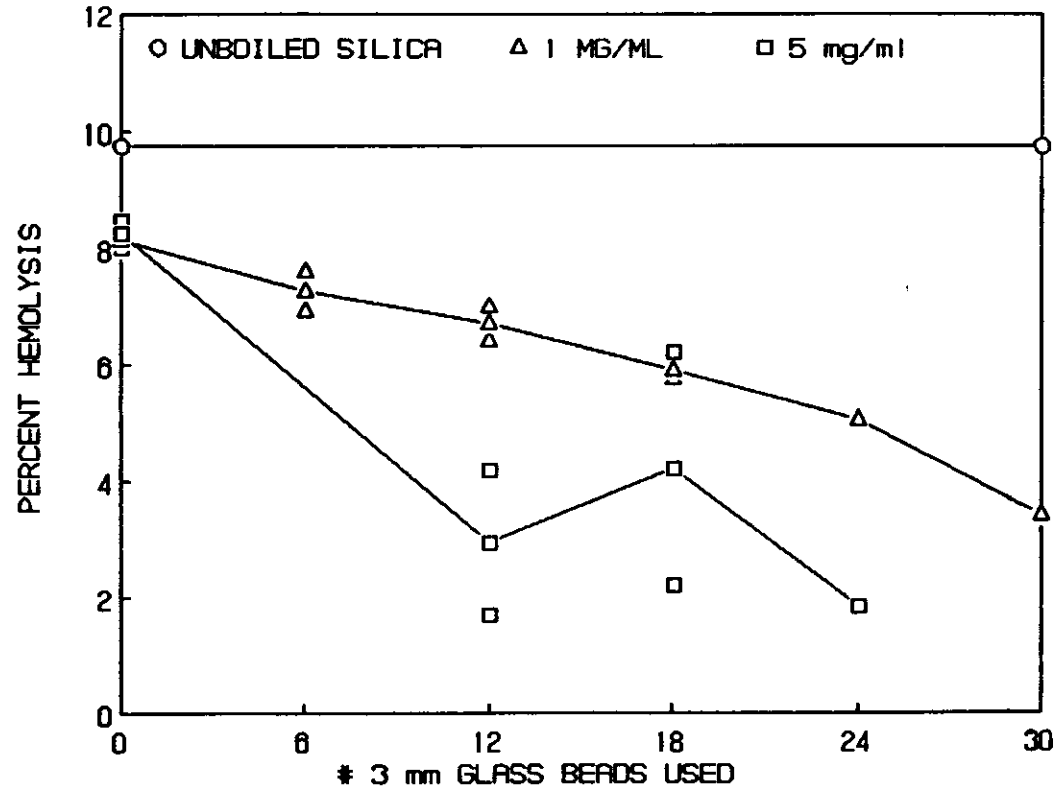

Figure 8. Quartz boiled 30° in polycarb W/glass beads.

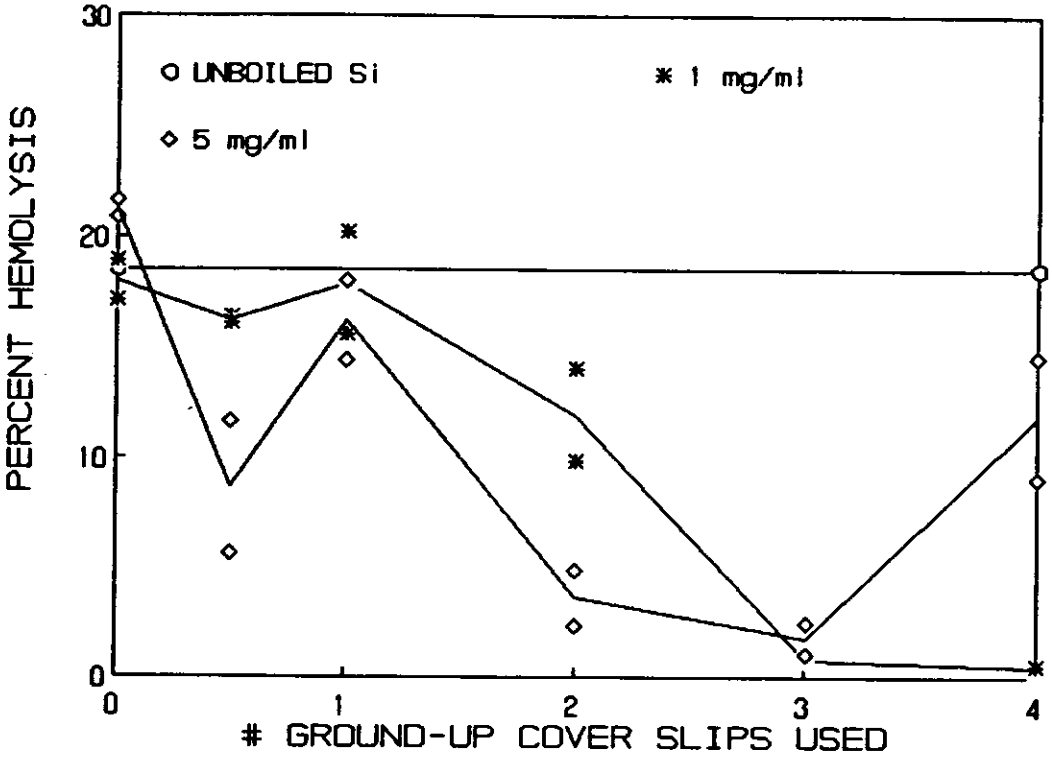

Figure 9. Quartz boiled 30° in polycarb W/glass pieces.

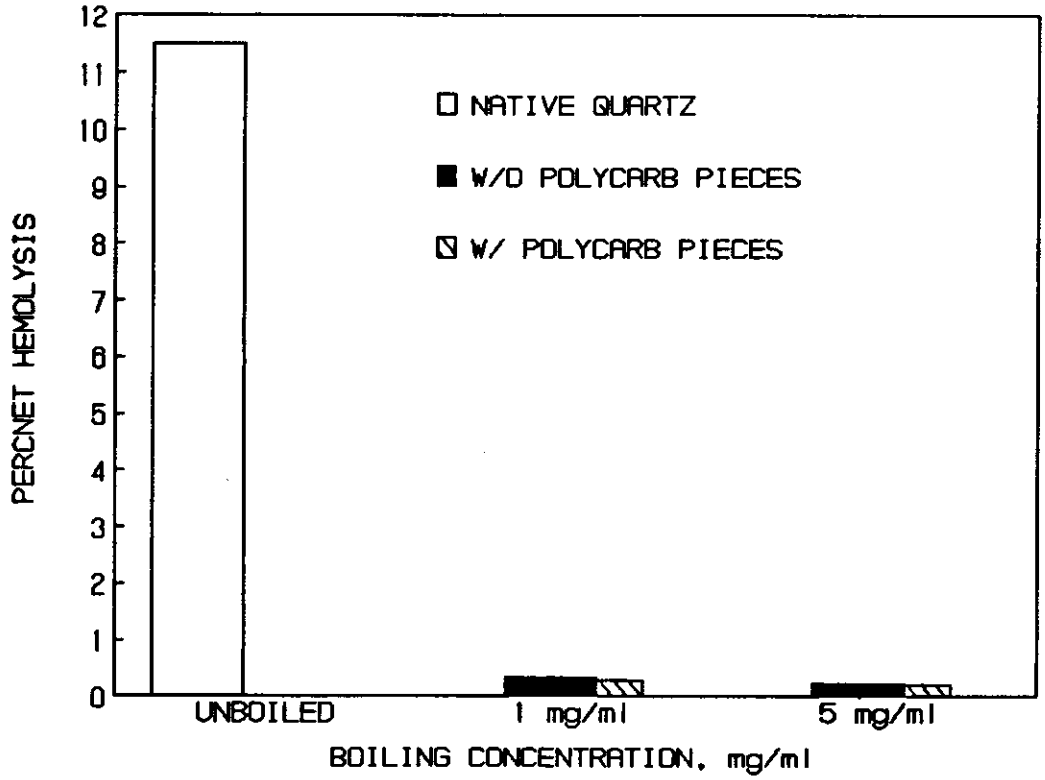

Figure 10. Hemolysis of quartz boiled in flint glass with and without polycarbonate pieces.

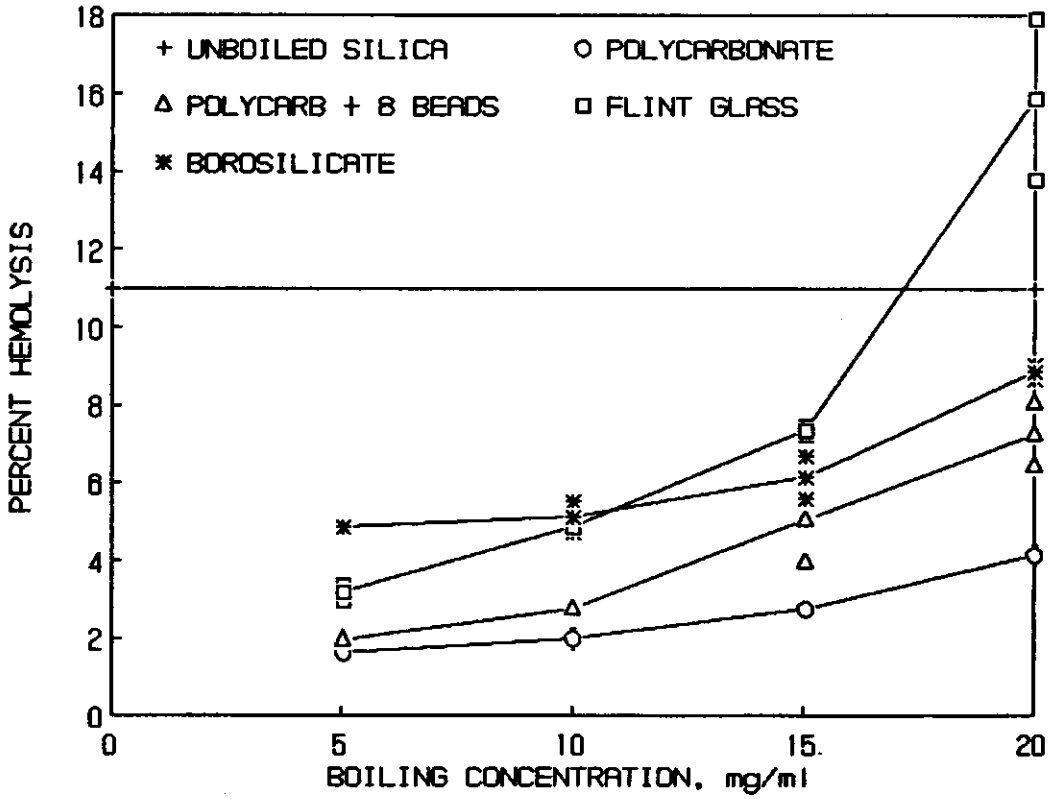

Figure 11. Hemolysis: quartz boiled in various tubes in contaminated water.

agreed with previous findings.In a limited investigation of this, quartz samples were boiled with sodium and calcium chloride solutions of several different concentrations; the effects were weak, slightly lessening the detoxification. (Figure 12)

Initial zeta potential measurements have been made on samples of unboiled quartz and on quartz boiled at 5 mg/ml in flint glass and in polycarbonate tubes. The zeta potentials for unboiled quartz and for quartz boiled in polycarbonate are essentially identical, while the samples boiled in flint glass show a less negative zeta potential. (Figure 13)

The boiling treatment was also applied to kaolin and alumina dusts. The kaolin dust, previously described,[1] was unaffected. A commercially obtained respirable sized alumina expressed hemolytic potential in its untreated state, and was detoxified upon boiling. (Figure 14) The untreated and treated alumina samples were subsequently analyzed by photoelectron spectroscopy, courtesy of the U.S. Department of Energy, Morgantown Energy Technology Center. The intention was to determine if the elemental composition of the alumina surface showed substantial levels of silicon in addition to aluminum after treatment. Results of the test showed, however, that the surface of the untreated alumina itself had a silicon-to-aluminum elemental ratio of about 4-to-1. This was reduced to about 1-to-1 after boiling. Studies using other dusts including asbestiform materials are ongoing.

CONCLUSIONS

At this point, several conclusions may be stated, and a partial working hypothesis formulated, namely:

- Quartz boiled in flint glass for times greater than ten minutes at concentrations between 1 and 10 mg/ml is partially to fully detoxified in the hemolysis assay.
- The effect is strongly concentration dependent between 10 and 30 mg/ml
- If a change is made to fresh boiling water midway in the process, then full detoxification occurs across the entire concentration range.
- The effect is present only in samples boiled in glass tubes, flint or borosilicate having been tested thus far; plastic tubes do not show the effect.
- The effect is only moderately time-dependent, tests having been limited to boiling times of 10 minutes or more thus far; at most concentrations the effect seems nearly complete at 10–15 minutes.
- The effect seems to persist on mild drying (overnight vacuum drying).
- Fully detoxified samples appear to show little or no cytotoxicity after soaking at room temperature in the supernatant from boiling for periods up to 4 days; partially detoxified samples show an increase with time.

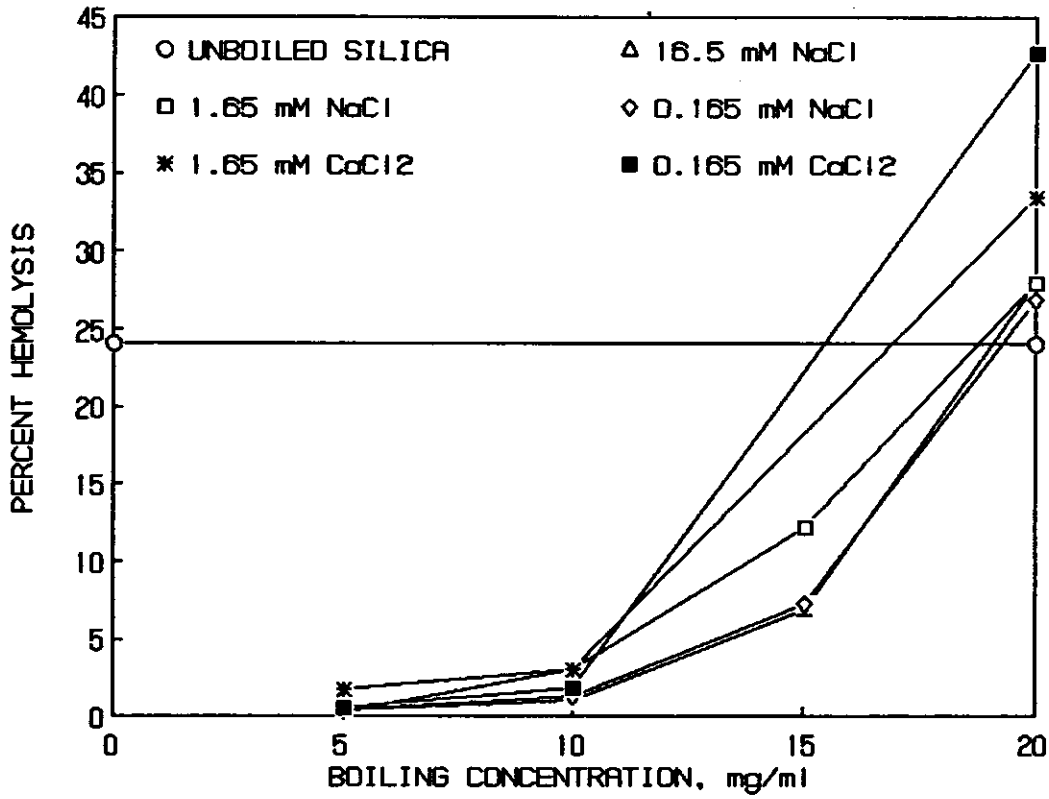

Figure 12. Hemolysis: silica boiled in NaCl and $CaCl_2$.

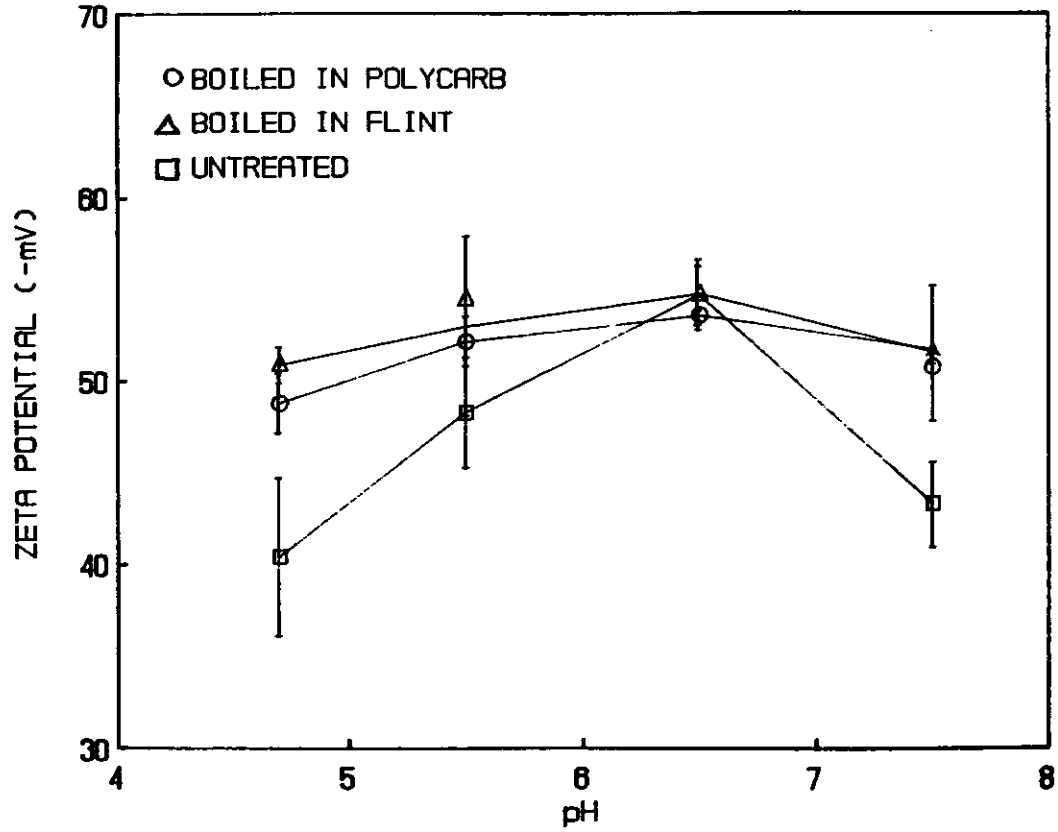

Figure 13. Zeta potential of quartz boiled in flint or polycarbonate.

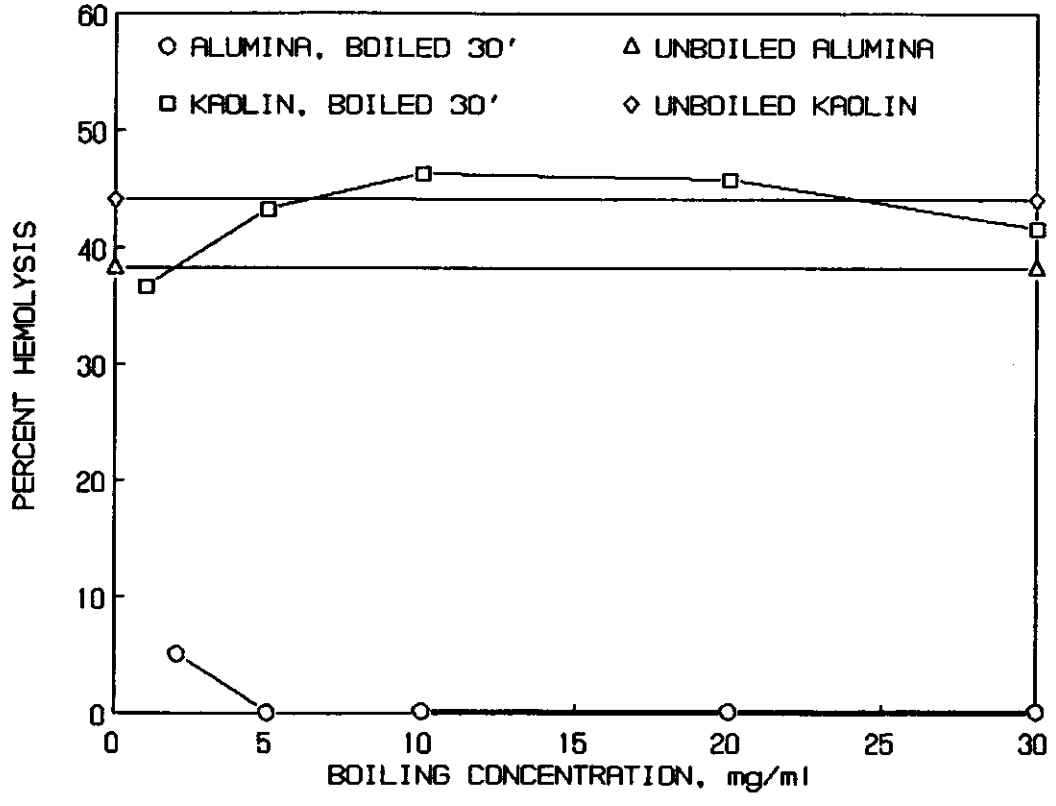

Figure 14. Hemolysis of boiled kaolin and alumina dusts.

- The detoxification shows some proportionality to available surface area of glass present during boiling.
- There is some indication that pre-boiling water with silica partly diminishes the detoxification effect for subsequently boiled quartz.

Further investigation is needed to more fully clarify the mechanism of quartz detoxification, but a partial hypothesis can be stated:

Boiling water releases a soluble or partially soluble factor, possibly silicic acid or sodium and/or calcium silicates or hydroxides, which, in monomeric or polymeric form, react or are physically adsorbed on the quartz surface, which fully or partially detoxify the mineral surfaces, as shown in *in vitro* cellular toxicity assays.

There is a significant amount of discussion in the literature concerning the dissolution of silica in water. Holt and King found that all sizes of quartz particles behave as if a soluble fraction of silica is leached from their surface, and that surface leached at pH 9 will rapidly adsorb the dissolved silica species.[5] Baumann measured the uptake of silicic acid by quartz from aqueous solution prepared by mixing silica gel in water.[6] In general, various silicates, including vitreous glass and quartz, are reported to have slight solubilities in aqueous media. The values found for quartz are on the order of one magnitude lower than the values obtained for glass under the same test conditions.[7] Iler states that the ability of quartz surface to hold water of hydration even after outgassing at 100C, in contrast to the behavior of amorphous silica, suggests a powerful hydrogen bonding capacity of the quartz surface silanol groups. He suggests this may be related to the peculiar power of quartz to adsorb multilayers of silicic acid as noted by Baumann.[8] This seems to favor a hypothesis that some soluble form of silica dissolves from both quartz particles and the glass container; that the "silicic acid" or a polymerized derivative re-adsorbs to the quartz; and this masks or otherwise passivates the quartz surface. Tests using pre-saturated medium raise the possibility that the quartz surface must undergo a desorption step or some conditioning before or in conjunction with adsorption of passivating species.

Suggested strategies for clarifying this would include radiolabel experiments to distinguish the source of surface silica groups after boiling treatment, and to determine if native quartz surface groups are exchanged with the medium in the passivation process; further investigation of the effect of treatment on the zeta potential of quartz; and the attempted use of surface spectroscopy methods, such as diffuse reflectance Fourier transform infrared spectrophotometry to identify surface structural changes following treatment. If acid-base reactions are involved, the pH dependence of detoxification should be looked at in detail.

The prime question raised here is under what moderate treatment conditions will quartz be surface modified so that it becomes biologically inert for cytotoxicity in cellular assays or for fibrogenicity *in vivo*. That is, what physical and chemical conditions are necessary and sufficient to passivate the quartz surface? This study has identified some parameters involved: the process proceeds in aqueous solution; glass surface must be present; there is a concentration dependence; details of the boiling procedure can significantly affect the results.

Another question is whether the passivation effect persists. The effect should be monitored in long term experiments involving physical and/or chemical methods, as well as *in vitro* assays, and possibly *in vivo* bioassays to determine the long term persistance in air and in physiological fluids.

The last question is whether this phenomenon is a feasible basis for prevention strategies. One major unknown here is the long term persistance of the effect under *in vivo* conditions.

In any event, the possibility exists for de-toxification of quartz by relatively mild treatment conditions. Seemingly innocuous preparation procedures used in biological assays of quartz could produce respirable dust surface property changes which are not readily detected by chemical or physical analysis, but which can confound interpretation of bioassay results. The possibility for such should be recognized in research protocols.

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CLINICAL ANALYSIS OF 22 CASES OF TOXIC PULMONARY EDEMA

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The pulmonary edema, caused by intoxication of irritant gases, is one of indications of severe intoxications. A violent or mild attack is depended on sorts and the concentration of the chemicals in the air. Being treated promptly, the courses would be commonly short and prognoses would be favourable. Three hundred and thirty-four cases of acute intoxication of irritant gases were treated in our institution in 1970–1987. Of these cases, 143 were the irritant reactions; 150 mild, 16 middle and 25 severe intoxication. There were 22 cases of pulmonary edema in the last group, accounting for 6.6% in all cases, 88% in the severe cases. They were 10 cases of nitrogen dioxide, 6 of chlorine, 2 of hydrogen sulfate, 1 of ammonia, 2 of dimethyl sulfate, 1 of phosgene intoxication. Twenty-one patients were recovered except a case of phosgene intoxication that died of ARDS. All patients were poisoned by breathing in high concentrations of irritant gases in a short time due to accidents. In two special cases, continuous localized rales could be found though the shadows on chest X-ray had been absorbed. The severity degrees, incubation periods, indications, X-ray showings and courses of pulmonary edema varied with the differences of sorts of poison, visiting times and treatment. Now we analyze these clinical data of 22 cases of toxic pulmonary edema by some poisons.

Cause of Poisoning

The cause of poisoning were breathing in high concentration of irritant gases in a short time period in accidents. Two pupils breathed in heavy chlorine and was poisoned in resident area in a chlorine leakage.

Clinical Data

The incubation periods were short in chlorine, dimethyl sulfate, hydrogen sulfate, ammonia. It took 30 minutes in a case of chlorine intoxication. While it was longer in nitrogen dioxide and phosgene intoxication, e.g., it took 24 hours in a case of nitrogen dioxide and 72 hours in a case of phosgene intoxication. The incubation periods of the rest 19 cases varied from 1 to 20 hours with a average of 4.3 hours. Most of the cases were between 1–7 hours (Table I).

The onset time and severity of symptoms and signs of pulmonary edema varied with different particularities (kinds) of irritant gases. For example, in pulmonary edema caused by water soluble poisonous gases, the upper respiratory tract symptoms were mild and the clinical expressions were generally the same, i.e., cough, suppressing in chest, breathlessness, white or pink sputum, hemoptysis, cyanosis, dyspnea, rales on chest (Table II).

In 10 cases of toxic pulmonary edema by nitrogen dioxide. Pulmonary signs disappeared earlier than shadows on chest X-rays. It took 13.7 days in average for the clearing of rales and 27.8 days for the shadows of pulmonary edema on chest X-rays to clear. In one special case we got reverse finding (Table III).

Treatment

After proper treatments, 21 cases were cured without any pulmonary sequela except one death with phosgene intoxication, the incubation period of which was 72 hours. In addition to symptomatic treatment, control of infection and pulmonary edema, the courses, to a great extent, were depended on whether administration of corticosteroid was given promptly or not. A short course was got when corticosteroid was given in time, otherwise, long courses were got with delayed or without such treatment (corticosteroid).

There were 3 cases in which the courses were more than 30 days and in which 2 cases were beyond 100 days without the administration of corticosteroid. It was established that pulmonary edema occurred in these 3 cases. The causes of delayed course were late visiting and no corticosteroid administration.

DISCUSSION

1. The clinical data of these 22 cases showed that incubation period of toxic pulmonary edema by irritant gases were related with the kinds, properties and concentration of poisons, e.g. the incubation periods of water-insoluble nitrogen dioxide were 5–11 hours mostly, those of water-soluble chlorine, were between 30 minutes to 1 hour. The incubation period, we should pay attention to this.

2. In 22 cases of toxic pulmonary edema, rale disappeared earlier than shadow on chest X-ray.

   On occasions when roentgenoscopy is not available, disappearance of rales should not be regarded as the criterion for the healing of pulmonary edema. In special cases continuous localized rales could be found though the shadows on chest X-ray had been absorbed. This may be due to the accumulation of secretions in the narrowed and deformed bronchioles damaged by poisons.

3. The course of pulmonary edema by irritant gases are closely related with administration of corticosteroid besides visiting in time, symptomatic treatment, prevention and control of infection. In cases with prompt

Table I
Incubation Periods of Various Poison Intoxications

Kinds	Cases	Incubation period (hours) 0.5	1	1.5	2	3	4	5	6	7	8	9	10	11	20	24	72
Chlorine	6	1	3		2												
Hydrogen Sulfate	2				2												
Ammonia	1					1											
Dimethyl Sulfate	2			1		1											
Nitrogen Dioxide	10							3		1	1	1		2	1	1	
Phosgene	1																1

Table II
Cases of Toxic Pulmonary Edema by Irritant Gases

Symptoms & Signs	Number of Case
Photophobia	1
Lacrimation	7
Ophthal Malgia	1
Coma	3
Headache	2
Dizziness	9
Nausea	8
Vomiting	4
Cough	18
Suppressing on Chest	16
Breathlessness	20
Chest Pain	3
Fever	8
Conjunctiva Congestion	8
Pharyngeal Congestion	6
Cyanosis	17
Dyspnea	17
Hemoptysis	4
Foamy sputum	11
Dry and Crepitant Rale	22

administration of corticosteroid after poisoning, the time of shadow absorption on chest X-ray were 7.4 days in average, while they were 98 days in cases without administration of corticosteroid and were 30 days in cases with delayed administration. There were 3 cases that their courses were more than 30 days and there were 2 cases their courses were beyond 90 days. These cases were believed that pulmonary edema occurred in initial poisoning.

The chronicity of these cases might be: (1) The chronicity of pulmonary edema, especially interstitial pulmonary edema state due to improper treatment; (2) The rebound phenomenon because the damaged epthelial cells had not completely recovered, even the minor infection would ignite recurrence of the edema state; (3) There might be obstructive bronchiolar alveolitis. There were reports that irreversible bronchiolar fibrosis might occur in the very rare untreated cases. What-

Table III

Comparison of Time for Rale and Chext X-ray Shadows Disappearance

Case	the Time of Rales (days) Clearing	the Time of Chest X-ray Shadow Disappearance (days)
1	5	8
2	6	9
3	7	7
4	3	6
5	10	10
6	7	4
7	6	8
8	15	95
9	19	30
10	19	101
Average	13.7	27.8

Table IV

In Influence of Administration of Corticosteroid on the Courses
(Disappearance of Shadow on Chest X-ray as the Criterion)

Groups	Number of Cases	Courses (days)
Prompt Steroid	7	7.4 (4-10)
Delayed Steroid	1	30
No Steroid	2	98 (95-101)

ever the causes, it can be completely cured without any symptoms left if corticosteroid is administered early.

In summary, the authors hold that in irritant gas intoxication, prompt treatment should be given and in the severe cases, especially if the symptoms of pulmonary edema appear, early and adequate administration of corticosteroid for a short course should be given.

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RESULTS OF A STUDY ON THE CHEMICAL COMPOSITION OF WOOD DUST AND THE ETIOLOGY OF BRONCHIAL ASTHMA IN WOODWORKERS

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The possible biological actions of wood dust are of an irritant, allergic, toxic, and carcinogenic nature. Besides the cutaneous disturbances, the most common pathologies found in workers at risk are respiratory and oculo-rhinitic; specifically, in the respiratory system wood dust can cause bronchial asthma, either of an allergic or pharmacoirritant nature. Therefore, studies have developed concerning: 1) the chemical composition of the type of wood, 2) *in vivo* and *in vitro* experiments regarding the toxicity of wood dust or its extracts and derivatives, 3) clinical and epidemiological observations of subjects at risk, and 4) environmental investigations in lumber workshops and yards.

This present work is related to the first group of research investigations in that it studies the chemical composition of the different types of wood through the use of TLC (thin layer chromatography); in relationship to the third group of studies it is related to clinical observations carried out in our occupational allergology out-patient clinic.

METHODS USED IN THE STUDY OF THE WOOD CHEMICAL COMPOSITION

Woods examined were chosen on the basis of information obtained from wood workers who came under our observation for respiratory disturbances, choosing those types of wood that were most often used or most often thought by the patients themselves to be responsible for their problems.

Before carrying out TLC, samples of the different types of wood were pulverized manually by rasping. Approximately 2 grams of finely ground and well dried wood dust were added to a solution of 95% ethanol and allowed to stand for 24 hours, to obtain an extract; an aqueous 1% HCl solution was added for the determination of alkaloids. We carried out chromatographic studies on these wood extracts, adapting a method recently proposed by the W.H.O. for phytopharmacological research,[6,7] which employs TLC. We used, for the TLC, plates of silica gel (Merk HF 254). For the elution of compounds containing different charges, a system of solvents analogous to that found in the literature[9] was used, according to the degree of polarity. After elution and subsequent drying in an oven, the plates were sprayed with several reagents in order to determine the main classes of compounds: Polyphenols, Terpenoids, Cardenolids, Alkaloids, Anthranoids and Coumarins. The eluents and the reagents used are listed in Table I. Furthermore, in lieu of specific reagents, the plates were sprayed with 2N H_2SO_4 to detect eventual organic compounds different from those studied above and which we shall call "non identified compounds"; at the moment, these shall not be taken into consideration.

It is noteworthy that TLC represents one of the most sensitive analytical techniques, capable of detecting quantities of substances on the order of a few micrograms (whereas the detection of compounds present in still smaller quantities requires a concentration of the extract). It reveals information not only regarding the categories of the substances extracted (polyphenols, alkaloids, etc.), but also their numbers (number of spots). At first, TLC can orient us as to the type of substance under examination, on the basis of its differential motion due to a difference of polarity (for example, if a terpene compound can be eluted with a low polar solvent, then it will be identified as a steroid terpene, while a saponine will be eluted with more polar solvents). Therefore, TLC analysis can be considered a preliminary step for deeper subsequent examinations.

The classes of compounds that we considered make up the major part of the secondary metabolites of woody plants that can be considered harmful for the organism: in fact, Polyphenols have irritative and sensitizing properties; Cardenolids have cardioactive effects; Alkaloids have systemic toxic effects and can bring about the liberation of histamine; Terpenoids have irritative and sensitizing effects and, in particular, saponins have hemolytic properties; some Coumarins have photosensitizing effects.[4]

RESULTS OF THE CHROMATOGRAPHIC ANALYSIS OF THE DIFFERENT TYPES OF WOOD AND COMMENTS

The results of the chromatographic examinations are contained in Table II and III. The woods tested are indicated with their commercial names followed by their scientific names and, in parenthesis, their family names. The results are expressed as the number of significant spots revealed in the nonconcentrated extracts; these spots are marked with an "x".

We grouped the woods into exotic and domestic and further distinguished the softwoods (conifers) from the hardwoods (latifolia). In general, exotic woods contain a moderate amount of Polyphenols and Cardenolids as well as Terpenoids, while the Alkaloids are present only in Asian Rosewood, Mansonian Walnut and Teak, and the Anthranoids only in Mansonian Walnut. Among the domestic woods there was a widespread presence of Polyphenols and

Table I

Eluents and Reagents Used for the Study of the Chemical Composition of Wood Dust Through the Use of TLC

ELUENTS (v:v) :	
E1	Toluene : Ethyl Acetate (1:1)
E2	Chloroform : Ethyl Acetate (1:1)
E3	Chloroform : Methanol (9:1)
E4	Chloroform : Acetic Acid : Water (50:45:5)
E5	1-Butanol : Acetic Acid : Water (4:1:5)
E6	Methyl Ethyl Ketone : Toluene : Methanol : Acetic Acid : Water (80:10:5:2:6)
E7	Toluene : Ethyl Acetate : Diethylamine (5:4:1)
REAGENTS :	
R1	Potassium Ferricyanide : Ferric Chloride (for Polyphenols: phenols, phenolic acids, flavonoids, tannins, catechins, coumarins, quinones, and stilbenes)
R2	Acetic Anhydride : Sulfuric Acid (for Terpenoids: terpenes, steroids, sterols, and saponins)
R3	Phosphomolybdic Acid (for reducing compounds: mainly appropriate for terpenes if associated with R2)
R4	3,5-Dinitrobenzoic Acid : Potassium Hydroxide (for Cardenolids)
R5	Basic Bismuth Nitrate : Acetic Acid : Potassium Iodide (for Alkaloids)
R6	Sulfuric Anisaldehyde (for Coumarins and Anthranoids, especially if associated with R1)

Terpenoids and a constant lack of Cardenolids, Alkaloids, and Anthranoids, that is, those classes of compounds having potential systemic pharmacological activity. In general, the larger amount of active substances contained in exotic woods with respect to domestic woods seems to account for the fact, at the present, that the former have a greater toxicity. Nevertheless, on the one hand, the presence of large amounts of accessory components in some domestic woods, such as Cherry, and, on the other hand, the scarcity of these components in some exotic woods, such as Obeche, make it unwise to generalize.

Instead, differences are less marked when comparing the presence of Polyphenols or Terpenoids; these were found in all examined except Mahogany, Obeche and Elm. It may be surprising that some softwoods (conifers), both domestic and foreign, examined by us contain no Terpenoids which are the most characteristic substances found in the Pine family; however, it is necessary to bear in mind that the analysis was carried out on well seasoned wood dust and, therefore, free of resins, and that some volatile terpene fractions can be lost during the initial phases of the techniques involved in chromatography. Furthermore, more work must be done on the "nonidentified substances" found in 3 of the 5 softwoods examined.

In the hardwoods (latifolia), in addition to the Terpenoids contained in Beech, Walnut, and Linden, large amounts of Polyphenols are present especially in Cherry, Walnut, and Olive. Because of the characteristics of such compounds chemical analysis allows us to confirm that these woods have a greater capacity for causing irritative and allergic reactions. Moreover, Colophony, contained in conifers, is a Terpene, and Plicatic Acid, found in Red Cedar, is a Polyphenol.[1,2] Such an observation, together with the results of clinical data, allows us to conclude that even domestic woods, rich in such substances, are to be considered as a potential cause of asthma, no less than exotic woods; in Italy, insurance protection exists only for the latter.

A first consideration that can arise from our study is a

Table II

Results of the Chromatographic Analysis of the Different Types of Wood (Exotic Woods)

Woods (commercial and scientific names)	Polyphenols	Terpenoids	Cardenolids	Alkaloids	Anthranoids & Coumarins	Non identified compounds
SOFTWOODS						
Douglas Fir Pseudotsuga douglasii Carr.	xxx	x	-	-	-	xxx
Pitch Pine Pinus spp	xx	-	-	-	-	x
HARDWOODS						
Afrormosia Afrormosia elata Harms.	-	xx	-	-	-	-
Asian Rosewood Dalbergia latifolia Roxb.	xxx	-	x	xx	-	-
Iroko Chlorophora excelsa Benth.	xxx	-	xx	-	-	-
Mahogany Shorea spp	-	-	-	-	-	-
Mahogany Entandrophragma utile Sprag.	-	-	x	-	-	-
Mansonian Walnut Mansonia altissima A. Chév.	xxxxx	x	xx	xx	x	-
Obeche Triplochiton scleroxylon K.	-	-	-	-	-	-
Padouk, Kejatt Pterocarpus spp	xx	x	-	-	-	xx
Ramin Gonystylus bancanus Kurz	-	xxx	-	-	-	-
Tanganyika Aniegré Aningeria altissima Aubr. P.	-	xx	-	-	-	-
Teak Tectona grandis L.f.	xxx	xx	-	x	-	-

deeper examination aimed at both woods with greater reactivity (Mansonia, Rosewood, Teak, Cherry, Larch, etc.), as well as woods that resulted in practically no reactivity (Such as Obeche), but which were reported in the literature as being responsible for pathological effects.[5] Another consideration that seems to derive from our study is the use of TLC methods in preliminary hygienic and sanitary investigations of work environments where lumber is employed for which adequate bibliographical references are lacking. A third line of development involves the chromatographic separation of the compounds through the use of TLC and the subsequent employment of the various fractions for pharmacological tests on animals, or for allergometric tests or bronchial challenge tests on workers at risk and symptomatic. For example, it is possible, using patch tests, to apply the single spots cut out from the chromatographic plates, and subsequently carry out skin tests or tests involving bronchial exposure with the same preliminary chromatographic fractions, dried and redisolved in controlled solutions. Furthermore, the analysis of different samples of the same wood did not always give rise to identical results (such as the Douglas Fir), and this can be explained, at least in part, by the different origin of the trees: and this is another reason for using, in the etiological research of the disturbances attributed to wood dust, the components extracted directly from the material supposed to be responsible.

CLINICAL CASES

We now report case history data regarding 86 wood workers observed during the past 5 years at the Institute of Occupational Health of the Catholic University of Rome for respiratory pathology problems. Table IV contains a summary of clinical history data concerning the subjects observed. The subjects were all of the male sex with an average age of 43 years and average work seniority of 18 years at that type of job. On the basis of the type of employment, they were divided into 2 groups: those exposed only to wood and those who were also exposed to paints (in this latter group we should take into consideration isocyanates and other components of paints as possible contributers to the genesis of the respiratory symptomology). All the subjects underwent a specialistic examination by an otorhinolaryngologist, a cranial radiography to evaluate the paranasal sinuses, a radiography of the chest, a spirometric examination, and

Table III

Results of the Chromatographic Analysis of the Different Types of Wood (Domestic Woods)

Woods (commercial and scientific names)	Polyphenols	Terpenoids	Cardenolids	Alkaloids	Anthranoids & Coumarins	Non identified compounds
SOFTWOODS						
Larch Larix decidua Mill.	xxx	-	-	-	x	x
Northern Redwood Pinus silvestris L.	-	xxx	-	-	-	-
Spruce Picea abies Karst	xx	x	-	-	-	-
HARDWOODS						
Ash Fraxis excelsior L.	xx	-	-	-	x	-
Beech Fagus sylvatica L.	-	xx	-	-	-	-
Cherry Prunus avium L.	xxxxxxx	-	-	-	-	-
Chestnut Castanea sativa Mill.	xx	-	-	-	-	x
Elm Ulmus campestris L.	-	-	-	-	-	xx
Linden Tilia cordata Mill.	-	xx	-	-	-	-
Maple Acer campestre L.	x	-	-	-	-	xx
Oak Quercus petraea Liebl.	x	-	-	-	-	-
Olive Olea europea L.	xxx	-	-	-	-	-
Walnut Juglans regia L.	xx	xxx	-	-	-	-

allergometric tests carried out by pick or i.d. test with allergens provided by the Lofarma Company and containing "Pollens," "Mycophytes," and "Inhalants" which include also 30 extracts of wood dust both from exotic as well as domestic woods. Furthermore, some of these subjects (chosen on the basis of history criteria, type of exposure, and type of referred pathology, and, moreover, excluding those that presented with serious impairment of respiratory functions of the obstructive type even at rest) underwent bronchial challenge tests which were both aspecific (with ultrasonic mist or methacoline) and specific with the more commonly used and suspected wood dust or with toluene diisocyanate (TDI) or both, depending on the circumstances. A reduction of at least 20% of the FEV_1 was considered as a positive result. In the meantime, it was not possible for us to carry out a skin test with TDI conjugated to human albumin. The more significant group of subjects with positive results for wooddust, that is, those 3 that responded to Tanganyika Aniegre both with the skin test as well as the bronchial exposure test, underwent a RAST for this type of wood.

RESULTS AND COMMENTS

After examining the results of our clinical case studies we can observe that the type of respiratory pathology found in the workers studied was made up of recurrent asthma crises in 45.3% of the cases, less than half of which also had oculorhinitic symptoms; in the remaining 54.7%, the symptoms were mainly bronchial. Among the clinical and functional findings observed in the 86 subjects, we noted: 1) the presence of chronic rhinopharyngitis in 58.2% of the cases; 2) radiological alterations of the paranasal sinuses in 46.7%; 3) an increase in the bronchovasal lung tissue in 73.3% of the cases and hyperdiaphany in 30%; 4) obstructive ventilatory deficit in 50% of the cases; and 5) mixed ventilatory deficit in 15% of the cases.

The cutaneous allergometric tests (Table V) were positive only in 13 subjects, amongst which 7 were positive for nonwork related allergens, 2 were positive for both work and nonwork related allergens, and 4 were positive only for work related allergens. The woods that resulted in a positive skin

Table IV
Clinical Data of Subjects Studied

Number	86	
Age (yr, mean and range)	43	(31-62)
Work seniority (yr, mean and range)	18	(5-38)
Current smokers	49	(56.9%)
Exposed only to wood	21	(24.4%)
Also exposed to paints	65	(75.6%)
Duration of symptoms at diagnosis (yr, mean and range)	4.6	(0.6-15)
Prevalence of symptoms (No. and %):		
Chronic cough and phlegm	47	(54.7%)
Asthma	39	(45.3%)
Work related:		
asthma	35	(40.7%)
eye symptoms	16	(18.6%)
nasal symptoms	23	(26.7%)
Clinical and functional findings (No. and %):		
Chronic rhinopharyngitis	50	(58.2%)
Radiological alterations of the paranasal sinuses	41	(46.7%)
Radiographic increase in bronchovascular marking	63	(73.3%)
Obstructive ventilatory deficit (in baseline FEV_1)	43	(50.0%)

Table V
Prevalence of Skin Reactivity to Common Allergens and Wood Dust Extracts (Prick or Intradermal Tests)

Subjects examined (No.)	86	
Positive for work related allergens	4(*)	(4.6%)
Positive for both work and non-work related allergens	2(°)	(2.3%)
Positive for non-work related allergens	7	(8.1%)
Negative	72	(84.8%)

(*) 2 positive to Tanganyika; 2 positive to Cherry
(°) 1 positive to Pine, Oak, Dermatophagoides pt., and some Mycophytes; 1 positive to Tanganyika and Graminaceous pollen

test in the 4 workers were the Tanganyika Aniegre (in 2 cases) and the Cherry (in 2 cases); in the two with mixed positive results, one case reacted positively to the Tanganyika Aniegre together with Graminaceous pollen, while the other reacted positively to Pine and Oak together with Dermatophagoides and some Mycophytes.

Table VI indicates those subjects who were positive only to the specific bronchial challenge test, both with woods and TDI; those subjects positive only to the aspecific bronchial challenge test, both with mist and methacoline; and those positive to both. The number of subjects who underwent the specific test was 25, of which 6 both for woods and TDI. Seven out of 13 subjects examined resulted positive to wood dust, and of these 7, 2 were also positive to ultrasonic mist. There were 10 out of 18 positive results to TDI; of these, 4 were also positive to mist and 1, in addition to mist, was also positive to Mansonian Walnut.

Table VI

Results of Bronchial Challenge Tests Both Specific (Wood Dust and TDI) and Aspecific (Metacholine or Ultrasonic Mist)

Subject examined (No.)	25 (of which 6 both for woods and TDI)		
Wood dust challenge test	Bronchial hyperreactivity test positive	negative	Total
positive	2 (*)	5 (°)	7
negative	3 (')	3 (")	6
TDI challenge test			
positive	4 (§)	6	10
negative	2	6	8
Total	11	20	31

(*) 1 positive to Tanganyika; 1 positive both to Mansonia and TDI
(°) 2 positive to Tanganyika; 2 positive to Mansonia; 1 positive to Cherry
(') of which 1 was negative to Pine and Oak, but had positive skin test with the same type of woods
(") of which 1 was negative to Cherry, but had positive skin test with the same type of wood
(§) of which 1 was also positive to Mansonia

The RAST for Tanganyika wood was done, according to the classical method, with an aqueous extract and binding the antigen to a solid polystyrol phase. The test resulted strongly positive in 2 out of 3 subjects (Table VII), while it resulted negative in that subject who had a positive skin reaction also for Graminaceous pollen and was also positive to the bronchial provocation test with ultrasonic mist. Our RAST results differ from those of other authors.[8]

A first finding of a certain interest obtained in our study is that in wood workers, harmful agents in professional exposure comprise not only wood dust but also many other factors that have irritative and allergic properties for the respiratory airways: in fact, the exposure to paints and solvents was significant in 75% of our cases. More than 50% of the carpenters observed by us presented prevalently with bronchial symptoms; but after an accurate history study involving the conditions of onset and the evolution of the symptomology, it was found that in about 50% of those subjects with bronchitis the disease had begun many years earlier with typical asthma crises, while the onset of the bronchitis was subsequent. We believe that this is due to the long time interval that elapsed between the beginning of the symptomology and the beginning of appropriate diagnostic examinations (on the average of 4.6 years in the entire group): it is worthwhile to emphasize the importance of carrying out allergometric examinations as early as possible, especially in those cases of asthma that arise in work environments.[3]

The clinical and functional findings stress a high incidence of alterations of the rhinopharynx and paranasal sinuses. This is in agreement with data found in the literature concerning damage produced by wood dust on the upper respiratory airways, with possible rhinitis that can also be hemorrhagic. In fact, the average diameter of wood dust is greater than 5 μ and this justifies its localization in the upper respiratory airways.[11]

In our case studies the allergometric skin tests, considered as a whole, were positive in 33.3% of the asthmatic subjects (excluding all those with bronchitis from the total) and this percentage is lower than that of other case studies conducted on non-professional subjects with asthma (up to 50–60% skin test positive). This could imply a prevalently non allergic cause for asthma due to wood dust. On the other hand, studies on the chemical composition of woods conducted by us have shown that in nearly all the woods examined there was a presence of Polyphenols or Terpenoids, compounds that have properties that are notoriously irritative or allergic. This, together with the consideration that the extracts on the market with which the allergometric tests are carried out are of a protein nature and, therefore, do not contain those substances which also have potential haptenic properties, tends to strengthen the hypothesis that, like for Plicatic Acid,[10] at least a part of the cases is due to sensitization to haptenes and another considerable part is due instead to a pharmacological-irritative type of reaction. In-

Table VII

Serum Rast Values for Tanganyika Extract Obtained in 3 Subjects Who Responded to This Type of Wood Both with the Skin Test as Well as the Bronchial Challenge Test

Subject	Age	Work seniority	Skin reactivity to common allergens	Bronchial hyperreactivity	RAST value
V. C.	43	15	-	-	+++ (15.0%)
S. A.	45	11	-	-	+++ (12.5%)
F. P.	37	12	+	+	- (0.9%)
5 control subjects			+		-

stead, in those cases with a positive skin reaction to the protein extract, we believe that an allergic pathologic mechanism is the most probable.

As far as the bronchial challenge tests are concerned, we note that only one subject had a positive result to mist, Mansonian wood, and TDI; one was positive to mist and Tanganyikan wood; and three were positive to mist and TDI. Five subjects who were positive to mist had negative results with wood dust or TDI; on the other hand, 5 subjects who were positive to wood dust and 6 who were positive to TDI had negative results with mist. Regarding the type of response to the specific test, in 9 cases it was immediate, in 6 it was diphasic, and in 2 it was delayed.

The results of the specific bronchial exposure tests would seem to confirm a certain selectivity in the response, even in those subjects with aspecific bronchial hyperreactivity; nevertheless, they give us no indication as to the pathogenetic mechanism of the broncospastic attack, which can be either pharmacoirritative or allergic. In 2 out of 3 subjects who had given a positive response both to skin tests and bronchial exposure provocation tests with Tanganyikan wood, the specific IgE dosage by RAST, was strongly positive, bringing us to the conclusion that there are specific IgE's towards protein constituents of the wood. In those subjects with a positive result to the bronchial challenge test with wood dust, but negative to the skin test with an extract of the same type of wood, an irritative cause of the bronchospasm could be an explanation. But another explanation could also be a sensitization to some non protein substance contained in this wood (a haptene). The next step of our research program is to carry out tests both in vivo (skin reaction, patch tests, bronchial challenge tests) and in vitro (RAST) with the fractions isolated with TLC.

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THE PREVALENCE OF BAKERS ASTHMA IN THE FR OF GERMANY —RESULT OF A PILOT-STUDY

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ABSTRACT

Chronic obstructive airways disease (COAD) of bakers is a serious occupational problem. Since atopic disease is very common, many bakers are at risk to develop allergy against flow dust and baking additives. We studied 367 bakers from a closed region to establish prevalence rates of COAD and bronchial hyperreactivity. Intracutaneous skin tests with several occupational and ubiquitous allergens were performed in combination with measurement of specific IGE (RAST) and histamin liberation of blood basophils. Prevalence of wheezing at working place was found in 8% of hyperreactivity 22% and pathological increase of basal airway resistance in 11% of all bakers. Bakers with positive tests to allergens and rhinitis had an increased risk in developing COAD but sensitivity of allergen testing and even rhinitis is too low, to clearly predict development of the disease. Allergy to flow dusts are common and often without clinical relevance. Controlling and minimizing exposure is most effective for prevention. There is no reason to exclude bakers from working place when only skin tests or other tests for allergy are positive. Early detection of COAD is the most important measure to prevent severe disease.

No Paper provided.

ASBESTOS-INDUCED LESIONS AND ASBESTOS BODY BURDENS IN PATIENTS WITH LUNG CANCER

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ABSTRACT

Lesions of asbestosis and small airway disease were scored and asbestos bodies (AB) counted in the lungs from 106 consecutive patients operated for bronchial carcinoma. The occurrence of pleural plaques detected by CT scan and during surgery was also recorded. Among the 106 cases, 19 were found to have high AB burdens when compared to a control autopsy population, essentially because of more frequent occupational exposures. The greater frequency of high AB burdens among men with lung cancer (19.4%) versus controls (3.9%) suggest thus a possible role of asbestos in the etiology of malignant disease. Lesions of minimal or slight asbestosis (peribronchiolar fibrosis and AB in sections) were detected in only 7 of the 19 cases (37%) and pleural plaques in 8 of 19 (42%). Nevertheless scores of fibrosis and pigmentation of the respiratory bronchioles were significantly higher in the patients with high AB lung concentrations than in the others, and these scores correlated strongly with smoking history (in pack-years). The results of this study suggest a synergistic effect between asbestos fibers and tobacco smoke in the development of bronchial carcinoma, even when there are no associated signs of asbestosis (or pleural plaques).

No Paper provided.

THE EFFECTS OF SILICA DUST EXPOSURE ON SMALL AIRWAYS

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INTRODUCTION

Recently Churg et al[2] have shown that dust-exposed workers may have markedly abnormal small airway pathologic findings. When this group was matched by age, sex and smoking habit to a dust-exposed worker group without pathologic abnormality they concluded that the first group had abnormalities of air flow greater than those induced by smoking alone. In fact we still do not know what role may smoking play on the pathogenesis of silica induced airway changes. Nery et al[7] have very recently shown that smoking and silica exposure may have an addictive effect on pulmonary epithelial permeability of ceramic workers.

The purpose of this investigation was to analyze the small airway function of non smoking silicotic ceramic workers with at least ten years of dust exposure.

MATERIAL AND METHODS

We studied 46 non smoking ceramic workers with the diagnosis of silicosis based on occupational history of silica dust exposure and on radiographic features. Their mean age were 48.3 ± 8.6 years (mean ± standard deviation) and the mean exposure time of the groups was 22.6 ± 5.4 (range from 10 to 40 years). Five patients had tuberculosis in the past and one was bronchitic.

Standard spirometric tests were performed using a 9.0 l Godart spirometer and measured forced vital capacity (FVCO, forced expiratory volume in one second (FEV_1) and forced expiratory flow at 25-75% (FEF 25-75%); it was calculated the ratio FEV_1/FVC. Forced spirometric curve was repeated 10 minutes after the inhalation of a beta two adrenergic drug (fenoterol—200 mcg) and FVC, FEV_1 and FEF 25-75% were calculated by the isovolume technique.[4]

Maximal expiratory flow volume curves were obtained with a "bag in box" system.[9] The bag dislocation was sensed by a Validyne differential pressure transducer ± 2 cmH_2O and volume was integrated electronically. Curves were registered on a X-Y Tektronics Storage oscilloscope and copied on a plastic card. They were obtained breathing air and then after three inspiratory vital capacities maneuvers of a mixture of 80% of helium and 20% of oxygen (HeO_2).[5] The best fit of three curves for air and HeO_2 were drawn and they were superimposed and matched at residual volume if the vital capacities were unequal. We calculated the flow at 50% and 25% of the curve breathing air ($\dot{V}$max 50% and $\dot{V}$max 25%) and at the volume were both curves had the same flow (Viso$\dot{V}$).[7]

Chest radiograms were classified according to ILO Classification, 1980.[3]

RESULTS

As there was a large variability in the radiological appearances concerning profusion, size and shape of the regular and irregular small opacities we grouped them according to the predominant lesion. We found 25 individuals with 1/1 profusion, 13 with 2/2 profusion and 8 with 3/3 profusion; 37 of them (80%) had a predominance of the p/p small opacities.

Spirometric parameters were considered as normal if the predicted values for FVC and FEV_1 were above 80%, above 60% for FEF 25-75% and above 70% for the ratio FEV_1 /FVC. Thirty five individuals (76.1%) were classified as having normal spirometry and 11 (23.9%) as having some degree of pulmonary impairment[9] predominantly obstructive and 2 restrictive).

The opposite was observed with the analyzis of flow-volume curve and isoflow volume; considering as an abnormal result the presence of at least one altered parameter ($\dot{V}$max 50%, $\dot{V}$max 25% or Viso$\dot{V}$) we observed that the abnormal results (71.7%) predominated over the normal ones (28.3%). These percentages differed significantly from the ones obtained with spirometry ($p < 0.05$).

The analysis of $\dot{V}$max 50%, $\dot{V}$max 25% and Viso$\dot{V}$in the 33 individuals with normal spirometry show that 24 of them had already some degree of airflow abnormality (Figure 1).

$\dot{V}$max 25% could significantly detect more abnormalities than the other 2 parameters ($p < 0.05$) (Table I).[6]

After 200 mcg of inhaled fenoterol 61.4% of the group (27 out of 44) increased their FEF 25-75% by at least 15% (46.1 ± 36.6% increase); 24 out of 27 increased by 25% or more. Twenty individuals of the responsive group had normal spirometry (74.1%) and showed an increase in FEF 25-75% of 47.2 ± 38.4%, a very similar increase presented by the 7 responsive silicotics with abnormal spirometry, 40.1 ± 30.4% (Table II).

There was no association between the small opacities pro-

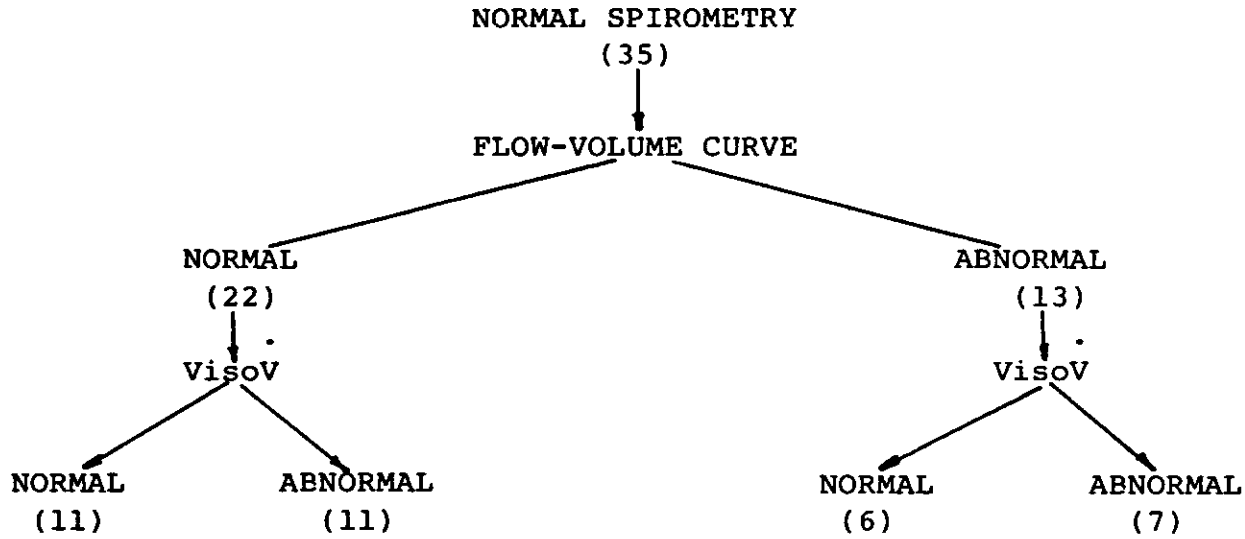

Figure 1. Diagram showing the distribution of the 35 individuals with normal spirometry after they performed a flow volume curve breathing air and helium for the analysis of $\dot{V}$max 50%, $\dot{V}$max 25% and Viso$\dot{V}$.

Table I

Distribution of Normal and Abnormal Values of $\dot{V}$max 50%, $\dot{V}$max 25% and Viso$\dot{V}$ in 46 Individuals Exposed to Dust Silica

	ABNORMAL VALUE	NORMAL VALUE	TOTAL
$\dot{V}$max 50%	12	34	46
$\dot{V}$max 25%	22	24	46
Viso$\dot{V}$	21	25	46

fusion and the response to bronchodilator (Table III) or flow volume-isoflow abnormalities (Table IV).[10]

DISCUSSION

We have shown that flow-volume curves breathing air and a mixture of HeO_2 are able to detect a large number of individuals with airflow obstruction that otherwise would be classified as normals. Isoflow volume was abnormal in 50% of the individuals with normal spirometry while $\dot{V}$max 25% alone would detect 33.3% of them. The combined use of $\dot{V}$max 50%, $\dot{V}$max 25% and Viso$\dot{V}$ were altered in 24 individuals with normal spirometry, a 66% early detection. Despite the fact that Viso$\dot{V}$ has been described for a long time as a tool for early diagnosis of small airway disfunction it has not largely been used in occupational medicine.[7,11]

There seem to be no influence of the length of exposure since the group exposed from 10 to 20 years and the one exposed over 20 years presented very similar Viso$\dot{V}$ values, 11.7% and 12.7%, with 40% of abnormal individuals in each group.

The second point we want to stress is the increased bronchial motor tonus these individuals presented; approximated 60% of the ones with normal spirometry (the same percent for the whole group) responded to inhaled fenoterol with an increase in their FEF 25-75%. There was a slight negative correlation between the initial value and the FEF 25-75%

Table II

Association of Bronchodilator Response (Concerning a 15% Increase in FEF 25–75%) to the Normality or Not of the Spirometric Values

BRONCHODILATOR RESPONSE	SPIROMETRY		
	NORMAL	ABNORMAL	TOTAL
POSITIVE	20 (60.6)	7 (63.6)	27
NEGATIVE	13 (39.4)	4 (36.4)	17
	33	11	44

Table III

Association of FEF 25–75% Increase (Positive Response) to Bronchodilating Drug and Small Opacities Profusion in the Chest X-ray of 44 Non-smoking Silicotics (Non Significant)

	X-RAY PROFUSION			
	1/1	2/2	3/3	TOTAL
POSITIVE	13	9	5	27
NEGATIVE	11	4	2	17
TOTAL	24	13	7	44

Table IV

Association of Altered $\dot{V}$max 50%, $\dot{V}$max 25% or Viso$\dot{V}$ to Small Opacities Profusion in the Chest X-ray of 46 Non-smoking Silicotics (Non Significant)

$\dot{V}$/V and Viso$\dot{V}$	X-RAY PROFUSION			
	1/1	2/2	3/3	TOTAL
NORMAL	18	7	8	33
ABNORMAL	7	6	0	13
TOTAL	25	13	8	46

response (r: -30, $p < 0.05$). As these individuals were not smokers and had no symptoms of asthma we conclude that silica dust is the causal agent of this abnormal response.

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EXPOSURE TYPE RELATED PULMONARY SYMPTOMS IN DENTAL LABORATORY TECHNICIANS—RESULTS OF A QUESTIONNAIRE SUPPORTED SURVEY

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ABSTRACT

Dental laboratory technicians (DT) are exposed to various dusts including quartz and alloys containing Co, Cr and Mo, both arising predominantly in model casting technique (MCT) presumably to be responsible for pneumoconiosis in DT. In order to assess the influence of occupational dust exposure on pulmonary symptoms questionnaires were mailed to 3,415 West German dental laboratories employing 24,588 DT. 5,238 questionnaires were returned; 4,328 qualified for assessment. 51.7% DT had experience in MCT, 69.7% in processing precious alloys (PAT), 85.9% in dental resins (DRT); ceramic techniques were less often used. Simultaneous practice of several techniques was common. ***Methods:*** In order to evaluate the effect of different exposure types on pulmonary symptoms by multivariate analysis we computed exposure time differences in MCT, PAT and DRT, controlling smoking habits, sex, age and even the total time of work in dental laboratories. ***Results:*** Male smoking DT who complained the following symptoms were significantly (WILCOXON) longer exposed in MCT than the nonsymptomatic: Dry cough ($p<0.01$), cough with phlegm ($p<0.05$) and breathlessness on exercise ($p<0.01$), conversely cough with phlegm was related to significantly shorter time in DRT for all subgroups. ***Conclusion:*** In concordance to casuistic reports and own clinical studies on 104 DT these epidemiological data strongly indicate a causal relationship between exposure in MCT (probable due to Co-Cr-Mo alloys and quartz) and pulmonary disease of DT. Cigarette smoking seems to exert an important synergistic influence.

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PROGRAMME FOR INTERVENTION AGAINST ASBESTOS RELATED DISEASES IN THE COUNTY OF TELEMARK, NORWAY

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INTRODUCTION

Although the relationship between exposure to asbestos and pneumoconiosis and lung cancer was revealed some 85 and 60 years ago respectively, scientists are still preoccupied with quantification of these relationships. Much work has been carried out both to remove asbestos and to minimize exposure in work places. Quite little has been done to reduce disease risk among the great number previously exposed subjects.

Attempts have been made to quantify the public health significance of past exposure to asbestos.[5,9] In Norway it has been estimated that 125–150,000 people have been exposed during the past four-five decades to an extent which is detectable in population based studies.[8] In our country no one has carried out intervention among people at high asbestos related risk. In fact, only few scientists have been willing to indulge in the task of stimulating risk reduction and assisting the high risk people to reduce their individual risk.

Our department, which is located in the county of Telemark, Norway, has diagnosed about 700 cases of asbestos-related illnesses during the past 10 years. The cases are mainly lung cancers, mesotheliomas, asbestosis, and pleural plaques. A number of cohort studies and case-control studies carried out among the county population has confirmed that past asbestos exposure has contributed 40 to 45 percent of the environmental causes of lung cancer among the local male population.[4,6,7,8] This high contribution to the "causal weight" is calculated by using etiologic fraction estimation.[7,8] Based on these and other local studies it has been estimated that 11–12,000 asbestos exposed persons are living in the county. We have collected exposure information on about 5,500 of these, mainly males. The lung cancer incidence in males in this county is about 30% higher than in the country as a whole.[1] The total male population in the county is about 80,000, of whom 33,400 are over 39 years old.[4]

These findings have inspired us to start an intervention study of determinants for increased asbestos related disease risk among males in the county. The purpose of the study is to reduce asbestos related disease risk and to prevent illnesses which otherwise would be caused by asbestos or by previous exposure to both asbestos and tobacco smoke. Methods

We have designed a programme in which these 5,500 subjects serve as base for recruitment of subjects assigned for intervention. As a large proportion of these subjects have been identified through a screening programme,[4] where age exceeding 39 years was one of the inclusion criteria, the majority of the subjects are over 40. Most of the other subjects, who have been identified as asbestos exposed through other epidemiologic studies or through clinical surveys, are also above 40 years of age.

We have decided to intervene only against those determinants which give high risk for development of asbestos related lung cancer in males as the primary activity in the early phase. The intervention is planned to comprise two elements;,

a) Information intervention among previously asbestos exposed present smokers, by doctor or nurse, counselling on the potential great lung cancer risk reduction among these combined exposed subjects; and

b) A programme for intensive screening for lung cancer among previously asbestos exposed previous and present smokers.

Evaluation of the results is planned to measure the effect on the smoking prevalence in the intervention group, and the long term effect on lung cancer incidence and mortality, mortality all causes, and mortality due to other asbestos related diseases.

We intend to estimate each participants a priori risk of developing lung cancer and subsequently to use this risk as criterion for determining to which of the two intervention groups the subject is to be assigned. For estimation of the individual a priori lung cancer risk, one needs to know; a) each subjects individual exposure history to lung cancer determinants, and b) to have a set of information from the literature which makes it possible to assess each subjects risk, when the accurate exposure history is known. At present it is not possible to take genetic disease determinants into account in the risk estimation.

For each participant we need to obtain accurate information on the duration and the intensity of past exposure to all major lung cancer determinants. By taking a detailed, individual occupational history, as well as history of exposure to tobacco smoke and alcohol, we have already obtained sufficiently detailed exposure information from about 2,000 subjects. From another 3,500 subjects we have obtained information on exposure to asbestos and tobacco smoke, but supplementary information is needed to be able to carry out assessment

of the lung cancer risk. It is also intended to continue collection of exposure information in another 22,000 subjects in whom we have obtained only that exposure information which has been needed to assign these subjects to job categories in previous epidemiologic studies.

From the data on cancer incidence in the total Norwegian population, which have been collected by the Norwegian Cancer Registry since 1953, it is known that the present average a posterior risk for lung cancer in the Norwegian male population increases from about 1×10^{-4} at the age of 40–44 to 15×10^{-4} and even higher at the age of 65–69 (Figure 1, line a).

These risk levels are average levels for experienced lung cancer risk in the general male population. The levels are outcomes from exposure to a range of disease determinants that characterize the past exposure situation for the general population. The individual risk levels, which have lead to these population based risk levels, ranges from low levels among subjects with hardly any exposure to high levels in subjects with previous exposure to a multitude of strong disease determinants.

It would be preferable to have access to reference levels for lung cancer which were uninfluenced by external disease determinants. However, such reference entities are not available. We have therefore decided to apply the national age standardized lung cancer incidence as reference entity for estimation of those risk levels which should serve as criteria for assignment to either of the two intervention groups.

We have chosen to assign those subjects to the subgroup for information intervention who, between five and 25 years from the date of enrollment, are extrapolated to have an a priori lung cancer risk five times or more higher than the national age adjusted background level (Figure 1, line b). Those subjects who are estimated to be at 10 times or higher lung cancer risk than the reference level at the time of enrollment, or who reach this risk level during the study, are to be enrolled into the lung cancer screening group (Figure 1, line c).

The means of intervention have been planned as follows:

a) The information intervention is designed with the purpose to reduce the a priori lung cancer risk by means of providing individually designed oral and risk-determined written information to the study subjects. The content of the information will be different for each subject, and is to be designed to meet each persons needs. These "needs" are determined on basis of the available information on the relevant disease determinants which has been collected beforehand by means of individual work histories an individual information on the non-occupational disease determinants. The magnitude of the a priori lung cancer risk is to be estimated by comparing each subjects past exposure with comparable group based exposure information in published literature. This literature information on relative rate ratios at given past exposures, is to be multiplied by the absolute a posteriori risk at the given ages in the cancer registry data. This approach also enables us to extrapolate the individual a priori lung cancer risk to different points in time in the future. These extrapolated risk estimates are also to be taken into account for the content of the information designed for each participant.

b) The lung cancer screening is planned to be based on two-angle pulmonary X-rays every four months and on yearly three-day exfoliative cytology examination among the members of the high risk groups aged 50 to 69, as these are defined above. Only those participants who exceed an estimated yearly a priori lung cancer risk of 80×10^{-4} will be assigned to triannual screening, as indicated by the broken line c in Figure 1. Those high risk members who do not exceed an estimated risk of 80×10^{-4}, will be screened biannually by two-angle pulmonary X-rays. (The risk among heavy smokers rarely exceeds 60×10^{-4}).

In order to make interpretation and evaluation of the study outcome possible, the study is in need of a kind of "unit" which is applicable both in presence and in absence of intervention. We consider "gained healthy years" among the members of the study group to be an adequate unit for judging the results. Reduced number of exposure-related lost years of life in the study cohort is assumed to be a natural consequence of increased number of healthy man-years. Therefore, gained years of life could also serve as a "unit" for measurement of the outcome of the two strategies for intervention.

DISCUSSION

The choice of frequent X-rays and the less frequent cytology examinations is based on recommendations from the Early Lung Cancer Cooperative Study,[1] which indicated that two-angle lung X-rays are about four times as efficient in detecting early lung cancer as is exfoliative cytology examinations.

We have also considered to chose fixed a priori levels for lung cancer risk as enrollment criteria for each of the two intervention groups. By doing that, assignment to either of the two intervention groups would have taken place when the estimated individual a priori risk exceeds either of these two fixed levels. However, as the experienced a posteriori risk for lung cancer increases with age, (Figure 1, line a) fixed a priori risk levels would have given older people preference before young subjects. It seems likely that individual information intervention may lead to a greater risk reduction when given to high risk groups at young age, than when given to older subjects with a comparable high a priori risk. Therefore, fixed risk level across the age groups might lead to reduced efficiency.

For interpretation and evaluation of the results, we are faced with the same difficulties as other researchers who have indulged in the problem of prospective health assessment.[10] A "controlled" study, in the sense that half of those subjects who are eligible for the study were assigned to the study group and the other half to the reference group, is one possible way to get a reference group. In the present study, however, where a positive outcome of the intervention seems likely, it is difficult to leave half of the group without intervention.

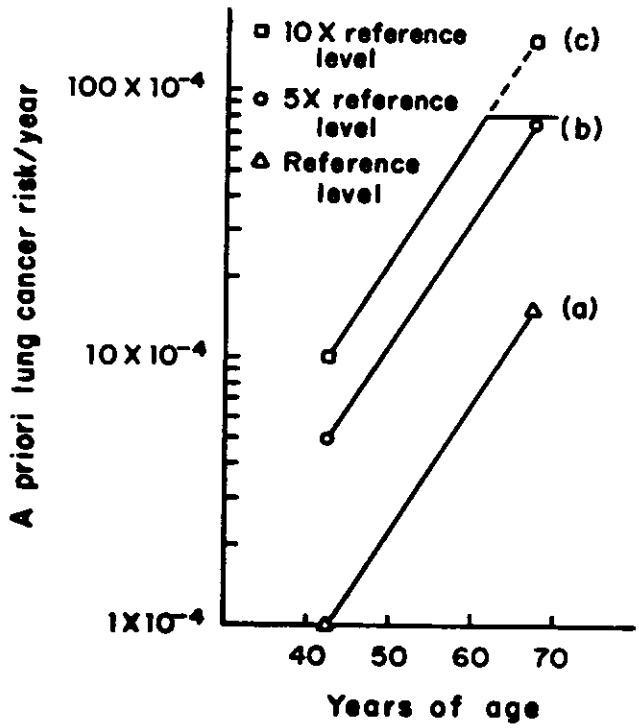

Figure 1. The figure illustrates the a posteriori experienced lung cancer risk (line a) and the a priori lung cancer risk criteria for assignment to the groups for information intervention (line b) and X-ray screening (line c), respectively. Those subjects with risk exceeding the horizontal part of line c are assigned to triannual screening.

We have decided to deal with the problem of evaluation in a similar way as was done in a New York study on the effect of smoking cessation in asbestos workers.[10] In this study the lung cancer mortality was compared among those who had stopped smoking and those who had not. As the numbers are likely to be small in the present study, such a method would allow us to apply intervention on the whole identified population, and subsequently use those who do not participate as reference entity.

In groups which have been heavily exposed to one or two major disease determinant, we consider screening for lung cancer useful only after a presumed development time ("latency period") of 15 to 20 years has elapsed from the first significant exposure. When applying this view, lung cancer screening has biological meaning in relation to the disease determinants at issue only after this presumed development time. When the past exposure has been low, screening only has biological meaning even later.

Depending on the obtained results, in the first place in terms of reduced smoking prevalence in the target group, and later in terms of reduced incidence of lung cancer, the study is intended to carry on as long as past asbestos exposure is considered to be a significant disease determinant in the target population. As reduction in smoking prevalence in the intervention group is to be a prime effect in the present study, one might also expect reduction in smoking related disease incidence and mortality. It is the intention to expand the study to include other major disease determinants in the local population. Such expanded intervention will be performed in close cooperation with the local general practitioners, occupational health physicians, and the hospital.

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BRAZILIAN PROGRAM FOR PNEUMOCONIOSIS PREVENTION

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Brazil is a developing country located in South America and has 135 million people out of which 55 million are active workers. Economically speaking, Brazil is the 8th largest country in the world.

Until 1950 Brazil was basically an agricultural country. From that time on, the manufacturing industry boomed, resulting in an increase of the mining activities. This made a large number of workers to be exposed to dust which are harmful to their health.

Figure 1 shows data related to this serious problem in Brazil and the continuous increasing number of potentially exposed workers. Due to the fact that until last year all measures in Occupational Hygiene and Medicine areas were taken individually in Brazil, to date there are no available data on this matter. Thus, Brazil Ministry of Labor and FUNDACENTRO have been led to set forth a program for Pneumoconiosis Prevention, following the evample of the developed countries.

PURPOSE

The purpose of this program is the control and the reduction of pneumoconiosis cases through primary, secondary and tertiary integrated preventive measures. Primary prevention consists of the workers' dust exposure elimination through the proposition and adoption of environmental control measures, as well as the diffusion of information about the exposure effects and its relationship with the workers''s personal characteristics. Secondary prevention implies the early detection of all pathological conditions of the workers, particularly before the onset of pneumoconiosis symptoms. And tertiary prevention involves the minimization of the medical-social complications resulting from pneumoconiosis by means of treatment of the disease and occupational rehabilitation.

In order to attain this purpose, short and medium-term measures were taken, such as:

a) identification, estimation and registration of the potentially exposed working population, and of the companies and activities which cause pneumoconiosis hazards;

b) workers and employers' awareness of health hazards caused by pneumoconiotic dust exposure. The diffusion of information about prevention risks and techniques by means of events and educative material will help the workers and employers' awareness;

c) training of experts for dust environmental evaluation and pneumoconiosis medical evaluation;

d) control of dust content in work places and medical control of the exposed population;

e) establishment of pneumoconiosis multidisciplinary centers comprising reference laboratories where environmental and medical analyses, including gravimetric, diffractometric, microscopic and radiological analyses may be carried out;

f) improvement of occupational safety and medicine legislation concerning the prevention of occupational pneumoconiosis;

g) subsidies for inspection measures provided by Brazil Ministry of Labor;

h) subsidies for implementation of epidemiological surveillance programs through epidemiological data obtained from cross-sectional and longitudinal studies of the population exposed to pneumoconiotic dust;

i) incentives to research into the occupational pneumoconiosis prevention in engineering and medicine areas, which can be developed at institutional level or in graduation and post-graduation courses.

COVERAGE

For a better use of the available material and human resources we decided, firstly, to develop the program in only six Brazilian states, where the largest number of mining and manufacturing industry workers are concentrated (70% of the whole working population in Brazil). Figure 2 shows the distribution of mining and manufacturing industry workers in Brazil.

In the beginning, we will control the exposure of workers only to coal and crystalline silicates, including silica and asbestos which are the causers of a high percentage of occupational pneumoconiosis cases. Figure 3 shows the district chosen for the development of the pilot plan, where the main Brazilian asbestos and coal mines, and the largest number of mining and manufacturing industry workers exposed to crystallized free silica dust are concentrated.

PROGRAM ACCOMPLISHMENT

The program is being carried out by the Ministry of Labor and the Jorge Duprat Figueiredo Foundation for Occupational

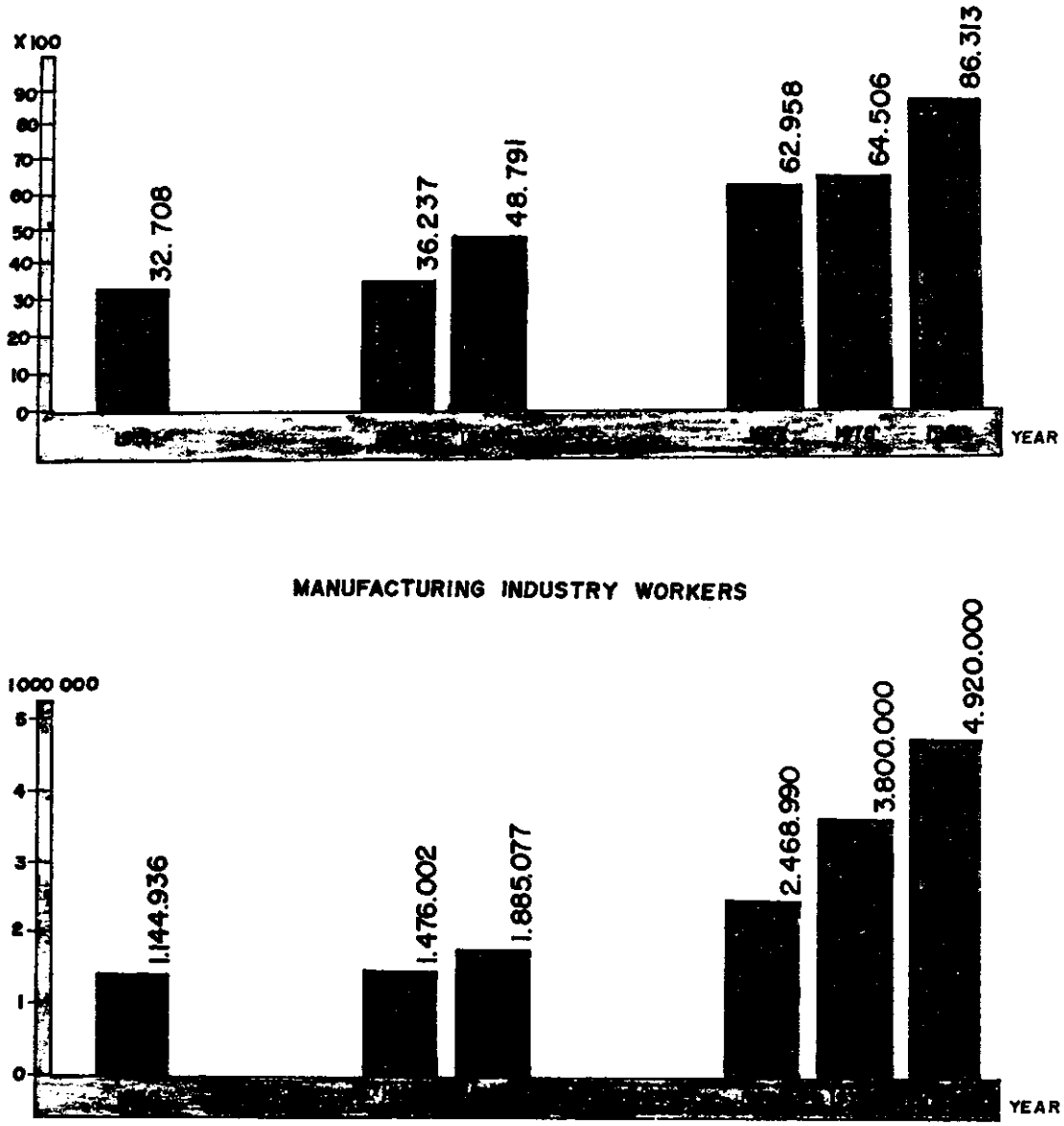

Figure 1. Labor comparative table (1950/1980).

Safety and Medicine—FUNDACENTRO—a nonprofitable entity, which is part of the Ministry of Labor. It was established to conduct research, develop occupational accident and disease prevention programs, and provide technical assistance to public and private organs responsible for occupational safety, hygiene and medicine policy. This program will be successful if workers, employers and Brazilian organs for the prevention of occupational diseases will participate actively in it.

In order to attain the predicted purposes, several steps were estipulated. Some of them will be carried out simultaneously.

In step I, data on exposed workers and data on pneumoconiotic dust exposure sources are being updated, and information channels are being created, since there is no organized information today about the exposure of workers to environmental agents in Brazil.

Questionnaires on administrative data, on registration of industries, and on operational data aiming at identifying the main hazardous operations, the products involved, and the existing control measures were prepared. The predicted number of questionnaires to be applied, in this first step, in all hazard industrial sections, such as mining, ceramics,

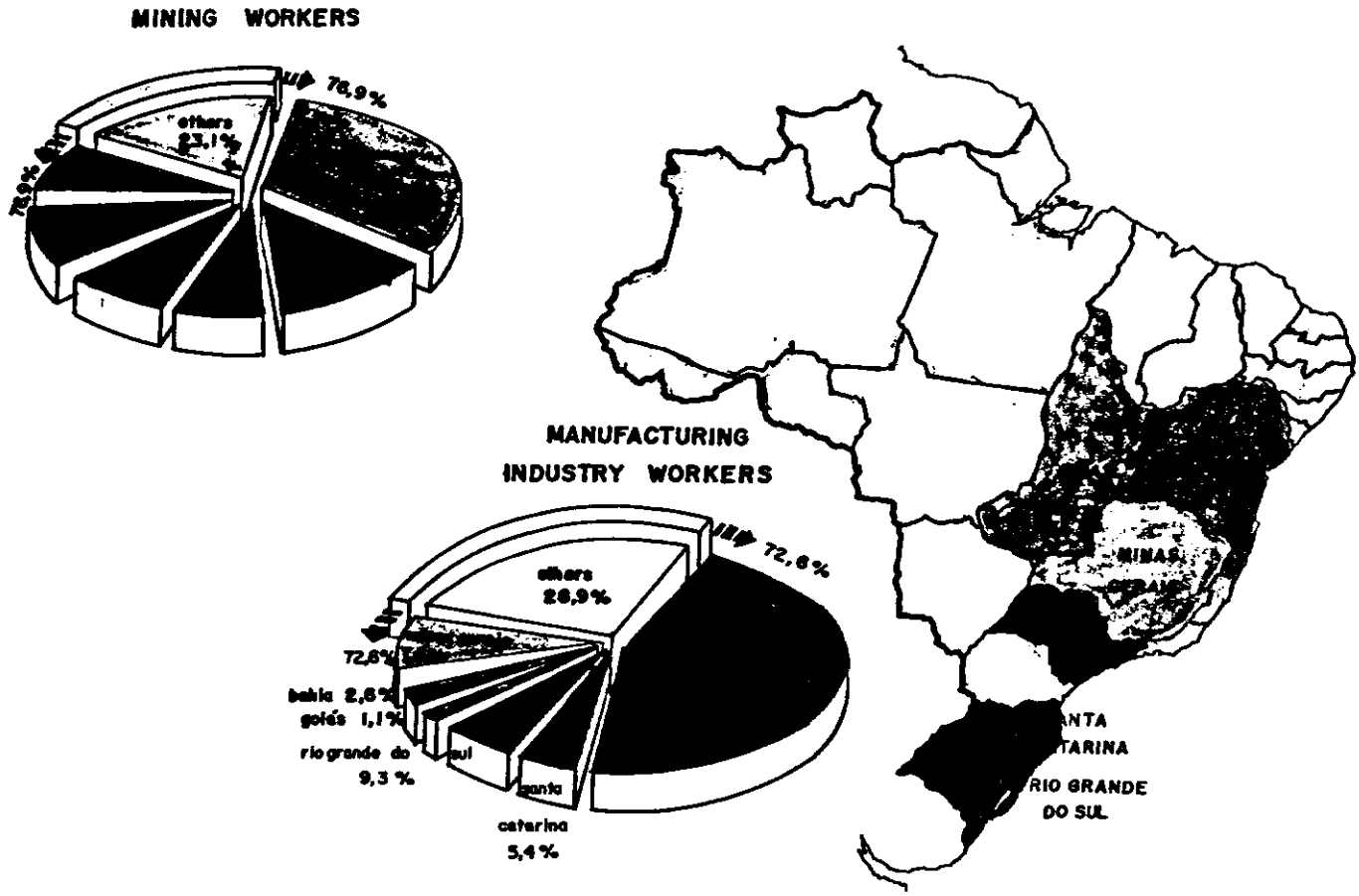

Figure 2

glass industry, foundries, refractories, abrasives, asbestos cement and friction materials is 10.000. 3

Posters and folders were also prepared, as well as technicians from FUNDACENTRO's Regional Unities and from the Ministry of Labor were trained to collect data.

The tabulated data wil define the measures to be taken in the next steps, and the information obtained will be widely spread around the community.

In step II, the identification and the evaluation of workers exposure to the hazards in the workplaces and of the effects on their health will be carried out by means of training courses, characterization of workers exposure, and diffusion of the results.

Training courses wil be promoted for multiplier agents (governmental and private enterprises professionals) aiming at:

a) enabling technicians for evaluating and controlling airborne dust, through recognition, sampling strategies, sample collection and analysis, and control measures;

b) giving credential to support laboratories and standardizing the analytical methodologies of environmental and biological samples by X-Ray diffractometry, gravimetry and microscopy;

c) training medical teams for pneumoconiosis epidemiology and clinic, comprising radiological classification, pulmonary function evaluation and field work methodology.

The characterization of dust exposure will be made through the joint analysis of environmental and medical data obtained during the visits that the specialized teams wil make to the previously selected industries, where they will collect airborne dust samples and will make radiological examinations of the exposed workers, following a methodology developed by FUNDACENTRO together with the Secretaria de Segurança e Medicina do Trabalho (Occupational Safety and Medicine Bureau) of the Ministry of Labor.

In step III, the workers exposure to pneumoconiotic dust and the incidence of pneumoconiosis wil be decreased through educative and informative programs, inspection measures, establishment of specialized centers, and improvement of the current legislation. Guidebooks on hazard awareness and on hazard control measures for workers and employers will be prepared based on data obtained in steps I and II. For spreading out information related to pneumoconiosis prevention, posters and folders will be distributed, and seminars and symposia will be held. Thus an intense inspection by the Ministry of Labor of the most hazardous industries, ac

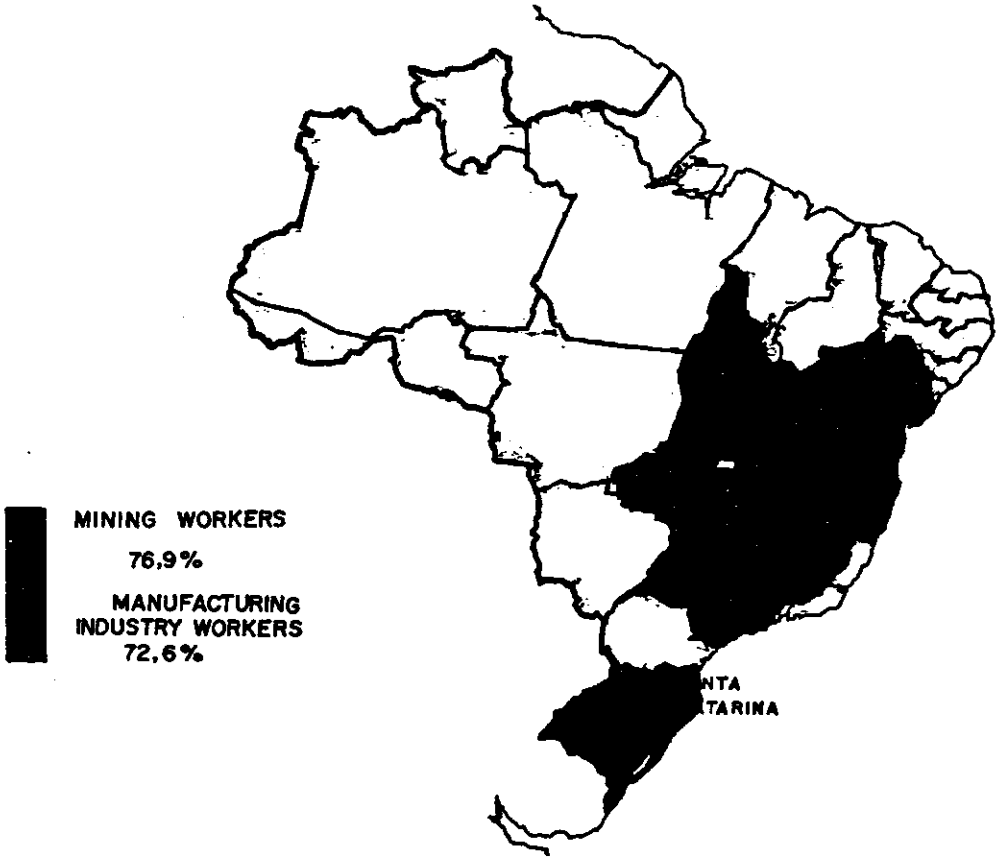

Figure 3. Map of pilot plan.

cording to data obtained in steps I and II, will be possible and efficient.

Additionally, specialized centers for environmental and medical control and evaluation will be established. Its quality will be controlled by National Reference Laboratories of Analytical Hygiene and Radiology being installed at FUNDACENTRO's National Technical Center.

A continuous review and improvement of the Brazi ian legislation wil be emphasized aiming at the effective protection of workers and the enforcement of periodical data supply on the industries in order to keep updated data on production processes and on medical and environmental evaluation.

Specific programs for pneumoconiosis epidemiological surveillance wil also be developed by the Ministry of Health together with the Ministry of Labor in order to evaluate the measures. This will also make possible the relationship between exposure and disease, the study on the respiratory symptoms prevalence of the exposed population, and the technical analysis of pneumoconiosis early detection.

Teams specialized in diagnosis, treatment, mitigation of pneumoconiosis and in professional rehabilitation will carry out the secondary and tertiary measures.

The program will be nationwidely coordinated by engineers and physicians of FUNDACENTRO's National Technical Center and the Secretaria de Segurança e Medicina do Trabalho (Occupational Safety and Medicine Bureau) of the Ministry of Labor and by representatives of the states involved. This coordination team is in charge of the elaboration, follow-up and evaluation of the measures.

CURRENT STATUS

A team has been preparing the material needed to support step 1 measures since 1987 second half.

An administrative questionnaire was prepared for registering the sources where exposure to pneumoconiotic dust can occur. It will be utilized to collect data on working hours, on the number of workers (number of men, women and underage workers), on medical attendance, on the number of trained technicians in occupational safety, hygiene and medicine, on the number of pneumoconiosis cases; on environmental monitoring, on medical examinations for the control of dust exposure, and on training courses. Through this questionnaire information on the specification and quantity of materials employed in the production wil be also known.

These questionnaires were on trial in a hundred industries in the state of São Paulo, and it will be applied in the states involved in the program next September.

Another questionnaire was prepared for collecting data on

the operations of industries which generate pneumoconiotic dust.

In order to attain this goal; small, medium and large-sized industries were visited. Based on these data a form was made so as to obtain information on the type of operation carried out in each industry, on the number of equipment used in each type of operation, and on the control measures (starting with the receiving of the raw material and ending with the finished product).

As cleanup is of utmost importance, we also try to know how it is done inside the industries.

In order to obtain the cooporation of workers and employers, posters and folders of the program are being sent to Labor Unions and to Trade Associations.

A previous qualitative analysis of the raw material used in the industries, to detect the presence of crystallized free silica, is being carried out so that priorities may be established after the tabulation of data obtained through the questionnaires.

Simultaneously, airborne dust measurements have been made in different types of industries for quantifying the hazards and making possible the accomplishment of steps II and III.

FINAL COMMENTS

The efficiency of the diffusion, awareness, and training will show a significant increase in the number of pneumoconiotic workers, since to date it is common practice in Brazil to retire workers with occupational respiratory diseases as if they suffered from ordinary diseases. This happens because working conditions at the workplaces and suitable techniques for clinical investigation are totally unknown.

The number of workers retired because of sickness will only start to decrease when the real number of pneumoconiotic workers will be registered. Therefore, this decrease will only be attained in a long period of time.

PREVENTION OF OCCUPATIONAL AND ENVIRONMENTAL LUNG DISEASES

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INTRODUCTION

In the normal lung, there is an extremely rapid turnover of proteins including collagen. This helps in the maintenance of vital function of the gas exchange and need for rapid adopatation in response to injury. Being unusual proximity to the environment, the lung is primary port of entry of noxious gases, fumes and dusts. The same thickness and delicacy that qualify the air-blood barrier for the rapid exchange of oxygen and carbon dioxide reduce its effectiveness as barrier to inhaled microorganisms, allergens, carcinogens, toxic particles and noxious gases. These exposure are normally tolerated by the host. Excess of these substances in the exposure, thus damage to lung not only impair life sustaining process of gaseous exchange but also the defence of organism against microorganisms. In addition, the lung is now recognized as a major site associated with many metabolic activities, the so called non-respiratory functions of the lung.

Like most other organs, the lungs, exhibits only a limited range of responses to damaging agents since the final common path of inflammation and repair involves a fairly limited number of cells. Although nearly 40 different types of cells are found in the lungs.[10] Thus a variety of initiating agents cause damage to host cells in a much more limited number of ways. The uniformity of the final common path response is even more striking when the late healing stage of widespread lung damage is considered. Thus a very wide variety of quite different acute inflammatory reactions, if persistent, will result in a uniform pattern of fibrous scarring. Assessment of hazards associated with inhalation of toxic particles is dependent on a number of factors. The toxic effects are effectively minimized by maintaining the concentration of contaminant below some level which has been deemed unlikely to cause detectable biological damage in people exposed over a long period. Besides, there are other factors that are not directly related to chemical properties that make a substance toxic.

In fact, lung diseases due to exposure of dusts are the most serious among occupational and environmental diseases. Dusts of free silica such as quartz and silicates, e.g. asbestos, talc and mica are known to produce diverse toxic effects which are very well documented.[5] However, inspite of several theories and a large number of experimental and clinical studies the exact molecular mechanism responsible for the pathomorphological and physiological lesions is not yet clear. There is considerable evidence pointing out that silicic acid dissolve from the dusts could be pathogenic fact or as postulated in solubility theory of king and its follow up studies.[3] Many theories on fibrogenic action of silica were put forward but real mechanism of fibrogenesis is not yet known.

PRESENT SITUATION

Although industry is spending unprecendented amount of money to protect its employees from all known hazards, today's technological advances are creating problems faster than we can handle them. In India 56 minerals are exploited through 3350 mines mostly comprising coal, iron ore, limestone, bauxite and manganese etc. The mining industry contributed quite a lot to the regional economic development, however, it has caused ecological and environmental damage to the proportions beyond retreval. The chemical industry in India made spectacular progress during last 4 decades. It is now well-established fact that chemicals play a key role in important sector of agriculture, clothing, housing, transport and health. The present societies have become dependent on the benefits of chemicals to an extent that is irreversible. But many of the basic chemicals which are, essential for the production or on great demand are hazardous—toxic to human and the environment.

EXPOSURE, DEPOSITION, CLEARANCE, TRANSLOCATION AND RETENTION

Once released into the environment, the main routes of entry of chemical into the body are through the lung, skin, eyes and gastrointestinal tract. The occurrence of pneumoconioses, neoplasms and infectious diseases resulting from particulate exposures depends on the deposition and clearance of particles in the respiratory tract.

Deposition is the process that determine what fraction of the inspired particulates will be caught in the respiratory tract and thus fail to exit with the expired air. It is likely that all particles deposit after touching a surface, thus the site of initial deposition is the site of contact. Clearance refers to the dynamic processes that physically expel the particulates from respiratory tract. It is the output of particulates previously deposited. Rapid endocytosis of insoluble particles prevents particle penetration through the alveolar epithelia and facilitates alveolar-bronchiolar transport. It has little possibility that macrophages laden with dust can re-enter the alveolar wall, only free particle appear to penetrate. Thus phagocytosis plays an important role in the prevention of the entry of particles into the fixed tissues of the lung.[1] Silica

dust which is cytotoxic has been found to be translocated in the tracheobronchial lymph nodes at a greater rate than the mica dust.[6,9] However, translocation of chemicals or dusts from lungs to lymph nodes may produce other serious effects and sequalae besides fibrotic replacement of nodal tissue could follow the increased accumulation of inhaled chemical substances in the lymph node. The actual amount of substance in the respiratory tract at any time is called the retention. When the exposure is continuous, the equilibrium concentration (achieved when the clearance rate matches the deposition rate) is also retention. When the accidental or sudden massive exposure of chemical occurs as in case of chemical accidents or disasters, the equilibrium between the deposition and clearance is not operative and retention is maximum in comparison to that of normal working conditions. In contrast as in the case of asbestos exposures, a dose too small to produce fibrosis i.e. asbestosis, may lead to lung cancer. A dose large enough to produce asbestosis may cause malignance if the worker does not die first from the pneumoconiosis. Recently the events which were naturally occurring or industrial related in which the release of toxic fumes or gas had occurred, the main route of entry of excess toxic substances is through inhalation (Figure 1). The pathological and physiological state of the individual may

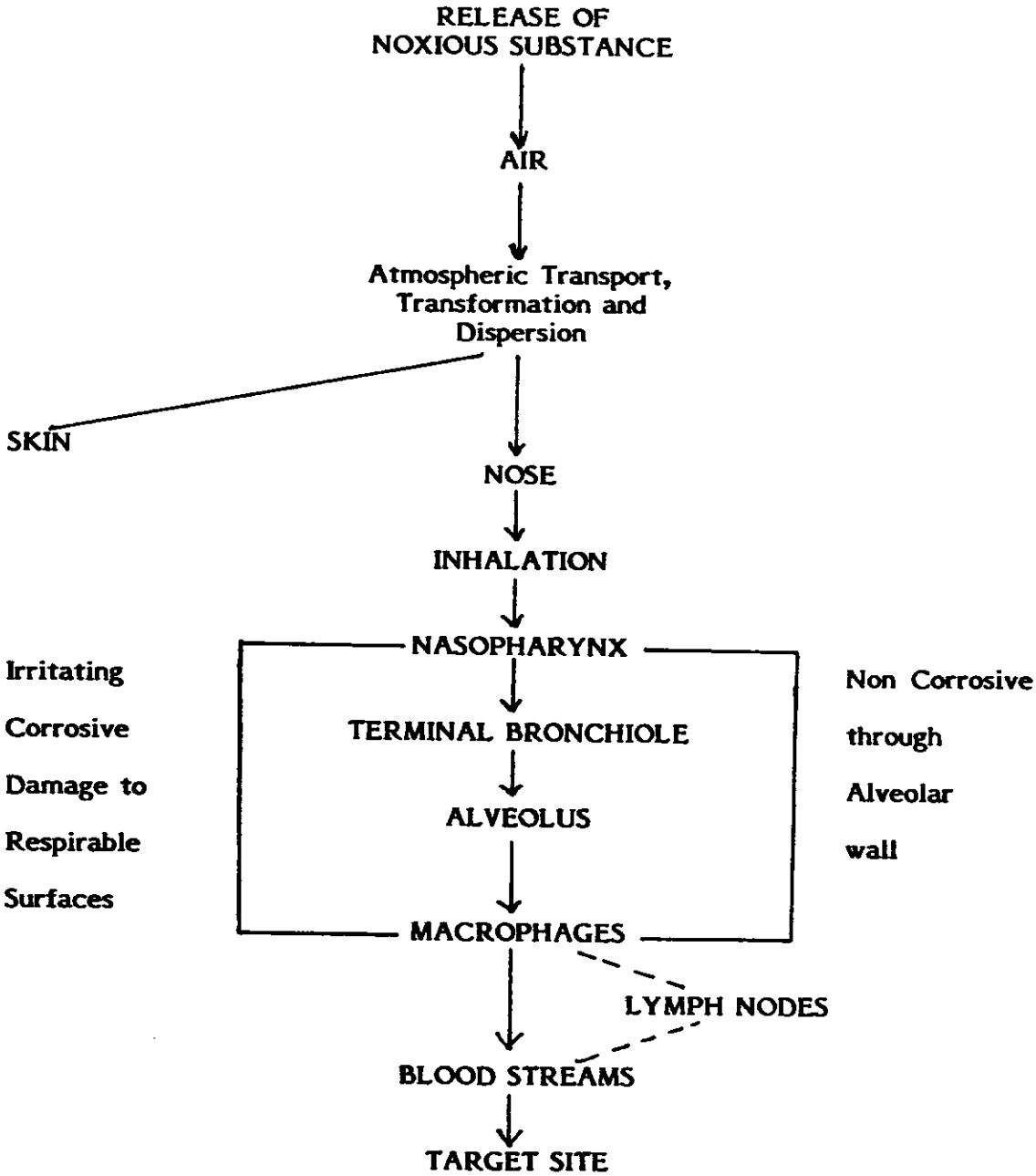

Figure 1. Fate of inhaled substance.

play a major role in biological response after exposure to dusts or chemicals.

PATHOLOGICAL STATES

Prolong inhalation of dust over an extended period of time can produce in certain individuals a respiratory disorders known as coal worker's pneumoconiosis, silicosis, asbestosis and silicatosis. Simple pathological states which are referred as simple silicosis or simple pneumoconiosis in coalworkers which are uncomplicated by any other factor and thus refers to the essential manifestation of the disease. Occupational diseases are associated with complex webs of causations and attributed to both environmental and genetic factors. The industrial workers are liable to all other diseases which affects man. Hence, the other factors such as age, sex, reproductive status, genetic make up, nutritional status, pre-existing disease states and status of immune system influence the disease process and a composite picture comes as clusters of diseases or symptoms. In the case of exposure to chemicals such as Toluene disocyanate (TDI) which affects various parts of the respiratory system. Sometimes it affects the nose and throat, sometimes the bronchial tube and/or the lung. The different pathological states may occur at different exposure level, if exposures are sufficient may affect growth and development, host susceptibility and pre-pathological changes. In case of massive exposure the terminal effect may be progressive fibrosis and mortality (Figure 2).

PREVENTION AND TREATMENT

The search that begun in the beginning of the century, the treatment of silicosis or asbestosis continues unabated to this date in what surely is one f the longest uninterrupted lines of unfulfilled inquiry in Pneumoconiosis Research. It is generally agreed that the dust must be suppressed at the point of origin. If all the preventive measures be introduced then there should not be pneumoconiosis but it is not possible in practice. We can reduce the number of fibres or particles (0.1 μm and greater) per unit area but the predominance of smaller submicroscopic dust particle may modify the type of disease. As electronmicroscopic analysis of isolated lung dust of asbestos exposed and nonexposed individuals revealed high fibre counts. The highest fibre counts were found in individuals exposed to asbestos and mixed dust.[11] At present there is no methods available to specifically interfere with the deposition of collagen in the injured organ. It seems that once the fibrogenic cell triggered by the message to produce more collagen it is already too late for any pharmacological interfere. While the progression of fibrosis might be halted, the actual removal of fibrosis is highly improbable. It is unlikely that alveoli in which fibrosis occur will ever return to normal. Although in the past various substances were tried to prevent silicosis such as Aluminum therapy and lately by the antisilicotic drug Polyvinylpyridine-N-Oxide (PVNO). The therapeutic and preventive effect of Tetrandine—an alkaloid of bisbenzyl isoquinoline (*Stephania*

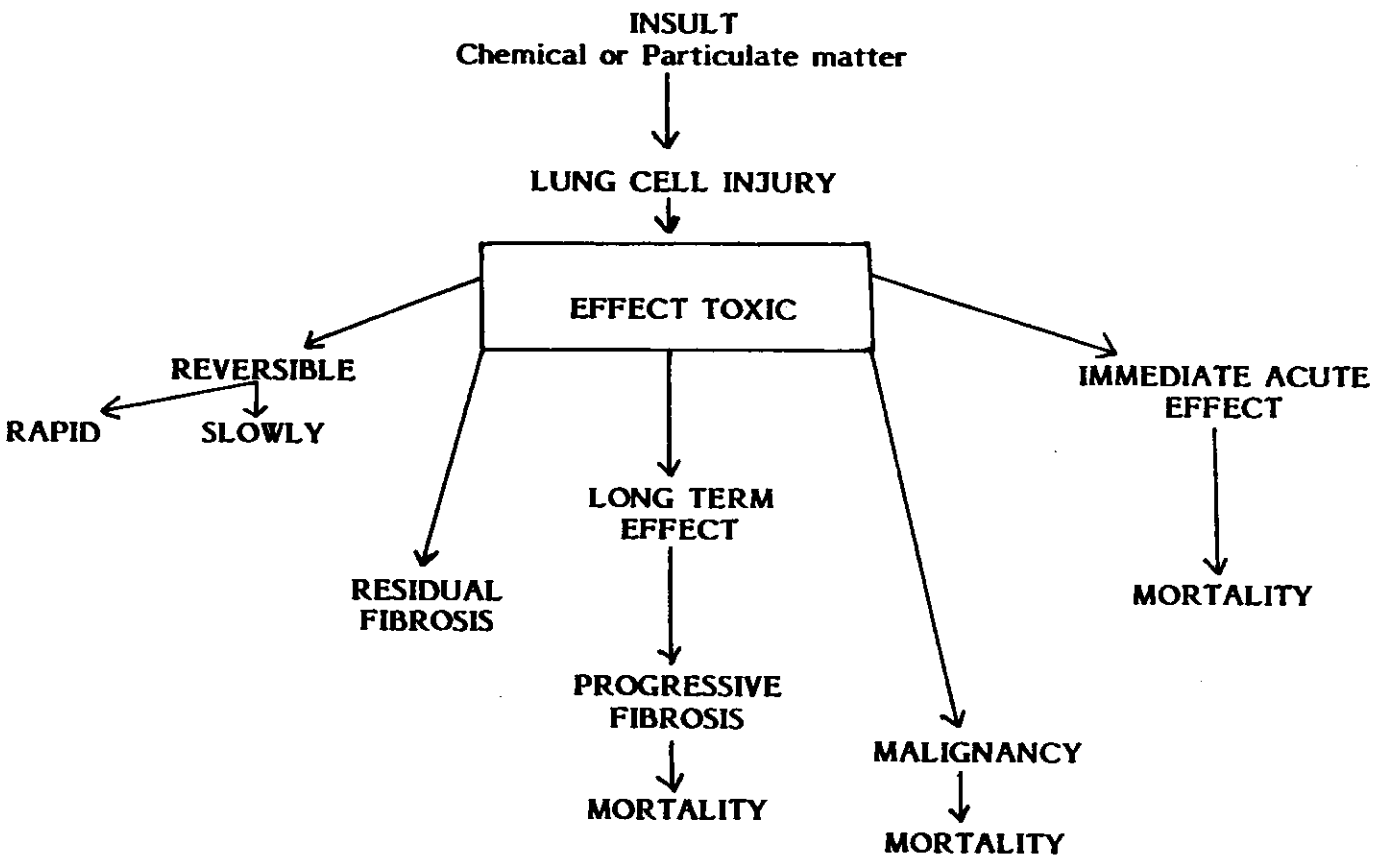

Figure 2. Injury to respiratory system due to exposure.

tetranda S. moor) in experimental silicosis in rats and monkeys as well as marked improvement in symptoms and chest X-ray of human silicotics.[2] Certain toxic effect of tetrandine on long term treatment were found in the form of degeneration and necrosis of cells of liver and kidney. Earlier, several experimental approaches have been attempted for the treatment of pulmonary dust diseases with only partial success using different types of aerosol therapy, hormonal therapy, vitamin therapy and other substances including dietetic factors.[12]

The animal experimentation conducted with various substances when introduced by intratracheal injection, massive pulmonary lesions may be produced, whereas exposing animals to same types of substance by inhalation, no pulmonary damage was found. The impairment in the equilibrium between deposition and clearance of dust particle may be the main source of retention in the lung and ultimately leading to respiratory disorder. We conducted some studies earlier to explore and verify the role of nutritive substance, on the pathogenesis of coal dust induced lung disorders in rats. The effect of Indian jaggery, where many microingredients play some protective role, firstly, by enhancing the physiological pathway of dust clearance and secondly on release of biologically active toxic substances. Naturally when the status of physiological pathway of clearance of host is enhanced then dust larger and/or submicroscopic particles may be expelled during course of exposure of dust through nasopharyngeal clearance mechanism. It has also some effect on the development of fibrosis and deposition of collagen in the lungs. Moreover, the transportation of dust from lungs to tracheobronchial lymph nodes were also altered and produced less fibrogenic lesions in the lymph nodes.

Our earlier studies[7,8] suggested a strong potential of jaggery as protective agent in coal induced lesions in the rat while regular consumption of jaggery is said to confer symptomatic relief in industrial and mine workers and jaggery is therefore routinely provided to workers in most of mining and industrial establishments in India. Moreover, in the case of exposure to gases and fumes only symptomatic treatment is provided. Even in case of long term effect of exposure of gases or fumes the treatment is available on the basis of symptoms only. The antibiotics have certainly saves many lives due to prevention of pneumonia. The better chemotherapy for tuberculosis which complicates many pulmonary disorders are now under control. Simple pneumoconiosis if not prevented may lead to more complicated disease pattern or neoplasia after prolong exposure.

CONCLUSIONS

1. Pulmonary fibrosis and lung cancer are severe and crippling disease, the prevention of the disease must be done by all possible engineering methods.

2. Animal experimental work and epidemiological studies in industries have led to identification of causative factor(s) but mechanism by which effects are produced are not known.

3. More detailed studies on the (a) mechanism of clearance of dust particles (b) enhancement of clearance (c) substances which can reduce the biological effect of dust on retention in the lung and (d) substance or drug which can prevent the fibrotic lesions, are required. Greater thoughts should be given to these steps to minimize the disease process. Care should be taken to ensure the best possible nutritional status and to treat active infections in industrial workers.

4. Lot more is needed to be done in the prevention of occupational and environmental lung diseases.

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PRECAUTIONARY MEDICAL EXAMINATIONS FOR EMPLOYEES EXPOSED BY QUARTZ FINE DUST IN THE FEDERAL REPUBLIC OF GERMANY

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ABSTRACT

In the Federal Republic of Germany, all employees exposed to quartz fine dust at the work station have to be examined on a regular basis by specially certified physicians. Continuation of employment depends on lack of medical objections based on these examinations, which are organized, paid for, and documented by the employer.

For several decades the STEINBRUCHS-BERUFSGENOSSENSCHAFT—the accident insurance institute for quarries—has been in charge of scheduling those medical examinations and keeping records of their results, including X-ray examinations. Hence, for all employees within the responsibility of the STEINBRUCHS-BERUFSGENOSSENSCHAFT, complete and up to date medical history information is available in case of a diagnosed disease.

Moreover, we have started in 1987 to keep records on the actual level of quartz fine dust exposures encountered by each employee in connection with individual job profiles and dust reduction devices. So far, we have accumulated data for about 20,000 employees. These data provide a basis for the physicians to probe the feasibility of and compliance with currently defined quartz fine dust concentration limits in the Federal Republic of Germany.

See Table of Contents, Part II, for Paper.

A METHODOLOGICAL PROBLEM IN INVESTIGATION OF PNEUMOCONIOSIS EPIDEMIOLOGY

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Pneumoconiosis epidemiology has brought to more and more people's attention. A problem frequently faced in statistical analysis to determine the significance of incidence reduction is the paucity of population data for exposure, as met by Hill in his investigation on chromicim chemical manufacture. Under the enlightenment of "Probability window analysis," author advanced a method of contrast analysis combining "the calendar year of beginning exposure" and "the exposure standing up to diagnosis"—the length of exposure years from beginning exposure to the date of diagnosis of pneumoconiosis which is abbreviated "exposurestanding contrast analysis." It proved that the method had certain significance in analyzing effects of dust prevention, evaluating dust harmfulness and handling health surveillance.

METHOD

According to the following conditions, selected plants A and B from the data of Liaoning Provincial Penumoconiosis Epidemiology Investigation as observation targets,

1. Time record was certain before and after a major change of dust prevention.
2. There were systematic data on health examination and environmental survey.
3. There were complete records of pneumoconiosis cases.

Then, draw "exposure-standing contrast" figures according to the following method:

1. On the common standard lattice paper, draw an abscissa and an ordinate which show "the calendar year of beginning exposure" and "the exposure standing up to diagnosis", respectively.
2. According to the two parameters mentioned above. Each pneumoconiosis case is plotted on the figures.

Contrast Method

Figure 1 shows the contrast between two periods. Each observation period included 20 years.

1. Draw three erect lines A, B and C upward from 1945, 1965 and 1985 on the abscissa.
2. Drow two oblique lines toward ordinate from 1965 and 1985 which intersect the lines A, B. Thus two triangular windows with equal size are drawn.
3. Count the number of pneumoconiosis cases in the triangular windows, then, do statistical test by binomial probability distribution.

Figure 2 shows the contrast among many periods including 5 years.

1. On the absicissa, from 1945, 1950, 1955, 1960, 1965, 1970, 1975, draw erect lines A, B, C, D, E, F, G, and I upward.
2. From 1965, 1975, and 1980 draw oblique line toward A,B,C, D, and E. Thus, five triangular windows with equal size are drawn.
3. Count the number of pneumoconiosis cases in the trapezoidal windows and do statistical test to avoid recounting to these same cases.

RESULTS

The history of dust prevention was divided into four periods in plants A and B:

- 1945—period of no dust prevention.
- 1950—period of poor dust prevention.
- 1955—period of wet drill and closed ventilation.
- 1960—period of comprehensive dust prevention.

Figures 1–4 provide plots for each pneumoconiosis cases in plants A and B by "calendar year of beginning exposure" versus "exposure standing up to diagnosis."

DISCUSSION

In Figure 1, 3, the left triangular windows contain pneumoconiosis cases who were first employed between 1945 and 1965. There were a total of 320 cases in plant A and 291 in plant B. The right triangle contains cases who were first employed between 1965 and 1985, no cases in plant A and 7 in plant B. The decline in cases before and after comprehensive dust prevention in 1965 is statistically significant ($p < 0.01$).

In Figure 2, 4, the equal sized windows contain cases who entered the plants A and B in the period of 1945–1959, 1950–1954, 1955–1959, 1960–1964, 1965–1969, 1970–1974, 1975–1979, respectively.

The number of reported pnuemoconiosis cases falling within the windows are 140, 182, 14, 1, 0, 0 in plant A and 216, 196, 30, 3, 4, 0 in plant B, respectively.

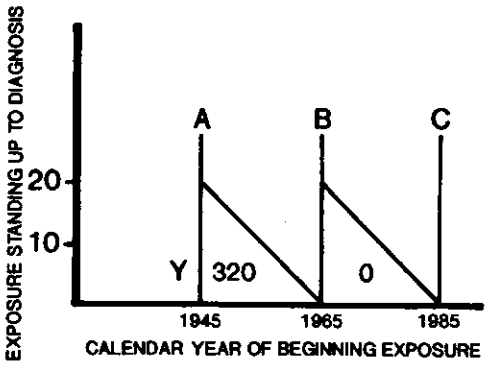

Figure 1. A comparison of pneumoconiosis incidence in equal size observational windows before and after a major dust prevention change in 1965 in A plant.

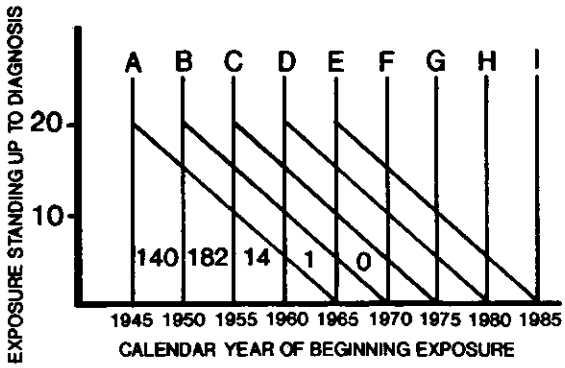

Figure 2. A comparison of pneumoconiosis incidence in equal sized observational windows before, between, and after major dust prevention change in 1960–1965 in A plant.

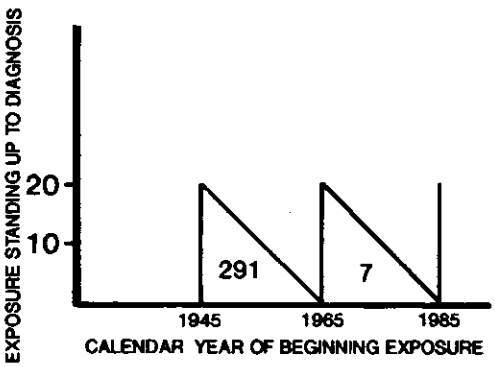

Figure 3. A comparison of pneumoconiosis incidence in equal sized observational window before and after a major dust prevention change in 1965 in B mine.

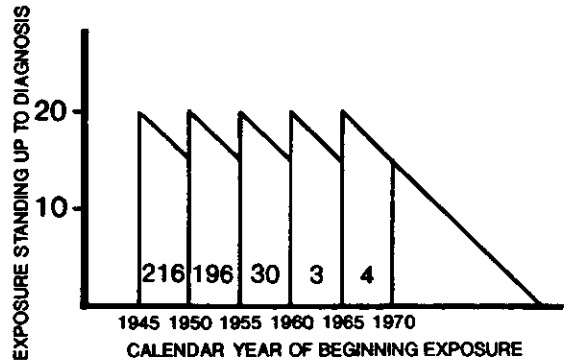

Figure 4. A comparison of pneumoconiosis incidence in equal sized observational windows before, between, and after major dust prevention change in 1960–1965 in B mine.

The results show that dust prevention plays an important role in reducing pnuemoconiosis incidence. The advantage of the method of "exposure-standing contrast analysis" is to be able to assess the probability that a change in the number of cases may have occurred at chosen point in time in the absence of data on exposed population.

When comparing the incidence according to type of works and work standing, it used to be difficult to deal with the following two problem,

1. The calculation was difficult when dividing standing into different groups after having divided types of work, because the divided layer were too many to have even distribution of cases.
2. When calculating the years of standing, it was confounded by the factor of different year of beginning exposure, so that the results might be false and misunderstood. For example, the duration of exposure may be the same of 10 year but the effect of 10 years exposure 20 years ago is different from that of latest 10 years. That is because the environmental and hygienic situation has been changing greatly in recent 20 years.

The method of "exposure-standing contrast analysis" is to do contrast analysis between two periods by combining two parameters of "year of beginning exposure" and "exposure standing up to diagnosis," so as to get a clearer picture that when (in what calendar year) the worker was exposed to dust and how long (years) the workers' standing was since then.

The concept has a important significance not only in assessing the preventing effects but also understanding the harmfulness to workers caused by dust pollution at workplace in different period. Hence, it has a reference value to carry out health surveillance and administration, analysis the results of body's examination and evaluate the trend of pneumoconiosis incidence change.

BRIEF SUMMARY

It is proved through study that the method of "exposure-

standing contrast analysis'' can be used to assess probability that a change in the number of cases may have occurred at a chosen point in time. In the absence of data on exposed population and proved the basis to evaluate preventing effects, medical surveillance, health guardianship and administration conditions.

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A COMPREHENSIVE PROGRAM FOR IMPROVED MANAGEMENT OF RESPIRATORY HEALTH

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INTRODUCTION

Morgan has described a medical condition of the lung, of nonsmokers in the industry trade, characterized by chronic cough productive of sputum and accompanied by mild obstruction of the large airways. Since X-rays of the chests of these workers exhibit few change, and therefore little parenchymal involvement of the lung, he termed this entity industrial bronchitis.[1] Other investigators have reported similar findings in studies of workers having long-term exposure to nuisance dusts.[2,3]

In a study of workers exposed to high total dust levels of bauxite and alumina for 20 or more years, Townsend *et al* in a cross-sectional study of pulmonary function test results demonstrated a statistically significant increase in numbers of workers with a forced expiratory volume in one second (FEV_1 of less than 80% of predicted.[4] A separately reported study of changes on chest X-ray of these high-dust-exposed workers compared to others with little exposure revealed only minimal nonsignificant X-ray changes.[5]

Because of this evidence of a decrement in FEV_1 of workers exposed to high levels of dust for twenty or more years, Alcoa's medical staff decided to plan and implement a standardized program for pulmonary surveillance at domestic locations.[6]

GENERAL DESCRIPTION OF ALCOA'S PULMONARY SURVEILLANCE PROGRAM

The goal of Alcoa's program for management of respiratory health is prevention of work-related lung impairment. We have identified two objectives which must be met in order to attain this goal. First, we must improve management of the multiple activities which are necessary for providing adequate respiratory protection, and secondly we must establish a mechanism to reevaluate continually the overall effectiveness of our efforts.

The major activities which must be managed for an effective program of respiratory protection are:

- Identification of hazardous exposures by air sampling;
- Education of employees about the respiratory hazards at work and the measures necessary for adequate protection;
- Provision of respiratory protection where indicated;
- Training of technicians to perform standardized testing of pulmonary function;

Pulmonary function testing of employees exposed to hazardous
materials;

- Identification of employees with lung function loss meeting some set of criteria;
- Medical referral of employees with confirmed functional loss for further diagnostic evaluation; and
- Modification of environmental controls to reduce health risks.

The resources we have developed for evaluating the overall effectiveness of our program for respiratory surveillance are:

- Creation of computer software to provide automatic storage of and access to data generated by spirometric testing;
- Development of criteria incorporated in the software for screening of spirometric test results; and
- Periodic analysis of data to determine the adequacy of the
surveillance program.

PULMONARY SURVEILLANCE SYSTEM

We have created a computer-based system to support functions in the plant medical departments as well as at the corporate medical level. The system is supported by a personal computer (Compaq 386) with a printer in each plant medical department and a mainframe computer in Pittsburgh. The plant-based computer interfaces with a spirometer and is programmed with algorithms to analyze and screen the results of each test as it is performed. If the medical staff wishes, at the end of a test, a report may be provided to the employee. The file of the Compaq 386 is sufficiently large to accommodate these functions as well as previous test results for each employee at a plant with about 1500 employees.

The plant-based computer is also programmed to permit periodic uploading of all interim test results to a Pittsburgh-based mainframe file.

The mainframe computer file contains test results for all employees at domestic locations, and the corporate medical

staff has access to this file for periodic assessment of the timeliness of testing at each plant as well as for determining the incidence of functional decrements experienced by employees exposed to irritating dusts.

The mainframe computer software also has a scheduling function to identify a future date for the next scheduled test for each employee. This new schedule for testing is downloaded to the plant personal computer. In this process the mainframe computer also downloads all job or demographic changes derived from another system maintained in Pittsburgh.

Criteria for Screening and Analysis of Spirometric Test Results

In Alcoa, pulmonary function testing is performed as a part of preplacement evaluations, non-occupational periodical medical evaluations, and periodic medical screening for hazardous work exposures.

Medical and industrial hygiene personnel have identified all plant materials which may be hazardous to the lungs. Arbitrarily we have identified an action level for triggering a medical exam. An action level is an exposure exceeding one-half the threshold limit value established by the American Conference of Governmental Industrial Hygienists.[7] Employees having such exposures have pulmonary function tests yearly. If test results are less than expected, the employee is retested in three months.

From Knudson's prediction equations[8] the plant personal computer has been programmed to calculate the predicted FEV_1 and the predicted forced vital capacity (FVC) based on the individual's age, sex, and height. Predicted values are adjusted for race. After corrections for BTPS the computer selects: the maximal FEV_1 and calculates a percent of predicted FEV_1 ; the maximal FVC and calculates a percent of predicted FVC; the maximal FEV_1 and calculates a percent of maximal FVC.

The criteria selected for the classification of respiratory impairment is consistent with the American Medical Association's guidelines for determination of respiratory impairment.[9] These criteria are: for normal function, a percent of predicted FEV_1 or FVC of 80 or better; for mild impairment, percent of predicted FEV_1 or FVC of less than 80 but 60 percent or better; and for moderate to severe impairment, a percent of predicted FEV_1 or FVC less than 60.

From the reports available, there appears to be considerable interest in developing sophisticated methods in the future for analyzing longitudinal pulmonary function data.[10,11,12] However, from a review of the recent literature there is insufficient information to support establishment with confidence of criteria for expected annual decrements in pulmonary function test results for an aging population.

In the absence of supporting information we have established arbitrary criteria to define significant loss of lung function over time (Table I). Because of the widely recognized variability in pulmonary function test results over time a worker, for his loss to be significant, must demonstrate a decrement in FEV_1 or FVC greater than 250 ml plus a yearly decrement 50 ml. (See Table I.)

Table I

Criteria for Defining Significant Lung Function Loss

Interim Between Tests	Decrement in FEV_1 or FVC
0 - 1 Years	> 300 ML
0 - 2 Years	> 350 ML
0 - 3 Years	> 400 ML
0 - 4 Years	> 450 ML
0 - 5 Years	> 500 ML
0 - 6 Years	> 550 ML
0 - 7 Years	> 600 ML
0 - 8 Years	> 650 ML
0 - 9 Years	> 700 ML
0 - 10 Years	> 750 ML

Medical referral for diagnostic testing is dependent on identification of employees exhibiting a significant loss in pulmonary function on successive tests. An employee with normal lung function (FEV_1 or FVC $\geq 80\%$ of predicted) will be referred for medical evaluation after he exhibits a significant loss on three successive tests or his test results indicate a change in status from normal to mild impairment (FEV_1 or FVC $< 80\%$ but $\geq 60\%$ of predicted).

A worker with mild impairment will be medically referred if he exhibits a significant loss on two successive tests or if his most recent test indicates a change in status from mild to moderate impairment (FEV_1 or FVC $< 60\%$ of predicted) his lung function becomes moderately impaired. A worker with existing moderate impairment will have a medical referral after exhibiting a significant loss on one test.

All plant medical technicians have received training in the conduct of standardized pulmonary function testing. At the end of August, 1988, computer-based testing is being done at two locations, and the corporate medical staff is preparing a schedule to complete implementation of the program at Alcoa's domestic locations over the next eight months. We think having a system to provide timely information about changes in lung function will permit us to achieve a high level of respiratory protection for Alcoans exposed to respiratory hazards.

Hazardous materials at all plants have been identified. Industrial hygienists have completed work on an employee educational package which will be distributed to all plants in the Fourth Quarter, 1988. We anticipate that the full program will be implemented at all domestic plants by mid-1989.

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"B-READERS" AND ASBESTOS MEDICAL SURVEILLANCE

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ABSTRACT

Civilian "B-Readers" certified in ILO methodology interpreted randomly distributed asbestos medical surveillance X-rays of more than 105,000 U.S. Navy employees. Analysis of 23 participating observers demonstrated a three hundred-fold prevalence of perceived "definite" pulmonary parenchymal abnormalities. There was an evident geographic component to interpretation habits, with east and west coast observers more likely to interpret films as abnormal than observers from the midcontinent. The most expert observers, a group who instruct the course leading to NIOSH certification in ILO methodology, also perceived fewer abnormalities than other readers. Instructors still exhibited a seven-fold prevalence range of positive interpretation. Under usual surveillance conditions, the habits of "B-Readers" appear to have a major impact upon the X-ray interpretation of asbestosis. Certification in "B-Reading" should not be the only quality assurance for radiographic surveillance programs, medical decision-making, nor related legal activities. Epidemiologic comparison between populations should account for the apparently wide spectrum of interpretation habits.

No Paper provided.

IS THE US COAL MINER CHEST X-RAY SURVEILLANCE PROGRAM SUCCEEDING IN CONTROLLING LUNG DISEASE?

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The 1969 Federal Coal Mine Health and Safety Act established a system of periodic chest X-ray examinations for underground coal miners in the United States.[1] The program, as operated by the National Institute for Occupational Safety and Health since 1970, has both surveillance and screening components.

The surveillance component of the program is directed toward observation of the incidence of coal workers' pneumoconiosis in the population of working miners. There is an expectation that the program can document decreasing disease incidence as exposure controls are put in place.

The purpose of medical screening is detection of asymptomatic disease in individuals at a point at which intervention will favorably affect disease outcome. It is a back-up mechanism to reduce impairment when environmental controls are insufficient to prevent disease in individual miners.

This paper explores whether the current surveillance and screening program is functioning adequately to contribute significantly to the reduction or elimination of lung diseases in underground coal miners. Both the surveillance and screening components depend upon the use of tests which can identify lung diseases of importance. They require high levels of participation by miners at greatest risk of disease and acceptance of preventive interventions. Ultimately, the measure of the success of the program is the extent to which the development of pulmonary impairment in coal miners is abated.[2]

PROGRAM STRUCTURE

The 1969 Coal Mine Health and Safety Act was the first legislation to establish a national program for medical surveillance. The X-ray program was continued under the Federal Mine Safety and Health Act of 1977 [MSHAct]. The MSHAct also contained an expanded mandate to utilize medical screening as a preventive strategy. When a determination is made that miners may suffer "material impairment of health or functional capacity" as a result of hazardous exposures, removal from exposure and reassignment must be offered.[3] To date, the periodic X-ray program is the only effort to fulfill the mandate for ongoing screening for dust diseases.

The MSHAct requires that all miners receive chest X-rays on entering the work force and after three years of work. Thereafter, periodic X-rays must be made available to coal miners at no less than five year intervals. The X-rays are offered at no cost to the miners and, according to regulation, at locations and times convenient to the miners. Acceptance of the later X-rays is voluntary.

The law provides for transfer of miners from areas of higher to lower dust exposure if they show signs of the development of pneumoconiosis on the basis of the X-rays or "other medical examinations." Alternatively, low dust levels can be achieved in the miner's current job through engineering controls. By regulation, exposure control for miners who participate in the program must be confirmed through frequent personal dust sampling.[4] Exercise of these transfer rights is at the discretion of the affected miner.

In practice, the right to transfer is offered only on the basis of X-rays read as positive for coal workers' pneumoconiosis utilizing the ILO method of X-ray interpretation.

TEST SELECTION

The MSHAct obligates the Secretary of Labor to develop mandatory health standards including, where appropriate, medical examinations to determine whether workplace exposures are adversely affecting a miner's health. The medical literature at the time the X-ray program was initiated concentrated on coal workers' pneumoconiosis as the characteristic and single important response of the lungs to inhalation of coal mine dust. Prevention of impairment from dust exposure was assumed to depend on elimination of Progressive Massive Fibrosis.[5] The transfer option is predicated on the assumption that PMF can be eliminated if the progression of simple CWP can be halted or slowed or through reduction of ongoing exposure in affected individuals.

The current literature is broader in its focus. Recent studies consistently demonstrate a range of pathological and physiological abnormalities in miners.[6] For example, pathologically confirmed emphysema is found more commonly in miners than non-miners even when the analysis controls for smoking status.[7,8,9] Symptoms of chronic bronchitis occur with increased frequency in both smoking and non-smoking miners as duration of coal mine dust exposure increases.[10] These symptoms may be associated with clinically significant impairment.[11,12] Miners with symp-

toms of chronic bronchitis tend to retire earlier with disability than those without these symptoms.[13]

Longitudinal studies in the US and UK demonstrate excess loss of FEV_1 in miners when compared to control populations.[14,15] This excess loss is related to dust exposure after the effects of cigarette smoking are considered. A subset of miners may develop severe pulmonary impairment in the absence of PMF.[11]

Further, both smoking and non-smoking miners have manifested abnormalities of gas exchange demonstrable on exercise testing.[16,17] Mortality studies of miners have consistently demonstrated that former coal miners die from chronic respiratory diseases at excess rates.[18]

People manifesting dust-related impairments do not necessarily have radiographically demonstrable CWP.[15,16] The chest X-ray appears to be neither sensitive nor specific for the identification of individuals with functional loss resulting from coal mine dust exposure. One cannot differentiate between miners with lung disease and those without through exclusive reliance on the chest X-ray.

PARTICIPATION

The periodic X-ray program has been plagued by low and diminishing participation by eligible miners. Administratively, program activities have been divided into four time periods or "rounds" thus far. If the compulsory films required of miners entering the work force are eliminated from consideration, approximately 32% of eligible miners participated in round three (1978–81), the latest round for which data is available. This is down from the 44% participation rate during round two (1973–8), and approximately 50% participation in the initial round (1970–3).[19]

The distribution of participants by mining experience is also significant. (see Table I) Approximately 35% of participants in round one had worked for twenty or more years in mining. In round two, only 12.4% of participants had worked this long. By round three, the percentage of participants with twenty or more years' experience was further reduced to 10.4%. In part this may reflect an evolution of the work force with older miners retiring and younger miners being hired. However, this hypothesis cannot be tested at this point; the necessary demographic data detailing the age and tenure distribution of the mining work force over time is lacking.[19]

A number of problems contribute to poor participation in the program. Some approved facilities are not, in fact, convenient for miners. Miners must take examinations during their off-work hours. Travel time can be as much as an hour from the mine site, and may be further from the miner's home. The facilities are selected by the employer and may be the same ones that provide pre-employment examinations as well as evaluative examinations used to contest workers' compensation claims. There is limited understanding of the nature and purpose of the program among coal miners, employers, and health care providers in the coal mining areas. Concerns about confidentiality and adverse impact on future employment are widespread.[20]

Miners who have worked longest on average have the greatest lifetime dust exposures. Low participation rates by the most experienced miners could distort understanding of disease patterns in the mining population and diminish the value of the screening function of the program.

TRANSFER ACCEPTANCE

The primary preventive intervention offered by the X-ray program is transfer with pay rate retention from a high to lower dust exposure job for individuals demonstrating CWP on chest X-ray. Miners are permitted to exercise this transfer option any time after notification of their eligibility status. Through the life of the program, 9138 miners have been eligible for transfer but only 2119 have exercised this option. The number of miners actually working who have exercised the option has declined from a total of 550 at the end of 1981 to 140 by the end of 1987.[21]

The consequences of delaying or failing to exercise transfer rights means that most miners who are identified through

Table I

Percentage Distribution of Participants in Rounds 1, 2, and 3, by Tenure Group. 1970–1981

Years in Mining	Round 1 (1970-73)	Round 2 (1973-78)	Round 3 (1978-81)
0-4	42.1	68.7	51.9
5-9	9.8	11.4	24.8
10-19	13.1	7.5	12.9
20-29	18.4	6.5	4.6
30+	16.6	5.9	5.8

(reproduced from reference 19)

the screening program as having CWP continue to be exposed to higher levels of coal mine dust than necessary.

IMPAIRMENT DEVELOPMENT

Despite the mandate of the MSHAct to eliminate occupationally-induced health impairments, miners continue to develop dust related disease. The extent to which this is happening is not currently measured. However, data from the surveillance program indicates that miners continue to demonstrate CWP on X-ray.[21]

Indirect evidence from the Black Lung Benefits program supports concern that some miners are developing severe pulmonary impairment in part or in whole from their workplace exposures. In fact, the number of retired miners who are awarded benefits for permanent and total pulmonary disability arising from coal mine employment is greater than the number of active miners being offered transfer rights. (see Table II) Even with a significant tightening of eligibility standards in 1981, over five hundred awards of disability benefits have been made each year to miners who applied after March 1, 1978.[22]

DISCUSSION

The surveillance and screening program for US coal miners was designed almost twenty years ago with a narrow focus on coal workers' pneumoconiosis. With minor modification, the program regulations have remained constant since its inception. The success of the surveillance component of the program is limited, in large measure, by poor participation and incomplete data. Nevertheless, the program has developed an invaluable data base through effective use of limited resources and the strong commitment of involved researchers. However, the surveillance activity has not yet been tied to the institution of primary exposure control measures.[23]

With almost twenty years' experience, it may be time to modify the program. Additional demographic data on both participants and non-participants should be collected. Also, efforts should be made to develop improved exposure information and to tie the surveillance program more directly to exposure control. The causes of non-participation in the program merit serious study. Attempts to overcome these should be continued.

The screening component of the program is more troublesome. It has operated in the shadow of the CWP surveillance activity maintaining the same narrow focus. The overall legislative mandate to identify miners with material health impairment from their workplace exposures and aid them in exposure elimination has remained largely unfulfilled. The current screening program relies exclusively on X-ray-diagnosable abnormalities and excludes consideration of dust induced functional derangement. Miners at greatest risk for the development of asymptomatic disease are least frequently screened. Only a limited number of miners avail themselves of the preventive intervention that is offered. At the same time, the number of miners qualifying for total disability benefits far exceeds the number participating in preventive options.

The screening component of the activity would improve to some extent with expanded participation in the current X-ray program. Nevertheless, until the medical screening focus is broadened to include efforts at early identification of other dust diseases in miners, the impact on overall health status will be quite limited. Part or all of the screening activity should be disaggregated from the surveillance program and new regulations developed. These would require consideration of the range of lung diseases caused by coal mine dust exposure, the methods available to detect them, and interventions that would prevent their progression. Each area presents difficult scientific issues which must be resolved. Nevertheless, it is not too soon to begin to fulfill the promise of the Mine Safety and Health Act of 1977 to "assure that no miner will suffer material impairment of health or functional capacity even if such miner has regular exposure to the hazards for the period of his working life."

Table II

Numbers of Miners Awarded Total Pulmonary Disability Benefits for Claims Filed After March 1, 1978, and Miners Offered Transfer Option. 1981–1985

Year	Awarded Benefits	Transfer Option Offered
1981	5148	245
1982	1145	119
1983	763	94
1984	556	271
1985	570	79

(source: references 21,22)

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EPIDEMIOLOGIC SURVEILLANCE BY A STATE HEALTH DEPARTMENT USING THE ILO CLASSIFICATION SYSTEM FOR PNEUMOCONIOSES

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Since October, 1985, the Wisconsin Division of Health has provided radiologic consultation using the ILO classification system for pneumoconioses. X-ray interpretations have been provided to physicians and to workers with a significant history of occupational exposure to silica or asbestos. The X-ray interpretations when evaluated in association with their respective occupational histories, provide a data source to complement other methods of epidemiologic surveillance. This project has reviewed 1124 X-rays in 2 and 1/2 years. Of these, 663 or 59% were normal; 233 or 21% showed abnormalities consistent with pneumoconiosis; the remainder showed other abnormalities judged not related to dust exposure.

Data sources available for occupational disease surveillance include death certificates, workers' compensation cases, hospital discharges and third party liability lawsuits. These data sources which focus on end stage disease apparently underestimate the incidence of pneumoconiosis when compared with the results of the voluntary radiologic consultation program using the ILO classification. For example, during the two and 1/2 years of this program, 36 of the approximately 100,000 death certificates filed with the State Health Department listed pneumoconiosis as a cause of death, whereas our program, which is not population based and which employs selective criteria for participation identified 233 individuals with X-ray abnormalities consistent with pneumoconiosis. Thus, the active provision of radiologic consulting services can effectively supplement existing passive data sources for epidemiologic surveillance.

A strength of this program has been the ability to use medical surveillance to identify and remedy exposure hazards before the exposure has resulted in end stage disease. Impediments to the program have included the lack of occupational histories in most patients' medical files, physicians' difficulties in recognizing occupational disease and the unexpected finding that 24% of the films reviewed were of marginal quality for ILO Pneumoconiosis Classification. The experience of this program indicates a need for quality assurance programs to maintain film quality if the ILO Classification system and the B reader programs are to be used to their full potential.

INTRODUCTION

Wisconsin enjoys a well deserved reputation as a America's Dairyland. As of 1986, Wisconsin was the leading producer in the United States of milk, butter and cheese. Wisconsin is also the leading producer of green peas, beets, cabbage and sweet corn for processing. Although 41% of Wisconsin's land area is devoted to agricultural production, Wisconsin's population is more industrial than agricultural, with only 6% of the population engaged in agriculture, compared to 28% employed in manufacturing. Wisconsin's strength as an industrial producer is less well known, but we lead the nation in the production of small horsepower gas engines, outboard motors, power cranes and other mining and construction equipment. The state also leads in the production of writing paper, sanitary tissue products and laminated and coated process paper.

Wisconsin has had a progressive record in terms of recognizing the occupational health issues resulting from industrialization. In 1911 Wisconsin passed the first Workers' Compensation law in the U.S. Wisconsin also was the first state to recognize asbestosis disability outside of a manufacturing context when in 1932, a maintenance worker was compensated for disease arising from handling and using insulation materials.[1]

Despite Wisconsin's history of concern and the passage of the Federal Occupational Safety and Health Act in 1970, there is evidence that problems persist. Industrial hygiene evaluations of Wisconsin foundries in the mid 1970's measured 1270 air concentrations of silica and found 41% to be above the federal OSHA standard.[2] Other national studies have confirmed that silica as well as asbestos problems are widespread throughout the U.S. A 1980 U.S. Department of Labor Report to Congress predicted that 6% of all workers in silica exposed industries would develop silicosis.[3] In Wisconsin, with 25,000 silica exposed workers, this would mean, at a minimum, 50 new cases a year for the next 30 years.

NIOSH has identified the pneumoconioses as one of their top ten priority diseases for improved surveillance and prevention activities and the U.S. Public Health Service has

set forth the goal, that "among workers newly exposed after 1985, there should be virtually no new cases of four preventable diseases, asbestosis, silicosis, byssinosis and Coal Workers Pneumoconiosis."[4]

Unfortunately it is difficult too for us to quantify progress toward these goals in the U.S., since with the exception of the coal miners' programs, there are no comprehensive national reporting systems in the U.S. for asbestosis, silicosis or other occupational diseases. Those systems which are used to estimate occupational disease incidence have severe limitations. A recent National Academy of Sciences report has concluded that occupational diseases are grossly under reported.[5] However, a number of states have established occupational disease surveillance systems. Since the 1930's, Wisconsin has had laws requiring occupational disease reporting, but compliance has been minimal.

PROGRAM DESCRIPTION

In 1985, with the support and cooperation of NIOSH, Wisconsin began to implement new surveillance efforts, including a review of existing databases. Currently in Wisconsin, for the surveillance of pneumoconiosis and other dust diseases, only three systems provide population based information, death certificates, the tumor registry and workers compensation files. These three systems all record cases of end stage disease. The hospital discharge and ambulatory care surveys provide a broad range of morbidity outcomes, but their usefulness is limited since these data sets are currently only small samples of the annual disease incidence. What all these systems have in common is that they require physician recognition and reporting of the occupational nature of disease. Physician resources in occupational health are limited. In Wisconsin there are only 8 board certified occupational physicians and 9 certified B readers. For the surveillance of occupational disease to be improved, occupational links must be noted at the point of entry into the medical system, when the patient first sees the physician. Also, if occupational disease recognition is to lead to intervention and preventive activity, then more cases of early stage diseases must be recognized. While end stage disease is easier to recognize, it has less utility for prevention. Early stage disease while harder to recognize, provides more opportunity for prevention. For these reasons, Wisconsin, in cooperation with NIOSH, decided to focus our surveillance activities in two directions, a continuous review of data from existing systems, combined with a new radiographic abnormality reporting and interpretation program designed to facilitate the detection of early stages of pneumoconiosis, thje "State pneumoconiosis Radiologic Consultative Program."

In reviewing the existing data, we found that there was no uniform radiographic description of pneumoconiosis used by Wisconsin radiologists with the exception of the B-readers using the ILO Classification system. Thus, in order to meet our surveillance objectives for prevention and to facilitate consistency and uniformity in reporting, we selected the ILO Classification System for a standard definition of radiographic abnormality. (Figure 1) For individuals with asbestos exposure, the case definition for abnormal consistent with pneumoconiosis requires a small opacity profusion of 1/0 or greater and/or pleural thickening or plaques. For individuals with silica exposure, the case definition involves a small opacity profusion of 1/0 or greater. Since few radiologists are familiar with or trained in the ILO system, it became necessary for the state to have a B reader interpret films of exposed workers so as to provide the required consistency of interpretation. From all participants we require that a chest X-ray and a brief occupational exposure history be submitted. In general, we limit participation to those whose first dust exposure occurred 15 or more years ago.

We have explored a variety of methods to promote the program's purposes and availability. These efforts have met with a variety of responses, ranging from indifference to enthusiasm. We have done mass mailings to 2000 physicians and to all AFL-CIO locals in the state and have found both efforts to be remarkably ineffective, generating less than ten requests for X-ray interpretation each. Face to face meetings with groups of exposed workers and physicians known to have an interest in occupational health have been more productive.

Another factor which may have influenced participation is the U.S. Department of Labor OSHA regulations concerning asbestos which were changed in June 1986 to require that physicians examining asbestos exposed workers have access to the standard X-rays prepared by the International Labor Office for the Classification of Pneumoconioses. It is difficult to assess the potential impact of these regulations on the utilization of our non-regulatory voluntary radiologic consultation program, but at a minimum, the 1986 OSHA regulations have increased the public awareness and the credibility of the ILO Classification System and the NIOSH B Reader certification program.

RESULTS

The X-rays received have been from diverse sources including employers, clinics, labor unions, individual workers, physicians and family members. From November, 1985 to July, 1988, multiple promotional activities have resulted in 1124 X-rays submitted. Of the 1124 X-rays submitted, 233 or 21% have shown abnormalities consistent with pneumoconiosis. (Figure 2)

It is interesting to compare the results of this targeted surveillance using the ILO system with the other, more traditional population-based epidemiological data sources available to us (Figure 3) Searching for both underlying and multiple contributing causes of death, silicosis was recorded as a cause of death on an average of 12 death certificates per year from 1981 to 1986. Asbestosis as a cause of death was recorded on an average of 4 death certificates per year during that time. Mesothelioma reports averaged 15 per year from 1981 to 1986 with increasing frequency. In 1987, 40 mesothelioma deaths occurred. In the workers compensation system slightly more silica disease and less asbestos disease has been recorded. From 1982 to 1986 an average of 17 silicosis and 6 asbestosis claims per year were closed. There were another 7 cases per year of other dust related diseases, such as mesothelioma. Our targeted X-ray surveillance system found an average of 86 new cases per year. In addition, our survey of other B readers in Wisconsin

found that they read approximately 600 Wisconsin films per year of which approximately 65 or 11% are abnormal consistent with pneumoconiosis. Although the case numbers from our active program are larger than in the existing data sources, our cases are not sufficiently representative to allow a population based description of the total impact of past dust exposure on the population.

In reviewing the industries which have participated in the program, (Figure 4) the paper industry, food processing machinery manufacturing, foundries and construction have contributed more than 60% of the X-rays. These same industries have contributed a similar proportion of the X-rays showing abnormalities consistent with pneumoconiosis. Evaluating the data concerning participation by occupational groups (Figure 5) a similar pattern emerges, with the number of abnormalities found in various occupations reflecting the degree of participation by the exposed group, rather than an indication of the relative risk of dust exposure by industry or occupation such as one could derive from an analysis of population based data.

Serves Two Purposes:

1. **Epidemiological:**

   Provide Information About Pneumoconiosis Incidence

   * **Offers Gradation of extent of abnormality**
   * **Offers Consistent, Uniform Descriptive Method**
   * **Can Be Easily Performed Outside Clinical Context**

2. **Service:**

   Supports Diagnostic Evaluation by Physicians

Figure 1. The ILO Pneumoconiosis Classification System as an epidemiological surveillance instrument.

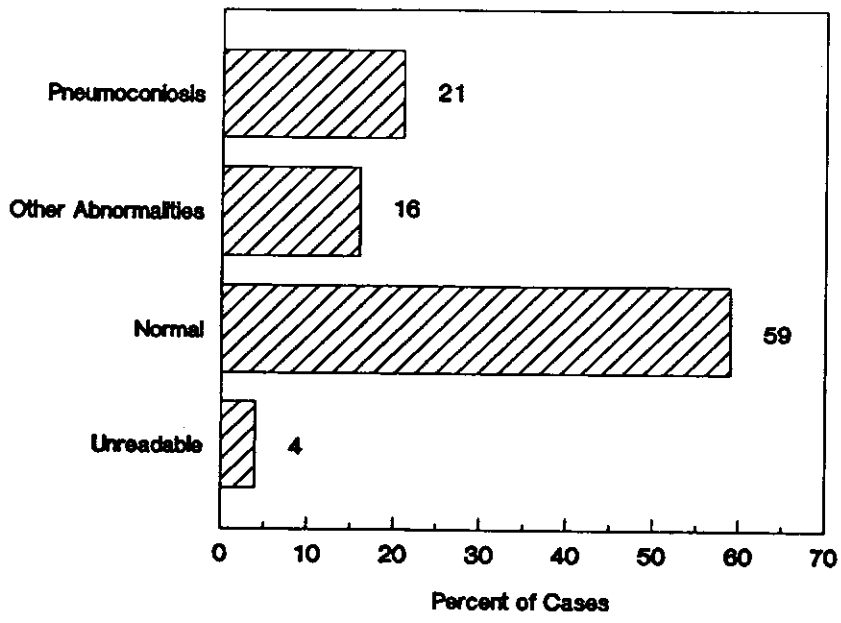

Figure 2. Summary of X-ray interpretations (1985–1988) using ILO Classification System—N: 1124.

Source	Time	Disease	Annual Incidence
* Death Certificates	1981-1986	Silicosis	12
		Asbestosis	4
		Mesothelioma	15
* Workers Compensation	1982-1986	Silicosis	17
		Asbestosis	6
* Third Party Suits	1980-1986	Asbestos Diseases	6
* Targeted Surveillance Using ILO System	11/85-7/88	Pneumoconiosis	86

Figure 3. Wisconsin occupational disease surveillance.

SIC	Industry Name	Number	(%)
2621	Paper Mills (with pulp mills)	315	(28.4)
3551	Food Products Machinery	171	(15.4)
3321	Gray iron foundries	157	(14.1)
1711	Plumbing, heating and air conditioning	85	(07.7)
3011	Tire manufacturing	51	(04.6)
3731	Ship building and repairing	51	(04.6)
3462	Iron and steel forgings	41	(03.7)
4911	Electric Services	34	(03.1)
4931	Electric and other services combined	30	(02.7)
1742	Plastering, drywall, acoustical and insulation	23	(02.1)
	All Other	153	(13.8)

Figure 4. State of Wisconsin, Department of Health and Social Services, Pneumoconiosis Surveillance Program. Industry participation in pneumoconiosis radiologic consultation program ranked by number X-rays submitted per standard industrial classification, November 1985 through July 1988 (N = 1111).

Census Code	Occupation	Number X-Rays	Percent of Total
777	Miscellaneous Machine Operators	102	(9.3)
783	Welders and Cutters	57	(5.2)
596	Sheetmetal duct installers	54	(4.9)
593	Insulators	50	(4.6)
709	Grinding, abrading, buffing and polishing machine operators	49	(4.5)
	All Other	784	(71.5)

Figure 5. State of Wisconsin, Department of Health and Social Services, Pneumoconiosis Program. Participation by occupations in pneumoconiosis radiologic consultation program ranked by number X-rays submitted per occupation, using 1980 U.S. census occupational classification system, November 1985 through July 1988 (N = 1096).

DISCUSSION

Our surveillance program has demonstrated some potential for disease prevention. We have conducted several follow-back field investigations prompted by groups of identified cases in single work places. In one facility, for example, the identification and confirmation of a single case led to an expanded screening program which found more radiographic abnormalities. This prompted a careful industrial hygiene survey and led to the eventual recognition and control of a previously unknown asbestos exposure in a paper making industry.

Two significant programmatic problems have persisted which must be addressed before the program can become more effective. We have had some difficulty obtaining thorough occupational histories. This problem will require increased effort to educate physicians, employers and employees on the value and importance of occupational histories in disease detection and prevention. These efforts will be strengthened by current Wisconsin regulations requiring such histories for hospital inpatients and cancer patients.

The other problem we have had concerns film quality. (Figure 6) This problem will be more difficult to correct. Of the films reviewed, 4% have been unreadable, while 19.7% have been category three or marginal quality for ILO classification. We have distributed the ILO guidelines for equipment and technology to those submitting large numbers of poor quality films, but we feel that more effort is needed in this area on national or international level.

There has been much attention to the errors or variability which may be introduced into the X-ray interpretation by the persons who read the films. For example, we have, in the U.S., a national program to train, test and certify physicians who interpret X-rays for pneumoconiosis. There have also been numerous studies which have evaluated inter-reader variability issues.[6,7] However, the effect of varying film quality on radiographic interpretation has not received sufficient attention. This is unfortunate, since inaccurate X-ray interpretations may result. Indeed, it is likely that poor quality films may introduce systematic bias into X-ray interpretations. Furthermore, if films must be repeated because of quality problems, unnecessary radiation exposure may result.

Originally intended as a program to provide coal miners with accurate readings of their X-rays through physician training and certification, the B reader program in the United States has expanded to included training and certification for physicians who read films of persons exposed to silica and asbestos. Maintenance of X-ray interpretation quality for coal miners' films is assured both by the certification of the physician readers and by the certification of the X-ray machines. A program to ensure the taking of high quality films for workers exposed to asbestos and silica dusts has not yet been implemented in the United States. We recommend that Congress, through NIOSH, establish a quality assurance program for facilities which provide X-rays for workers exposed to silica and asbestos, either on a voluntary or mandatory basis. The program which currently certifies and evaluates film quality for coal miners' X-rays could serve as a model.

RECOMMENDATIONS

We recommend: (1) the initiation of studies to determine the impact of film quality on X-ray interpretation using the ILO classification; (2) the development and distribution of instructions to radiology technicians as to how to achieve better film quality on X-rays taken for the evaluation of pneumoconioses; and (3) the development of quality assur-

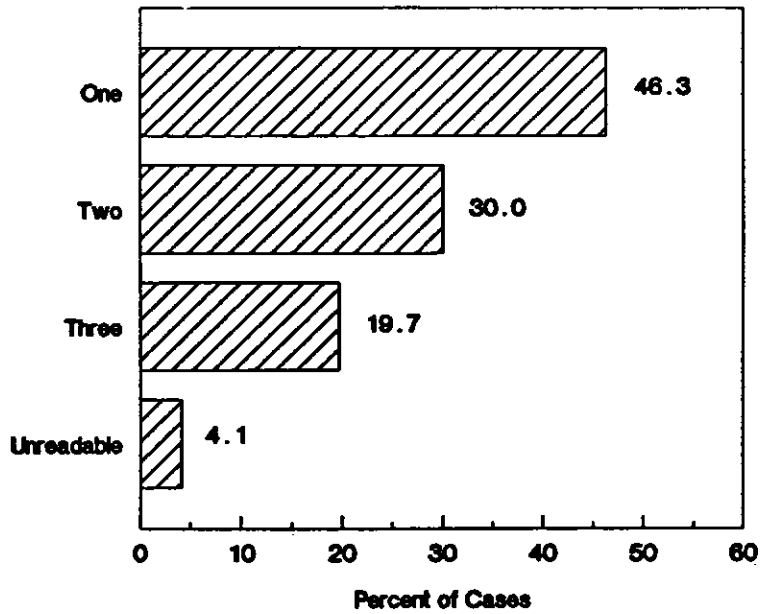

Figure 6. Film quality—total N: 1124 1985–1988.

ance programs for facilities providing X-ray services for the evaluation of workers exposed to silica and asbestos.

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UNIVERSITY PARTNERSHIP FOR WORKSITE MEDICAL PROGRAMS WITH INDUSTRY

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INTRODUCTION

Partnerships in the name of prevention between coal companies and university staff can be mutually beneficial, with worker well-being a positive outcome. Cyprus Minerals, a major American mining corporation based in the Denver, Colorado area, has joined with the Department of Preventive Medicine and Environmental Health of the University of Kentucky College of Medicine in Lexington to operate a preventive occupational medicine program at its coal mining operations in eastern Kentucky. Located in the heart of the Appalachian coal fields, Cyprus is one of the leading coal producing companies in the leading coal producing state. Operating both underground and surface mines, and having washing units, laboratories, and office staff, the approximately 1,000 employees in geographically dispersed facilities have access to, and are kept under medical surveillance by, a medical team from the University. This relationship is now four years old, having begun a year after the establishment of the Department of Preventive Medicine and Environmental Health at the College of Medicine, and continues as an ongoing program.

NEEDS AND SERVICES PROVIDED

There are a wide variety of services provided as part of the occupational medicine program. These begin with pre-employment examinations, which include standard medical evaluations with special attention being paid to pulmonary function results, chest X-ray, and a mandated drug screen. A program for yearly interim exams has been established for all "at-risk" individuals, defined as any person who spends significant or regular time at a mine site. These yearly interim exams are offered to all employees and are conducted on all three shifts at a location at the mine work sites. The focus of these examinations are on pulmonary function, hearing and vision testing, and a review of the general health status of the individual. Given the locations of the mine, washer, and office sites, there is a background of traditional Appalachian health problems.

These background problems include elevated rates of heart disease, diabetes, and other nutritional problems, as well as problems associated with either poverty or lack of education. Nutritional research specifically done on miners has demonstrated poor eating patterns and it does not appear as if working miners, with their adequate income, will pursue an improved diet with the money available to them.

In addition to the yearly interim exams, the company has established a program for periodic examinations of all employees, cycled by birthmonth, the periodicity depending on age, job category, and similar factors. These exams are offered on a voluntary basis and include a thorough medical review, physical examination, and appropriate laboratory tests.

In addition to these services, many of which serve a preventive function, there is care given for injury evaluations, non-occupational illness evaluations, and follow-ups for disabled mine employees, both those on short-term and long-term disability. University personnel assist employees with appropriate referrals for both work-related and non-work-related conditions, and the medical staff participates in special projects such as health education, some of which is done through miner re-training activities, and other medically-related activities, such as local blood drives.

PROBLEMS OF SPECIAL IMPORTANCE

Clearly, in any mining population attention to pneumoconioses is of special importance. As part of the establishment of this program a chest X-ray was obtained on all personnel, with a follow-up scheduled for the near future. The prevalence rate of pneumoconioses was small, and the patterns found on X-ray correlated well with specific occupational histories.

As might be expected, a small number of what appeared to be traditional coal workers' pneumoconiosis (CWP) cases were detected. These generally occurred in older miners, most of whom were still working underground. However, a few cases were noted in previous underground miners who were now working at surface operations. Other X-ray abnormalities were more compatible with silicosis, in workers such as drillers and driller helpers who had had a life-long career working in surface operations and who rarely were exposed to coal dust per se.

As might be expected in any general population, other X-ray abnormalities were detected, such as a high prevalence with what appeared to be old histoplasmosis, a common finding in Kentucky, and evidence of old tuberculous infections, as well as pulmonary abnormalities not directly related to mining activity. Each employee was sent a letter with the findings as noted, sharing with them the fact that their X-ray was either normal or abnormal, and a copy of the official report was sent with the suggestion to review matters with one's personal physician or to come to the medical department for further assistance. A significant number of employees who received letters noting a wide range of abnormalities availed themselves of visiting or calling the medical department. Ongoing attention is given to the matter of dust levels at the workplace. With modern mining techniques and ventillation, the dust levels in underground facilities are kept at low levels. At surface operations there is the use of dust-suppression techniques as well as a program for using respirators, as required.

Another special problem related to workers engaged in mining activity is the matter of noise exposure. Baseline audiograms on all employees and all new hires, show that some level of hearing deficit is a common finding in this population. Complicating matters, but amenable to study, is the fact that many employees have other significant non-occupational noise exposures such as hunting and/or trap shooting, motorcycle use, exposure to loud music, use of chainsaws, and other noisy activities. The majority of newly hired individuals also demonstrate hearing loss of some degree, but as part of the preventive health program for company employees a hearing conservation program has been developed, as well as hearing protection being made available to workers.

As noted above, there are special problems in this group of workers related to the background of disease in this area, factors not related to employment.

PROBLEMS IN ESTABLISHING A PROGRAM

Although there has been an excellent four-year cooperative effort between Cyprus Minerals and the Department of Preventive Medicine and Environmental Health, this program was established only after some education on both sides. From a corporate perspective, there was the need to educate both central and local administrators as to the role of an organized medicine program, especially one utilizing the services of a university based 125 to 150 miles from the actual operations. There was some initial resistance by the existing local medical community to the idea of university-based personnel developing and operating a medical program. Another logistical problem was to staff facilities, attempting to utilize as much as possible, local personnel. Because of the relative small size of the medical communities and the small number of well-trained personnel, this in particular has proven difficult.

SOLUTIONS TO PROBLEMS

Needless to say, most real or potential problems were successfully dealt with, which allowed this program to become established and continue to do well over the years. University personnel met with corporate and local managerial staff and there was a mutual exchange of views. The possibility for potential conflict in operating a program was minimized, since corporate policies, passed on from the corporate medical director in Denver, guide the program. The on-site medical staff always remembers that the best interests of the patient comes first and fortunately, corporate and patient interests most often coincide. It was clear that the university staff had much to learn about the day-to-day operation of coal company facilities, and there was a period of education of the members of the Department so that they could better understand the working realities of coal operations. Much of this was done by sharing information. Initially there were many field trips made to mine facilities, including visiting drag line operations, work in active mining pits, washing facilities, laboratory facilities, and underground mines. One continuing aspect of the program is a series of on-going, on-site visits by medical personnel on a regular basis to all operations. This not only continues to educate and reinforce the experience of the medical staff, but allows on-site interaction between the medical staff and miners at times other than those related directly to medical examinations.

The staffing for the occupational medicine program comes from the Department of Preventive Medicine and Environmental Health, based in Lexington. At the most distant facility at the southeastern corner of the state in Middlesboro, there is the main medical department office where all health records are maintained. A medical assistant on the staff is available daily to interact with patients, management, and others as necessary. Traveling from Lexington each week is an occupational physician assistant who spends one day at the medical office in the Hazard, Kentucky area and then travels on to Middlesboro the second day, performing the necessary hands-on medical evaluations required. A board-certified specialist in occupational medicine regularly goes to both sites and is responsible for all patient management questions and oversight of all patient records. Twenty-four hour communications is maintained to mine management for any routine or special problems that may arise.

Recognizing that there is a need for on-site medical evaluations that may occur on days when the Lexington staff are not present, arrangements have been made in both communities served by this program to have local physicians act as surrogates. These local practitioners serve at the request of the program director in Lexington and communicate with him regarding any substantive matters requiring decision making. By having such backup, no time is lost in processing new hires, evaluating injured workers, or in any other way in taking care of the company's needs.

Another aspect of the program which facilitates corporate/university interactions has been the establishment of a joint occupational health committee, which includes the corporate medical director, the director of the university program, safety personnel, and senior human resources management personnel. These individuals act frequently on an informal basis and come together formally to review the status of the program, discuss on-going or potential future difficulties, and to provide general oversight and direction for the program. It is through this mechanism that arrangements can be made to minimize disruption of production time when

yearly interim exams are scheduled, which as noted above are done on all three shifts at the mine sites. For such examinations no more than two hours, and often less, is required to have the individual report for their exam, complete the procedures, and return to their regularly assigned duties.

Another aspect of the program is active involvement and participation with members of the local medical communities. Although based at a University hospital in Lexington, the program director holds courtesy appointments at the two major community hospitals in Hazard and Middledboro, and meets from time to time with individual physicians, medical boards, and hospital administrators. Initial apprehensions that a program such as this would diminish the patient activities of the local practitioners was quickly dispelled as these yearly examinations uncovered many previously unknown conditions, including diabetes, hypertension, heart disease, and other similar problems, which were then referred back to the local practitioners in the community.

ADDITIONAL UNIVERSITY RELATIONSHIPS

In addition to the medical program described above, the interaction between the corporation and the University has been fruitful in other areas. The University has the BRASH (Behavioral Research Aspects of Safety and Health) working group, a research and service organization comprised of individuals from many disciplines. Principle members of this group include educational psychologists, professors in public administration, community health nursing, and behavioral science, as well as the occupational physician who oversees the Cyprus-sponsored medical program. In addition, other associate members of the group include epidemiologists, nutritionists in both home economics and medical anthropology, and many other professional staff from the University. The presence of this group and the excellent working relationship with the coal company have fostered research activities in several areas. The ergonomics group at the University have used miners from Cyprus facilities for simulated mine activities and to better understand oxygen demand and other factors related to mine work. Nutritional work, including detailed surveys by a medical anthropologist, have been carried out by mutual agreement with Cyprus. The offices of the coal company and the activities of the medical program are utilized as a training site for residents in occupational medicine, and these physicians are made welcome at the mine site to learn first-hand about the mining industry. Free access to information has even allowed students in the University's Master of Science in Public Health degree program to utilize corporate medical records for analytical purposes, such as relating hearing loss with particular pieces of equipment and non-occupational causes of hearing loss among the mine employees. As a spinoff from this research, other activities are facilitated and the BRASH group has been especially successful in securing research funds from the United States Bureau of Mines, the NIH, and other similar agencies.

CONCLUSION

The success of this program, focusing as it does on the particular health problems of miners but also providing a wide range of preventively-oriented services, demonstrates that a university medical staff in the field of preventive medicine with its traditional population-oriented approach can successfully cooperate with a centrally-located corporate medical department and local mine management to provide health care services to miners. These mutually agreed to activities make resources available that go beyond the scope of any single practitioner and eliminate many logistical problems for the coal company. This successful university/corporate partnership demonstrates how mutual interactions can be beneficial to both parties.

HEALTH EFFECTS OF TREMOLITE, ACTINOLITE, AND ANTHOPHYLLITE

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ABSTRACT

On June 20, 1986, the Occupational Safety and Health Administration promulgated revised asbestos standards for general industry and construction. The standards regulate occupational exposure to asbestos and to all types of tremolite, actinolite, and anthophyllite, including nonasbestiform varieties.

We have examined the scientific basis for regulating, in the same manner as asbestos, exposure to nonasbestiform varieties of tremolite, actinolite, and anthophyllite. From our review of several hundred articles, we found strong evidence that pneumoconiosis and malignancies in both experimental animals and humans are associated with asbestos forms of these minerals. We found no experimental or epidemiologic evidence to indicate such pathogenic effects from exposure to nonasbestiform varieties of tremolite, actinolite, and anthophyllite.

Although scientific studies of the health effects of exposure to nonasbestiform varieties of tremolite, actinolite, and anthophyllite are limited, nonasbestiform tremolite and actinolite did not cause pulmonary fibrosis or excess tumors in three animal studies. We lack relevant human data to examine the health effects of exposure to nonasbestiform types because the several occupational cohorts reported in the literature were all exposed to a mixture of asbestiform and nonasbestiform minerals.

We conclude that the literature supports the regulation of the asbestiform variety of tremolite, actinolite, and anthophyllite. However, it does not support the regulation of the nonasbestos forms of these minerals in the same manner as asbestos.

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EFFECTS OF TOXIC GAS INHALATION ON RESPIRATORY SYSTEM IN BHOPAL GAS VICTIMS

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INTRODUCTION

Toxic gas leak at about mid-night from Union Carbide pesticide plant affected majority of the citizens of Bhopal, on 3rd December, 1984. Since it was a comparatively cold and humid night the gas formed almost an aerosol and settled on the adjoining area in the shape of a mushroom; engulfing the population in the affected area and then gradually spreading to the neighboring area after reaching the ground level. It resulted in immediate death of approximately 2500 victims and a large number of those who survived developed irreparable damage to lungs and other systems which has crippled them for their life. The present report summarizes the effects of toxic gas inhalation on respiratory system including clinical, radiological and physiological abnormality, which was studied in depth, soon after the disaster.

MATERIAL AND METHODS

Selected cohort of severely affected individuals, as well as a control population is being followed for studying the long term effects of toxic gas inhalation. 978 patients were admitted in Medical College Hospital,[1] out of which 458 (46.8%) were males and 520 (53.2%) were females. Age and sex distribution of 544 victims admitted on first day is shown in Table I.

OBSERVATIONS

Of 978 victims analysed 733 hailed from areas within 1 km. of Union Carbide Factory, 127 were within 1–2 Km. and rest 117 were from areas situated more than 2 Kms. from factory. Thus all of them were exposed to gas in a sufficient concentration. All the hospitalized patients had respiratory complaints. They described that toxic gas had a curious odour, unfamiliar smell that they had never experienced. Soon after inhalation they developed an extreme degree of irritation in nose and throat, almost resulting in a sense of suffocation. They found it extremely difficult to breathe and some of them died in the same state almost instantaneously.

Main respiratory symptoms noted in a series of 544 patients were breathlessness, cough with scanty expectoration, presence of pink froth, irritation in throat and a choking sensation, pain in chest, haemoptysis and hoarseness of voice. Symptoms are illustrated in Table II.

Most of the victims had tachycardia, pulse rate above 100/mt. and almost all of them were afebrile (except 2%), which is remarkable, as with so much of pulmonary congestion to oedema in most of the cases, they did not develop frank infection, which possibly is due to lethal action of the toxic gas on the microbials. Almost all of them had tachypnoea. Ronchi and crepitations were present in 452 (83.08%) cases, pleural rub was recorded in 7 cases. When compared with radiological picture physical signs appeared to be much less.

Symptoms and physical signs decreased with passage of time but a few victims developed paroxysmal dyspnea of considerable severity. Dyspnea was of considerable severity soon after the episode but with passage of time both the severity and frequency of episode of dyspnea decreased.

At the end of three months and six months follow up respiratory symptoms mainly cough and pain in chest had decreased, clinical score had gone down; but breathlessness persisted in all patients almost with the same severity.

Radiological Abnormalities

There were X-Ray abnormalities in almost all cases. Most of them had diffuse non-homogenous opacities, mostly in mid and lower zones; in some of the severely exposed cases almost whole of the lung fields were opacified with ground-glass like appearance. The opacities in lungs started decreasing at the end of first week and there was considerable radiological clearing by the end of second week.

X-Rays of 500 patients who were symptomatic were taken sequentially to study the changes with the passage of time.

Various types of radiological lesions observed were:

1. Interstitial lesions.
2. Combined interstitial and alveolar lesions.
3. Destructive lesions.
4. Parenchymal opacities:linear, punctate, nodular—micro and macro-nodular, and reticular, alone or in combination.
5. Evidence of pre-existing lung disease was detected in few X-Rays, along with fresh changes due to toxic gas inhalation.

Interstitial lesions:

In 207 victims out of 500 interstitial pulmonary lesion was detected leading to pulmonary oedema of various grades, most of them having involvement of both mid and lower zones and in some whole of the lung was opacified. It appears that inhalation of toxic gas caused exudation of large amount of fluid in the interstitium not capable of being drained by lymphatic channels. This resulted in an increas-

Table I
Showing Age and Sex Distribution of Victims Studied

Age Group	Male	Female
Under 15 years	45	42
Between 15–30 years	100	154
Between 31–45 years	66	60
Between 46–60 years	43	16
Above 60 years	10	8

Table II
Showing Symptoms of the Victims in Early Phase

SYMPTOMS (n=544)	No.of patients	Percentage
Breathlessness	538	98.89
Cough	516	94.84
Presence of pink froth	283	52.00
Irritation in throat/choking	250	45.95
Pain in chest	136	25.00
Expectoration	87	15.99
Haemoptysis	66	12.60
Hoarseness of voice	11	2.00

ing streaky shadows developing and miliary shadows developing in the interstitium of the lung.

Alveolar lesions:

Alveolar pulmonary oedema was seen in 203 out of 500 victims whose serial X-Rays were analysed. 184 cases had bilateral involvement. In 94 cases all the six zones were effected, in 90 there was involvement of lower zones only. 19 victims had unilateral involvement only. Confluent fluffy shadows indicated alveolar lesions. Alveolar lesions could have resulted from higher dose of toxic gas than was inhaled by those patients who has only interstitial lesions, where exudation took place only in interstitial spaces. With increased amount of exudate it poured into alveolar spaces, resulting in alveolar oedema as well.

Destructive lesions:

In 40 victims lesions such as surgical emphysema, pneumomediastinum and pneumothorax were seen, in addition to alveolar lesions. These abnormalities indicate that a higher

dose of the toxic gas led to break down of lung tissue resulting in leaking of air into soft tissues and mediastinum. A few cases had pleural effusion obliterating costophrenic sinus, which tended to disappear with passage of time, resulting from inflammation of underlying pulmonary tissue.

Pre-existing lesions:

Evidence of pulmonary tuberculosis and emphysema was found in 36 cases. Evidence of chronic obstructive airway disease was found in many X-Rays, mostly in smokers. All of them had evidence of lesions resulting from inhalation of toxic gas, described above, besides evidence of pre-existing disease. In many cases hyperinflation was observed due to air-trapping resulting from involvement of airways limiting airflow following inhalation of toxic gas.

In another study of radiological changes in 113 victims,[2] X-rays were taken soon after disaster and after three months. 2 victims showed normal picture. Emphysema was seen in 15%, pleural scars in 21%, consolidation in 4%. In lung parenchyma interstitial deposits were seen in almost all cases, 82% had linear and 37% punctate deposits. These deposits tended to clear with the passage of time. 36% had infiltrates in 2 zones, 40% in 3–4 zones and 24% in more than 4 zones. Evaluation of X-Rays taken three months later 38% showed some improvement, while some deterioration was seen in 16%.

Some victims developed episodes of paroxysmal dyspnea following toxic gas inhalation. Radiological studies of these subjects showed evidence of air-trapping indicated by hyperinflation in upper zones with evidence of infiltrates in lower zones mostly on right side, perhaps because right bronchus is direct continuation of trachea. A few of these subjects showed evidence of hypersensitivity pneumonitis and evidence of patchy consolidation in others.

Pulmonary Functions

Pulmonary functions were estimated in the victims to observe the abnormality that the toxic gas inhalation produced, immediately after the episode and are being followed in a longitudinal fashion to find out the long term changes in the victims with a control group.

224 gas exposed victims were studied,[3] soon after the episode. For the purpose of analysis of results they were divided into four groups on the basis of FVC and FEV_1 values, as shown in Table III.

All the victims showed involvement of peripheral (small) airways thus it appears that main brunt of the toxic gas inhalation was borne by the small airways. Almost half of the gas victims showed normal pulmonary functions as far as FVC and FEV_1 values are concerned, rest were almost equally distributed amongst those having obstructive (24), restrictive (38) and combined (36) abnormality.

Blood Gases

Arterial blood gases and pH were studied in the gas victims after the acute episode. PCO-2 values were slightly on the hypocapnoeic side, indicating that these victims were hyperventilating. There was slight hypoxaemia in a few subjects but most of them had a value above 70 m.m., only 7 out of 46 had values of PO-2 below 70 m.m. and only 2 out of these 7 had values below 60 m.m. All of them had normal pH.

COHb was studied in 70 cases, it was raised in 94.3%; in 11.4% it was higher than 6%.[4] Repeat study after 3 months showed that COHb values had returned to within normal limits in almost all cases. MetHb. was estimated in 111 subjects, and in 83% it was raised but declined to almost within normal range after 3 months.

Table III

Showing Distribution of Victims as per Pulmonary Function Abnormality (n=224)

Group	Pulmonary function abnormality	No.of cases
I.Normal	Normal FVC and FEV-1	126
II.Combined	Reduced FVC and FEV-1	36
III.Obstructive	FVC normal FEV-1 reduced	24
IV.Restrictive	FVC reduced FEV-1 normal	38

Oxygen uptake studies revealed that oxygen uptake had improved after 3 months, which was low initially but the improvement was not significant. Values of VO_2 being 1122.6 ± 280.4 initially and 1157.0 ± 402.6 after 3 months.

In an attempt to correlate pulmonary functions with clinical status of the gas victims, it was found that initial FVC and FEV_1 before bronchodilator and FEV_1 after bronchodilator were inversely proportional to symptoms score ($r=0.76$ for FVC and -0.79 and -0.85 in FEV_1 before and after bronchodilator therapy). There was no correlation of pulmonary functions with oxygen uptake at rest; and of pulmonary function and radiological abnormalities.

Flow Volume Loop Studies

There were four types of flow volume loops:

1. Doming: inability to sustain peak flow indicating fixed central obstruction.
2. Hesitation: poor starting flow with fluctuations due to incoordination of inspiration.
3. Saw tooth: incoordination of inspiratory movement indicating variable intra or extra-thoracic central obstruction.
4. Concavity: indicating small airway obstruction.

No correlation was found between these patterns and the initial severity of symptoms. Changes did not seem to improve significantly at the end of 3 months period. Bronchodilator therapy produced an improvement only upto 15% in small percentage of cases but most of them did not respond to bronchodilators, suggesting irreversible airway obstruction.

Bronchoalveolar Lavage:

Bronchoalveolar lavage was carried out in 12 subjects soon after the episode. 4 out 8 victims who were studied in first 4 weeks showed swelling of tracheo-bronchial mucosa and distortion of lumen. There was patchy congestion in 3, ulceration in 2, and suspected lymphoid hyperplastic follicles in 3 cases. B.A.L. showed a rise in total cell count indicating continuing inflammatory status even after 4 weeks of the acute episode. Mean cell count of 344 m./c.mm. (normal upto 150 m./c.mm.). In nine samples neutrophils were raised (more than 3%; total mean 14 ± 25%, range 1 to 93), in two macrophages were raised (above 94%), while in five they were lower than normal. In one case there were eosinophilia (14%). In another case there was 11% lymphocytosis.

Lung Histo-Pathology

Lung biopsies were performed in 3 patients by open biopsy technique and adequate tissue could be obtained.

Histology showed pleural fibrosis with focal mesothelial proliferation thickened inter-alveolar septa, mono-nuclear infiltration in bronchial and peri-bronchial tissues, with patchy evidence of peri-bronchial and peri-vascular fibrosis, with destruction of bronchial wall and epithelium. No desquamation was seen. Muscular arteries and arterioles showed intimal hyaline thickening in one case suggestive of hypersensitivity. In another patient who had a severe exposure to gas besides changes described, the bronchioles were full of inflammatory exudate obliterating the lumen completely with round cell infiltration around, a typical picture of Bronchiolitis Obliterans; which seems to be a feature of toxic gas inhalation.

DISCUSSION

Methyl iso-cyanate is highly irritant to respiratory mucosa and can produce irreversible damage, as has been proved by experimental studies, data which was not available at the time of the episode, which was a main handicap in dealing with the patients; as well as lack of its toxicological data and availability of antidote, presented enormous problem in the management of the patients. Toxicity to human beings was reported in a study from U.K. due to accidental release of TDI in 35 fireman, toxicity of phenyl isocyanate, hexyl isocyanate and hexyl di-isocyanate has also been reported, but there was no documented study on MIC at the time of acute episode. Toxicity and pulmonary irritation described in these studies is very close to observed effects in gas victims in lungs. Exposure to TDI has led to development of hypersensitivity 'isocyanate asthma'. A few patients in our series had paroxysmal dyspnea following gas exposure perhaps due to sensitisation with single large exposure to the gas (R.A.D.S.).

All victims who had a severe exposure to the gas developed pulmonary infiltrates and many of them developed pulmonary oedema, which cleared with the passage of time, leaving evidence of either radiological or functional pulmonary abnormality. All the subjects were symptomatic. Patients who were managed with high dose steroids (Methyl prednisolone 1 gm I.V. repeated after 12–24 hrs., if necessary) showed much better response than those who did not receive it.

Although after the acute episode there was slight improvement in the condition of the victims but most of them continued to be symptomatic, many showed radiological shadows, and had abnormal pulmonary functions, indicating continuing inflammatory process, supported by histopathological finding. A long term follow up of a cohort is being conducted to study the ill-effects of toxic gas inhalation.

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A STUDY OF SPANISH SEPIOLITE WORKERS

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ABSTRACT

Sepiolite is a naturally occurring fibrous clay which has a wide variety of commercial applications. It can occur as long thin lathe-like crystals which have similar dimensions to asbestos fibres. This has prompted concern that both materials may have similar biological properties. Sepiolite has been processed at a site close to Madrid for the past 30 years. We report here a cross-sectional study of this workforce and mortality data for the total work population.

All 218 current workers provided personal, occupational and smoking histories and all had a full-size chest X-ray. Data from previous environmental sampling was available to help derive measures of total exposure. Our study shows significant relationships between age and small opacities on the chest X-ray (as expected) but no relationship between years worked and chest X-ray appearance. There is a relationship between types of occupation and small opacities on the chest X-ray but this was less than the relationship with age.

There appears to be no excess mortality in this population from lung cancer or other disease and no cases of mesothelioma have been reported. This supports the contention that exposure to sepiolite dust does not present a hazard.

No Paper provided.

CHEST RADIOGRAPHIC FINDINGS AMONG TIRE MANUFACTURING WORKERS —INITIAL RESULTS FROM A CROSS-SECTIONAL SURVEY

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ABSTRACT

Tire and rubber manufacturing has been associated with a wide spectrum of occupational hazards. Cancer risk has been suggested by some investigators.

Because of potential for exposure to inorganic dusts in these industrial processes, a cross-sectional chest roentgenologic survey was conducted of 475 individuals with long-term employment in tire manufacturing.

A high prevalence of chest radiographic abnormalities consistent with effects of inorganic dust was found. One hundred thirty one (28%) had parenchymal changes graded as $\geq 1/0$ according to the ILO Classification of Radiographs of Pneumoconioses, 1980. They appeared primarily as small, irregular opacities. Bilateral pleural thickening was present in 142 (30%) of the examined workers, and 72 additional workers had unilateral pleural abnormalities. Sixty four percent of those with abnormal parenchymal findings also had signs of pleural thickening. These findings are consistent with effects of significant exposure to airborne asbestos. Potential sources of such exposure in this trade will be discussed.

No Paper provided.

DOSE-RESPONSE RELATIONSHIPS FOR CAUSE-SPECIFIC MORTALITY AND CANCER MORBIDITY AMONG ASBESTOS-CEMENT WORKERS

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ABSTRACT

Cause-specific mortality (1952–1986) and cancer morbidity (1958–1985) were studied among male, Swedish asbestos-cement workers (N=1,929) employed for at least 3 months 1907–77. Individual dose-estimates were calculated from dust-measurements performed 1956–1977, data on technical changes, and work histories (N=1,503). The median estimated intensity of exposure was 1.2 fibers/ml and the median cumulated dose 2.3 fiber-years/ml. The mineral-fiber content in lung tissue was analyzed in 76 dead workers, and tissue review was performed for respiratory and gastrointestinal cancers.

Chrysotile was the major fiber type in lung tissue, which is in accordance with the asbestos used in the factory (>95% chrysotile). A remarkably increased risk was found for death from pleural mesothelioma (13 cases out of 560 deaths in workers with a latency time of at least 20 years). Three of the mesotheliomas were epithelial, seven mixed, and three fibrous. Material for immunohistochemistry was available for 12 of these, which all showed a staining pattern consistent with mesothelioma. The mesothelioma cases had a much higher crocidolite content in tissue, than the non-cases. There was also an increased risk for cancer in the colon and rectum (SMR=1.6; 95% confidence level; CI=1.1–2.4; histopathological review revealed no peritoneal mesothelioma). The dose-response relationships (duration of employment and cumulated dose) were steeper than usually reported. Totally mortality (SMR=1.2, CI=1.1–1.3), mortality from non-malignant respiratory disease (SMR=1.7, CI=1.3–2.3), and lung cancer mortality (1969–1986; SMR=1.7, CI=1.2–2.4; after histopathological review) were also increased, but with no dose-response relationships.

INTRODUCTION

We have earlier presented the cause-specific mortality and cancer morbidity in a cohort of asbestos-cement workers and a referent cohort.[1] This study includes a further six years of follow-up of the same cohorts, and a more detailed analysis of dose-response relationships. Additionally, the mineral-fiber content in lung tissue among asbestos-cement workers, with and without mesothelioma, has been analyzed.

EXPOSURE

The plant operated 1907–1977, producing asbestos-cement products from mainly chrysotile asbestos (>95%). Before 1966, some crocidolite was also used, and amosite was used for a few years during the 1950's. All asbestos was disintegrated before mixing with the cement. The cement had a low content of crystalline silica.

Dust measurements were performed from 1956, but before 1969 only Impinger or gravimetric counts exist. The individual cumulated dose was estimated in fiber-years/ml (f-y/ml) from data on dust measurements, changes in the production, and dust control.

MATERIAL

Lists were made including all male, Swedish workers who had been employed at least three months (N=1,929). Work histories were available for 1,503 (78%) of these. The median estimated intensity of exposure was 1.2 (range 0–10)f/ml, and the median cumulated dose 2.3 (0–420) f-y/ml. Only 57 persons were assigned a dose of 50 f-y/ml or more.

A referent cohort (N=726) was set up, including industrial workers from the same region, fulfilling the same requirements as the asbestos-cement workers, but without known exposure to asbestos.

METHODS

Follow-Up

Vital status was determined for the two cohorts up to December 31, 1986. Loss in follow-up was 1.5% in the exposed cohort and 0.3% in the referent cohort. Death certificates were obtained and recoded according to the International Classification of Disease (8th revision). Both cohorts were matched with the national (1958–1983) and regional (1958–1985) cancer registries.

The respiratory and gastro-intestinal cancers in the exposed cohort were reviewed. The pleural tumours were also classified as to type of mesothelioma, according to the 1982 WHO Classification, using light microscopy and stained for immunohistochemical analysis.

The mineral-fiber content in lung tissue in 76 of the asbestos-cement workers (7 with and 69 without mesothelioma) was determined by transmission electron microscopy.

Statistics

The mortality (1952–1986) and cancer morbidity (1958–1985) in the two cohorts were compared with the general population in the county, using annual rates (1958–1985), grouped in five-year age intervals. SMRs (standardized mortality/morbidity ratios) and 95% confidence intervals (CI), were calculated. Due to coding problems for the period before 1969, reliable rates for lung cancer mortality are available only since then.

Since the distribution of dose, even within each exposure category was skew, the median was used as a co-variate in the calculation of the dose-response relationships. These were analyzed by testing for trends in SMR.[2] The rate in the referent cohort was included in the analysis as a crude correction for the bias introduced by deriving the expected values from the general population. To evaluate the potential bias introduced by unequal age-distribution in different strata of exposure, an age-standardized SMR (SSMR) was calculated.[3] A minimum induction/latency time of 20 years since onset of employment was employed in all analyses. All tests are two-tailed.

RESULTS

Comparison with the General Population

When compared with the general population in the county, the *exposed cohort displayed* an increased overall (Observed (O)=560, SMR=1.17, CI=1.08–1.27), as well as cause-specific mortality from respiratory cancer (O=46, SMR=1.98, CI=1.46–2.66), non-malignant respiratory disease (O=54, SMR=1.73, CI=1.31–2.27), gastro-intestinal cancer (O=47, SMR=1.46, CI=1.08–1.95), and cancer of the colon and rectum (O=26, SMR=1.64, CI=1.09–2.44). The SMR for stomach cancer was slightly above one (SMR=1.35, CI=0.82–2.16).

The overall *cancer morbidity* was also increased (O=231, SMR=1.29, CI=1.13–1.47), as well as the malignant tumours in the gastrointestinal tract (O=58, SMR=1.39, CI=1.06–1.81), due to an equally raised rate in the upper and lower part. The risk estimate for the total respiratory cancer morbidity was slightly lower than for the corresponding mortality (O=39, SMR=1,55, CI=1.11–2.14), especially when only lung cancer was considered (O=30, SMR=1.39, CI=0.95–2.01)

The referent cohort showed no significant deviation from the general population but tended to have a raised rate of deaths from stomach cancer (O=9, SMR=1.90, CI=0.87–3.61). As to cancer morbidity, only the risk for stomach cancer (O=10, SMR=2.11, CI=1.01–3.88) was statistically significantly increased.

Tissue Review

For nine of the respiratory cancers, the diagnosis of mesothelioma, or pleural tumour, was given on the death certificate. An additional four cases were diagnosed when the histopathology of the respiratory tumours was reviewed. Three were epithelial, seven mixed and three fibrous. Material for immunohistochemical staining was available for all but one of the cases. These were all CEA negative.

When the result of the review of the respiratory cancers was accounted for in the mortality analysis, the rate of lung cancer was still increased (SMR=1.7, CI=1.2–2.4; 1969–1986).

Thirty-two of the totally 44 cancers in the stomach, colon and rectum (73%) were available for histopathological review. The diagnosis was not changed for any of these cancers; no peritoneal mesothelioma was found.

Pulmonary Mineral-Fiber Content

Among the 69 asbestos-cement workers without mesothelioma, chrysotile was the major asbestos type (median count 41 of totally 50×10^6 total asbestos fibers per mg dry weight), and the crocidolite content was low (median 1.8×10^6). For the mesothelioma cases, however, chrysotile was still the major asbestos type (62×10^6), but the total amount of asbestos fiber was higher (189×10^6), and especially so the crocidolite content (54×10^6). The tremolite count also differed between the two groups, but to a much lesser degree.

Dose-Response Relationships

A significant relationship was found between mortality from respiratory cancer and duration of employment (p=0.0016), as well as cumulated dose (Table I). More than half of the respiratory cancer deaths were due to mesothelioma (using the information from the histopathological review) in the two highest exposure strata, corresponding to 5–6% of all deaths. The remaining lung cancers displayed no dose-response relationship. The same applied for the cancer morbidity from these causes.

Mortality from gastro-intestinal cancer displayed no significant relationship with duration of employment, but an association was found with cumulated exposure. This was due to a dose-response relationship for cancer in the colon and rectum, while stomach cancer displayed no such pattern (Table I). The cancer morbidity for the corresponding diagnoses showed no statistically significant dose-response relationships, but a tendency towards such a relationship was found between cumulated dose and cancer in the colon and rectum (p=0.11).

No dose-response relationships were found for non-malignant respiratory disease, nor overall mortality, neither with duration of employment nor cumulated dose.

DISCUSSION

The estimated cumulative exposure in the cohort was low; only about 3% were assigned a dose of 50 f-y/ml or more. This offers a possibility to assess risks directly at rather low doses, but provides low power for detection of moderately increased risks at intermediate to high exposure.

Table I

SMR for Cause-Specific Mortality, Stratified by Cumulative Exposure, Among Asbestos-Cement Workers and Referents

		Asbestos-cement workers Cumulative exposure (fiber-years/ml)					
Cancer site	Referents	<1	1-4.99	5-14.99	15-39.99	>40	P-value [1]
Respiratory							
Observed	5	7	9	4	12	5 [2]	
SMR	0.67	1.64	1.92	1.32	3.30	2.61	0.028
CI [3]	0.22-1.6	0.66-3.3	0.88-3.6	0.36-3.4	1.7-5.7	0.85-6.1	
SSMR [4]	0.64	1.51	2.01	1.40	3.78	2.61	
(Mesothelioma [5]							
Observed	0	1 (1)	0 (0)	0 (1)	5 (6)	2 (4)	-)
Gastro-intestinal							
Observed	14	8	5	7	9	8	
SMR	1.22	1.30	0.76	1.72	1.76	2.47	0.042
CI	0.67-2.1	0.56-2.6	0.25-1.8	0.69-3.5	0.8-3.3	1.1-4.9	
SSMR	1.25	1.30	0.99	1.67	1.57	2.47	
Colon, rectum							
Observed [6]	4	6 (4)	2 (1)	4 (3)	3 (2)	6 (5)	
SMR	0.70	2.00	0.63	2.00	1.20	3.88	0.009
CI	0.19-1.8	0.74-4.4	0.08-2.3	0.54-5.1	0.25-3.5	1.4-8.5	
SSMR	0.73	1.96	0.90	2.35	1.11	3.88	
(Dose; median)	(0)	(0.5)	(2.0)	(8.3)	(24.7)	(67.0)	
(Person-years)	(7,677)	(4,287)	(4,264)	(2,687)	(2,719)	(1,501)	

1. Test for trend across exposure strata, including referents; two-tailed tests.
2. One mesothelioma mis-classified as ICD 215 not included here,but among the mesotheliomas.
3. 95% confidence intervals.
4. SMR standardized to age distribution in the highest exposure category.
5. Diagnosis stated on death certificate (diagnosis according to tissue review within brackets).
6. Cases verified by review of histopathology within brackets.

An increased mortality and morbidity from respiratory cancer was found, with a dose-response relationship with duration of employment, as well as with cumulated dose. Several deaths were attributed to pleural mesothelioma on the death certificates, a finding which was confirmed and amplified by tissue review. The life-time risks in the highest exposure categories (>20 years of employment or >15f-y/ml) are very high, and compatible only with the experience from cohorts of insulators,[4] factory workers,[5] and one of the cohorts of asbestos-cement workers,[6] but considerably higher than reported from other asbestos-cement plants.[7-9] The analysis of the mineral-fiber content in lung tissue among workers without mesothelioma confirms, that the cohort has mainly been exposed to chrysotile asbestos, since this was the major asbestos type observed in the tissue, in spite of the much higher persistence of amphibole fibers. The comparatively much higher amphibole (especially crocidolite) content among the workers with mesothelioma, is in agreement with former observations that these fibers are especially liable to produce mesothelioma. No dose-response relationships were found for lung cancer, but our data are not incompatible with previous estimates of such relationships, since the present median exposure was low.

An important finding was the increase of cancers in colon and rectum. This has formerly been observed among workers in chrysotile mines,[10] but the dose-response relationship in our study is much steeper. This is not likely to be due to misclassified peritoneal mesotheliomas, since most of the cancers could be verified by tissue review, and all but one in the highest exposure category. We found no evidence for a dose-response relationship for stomach cancer at these levels of exposure.

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EPIDEMIOLOGICAL INVESTIGATIONS OF THE FIBRE CEMENT INDUSTRY IN THE FEDERAL REPUBLIC OF GERMANY (1981–1986)

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INTRODUCTION

The present study is based on an analysis of death causes in 9 plants of the Association of the Fibre Cement Industries in the Federal Republic of Germany. These represent the entire West-German fibre cement industry. It is a continuation of the epidemiological investigations conducted in 1976–1980.[1,2,3] In order to extend the conclusions drawn from the results of the first study phase (1976–1980) it was followed by a second phase (1981–1986) for comparison and crosschecking;[4] in this case the registered death cases were already considered following a minimal exposure period of 5 years as compared to 10 years in the first study. Of the workers exposed for at least 5 years, 325 cases of the death were registered by the plants of the Association of the Fibre Cement Industries between January 1, 1981, and December 31, 1986. A total of 290 cases were recorded. The remaining 35 cases could not be included in the investigation due to the lacking consent of the next of kin until the beginning of the evaluation. Thus a response rate of 89% was obtained. Furthermore, not all criteria of interest could be ascertained leading to different sample sizes for the individual criteria. As there was only one female worker among the deceased, as 4 cases were already reported in 1980 and as the duration of exposure was less than 5 years in 5 cases, only 280 cases could be included in the evaluation.

METHODS

In the present communication it was attempted to analyse the proportional mortality rates (SPMR) with regard to the ICD classification of the observed death causes in order to derive indications concerning the health hazards due to asbestos exposure of the employees in the asbestos industry. In addition this allows a comparison with the results of the study executed in 1976–1980. The SPMR was determined according to the method of Rao and Marsh.[8] The mortality of the total male population (German Federal Office of Statistics) was adjusted according to the age of the test population. For the calculation of the probability that the various diagnoses or diagnostic groups occurred at the observed rate or at more extreme frequencies, it was assumed that the observed instances followed a Poisson distribution.

RESULTS

Of the registered 280 death cases 160 died in hospital and 118 at home, of 2 cases the location was unknown. The dates were taken from the following documents or records: 280 death certificates, 156 medical records (56%), 73 pathological reports (26%) and 81 histological reports (34%); an occupational disease was recorded in only 10 cases (3.6%). The average age at entry into employment of the employees of the first phase was 50 years and of the second phase $x = 42.5$ years (median = 44 years).

The average age at death is $x = 69.5$ with a median of 72 years; the exposure time $x = 18.7$, median = 17 years, and the survival time (time from start of exposure to death) $x = 27.2$, median = 27 years. The employment and survival times of the registered deceased correspond approximately to earlier data on the actual exposure time and also confirm the results of the first phase of our study. With regard to the distribution of the death causes according to the ICD classification the diseases of the cardiovascular system (ICD 460–519) are in the foreground, followed by malignant neoplasms of all organs (ICD 140–239) and the diseases of the respiratory organs (ICD 460–519). Firm distinctions between the diseases of the circulatory and respiratory systems cannot be drawn. This corresponds to expectation and does not differ essentially from the most frequent diseases of the total male population of the FRG and thus confirms the results of the first study period as well.[1,2,3]

Malignant neoplasms of the respiratory system (ICD 160165) were registered in 29 deceased, among them pleural mesotheliomas (ICD 163) in 7 and malignancies of the digestive tract and peritoneum (ICD 150159) in 9 cases. In 21 of the deceased workers asbestosis was diagnosed. This agrees with previous experience concerning the incidence of this disease in the asbestos cement industry during the time without sufficient dust protection measures.

For the evaluation of the incidence of the observed death causes the SPMR was calculated. A clear excess incidence (SPMR 1.7, $p < 0.01$) compared to the general population was noted with regard to respiratory diseases excluding cancer (ICD 460–519). The incidence of bronchitis, bronchial asthma and lung emphysema (ICD 490–493) is even higher (SPMR 2.1, $p < 0.001$). This is typical of industries with high dust concentrations (Table I). Malignancies of the respiratory organs (ICD 160–165) are more frequent in the exposed group than in the general male population (SPMR 1.36, $p = 0.09$). Less frequent are the total malignant neoplasms (ICD 140–239) in asbestos workers; this lesser incidence leads to a SPMR of 0.77 and $p = 0.05$. Similarly there is a clearly less frequent incidence of cancer of the

Table I

Analysis of the Proportional Mortality (n=262) 1981-1986

ICD-Classification	Observed*	Expected	SPMR	(chi)²	p
390-459 Diseases of the cardiovascular system	103	125.2	0.82	3.9	0.048
140-239 Total malignant neoplasms	55	71.5	0.77	3.8	0.050
160-165 Malignant neoplasms of the respiratory organs	29	21.3	1.36	2.8	0.095
160-162, 164-165 Malignant neoplasms of the respiratory organs without mesotheliomas	22				
163 Pleural mesotheliomas	7				
150-159 Malignant neoplasms of the digestive tract and peritoneum	9	23.1	0.39	8.6	0.004
150-157, 159 Malignant neoplasms of the digestive tract	9				
158 Peritoneal mesotheliomas	-				
460-519 Diseases of the respiratory organs without malignant neoplasms	33	18.7	1.7	10.9	<0.001
490-493 Bronchitis, emphysema, asthma bronchiale	25	11.9	2.1	14.4	<0.001
501 Asbestosis	5				
800-999 Accidents	4				
303, 570-577 Alcoholism, hepatic cirrhosis	12	46.6	1.52	12.7	<0.001
Other death causes	55				

The calculation of the expected values is based on the distribution of age at death in 1981 - 1986. * 18 cases are excluded due to lacking data concerning age at death or year of death; p is stated in a two-tailed manner.

digestive organs and the peritoneum (ICD 150–159; SPMR 0.39, p = 0.48). The same behaviour can be observed in diseases of the circulatory system (ICD 390–459) with a SPMR of 0.82, p = 0.48.

DISCUSSION

The average age at death (72 years) of the deceased employees in our study does not essentially differ from the average age at death of the general population of the FRG. The mean age at entry into employment of the group of the first study period was 50 years, 50% of these had an age of 40–55 years. It was 42.5 years in the employees of the second phase of the study with a 50% interquantile of 36–50 years.[4] Why the mean age at entry of the employees in the asbestos cement industry is relatively high, especially in the first phase, could not be elucidated. There was a critical discussion that this elevated age at entry impairs the significance of the results of the first phase in the sense that the tumour expectancy would be significantly greater with an earlier age at entry. However, the age correlated expected value has been used for the calculation of the SPMR. In addition, this argument can be countered with results of other authors. In the study by Neuberger et al.[7] the age at the beginning of employment was higher in asbestos-associated cancer death cases than in the not asbestos-associated death cases. In their evaluation of the results of 11 international epidemiological studies of lung cancer mortality in employees of the asbestos cement industry, Gardner and Powell[5] stated latency periods from first exposure to tumour manifestation of at least 5 and maximally 20 years. This is in accordance with the concept of the present study where a minimal exposure time of 5 years has been used as criteria of inclusion and in which an exposure time of 20 years could be observed.

The present investigations of the first as well as the second study phase confirm essentially the results of Lacquet et al.[6] and of Weill et al.[11] Thomas et al.[10] examined a cohort of comparable size of deceased employees of the British asbestos cement industry and obtained results largely in accordance with those of the present study, particularly with regard to the expected and observed cases of all malignant neoplasms and of cancer of the respiratory organs and the digestive system. The studies by Ohlson and Hogstedt[8] and Gardner and Powell[5] are also in agreement.

Neuberger et al.[7] conducted a recent investigation of ca. 2800 employees of the Austrian asbestos cement industry using the general population as controls just as in the present study. Based on official death certificates death from lung cancer was diagnosed in 535 cases exceeding the mortality of the age and sex adjusted general population by 1.7. This excess mortality was explained by the authors as due to the higher tobacco consumption of the employees as compared to the general population. In the same study 5 cases of mesothelioma were demonstrated and attributed to the earlier use of crocidolite in the production of asbestos cement pipes. The findings of the present study also point to a possible correlation between mixed dust exposure with crocidolite and chrysotile and the incidence of 7 pleural mesotheliomas

($p = 0.08$). In the review by Gardner and Powell[5] cited above this is also stressed with regard to the SPMR of lung cancer which lies in the range of 5.2–0.8 in plants with previous mixed dust exposure (chrysotile and crocidolite) and 1.5–0.9 in those with pure chrysotile exposure, while the SPMR of the present investigation is 1.4. Of the three mesotheliomas listed in the review two are attributed to mixed exposure with chrysotile and crocidolite and one to exposure with chrysotile and amosite.

According to these results and those of the authors cited above a distinction should be made between crocidolite and chrysotile asbestos with respect to their carcinogenic effects. Thus inhalable crocidolite fibres possess a stronger oncogenic potential than the corresponding chrysotile fibres. The higher durability of crocidolite in the reacting tissue may explain its pathogenetic importance for the development of pleural or peritoneal mesothelioma. Under present-day working conditions and with the considerably restricted use of crocidolite only for exceptional technical products (pipes) a reduction of the increased mesothelioma hazard appears possible. With the sole exposure to chrysotile the relative risk of mesothelioma is expected to be low (see also Neuberger et al.)[7]

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LUNG CANCER AND NNRD MORTALITY SIMILARITIES OF VERMONT AND NEW YORK STATE TALC WORKERS

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ABSTRACT

The 741 employees of a New York talc plant observed from 1947 to 1978 had statistically significant excesses of lung cancer mortality among short-term workers and of non-infectious, non-malignant respiratory disease (NNRD) among workers with at least one year of employment. Occupational exposures to elongated particulates were greater in the mill than in the mine. However, the excess lung cancer risk was limited to the miners. Some analysts have asserted that there was asbestos in the talc at this New York plant, in contrast to the talc at the Vermont talc plants. However, the only difference in pulmonary mortality observed between the New York and the Vermont talc workers was a greater risk of NNRD among the Vermont talc millers than among the New York state talc millers. Miners but not millers showed a statistically significantly increased risk of lung cancer in both the Vermont and the New York plants. Millers but not miners showed a statistically significantly increased risk of NNRD only in the Vermont plants but not in the New York plant. Thus, epidemiologic assessment of the mortality of the NY talc workers does not support the hypothesis that they have been exposed to asbestos.

No Paper provided.

EPIDEMIOLOGIC STUDIES OF MINING POPULATIONS EXPOSED TO NONASBESTIFORM AMPHIBOLES

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INTRODUCTION

Current standards for the control of asbestos exposures have resulted from proven and serious health effects caused by commercial asbestos, principally chrysotile, amosite and crocidolite. There is more limited information from asbestiform tremolite, actinolite, and anthophyllite. The latter amphibole minerals are also commonly found in nonasbestiform habits. It has become a matter of considerable scientific, social, and economic importance to define precisely which elongated and asbestos-like particles are hazardous to health. Of particular interest is to determine whether or not there is any need to regulate exposures to acicular particles, such as cleavage fragments of nonasbestiform tremolite, actinolite, and anthophyllite as well as the nonasbestiform varieties of other amphiboles. Particles of these minerals found in the environment may meet the currently accepted 3:1 length-to-width (aspect) ratio used to define fibers, but not be asbestiform. The mining populations to be discussed in this report supply information on the health effects of such exposures.

Although not addressed in detail, important related questions pertinent to the biologic effects of elongated particles are: (1) What should be the minimal particle length subject to control, i.e. should fibers shorter than 5 micrometers be included? (2) Since there is considerable doubt as to whether particles with aspect-ratios below 1:10 or 20:1 are hazardous, is it proper to use an aspect-ratio of 3:1? These important questions are discussed in detail in mineralogic references cited in the bibliography.[5,6,17,24,33,38,39,41,42,43,44,45,46]

MINING POPULATIONS THAT WERE STUDIED

Four areas were identified where there have been health studies of mining populations known to have been exposed to nonasbestiform amphiboles. In each there had been concern about the potential for asbestos-like effects. These were (1) taconite mines in the eastern Mesabi Range in Minnesota; (2) the Homestake gold mine in western South Dakota; (3) the Sydvaranger iron mine in northern Norway; (4) iron mines in southwestern Labrador.

MINNESOTA TACONITE OPERATIONS

Minnesota taconite mines came under active study after the discovery in 1972 of asbestos-like particles in the water supply of Duluth.[23,27] These were attributed to the discharge into Lake Superior of tailings from the Reserve mining operation located at the eastern end of the Mesabi Range. The mining of taconite as a major source of iron had begun in this area in the early 1950's with pilot operations starting about 1947. The consensus of mineralogic and environmental studies[2,3,15,32,35,36,39,40,45] is that (a) ore bodies in the eastern portion of the range contain amphiboles, principally cummingtonite, grunerite, actinolite and hornblende; (b) there are many cleavage fragments that meet the regulatory definition of fibers by having 3:1 aspect-ratios; and (c) asbestiform particles are rare, although a small amount of asbestiform ferroactinolite was found in one area.[9,10] Dust exposures in some locations were sufficient to cause concern as to possible silicosis. Langer in 1981[22] summarized the major issue in the Minnesota taconite mines as being "the biological activity of acicular (needle-like) cleavage fragments of grunerite..."

Clinical studies of Reserve miners and millers by Clark et al.[8] and Higgins et al.[18] showed no evidence of asbestos-like effects, but there was radiographic evidence of possible early silicosis. An analysis of mortality in 5,751 Reserve workers who had been employed for one or more years in the period 1952–1976 showed 15 lung cancer deaths with 17.5 expected for an SMR of 84.[19] During the observation period 15 or more years after hire, the SMR was 102, based on 8 deaths from lung cancer.

Cooper et al.[11] analyzed mortality in 3,444 taconite miners and millers employed by the Erie Mining Company or by U.S. Steel for 3 months or more between 1947 and 1958. There were 801 deaths, with 41 due to respiratory tract cancer, 61% of the number expected using U.S. death rates or 85% of expected using Minnesota rates. There were small but not statistically significant excesses in deaths from kidney and lymphatic cancers. There was one death from pleural mesothelioma, which was not attributable to mine exposures, since it occurred only 11 years after hire and there had been probable pre-employment asbestos exposures.

One can conclude that there is no evidence of asbestos-related disease associated with employment in the Reserve, Erie and U.S. Steel iron mines in Minnesota, where there have been opportunities for exposure to nonasbestiform amphiboles in the taconite ore deposits.

HOMESTAKE GOLD MINE

In 1974 it was recognized that the ore body of the Homestake

gold mine in western South Dakota contained cummingtonite-grunerite similar to that which was of concern in Minnesota. Since Homestake mining operations had begun in 1876 and past dust exposures had been relatively high, it was realized that epidemiologic studies could yield valuable information.

There have been a number of mineralogic and environmental studies.[1,4,12,29,30,39] There is general agreement that cummingtonite-grunerite, tremolite-actinolite and hornblende are present, that acicular fragments are common, and that there are few if any asbestiform particles. Current exposures to acicular fragments corresponding to 3 f/ml were reported, with estimates of time-weighted average exposures to such particles ranging from 0.25 to 1.72 per ml.[47]

There have been three published epidemiologic studies of Homestake miners. The first, by Gillam et al. in 1976[14] reported 10 deaths from respiratory tract cancer with 2.7 expected as well as 8 deaths from non-malignant respiratory disease with 3.2 expected. The authors attributed the latter to asbestos. This study was seriously flawed, and later analyses of mortality in larger cohorts have not confirmed the authors' conclusions. McDonald et al.[28] in 1,321 Homestake workers employed for 21 years or more found no excess lung cancer deaths (17 with 16.5 expected) but there were 37 deaths from pneumoconiosis and 39 deaths from tuberculosis (SMR = 1,038, or over 10 times the number expected). A single mesothelioma death was observed, in a surface worker who during a relevant time period (22 to 26 years before death) had worked in machine maintenance with probable exposures to asbestos. In a more recent study sponsored by NIOSH, Brown et al.[4]) similarly found no excess lung cancer deaths in a population of 3,328 underground Homestake miners (43 with 42.9 expected). There were 53 deaths from nonmalignant respiratory disease observed with 19 expected, due to a large number of deaths from silicosis and silicotuberculosis.

In describing the exposures of workers in their study, Brown et al.[4] stated that cummingtonite-grunerite, silica, arsenopyrite, and radon were possible hazards. Their results were consistent with the conclusion that silica was of major importance. With respect to amphibole exposures, they stated that the mean time-weighted-average exposures of all miners to C-G particles longer than 5 micrometers was 0.44 such particles per cubic centimeter, based on a 1977 survey. Early exposures had probably been greater.

One can conclude that despite dust exposures sufficient to cause severe and often fatal silicosis, with concurrent exposures to nonasbestiform amphiboles, there was no evidence of excess deaths attributable to asbestos, i.e., lung cancer, mesothelioma, or asbestosis.

SYDVARANGER IRON MINE

Iron mining began near Kirkenes in the northernmost county of Norway in 1907. The ore body resembles that in Minnesota, containing cummingtonite-grunerite, actinolite, and hornblende. These amphiboles occur in elongated fragments, many of which are over 5 μm in length with aspect-ratios as high as 11:1.[16] Amphibole bodies have been found in the lungs of deceased miners by Gylseth et al.[16] There are no reports to indicate that any of the elongated particles are asbestiform, nor is there any evidence to date to indicate asbestos-related disease. Gylseth et al.[16] stated that an analysis of deaths during the period 1949 through 1963 showed no excess lung cancers. Saugstad in 1980[34] studied deaths from lung cancer in Finnmark County where the mine is located. While the county had a higher lung cancer incidence than Norway as a whole, this did not appear to be related to working in or living near the iron mine. Data from the Norwegian Cancer Registry have not shown any excess mesothelioma deaths in the area.

LABRADOR IRON MINES

During the early 1970's it was discovered that iron ore deposits in the Wabush Range in southwestern Labrador contained amphibole minerals, including cummingtonite-grunerite. The two iron mines in the area, one operated by the Iron Ore Company of Canada (IOCC) and the other by the Erie Mining Company, had begun operations in 1962 and 1965 respectively. They had been alerted to dust hazards because radiographic changes consistent with pneumoconiosis had been found during surveillance programs required because of potential quartz exposures. Because of concern that there might be asbestos-related disease, a major study was started in 1979. Financed by industry, it was coordinated and supervised by the provincial government and a distinguished scientific committee selected by industry, government, and labor. The actual investigation, the Labrador West Study, was carried out by the Labrador Institute of Northern Studies, based in the University of Newfoundland.

The results of the Labrador West Study were made available in 1982.[21] They confirmed the presence of cummingtonite-grunerite and other amphiboles, but the concentrations of fibrous particles (i.e. those with aspect-ratios 3:1 or more) were relatively low and 98.5% were shorter than 5 micrometers. Very few were considered to be asbestiform. Lee and Fisher[25] and Lee et al.[26] reported more detailed mineralogic findings in the Labrador mine which were in essential agreement.

Medical studies[7,13,21] have confirmed the presence of a mixed-dust pneumoconiosis, presumably due to combined exposures to iron oxides and silica. Although the original detailed report[21] contained a section which suggested that there was evidence of pleural thickening in some of the chest films, this was not mentioned in the published report of the the radiographic findings.[7] Review of films reported as positive for pneumoconiosis by Cooper and Sargent (personal observation) showed no changes suggestive of asbestos effects.

The Labrador populations have not been the subject of a cohort mortality analysis. They are reaching a time period, 23 to 26 years after the start of operations, where meaningful results might be obtained.

SUMMARY AND CONCLUSIONS

In four mining areas where exposures to elongated but nonasbestiform amphibole particles have been confirmed, there has been no evidence of asbestos-like effects. The negative evidence is strongest in the Homestake gold mine,

because of the proven high dust exposures in the past as shown by the high silicosis incidence, and the opportunity for observation after long latency. The evidence is convincing in the Minnesota taconite miners. Although the exposures were lower, the populations are large and there has been ample time for latent disease to appear. The information from the Sydvaranger iron mine and the Labrador mines is also reassuring, but it would be of value to have historical-prospective cohort studies of mortality to augment the existing negative evidence.

Cumulatively, these studies do not indicate that there is any reason to control nonasbestiform amphiboles in a manner comparable to that required for commercial asbestos.

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