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

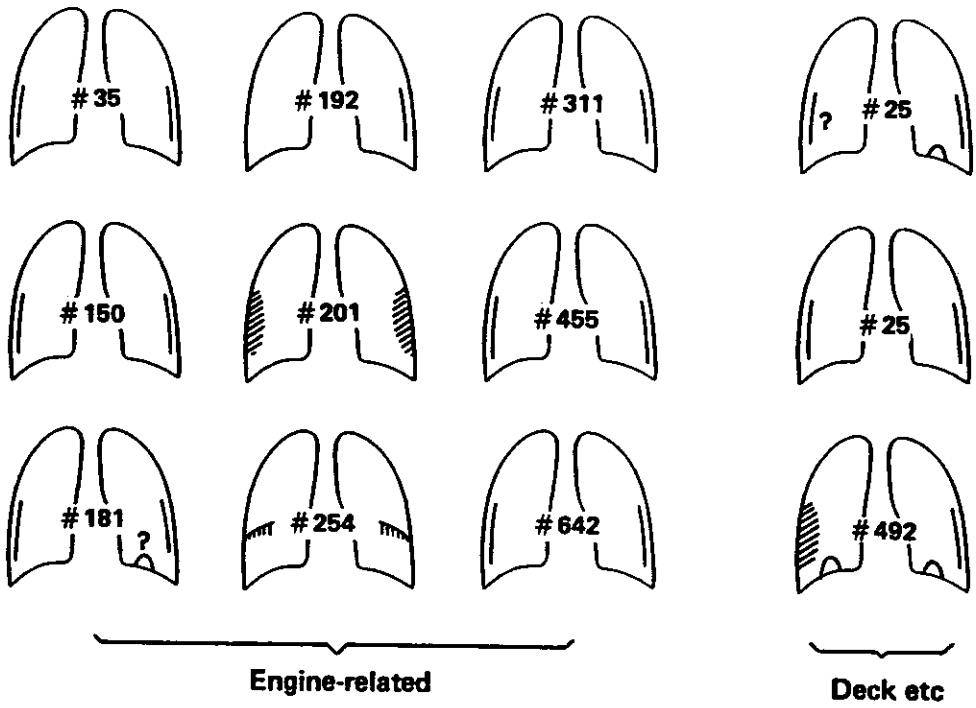

Figure 1. Plaque cases according to jobs.

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

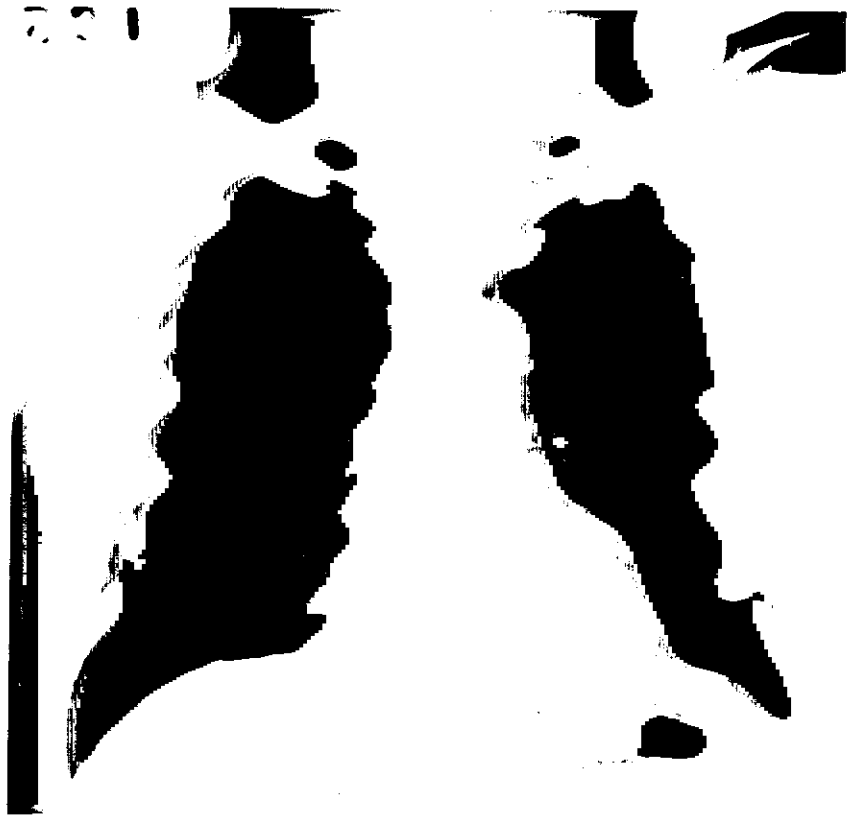

Figure 2. A 55-year-old male who had entered the company as a fireman in 1948 and worked for 36 years.

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)

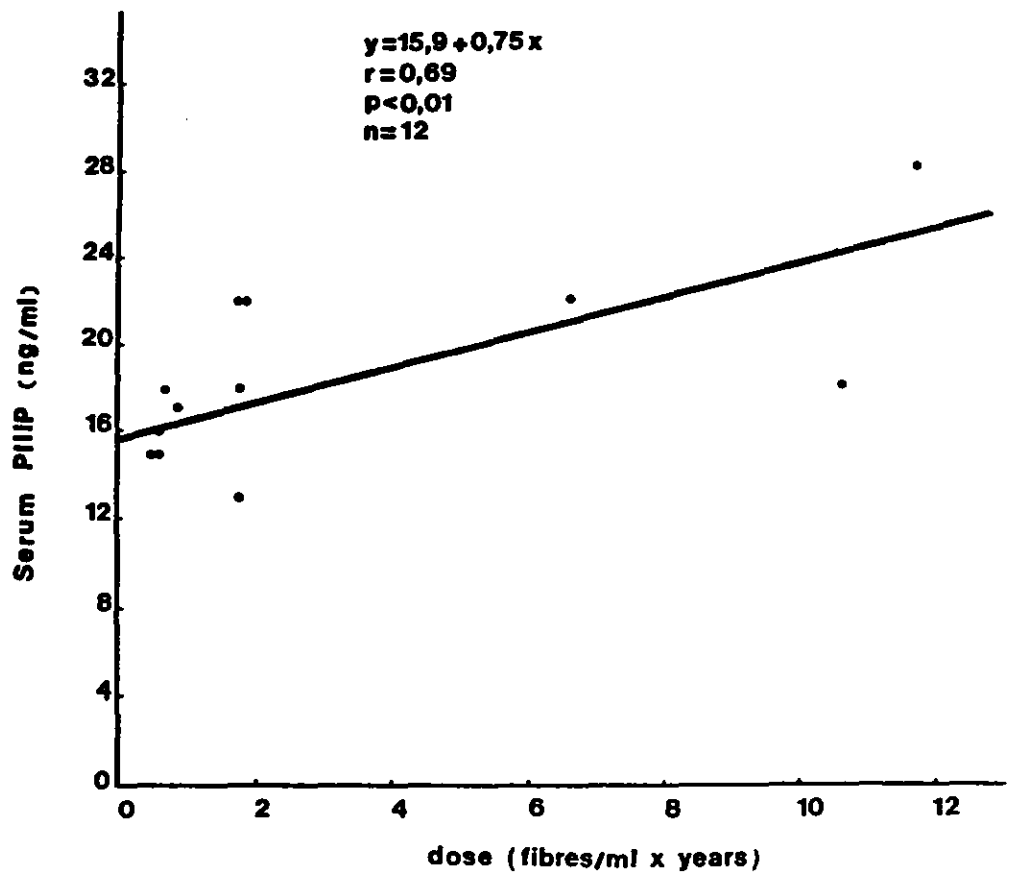

Figure 1. Relationship between asbestos dose (fibres/ml × years of exposition) and serum PIIIP values in the exposed workers.

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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