PULMONARY REACTIONS TO MISCELLANEOUS MINERAL DUSTS, MAN-MADE MINERAL FIBERS, AND MISCELLANEOUS PNEUMOCONIOSES

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INTRODUCTION

The miscellaneous pneumoconioses represent a group of occupational lung disorders caused by the inhalation of a variety of different dusts. The entity does not include the dusts of silica, asbestos, silicates, coal and carbon products, various clays, beryllium, or organic dusts. Most miscellaneous pneumoconioses are due to inorganic materials, mainly metals of one sort or another. In reviewing the miscellaneous pneumoconioses, the definition provided by Parkes has been adapted: "The presence of inhaled dust in the lungs and their nonneoplastic tissue reaction to it."

A large number of different occupations, industrial processes, and materials must be considered. As a group, the miscellaneous pneumoconioses can potentially affect an estimated working population of ten million. While the total number of exposed workers at risk may be large, the actual number of individuals employed in any single industry or exposed to any specific agent may not be large when compared to inorganic dusts such as asbestos, coal, or silica. Only aluminum and iron, with perhaps several million potentially exposed workers, approach the population exposure magnitude of these other dusts.

A problem in identifying affected individuals may be related to the fact that only a small number of workers are usually employed in any single operation/industry and thus exposed to one of the dusts. Consequently, medical and environmental information is not as readily available as it is in larger industries where occupational health programs are better developed, regulated, and supervised. Another consideration is that many of the miscellaneous pneumoconioses cause only chest radiographic alterations but are not associated with medical disability or symptomatology. Because of this, there is less interest or impetus to monitor these workers. On the other hand, the agents to be described in this chapter have extremely important, often critical, uses and demands in this country, as well as throughout the world. The demand for these agents will be generally increased over the next 10 years, consequently increasing the number of workers exposed to them. It is important to be familiar with the miscellaneous pneumoconioses and to make practicing physicians more aware of their presence, of their manifestations, and of the occupations where these lung diseases are likely to occur.

ALUMINUM

Introduction

The primary sources of aluminum are the ores of cryolite and bauxite; the metal is never found in its elemental state (Al). Aluminum's effect on the lungs differs depending upon the composition of the inhaled aluminum-containing dust. Cases of pulmonary fibrosis sometimes called "Aluminum Lung" (25), as well as asthma have been reported in workers involved in various manufacturing processes.

List of Causative Agents (Manufacturing Processes)

The estimated annual capacity of primary aluminum production is 14 million tons (27). There are three major steps in aluminum production beginning with mining of the ore (bauxite) and leading to production of metal ingots. Bauxite mining consists of strip mining or underground mining depending upon the type of vein to be quarried. Bauxite contains alumina which is mixed with 40% to 50% iron and other oxides. Extraction of alumina (aluminum oxide, Al_2O_3) from the ore involves preferentially

dissolving it out by autoclave treatment with soda (Bayer Process). Filtration of the caustic mixture leaves a residue known as red mud and a solution of pure alumina in soda. Alumina is then precipitated from the soda by means of a seeding process. The solution is allowed to settle, then filtered and calcined from drygin to yield the alumina—a white, floury powder (27). The final step is carried out either in smelters or reduction plants. The basic reduction process involves an electrolytic decomposition: alumina is first transformed into a liquid form in order to allow a direct electric current to pass through it. Because alumina has such a high melting point (close to 2,000 °C), operations at such temperatures are impractical, if not impossible. To get around this problem, a fluorinated compound of sodium and aluminum (cryolite) is used. It melts at approximately 1,000 °C and in a molten state is capable of dissolving up to about 8% of alumina (27). Thus, alumina is obtained in a liquid form by dissolving it in molten cryolite at a temperature below 1,000 °C where it is technically more practical and feasible to carry out electrolysis. The molten aluminum produced by electrolysis has a slightly higher specific gravity than molten cryolite and therefore will settle into the bottom of the cell from whence it can periodically be extracted by some kind of vacuum trapping technique. The electrolytic process is done in an electrolytic cell (called the pot) which consists of steel-coated shells lined with insulating materials and contains an electricity-conductive bottom made of carbon connected to a negative polarity power source. Carbon anodes connected to positive polarity hang above and dip into the cryolite-alumina melt. When electric current flows from the anode to the cathode bottom, alumina is split into metallic aluminum spreading over the bottom and evolving oxygen. The capacity of a common pot is approximately 150,000 amps and yields more than one metric ton of aluminum each day (27).

There are various pot-fume emissions that have been identified (27). Molten cryolite releases gaseous hydrofluoric acid and fluoride dust. Fluoride emissions are low during quiet operations but increase during crust breaking, taping, and anode-changing (27). In addition to the generation of cryolite dust, there is also production of alumina and carbon dusts, the proportions depending upon the raw materials used. During the burning of the anodes, sulfur dioxide is emitted, having originated from the sulfur present in the petroleum coke used for anode making. Anode burning involves oxygen during electrolysis and results in the evolution of carbon monoxide and carbon dioxide gases.

Depending on the type of pot used, there are also emissions of various pitch volatiles and polynuclear aromatic compounds. Identifying specific etiologic agents causing lung disease among reduction workers is difficult because they may be exposed not only to alumina but also to a number of other air contaminants including: asbestos, which is sometimes used as insulation in the pots or as marinite in casting operations; carbon, used to make cathodes and anodes; fluorides, emitted both as a particulate and gas which are constituents of cryolite and of the electrolytic bath; and particulate polycyclic organic matter, originating from the binder used in the electrodes (40). Secondary chemical contaminants that are present include: carbon monoxide, a by-product of incomplete combustion which can be present at low levels in potrooms having inadequate ventilation; copper fumes and dust which occur from some anode rods and fluxes as well as from welding and sanding; cyanide, which may be emitted in spent cathode material but is usually not a problem unless acidified; mercury, contained in electrical rectifiers which may be present during maintenance work; perchlorethylene, used as a solvent degreaser on electrical parts and motors; silica, sometimes used in sandblasting and also found in discarded refractory bricks; and sulfur dioxide, a by-product of sulfur-bearing coke. Various welding fumes may also be present in the working environment: chlorine gas may originate from fluxing and casting operations; hydrogen chloride can be formed during casting from chlorine and water; manganese fumes can occur during processing metal alloys; ozone can be produced as a by-product in electrical discharge and welding; and phosgene can result from combustion products of halides (39).

There are two major types of aluminum products produced—flakes and granules. Particle size as small as 0.6 μ have been noted in the flaked type, which are prepared in a stamp or ball-mill from cold metal or foil (25); the granular type is made from molten metal (25). Stearin, a mixture of fatty acids created by hydrolysis of fats or paraffin, is usually added to allow separation of particles (24). Many of

the early cases of pulmonary fibrosis attributed to aluminum exposure were reported in Germany during World War II when stearin was not added to the flakes (25). Furthermore, there are reports of pulmonary fibrosis among English and Swedish stamping mill workers, where stearin was either reduced or replaced by mineral oil (25).

Small-sized, flaked particles (pyro) are used in the manufacture of explosives and incendiary devices and fireworks. Some occupations in which exposures may occur to the flaked variety include: aluminum alloy grinders, reduction plant workers, ammunition makers, fireworks makers, foundry workers, petroleum refinery workers, plastic workers, and rubber makers.

Hazardous exposures may occur during smelting and refining processes. Aluminum may be alloyed with copper, zinc, silicone, magnesium, manganese, or nickel (34). Special additives may include chromium, lead, bismuth, titanium, zirconium, and vanadium (34). Aluminum and its alloys can be extruded or processed in rolling mills, fireworks, forges, or foundries and are used in ship building, electrical building, aircraft, automobile, light engineering, and jewelry industries. Aluminum foil is widely used in packaging.

Powder aluminum is used in patients and pyrotechnic industries (34). Alumina has been utilized as abrasives, refractories, catalysts, and in the past, in the first firing of china and pottery (34). Aluminum chloride is used in petroleum processing and in the rubber industries. Heyl aluminum compounds are used as catalysts in the production of polyethylene.

Bauxite, a noncrystalline mineral, has a composition of $Al_2O_2 \cdot 2H_2O$ and theoretically contains 74% alumina (usually closer to 50-60%). It is the major aluminum ore, but is also used in the manufacture of abrasive aluminum salts, refractories, white cement, and as a replacement for fuller's earth for decolorizing oil (2). Bauxite contains varying amounts of silica (2-10%), iron oxide (2-26%), and titanium oxide (2-4%) (2). Aluminate cement is a construction cement containing bauxite as a raw material. It has quick-setting properties, reaching a strength in 24 hours as high as that obtained by ordinary cement in 28 days; thus it is useful in laying roads or bank walls. American bauxite found in Arkansas, Georgia and Alabama is valued for aluminum production because of its low silica content (2).

Alumina, the natural crystalline form of aluminum (Al_2O_3) is used as an abrasive and for gem stones (2). It is an important constituent of clay, used for making porcelain, bricks, pottery, and refractories. It may also be used as a mordant in dyeing. Hydrated alumina is used as catalyst carrier and has particles which are 0.1 μ to 0.6 μ in size. It can also be used as a filler in plastics and cosmetics. Calcined alumina is alumina that has been calcined to a degree that prevents absorption of more than 0.5% to 2% water. It is a fine powder and is used for electrical insulators, abrasives, and in porcelain and ceramic enamel mixes. Aluminum hydrate is a white, bulky water-insoluble aluminum powder ($Al(OH)_3$) produced by the reaction of soluble aluminum salt and alkali and precipitated from a solution (2). It is used as a base for lake pigment, for making glass white, as a water repelent agent, and for fabric and paper coatings. Hydrated alumina coated with stearic acid is used as a reinforcing pigment for rubber.

Aluminum is a bluish-white metal with countless uses. It is used for automotive and airplane construction, for moving parts of machinery, for ornamental or architectural work, and for cooking utensils. The metal is transparent to x-ray and is used in thin sheets as a ray filter. Its lightness makes it valuable for transport equipment; about 25% of its entire production is used for this purpose. It is resistant to corrosion and is nonmagnetic even when alloyed with iron (2). Aluminum sheets as thin as 0.0005 inch are rolled into aluminum foil. Aluminum, in powder form, is used in paints and fireworks. Its physical properties are greatly affected by even slight additions of other elements. So great is the effect of alloy elements in aluminum that a commercial aluminum 99.2% pure will have a strength 25% greater than 99.9% pure aluminum. Pure aluminum is next to gold in malleability. Aluminum alloys are usually aluminum-copper alloys with or without other alloying elements. Copper hardens and strengthens aluminum. The alloy is easy to cast; 8% copper is considered the economic point for balancing strength and low specific gravity. When zinc and tin are added to aluminum alloys, they cause hot-shortness; silicon adds fluidity and decreases luster; magnesium inhibits grain growth and gives age hardening; titanium gives corrosion resistance; and iron in small amounts increases

strength. Nickel, replacing copper in the alloy, makes it stronger, more corrosive resistant and improves luster (2).

Aluminum oxide (Al_2O_3) may be made commercially and, because of its high melting point, is valuable as a refractory material. The crystalline type is used as an abrasive. Aluminum oxide is also employed in making refractory linings and crucibles. Aluminum oxide grains can be made into pellets with a ceramic bond for use as a catalyst carrier in the chemical industry. Alumina, the natural-occurring crystalline aluminum oxide is called corundum; the synthetic crystals used for abrasives are designed as aluminum oxide or marketed under trade names. It is an important constituent of clays for making porcelain, bricks, pottery, pigments, catalyst carriers, chemicals, and refractories—although aluminum metal production and abrasives are its major uses. Ultrafine aluminum abrasive powders are of two types: alpha-alumina with hexagonal crystals and gamma-alumina with cubic crystals. The alpha type cuts faster but the gamma type gives a finer finish. The aluminum oxide most frequently used for refractories is beta-alumina with hexagonal crystals heat-stabilized with sodium.

The Hindu word, corundum, was originally applied to gemstones (2). Rubies and sapphires are corundum crystals colored with oxides. Oriental topaz is yellow corundum containing ferric oxide. Oriental emerald is a rare green corundum. Corundum is now largely replaced by the more uniformly manufactured aluminum oxide. Foamed aluminum or aluminum foil is made by foaming aluminum metal with zirconium hydride or other metal hydride (2). Released hydrogen expands the metal into cellular structures of good strength and controlled densities which can be used for insulating roofing or for building panels.

Aluminum powder or flake, made by a stamping process, is used as a pigment in paints and printing inks, in silvering rubber articles, and in plastics. Spherical-shaped particles of aluminum free from grease (granulated aluminum) are used in coloring and for pyrotechniques and explosives, fat reacting fuels, and incendaries. Aluminum powder may be used to increase thrust in solid-fuel rockets, for metallurgical purposes, for paints and enamels.

Aluminum-silicon alloys refers to casting alloys containing 5-22% silicon. They are characterized by their ease of casting, corrosion resistance, lightness, and ease of welding. They are frequently used for engine cylinders, pistons, and casting dies. Aluminumized steel consists of dip-coating and diffusing aluminum into steel at a temperature of about 1,600 °F to form an aluminum-iron-alloy coating. The process is used for wire, sheet, and marine hardware.

List of Occupations and Industries Involved

Exposure to aluminum as a powdered metal occurs in a number of occupations where aluminum is used or processed:

- Aluminum workers
- Aluminum smelting
- Aluminum alloy grinders
- Ammunition makers
- Fireworks maker
- Aluminum paint makers
- Aluminum propeller grinders
- Petroleum refining
- Plastic makers
- Rubber makers

Exposure to aluminum oxide is seen in:

- Abrasive manufacturers
- Pot-room workers
- Catalyst makers
- Aluminum grinders
- Potteries
- Refractories

Epidemiology

Shaver and Ridell described a lung disease in Canadian pot-room workers exposed to fumes which evolved during the making of abrasive corundum (naturally occurring A_2O_3 in alpha or hexagonal crystals, usually containing lime and other impurities) (29)(30). During the operation, dense white fumes were noted to evolve and tended to be carried upward by the heat draft from the furnaces, with most of the fumes escaping through openings in the roofs of the furnace rooms. Nonetheless, considerable contamination occurred in the work area surrounding the furnaces where workers were stationed (29)(30). A total of 23 cases of pulmonary fibrosis were described—ages ranging between 25 and 61 years and length of exposure 29 months to 15 years. The majority of affected employees worked as "furnace feeders." An additional 25 workers were studied and 13 showed "early" or "doubtful" pulmonary fibrosis. Symptoms varied in intensity but were found to correspond to the

amount of lung involvement present as indicated by a chest x-ray (30).

Shaver commented on the high concentrations of alumina and silica in a finely divided state evolving from the reduction process. The atmosphere contained 32.3% silicon dioxide and 56% aluminum oxide. The silica, however, was present in an amorphous nonfibrogenic form (14). Particles were extremely small, 0.02 to 0.5 μ in diameter. The disease was fatal in seven cases, and in several other cases progressed rapidly, producing serious disability. Of 245 individuals exposed in four different plants, 35 had "definite" x-ray changes of disease, and 13 had lung changes classified as "doubtful." The etiology of the fibrosis was uncertain.

Pulmonary fibrosis was noted in workers exposed to very fine aluminum powder used for fireworks and aluminum paints (20). The powder was produced by pounding cold metal into fine flakes used for fireworks (pyro) and paint powders (20). Exposure to high concentrations of dust occurs when machines are emptied and filled and during certain weighing and screening processes (29). Goralewski reported that German workers engaged in the manufacturing of pyro-aluminum powder not coated with stearin developed acute respiratory illnesses within a few months of starting work (10). The development of illness was rapid and showed no relationship to length of exposure to aluminum.

Hunter reported on airplane propeller grinders in England during the war (14). Duraluminum is an alloy containing 95% aluminum, 3.5-4.5% copper, 0.04-0.7% iron, and 0.3% titanium. It was used for making aircraft propellers, and during this process propellers were ground smooth with alundum wheels (calcined aluminum oxides 95-97%, ferric oxide 0.3-0.6%, titanium oxide 2.2-2.8%, and silica 0.2-0.4%) which created much dust. Despite good ventilation, workers were covered with dust and were said to assume an aluminum color. The average concentration of aluminum in the breathing zone of operators was 3-5 mg/m^3. At polishing vents, dust levels were on the order of 50-100 mg/m^3, depending on the direction of the buffing wheel. The dust was almost exclusively large aluminum particles, although a significant number of particles below 2 μ were present. Clinical examinations revealed no excess illness recorded in medical records, nor were there abnormal chest x-rays noted in 92 workers examined.

Mitchell reported a fatal case of progressive pulmonary fibrosis in a young man occupationally exposed to high concentrations of fine aluminum dust (23). On postmortem examination there was a generalized pulmonary fibrosis present, most marked in the upper lobes. Many jagged particles were identified in lung tissue and gave histochemical reactions for aluminum. The average content of aluminum oxide per dry weight of lung was 640 ppm (23). While the particle size of the powder was generally large, dust levels of about 10 mg/m^3 consisted of dust particles less than 5 μ. The dust was mixed with approximately 0.5% stearin.

Mitchell et al. reported on 27 individuals in a fireworks factory exposed to pyro (finely powdered aluminum); six workers had evidence of pulmonary fibrosis (24). This study involved exposures to fine, flaked aluminum powder which is made by stamping cold metal. Whereas flaked powder is flattened and has a peculiar leafing characteristic, granulated powder consists of larger particles which are spherical in shape and is widely used in aluminum paints. Large quantities of stearin were used for paint powder to prevent aggregation of particles, but the making of pyro powders required the quantities of stearin to be kept as low as possible and replaced largely by mineral oil. Exposure to high concentrations of dust took place while aging and emptying machines during certain weighing and screening processes. Mean total dust concentration in the pyro stamping room during emptying and refilling of machines was 6.5 mg/m^3 and 68 mg/m^3 (24); respirable dust was 51 and 52 mg/m^3 (respirable dust was 8% of the total dust). There was a mean concentration of 95 mg/m^3 of respirable dust in the screening room. Chemical analysis of dust revealed that aluminum represented 81.4% and stearin approximately 3.5%. Semiquantitative spectrographic analysis showed 0.5% silicon dioxide and approximately 0.1% copper manganese and iron to be present; beryllium was not detected.

One of the first cases of pulmonary fibrosis was reported in German aluminum workers by Baader in 1934 (24). After World War II, cases of pulmonary fibrosis were reported in men working with aluminum powder for ammunition (24). Goralewski reported on 62% of the workers from six factories and noted more than 26% had pulmonary fibrosis (9). Koelsch, summarizing German workmen's compensation cases, re-

ported 65 cases in which 26 were considered cases of "aluminum lung" (19). In Japan, Ueda recorded a case of a patient who died of an aluminum-associated lung disease three years after stopping employment (36).

Jordan reported pulmonary fibrosis in a young woman employed for five years as a "flash filler" in a fireworks factory and exposed to high concentrations of aluminum powder (17). Pulmonary function studies showed reduced lung volumes and severely impaired carbon monoxide diffusion (17).

Clinical, radiographic, pathologic, and environmental features of a case of extensive pulmonary fibrosis were reported in a 49-year-old man who worked 13½ years in a ball-mill room of an aluminum powder factory and died with progressive encephalopathy and seizures (21). There were no presenting pulmonary symptoms. Chest x-ray examinations of 53 other workers in the same factory and pulmonary function studies of 23 individuals revealed no significant abnormalities. The concentration of aluminum in lung and brain tissue was about 20 times normal and in the liver, 122 times more than in the normal controls. Microscopic studies of lung tissue revealed aluminum particles in areas of fibrosis. Chemical analysis confirmed the presence of aluminum in the lung. Sections of brain tissue also indicated aluminum deposition in brain tissue.

Posner and Kennedy reported on china biscuit placers, more than half of whom were working with aluminum for more than 15 years. No cases of radiologically manifest pulmonary fibrosis were identified (26).

Discher and Breitenstein reported a prevalence of chronic pulmonary disease in 457 male aluminum pot-room workers compared to a 5.3% prevalence rate in 228 skilled laborers (7). No difference was noted in respiratory symptoms or spirometric measurements between the two groups. Jephcott reported that the bauxite used by the plants reported by Shaver contained between 77.5% and 85.2% Al_2O_3 and 4.5-7.2% SiO_2 (16). Chemical analysis of fumes indicated concentrations of SiO_2O_3 of 30.7-62.1%. Analysis of lung tissue from the autopsy of six workmen exposed to the fumes showed silica concentrations of 0.86-2.45% per dried lung and alumina content of 1.2-2.6%. The amount of alumina and silica were in excess of the quantities observed in lungs of unexposed persons and indicated that significant amounts of inhaled fumes were retained by the lungs. X-ray defraction analysis of dried lung revealed both alpha and gamma alumina.

Estimates of Population Exposed

The National Occupational Hazard Survey (NOHS) conducted by NIOSH estimates that there may be more than three million workers potentially exposed to various aluminum compounds. About 1.8 million are exposed directly to alumina (Al_2O_3)—perhaps 112,000 on a full-time basis. It is estimated that 1.6 million are exposed to aluminum coated with stearin—25,000 on a full-time basis, and that 500,000 are directly exposed to aluminum metal (35).

Pathology

Autopsy studies on gross examination have shown the lungs are usually either small or normal in size and weight, but sometimes markedly shrunken (28). Pleural surfaces are pigmented and may have a somewhat pebbled appearance. On occasion, there may be extensive thickening of the pleura, with emphysematous blebs and large bullae present on the surfaces. The darkly pigmented fibrous masses and bands are scattered throughout lung substance tissues on cut sections of the lung. Central portions of the lung between the pleural surface and hilum are most heavily involved, demonstrating areas of dense fibrosis (28). Fibrous extensions cross interlobular septums to the pleura and appear to pass inward toward the hilum along the bronchi and blood vessels. The bronchi appear to be of normal appearance grossly, but may be dilated, containing clots of coagulated exudates. Moderate thickening of the vessels is noted. Lymph nodes are pigmented and firm, but may be slightly enlarged.

Microscopic examination discloses diffuse nonnodular fibrosis of the lung. The fibrous tissue is said to be hyaline in nature with a few areas of interstitial inflammation. Alveolar spaces may be partially occluded and compressed between bands of collagen. Some airspaces contain masses of phagocytes filled with blackish pigment, giant cells containing cholesterol crystal clefts, and cellular debris. The alveolar walls are thickened and lined with cuboidal epithelium. Dilated bronchi containing mucus may be seen in some areas; the submucosa is often thickened

and shows inflammatory cell reaction. Vessels, while usually normal, may show perivascular fibrosis and occasionally endarteritis. Lymphoid tissue reveals evidence of lymphadenitis, with large numbers of phagocytes filled with pigment particles within lymph nodes (28)(40).

One mechanism, which could explain the fibrogenic effects of aluminum on lung tissue, proposed that in the presence of protein and chloride ions, the protein is tanned and is then co-precipitated with an aluminum hydroxide complex which covers the partly dissolved aluminum particles (15). This complex is relatively insoluble and not likely to be phagocytized (3)(4)(15). Koelsch believed that the reported lung disease was the result of poor workroom ventilation present in blackouts during World War II, and that this led to high concentrations of aluminum dust accumulating in the ambient air of the work environment (19). The observation that excessively high workplace concentrations of aluminum dust are important in disease production is supported by studies of Gross et al. (11), who investigated pulmonary reaction to three types of aluminum powder: 1) British pyro powder, composed of flake-like particles; 2) American-made flake-like powders; and 3) American atomized spherical particles. Pulmonary fibrosis did not develop in guinea pigs and hamsters following inhalation of large dust burdens. Intratracheal injection of large doses of aluminum powder, however, did cause focal fibrosis. This was believed to represent an artifact due to the method of administration and the high concentration of dust used (11). Instillation of lower concentrations of aluminum dust, for instance, did not cause fibrosis.

Pulmonary fibrosis has not been reported in workers exposed to granular type alumina dust (Al_2O_3), such as when working in stamp mills that produce aluminum powder for paint and ink manufacturing (5); in aluminum reduction plants (18)(22); in potteries (26); or among Duralumin airplane propeller polishers (14). A proposed mechanism to explain the lung damage suggests that the introduction of mineral oil into the stamping industry, in place of stearin, permitted the powder to react with water, whereas it did not before. Lung damage was, therefore, caused by contact with the soluble aluminum. When pulmonary fibrosis has been reported, the incriminated dust has usually been flaked aluminum in which mineral oil was used to coat the flakes, either partially or wholly replacing stearin (9)(24). (There is an exception, however, in a case reported by McLaughlin et al. (22).) Thus aluminum oxide covering granular powder particles and stearin covering flake particles, was thought to prevent metallic aluminum from exerting a fibrogenic effect (11). Animal studies, however, do not support this theory since intratracheal instillation of fine aluminum flakes coated with either stearin or mineral oil were fat- free (3), but caused fibrosis of equal severity. Granular aluminum powder, however, had a negligible effect and was essentially inert (3).

It has also been suggested that silica, present in cryolite, was a responsible factor (1). This seems unlikely since quartz probably would be converted to glass at the operating temperature of the furnaces and identification of tridymite or cristobalite in the fumes had not been reported (25). Metallic aluminum, when heated in fumes, evolves mainly gamma-type Al_2O_3 (8), which causes fibrosis in rat lung, whereas alpha-type Al_2O_3 does not (32). Styles et al. tested alumina in cell cultures and in animals to assess its cytotoxicity and tissue reaction (33). The toxicity of alumina to rat peritoneal macrophages in cell culture was low when compared to asbestos. However, alumina fibers caused more fibrosis than zirconia fibers when injected intraperitoneally in animals (33). Although an immunologic reaction in aluminum workers with lung fibrosis has been described there is no conclusive evidence to support this hypothesis.

Thus, the role of aluminum dust or fumes in the pathogenesis of lung fibrosis is uncertain. The variability of animal study results makes it difficult to correlate with human disease. Even so, there are a number of reports of workers who have been exposed to both dust and fumes, and who have developed pulmonary fibrosis without identifying any other causal factor for their lung disease. It can be concluded, therefore, that aluminum may sometimes be responsible for causing pulmonary fibrosis, but the exact occupational circumstances and conditions are not yet completely clear.

Clinical Description

The pulmonary fibrosis attributed to aluminum is associated with two different inhalable materials (25): fumes derived from the smelting of bauxite (Al_2O_3), (known as Shaver's disease after Shaver jointly described the association in

1947 (30)); and inhalation of aluminum dust (25).

Shaver described unilateral or bilateral spontaneous pneumothoraces (30). Chest x-rays, when reviewed, showed well-established pulmonary fibrosis. Dyspnea on exertion was an outstanding symptom with attacks of extreme breathlessness frequently described. Attacks of breathlessness were occasionally interspersed with periods of symptom improvement. The majority of workers gave a history of cough and sputum production. The sputum was described as white, fluffy, or frothy in character, sometimes mucopurulent. In addition, there were complaints of substernal chest discomfort or tightness and occasionally actual chest pain. Weakness, fatigue, and inability to sleep were seen in individuals with severe dyspnea. No specific abnormal physical findings were noted in individuals with early disease, but in those with advanced disease, weight loss and loss of appetite were apparent. Chest signs, when present, were variable and largely depended on the presence or absence of pneumothorax and the amount of pulmonary fibrosis. More advanced cases showed cyanosis and limited chest expansion. Furthermore, decreased percussion noted on physical examination was generally found to correspond with extensive pulmonary fibrosis or pleural thickening. In some instances there was elevation of the diaphragm. Hyperresonance and decreased breath sounds were associated with the presence of pneumothorax. Some individuals demonstrated friction rubs; rales, and rhonchi were noted on chest auscultation (30).

In most cases chest x-ray showed widening of mediastinal shadows and irregular borders of the diaphragm shadow. The diaphragm was often tented and markedly elevated. Interstitial changes noted on chest x-ray were more pronounced in the upper lung fields, more intense towards the hilum, and less toward the periphery. Coarse shadows throughout the lung field occurred in more advanced cases. Emphysematous changes were often present and associated with bleb formation (30).

In workers exposed to fine aluminum powder, there were complaints of dry cough, pleuritic-like chest pain, shortness of breath, poor appetite, and gnawing abdominal pain (13) (24). Spontaneous pneumothorax occurred in some workers. Eosinophilia as high as 10% in some workers was present; erythrocyte sedimentation rate was normal in the majority of workers. A restrictive lung defect was noted on pulmonary function studies with decreased vital capacity. X-rays showed pulmonary fibrosis affecting mainly the upper part of the lung. Increased markings in the upper and middle thirds of the lung fields provided a reticular appearance, which later increased to become confluent. In general, symptoms and signs were similar to those in Shaver's disease.

There have also been a number of reports of an asthma-like syndrome associated with working in the pot-room environment (18)(31) (37)(38). Clinically there is an immediate asthmatic response while workers are actively working in the pot-rooms, usually precipitated by high exposures to pot fumes. A second, delayed response occurs 4 to 12 hours after leaving the cell room; a third, or dual-type, occurs in individuals both at work and sometimes after work (6). The asthmatic syndrome seems to occur following exposures to both pot-room fumes and dust (38). The immediate type of response usually develops within three months of employment; delayed responses usually occur after three months or as late as three years following beginning employment (6). Those with dual responses usually develop asthma within 6-12 months. Asthma occurs equally in both atopic and nonatopic individuals. The syndrome may appear after only one pot-room exposure. A major complaint is a nonproductive cough. Dyspnea is a more prominent symptom in individuals with immediate-type responses, whereas wheezing is prominent in workers with the delayed-type response. Those with the dual-type syndrome have severe exertional dyspnea (6). The exact cause of the asthma from pot-room exposure has not been identified.

Diagnostic Criteria

The most difficult problem is to distinguish this disease from mixed dust fibrosis and sometimes asbestosis. Differentiation is possible only when an appropriate and complete occupational history is taken and all exposures are identified. There are no specific diagnostic features of the history, physical exam, pulmonary function tests, or chest x-ray which differentiate this disease from other forms of pulmonary fibrosis.

Methods of Prevention

There are a number of fume control devices. Pots are generally fitted with a primary collection system and may also have a secondary system (27). The fumes collected by the primary collection system are concentrated and can be treated using either an electrostatic filter or bag filter, or a dry scrubbing system (27). A secondary system does not exist in every smelter but usually consists of a water scrubbing system on the roofs of the building, abating the pollutants that may have escaped during the primary system.

Research Needs

The exact mechanisms to explain the pulmonary fibrosis described in aluminum workers needs to be elucidated. It is not clear whether aluminum alone, or in combinations with other materials, is capable of inciting a fibrotic response. The specific etiological agents responsible for asthma among pot-room workers need identification.

Bibliography

1. Ahlmark, A., Bruce, T., and Nystrom, A.: Silicosis and other pneumoconiosis in Sweden. London: Heinemann, 1960.
2. Brady, G. S. and Clauser, H. R.: Materials Handbook 11th edition. New York: McGraw Hill Book Company, 1977.
3. Corrin, B.: Aluminum pneumoconiosis: I. In vitro comparison of stamped aluminum powders containing different lubricating agents and a granular aluminum powder. Br J Ind Med *20:* 264-267, 1963.
4. Corrin, B.: Aluminum pneumoconiosis: II. Effect on the rat lung of intratracheal injections of stamped aluminum powders containing different lubricating agents and of a granular aluminum powder. Br J Ind Med *20:*268-276, 1963.
5. Crombie, D. W., Blaisdell, J. L., and MacPherson, G.: Treatment of silicosis with aluminum powder. Can Med Assoc J *50:*318-328, 1944.
6. Dinman, B. D.: The respiratory condition of potroom workers: Survey preliminary report. In: *Health Protection in Primary Aluminum Production,* ed. by James P. Hughes. London: New Zealand House, pp. 95-100, 1977.
7. Discher, P. and Breitenstein, B. D.: Prevalence of chronic pulmonary disease in aluminum potroom workers. JOM *18:*379-386, 1976.
8. Finlay, G. R.: In pneumoconiosis: Sixth Saranac Symposium, p. 493-497, by A. J. Vorwald New York: Hoeber, 1950.
9. Goralewski, G.: Dic aluminum lunge: Eine Neue Gewerbeer Kran Kung. Z Ges Inn Med *2:*665-673, 1974.
10. Goralewski, G.: Die aluminum lunge (Arbeithsmedizin, No. 26) Leipzig, 1950.
11. Gross, P., Harley, R. A., and DeTreville, R. T. P.: Pulmonary reaction to metallic aluminum powders. Arch Environ Health *26:*277-236, 1973.
12. Hatch, T. F.: In pneumoconiosis: Sixth Saranac Symposium p. 498-501, Ed. by A. J. Vorwald New York: Hoeber, 1950.
13. Hunter, D.: The diseases of occupations. London: Hodder and Stoughton, 1975.
14. Hunter, D., Milton, R., Perry, K. M. A., and Thompson, D. R.: Effect of aluminum and alumina on the lung in grinders of duralumin aeroplane propellers. Br J Ind Med *1:*159-164, 1944.
15. Jaeger, R. and Jaeger, F.: Kolloidchemisches und histochemisches zur frage der lungenschadigungen durch aluminum staub. Arch Gewerbepath Gewerbehyg *11:*117-130, 1941.
16. Jephcott, C. M.: Fume exposure in the manufacture of alumina abrasives. JOM *5:*701-709, 1948.
17. Jordan, J. W.: Pulmonary fibrosis in a worker using an aluminum powder. Br J Ind Med *18:*21-23, 1961.
18. Kaltreider, N. L., Elder, M. J., Cralley, L. U., and Colwell, M. O.: Health survey of aluminum workers with special reference to fluoride exposure. JOM *14:*531-541, 1972.
19. Koelsch, F.: Beitr Klin Tuber *97:*688, 1942. (Cited by Hunter, D., et al., Br J Ind Med *1:*159-164, 1944.
20. Levy, S. A.: Occupational pulmonary diseases p. 117-155 In: *Occupational Medicine,* ed. by Carl Zenz, Chicago: Year Book Medical Publishers, Inc., 1975.
21. McLaughlin, A. I. G., Kazantzis, G., King, E., Teare, D., Porter, R. J., and Owen, R.:

Pulmonary fibrosis and encephalopathy associated with inhalation of aluminum dust. Br J Ind Med *19*:253-263, 1962.
22. Medical Research Council: Industrial pulmonary disease committee. Br Med J *2*:1273-1275, 1936.
23. Mitchell, J.: Pulmonary fibrosis in an aluminum worker. Br J Ind Med *16*:123-125, 1959.
24. Mitchell, J., Manning, G. B., Molyneux, M., and Lane, R. E.: Pulmonary fibrosis in workers exposed to finely powdered aluminum. Br J Ind Med *18*:10-20, 1961.
25. Parkes, W. Raymond: *Occupational Lung Disorders.* London: Butterworth and Co., Lts., 1974.
26. Posner, E. and Kennedy, M. C. S.: A further study of china biscuit placers in stroke-on-trent. Br J Ind Med *24*:133-142, 1967.
27. Ravier, E. F.: Technology of alumina reduction. p. 17-22. In: *Health Production,* ed. by James P. Hughes. London: New Zealand House, 1977.
28. Riddell, R. R.: Pulmonary changes encountered in employees engaged in the manufacture of alumina abrasives. JOM *5*:710-717, 1948.
29. Shaver, C. G.: Pulmonary changes encountered in employees engaged in the manufacture of alumina abrasives. JOM *5*:718-728, 1948.
30. Shaver, C. G. and Riddell, A. R.: Lung changes associated with the manufacture of alumina abrasives. J Ind Hyg Toxicol *29*:145-157, 1947.
31. Smith, M. M.: The respiratory condition of potroom workers: Australian experience p. 79-85. In *Health Protection in Primary Aluminum Production,* ed. by James P. Hughes, London: New Zealand House, 1977.
32. Stacy, B. D., King, E. J., Harrison, C. V., Nagelschmidt, G., and Nelson, S.: Tissue changes in rat lungs caused by hydroxides and phosphates of aluminum and iron. J Pathol Bact *77*:417-426, 1959.
33. Styles, J. A. and Wilson, J.: Comparison between in vitro toxicity of two novel fibrous mineral dusts and their tissue reactions in vivo. Ann Occup Hyg *19*:63-68, 1976.
34. Tabershaw, I. R., Utidjian, H. M. D., and Kawahara, B. L.: Chemical Hazards, p. 131-149. In: Occupational Diseases, DHEW (NIOSH) Publ. No. 77-181, by U.S. Department of Health, Education, and Welfare, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, Washington, D. C.: U.S. Government Printing Office, 1977.
35. U.S. Department of Health, Education, and Welfare, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health. National Occupational Hazard Survey, Vol. III Survey analysis and supplemental tables. DHEW (NIOSH) Pub. No. 78-1114. Washington, D. C.: U.S. Government Printing Office, 1977.
36. Ueda, M., Mizoi, Y., Maki, Z., Maeda, R., and Takada, R.: Kobe J Med Sci *4*:91, 1958. Cited in Ind Hyg Dig *24*:3, 1960.
37. Vale, J. R. and Johansen, B.: The respiratory condition of potroom workers: Present knowledge. p. 73-77, In: Health Protection in Primary Aluminum Production, ed. by James P. Hughes. London: New Zealand House, 1977.
38. Van Voorhout, H. C.: The respiratory condition of potroom workers: Netherland experience, p. 91-93. In: *Health Protection in Primary Aluminum Production,* ed. by James P. Hughes. London: New Zealand House, 1977.
39. Walker, T. J.: Hygienic aspects of aluminum reduction. p. 23-30. In: *Health Protection in Primary Aluminum Production,* ed. by James P. Hughes. London: New Zealand House, 1977.
40. Wyatt, J. P., and Riddell, A. C. R.: The morphology of bauxite-fume pneumoconiosis. Am J Pathol *25*:447-460, 1949.

ANTIMONY

Introduction

Antimony is an extremely brittle metal, bluish-white in color and crystalline-like in texture. Like arsenic and bismuth, it is sometimes referred to as a metalloid; it should be called a semimetal. It does not have the free cloud-like electrons that occur in metal atoms, thus it lacks

plasticity and is a poor conductor of electricity. It is used only in alloys or in chemical compounds. It is easily reduced to powder and is neither malleable nor ductile (2).

List of Causative Agents (Manufacturing Processes)

The chief uses of antimony are in alloys, especially as a hardener for lead-base alloys (2). It imparts hardness and a smooth surface to soft-metal alloys because it expands on cooling. Alloys containing antimony are useful because they can reproduce the fine detail of a mold, thus making it valuable for type metals. When alloyed with lead, tin, and copper it forms babbitt metals that can be used for machinery bearings. Antimony compounds are also widely used for pigments, particularly as a paint pigment for coloring red rubber and in safety matches.

The chief antimony ore is stibnite (SbS_3). Other antimony ores are valentinite, an oxide with a rhomboid structure; cervantite or antimony tetraoxide (Sb_2S_2O); stibiconite ($Sb_3O_4 \cdot H_2O$); kermesite (Sb_2S_2O), a mineral resulting from the partial oxidation of stibnite; Jamesonite ($Pb_2Sb_2S_3$), another sulfide ore of antimony; and stephanite, ore of silver sulfantinonite ($AgSbS_4$). Antimony is obtained chiefly as a by-product or co-product of base material and silver ores and is used in a variety of industries (27). Most industrial exposures are to antimony dusts rather than to antimony fumes, with antimony trioxide dust being the most common.

Antimony is used in electronic semiconductors and thermoelectric devices because of its excellent specific heat and electrical resistance (26)(27). The light transmitting qualities of antimony compounds, particularly antimony trioxide, make them ideal pigments for ceramics, glass, metalware, and enamels. Plastic flame-retardant chemicals are also important products (25).

U.S. consumption of primary antimony was slightly more than 15,000 short tons (21). Antimony is alloyed with other metals such as tin, lead, and copper. Metallurgical processes utilizing antimony compounds include the use of lead-antimony for the manufacture of storage battery grinds, pewter, type metal, printers' type, lead shot, lead electrodes and bearing metals, collapsible tubes and foil, sheet pipe, solder, cable covering, and castings. Antimony compounds are used in the rubber industry especially in the compounding of rubber. Antimony trioxide is used in flame-proofing materials for application to textiles and as a flame retardant in paint pigment. Oxides are used as opacifiers in enamels and as a decoloring and refining agent in glass manufacture. Other uses include bronzing powder for metals and plaster, ammunition primers, and fireworks (4)(21)(27). NIOSH estimates that there are approximately 50 potentially hazardous antimony compounds (12).

About 25 countries throughout the world are involved in antimony production (27). In 1976, the United States imported roughly 24,000 tons of antimony metal oxide and ore for consumption (21). U.S. production totaled approximately 35,000 tons, of which approximately 42% came from primary sources such as ore and primary smelters and 58% was secondary or recycled metal (21). Secondary antimony is recovered chiefly from battery scraps.

List of Occupations and Industries Involved

Table II-29 lists occupations and industry in which exposure to antimony may occur (12).

Epidemiology

Renes reported pneumonitis, tracheitis, laryngitis, and bronchitis among workers exposed to antimony trioxide (22). Karjovic demonstrated x-ray evidence of pneumoconiosis in 14 of 62 workers in an antimony smelting operation exposed to concentrations of poorly defined mixed dust (ranging from 16-248 mg/m^3). The dust contained antimony oxides and some silica. While the antimony oxides represented the bulk of the dust, it was not clear what role silica had (10). Exposure to antimony trioxide and other metal dusts produced x-ray changes in 44 of 262 workers (17). Workers with abnormal chest x-rays were essentially asymptomatic. Microscopic examination of tissue from one worker who died showed an accumulation of dust particles and dust-laden alveolar macrophages within alveolar septa and perivascular tissue. There was no evidence of pulmonary fibrosis or interstitial inflammatory response (15)(16). Cooper et al. reported three definite and five suspicious cases of pneumoconiosis based on chest x-ray changes in a group of 28 workers exposed to antimony ore and antimony trioxide (4). LeGall reported reticulonodular x-ray changes in 10 of 40 workers exposed to a mixed dust (including silica) containing an-

Table II-29

OCCUPATIONS WITH POTENTIAL EXPOSURE TO ANTIMONY

Antimony ore smelters	Metal bronzers
Antimony workers	Miners
Babbitt metal workers	Monotypers
Battery workers, storage	Mordanters
Brass founders	Organic chemical synthesizers
Britannia metal workers	Paint makers
Bronzers	Painters
Burnishers	Perfume makers
Cable splicers	Pewter workers
Ceramic makers	Pharmaceutical workers
Compositors	Phosphor makers
Copper refiners	Pigment makers
Dye makers	Plaster cast bronzers
Electroplaters	Porcelain workers
Explosive makers	Pottery workers
Fireworkers makers	Printers
Flame retardant workers	Pyrotechnics workers
Foundry workers	Rubber makers
Glass makers	Semiconductor workers
Glaze dippers, pottery	Solder makers
Gold refiners	Stereotypers
Insecticide makers	Stibnite miners
Insulators, wire	Textile dryers
Lake color makers	Textile flame-retardant workers
Lead burners	Textile printers
Lead hardeners	Type metal workers
Lead shot workers	Typesetters
Linotypers	Vulcanizers
Match makers	Zinc refiners

timony metal and trioxide (13). Some workers reported symptoms of shortness of breath, cough, and sputum production and demonstrated some abnormal physical findings. The role of silica and of SO_2 in the production of the lung changes and symptoms was not clear (13). One affected worker, however, worked only at the antimony oxide furnace where antimony exposure was reported to be high and silica concentrations low or nonexistent.

Estimate of Population at Risk and Prevalence of Disease

NIOSH estimates that 1.4 million U.S. workers are potentially exposed to antimony in their occupational environment (25). Exposures are largely to metal alloys and to metal oxide and sulfides.

Pathology

Histological examination of antimony workers' lungs reveal only dust accumulation and no fibrosis (16). Alveolar macrophages containing dust particles congregate in alveolar walls and around small vessels (16). No fibrosis or significant inflammatory reactions have been reported (16).

While antimony ore or antimony trioxide have not been reported to cause significant fibrosis in experimental animals (4), there have been reports of pulmonary reactions to certain antimony compounds in man following exposure by several routes (10)(13)(15)(17)(22)(24). A pneumonitis occurs following inhalation of antimony trioxide in guinea pigs (6). Animals with more than 50 mg of antimony in their lungs

showed scattered subpleural hemorrhages (6). Lipoid pneumonia was noted to occur in rats following inhalation of antimony trioxide for 25 hours per week over 14.5 months (8). Pathologically, there was evidence of cellular proliferation and swelling and desquamation of alveolar lining cells. Subsequent studies reported more deaths due to pneumonia among the exposed animals and evidence of extensive interstitial pneumonia and some fibrosis. The initial pathologic response was an acute chemical pneumonitis (4). By two months, only alveolar accumulation of macrophages was noted. No fibrosis was noted in animals followed as long as one year after termination of exposure. Single instillations of 2.5-20 mg of antimony trifluoride intratracheally in rats are invariably fatal (14) and result in acute hemorrhagic pulmonary edema. Tracheal instillation of antimony trisulfide or pentasulfide results only in macrophage accumulation, slight perivascular and peribronchial cellular inflammatory reactions, and scattered areas of atelectasis (14).

Clinical Description

There are no specific clinical symptoms or abnormal physical findings in workers exposed to antimony compounds (19). Health problems from antimony include dermatitis, mucous membrane irritation, electrocardiographic alterations, liver involvement, and hematologic changes (2)(3)(4)(5)(7)(10)(11)(13)(15)(17)(18)(22)(23). Many of the symptoms ascribed to antimony may be due to arsenic which is a common contaminate of antimony ores and antimony compounds used in industry.

Pulmonary Function Studies

There are no abnormalities of lung function reported.

Radiographic

There have been occasional reports of chest x-ray changes. Usually this consists of small, dense opacities similar to those noted in siderosis or stanosis (4)(15)(17). Large, confluent shadows do not occur. Densities may be denser near the hilar regions with loss of well-defined hilar vascular shadows (19). X-ray changes can develop within two to three years and involve all portions of the lung. Opacities are regular, usually 1-3 mm in size (9)(20). There are no detrimental effects upon health or life expectancy. Unlike siderosis and barium inhalation, there is no evidence of decrease in the x-ray appearance with progression of time following cessation of exposure (19).

Diagnostic Criteria

Antimony pneumoconiosis is a rare condition which can be overlooked if an accurate occupational history is not obtained. Differential diagnosis is similar to that for other inert dusts which are of high radio densities, such as tin or barium (which may produce identical x-ray appearances). Miliary tuberculosis can be easily excluded because of its clinical presentation; its opacities also are reported to be less dense and well-defined and may be more profuse in the mid zones of the lung (19). Sarcoid may present with a nodular pattern but is usually associated with large hilar adenopathy and other characteristic features of this disorder. Opacities seen with pulmonary hemosiderosis are due to repeated capillary hemorrhage and should be easily differentiated by hemoptysis, anemia, clubbing, and heptatosplenomegaly.

Methods of Prevention

NIOSH has recommended concentrations of antimony in the workplace should not exceed 0.5 mg/m^3 as determined by a time-weighted-average concentration for up to a 10-hour workshift in a 40-hour week. A workplace medical program should include both preplacement and periodic examinations including chest x-rays and pulmonary function studies (25).

Proper protective clothing may be necessary and should include gloves, coveralls, head and neck protection, and also eye and face protection if necessary. Respiratory protection is only indicated when engineering controls have not yet taken place; in situations where installation and testing of engineering controls are occurring; during performance of certain maintenance or repair procedures; and during emergencies where high dust levels may be expected.

Research Needs

More epidemiologic studies are needed to better define the prevalence of disease if it does occur. Animal studies might be designed to better identify which of the antimony salts is more likely to be toxic.

Bibliography

1. Belyaeva, A. P. [The effect of the antimony on reproductive function.] Gig Tr Prof

Zabol *11*:32-37, 1967 (Rus.).
2. Brady, G. S. and Clauser, H. R.: Materials Handbook, 11th ed. New York: McGraw-Hill Book Company, 1977.
3. Brieger, H., Semisch, C. W., Stasney, J., and Piatnek, D. A.: Industrial antimony poisoning. Ind Med Surg *23*:521-523, 1954.
4. Cooper, D. A., Pendergrass, E. P., Vorwald, A. J., Maylock, R. L, and Brieger, H.: Pneumoconiosis among workers in an antimony industry. Am J Roentg *103*:495-508, 1968.
5. Davies, T. A. L.: The health of workers engaged in antimony oxide manufacture — A statement. London Department of Employment: Medical Advisory Service, 1973.
6. Dernehl, C. U., Nau, C. A., and Sweets, H. H.: Animal studies on the toxicity of inhaled antimony trioxide. J Indust Hyg Toxicol *27*:256-262, 1945.
7. Gallina, R. and Luvoni, R.: Occupational poisoning from antimony—clinical observations. Rass Med Ind *27*:27-28, 1958 (Ita).
8. Gross, P., Brown, J. H. U., and Hatch, T. F.: Experimental endogenous lipoid pneumonia. Am J Pathol *28*:211-221, 1952.
9. I. L. O. Classification of radiographs of pneumoconioses, Geneva, 1958. Occupational Safety and Health, Vol. 9, 1959.
10. Karajovic, D.: [Pneumoconiosis in workers at an antimony smelting plant.] p. 370-374. In: Proceedings of the 12th International Congress on Occupational Health, Helsinki, 1958 (Ger.).
11. Klucik, I. and Ulrich, L. [Electrocardiographic examination of workers in an antimony metallurgical plant.] Prac Lek *12*:236-243, 1960 (Cze.).
12. Kusnetz, S. and Hutchison, M. K., eds.: Antimony. In: A Guide to Work-Relatedness of disease, 2nd ed., U.S. Department of Health, Education and Welfare, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, Washington DC: U.S. Government Printing Office, 1978.
13. LeGall: [Pneumoconiosis and Antimony] Arch Mal Prof *30*:361-362, 1969 (Fr.).
14. Levina, E. N. and Chekunova, M. P.: Toxicity of antimony halides. Fed Proc (Part II) *24*:608-610, 1965.
15. McCallum, R. K.: The work of an occupational hygiene service in environmental control. Ann Occup Hyg *6*:55-64, 1963.
16. McCallum, R. I.: Detection of antimony in process workers' lungs by x-radiation. Trans Soc Occ Med *17*:134-138, 1967.
17. McCallum, R. K., Day, M. J., Underhill, J., and Aird, E. G. A.: Measurement of antimony oxide dust in human lungs *in vivo*. In: Inhaled Particles II. Ed. by W. H. Walton. Old Working, Surrey England, Gresham Press: Unwin Brothers Ltd., 1971.
18. Oliver, T.: The health of antimony oxide workers. Br Med J *1*:1094-1095, 1933.
19. Parkes, W. R.: Occupational Lung Disorders. London: Butterworth and Co., Ltd., 1974.
20. Radiologic classification of pneumoconiosis for Anglo-American radiographic reading exercise and study of the International Labor Office classification of pneumoconiosis cooperative study. AMA Arch Environ Health *12*:314-330, 1966.
21. Rathjen, J. A.: Antimony — Reprint from the 1976 Bureau of Mines Minerals Yearbooks. U.S. Department of the Interior Bureau of Mines, Washington, DC, U.S. Government Printing Office, 1978.
22. Renes, L. E.: Antimony poisoning in industry. AMA Arch Ind Hyg Occ Med *7*:99-108, 1953.
23. Selisky, A. B.: [Occupational skin injuries by antimony salts in the textile industry]. Dermatol Wochenschr *86*:723-727, 1928 (Ger.).
24. Taylor, P. J.: Acute intoxication from antimony trichloride. Br J Ind Med *23*:318-321, 1966.
25. U.S. Department of Health, Education and Welfare, Public Service, Centers for Disease Control, National Institute for Occupational Safety and Health. Occupational Exposure to Antimony, Washington, DC, U.S. Government Printing Office, 1978.
26. Windholz, M., Budavari, S., Stroumtsos, L.

Y., and Fertig, M. N., eds. The Merck Index: An Encyclopedia of Chemicals and Drugs, 9th ed. Rahway, New Jersey: Merck and Co., Inc., 1976.
27. Wyche, C.: Antimony, p. 79-91. In: Mineral Facts and Problems, Bulletin, No. 667. U.S. Department of the Interior, Bureau of Mines, Washington, DC: U.S. Government Printing Office, 1975.

BARIUM

Introduction

Barium is a silver-white metallic element found in the widely distributed minerals witherite and barite. Although barium can be obtained by electrolysis from barium chloride, it oxidizes so readily it is difficult to process in the pure metallic state. Because of this, barium compounds find the most extensive uses.

Baritosis, first described by Arrigoni among barytes miners in Italy (1)(2), results from the inhalation of respirable particles of barium sulfate causing dense radiologic opacities but no functional impairment.

List of Causative Agents (Manufacturing Processes)

Barium may be extracted from barium oxide by heating with aluminum in vacuo at about 1,200 °C and then condensing the barium vapor in the cool end of a tube. It may also be extracted with ferrosilicon at a temperature about 50 °C higher. Lead barium-calcium alloys are prepared by electrolysis of the chlorides in cells with molten lead at the cathode (3).

Barium sulfate is insoluble and is used as a radiopaque contrast media for radiologic studies. It is not absorbed by the gut. On the other hand, soluble salts of barium are generally toxic. For example, barium carbonate, barium chloride, barium nitrite, and barium sulfide are rapidly absorbed by the gastrointestinal tract and are fatal to man in amounts of less than one gram (6). This type of intoxication is not often recognized clinically; it is usually noted only at postmortem examinations.

Barytes are widely distributed through the world and occur in combination with other minerals such as fluorite, calcite, limestone, witherite, quartz, and chert which may be intermixed according to the type of deposits (10). Barytes from some areas contain significant amounts of free silica. In the United States, the major states producing barytes are Nevada, Missouri, Arkansas and Georgia.

List of Occupations and Industries Involved

Barium compounds are used in the manufacture of lithopone (a white pigment utilized in paints), chlorine, sodium hydroxide, valves, and green flares (14). Barium compounds are used in synthetic rubber vulcanization, x-ray diagnostic work, glass making, paper making, meat-sugar purification, and animal and vegetable refining (14). Compounds are also used in the manufacturing of brick and tile, pyrotechnics, and in the electronics industries. In addition, they are used as additives to lubricants, pesticides, glazes, textile dyes and finishes, pharmaceuticals, and in cements which will be exposed to salt water. Barium is used as a rodenticide; as a flux for magnesium alloys; as a stabilizer and mold lubricant in the rubber and plastics industry; as an extender in paints; as a loader for paper, soap, rubber, and linoleum; and as a fire extinguisher for uranium and plutonium fires. It is used as an extender or filler in cement, paint, paper, soap, rubber, linoleum, plastics, ceramics, electronics, and in the glass industry, and in compounds containing matches, and in art paint pigments.

A list of jobs where exposure to barium compounds may occur includes: textile workers, chemical workers, tile makers, lithopone manufacturers, fire extinguisher makers, oil workers, pesticide(s) manufacturers, x-ray diagnostic contrast material workers, and barium miners (baryte ore).

During mining of the crude baryte ore, high concentrations of dust are produced, which may include silica in cases where the surrounding rock contains silica in hydrothermic deposits or chert. Baryte is supplied to industries in crude form, after removal of contaminants (10). Chances of dust inhalation during this procedure are low because operations are usually accomplished in the wet state. During drying and bagging of ground barytes, high concentrations of dust may be produced (10).

Ground baryte is used in the oil industry as a wetting agent for drilling mud; as a filler with weight increasing properties in some types of paper; as an additive in linoleum, textile, rubber, brake linings, and enamel paints; and in glass industries to increase the fluidity of molten glass

(10). It was used in records until the introduction of microgroove records in about 1948. Lithopone, a widely used pigment and filler until recent years, was made by roasting crude silica-free barytes with carbon in a rotary kiln, bleaching out the product and then adding zinc sulfate. The resulting precipitate was washed, filtered, dried, and calcined. At some stages of the process, a mixture of barytes and carbon dust was present. Coal was often used as a source of carbon and grinding was a dusty process. Because of this, the possibility of coal or carbon pneumoconiosis coexisted with baritosis. Today, the production of lithopone has markedly decreased.

Barium, in the form of barytes or witherite, is used in large quantities by the chemical industry. Because of its electromagnetic properties, barium titanate has been used for electronics and ultrasonic devices including transducers and digital computers. Accidental inhalation of barium sulfate during x-ray contrast studies (such as upper GI series) sometimes occurs, but it is not likely to be confused with baritosis of industrial origin.

Epidemiology

Doig reported nine cases of baritosis occurring in a small factory in which baryte was crushed, grated, and milled (4). Two of the cases occurred after 18 and 21 months of exposure; 9 of the 10 men employed for more than 1-1/2 years had baritosis. Five of the affected men examined—who left the industry and had no further exposure—showed clearing of radiologic abnormalities.

Pendergrass reported a case of a man working in a lithopone plant who was exposed to finely divided particles of barium sulfate (11). The worker also had been a coal miner for 4 years and an engine cleaner in a railroad shop for 12 years. During his employment he was also exposed to silica and carbon dust, but mainly barium dust. Chest x-ray showed nodular-like opacities distributed throughout both lung fields. Autopsy examination of lung tissue revealed the presence of irregular masses of dense fibrous tissue scattered throughout the lung. Some of the nodules were characteristic of silicosis but shaded with heavy carbon deposits. Polarized light examination indicated refractile crystals which were probably silica. Within the alveolar lumen there were numerous macrophages, most containing pigmented granules. Spectrographic and x-ray defraction studies as well as chemical analysis documented the presence of barium sulfate within the lung. The case was interpreted as being that of baritosis along with anthrosilicosis.

Estimate of Population at Risk

Baritosis is a rare condition. According to NIOSH data, however, there are approximately 800,000 exposed workers.

Pathology

Barium in the soluble form is a powerful, smooth and striated muscle stimulant (6). Accidental ingestion causes vomiting, severe colic, diarrhea, possibly gastrointestinal hemorrhage, elevation of blood pressure, convulsions, and skeletal and muscle tremors. Death occurs within one to several hours depending on the amount of barium ingested and is due to either cardiac arrest or paralysis of the central nervous system.

When free silica dust exposure occurs along with baryte dusts, both baritosis and silicosis may be present. There is no evidence that the silicotic lesion is modified by the accompanying barytes (10).

In cases of pure baritosis, cut sections of lung tissue show discrete macules located close to the pleural surface and may resemble the pathologic findings seen in stannosis (10). No confluent masses, evidence of fibrosis or hilar lymph node enlargement are noted. Microscopic examination demonstrates macular lesions similar to those seen with inhalation of tin or iron with a little reticulin and no fibrosis (10). Approximately 12 hours after endotracheal instillation of barium sulfate into rats, there is a polymorphonuclear inflammatory response in lungs containing the barium suspension (7). By 24 hours, the polymorphonuclear cells show some degeneration and are reduced in numbers. The next stage reveals mononuclear cell infiltration within the areas containing the barium suspension. By 30 days, the mononuclear cells are still present within the interstitial tissue, but may have lost their cell outline and appear to become fused together; other cells have ruptured, liberating barium salt which appears as aggregated refractile masses. By 94 to 120 days, only a mild tissue reaction remains. There are only a few areas in the lung where refractile masses remain, as well as a few lymphocytes and mononuclear

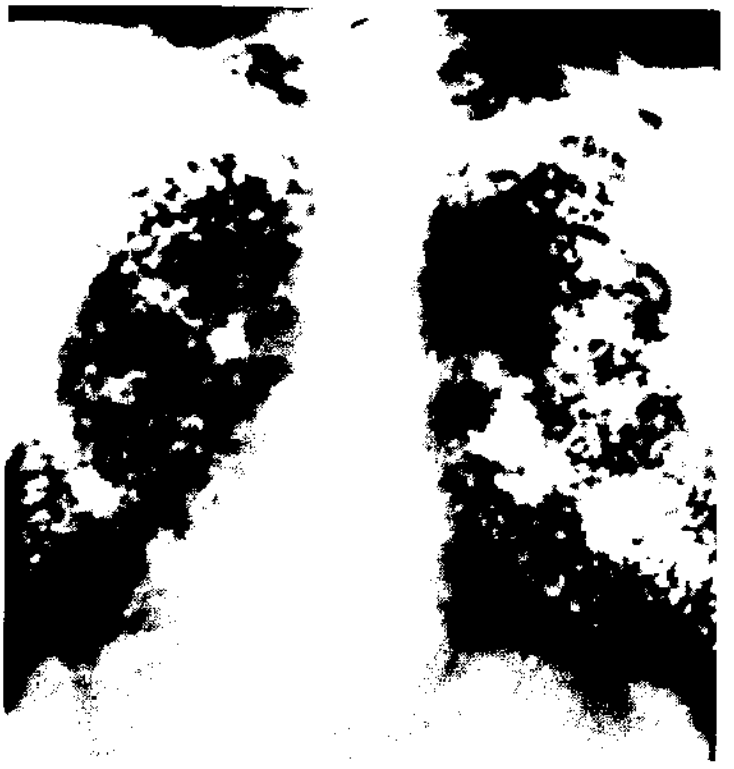

Figure II-43.

cells. There may, on occasion, be evidence of early granuloma formation, but no evidence of pulmonary fibrosis. These animal studies indicate that barium sulfate is a relatively inert substance which may cause mild tissue reaction but does not produce pulmonary fibrosis.

Clinical Description

Baritosis is symptomless and causes no abnormal physical signs. There are no symptomatic toxic effects because the baryte is a relatively insoluble, chemically inert substance.

Lung Function

No abnormalities of lung function have been recorded.

X-ray Appearance

There are discrete small opacities distributed throughout all the lung fields (see Figure II-43). They may develop with only a few months of dust exposure (9). Kerley B-lines are prominent and hilar lymph nodes are opaque but not enlarged. As in a case of siderosis, a very gradual clearing of opacities due to elimination of the dust may occur after cessation of industrial exposure (8)(13).

The outstanding feature of the x-ray is the intense radiopacity of the discrete opacities which are usually profusely disseminated throughout the lung fields (4). The appearance is always of a simple pneumoconiosis with no massive shadows. However, when the opacities are very numerous, they may almost appear confluent (12). Gambos described a background of fine, reticular, micronodular-sized opacities the size of fine sand with edges thin and sharp, contrasted and well outlined (5). In some series, the intensity and profusion of the shadows varied. The size of the shadows varied between 1-4 mm; most were 3 mm or smaller; an occasional shadow reached 5 mm (4). Nodules generally were irregular in shape, some being reticular or dendritic and occasionally round. The general distribution in the lung fields was usually uniform for the upper and lower lung fields (4). In earlier cases shadows were round and small (perhaps 1-2 mm in size) and less dense. There were no abnormalities of thoracic structure; hilar nodes were not enlarged; mediastinal distortion did not occur; and there were no adhesions or evidence of pleural thickening (4).

The presence of barytes within the lung is not known to have any adverse effects upon

health or life expectancy. On the other hand, toxic effects occur with exposure to the soluble forms of barium. There is currently no threshold limit value for barium dust classified as inert or as nuisance particulates by the American Conference of Governmental Industrial Hygienists (ACGIH).

Diagnostic Criteria

An accurate occupational history is necessary in order to diagnose barium pneumoconiosis. The marked density of opacities on chest x-ray should suggest the possibility of baritosis. When exposure to dust has been slight, or if there are only a few opacities, the x-ray may be confused with other causes of dense lung opacities. Among barytes miners where silica exposure is common, x-ray changes may be due to inhalation of silica dust (10).

Baritosis is rare among workers today, found usually in older or elderly workers who have left the industry years before. Sporadic new cases may occur, especially when men who were exposed to dust for a number of years have a chest x-ray taken for the first time (10).

Methods of Prevention

This is a rare condition. Usual procedures to reduce environmental dust levels are necessary. Soluble barium compounds should be handled carefully.

Research Needs

There are only a few reported cases of lung involvement in humans. Experimental studies on animals are limited. Further research in a multitude of areas seems appropriate.

Bibliography

1. Arrigoni, A.: La Pneumoconiosis da Bario. Clin Med Ital *64:*229, 1933.
2. Arrigoni, A.: La Pneumoconiosis da Bario. Med Lavoro *24:*461, 1933.
3. Browning, E.: Toxicity of Industrial Metals 2nd ed. New York: Appleton-Century-Crofts, 1969.
4. Doig, A.T.: Baritosis: A benign pneumoconiosis. Thorax *31:*30-39, 1976.
5. Gambos, B.: Pulmonary nodulation from inhalation of barium dust. Pracouni LeKarstui *9:*399, 1957.
6. Goodman, L. and Gilman, A.: The pharmacological basis of therapeutics, 2nd ed. New York: The Macmillan Company, 1956.
7. Huston, J., Wallach, D. P., and Cunningham, G. J.: Pulmonary reactions to barium sulfate in rats. AMA Arch Path *54:*430-438, 1952.
8. Levi-Valensi, P., Drif, M., Dat, A., and Hadjadj, G.: A'Propos de 57 observations de barrytose pulmonaire. J Fr Med Chir Thorac *20:*443-454, 1966.
9. Pancheri, G.: Su Alcune Forme di Pneumoconiosis Particolarmente Studiate in Italia. Medna Lav *41:*73-77, 1950.
10. Parkes, W. R.: Occupational Lung Disorders. London: Butterworth and Company, Ltd., 1974.
11. Pendergrass, E. P. and Greening, R. R.: Baritosis industr. Hyg Occ Med *7:*44-48, 1953.
12. Preti, L. and Talini, P. C.: La Pneumoconiosi de Bario Nel Quandro Radiologica, pp. 963-965. In Bericht U. den VIII. Internal Kongr fur unfallund und Berufskrakhiten Leipzig, 1939.
13. Spedini, F. and Valdin, P. L.: Contribute Allo Studio Della Pneumoconiosi da Barite. Radiologia Med *26:*1-31, 1939.
14. Tabershaw, I. R., Utidjian, H. M. D., and Kawahare, B. L.: Chemical Hazards, p. 131-443. In Occupational Diseases, U.S. Department of Health, Education, and Welfare, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health. Washington, DC: U.S. Government Printing Office, 1977.

COBALT

Introduction

Cobalt is a silver-gray, hard, brittle, magnetic metal obtained mainly as a by-product of other metals, especially copper and silver (1)(16). It is recovered from ores by smelting in blast furnaces and then precipitated out as cobalt hydroxide; this can be inhaled, resulting in an acute tracheobronchitis (1). It has not been adequately determined whether cobalt is capable of causing pulmonary fibrosis. Cases of pulmonary fibrosis in tungsten-carbide workers have been attributed to cobalt constituents.

List of Causative Agents (Manufacturing Processes)

Cobalt is recovered as a by-product from copper and silver mining. The most important primary minerals which contain cobalt are cobalite, smaltite, and linnalite (6). Cobalt is obtained when copper-cobalt ores are reduced in electric furnaces to a crude alloy which contains about 33% to 44% cobalt mixed with iron and copper (2). Digestion with hot sulfuric acid enables the copper to be removed to filtration and the ferrous sulfate to be oxidized (2). This is then precipitated with chalk and finally filtrated. Cobalt oxides are produced from the filtrate by adding sodium carbonate, leaching it with an ammonium chloride solution, and reducing it to the metal by heating in hydrogen at a temperature of 1,000°C. An electrolytic process can also be used since deposits of cobalt are harder than those of nickel (2).

List of Occupations and Industries Involved

Cobalt is used in the manufacture of alloys with chrome, nickel, aluminum, copper, beryllium, and molybdenum, especially in the electrical, automobile, and aircraft industries (2). Cobalt steels possess some of the properties of nickel and tungsten steel; its addition to steel improves cutting qualities of tools (2)(6). A major use of cobalt is in the manufacture of pigments, especially blues for coloring glass, enamel, pottery glaze, and paints (6). Cobalt alloys are found in jet engine parts; a cobalt-chromium molybdenum alloy, vitallium, is used in orthopedic surgery because of its resistance to corrosion from body fluids (6). Ferrous and non-ferrous cobalt alloys are utilized for making powerful magnets capable of lifting loads 60 times the weight of the magnet. Corrosion resistant steel containing cobalt is used for safety razor blades and surgical instruments. Cobalt is used as a binder for tungsten-carbides and similar hard cutting materials. Cobalt may be used as a catalyst for promoting the oxidation of vegetable oils in paints. Cobalt adds a hard and brilliant surface in electroplating. Radioactive cobalt has been used for treating breast cancer (2).

A list of occupations in which exposure to cobalt may occur include: Catalyst workers, ceramic workers, drug makers, electroplaters, glass colorers, nickel workers, paint dryer makers, porcelain colorers, rubber colorers, synthetic ink makers, magnet makers, and tungsten carbide workers (16).

Epidemiology

While there have been reports of respiratory symptoms and abnormal chest x-rays among workers in the tungsten carbide industry, opinion differs as to whether it is cobalt or tungsten carbide that is the toxic agent (2). A study by Lindgren and Ohman reported a worker who died with evidence of marked pulmonary fibrosis and bronchiectasis (8). The cobalt content of the working atmosphere dust was 2.8%. Higher concentrations of titanium and solfram were present; therefore, it was not possible to determine which dust component was actually responsible for the pulmonary fibrosis. Fairhall found no ill effect except conjunctivitis and upper respiratory irritation in workers exposed to cobalt dust (3). Miller and Davis reported three cases where chest x-rays showed increased perivascular and peribronchial markings and attributed this to cobalt (9). One case improved after removal from exposure (9). There is anecdotal data of similar cases showing clearing of chest x-rays within 18 months (9). These cases are probably due to hypersensitivity reactions. Only a few workers were affected and pure metallic cobalt did not produce similar changes.

Estimate of Population at Risk and Prevalence of Disease

It has been estimated by NIOSH that there are approximately 260,000 workers exposed to cobalt materials (19).

Pathology

Although cobalt is essential for animals' nutrition, it is probably not essential to plants (11). It is found in trace amounts in all plants except those growing on cobalt deficient soil (10)(11). Anemia develops in animals fed a cobalt-free diet; it is reversed by adding cobalt (2). Cobalt is important in the synthesis of vitamin B_{12} (12)(15)(18).

Acute pulmonary edema and hemorrhage occur after inhalation of metallic cobalt or intratracheal instillation of soluble salts in animals (2). Harding and Delahant found that cobalt metal dust was the most toxic component of the various mixtures of substances used in the tungsten-carbide industry (5). Repeated inhalations of a mixture of 75% tungsten carbide and 25% cobalt produced pulmonary lesions while tung-

sten carbide alone and other components of the mixtures did not. Schepers reported a bronchiolitis obliterans following intratracheal cobalt metal instillation. Cobalt oxide exposed animals developed interstitial pneumonitis and diffuse granulomatous pneumonia (13). Fibrosis of alveolar septa occurred along with bronchial and bronchiolar epithelial cell hyperplasia, bronchiolization of alveolar epithelium, marked metaplastic changes, and focal emphysema and/or atelectasis. Inhaled dust was phagocytized by alveolar macrophages. The degree of pulmonary changes in cobalt oxide exposed animals generally was a function of the cumulative exposure time and was not significantly affected by cigarette smoke. There was almost complete clearing by one year (14).

In order to explain the lower toxicity of cobalt oxide compared to cobalt metal, it was suggested that cobalt oxide is converted to hydroxyl groups in body fluid, whereas cobalt metal releases cobalt ions (14). It has also been suggested that the toxic effects of cobalt are related to interference with oxidative metabolism with fixation and loss of sulfhydryl compounds in tissue (4). Cysteine, interestingly, has a detoxifying effect on cobalt (4).

Kerfoot reported animal inhalation studies in miniature swines exposed to cobalt metal powder (7). Pulmonary function testing demonstrated a decrease in lung compliance while electron microscopy showed increased septal collagen accumulation. Wehner exposed hamsters to cobalt oxide and produced acute pulmonary changes (20). The concomitant addition of cigarette smoke significantly increased the incidence of tumors but not pneumoconiotic lesions. Histological sections showed chronic-inflammatory cell infiltration of the alveolar walls and focal accumulations of cobalt oxide adjacent to bronchial and vessel walls.

Clinical Description

While there have been reports of respiratory symptoms and abnormal chest x-rays among employees in the tungsten carbide industry, opinion on the actual incrimination of cobalt as the essential toxic agent is conflicting (2). Acute conjunctival irritation and cough from respiratory irritation may occur after exposure (3). An asthma syndrome has also been described (16).

Signs

There are no specific findings.

X-rays

In general, there is no specific x-ray anomaly reported for workers exposed to cobalt except perhaps the changes described as increased vascular or bronchial lung markings (9).

Diagnostic Criteria

There are no specific diagnostic criteria identifying cobalt exposed workers other than a complete occupational history.

Prevention

NIOSH has recommended a threshold limit value of cobalt of 0.05 mg/m^3 (17).

Research Needs

The role of immunologic factors in disease causation needs to be studied further. The role of cobalt in the pathogenesis of lung disease in tungsten carbide workers needs to be better defined.

Bibliography

1. Brady, G. S. and Clauser, H. R.: Materials Handbook, 11th ed. New York: McGraw-Hill Book Company, 1977.
2. Browning, E.: Toxicity of Industrial Metals, 2nd ed. New York: Appleton-Century-Crofts, 1969.
3. Fairhall, L. T., Castberg, H. T., Carrozzo, N. J., and Brinton, H. P.: Industrial hygiene aspects of the cemented tungsten carbide industry. JOM *4*:371, 1947.
4. Griffith, W. H., Pavcek, P. L., and Mulford, P. J.: The relation of the sulphur amino acids to the toxicity of cobalt and nickel in the rat. J Nutr *23*:603, 1942.
5. Harding, H. E.: Notes on the toxicology of cobalt metal. Br J Ind Med *7*:76-78, 1950.
6. Hunter, D.: The Diseases of Occupations. London: Hodder and Stoughton, 1975.
7. Kerfoot, E. J., Fredrick, W. G., and Domeier, E.: Cobalt metal inhalation studies on miniature swine. Am Ind Hyg Assoc J *36*:17-25, 1975.
8. Lindren, K. D. and Ohman, H.: Pneumokoniose in der hartmetallindustrie virchows. Arch Path Anat *325*:259, 1954.
9. Miller, C. W., Davis, M. W., Goldman, A., and Wyatt, J. P.: Pneumoconiosis in the tungsten carbide tool industry. Arch Industr Hyg *8*:453, 1953.

10. Monier-Williams, G. W.: Trace elements in food. London: Chapman and Hall, 1949.
11. Neal, W. M. and Ahmann, C. F.: Cobalt as an essential element in animal nutrition. Science *86:*225, 1937.
12. Rickes, E. L., Brink, N. G., Koniusky, F. R., Wood, T. R., and Folkers, K.: Vitamin B_{12}: A cobalt complex. Science *108:*134, 1948.
13. Schepers, G. W. H.: The biological action of cobaltic oxide. AMA Arch Industr Health *12:*124-126, 1955.
14. Schepers, G. W. H.: The biological action of particulate cobalt metal. AMA Arch Industr Health *12:*127-133, 1955.
15. Smith, E. L.: Presence of cobalt in the anti-pernicious-anemia factor. Nature *162:* 144, 1948,
16. Tabershaw, I. R., Utidjian, H. M. D., and Kawahara, B. L.: Chemical Hazards, p. 131-439. In: Occupational Diseases, DHEW (NIOSH) Publ No. 77-181 by U.S. Department of Health, Education and Welfare, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, Washington, DC: U.S. Government Printing Office, 1977.
17. Thiessen, J. W.: Director, Occupational and Environmental Health, personal letter to Vernon E. Rose, Director, Division of Criteria Documentation and Standards Development, National Institute for Occupational Safety and Health, Rockville, Maryland, September 12, 1978.
18. Trufanov, V. A.: Vitamin B_{12} (Cobalamin). Clin Chem *5:*335, 1959.
19. U.S. Department of Health, Education and Welfare, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, National Occupational Hazard Survey, Vol. III Survey Analysis and Supplemental Tables. Washington, DC: U.S. Government Printing Office, 1977.
20. Wehner, A. P., Busch, R. H., Olson, R. J. and Craig, D. K.: Chronic inhalation of cobalt oxide and cigarette smoke by hamsters. Am Ind Hyg Assoc J *38:*338-346, 1977.

SIDEROSIS

Introduction

Iron is a malleable silver-gray metal found throughout the world, but it does not occur in its native state except in meteorites. Inhalation of metallic iron or iron compounds causes siderosis, a condition first described by Zenker in 1866 (1). Siderosis is a relatively benign pneumoconiosis, characterized by large accumulations of inorganic iron containing macrophages in the lungs with minimal reactive fibrosis. In its pure form, the condition probably does not progress to true nodulation as seen with silicosis and is usually asymptomatic. Siderosis is known chiefly for the abnormal changes produced on chest x-rays.

When iron is inhaled in conjunction with other fibrogenic mineral dusts, pulmonary fibrosis results. This is referred to as mixed dust pneumoconioses or silicosiderosis (22). The entity known as hematite pneumoconiosis occurs in iron miners who are exposed to iron oxide in combination with free silica and silicates.

List of Causative Agents (Manufacturing Processes)

Iron is the most common commercial metal utilized in industry today. It melts at 1,525 °C and boils at 2,400 °C. Very small additions of carbon reduce the melting point. All commercially used irons, except ingot iron and electrolytic iron, contain some quantities of carbon which affect its properties. Iron containing more than 0.15% carbon is termed steel. Iron hardens when cooled suddenly from a red heat and when pure is very ductile. The addition of small amounts of sulfur (as little as 0.03%) causes it to become "hot-short" or brittle when red hot (3). As little as 0.25% phosphorous makes iron "cold-short" or brittle when cold. Iron is capable of forming carbonates, chloride, oxides, sulfides, and other compounds. It oxidizes easily under atmospheric conditions and is reactive to many acids. Reduced iron has special chemical uses and is made by reducing iron oxide by heating it in a stream of hydrogen.

Iron ores are iron-bearing minerals from which iron can be extracted on a commercial scale (3). Chief iron ores in order of importance are hematite, magnetite, limonite, and siderite.

The greatest producers are the United States, France, Russia, Great Britain, Brazil, and Germany. More than 90% of the iron ore mined in the United States is red hematite (Fe_2O_3) which theoretically contains 70% iron but usually not over 60%. Ores containing more than 50% iron are considered high grade. Pulverized hematite is used as a paint pigment, "Indian Red." Magnetite or magnetic iron ore ($FeO.Fe_2O_3$) is found in northern New York, New Jersey, and Pennsylvania and theoretically contains 62.4% iron; it also contains some nickel or titanium. A natural magnet known as lodestone is a magnetite.

Siderite, the chief ore in Great Britain, is an iron carbonate ($FeCO_3$) theoretically containing 48.2% iron, but perhaps more likely 35% iron. Limonite, or brown hematite ($2Fe_2O_3.3H_2O$) is formed by the water solution of other iron minerals, and theoretically contains 59.8% of iron but usually 30% to 55%.

Emery is a naturally occurring rock which contains approximately 50% aluminum oxide (corundum), 30% hematite or magnetite, and a remainder of complex aluminum salts (2). It is frequently used as an abrasive, although synthetic materials are now also used. Emery was used by ancient Egyptians for hollowing stone vessels and cutting stone blocks and has been used since classical times for polishing marble. A pneumoconiosis has been described in metal polishers using emery (2).

Silverware is polished with "rouge" or "crocus," both of which contain iron oxide powder. The powder is applied either by hand or by a mechanical polishing wheel called a "dolly." A type of siderotic lung disease found among silver polishers has also been described (20).

Ocher has important coloring properties and qualities with such varied industrial applications as manufacture of varnish, lacquer, and linoleum. Ocherous material consists of sand mixed with clay and ferrous oxide, the latter giving ocher its yellow color. The clay consists of iron silicates or a mixture of silicates of aluminum potash or soda. The percentage of pure silica in clay is variable, but typical ocher contains about 17% iron oxide, 51% silica, and 23% aluminum oxide. Individuals who work with ocher or handle ocherous materials are thus exposed to dust which is composed mainly of silica and iron (25).

Industries and Occupations Involved

Occupational exposures to iron occur during mining, transporting, and preparing of ores; during the production and refining of metals and alloys; or while using certain iron-containing minerals. Exposure to dust of metallic iron and iron oxide may occur in a number of industries and processes (23). Metal strips in iron and steel rolling mills are agitated causing the production of rust and iron-scaled dust.

Steel grinding generates metallic dust. Welding processes utilizing electric arc and oxyacetylene torches produce iron oxide fumes (7)(13). The fume concentration may be very high for welders working in confined and poorly ventilated spaces such as tanks, boilers, and hulls of ships. Polishing of silver and steel often requires using iron oxide powder in a finely divided state, usually a specifically pure form of ferric oxide referred to as "rouge" or "crocus" (1). Ferric oxide is also used to polish plate glass, stone, and cutlery. Occupations such as fetting, chipping, and pressing castings in iron foundries are particularly risky jobs for developing x-ray changes. Siderosis may occur alone, but many times iron is mixed with silica causing a mixed-dust fibrosis or typical silicosis. Boiler scalers clean fire boxes of flues and water tubes in enclosed spaces in boilers of ships, factories, and power stations. High concentrations of dust may be generated which contain iron and perhaps carbon in coal-fired but not oil-fired boilers. Silicate and small quantities of quartz may also be present from the coal utilization; while siderosis alone may be produced, mixed-dust fibrosis also occurs. Mining and crushing of iron ore is another occupational source of iron exposure (22). High concentrations of emery dust have been reported during the manufacture of emery cloth and papers, in the setting up of polishing wheels, mops, and abrasive paste, and as a wear-resisting component of concrete floors. Emery consists of fine crystals of aluminum oxide embedded in a matrix of iron oxide. It is an impure variety of the mineral corundum (Al_2O_3) which, next to diamond, is the hardest natural mineral known. Mining, pulverizing, and mixing natural minerals such as hematite, limonite, and magnetite may result in significant exposures (16)(20). Siderosis

may occur in workers who pulverize and mix natural pigments or prepare synthetic pigments (23).

Epidemiology

Prolonged inhalation of fumes originating from melting or boiling iron materials during arc welding or oxyacetylene cutting may result in siderosis (5-8)(11-13). In some reported cases, clinical impairment and abnormal pulmonary function tests have been reported (22). Silver polishers (1)(19), iron ore workers (9)(15)(22)(27), workers exposed to emery dust (2), foundry workers (11), magnetite workers (16)(20) and others (25) may develop siderosis secondary to prolonged exposure to various iron-containing materials. In general, pulmonary fibrosis occurs only when there is an associated fibrogenic dust component, such as silica, also present in the work environment (See section on mixed dust pneumoconioses).

Estimate of Population at Risk and Prevalence of Disease

NIOSH estimates approximately 5 million individuals are currently exposed to iron and iron compounds (28). This includes approximately 2,700 iron ore miners and more than 4 million other workers exposed to iron oxides. The prevalence rate for siderosis among welders was reported to be 17.6 per hundred in a survey at a Sheffield steel foundry (11). The mean age of disease onset was 46.4 years with the majority of cases occurring in individuals 40 years of age and older; cases were also reported in workers less than 35 years of age. In the same study, the mean onset age for silicosis was 52.2 years. Average years of exposure was 21.9 years for welders with siderosis, 31.7 years for workers with silicosis, and 33 years for individuals with coal workers' pneumoconiosis. Hunnicutt, et al. reported x-ray changes occurred in 34% of electric arc welders (14). Data on prevalence of disease is not available for other occupational causes of siderosis.

Pathology

In the pure form of siderosis, gross pathologic examination demonstrates no obvious underlying fibrotic disease. The visceral pleural surface is rust or brick-red in color. The lung, when cut, has a brownish surface on which are superimposed darker macular areas 1-4 mm in diameter. In some areas it is difficult to identify individual macules, many appearing to blend together or with surrounding pigmented lung tissue.

Microscopically, iron particles are seen to accumulate mainly around small vessels and bronchioles. When the dust burden is large many alveoli may be completely filled with brown pigmented macrophages containing iron. Iron may also lie free within alveolar spaces. There may be a slight reticulin response to the dust, but even in the presence of large quantities of iron pigment, fibrosis is notable by its absence (23).

Hematite Miner's Lung

Lung disease has been particularly prevalent among hematite miners since the introduction of the pneumatic drill in 1913. Hematite pneumoconiosis results from the inhalation of dusts from pulverized siliceous rock containing both iron and free silica particles (26). Stuart and Faulds divided the hematite lung into three pathologic types: diffuse, nodular, and massive fibrotic (27). The diffuse variety is characterized by a brick-red colored lung surface with superimposed darker dust foci and surrounding centrilobular emphysema. It has been likened to the simple form of coal workers' pneumoconiosis (26). The nodular type is characterized by dark, reddish-black fibrous nodules up to 1 cm in diameter located primarily in the upper zones of the lung. Thickening of the pleura was noted in many cases. Microscopically, the lesions have a concentrically whorled collagenous center surrounded by iron containing macrophages and thus closely resemble silicosis. The legions of massive fibrosis in hematite lung are similar to those seen in coal workers' pneumoconiosis and silicosis. They are usually confined to the upper lobes and have sharply demarcated borders. Dense pleural adhesions are common and the fibrotic mass may encroach and obstruct pulmonary vessels and bronchi.

In general, the greater the amount of pulmonary fibrosis, the greater the lung tissue silica content (9).

Other Pneumoconioses Characterized by Heavy Exposure to Iron Containing Dusts

A type of pneumoconiosis has been described in lungs of silver polishers exposed to large amounts of iron oxide (rouge) in polishing material. The lesions included massive fibrosis despite the absence of silica in the dusts (1)(26). Pulmonary lesions have also been described in other workers simulating nodular silicosis, with

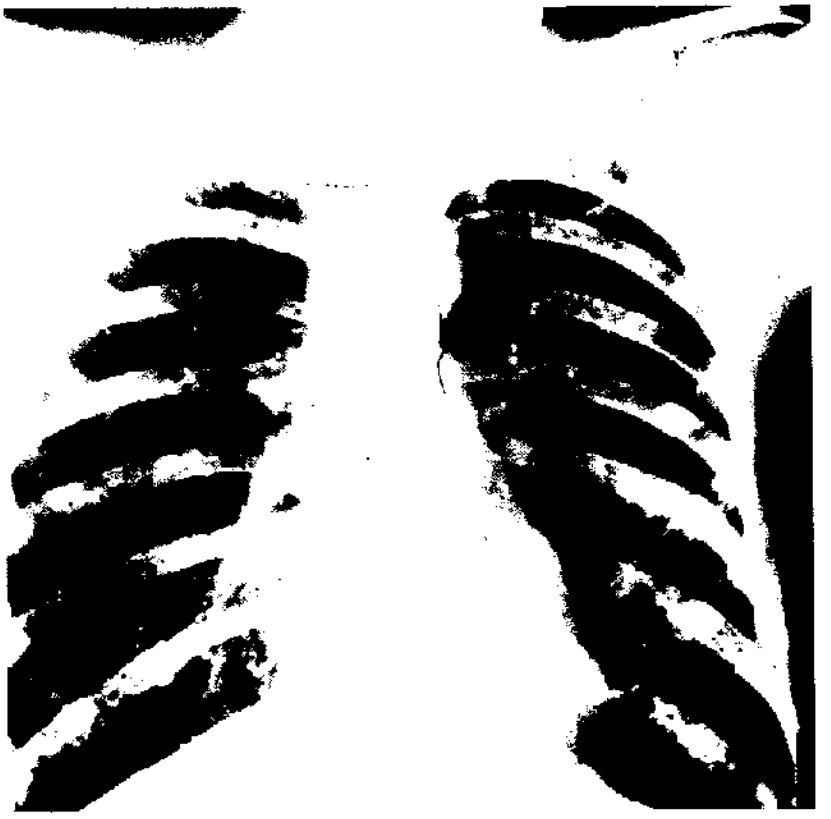

Figure II-44
Source: Morgan and Kerr (21).

extensive fibrosis and necrosis (25).

A number of investigators have described postmortem changes in electric arc welders (5)(6)(8)(12)(13)(17)(18). On gross examination, the lungs are dark and appear anthracotic. Microscopically, the perivascular and subpleural alveoli are filled with macrophages loaded with coarse black granules of iron oxide. In the majority of cases examined, pure iron oxide alone was not thought to be responsible for the fibrosis (7)(13). X-ray changes noted in arc welders are caused by radiodense iron-oxide deposits within alveolar, septal, and perivascular walls.

Morgan and Kerr obtained lung biopsies in four welders with siderosis (21). There was an absence of fibrosis despite the presence of large amounts of iron in the distal air passages and lymphatics. The iron content of lung tissue was reported to be 15 to 20 times greater than normal values. It appears that the nodular x-ray appearance resulted from the deposition of iron in the perivascular lymphatics (see Figure II-44).

Levy and Margolis reported a case of a gas-torch cutter with siderosilicosis, diffuse interstitial fibrosis, and highly atypical alveolar epithelium (17). Studies of lung tissue from an autopsy of a 58-year-old arc welder with arc welder's pneumoconiosis emphasized the diagnostic usefulness of scanning electron microscopy combined with backscattered electron imaging and x-ray analysis for *in situ* identification of mineral dusts (12).

Clinical Description

Diagnosis is largely dependent on obtaining an appropriate occupational history, demonstrating airborne iron dust in the work environment, and obtaining a chest x-ray compatible with the findings of siderosis. The worker is rarely symptomatic and usually is unaware of his disease until the chest x-ray is obtained. The changes noted on x-ray may be difficult to distinguish from simple silicosis (22). Nodular opacities are well circumscribed but may appear more radiodense than typical silicotic nodules. Aggregation of nodular shadows does not occur, and the x-ray shadows may resolve if there is no

further exposure to iron oxide dust. Pulmonary function tests are rarely abnormal (22).

Diagnostic Criteria

Diagnosis is dependent upon an appropriate occupational history which documents the iron oxide dust and the characteristic chest x-ray findings. The recent application of magnetopneumography to the study of the pneumoconioses may be a valuable tool for the documentation and quantification of ferromagnetic mineral dusts in human lungs (10).

Methods of Prevention

The siderosis that occurs in welders is usually seen in those individuals who work indoors in poorly ventilated workrooms. Exposure can be reduced by proper ventilation or by having the employees work outside. In general, control of dust levels requires the same procedures and techniques described for silica.

Research Needs

More sophisticated physiologic testing, including measurement of the lung's mechanical properties, is required to better document lung function changes that may occur following inhalation of iron-containing dusts. *In vitro* studies or animal experimentation might be helpful in determining dose-response relationships, understanding lung clearance mechanisms for iron, and elucidating any fibrogenic properties of various ferrous compounds.

Bibliography

1. Barrie, H. J. and Harding, H. E.: Argrosiderosis of the lung in silver finishers. Br J Ind Med *4:*225-228, 1947.
2. Bach, A. O., Kipling, M. D., and Zundel, W. E.: Emery pneumoconiosis. Transactions of the Association of Industrial Medical Officers *15:*110-115, 1965.
3. Brady, G. S. and Clauser, H. R.: *Materials Handbook*, 11th ed., New York: McGraw-Hill Book Company, 1977.
4. Byers, P. D. and King, E. J.: Experimental infective pneumoconiosis with mycobacterium tuberculosis (Var. Muris) and haematite by inhalation and by injection. J Pathol Bact *81:*123-134, 1961.
5. Charr, R.: Pulmonary changes in welders. Ann Intern Med *44:*806, 1955.
6. Charr, R. Respiratory disorders among welders. Am Rev Tuberc *71:*877, 1955.
7. Doig, A. T. and McLaughlin, A. I. G.: X-ray appearances of the lung of electric arc welders. Lancet *1:*771-775, 1936.
8. Enzer, N. and Sander, O. A.: Chronic lung changes in electric arc welders. J Ind Hyg Toxicol *20:*333-350, 1938.
9. Faulds, J. S. and Nagelschmidt, G. S.: The dust in the lungs of haematite miners from Cumberland. Ann Occ Hyg *4:*225-263, 1962.
10. Freedman, A. P., Robinson, S. E., and Green, F. H. Y.: Magnetopneumography as a tool for the study of dust retention in the lungs. In *Inhaled Particles*, Vol. 5, W. H. Walton, Ed. Oxford: Pergamon, in press.
11. Gregory, J.: A survey of pneumoconiosis at a Sheffield steel foundry. Arch Environ Health *20:*385-399, 1970.
12. Guidotti, T. L., Abraham, J., DeNee, P. B., and Smith, J. R.: Arc welders' pneumoconiosis—application of advanced scanning electron microscopy. Arch Environ Health *33:*117—124, 1978.
13. Harding, H. E.: Clinical radiographic and pathological studies of the lungs of electric arc and oxyacetylene welders. Lancet *2:*394-398, 1958.
14. Hunnicutt, T. N., Cracovaner, D. J., and Mylers, J. T.: Spirometric measures in welders. Arch Environ Health *8:*661-669, 1964.
15. Jaiswal, A. K., Kaw, J. L., Rahman, Q., Viswanathan, P. N., and Zaidi, S. H.: Pulmonary response to haematite dust: A biochemical and histopathological study in guinea pigs. Industr Health *15:*117-122, 1977.
16. Kleinfeld, M., Messite, J., and Shapiro, J.: A clinical roentgenological and physiological study of magnetite workers. Arch Environ Health *16:*392-397, 1968.
17. Levy, S. A. and Margolis, I.: Siderosilicosis and atypical epithelial hyperplasia. JOM *16:*796-799, 1974.
18. Mann, B. T. and Lecutier, E. R.: Arc welders' lung. Br Med J *2:*921, 1957.
19. McLaughlin, A. I. G., Grout, J. L. A., Barrie, H. J., and Harding, H. E.: Iron oxide dust and the lungs of silver finishers.

Lancet *1*:337-341, 1945.
20. Morgan, W. K. C.: Magnetite pneumoconiosis. JOM *20*:762, 1978.
21. Morgan, W. K. C. and Kerr, H. D.: Pathologic and physiologic studies of welders siderosis. Ann Intern Med *58*:293-304, 1963.
22. Morgan, W. K. C. and Seaton, A.: *Occupational Lung Disease*. Philadelphia: W. B. Saunders Co., 1975.
23. Parkes, W. R.: *Occupational Lung Disease*. London: Butterworths and Co., LTD, 1974.
24. Pendergrass, E. and Leopold, S. S.: Benign pneumoconiosis. JAMA *127*:701-705, 1945.
25. Roche, A. D., Picard, D., and Vernhes, A.: Silicosis of ocher workers. Am Rev Tuber *77*:839-846, 1958.
26. Spencer, H.: *Pathology of the Lung*, 2nd ed. Oxford: Pergamon Press, 1968.
27. Stewart, M. J. and Faulds, J.S.: The pulmonary fibrosis of haematite miners. J Pathol Bact *39*:233-253, 1934.
28. U.S. Department of Health, Education and Welfare, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, National Occupational Hazard Survey, Vol. III. Survey Analysis and Supplemental Tables, Washington, DC, U.S. Government Printing Office, December, 1977.
29. Zaidi, S. H., Dogra, R. S., Sahu, A. P., Khana, S., and Shanker, R.: Experimental infective pneumoconiosis: Effects of Canadia albicans and iron ore dust on the lungs of guinea pigs. Industr Health *15*:123-129, 1977.

SILVER

Introduction

Silver (Ag) is a white, very malleable and ductile metal which is classified as a precious metal. The chief effect of excessive silver absorption is argyria, the local or generalized impregnation of tissue with silver. This normally does not produce a recognizable disturbance of health. The inhalation of dust containing silver may result in pathologic changes by combining with proteins in the lung and causing the elastic tissue to be stained black. Because of this, silver is regarded as a form of pneumoconiosis, although no clinical, physiologic, or x-ray changes occur in individuals exposed.

List of Causative Agents (Manufacturing Processes)

Silver is present in many ores, the most important being argenite (Ag_2S). It is estimated to be present in the earth's crust in amounts of about 0.1 gm per ton (3). Copper, lead and zinc ores frequently contain small amounts of silver. In fact, about 70% of all production of silver is a by-product of the refining of these metals. Mexico and the United States produce more than half of the silver in the world (2). Nearly 99% of the silver is produced in Arizona where it originates from copper ore; most silver produced in California is a by-product of gold quartz mining.

Silver can be extracted from ores by a cyanide process in which the crushed ore is ground into cyanide solution, the resultant pulp agitated by jets of compressed air, and the silver precipitated by the addition of a zinc dust emulsion (3). A second method is based on the greater affinity of zinc than lead for silver present in lead-silver ores. There is also an electrolytic process where silver is recovered from the anode slimes obtained in electrolytic lead refining (3).

Because silver is such a soft metal, it is not normally used in industry in its pure state; it must be alloyed with a hardener, usually copper. Sterling silver is the name given to a standard high-grade alloy containing a minimum of 925 parts silver per 1,000.

List of Occupations and Industries Involved

Silver has many uses including: the manufacture of silverware and jewelry; in alloys with copper to increase strength and hardness; with aluminum in the manufacture of scientific instruments; with cadmium and copper in automobile bearing alloys; with lead to increase corrosion-resistance to sulfuric acid; with lead and antimony in grids for storage batteries; and with chrome-nickel and steels, especially steel dies (3). It is also used in solders and brazing alloys; as bearing linings in air-cooled aircraft engines; in manufacturing pipes and valves; in pasteurizing coils and nozzles; in milk, cider, and brewing trades; in the acetate rayon silk industry; in application of metallic film in glass and ceramics; as an electroplated undercoating for nickel and chrome; in photography; and as a bactericide (3). Jewelers' rouge is used for polishing and the dust

generated during polishing consists of silver and iron oxide particles (9). Silver is also used as busbars and winding in electrical plants, in dental amalgams and as a chemical catalyst in the synthesis of aldehydes (10). Some of the compounds are of medical importance as antiseptics or astringents and in the treatment of certain diseases, particularly in veterinary medicine.

Some occupations in which exposure may occur include:

alloy makers
ceramic makers
chemical laboratory workers
drug makers
food product equipment makers
hair dye makers
ivory etchers
organic chemical makers
silver polishers
bactericide makers
coin makers
dental alloy makers
electric equipment makers
glass makers
hard solder workers
mirror makers
photographic workers
water treaters

Epidemiology

There are only individual cases of argyria reported and only limited epidemiologic studies.

Estimate of Population at Risk and Prevalence of Disease

There are probably too few workers to provide any estimate of any accurate prevalence or population at risk, although estimates from census data and disease prevalence studies suggests that there are potentially 60,000 exposed workers.

Pathology

No human pathological material has been adequately described. Implantation of small silver particles into the skin may cause permanent skin discoloration (10). Silver nitrate dust can cause skin irritation, as well as conjunctival burns leading to blindness (10). There may be resultant pigmentation of the skin, eyes, nasal septum, and tonsillar pillars. Once silver enters the body, very little is excreted (10). Studies on the occurrence of argyria following injection of silver arsphenamine reveals development of observable disease with a total dose of 0.9 gms of silver (10). Argyria may develop in workmen who inhale or handle silver oxides or salts (nitrate, fulminate, or cyanide) (10). In workmen who are affected, there are no constitutional symptoms, but there may be permanent pigmentation of skin and eyes. When biopsies of nasal or bronchial tissue have been made, tissues have been found to be heavily laden with particles of silver salts which have also been noted to be scattered along lymphatics (3). Additionally, the bronchial mucous cells have revealed basal membrane deposits.

The inhalation of metallic silver by silver finishers using "rouge" (an iron oxide) caused a fine granular pigmentation of the elastic fibrils in the alveolar walls (7). Hardin described a 63-year-old man who spent all of his working life as a silver finisher (6). At autopsy, histology sections of lung tissue showed some subpleural and periarterial fibrosis. A great deal of pigment was present in and around the areas of fibrosis, some within alveoli. There were perivascular aggregates that showed no fibrosis. Incinerated sections of lung tissue showed that most of the pigment was iron, but with silver deposited on elastic laminae. The amount of silica seen by polarized light was small and appeared to be no more than in normal controls. Chemical examination of lungs show that ash constituted 8.38%; iron (Fe_2O_3) 3.5%; total silica 0.22%; free silica nil; and silver (as metal) 0.36% of the dry weight (6). It was suggested this worker was particularly sensitive to the presence of the inhaled iron oxide which caused the pulmonary fibrotic changes. However, the amount of fibrosis in the lungs was small and the fibrotic areas, noted only on microscopic examination, were well separated.

There have been other reports of silver finishers in which heavy loading with iron oxide was not accompanied by pulmonary fibrosis (1)(7). Furthermore, iron oxide used in the finishing of silver and silver-plated articles did not produce fibrosis in the lungs of experimental animals (3)(4)(5).

Clinical Description

There are no clinical signs, symptoms, or specific chest x-ray findings that result from the

inhalation of silver. Diagnosis is made by occupational history and by noting the discoloration that may occur on the skin and mucous membrane of conjunctiva. Characteristically, the workmen's faces, hands, and arms develop a dark slate-gray color which is uniform in distribution and varies in depth depending on the degree of exposure. There may also be discoloration of the fingernails, bronchial mucosa, and toenails. Covered parts of the body are affected to a lesser degree by the discoloration process (10). Dust may be deposited in the lungs and produces no fibrosis. There is no specific treatment for this condition.

Diagnostic Criteria

Diagnosis depends on an occupational history and the presence of skin, mucous membranes, and conjunctiva discoloration. Chest x-ray is not abnormal. Urine silver analysis is not helpful because very little silver is excreted in the urine. Argyrosis of the respiratory tract with generalized argyria has been described in two men who were employed in the manufacture of silver nitrate (8). There were symptoms of mild chronic bronchitis, but there was no discoloration of the skin, eyes, or mouth. Nasal mucosa showed bilateral symmetrical dark pigmentation of the walls of the middle and upper regions. In the more severe case, bronchoscopy showed isolated plaques of pigmentation at the tracheobronchial bifurcation and uniform zones of greyish-yellow coloration around the orifices of the smaller bronchi, but the intermediate bronchi remained free. Biopsy of the nasal or bronchial mucous membrane demonstrates deposition of silver.

Research Needs

More studies are necessary, but may be limited because of the cost of conducting animal experimentation.

Bibliography

1. Barrie, H. J. and Harding, H. E.: Argyrosiderosis of the lungs in silver finishers. Br J Ind Med *4:*225-228, 1947.
2. Brady, G. S. and Clauser, H. R.: Materials Handbook, 11th ed. New York: McGraw-Hill Book Company, 1977.
3. Browning, E.: Toxicity of Industrial Metals, 2nd ed. New York: Appleton-Century-Crofts, 1969.
4. Harding, H. E.: Fibrosis in the lungs of a silver finisher. Br J Ind Med *5:*70-72, 1948.
5. Harding, H. E.: Radiographic and histological appearances of the rat lung after intratracheal injection of roughe (Fe_2O_3). Br J Ind Med *2:*32-35, 1945.
6. Harding, H. E., Grout, J. L. A., and Lloyd-Davies, T. A.: the experimental production of x-ray shadows in the lungs by inhalation of industrial dusts. I. Iron Oxide. Br J Ind Med *4:*223-224, 1947.
7. McLaughlin, A. I. G., Grout, J. L. A., Barrie, H. J., and Harding, H. E.: Iron oxide dust and the lungs of silver finishers. Lancet *1:*337-341, 1945.
8. Montaudon, M. A.: Argyrose de la voie respiratoire, Arch Mal Prof *20:*419, 1959.
9. Morgan, W. K. C. and Seaton, A.: Occupational lung diseases. Philadelphia: W. B. Saunders Company, 1975.
10. Tabershaw, I. R., Utidjian, H. M. D., and Kawahara, B. L.: Chemical Hazards, p. 131-439. In Occupational Diseases DHEW (NIOSH) Pub. No. 77-181 by U.S. Department of Health, Education, and Welfare, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health. Washington, DC: U.S. Government Printing Office, 1977.

MIXED DUST PNEUMOCONIOSES (Iron and Other Compounds and Silica)

Introduction

Mixed dust fibrosis—a term first coined by Uehlinger in 1946 and adopted by Harding, Gloyne, and McLaughlin in 1950—is applied to pulmonary lesions caused by the inhalation of silica dust (or a fibrogenic dust) in combination with other (usually nonfibrogenic) dusts (7). Mixed dust fibrosis does not include lung disease which occurs when the dusts are inhaled separately and at different times. In the majority of instances, dusts of iron or its compounds are inhaled along with silica. The term nonferrous refers to alloys containing a copper (brass, bronze, and gunmetal), aluminum, or magnesium base.

List of Causative Agents (Manufacturing Processes)

Mixed dust pneumoconioses occur in industries where there is exposure to dust combinations. This includes crystalline silica in combination with nonfibrogenic dusts; iron and iron products; and brass, bronze, aluminum, or other nonferrous alloys.

List of Occupations and Industries Involved

Mixed dust pneumoconioses occur in industries where there is exposure to both free silica and to iron or iron products. This includes iron, steel, and nonferrous foundries; hematite mining; cleaning and scaling of boilers; electric arc welding and oxyacetylene cutting (when concomitant exposure to silica dust is present); and potteries (14).

Epidemiology

Steam-driven ships periodically require docking in order to have their boilers scaled and cleaned. Men employed full time in this occupation must work in confined spaces, crawling along with lamps and hammers, chipping off scales as they go, and often working in a hot atmosphere (8). Considerable amounts of dust are created from the breaking off of scales deposited in the boilers and from flue dust in the fire tubes originating from the use of coal and other fuels. Silica content of flue dust has ranged between 6.1% and 26.4% (3)(10). Pneumoconioses has been reported in these workers (8).

Brass and bronze molders and casters working with sand molds may inhale mixtures of dust sand fumes (9). The sand that is used has a lower free silica content (about 80%) than the sand used for steel casting (about 95%), because the temperatures used for nonferrous metals are lower than those used for steel and iron and the melting temperatures are different. Fettlers who remove burnt-on sand from castings have significant dust exposures. High levels of dusts are also generated during the application of parting powders and molding dress, exposing molders and casters who perform this work. Before 1950, parting powders had high silica concentrations (9). There are other exposures including dusts and fumes of various metal oxides including zinc, tin, and lead. It has been reported that mixed dust fibrosis occurs sooner in iron fettlers than brass fettlers because the melting temperature of iron is higher than that of brass and there is, therefore, more burnt-on sand found on iron castings (9).

Estimation of Population Exposed

The 1976 Metal Casting Industry Census Guide reported that there were 4,938 foundries in the United States employing 490,000 people with a total capacity for producing 33,700,000 tons/year of ferrous and nonferrous castings (5). Of the large numbers of foundry men casting ferrous alloys, almost half of them worked in foundries employing 100 and 500 people, while the majority of nonferrous foundry men worked in foundries employing less than 100 people (5).

Pathology

In mixed dust pneumoconioses, the gross appearance of the lungs reveals a thickened pleura, possibly with evidence of underlying fibrotic masses and occasionally bullae. On sectioning the lung, punctate, irregular, or stellate-shaped areas of fibrosis are noted which vary in size from 3-4 mm. Occasionally larger and more confluent masses are seen, but typical silicotic nodules are not seen. When changes similar to progressive massive fibrosis occur, the lesions are pigmented brick-red color in contrast to the black-pigmented lesions of coal workers' pneumoconiosis. The varying sized lesions are more numerous in the upper lobes.

On microscopic examination, particles of iron and silica are identified accumulating within alveolar walls and adjacent to respiratory bronchioles and small arteries. (Also see Pathology section of Siderosis chapter page 423.) The amount of pulmonary fibrosis occurring seems to be determined by the amount of quartz present. Fibrotic lesions are seen surrounding bronchioles and small vessels. There may be obliteration of surrounding alveoli. Individual fibrotic lesions are irregular in shape, perhaps stellate-shaped, and are not concentrically nodular such as seen in silicosis. The lesions have a characteristic "Medusa head" picture (14). When silicotic nodules are present, the nodular components are said to appear immature (14). In addition to quartz dust, carbon, iron, and other metallic dust particles are present in large quantities within lung tissues. When progressive massive fibrosis lesions occur, they contain a great deal of dust which is randomly arranged and extra-cellular in location (4)(13)(14). Contraction and distortion of tissue may produce irregular emphy-

sematous scars and bullae. In hematite miners, the lung tissue contains hematite, silica, and mica (4)(14). Silica makes up perhaps 4% of the total dust with greater quantities noted in lungs containing more fibrosis (4).

Mixed dust fibrosis appears to be a modification of the effects of small quantities of free silica by the accompanying nonfibrogenic dust. Iron oxides, for example, have been shown to inhibit the fibrogenic effects of quartz (11). Hematite produced no fibrosis when administered to experimental animals (1). Organic iron (as ferritin) engulfed by alveolar macrophages may shorten a cell's life and cause disruption of the cell and release of collagen-stimulating substances (2). It is not clear whether iron influences collagen formation but, experimentally in mixtures, it inhibits the fibrogenic potential of quartz (14).

Nagelschmidt examined 144 lungs with mixed dust fibrosis and reported that the concentration of iron oxide per pair of lungs varied between 9-45 gms (13). The average lung dust composition was approximately 80% hematite, 5% quartz and 15% mica. The amounts of dust found in the lungs with massive fibrosis ranged between 30-85 gms, perhaps two to three times as high as the dust content of the lungs of coal miners. Gerstel found that the total iron oxide content of the lungs of silicotic coal miners, lead and zinc miners, iron ore miners, and ceramic workers ranged between 0.4-5 gms (6). In some cases of fibrosis there may be as much as 100 gms of dust with little or no silica (13).

In order to demonstrate the relationship between the total dust and quartz concentration, Nagelschmidt plotted the average amount of quartz against the average amount of total dust in lungs of individuals who died with pulmonary fibrosis (13). Included were coal miners, foundry workers, hematite miners, and quartz-free massive fibrosis.

Mixed dust fibrosis accompanied by areas of focal emphysema are common findings in nonferrous (mainly brass) foundry workers as well as iron and steel foundry workers (9). Whorls of silicotic nodules are occasionally found. There is a rough correlation between the percentage of free silica present and the amount of fibrosis.

Clinical Description

The clinical picture of mixed dust fibrosis is similar to that found in nodular silicosis.

Nodular opacities appear on chest x-rays resembling silicosis or coal workers' pneumoconiosis. When larger opacities occur, they are usually found in upper and mid zones and may, on occasion, be confused with tuberculosis. Large, well-circumscribed opacities similar to conglomerate masses in complicated silicosis rarely occur. Calcification does not occur in lesions unless caused by tuberculosis and egg-shell calcifications of hilar lymph nodes are seen. Small radiodense opacities may also be present in iron foundry workers or occupations where iron dust is inhaled (7)(12)(14).

In siderosis, as in nonfoundry welders, silver finishers, etc., aggregation of nodular shadows is not seen (12). The x-ray shadows even resolve if there is no further exposure to iron oxide dust (16). By contrast, in mixed dust fibrosis, when nodular shadows are seen, the lesions may coalesce and remain even if workers are removed from exposure.

Diagnostic Criteria

Diagnosis is dependent upon an appropriate occupational history which documents the mixtures of dust, especially iron and silica, and the characteristic chest x-ray findings.

Prevention

This is much the same as in silicosis.

Research

Well controlled epidemiologic studies accurately documenting environmental dust mixtures are needed. Animal and *invitro* studies comparing the effects of ferrous and nonferrous materials on the fibrogenic properties of silica seem appropriate. Newer developments in alveolar macrophage technology would allow proper investigations of the effects of mixed dusts on these cells.

Bibliography

1. Byers, P. D. and King, E. J.: Experimental infective pneumoconiosis with mycrobacterium tuberculosis (var Muris) and haematite by inhalation and by injection. J Pathol Bact *81:*123-134, 1961.
2. Chvapil, M. and Huyrch, J.: Control of collagen biosynthesis. In: International Review of Connective Tissue Research, Vol. 4, D. A. Hall, Ed., New York Academic Press, p. 97, 1968.
3. Cooke, W. E.: Pneumoconiosis due to flue dust. Br Med J *2:*816-817, 1930.

4. Faulds, T. S. and Nagelschmidt, G. S.: The dust in the lungs of haematite miners from Cumberland. Ann Occup Hyg *4*:225-263, 1962.
5. Foundry Management and Technology, Metal Casting Industry Census Guide. Cleveland, Ohio: Penton/i.p.c. Penton Plaza, 1976.
6. Gerstel, Arch Gewerbepath. Gewerbehyg, *10*:616, 1941.
7. Harding, H. E., Gloybne, S. R., and McLaughlin, A. I. G.: Industrial lung disease in iron and steel foundry workers, A. I. G. McLaughlin, Ed., London: HMSO, 1950.
8. Harding, H. E. and Massie, A. P.: Pneumoconiosis in boiler scales. Br J Ind Med *8*:256-264, 1951.
9. Harding, H. E. and McLaughlin, A. I. L.: Pulmonary fibrosis in non-ferrous foundry workers. Br J Ind Med *12*:92-99, 1955.
10. Harding, H. E., McRae Tod, D. L., and McLaughlin, A. I. G.: Br J Ind Med *1*:247, 1944.
11. Kettle, E. H.: The interstitial reactions caused by various dusts and their influence on tuberculous infections. J Path Bact *35*: 395-405.
12. McLaughlin, A. I. G. and Harding, H. E.: Pneumoconiosis and other causes of death in iron and steel foundry workers. AMA Arch Ind Health *14*:350-378, 1956.
13. Nagelschmidt, G.: The relation between lung dust and lung pathology in pneumoconiosis. Br J Ind Med *17*:247-259, 1960.
14. Parkes, W. R.: Occupational Lung Disorders, London: Butterworths and Co., Ltd., 1974.

MISCELLANEOUS PULMONARY REACTIONS

Bakolite Pneumoconiosis

Bakolite is a phenolic plastic obtained by the polymerization of phenol and formaldehyde by heat and pressure (17). It has multiple industrial uses, but is particularly used in electric and telephone equipment. There are several reports of nodular chest x-ray changes occurring in workers exposed to bakolite dust along with other organic dust (1)(17). Pulmonary granulomatous lesions have been reported in two workers exposed to bakolite dust (17). One was a cabinet maker exposed to bakolite dust during a polishing procedure of exotic wood for three years; the second was exposed for 15 years to bakolite objects used for electrical appliances. Chest x-ray showed bilaterally diffuse mottling and enlarged hilar lymph nodes. One case showed evidence of interstitial fibrosis. On pathological examination there were sarcoid-like granulomas noted. The granulomas were characterized by intracellular inclusions which gave a positive chemical reaction for phenol compounds. In an animal model, pulmonary fibrosis was noted to develop (17). Further studies are necessary in order to determine the significance of these findings.

Manganese

Manganese is a silvery-white metal but as usually prepared is reddish-gray in color, brittle, and intensely hard. The most important ore is pyrolusite or black dioxide (MnO_2). Less important manganese minerals include: braunite, Mn_2O_3 H_2O and hausmannite, Mn_3O_4. It also occurs as a sulfide (hauserite) in a manganese blend; as a carbonate in managesestat; and as a silicate in tebhrorite, kneblite, and rhodomite (6).

Manganese is widely distributed in the earth's crust and is calculated to be the twelfth most abundant element (25). Chief countries supplying ores are Russia, India, South Africa, Ghana, Brazil, and Morocco. The ores found in the United States are of low grade quality (6). The mining of manganese can result in significant dust exposure, particularly during drilling with pneumatic drills (25). Grinding of ores is responsible for a great number of manganese poisoning cases (25).

Manganese is used in steel manufacturing and as a part of alloys with copper, aluminum, magnesium, and iron. More than 90% of the manganese used in the United States is found in the production of steel and iron (25).

Poisoning has been reported to occur among workers making ferromanganese alloys; during crushing and screening of ferromanganese; and among arc welders burning steel containing low concentrations of manganese (25). Crane operators in a vicinity of manganese ore smelting may also be affected. Manganese dioxide ores are used in the chemical industry for the production of hydroquinone, potassium permanganate and manganese sulfate. Manganous oxide (MnO) is added to animal and poultry feed. Dry-cell batteries use manganese dioxide as a depolarizer in a cell

for the readily obtained oxygen it contains. Cases of poisoning have occurred among workers in the dry-battery industry (8). Chemicals containing manganese are used in the ceramics industry to color glass, face brick, and ceramic products. Welding rods and fluxes contain manganese. Manganese dioxides and other compounds are used in the manufacture of dyes, paints, varnish, dryers, fungicides, and pharmaceuticals. Manganese compounds may be added to chemicals used as smoke inhibitors, as additive to fuels, and as oil and anti-knock additives to gasoline supplementing lead anti-knock compounds.

It has been estimated by NIOSH that approximately 168,000 workers are exposed to manganese compounds (26).

The two major toxic pathologic effects of manganese relate to a chronic central nervous system disorder similar to Parkinson's disease and manganese pneumonia. In the early part of the century, Brezina reported 5 cases of death from pneumonia among 10 manganese workers in an Italian pyrolusite industry in 1929 (25). An epidemic of lobar pneumonia was reported from Norway in 1939 (25). Smoke from a ferromanganese smelting plant containing silica and manganese oxides polluted a town. During the year with heavy pollution, lobar pneumonia accounted for 32.2% of all deaths in the community. Corresponding figures for all of Norway were 3.65% (25). The incidence of pneumonia among men exposed to manganese oxide dust as part of the manufacturing of potassium permanganate was 36 times higher than an unexposed comparison group (14). Confirmation of human studies is born out by inhalation studies of mice which reveal that manganese is toxic to respiratory epithelium and produces an intense interstitial inflammatory response (14). Studies on guinea pigs also confirm that the toxic effect of manganese dioxide dust might augment concomitant respiratory infections (28). Manganese, in combination with candida albicans, caused pulmonary fibrosis (28). However, exposure to MnO_2 dust did not significantly affect rat lung enzymes or microsomal fractions even though manganese was significantly increased in tissues remote from the lung (indicating translocation of dust from intrapulmonary locations) (21).

In acute manganese pneumonia, symptoms are similar to other types of pneumonia. There are no characteristic pulmonary function or x-ray changes. Diagnosis depends on careful occupational history and appropriate clinical picture.

Polyvinyl Pyrolidine (Thesaurosis)

Individuals exposed to hair lacquer sprays may develop a lung disease known as thesaurosis. There are three basic types of hair sprays. These include polyvinyl pyrolildone (p-type) where PVP is combined with trichlorfluoromethane and dichlorfluoromethane as aerosol propellant in metal dispensers; shelactitie made of dewaxed shellac mixed with castor oil in some sort of aerosol propellant in metal dispensers; and a mixture of the two (16). Workers most likely to be affected are beauticians or hairdressers. However, men and women using or children playing with hair sprays may also be exposed.

Disease attributed to hair sprays have included interstitial fibrosis, hilar adenopathy, and sarcoid or foreign body-type granuloma (2)(3)(9)(15). PAS positive intracytoplasmic granules have been identified within macrophages, lung tissues, and lymph nodes (3). However, similar staining granules have been reported in sarcoid and other granulomatous diseases. Chemical analyses of lung tissue have not demonstrated PVC which is readily soluble in water and chemically inert (16). It has been suggested that lubricants in PVP or in the mixed sprays cause the pulmonary lesions and not the PVP itself (7).

X-ray surveys performed on a large number of hairdressers have not demonstrated any significant pulmonary disease ascribable to sprays (10)(12). In cases where lung disease has been reported, the average duration of exposure before diagnosis of disease was approximately 2.9 years, ranging from six months to eight years (9). The youngest patient was eight years of age (9). Symptoms described were nonspecific and included exertional dyspnea, cough, and occasional fever. Chest x-rays revealed patchy or linear opacities; occasionally hilar lymph nodes were enlarged (9). When sprays were discontinued, chest x-rays have shown clearing of lesions within six months, but in a few it has taken as long as two years (9).

Titanium

Titanium, present in a variety of minerals, is an abundant element. It is considered rare because it is difficult to separate. It is used as ferrotitanium for deoxidizing and denitrogeniz-

ing steel and in alloyed steel to increase tensile strength, toughness, and hardness. In chromium steel it minimizes intergranular corrosion (4). Titanium oxide is used as a paint pigment while titanium tetrachloride has been used for making smoke screens and for skywriting. Titanium tetracarbide is used with tungsten carbide for the manufacturing of tools (5). There is one report that titanium oxide may cause radiographic changes, similar to those seen following inhalation of iron or tin, without functional impairment (20).

Vanadium

Vanadium is obtained by roasting the ores from the thermal decomposition of iodide or petroleum residues, from slags resulting from ferrovanadium production, or from soot obtained by oil burning (24). Because high temperatures are necessary and vanadium has a tendency to reoxidize, pure vanadium is difficult to obtain, even on a small scale (11). Vanadium is found in combination with other elements in rocks and some petroleum deposits because the blood of certain fossilized remains consists in part of vanadium (16).

Vanadium ore is crushed and dried and then finely ground and roasted. After mixing with sulfuric acid, the resulting precipitate is dried as vanadium pentoxide and packed in bags. Roasting and bagging processes produce the most dust; grinding and crushing produces less (16).

Vanadium is used in the steel industry because of its powerful oxidizing capacity, ability to increase hardness, malleability, and resistance to fatigue. It is used as a catalyst in the manufacture of phthalic anhydride and sulfuric acid and in the oxidation of ammonia and nitric acid. Vanadium is used for the manufacture of dyes and inks, paints and varnish dryers, insecticides, and in photography. Animal studies indicate the pulmonary effects of vanadium are primarily irritant in nature (18)(19). Animals exposed to vanadium dusts develop profuse mucoid nasal discharge, sneezing and wheezing, bronchitis, and bronchopneumonia. Dust accumulates within cells and there may be some interstitial fibrosis (18). In humans, the irritative nature of vanadium causes bronchitis symptoms, and conjunctival and nasal irritation (5)(13)(22)(23)(27) (29). Acute bronchospasm may develop when high concentrations of vanadium dusts are present. Although the radiodensity of vanadium is less than that of iron, there is no evidence that it causes x-ray changes. This may be due to its rapid absorption from the lung (16).

Bibliography

1. Abe, A. and Ishikawa, T.: Studies on pneumoconiosis caused by organic dusts. J Science Labour *43:*19-41, 1967.
2. Bergmann, M., Flance, I. J., and Blumenthal, H. T.: Thesaurosis following inhalation of hair spray. N Eng J Med *258:*471-476, 1958.
3. Bergmann, M., Flance, I. J., Cruz, P. T., Kiam, N., Aronson, P. R., Joshi, R. A., and Blumenthal, H. T.: Thesaurosis due to inhalation of hair spray. N Eng J Med *266:*750-755, 1962.
4. Brady, G. S. and Clauser, H. R.: Materials handbook, 11th ed., New York, McGraw-Hill Book Company, 1977.
5. Browne, R. C.: Vanadium poisoning from gas turbines. Br J Ind Med *12:*57-59, 1955.
6. Browning, E.: Toxicity of industrial metals, 2nd ed., New York, Appleton-Century-Crofts, 1969.
7. Brunner, M. J., Giovacchini, R. P., Wyatt, J. P., Dunlap, F. E., and Calandra, J. D.: Pulmonary disease and hair spray polymers: A disputed relationship. JAMA *184:*851-857, 1963.
8. Emara, A. M.: Chronic manganese poisoning in the dry battery industry. Br J Ind Med *28:*78, 1971.
9. Gowdy, J. D. and Wagstaff, M. J.: Pulmonary infiltration due to aerosol thesaurosis. Arch Environ Health *25:* 101-108, 1972.
10. Haung, H. P.: Zur frage der speicherkrankheit in det lunge nach gebrauch von haarspray. Dt Med Wschr *89:*87-92, 1964.
11. Hunter, D.: The diseases of occupations. London, Hodder and Stoughton, 1975.
12. John, H. H.: Thesaurosis: A survey of those at risk. Med Off *109:*399-400, 1963.
13. Lewis, C. E.: The biological effects of vanadium. II. The signs and symptoms of occupational vanadium exposure. AMA Arch Ind Health *19:*497, 1959.
14. Lloyd-Davies, T. A.: Manganese pneumonitis. Br J Ind Med *3:*111-135, 1946.

1946.
15. McLaughlin, A. I. G., Bidstrup, P. L., and Konstam, M.: The effects of hair lacquer sprays on the lungs. Food Cosmet Toxicol *1:*171-188, 1963.
16. Parkes, W. R.: Occupational lung disorders. Butterworths and Co., Ltd., London, 1974.
17. Pimentel, J. D.: A granulomatous lung disease produced by Bakelite. Am Rev Respir Dis *108:*1310, 1973.
18. Roschin, I. V.: Effect on organisms of vanadium trioxide. Fed Proc *24:*611, 1965.
19. Roschin, I. V.: Toxicology of vanadium compounds used in modern industry. Gig Sanit *32:*26, 1967.
20. Schmitz-Moorman, P., Horlein, H., and Hanefeld, F.: Lungenverander unger bei titandioxyd staub exposition beitr. Silikose Forchung *80:*1, 1964.
21. Singh, J., Kaw, J. L., and Zaidi, S. H.: Early biochemical response of pulmonary tissue to manganese dioxide. Toxicology *8:*177-184, 1977.
22. Sjoberg, S. G.: Vanadium pentoxide dust — a clinical experimental investigation on its effect after inhalation. Acta Med Scand Suppl *238:*1-188, 1950.
23. Symanski, J.: Industrial vanadium poisoning its origin and symptomatology. Arch Gewerbepathol Gewerbehyg *9:*925-313, 1939 (Ger.).
24. Tabershaw, I. E., Utidjian, H. M. D., and Kawahara, B. L.: Chemical hazards. In: Occupational Diseases, DHEW NIOSH, Pub. No. 77-181, by U.S. Department of Health , Education, and Welfare, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, U.S. Government Printing Office, Washington, DC, p. 131-439, 1977.
25. Tanaka, S.: Manganese. In: Occupational Medicine, Carl Zenz, Ed., Year Book Medical Publishers, Inc., Chicago, p. 659-668, 1975.
26. U.S. Department of Health, Education, and Welfare, Public Health Service, Centers for Disease Control, National Occupational Hazard Survey, Vol. III: Survey Analysis and Supplemental Tables, U.S. Government Printing Office, Washington, DC, 1977.
27. Williams, N.: Vanadium poisoning from cleaning oil-fired boilers. Br J Ind Med *9:*50, 1950.
28. Zaid, S. H., Dogra, R. K. S., Shanker, R., and Chandoa, S. V.: Experimental infective manganese pneumoconiosis in guinea pigs. Environ Res *6:*287-297, 1973.
29. Zenz, C., Bartlet, J. P., and Thiede, W. H.: Acute vanadium pentoxide intoxication. Arch Environ Health *5:*542-546, 1962.

TIN

Introduction

Tin is a soft, malleable metal slightly harder than lead. It is resistant to atmospheric corrosion and it may be dissolved in mineral acids (4). It is used to make brasses, bronzes, and babbitts, and in soft solders. It is more radiopaque than iron, and when inhaled and deposited in the lungs, it produces dense x-ray shadows, a condition known as stannosis.

List of Causative Agents (Manufacturing Processes)

Next to gold and copper, tin is the earliest metal known to man (20); it was first obtained from ores about 5,000 years ago (10). Tin smelting probably began in northwest Persia about 1600 B. C. (10). It was soon discovered that copper, combined with tin, produced an alloy that was stronger and easier to cast in a mold and thus was preferable for weapons production. The bronze age began in Egypt 1,000 years before spreading to northern Greece but occurred in Great Britain between 1800 and 1600 B. C. (15). Tin was known to Homer between 900 and 750 B. C.; in the "Iliad," Agamemnon's shield had 20 knobs of tin making a circle around the dark enamel boss (17).

Cassiterite (SnO_2) is the primary ore from which tin is obtained. An important use of tin is providing a protective coating for other metals, particularly in the food and beverage canning industry, roofing tiles, silverwares, coated wire, household utensils, electronic components, and pistons. Electroplated tin provides a durable protective finish and produces a lubricating effect on bearing surfaces (4). Common tin alloys are phosphor bronze, light brass, gunmetal, high ten-

sile brass, manganese bronze, die casting alloys, bearing metals, pipe metals, and pewter (23). Tin is used for solder, fillers in automobile bodies, castings for hydraulic brake parts, aircraft landing gear, and engine parts. Metallic tin is used in the manufacture of collapsible tubes and foil for packaging. Organic and inorganic compounds are used in the production of drill-glass ceramic, porcelain, enamel, glass, and inks. They are also used as a mordant in production of fungicides, anthelmintics and insecticides, and as a stabilizer polyvinyl plastics and chlorinated rubber plants and in plating baths (23). Stannous chloride is used in the chemical industry as a reducing agent, for immersion, tinning of metal, and for sensitizing glass and plastics before metalizing. Tin oxide is used as a opacifier in ceramic enamels, as a ceramic color, as an abrasive, and as a coating for conductive glass. The term organotin refers to butyl compounds which are used as catalysts, or heat and light stabilizers, in vinyl polymers and chlorinated latex paints. Tins in paints act as stabilizers to prevent darkening (9).

List of Occupations and Industries Involved

Exposure to tin occurs during mining, smelting, refining, and in production and use of tin alloys and solders. Occupations in which exposure to tin may occur include: (23)

Babbitt makers (tin-copper)(antimony)

Britannia metal workers (tin-copper-antimony)

dye workers

pewter makers

textile workers

Herth tinners

valuing of tin oxide (detinning furnace tender)

brass founders (copper and zinc)

bronze founders (tin-copper)

fungicide workers

pigment workers

solder makers

type metal makers (lead-antimony tin)

scrap metal recovery plant operators

tin miners

The amount of tin in crude ore is so small that mining procedures involving drilling and loading of ore do not cause stannosis. The silica in the dust, however, may cause silicosis (13). Tin dust and fumes are generated when emptying bags of crude ore into ships, and in the milling and grinding of ore (12); shoveling of split ore, tipping of crushed ore into calcination furnaces; charging smelting furnace with calcined ore producing tin oxide fumes (21); shaking out of the refinery furnace which contains high percentages of tin oxide; melting down tin scraps in order to recover tin oxide (7); and in procedures where material to be plated is dipped by hand into molten tin (5).

Epidemiology

Pendergrass and Pride reported a 45-year-old man whose job consisted of bagging tin oxide for a period of 15 years (14). Abnormalities on chest x-ray were noted during a routine survey but the worker complained of no symptoms or disability. Bartak and Tomecka (2), described an enamel factory worker who charged furnaces in which tin was converted (burned) to tin oxide for 18 years. He complained of no symptoms and demonstrated no abnormal physical findings. Chest x-ray showed diffusely scattered radiodense shadows. In the same factory, 6 of 16 co-workers showed similar x-ray findings. These individuals were exposed to tin oxide dust for periods ranging between 6 months and 25 years. Robertson and Whitaker reported chest x-ray changes suggesting pneumoconiosis in 121 of 215 workers in a tin refinery who did not demonstrate clinical findings (19). Cutter et al. described two cases with x-ray findings showing nodules 1-2 mm in diameter not accompanied by any pulmonary dysfunction (6). A report of the autopsy findings of an asymptomatic tender of a detinning furnace revealed concentrations of tin in his lungs of 110 mg per 100 gms of wet lung tissue which was approximately 2,000 times the normal value (7). X-ray defraction analysis confirmed that tin oxide was the only metal or mineral present. Cases reported by Spencer and Wycoff, Robertson and Whitaker, and Oyanguren had no disability but abnormal chest x-rays (11)(19)(21). Dundon and Hughes suggested that tin fumes were a more important source of exposure than tin oxide dust (7). However, studies by Robertson and Whitaker suggested that the two most important factors in causing lung deposition were the quality of the dust and duration of exposure (19).

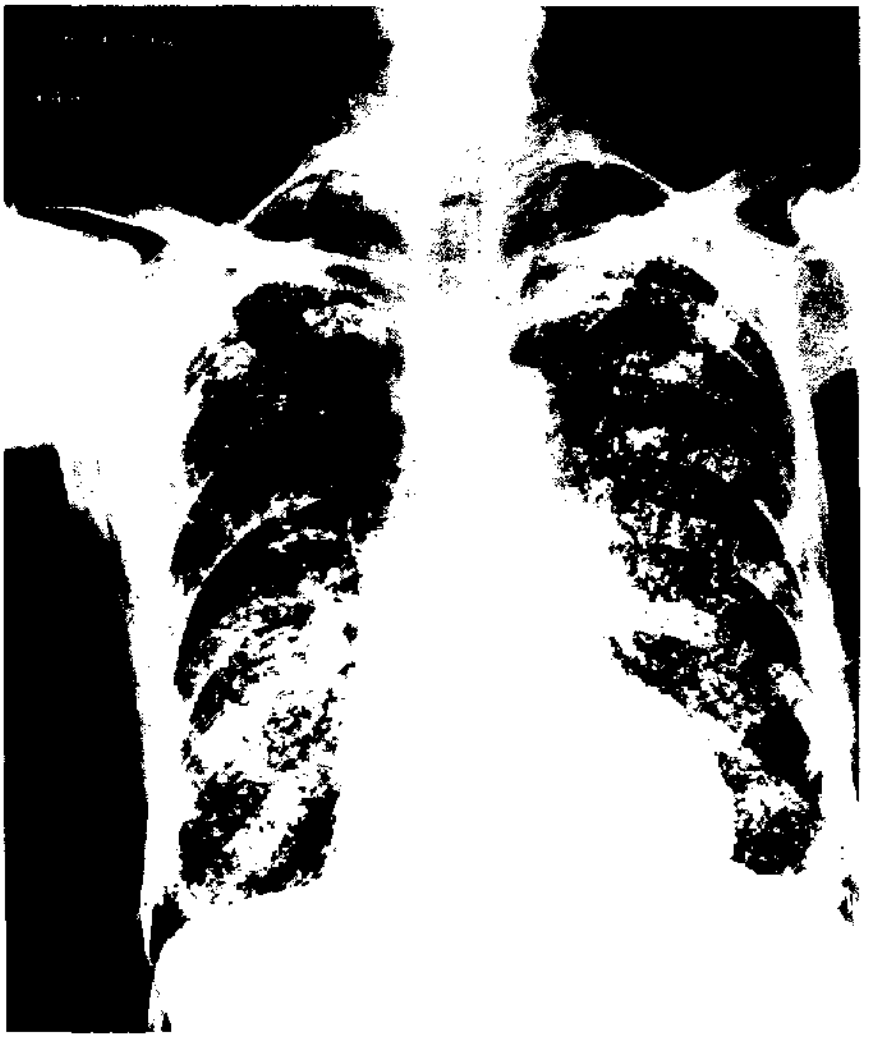

Figure II-45.

Estimate of Population at Risk

Stannosis seems to be an uncommon cause of pneumoconiosis with only approximately 140 recorded cases (13). However, NIOSH estimates that there are perhaps 250,000 workers exposed to tin or tin oxide.

Pathology

Examination of the cut surface of the lung reveals numerous 1-3 mm size gray-black, rounded densities scattered throughout the lung tissue (13). They are primarily located in the subpleural area and in interlobular septal tissue (22).

On microscopic examination, macrophages containing dust particles are deposited within alveolar walls, around vessels and bronchioles, and beneath the pleural surface. Aggregations of dust particles accumulate in hilar lymph nodes. The dust-ladened macrophages aggregate around the perivascular and peribronchiolar tissue producing macules which are similar to those seen in coalworkers' pneumoconiosis and siderosis (13). Massive fibrosis does not occur and little reticulum or collagen fiber formation develops. The dust does not cause bronchitic changes. No appreciable chronic lung changes such as emphysema or fibrosis have been observed (22), even after 50 years of exposure to tin oxide (18).

Tin oxide crystals are strongly birefringent in contrast to silica which is poorly birefringent.

X-ray defraction analysis provides definite identification of the pigmented particles. Following microincineration of lung tissue, carbon particles disappear while tin particles remain. Tin concentrations in lung tissue in stannosis cases have been reported to range between 0.5 and 3.3 gms per lung, in cases where duration of exposure has been 11 and 50 years (18). There is a good correlation between the quantity of tin in the lung and x-ray changes (18). Tin oxide does not cause lung fibrosis in experimental animals (8)(16).

Clinical Symptoms

Tin pneumoconiosis or stannosis was first described by Beintker in 1944 (3). There are no reported symptoms or abnormal findings on physical examination. Pulmonary function tests usually are normal. Chest x-ray appearance may resemble siderosis. Following heavy prolonged exposure to tin oxide dust, many small, dense radiopacities develop and are scattered relatively evenly throughout lung fields (13)(see Figure II-45). Opacities are usually 2-4 mm in size, somewhat irregular in outline and extremely radiopaque. In the upper lung zone, dense linear opacities may be seen and Kerley B-line may be seen throughout the lungs (13). Exposures that are less intense produce fewer and less dense opacities on chest x-ray. Large confluent opacities and hilar adenopathy do not occur.

Diagnostic Criteria

Diagnosis is made by obtaining an occupational history of significant tin exposure, lack of clinical symptoms and physical findings, and the presence of very radiodense opacities on chest x-ray. In the absence of a history of exposure and when opacities are few in number, the pneumoconiosis may be mistaken for siderosis and possibly silicosis. X-ray diffraction analysis of lung tissue may provide definite identification.

Prognosis

Stannosis has no known effect on health or life span. It has not been well documented whether termination of exposure results in gradual disappearance of the x-ray opacities.

Methods of Prevention

Prevention depends mainly on efficient dust supression, good exhaust ventilation, and good factory housekeeping. Tin oxide is classified as an inert or nuisance particulate by the ACGIH (13).

Bibliography

1. Aitchison, L.: A history of metals. London: 1960 cited by A. John Robertson. In the Romance of Tin. Lancet *1:* 1229-1293, 1964.
2. Bartak, F. and Tomecka, M.: Proceedings of the Ninth International Cong. of Industrial Medicine. London: Wright, Bristol, 1949.
3. Beintker, E.: Reichsarbeitsblatt *3:*37, 1944. (Cited by Robertson, A. J.: The Romance of Tin, Lancet 1229-1236, 1964.)
4. Brady, G. S. and Clauser, H.R.: Materials Handbook, 11th ed., McGraw-Hill Book Company, New York, 1977.
5. Cole, C.W.A., Davies, J.V.S.A., Kipling, M.D., and Ritchie, G.L.: Stannosis in hearth tinners. Br J Ind Med *21:*235-241, 1964.
6. Cutter, H.C., Faller, W.W., Stocklen, J. B., and Wilson, W. L.: Benign pneumoconiosis in a tin oxide recovery plant. J Ind Hyg Toxicol *31:*139-141, 1949.
7. Dundon, C.C. and Hughes, J.P.: Stannic oxide pneumoconiosis. Am J Roentgenol *63:*797-812, 1950.
8. Fischer, H. W. and Zimmerman, G. R.: Long retention of stannic oxide. Arch Pathol *88:*259-264, 1969.
9. Hampel, C. and Hawley, G.: The Encyclopedia of Chemistry, 3rd ed., Van Norstrand Reinhold Company, New York, 1973.
10. Hoover, H.C. and Hoover, L. H.: Footnotes in Agricola's De Re Metallica, 1556. London, 1912 cited by A. John Robertson. In: The Romance of Tin. Lancet *1:*1229-1293, 1964.
11. Oyanguren, H., Haddad, R., and Maass, H.: Stannosis-inhalation of dust and fume. Ind Med Surg *27:*427, 1958.
12. Oyanguren, H., Schuler, P., Cruz, E., Guijon, C., Maturana, V., and Valenzuela, A.: Estanosis: Neumoconiosis benigna debida a inhalacion de polvo y humo de estano. Reuta Med Chile *85:* 687-695, 1957.

13. Parkes, W. R.: Occupational Lung Disorders. Butterworth and Co Ltd., London, 1974.
14. Pendergrass, E.P. and Pryde, A.W.: Benign pneumoconiosis due to tin oxide. J Ind Hyg Toxicol *30:*119-123, 1948.
15. Piggott, S.: In culture and environment. A.L. Foster and L. Alcock, Ed. London 1963, cited by A. John Robertson. In: The Romance of Tin. Lancet *1:*1229-1293, 1964.
16. Robertson, A.J.: Pneumoconiosis due to tin oxide. In: Industrial Pulmonary Diseases, E. J. King and C.M. Fletcher, Ed: Churchill, London, 1960.
17. Robertson, A.J.: The Romance of Tin. Lancet*1:*1229-1293, 1964.
18. Robertson, A.J.,Rivers, D., Nagelschmidt, G., and Duncomb, P.: Stannosis: Benign pneumoconiosis due to tin dioxide. Lancet *1:*1089-1095, 1961.
19. Robertson, A.J., and Whitaker, P.H.: Tin smelters' pneumoconiosis. J Facult Radiol *6:*224, 1955.
20. Singer, C., Holymyard, E.G., and Hall, A.R.: History of technology Vol. 1. Oxford, 1954 cited by A. John Robertson. In: The Romance of Tin. Lancet *1:* 1229-1293, 1964.
21. Spencer, G.E. and Wycoff, W.C.: Benign tin oxide pneumoconiosis. Arch Ind Hyg *10:*295-297, 1954.
22. Spencer, H.: Pathology of the lung, 2nd ed. Pergammon Press, Oxford, 1968.
23. Tabershaw, I.R., Utidjian, H.M.D., and Kawahara, B.L: Chemical hazards. In: Occupational diseases DHEW (NIOSH) Pub. No. 77-181 by U.S. Department of Health, Education and Welfare, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health. U.S. Government Printing Office, Washington, DC, pp. 131-439, 1977.

TUNGSTEN CARBIDE (Hard Metal Disease)

Introduction

Tungsten, a greyish metal, is classified as a transition element and closely resembles molybdenum in its physical and chemical properties. Wolframite ($(FeMn)WO_4$) is the most important ore containing tungsten, while Scheelite ($CaWO_4$) is a principal domestic ore (45).

Currently, approximately 70% of the tungsten production in the United States is used in the manufacture of cemented tungsten carbide or "hard metal" (a mixture of tungsten carbide, cobalt, and/or other metals and their oxides or carbides) to form a material with a hardness nearly equal to diamonds (7)(43). It is used as an abrasive or briquetted with cobalt or other binders into tools for high-speed cutting of metals or hard materials. Tungsten compounds and cemented tungsten carbide are reported to cause both transient and chronic pulmonary disease.

Table II-30

OCCUPATIONS WITH POTENTIAL TUNGSTEN EXPOSURE

Alloy makers	Melting, pouring, casting workers
Carbonyl workers	Metal sprayers
Ceramic workers	Ore-refining and foundry workers
Cemented tungsten carbide workers	Paint and pigment workers
Cement makers	Paper makers
Dye makers	Penpoint makers
Dyers	Petroleum refinery workers
Flameproofers	Photographic developers
High-speed tool steelworkers	Spark-plug makers
Incandescent-lamp makers	Textile dryers
Industrial chemical synthesizers	Tool grinders
Inkmakers	Tungsten and molybdenum miners
Lamp-filament makers	Waterproofing makers
Lubricant makers	Welders

Source: (43)

List of Causative Agents (Manufacturing Processes)

The major compounds of tungsten to which workers are exposed are ammonium-P-tungstate, oxides of tungsten (WO_3, W_5O_5, WO_2), metallic tungsten, and tungsten carbide (43).

Tungsten carbide is produced by blending and heating tungsten and carbon in an electric furnace, and then mixing in a ball mill with cobalt to form a matrix for tungsten carbide crystals and other metals such as chromium, nickel, and titanium. Tantalum may be added depending on the properties required (28). All constituents are present in a finely divided state with a mean diameter reported to be about 1.5 μ (10). The powdered metal is then pressed into ingots and fused. All processes of drying, grinding and drilling, finishing, and cleaning equipment are dusty (28). In the production and use of tungsten carbide, exposure to the cobalt or nickel used as a binder or cementing substance may be an important hazard to workers (29)(42).

Tungsten carbide usually constitutes 80% or more of the hard metal; the content of cobalt is usually less than 10%, but may be as high as 25% (43). When the cobalt content is greater than 2%, there is a potential cobalt health hazard, perhaps exceeding that of tungsten carbide; a nickel content greater than 0.3% represents a significant health hazard risk from nickel (43). In addition, the tungsten carbide industry uses other metals such as tantalum, titanium, nosibium, chromium, and vinadium during the manufacturing process which also represent potential health risks.

List of Occupations and Industries Involved

See Table II-30, page 438.

Epidemiology

Diffused pulmonary fibrosis (2)(3)(6)(10)(12)(15)(20)(24)(26)(38)(44) and bronchial asthma (5)(6)(9)(10)(14)(17) have been reported following either short-term or long-term occupational exposure to tungsten and its compounds in the cemented tungsten carbide industry. Changes have been reported for individuals exposed only to tungsten carbide (10)(14)(20)(26). It has been estimated that perhaps 9-11% of hard metal workers exposed to tungsten carbide develop pulmonary fibrosis (20)(26). While animal studies document the specific pulmonary toxic effect of tungsten and some of its compounds (8)(13)(26)(27)(34), most reports of occupational exposure concern the effects of mixed dusts which contain not only tungsten carbide but also cobalt and other materials (4)(5)(6) (9)(10)(14)(15)(19)(32)(38)(39). Concentrations of tungsten are reported in only a few cases (28). Dust particles that are generated in operations where tungsten is processed are largely respirable, the majority being less than 5 μ in diameter (6)(14)(16)(26)(30).

Estimated Population at Risk

NIOSH estimates that there are at least 30,000 employees in the U.S. who are potentially exposed to tungsten and its compounds (43). These figures are based on actual observations reported in the National Occupational Health Survey (NOHS). There are perhaps 15,000 to 20,000 persons potentially exposed to dusts in the hard-metal industry throughout the world (28). Only a small portion of exposed persons appear to develop respiratory disease (10). It has been estimated the 9-11% of hard metal workers exposed to tungsten carbide develop pulmonary fibrosis (20)(26). However, in one industry, only 9 of 1,500 workers were reported to have pulmonary disease (10).

Pathology

There are two major types of pulmonary reactions that occur among workers exposed to tungsten carbide: an asthma syndrome and diffuse interstitial pulmonary fibrosis. The interstitial fibrosis does not appear to differ from interstitial fibrosis produced by other agents (10). On microscopic examination, the lung shows an interstitial cellular infiltration and variable fibrosis. There are dilated alveolar spaces, lined by epithelium showing metaplastic changes. In some areas there are accumulations of what appear to be Type 2 alveolar pneumocytes and alveolar macrophages within alveoli lumen. Large mononuclear and even occasional multinucleated giant cells may be present. Electron microscopic changes are consistent with those observed by light microscopy (10). X-ray defraction analysis shows the presence of tungsten carbide and mass spectrometric analyses document the presence of tungsten carbide and cobalt in lung tissue (10). In the study of 12 cases of diffuse pulmonary fibrosis reported by Coates and Watson, a lung biopsy sample contained 2.0 mg of tungsten, 2.0 titanium, and 0.1 μg of cobalt/

gm of wet lung (10). There was no correlation between cobalt content of lung tissue and severity of disease. In another study by Coates et al., light and electron miscroscopic examination were performed on specimens from a case of diffuse interstitial fibrosis, a second with subacute interstitial pneumonitis, and a third asymptomatic worker with clinically normal lungs (11). There were deposits of collagen and elastic tissue in alveolar areas associated with multifaceted crystals which appeared to cause tears in cells; the crystals were believed to be tungsten carbide. Finer, needle-like crystals were noted lying in macrophage lysosomes. There were alterations of alveoli Type I pneumocytes, with swelling and formation of microvilli. There were also occasional alterations of the capillary endothelial cells. In the asymptomatic individual, no abnormalities were noted in the alveoli or endothelial cells.

Beck reported the results of 12 workers with hard metal disease, 8 of whom died because of pulmonary disease (6). In general, there were varying degrees of interstitial fibrosis present. No correlation was noted between the duration of exposure and development of interstitial fibrosis. Baudouin reported electron microscopy of biopsied lung tissue in a man who worked in a hard metal factory (4). Crystalline particles, possibly tungsten carbide, were noted in alveolar macrophages. Examination of lung tissue by x-ray fluorescence demonstrated large amounts of tungsten, greater than usual amounts of titanium, and small amounts of tantalum and nosibium. X-ray defraction studies documented the presence of tungsten carbide and titanum carbide. The number of airspaces was decreased because of excessive mucus production and hyperplasia of alveolar epithelial lining cells. Alveolar macrophages containing foreign material were present. Spectroscopic and histochemical analysis of biopsy specimen material reported by Scherer indicated the presence of 2-10 times the normal amount of tungsten, but no cobalt was found (38). On the other hand, lung tissue analysis from a 46-year-old woman who worked with hard metal mixtures and was exposed to tungsten carbide and cobalt revealed an emission spectrographic analysis of lung tissue which showed no detectable levels of tungsten, titanium, or cobalt—possibly because of the small sample size (32). There was significant x-ray and pulmonary function test improvement when she left work; this worsened when she resumed her job.

Rats exposed to metallic tungsten by intratracheal injection or inhalation, showed a mild interstitial and perivascular inflammatory cell response (26). Increased collagen tissue was noted by eight months. Although tungsten itself caused mild interstitial fibrosis in rats, no significant response was noted following intratracheal injection of pure tungsten carbide (27). Because of this, it was speculated that the pulmonary fibrosis described in the hard metal industry was caused not by the tungsten carbide, but by coexisting exposure to cobalt. Delanhant's studies support this; tungsten carbide produced little effect on guinea pig lungs (13). Experiments were undertaken to determine which of the metallic components in cemented tungsten might provoke lung lesions. Tungsten metal, tungsten carbide, and carbon dust produced relatively little tissue response. Mixtures of tungsten carbide and carbon were more harmful to guinea pig lung tissue than tungsten metal alone (13)(33)(36). Particulate tungsten metal and a mixture of tungsten carbide and carbon appeared to be relatively inert, but when cobalt was mixed with tungsten carbide, an acute hemorrhagic pneumonia developed; this response seemed to characterize the cobalt component (33). A mixture of tungsten carbide and cobalt produced pulmonary fibrosis in guinea pigs, especially in areas where there was dust deposition (37). Even one year after injection, dust particles remained within alveolar spaces together with residual pneumonitis, mild cellular reaction, and fibrotic reaction around the dust deposits.

Schepers theorized that the marked proliferative and metaplastic epithelial changes noted could reflect a synthesizing property of cobalt (37). While changes in lungs following various mixed dusts exposures are similar, they are most marked when cobalt is one of the constituents. This suggests the activity of cobalt is enhanced when tungsten and cobalt combine (21). This may be due to the solubility of cobalt which is increased in the presence of tungsten (21).

Magnesium tungstate was very reactive in producing pulmonary lesions (34) whereas tungsten silicide caused hyperplastic lymph nodes, focal thickening of alveoli walls, perivascular lymphocyte infiltration, and nodular accumulations of fibroblasts, lymphocytes, and macrophages (8).

cytes, and macrophages (8). Rats exposed to tungsten hexachloride inhalation died of pulmonary edema (40). Interstitial pulmonary inflammatory responses occured after administration of calcium-magnesium-tungstate phosphor in rats; the most accentuate lesions appeared in areas of dust accumulation (16). Animal studies comparing tungstic oxide, sodium tungstate, and ammonium-p-tungstate demonstrated greater mortality rates in animals as the tungsten content of their diet was increased, especially when it was greater than 2% (22).

While total dust levels and cobalt concentrations are reported in many studies, actual tungsten concentrations are documented in only a few cases. The size of the dust particles generated during various operations in which tungsten is processed and used is generally less than 5 μ in diameter (6)(14)(16)(26)(30).

Clinical Description

There are two major types of respiratory disease seen among tungsten carbide workers: reversible, rather acute airways obstructive syndrome (asthma) and diffuse interstitial fibrosis.

The acute asthmatic syndrome is characterized by productive cough and chest tightness which usually develops towards the end of the workday or in the evening (9)(10)(14). Symptoms improve during weekends and vacations but again recur within the first few days after returning to work. The airways obstructive disease is reversible, showing improvement following administration of bronchodilators; it is eliminated by removal from exposure (9). Atopic and nonatopic individuals are affected equally (9).

Individuals with interstitial pulmonary fibrosis develop a rapid onset of cough, sputum, and dyspnea on exertion (28). On physical examination, basilar rales are heard. The chest x-ray is abnormal and characterized by linear or ill-defined irregular opacities; there is some prominence near the hilar area. Disease onset usually occurs within one or two years after beginning employment. In some cases, resolution of symptoms are noted following removal from work (4)(14)(25)(27)(35). Although lung biopsies obtained early in the course of the disease show a desquamative interstitial pneumonia, biopsies taken later reveal a more chronic disease, characterized by diffuse interstitial fibrosis (35). Fibrosis develops in some workers within 2 years, but in others it may not develop until 25 years of employment; usually it occurs after 10 years of work (1)(6)(10)(18)(19)(25)(27)(31)(35). The clinical, physiologic, and x-ray features are similar to those of other types of diffuse interstitial fibroses. In a few cases, individuals have died with respiratory or cardiac failure. Opacities on chest x-ray do not appear more radiodense even though the atomic number of tungsten is 74. Increased gamma globulinemia has been reported in some affected individuals (27).

Treatment with corticosteroids may be indicated, particularly in the desquamative interstitial phase (28).

Diagnostic Criteria

Diagnosis depends on obtaining the proper occupational history as well as demonstrating characteristic x-ray and pulmonary function abnormalities consistent with an interstitial fibrotic response. This is also true for the asthma syndrome.

Methods of Prevention

Because of the 9-10% incidence of pulmonary fibrosis, NIOSH has recommended that employees exposed to tungsten alone, without cobalt exposure, have a recommended 10-hour shift (40-hour week) Threshold Limit Value of 1 mg/m^3, measured as tungsten. Because the major industrial exposure in the cemented tungsten industry occurs along with exposure to cobalt with mixture percentages ranging from 3-25%, NIOSH has recommended that employees exposed to cemented tungsten carbide which contains more than 2% cobalt have limited exposure. Exposure should be similar to the current standard for cobalt which is 0.1 mg/m^3 measured as a time-weighted-average concentration. When tungsten carbide is made with nickel as a binder rather than cobalt and the nickel content exceeds 0.3%, NIOSH has recommended that the TLV for nickel of 15 μg/^{3} should apply (43).

Medical surveillance should include a preplacement evaluation consisting of a medical and physical examination, chest x-ray and pulmonary function tests, as well as periodic examinations with similar laboratory and medical studies. Engineering controls, such as enclosures and local exhaust ventilation, should be used to keep the concentrations of airborne dust at or

below the appropriate time-weighted average exposure limits. Respiratory protective equipment should not be used in place of engineering and ventilatory controls. Care should be taken by employees when pouring or scooping powdered material in order to avoid excessive dust generation (43).

Research Needs

Epidemiology studies are needed to better assess the long-term effect of tungsten exposure by itself. Studies are necessary to determine whether there are synergistic or potentiating effects from other metals (e.g., cobalt and nickel) and compounds commonly found with the tungsten compounds used.

Bibliography

1. Ahlmark, A., Bruce, T., and Nystrom, A: Silicosis and other pneumoconioses in Sweden. London: Heinemann, 1960.
2. Barborik, M.: [Hard metal disease in workers employed in production of tungsten carbide]. Prac Lek *18:*241-247, 1966 (Cze).
3. Bartl, M.D. and Lichtenstein, C.I.H.: Tungsten carbide, pulmonary fibrosis—a case report. Am Ind Hyg Assoc J *37:*668-670, 1976.
4. Baudouin, J., Jobard, P., Moline, J., LaBandier, M., Roullier, A., and Homasson, J.P.: [Diffuse interstitial pulmonary fibrosis-responsibility of hard metals]. Nouv Presse Med *4:*1353-1355, 1975 (Fre).
5. Bech, A.O.: Hard metal disease and tool room grinding. J Soc Occ Med *24:*11-16, 1974.
6. Bech, A.O., Kipling, M.D., and Heather, J.C.: Hard metal disease. Br J Ind Med *19:*239-252, 1962.
7. Brady, G. S. and Clauser, H. R.: Materials Handbook, 11th ed. New York: McGraw-Hill Book Company, 1977.
8. Brakhnova, I. T. and Samsonov, G. V. [Comparative assessment of the effect on the organism of silicides of the transitional metals]. Gig Sanit *35:*42-45, 1970 (Rus).
9. Bruckner, H. C.: Extrinsic asthma in a tungsten carbide worker. JOM *9:*518-519, 1967.
10. Coates, E. O. and Watson, J. H. L.: Diffuse interstitial lung disease in tungsten carbide workers. Ann Intern Med *75:*709-716, 1971.
11. Coates, E. O. and Watson, J. H. L.: Pathology of the lung in tungsten carbide workers using light and electron microscopy. JOM *15:*280-286, 1973.
12. Collet, A., Liot, F., Gallouedec, C., Roussel, G., Martin, J., Reuet, C., and Brouet, G.: [Electron microscopy study of various cellular aspects of a pulmonary fibro-adenomatoses with diffusion disorders—discussion on the etiologic role of cobalt and tungsten carbide]. Rev Tuberc Pneumol *27:*275-381, 1963 (Fre).
13. Delanhant, A. B.: An experimental study of the effects of rare metals on animal lungs. Arch Ind Health *12:*116-120, 1955.
14. Dorsit, G., Girard, R., Rousset, H., Brune, J., Wiesendanger, T., Tolot, T., Bourret, J., and Galy, P.: [Pulmonary fibrosis in three individuals working in the same factory and exposed to cobalt and tungsten carbide dust-pulmonary problems in the hard metal industry]. Sem Hop *46:*3363-3376, 1970 (Fre).
15. Fairhall, L. T., Castberg, H. T., Corrozzo, N. J., and Brinton, H. P.: Industrial hygiene aspects of the cemented tungsten carbide industry. JOM *4:*371, 1947.
16. Goldman, E. I., Mezentseva, N. V., and Mogilerskaya, O. Y.: Industrial dust of luminophores, p. 170-181. In: Toxicology of Rare Metals, NTIS, AEC, TR 6710. Ed. by Z. I. Izrael'son. Springfield, VA: U.S. Department of Commerce, National Technical Information Service, 1967.
17. Heuer, W.: [Pulmonary fibroses among hard metal production workers]. Arch Gewerbepath Gewerbehyg *19:*613-632, 1962.
18. Jobs, H. and Ballhausen, C.: 1940. Quoted by Bech, A. O., Kipling, M. D., and Heather, J. C. In: Hard Metal Disease. Br J Ind Med *19:*239-252, 1962.
19. Joseph, M.: Hard metal pneumoconiosis. Aust Radiol *12:*92-95, 1968.
20. Kaplun, Z. S. and Mezentseva, N. V.: [Hygienic evaluation of aerosols formed in the manufacture of hard alloys]. Gig Sanit *24:*16-22, 1959 (Rus).
21. Kaplun, Z. S. and Mezentseva, N. V.: In-

dustrial dusts encountered in powder metallurgy (hard alloys). p. 155-163. In: Toxicology of the rare metals-NTIS-AEC-TEC 6710. Ed. by Z. I. Izrael'son. Springfield, VA: U.S. Department of Commerce, National Technical Information Service, 1967.
22. Kinard, F. W. and Van de Erue, J: The toxicity of orally ingested tungsten compounds in the rat. J Pharmacol Exp Ther *72:*196—201, 1941.
23. Kopelman, B. and Smith, J.S.: Wolfram In: Kirk-Othmer Encyclopedia of Chemical Technology 2nd ed. New York: Interscience Publishers *22:*344-346, 1971.
24. Lichtenstein, M. E., Bartl, F., and Pierce, R. T.: Control of cobalt exposure during wet process tungsten carbide grinding. Am Ind Hyg Assoc J *36:*879-885, 1975.
25. Lundgren, K. D. and Ohman, H.: Pneumokoniose in der hartmetalindustrie virchows. Arch Path Anat Physiol *325:* 259-284, 1954.
26. Mezentseva, N. V.: Tungsten. p. 28-35. In: Toxicology of Rare Metals. NTIS-AEC-tr 6710. Ed. by Z. I. Izrael'son, Springfield, VA. U.S. Department of Commerce: National Technical Information Service, 1967.
27. Miller, C. W., Davis, M. W., Goldman, A., and Wyatt, J. P.: Pneumoconiosis in the tungsten carbide tool industry. AMA Arch Ind Hyg Occ Med *8:*453-465, 1953.
28. Parkes, W. R.: Occupational Lung Disorders. London: Butterworths and Co., Ltd., 1974.
29. Plant Observation Reports and Evaluation, Menlow Park, California. S. R. I. International, March 1977. (Submitted to NIOSH under contract No. CDC-99-74-31).
30. Reber, E.:[Investigation on dust hazards accompanying the production and machining of hard metals.] Staub-Reinhalt Luft *29:*57-62, 1969 (Ger).
31. Reber, E. and Burckhardt, P.: Uber hartmetallstanblungen in der schwelz respiration *27:*120-153, 1970.
32. Rochemaure, J., Anola, M., Triquet, G., and Meyer, a.: [A case of pulmonary fibrosis-possible role of exposure to tungsten dust.] J Fr Med Chir Thorac *26:* 305-312, 1972 (Fr).
33. Schepers, G. W. H.: Biologic action of tungsten, carbide and carbon. AMA Arch Ind Health *12:*137-139, 1955.
34. Schepers, G. W. H.: Lung tumors of primates and rodents. Ind Med *40:*48-53, 1971.
35. Scherer, M.: Paramabadathumalail, A., Burki, H., Senn, A. and Zurcher, R.: Drei falle von hartmetallstaublunge. Schweiz Med Wschr *100:*2251-2255, 1970.
36. Schepers, G. W. H.: The biological action of particulate tungsten metal. AMA Arch Ind Health *12:*124-136, 1955.
37. Schepers, G. W. H.: The biological action of tungsten carbide and cobalt. AMA Arch Ind Health *12:*140-146, 1955.
38. Scherer, M.: [Three cases of hard metal pneumoconiosis.] J Suisse Med *100:*2251-2255, 1970 (Ger).
39. Sivjakou, K. I. and Braun, H. A.: The treatment of acute selenium, cadmium and tungsten intoxication in rats with calcium disodium ethylenediaminetetraicetic acid. Toxicol Pharmacol *1:*602-608, 1959.
40. Spiridonova, V. A. and Suvoron, S. V.: [On the mechanism of the acute toxic action of chlorides of rare metals]. Gig Sanit *32:*79-82, 1967. (Rus).
41. Totot, F., Girard, R., Doritit, G., Tabousin, G., Galy, P., and Bourret, J.: Manifestations pulmonaires des "metaux durs": Troubles irritatifs et fibrose (Equete et observations cliniques). Arch Mal Prof Med Trav *31:*453-470, 1970.
42. Tungsten, p. 128-129. In: Industrial toxicology. Ed. by L. T. Fairhall. Baltimore: Williams and Wilkins Co., 1957.
43. U.S. Department of Health, Education, and Welfare, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, Occupational Exposure to Tungsten and Cemented Tungsten Carbide, Washington, DC, U.S. Government Printing Office, 1977.
44. Vengerskaya, K. T. and Salikhodzhaev, S. S.: [Some problems relating to the effects of tungsten powder on humans.] Gig Tr Prof Sabol *6:*27-29, 1962 (Rus).
45. Zadra, J. B.: Milling and Processing Tungsten. p. 120. In: Toxicology of the Rare

Metals. NTIS-AEC tr 6710, ed. by Z. I. Izrael'son, Springfield, VA, U.S. Department of Commerce, National Technical Information Service, 1967.

FIBROUS GLASS AND OTHER MAN-MADE MINERAL FIBERS

Introduction

Man-made mineral fibers are those made from glass, natural rock or any readily fusible slag. They differ from naturally occurring fibers, such as asbestos, which are crystalline in structure and differ chemically (27). Glass fibers are composed of either borosilicate or calcio-alumina silicate glass. They contain no trace elements of biological significance. A glass fiber refers to any glass particle with a length to diameter ratio of at least three to one. The health effects of man-made mineral fibers may be different depending on the length and diameter of individual fibers.

List of Causative Agents (Manufacturing Processes)

Slag wools, rock wools, and glass wools and filaments are all glass-heated mineral fibers behaving in much the same manner but having important differences and individual properties. Some of the important differences relate to structure, frequency of occurrence, and chemical resistance—particularly solubility.

Mineral wool, originally obtained as a natural product of volcanic craters in Hawaii, usually consists of fine, pliant, vitreous fibers which are incombustible and nonconductors of heat. Rock wool, made by blowing molten rock, is more uniform than mineral wool and has physical characteristics which depend on the class of rock used. For instance, rock wool made from high-silica limestone is used for insulating oven walls requiring temperatures up to 1,000 °F.

Man-made mineral fibers can be manufactured to various diameters and fall into three broad category groups: (1) Continuous filament, which is used in textiles and as a reinforcement in plastics and other materials. The filaments are of relatively large diameter, perhaps 9-25 μ in size. Production methods give a narrow variation of diameter size around a normal size. (2) Insulation wool is usually about 6 μ in diameter and has a much wider distribution around a nominal diameter. A high proportion of fibers may have diameters less than 3 μ which can be used for special application such as acoustic insulation. (3) Small (and sometimes uncoated) fibers below 1 μ in diameter are produced for a limited, specialized market—representing only about 1% of all production. Continuous filament and special purpose submicron range fibers are made exclusively from glass, whereas insulation wools can be manufactured from rock or slag (27).

Mineral fibers are glassy cylinders and, therefore, can never split longitudinally; they only break across. As they are destroyed, they form fragments which no longer have the character of fibers. The structure of technically-used asbestos fiber is totally different; it is always present as bundles, never as a single fiber. Individual fibrils may be as small as 2-30 mm in diameter. Because of the size of individual asbestos fibers, a bundle of asbestos fibers of the same diameter as mineral fibers would contain about 785,000 fibers. Fibrous glass processes may be classified as "textile" or "wool" operations (41). Textile fibers, formed as continuous filaments, have diameters greater than 3.0 μ and have wide application in textile, fabrics, and reinforced plastics industries. Fibers produced by wool-forming methods may be as small as 0.5 μ in diameter and less than 1 μ in length (16) and are mainly used for thermal insulation. Fibrous glass structure has silicon dioxide (SiO_2) as a major network form, with boron and aluminum oxides also contributing as network formers. The three dimensional network and tetrahedral configuration of SiO_2 molecules provide important and unusual properties which can be varied and adjusted by addition of various modifying ingredients (14).

Wool-type fibrous glass provides effective insulation because fibers are formed into interlocking network masses which entrap air into many small cells and restrict flow of heat. Thus, the density and diameter of fibrous glass fibers influence insulation properties by affecting the size of air cells and the structure of the interlocking glass fiber blanket. Decreased thermal conductivity and better insulation result as fiber diameter decreases. However, the linear relationship between fiber diameter and thermal conductivity no longer occurs when fiber diameters are very small.

Other important properties of fibrous glass besides insulation properties include chemical resistance, high tensile strength, and acoustic

insulation.

Man-made mineral fibers are usually coated with a binder (mainly a thermosetting resin) such as urea-formaldehyde type which is fully polymerized in the finished product. Rock wool may be produced with only an oil as a lubricant and for special application. Some glass fibers are of very fine-diameter and produced without any coating at all. Surface treatments are performed in order to bind and protect fibers and to reduce the effects of impact and friction (35)(43)(47). This treatment may introduce occupational health problems (41).

Estimation of environmental exposure to fibrous glass may be made gravimetrically by determining the weight of dust-per-volume of air sampled or quantitatively by the number of actual fibers counted per volume of air sampled. In general, gravimetric analyses provide an indicator of fibrous glass exposure to larger diameter fibers, i.e., greater than 3.5 μ. It does not accurately measure exposure to small diameter fibers. The relationship between fiber number and fiber weight varies considerably with fiber dimensions (16). The weight of fibrous glass dust is independent of the numbers of small fibers present and is more a function of the square of fiber diameter. A disproportionately greater number of very large-diameter fibers can increase the weight of the fibrous glass dust sample appreciably, and if large fibers constitute a small part of the dust, then a marked disagreement between gravimetric and fiber count may occur. Therefore, counting fiber numbers provides a more accurate estimate of exposure to small diameter fibers, i.e., less than 3.5 μ.

NIOSH has recommended fiber count for estimating numbers of small diameter fibers present and gravimetric analysis for determining large diameter-size fibers (52).

In the majority of occupational exposures to fibrous glass, there are fibers of varying diameters present, including a substantial percentage of fibers of respirable size. A number of industrial hygiene surveys have related different occupational and environmental sources of fibrous glass (1)(4)(11)(13)(16)(20)(28)(29). In most facilities using or producing fibrous glass with diameter size more than 3.5 μ, fiber counts of less than 1,000,000 fibers/M^3 (or one fiber/cc), and gravimetric measurements of less than 2.0 mg/m^3 (1-5 mg/m^3) have been noted (1)(11)(13)(16)(20)(29)(31)(50). In operations where fiber diameters are less than 3.5 μ, higher mean fiber counts are noted, ranging between 1,000,000 and 21,000,000 fibers/m^3, with an average of 3,000,000 fibers/m^3 (16)(20)(28)(31).

List of Occupations and Industries Involved

There are normally small amounts of fibrous glass present in urban air, reflecting its presence in our society (3). Concentrations range between less than 1,000 and up to 10,000 fibers /m^3 of air with levels of 30-130 fibers /m^3 being found even in remote rural areas. While fibrous glass used in ventilation ducts potentially represents a source of glass fibers in the air of buildings (7), the air concentrations of such fibers is extremely low, averaging about 1,000 fibers/m^3 of air (2)(12).

The major use for fibrous glass products is in thermal and acoustical insulation, and as reinforcement for various processes especially in the plastics industry (i.e., boats, shower stalls, etc.). Building insulation used in homes is installed between roof rafters and studs of sidewalls. A flexible fibrous glass blanket provides a lining for refrigerators, stoves, furnaces, and hot water heaters. A molded type insulation is used for automobile hoods, car bodies, refrigerator ships, acoustic and thermal insulation, and also for decorative purposes. Rigid board-type material may provide ceiling board and roof insulation for factory or warehouse decks. Fibrous glass-pipe insulation controls heat on steam lines and is used for temperature control and coal applications in chemical processing plants, utility plants, and commericial and mechanical applications (5). A semi-rigid type of fibrous glass boards is used in chemical processing tanks as low velocity air transmission systems for ducts and for metal building insulation such as on the roofs of prefabricated buildings.

Dust and fumes are produced when fibrous glass products are trimmed, chopped, cut or sawed, or during oven curing of the binder systems. Dust is not a problem during the basic fiber wool forming process. Packing processes with application of mechanical pressure to reduce product volume are often dusty. In industries utilizing wool-type fibers, dust is generated when producing loose fibers, or from pouring and blowing wools (31). Airborne fiber counts are reported to be low for textile-type fibers as they are processed into finished products during spinning, weaving, twisting, plying, and chopping opera-

tions (21). High dust levels are noted in operations involving insulation. Fibrous glass dust exposure occurs when rolled fabrics are cut to various shapes, during spraying when fibers are chopped simultaneously with application of catalyst resins, and during finishing operations when material is removed and imperfections are ground.

Epidemiology

The majority of human cross-sectional prevalence studies have reported no significant pulmonary effects from fibrosis (17)(22)(28)(38)(54)(57). Studies utilized pulmonary function tests and chest x-rays. Workers were employed up to 30 years and, in most cases, exposure was to fibers having a diameter of about 6 μ with fiber concentrations averaging about 70,000 fibers/m^3 (11)(57). Only a few human studies are available to suggest chronic health effects occur from fibrous glass exposure; these studies mainly report an excess mortality from nonmalignant respiratory disease (19). However, in a 1977 report prepared for the medical and scientific committee on the Thermal Insulation Manufacturers Association, Enterline and Marsh presented preliminary information on a mortality study of 5,443 fibrous glass workers from five plants and 955 mineral wool workers from three plants, who had worked at least one year during the period January 1, 1945, through December 31, 1963 (19). No excess mortality risks were observed for malignant or nonmalignant respiratory disease, nor were excess lung cancer deaths observed in two plants which manufactured small diameter (1-3 μ) fibers. There was no association between intensity of exposure and death from malignant and nonmalignant lung diseases. The investigators stressed the preliminary nature of their findings and withheld final conclusions until all data was analyzed.

Carcinogenic responses in animals, particularly rodents, following intrapleural or intraperitoneal fibrous glass administration is similar to the responses found after implantation of any foreign material such as polyethylene, asbestos, nylon, cellophane, or teflon (10)(15)(40)(46)(55). Tumor development in laboratory animals following pleural or intraperitoneal administration of fibrous glass material probably represents a nonspecific foreign body response. The response depends on the physical characteristics of the fibrous glass, the most important being size and shape; certain characteristics of the animal; and the length of time the fibrous glass is present in the animal (a critical factor). On the basis of present information, fibrous glass cannot be considered a carcinogenic agent.

NIOSH has recommended that occupational exposure to fibrous glass having diameters equal to or less than 3.5 μ (53) and lengths more than 10 μ be limited to a 10-hour time-weighted-average concentration of 3,000,000 fibers/m^3. This should especially protect workers in operations using small diameter fibers. NIOSH also recommends limiting dust exposures (measured gravimetrically) to 5 mg/m^3 so as to also reduce exposure to larger diameter fibers. The recommendations are designed to control exposure to both small diameter fibers, which might have potential long-term adverse health effects, and larger diameter fibers, which can cause skin, eye, and respiratory tract irritation (18)(25)(26)(33) and possibly increased mortality due to nonmalignant respiratory disease (6)(19). Most fiberglass irritation effects can be minimized when proper work practices are followed. Workers having dermographism and atopic dermatitis probably should not work with fibrous glass (39). Periodic examinations of workers—including pulmonary function testing and chest x-rays—seem necessary because of potential respiratory disease as a result of fiberglass exposure (6)(19)(30)(36)(37).

When workers are exposed to fibers less than 3.5 μ in diameter, a lung cancer screening program seems reasonable. Respiratory protection becomes necessary only when large amounts of dust are generated, and where environmental exposure cannot be adequately handled by engineering controls. Good personal hygiene by workers is important in order to avoid or minimize skin problems. There should be washing facilities and showers available at work before workers change into street clothes and employers should provide laundered work clothes. Gloves or other types of protective clothing may be helpful in reducing direct contact with fibrous glass and subsequent skin problems. Good housekeeping practices are extremely important in minimizing exposure (42)(43). Vacuuming, cleaning, washdown procedures, and wet sweeping can be helpful in reducing dust concentrations. On the other hand, dry sweeping or blow-down with compressed air generates dust and should be

discouraged. Scrap material and debris should not be allowed to accumulate; waste material should be disposed of properly. Finally, concern for other potentially hazardous substances such as resins, solvents, and pesticides used with fibrous glass is also necessary.

Estimate of Population at Risk

According to NIOSH about 200,000 workers in the United States are exposed to fibrous glass in the manufacturing of about 20,000 products (53). The amount of fibrous glass insulation has increased since the government required that 36,000,000 homes meet Federal insulation standards by 1963 (53). Approximately 3,000 workers are exposed to mineral wool.

Pathology

The behavior of a glass fiber in air is mainly determined by its diameter and less by its length.

Timbrell reported that fibers with aerodynamic diameters larger than 3.5μ were primarily deposited in the nasopharynx, trachea, and bronchil; fibers with diameters less than 3.5 μ penetrated into the alveoli; maximal alveolar deposition occurred with fibers of 2 μ diameter and decreased to a minimum deposition of about 20% with fibers 0.4 μ in diameter (52). Mathematical models estimate approximately 30% of fibers 25 μ long and with a proper diameter could be deposited in the alveoli (23)(24); perhaps 1-3% of the fibers could be deposited in alveoli when fiber length increased up to 200 μ.

A number of animal studies have been performed exposing animals to fibrous glass by various routes (21)(32)(34)(48)(49)(55)(56). In studies addressing the fibrogenic potential of fibrous glass, length and diameter are important factors (21)(32)(43)(56). Fibers having a length greater than 10 μ are more likely to produce pulmonary fibrosis in animals; fibers shorter than 5 μ generally do not. Kuschner and Wright studied the effects of glass fibers of different dimensions (32). Groups of 30 guinea pigs were intratracheally injected with one of six possible categories of glass fibers differentiated according to dimensions. No fibrosis was found after exposure to short fibers. Exposure to long fibers (greater than 10 μ) resulted in an interstitial reaction around respiratory bronchioles and proximal alveoli. Thin (less than 1 μ) and long fibers caused a fibrotic reaction whereas thin and short fibers did not. Short and thick fibers caused some interstitial fibrosis after two years. Long and thick fibers caused focal areas of interstitial fibrosis.

There have been a number of pathologic studies of human lungs reported (8)(9)(22)(41)(47). Postmortem studies performed on lungs of 20 workers who had been exposed to various concentrations of fibrous glass for 16-32 years were compared with the lungs of 26 urban dwellers of both sexes who presumably had not been occupationally exposed to fibrous glass dust (22). Quantitative analyses of lung tissue of fibrous glass workers demonstrated total dust levels of about 2% (range, 0.8-4.2%); actual fiber content was approximately 95,000 fibers per gram of dry lung (range, 20,000-200,000). These fiber counts were no different from fiber counts noted in the lungs of controls. There was no correlation between lung fiber count and duration of severity of occupational exposure. The highest percentage of fibers grouped according to length were between 16 μ and 25 μ, with 90% of the fibers having diameters less than or equal to 3 μ. No specific tissue change was identified in the lungs of fibrous glass-exposed workers who became ill following a heavy exposure to fibrous dust from the insulaton of an old hot water heater (37). Examination of lung tissue obtained following a right lower lobectomy revealed multifocal abscesses containing minute fiberglass particles, similar to the particulate matter obtained from the actual insulating material. Adverse health effects reported from large diameter fibers have included mainly skin, eye, and upper respiratory tract irritation (18)(25)(26)(33). There are no indications that fibrous glass acts like asbestos in humans except possibly where there are high concentrations of submicron fibers. This condition occurs rarely, if ever, and is not expected to occur significantly in the future. Larger diameter fibers have different biological characteristics than smaller diameter fibers (32); fibers with a diameter of 3.5 μ and smaller penetrate into alveoli (13)(16)(22)(31)(51)(52). Fibers of longer length, i.e., 10 μ or greater, appear to be more biologically active than shorter length fibers. Health effects reported to occur with exposure to small diameter fiberglass are rare and generally confined to skin and respiratory tract irritation. Small diameter fiberglass is a relatively new material and population exposures for long

periods of time have not yet occurred. Chronic effects similar to those observed with asbestos have not been noted in individuals occupationally exposed to fibrous glass. Although fibrous glass was first manufactured in the 1930's, its extensive use did not occur until the 1940's and 1950's. Fibers having diameters less than 3.5 μ did not have large-scale use until the 1960's (41)(47). Therefore, chronic health hazards from small diameter fibers may not be appreciated since sufficient exposure in terms of numbers of people exposed and duration of exposure may not have occurred, nor has enough time lasped for potential chronic effects to be recognized. There has been concern that occupational exposure to fibrous glass having fiber dimensions similar to those of asbestos might lead to similar chronic effects. There are a number of factors which might mitigate against this, including the presence of fewer numbers of small diameter fibers in fibrous glass workplaces than usually existed in asbestos operations (53).

Unlike asbestos, fibrous glass does not fracture linearly to produce small diameter fibrils. Furthermore, fibrous glass is less durable than asbestos and is more easily fragmented and rapidly cleared from the lungs (8)(9).

Clinical Description

There are no specific clinical, x-ray, or pulmonary function test changes that are reported to be characteristic of fibrous glass exposure. Surveillance should be conducted because of the potential chronic health effects.

Diagnostic Criteria

No special diagnostic test is appropriate.

Research Needs

More information is needed on the health effects of fibrous glass of small diameter size, particularly since glass fibers less than 3.5 μ diameter are relatively new in industry. Especially needed are studies of very small diameter fibers i.e., less than 1 μ. There are still a number of unanswered questions concerning health effects of fibers with diameters larger than 3.5 μ. Studies are necessary to determine the chronic long-term effects of inhalation of fibers of various dimensions and to identify potential mechanisms of fibrogenesis and possible carcinogenesis. More industrial hygiene data is needed to characterize the extent of exposure to fibers with diameters less than 3.5 μ. Improvement in analytical methods for fibrous glass is necessary in order to determine precision and accuracy. The importance of physical features of fibers needs to be explored such as fibers splitting, role of fiber fragmentations, and importance of fiber solubility in relation to tissue effects.

Bibliography

1. American Conference of Governmental Industrial Hygienists, Committee on Industrial Ventilation: Industrial Ventilation:—A Manual of Recommended Practice, 12th ed. Cincinnati, 1972.
2. Balzer, J. L.: Environmental Data: Airborne Concentrations Found in Various Operations. p. 83-89. In: Occupational Exposure to Fibrous Glass: Proceedings of a Symposium HEW (NIOSH) Pub. No. 76-151, by U.S. Department of Health, Education, and Welfare, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, Washington, DC: U.S. Government Printing Office, 1976.
3. Balzer, J. L., Cooper, W. C., and Fowler, D. D.: Fibrous glass-lined AIR transmission system-An assessment of their environmental effects. Am Ind Hyg Assoc J *32:*512-518, 1971.
4. Balzer, J. L., Fowler, D. P., and Cooper, W. C.: Glass Fibers in Ambient Air—Report to Health and Safety Committee, National Insulation Manufacturers Association, Berkeley, California, School of Public Health, Division of Environmental Health Sciences, 1971.
5. Barnhart, J. M.: History of the Uses/Applications of Fibrous Glass. p. 27-29. In: Occupational Exposure to Fibrous Glass: Proceedings of a Symposium, HEW (NIOSH), Pub. No. 76-151 by U.S. Department of Health, Education, and Welfare, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, Washington, DC: U.S. Government Printing Office, 1976.
6. Bayliss, D., Dement, J., Wagoner, J. K., and Blejer, H. P.: Mortality patterns among fibrous glass production workers. Ann NY Acad Sci *271:*324-325, 1976.

7. Bobroff, A.: Itching from ventilation-borne fiberglass particles. JAMA *186:*80-81, 1963.
8. Botham, S. K. and Holt, P. F.: Comparison of effects of glass fibre and glass powder on guinea pig lungs. Br J Ind Med *30:*232-236, 1973.
9. Botham, S. K. and Holt, P. F.: The development of glass-fiber bodies in the lungs of guinea pigs. Am J Path *103:*149-156, 1971.
10. Brand, K. G., Johnson, K. H., and Buoen, L. C.: Foreign body tumorigenesis. Crit Rev Toxicol *4:*353-394, 1976.
11. Cholak, J. and Schafer, L.J.: Erosion of fibers from installed fibrous-glass ducts. Arch Environ Health *22:*220-229, 1971.
12. Cholak, J., Schafer, L.J., and Yeager, D.: On an Environmental Survey of the Plant of Owens-Corning Fiberglass Corporation at Newark, Ohio. Cincinnati, University of Cincinnati, College of Medicine, Department of Preventive Medicine and Industrial Health, Kettering Laboratory, 1963.
13. Corn, M. and Sansone, E.B.: Determination of total suspended particulate matter and airborne fiber concentrations at three fibrous glass manufacturing facilities. Environ Res *8:*37-52, 1974.
14. Criteria for a Recommended Standard Occupational Exposure to Crystalline Silica, HEW Pub. No. (NIOSH) 75-120, by U.S. Department of Health, Education, and Welfare, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health,Washington, DC: U.S. Government Printing Office, 1974.
15. Davis, J.M.G.: The fibrogenic effects of mineral dust injected into the pleural cavity of mice. Br J Exp Path *53:*190-201, 1972.
16. Dement, J.M.: Environmental Aspects of Fibrous Glass Production and Utilization. p. 97-109. In: Occupational Exposure to Fibrous Glass — Proceedings of a Symposium, HEW (NIOSH), Pub. No. 76-151. U.S. Department of Health, Education, and Welfare, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, Washington, DC: U.S. Government Printing Office, 1976.
17. de Treville, R.T.P., Hook, H. L., and Morrice, G.: Fibrous Glass Manufacturing and Health. Results of a Comprehensive Physiological Study, Part II, Read before the 35th Annual Meeting of the Industrial Health Foundation, Pittsburgh, 1970.
18. Duvoir, M., Derobert, L., and Lesire, L.: [Pruritic Dermatitis from Fiberglass]: Ann Dermatol Syphiligr (Paris), 1943, *3:*297-298 (Fre).
19. Enterline, P. E. and Henderson, V.: The health of retired fibrous glass workers. Arch Environ Health *30:*113-116, 1975.
20. Fowler, D., Balzer, J. L., and Cooper, W. C.: Exposure of insulation workers to airborne fibrous glass. Am Ind Hyg Assoc J *32:*86-91, 1971.
21. Gross, P., Kaschak, M., Tolker, E. B., Babyak, M. A., and de Treville, R. T. P.: The pulmonary reaction of high concentrations of fibrous glass dust: A preliminary report. Arch Environ Health *20:*696-704, 1970.
22. Gross, P., Tuma, J., and de Treville, R.T.P.: Lungs of workers exposed to fiber glass. Arch Environ Health *23:* 67-76, 1971.
23. Harris, R.L.: Aerodynamic Considerations: What is a Respiratory Fiber of Fibrous Glass? p. 51-56. In: Occupational Exposure to Fibrous Glass: Proceedings of a Symposium HEW (NIOSH) Pub. No. 76-151 by U.S. Department of Health, Education, and Welfare, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, Washington, DC: U.S. Government Printing Office, 1976.
24. Harris, R. L. and Fraser, D. A.: A model for the deposition of fibers in the human respiratory system. Am Ind Hyg Assoc J *37:*73-89, 1976.
25. Heisel, E. B. and Hunt, F.E.: Further studies in cutaneous reaction to glass fibers. Arch Environ Health *17:*705-711, 1968.
26. Heisel, E.N. and Mitchell, J.H.: Cutaneous reaction to fiberglass. Ind Med Surg *26:*547-550, 1957.
27. Hill, J.W.: Health aspects of man-made mineral fibers: A review. Ann Occ Hyg *20:*161-173,1977.

28. Hill, J. W., Whitehead, W. S.,Cameron, J.D., and Hedgecock, S.A.: Glass fibers: Absence of pulmonary hazard in production workers. Br J Ind Med *30:*174-179, 1973.
29. Johnson, D.L., Healey, J.J., Ayer, H.E., and Lynch, J.R.: Exposure to fibers in the manufacture of fibrous glass. Am Ind Hyg Assoc J *30:*545-550, 1969.
30. Kahlau, G.: [Fatal pneumonia following inhalation of a glass dust as a result of working with a synthetic material made of fiberglass]. Franz Z Pathol *59:* 143-150, 1947 (Ger).
31. Konzen, J.L.: Results of Environmental Air Sampling Studies Conducted in Owens-Corning Fiberglass Manufacturing Plants. p. 115-120. In: Occupational Exposure to Fibrous Glass: Proceedings of a Symposium HEW (NIOSH) Pub No. 76-151 by U.S. Department of Health, Education, and Welfare, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, Washington, DC: U.S. Government Printing Office, 1976.
32. Kuschner, M. and Wright, G.: The Effects of Intratracheal Instillation of Glass Fiber of Varying Sizes in Guinea Pigs. P. 151-168. In: Occupational Exposure to Fibrous Glass: Proceedings of a Symposium HEW (NIOSH) Pub. No. 76-151, by U.S. Department of Health, Education, and Welfare, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, Washington, DC: U.S. Government Printing Office, 1976.
33. Longley, E.O. and Jones, R.C.: Fiberglass conjunctivitis and keratitis. Arch Environ Health *13:*790-793, 1966.
34. Maroudas, N.G., O'Neill, C.H., and Stanton, M.F.: Fibroblast anchorage in carcinogenesis by fibers. Lancet *1:*807-809, 1973.
35. Mettes, D.G.: Glassfibers in Handbook of Fiberglass and Advanced Plastics Composites. Ed. by G. Lubin, New York, Van Nostrand Reinhold Co., 1969.
36. Milby, T.H. and Wolf, C.R.: Respiratory tract irritation from fibrous glass inhalation. JOM *11:*409-410, 1969.
37. Murphy, G.B.: Fiber glass pneumoconiosis. Arch Environ Health *3:*102-108, 1961.
38. Nasr, A.N.M., Ditchek, T., and Scholtens, P.A.: The prevalence of radiographic abnormalities in the chest fiber glass workers. JOM *13:*371-376, 1971.
39. Possick, P.A., Gellin, G.A., and Key, M.M.: Fibrous glass dermatitis. Am Ind Hyg Assoc J *31:*12-15, 1970.
40. Pott, F., Huth, F., and Friedrichs, K.H.: Results of animal carcinogenesis studies after application of fibrous glass and their implications regarding human exposure. p. 183-191. In: Occupational Exposure to Fibrous Glass: Proceedings of a Symposium HEW (NIOSH) Pub. No. 76-151 by U.S. Department of Health, Education, and Welfare, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health. Washington, DC: U.S. Government Printing Office, 1976.
41. Pundsack, F.L.: Fibrous Glass Manufacture, Use and Physical Properties. p. 11-18. In: Occupational Exposure to Fibrous Glass, Proceedings of a Symposium, HEW (NIOSH) Pub. No. 76-151, by U.S. Department of Health, Education, and Welfare, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, Washington, DC: U.S. Government Printing Office, 1976.
42. Recommended Health Safety Practices for Handling and Applying Thermal Insulation Products Containing Mineral Fibers, New York, National Insulation Manufacturers Association.
43. Schepers, G.W.H. and Delahant, A.B.: An experimental study of the effects of glass wool on animal lungs. Arch Ind Health *12:*276-279, 1955.
44. Schwartz, L. and Votvinick, L.: Skin hazards in the manufacture of glass wool and thread. Ind Med *12:*142-144, 1943.
45. Shand, E.B.: Composition and Properties of Fibers. In: Glass Engineering Handbook, 2nd ed., New York: McGraw-Hill Book Company, Inc. 1958.
46. Sincock, A. and Seabright, M.: Induction of chromosome changes in Chinese hamster cells by exposure to asbestos fibers.

Nature *257*:56, 1975.
47. Smith, H.W.: History, Processes, and Operations in the Manufacturing and Uses of Fibrous Glass—One Company's Experience. p. 19-29. In: Occupational Exposure to Fibrous Glass, Proceedings of a Symposium, HEW (NIOSH) Pub. No. 76-151, by U.S. Department of Health, Education, and Welfare, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, Washington, DC: U.S. Government Printing Office, 1976.
48. Stanton, M.F. and Wrench, C.: Mechanisms of mesothelioma induction with asbestos and fibrous glass. J Natl Cancer Inst *48*:797-821, 1972.
49. Stanton, M.F., Layard, M., Miller, M., May, M., and Kent, E.: Carcinogenicity of fibrous glass: Pleural response in the rat in relation to fiber dimensions. J Natl Cancer Inst *58*:587-603, 1977.
50. Talvitie, N.A. and Hyslop, F.: Colorimetric determination of siliceous atmospheric contaminants. Am Ind Hyg Assoc J *19*:54-58, 1958.
51. Timbrell, V.: The inhalation of fibrous dust. In: Section V: Human Exposure to Asbestos—Dust Controls and Standards. Ann NY Acad Sci *132*:255-273, 1965.
52. Timbrell, V.: Aerodynamic Consideration and Other Aspects of Glass Fiber. p. 33-50. In: Occupational Exposure to Fibrous Glass: Proceedings of a Symposium HEW (NIOSH) Pub. No. 76-151 by U.S. Department of Health, Education, and Welfare, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health. Washington, DC: U.S. Government Printing Office, 1976.
53. U.S. Department of Health, Education, and Welfare, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, Occupational Exposure to Fibrous Glass, DHEW (NIOSH) Pub. No. 77-152. Washington, DC: U.S. Government Printing Office, 1977.
54. Utidjian, H.M.D.: I.H.F. Statistical Studies of Health of Fibrous Glass Workers, read before the Fibrous Dust Seminar of the Industrial Hygiene Foundation and Mellon Institute, Pittsburgh, 1968.
55. Wagner, J.C., Berry, G., and Skidmore, J.W.: Studies of the Carcinogenic Effects of Fibrous Glass of Different Diameters Following Intrapleural Inoculations in Experimental Animals, p. 193-197. In: Occupational Exposure to Fibrous Glass, Proceedings of a Symposium HEW (NIOSH) Pub. No. 76-151, by U.S. Department of Health, Education and Welfare, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, Washington, DC: U.S. Government Printing Office, 1976.
56. Wenzel, M., Wenzel, J. and Irmscher, G.: The Biological Effects of Glass Fiber in Animal Experiment. Int Arch Gewerbepathol *25*:140-164, 1969 (Ger).
57. Wright, G.W.: Airborne fibrous glass particles. Chest roentgenograms of persons with prolonged exposure. Arch Environ Health *16*:175-181, 1968.

ZIRCONIUM

Introduction

Zirconium is a silvery-white metal, more abundant than nickel, but difficult to reduce to metallic form since it combines so readily with oxygen, nitrogen, carbon, and silicon (1). Animal experiments have indicated that zirconium compounds are capable of causing both pulmonary granulomas and interstitial fibrosis (2)(10). There are no well-documented similar effects in humans.

List of Causative Agents (Manufacturing Processes)

Zircon (ZrS_1O_2) and baddalyte (ZrO_2),the most common naturally occurring forms of zirconium, are derived from igneous and sedimentary rock and recovered commercially from beach sands and river gravel (9). Zirconium occurs mixed in the form of platelets, flakes, or bluish-black amorphous powder but is never found in a free state. While it is generally regarded as a rare metal, it is present in the earth's crust in amounts larger than lead, copper, or zinc, with concentrations about 0.22% (15).

Zirconium may be prepared by chlorination—either of zircon or of a carbide made from it by heating with carbon (3). This mixed tetrachloride of zircon and silicon are then separated and the crude zircon tetrachloride is

further purified by sublimation in hydrogen gas. This is further reduced in vapor from magnesium or sodium, the residual zirconium being in the form of a sponge which is highly reactive and must be conditioned before being exposed to the atmosphere. A second method of preparation is by thermal dissociation of the zirconium tetraiodide on contact with a hot filament at a temperature of approximately 1,300 °C (3).

Pure zirconium has important properties, especially that of high resistance to corrosion by alkalis and most acids (4). It is very reactive, especially in the moist powder form and is likely to cause an explosion. This is an onerous problem since the ignition temperature of zirconium is low (20 °C) and it can readily be ignited by sparks or small flames. Zirconium fires should not be extinguished by water because this may cause a violent explosion (7).

List of Occupations and Industries Involved

Zirconium oxide (ZrO_2) is a fine crystalline powder which is used for fused or sintered ceramics and for crucibles and furnace bricks (1). Zirconia bricks have been used for lining electric furnaces. Zirconia foam is marketed in bricks and various shapes are used for thermal insulation (1). Stabilized zirconia has a low coefficient of expansion and white-hot parts can be plunged into cold water without breaking. Zircon crystals are valued as gemstones since the high refractive index gives it a great brilliance. Zirconia fibers are used for high temperature textiles and are produced from zirconia with about 5% lime for stabilization. Zirconia fabrics are woven, knitted, or felted of short-length fibers and are flexible.

Zirconium powder is very reactive and is used for making sintered metals or making sintered parts. Alloys are frequently produced including zirconium copper, nickel, or cobalt. Zirconium alloys with high zirconium content have atomic applications. Small amounts of zirconium are used in many steels, zirconium being a powerful deoxidizer which removes nitrogen and combines with sulfur. It reduces hot-shortness and gives steel ductility (1). Zirconium carbide (ZrC_2) is produced by heating zirconia with carbon at about 2,000 °C. The crystalline powder is used as an abrasive and for hot-pressing in heat resistant and abrasion-resistant parts. Zirconium ceramics are valued for electrical and high-temperature parts and refractory coatings.

Zirconium has industrial uses: for nuclear reactors; as a shielding material in high vacuum tubes and radio valves, chiefly because of its affinity for various gases; in steel manufacture as an alloy with silicon and manganese; as a constituent of alloys such as nickel and cobalt in order to increase wear resistance, or with nisobium and tantalum in the manufacture of noncorrosive chemical apparatus;as a substitute for platinum; in cast iron manufacture; as a refractory lining for electric furnaces; as an igniter for photoflash bulbs; as an alloy with lead for lighter flints; as a substitute for mercury fulminate for detonators; in a concentrated arch lamp which gives the nearest approach to a point source; in the ceramic and glass industries as an opacifier and a polishing powder for lenses in television tubes; as pigments in plastics; and as a catalyst in organic reactions (3). Zirconium is utilized as a foundry sand and abrasive; as a refractory in combination with zirconia; as a coating for casting mold; a catalyst in alkyl and alkenyl hydrocarbon manufactures; as a stabilizer in silicone rubbers; and as a gem stone. In ceramics it functions as an opacifier for glazes and enamels and it is used in unfrittered glass filters. Zirconia itself is used in die extrusion of metals and in spout linings for pouring metals as a substitute for lime in oxyhydrogen light (16). It is also used as a pigment, in metal cutting tools, thermocouple jackets, waterproofing textiles, and treating dermatitis and poison ivy.

A list of occupations in which exposure to zirconium may occur includes (16):

abrasive makers
ceramic workers
crucible makers
deodorant makers
enamel makers
explosive workers
foundry workers
incandescent lamp makers
pigment makers
refractory material makers
vacuum tube makers
glass makers
metallurgy
raylon spinneret makers
textile waterproofers

Epidemiology

There have been no detailed epidemiologic studies.

Population at Risk

It has been estimated by NIOSH that there are approximately 1.3 million employees exposed to zirconium compounds, especially zirconium oxide (17).

Pathology

Early animal studies indicate that zirconium is inert and does not produce any significant pulmonary pathology (5)(6). Suspension of finely ground zirconium, when injected intravenously, intraperitoneally, or intratracheally, is without apparent effects and no significant pathological changes have been noted (5). When rats were exposed to very high concentrations of zircon dust daily for several months and then killed, dense radiologic shadows were noted on radiographed sections (6). These shadows were produced by aggregations of phagocytes containing zircon particles. There was also a slight inflammatory response, but essentially no significant lung reaction. Animal exposure studies with zirconium metal were generally negative (11). Skin granulomas from deodorant sticks containing zirconium salts have been described (12)(13)(14)(18). A typical zirconium deodorant stick is a gel containing sodium stearate, ethyl alcohol, carbotol, and water with about 10% of an aqueous 45% solution of sodium zirconium lactate (approximately 0.5%) (3). The skin granulomas were described as reddish-brown papules being 1-4 mm in diameter. Biopsied lesions did not reveal zirconium in the granulomas even with examination by x-ray fluorescence and emission spectrometry (3). The skin eruptions were described after several months of use. They generally disappeared spontaneously but slowly, sometimes persisting for months or years (14) (15). These skin reactions were believed to be due to a hypersensitivity to zirconium (14)(15).

There are no reports available of good pathological studies on human lung. Peribronchial granulomas have been produced in rabbits following inhalation of sodium zirconium lactate (10). Diffuse pulmonary fibrosis has been reported to occur in a variety of experimental animals after prolonged inhalation of zirconium lactate (2). Reed reported a case of a pulmonary granulomous reaction in a chemical engineer associated with the process of a purification and reduction of zirconium metal (11). Twenty-two workers who had been exposed to the fumes of this process for 1-5 years were also evaluated (11). None of these workers showed granulomatosis and 15 had no pulmonary symptoms; 5 had symptoms of chronic bronchitis, 3 of whom were also exposed to chlorine gas. The original case, which was believed to have zirconium-induced disease, was subsequently found to have chronic beryllium disease and had been exposed to beryllium seven years previously.

Clinical Description

There appear to be no clinical effects of zirconium and zirconium compounds in man. There are no lung function studies on record.

No x-ray changes attributable to zirconium were reported by Reed in 22 workers exposed for a period of 1-5 years in a zirconium plant (11). McCallum reported the presence of small densities (Categories 1-3) on chest x-rays of eight men working in a zirconium process plant adjacent to an antimony smelting plant (8). The significance of the x-ray changes is not known.

Diagnostic Criteria

Since zirconium is widely used in industry, it is possible that a pneumoconiosis could be caused by zirconium dust. Perhaps the occasional report of small opacities seen on chest x-ray in molders and knockout foundry men using molding sand and parting powders containing zircon are caused by zirconium rather than iron. One must be cognizant, therefore, in light of changes noted in animals, of the possibility that zirconium compounds may cause chest x-ray opacities and perhaps diffuse granulomatous pneumonitis and interstitial fibrosis (9).

Methods of Prevention

Dust concentrations should be kept to a minimum. Good general housekeeping and safety practices are in order, as they are for any occupational exposure.

Research Needs

More studies are needed to determine whether zirconium compounds are capable of producing significant pulmonary disease in exposed individuals.

Bibliography

1. Brady, G.S. and Clauser, H.R.: Materials Handbook, 11th ed. New York: McGraw-Hill Book Company, 1977.
2. Brown, J.R., Mastromatteo, E. and Horwood, J.: Zirconium lactate and barium zirconate. Industr Hyg J *24:*131-136, 1963.
3. Browning, E.: Toxicity of Industrial Metals, 2nd ed. New York: Appleton-Century-Crofts, 1969.
4. Gegner, P.J. and Wilson, W.L.: Corrosion resistance of Ti and Zr in chemical plant exposures. Corrosion *15:*341, 1959.
5. Harding, H.E.: The toxicology of zircon: Preliminary report. Br J Ind Med*5:* 75-76, 1948.
6. Harding, H.E. and Loyd Davies, T.A.: The Experimental Production of Radiographic Shadows by the Inhalation of Industrial Dusts, Part II: Zircon (Zr Si Oy). Br J Ind Med *9:*70-73, 1952.
7. Hartman, I.: Explosion and Fire Hazards of Combustible Dusts, p. 549-578. In: Industrial Hygiene and Toxicology, 2nd ed., Vol. I. Ed. by Frank A. Patty. New York: John Wiley and Sons, Inc., 1963.
8. McCallum, R.I.: The work of an occupational hygiene service in environmental control. Ann Occup Hyg *6:*55-63, 1963.
9. Parkes, W.R.: Occupational Lung Disorders. London: Butterworths and Co., Ltd., 1974.
10. Prior, J.T., Crouk, G.A., and Ziegler, D.D.: Pathological changes with the inhalation of sodium zirconium lactate. Arch Environ Health *1:*297-300, 1960.
11. Reed, C.E.: A study of the effects on the lungs of industrial exposure to zirconium dusts. AMA Arch Ind Health *13:*578-580, 1956.
12. Rubin, L., Slepyan, A.H., Weber, L.F., and Neuhauer, I.: Granuloma of the axilla caused by deodorants. JAMA *162:*953, 1956.
13. Sheard, C., Zirconium Cornice, F.E., Atkinson, S.C., and Worthington, E.L.: Granulomatous reactions to deodorant stick. JAMA *164:*1085, 1957.
14. Shelley, W.B. and Hauley, H.J.: Experimental evidence for allergic basis for granuloma formation in man. Nature *180:* 1060, 1957.
15. Shelley, W.B. and Hauley, H.J.: The allergic origin of zirconium deodorant granulomas. Br J Dermatol *70:*75, 1958.
16. Tabershaw, I.R., Utidjian, H.M.D., and Kawahara, B.L.: Chemical Hazards, p. 131-439. In: Occupational Diseases DHEW (NIOSH) Pub. No. 77-181 by U.S. Department of Health, Education, and Welfare, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health. Washington, D.C.: U.S. Government Printing Office, 1977.
17. U.S. Department of Health, Education, and Welfare, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health. National Occupational Hazard Survey, Vol. III. Survey Analysis and Supplemental Tables. Washington, D.C.: U.S. Government Printing Office, 1977.
18. Weber, L.R., Rubin L., Slepyan, A.H., and Shellow, H.: Granuloma of axilla. JAMA *162:*65, 1956.

RARE EARTHS

Introduction

The term rare earths usually refers to the lanthanum (or lanthanons) series of metals having atomic number 57-71, and includes yttrium with atomic number 39 (11). They are part of the transition metals Group 3, being the first series of the periodic tables and having similar molecular structures. They are found together in various combinations in many ores: the most important are monazite and bastnaesite, but also xenotime, gadolinite, samarskite, fergsonite, apatite, and euxenite. Cerium, atomic number 58, is the most abundant rare-earth metal, but thorium oxide is also present in small amounts in monazite and yttrium. Norway, Sweden, the United States (Idaho, California and South Carolina), Ontario, Canada, and Brazil are the principal suppliers of rare earths. In the series with atomic number 57-71, each metal has 2 outer electrons and 8 or 9 electrons in the next inner shell. The metals vary in their third shell from the outside, with each element above lanthanum having one electron more in the third layer than the element below it (57). This makes the mass and atomic weight larger, but the additions of these electrons make little difference in the physical properties of the metals (11). Con-

sequently the rare earths are very similar and separation of them is difficult (12).

List of Causative Agents (Manufacturing Processes)

The rare-earth metals are usually found together in ore. The metals with atomic number 57-63 and including cerium (58) have also been referred to as light rare earths (3). Yttrium (atomic number 70) is also included in this group because of its light weight.

When thorium is separated from monazite ore, the residual matter may be reduced by electrolysis to an alloy which contains about 50% cerium together with other rare metals (3), and is called misch metal, a German name for mixed metal. Misch metal is used for making aluminum alloys and some steels and iron. It is useful in removing sulfur and oxides and completely degassifies steel. It is used as a precipitation and hardening agent for stainless steel. Another important use of misch metal is in the manufacturing of magnesium for aircraft castings.

Cerium oxide, a pale yellow, heavy powder, is used for coloring ceramics, for producing distortion-free optical glass and for decolorizing crystal glass. Cerous oxide (CE_2O_3) makes glass completely absorbent to ultraviolet rays and is thus an excellent opacifier for ceramics. Neodymium is used in magnesium alloys to increase strength and elevate temperatures and is used in some glasses to reduce glare (3). Lanthanum oxide, a white powder, is used for absorbing gas in vacuum tubes; the bromine is used as an electron admitter for maintaining a constant active cathode surface and has a high electric conductivity.

Didymium is not an element but a mixture of rare earth without cerium. It contains the oxides of lanthanum, neodymium, praseodymium, samarium, and other oxides. It is really the basic material in which the rare metals are produced. It gives glass a neutral grey color and is used in glass for welders' goggles because it absorbs yellow light and reduces glare and eye fatigue.

Dysporsium has high corrosion resistance and has good neutron-absorption ability. It is used in nuclear reactor control labs, in magnetic alloys, and in serrites for microwave use. It is also used in mercury arc lamps.

Cerium is used in coloring glass yellow, but can also be used to enhance the clarity of white glass (11). It gives a blue fluorescent quality to glass when made in reducing conditions, but if made in an oxidizing process, it produces no fluorescence. It is also used to prevent color changes in glass when exposed to ultraviolet. Cerium has replaced rouge in polishing glass. It is also used as a dye in the textile industry for mildew-proofing. Cerium constitutes about 50% of the makeup of misch metal used in magnesium and ferrous alloys.

Praseodymium is used to color glass, to make carbon arc cores for light and theater projection machines, search lights, and other intense lighting sources.

Neodymium is used to make purple glass and also used for stopping glass lasers.

Promethium is an important radioactive source and is used for luminescent dials.

Samarium is used in making infrared-absorbing glass and is a constituent of nuclear reactors.

Gasolinium has a high neutron absorption factor and is used in control rods and reactors. As an alloy, it improves high temperature characteristics of iron and chromium.

Metallic thorium is used in nuclear reactors to produce nuclear fuel, in the manufacture of incandescent lamps, and as an alloying material (18).

List of Occupations and Industries Involved

A partial list of occupations in which exposure to rare earths may occur includes:

ceramic workers
incandescent lamp workers
metal refiners
organic chemical synthesizers
aircraft castings maker
gas mantle workers
alloy metal workers
nuclear reactor workers
nocium tube makers
glass (vitreous) makers
rocket fuel makers
light flint makers
textile workers
ink makers
phosphor makers
metal refiners
enamel makers
workers exposed to carbon arc lamps

Epidemiology

There have been essentially no significant epidemiologic studies of individuals exposed to rare earths. A few case reports are described in the section on Clinical Description.

Estimate of Population at Risk

The overall population at risk is unknown. NIOSH estimates that there are about 7,000 workers potentially exposed to cerium oxide.

Pathology

No pathological studies of human lungs appear on record and the rare earths are believed to be relatively nontoxic. However, skin changes have been described following exposure to some of the rare earths (7)(9). The chlorides of the rare earths may cause eye irritation and transient conjunctivitis. Corneal damage has been described with terbium and opacities have been noted with lantanum (15). Intratracheal administration of the oxide of yttrium, neodymium and cerium in rats produce lung granulomas (7)(9). In large quantities inhalation may produce an acute chemical pneumonitis and bronchitis in animals (11). In other studies when rare earths were inhaled or injected by intratracheal routes into experimental animals there was no evidence of pulmonary fibrosis or other types of pulmonary reaction (10).

Cochran, et al. reported that lanthanum compounds exhibited low toxicity when administered orally to rats (4). Mice exposed to gadolinium oxide aerosol for 20-120 days demonstrated an increased number of deaths due to pneumonia five weeks after exposure. There was a trend toward shorter life spans in mice who survived exposure (2). There was also evidence that this compound was cleared completely from the lung. Histological features supported the evidence of its low-grade toxicity. There were focal areas of interstitial thickening and areas of macrophage accumulation containing rare earth dust particles. An unusual histological feature was pulmonary calcification in the region of the outer basement membrane and elastic lamina of small pulmonary vessels of exposed mice (2).

Schepers introduced a blend of rare earths with a high oxide content into the lungs of guinea pigs by intratracheal injection and noted fatal chemical pneumonitis in one-third of the animals. In those that survived, cellular eosinophilia was a prominent feature (17). Most of the dust was trapped within areas of focal atelectasis, but no pulmonary fibrosis was noted At one month, there was evidence of intraalveolar accumulation of pigment and engulfment of dust by alveolar macrophages. There was some dust transport to perivascular lymphatics. After one year, in animals that survived, there was peribronchial accumulation of dust and minimal scarring. In animals studied at 570 days, there were perivascular pulmonary granulomas without much pigment noted. Hilar lymph nodes showed focal aggregation of rare earth dust without inflammatory reactions. When blends of rare earth compounds, predominantly composed of fluorides, were introduced intratracheally, an acute transient chemical pneumonitis was produced followed by a subacute bronchitis and bronchiolitis (16). Graca et al. did a comparison study of stable rare earth compounds and found only transient but no permanent pulmonary changes (5)(6).

Clinical Description

There are no symptoms or abnormal physical signs or alterations reported for rare earths. No change in pulmonary physiology has been attributed to these inhaled dusts.

X-ray appearance

Hueck and Hoschek reported that 3 of 67 persons working in a photographic department of an offset printer, and in contact with carbon arc lamps, demonstrated opacities on chest x-ray similar to those of baritosis; they believed that the changes were due to cerium and other rare earths (10). In order to increase the brightness, the rods in arc lamps were equipped with cored carbon. An essential component of the rods is made up of rare earth fluorides. Parkes reported a similar case of an individual with dense opacities on chest x-ray who worked with cerium dioxide for six years (14). A French report describes two subjects with a miliary disease on chest x-ray, possibly due to the inhalation of cerium oxide (13).

Diagnostic Criteria

Differential diagnoses similar to other high-density dusts are in order. One may demonstrate radioactive thorium-228, in the expired breath by whole-body counter (14). Perhaps most important, a detailed occupational history will

establish the diagnosis of rare earth pneumoconiosis.

Analysis of tissue for rare earths by a quick and inexpensive means is not available; it is complex, especially when identifying for specific rare earths. Total rare earths content can be found by chemical methods (11). Absorption and x-ray fluorescence spectra can also be used for identifying a variety of rare earths (11). Flame photometry is not suitable for most rare earths because of interferences, but it can be used for lanthanon, neodymium, and ytterbium (12). Spectrographic analysis can be used for identifying rare earths especially when they are present in trace amounts. With the exception of cerium, atomic absorption spectrometry is the method of choice for quantitative determination for rare earths (11).

Method of Prevention

Environmental control is mainly designed to decrease inhalations since ingestion is harmless. Heated rare earths may give off toxic fumes that should be controlled. Dusts should be ventilated adequately (11). There is no TLV for any of the rare earths elements, although yttrium has an arbitrary TLV varying between 1 and 5 mg/m^3, which was based on no clinical experiences or inhalation experiments (11). The TLV for yttrium can probably be applied to all rare earths. Gloves, protective eye wear and other protective equipment is necessary to prevent skin contact, especially with terbium. Employees with corneal injuries, kerato-conjunctivitis or conjunctivities should not be exposed to the dusts. When there is thorium exposure, the amount of α-emitting radon daughters in air should be kept as low as possible, although no specific level has been yet generally agreed on.

Research Needs

Since there have been so few clinical pathologic studies available it is obvious that more information is needed. Little is known about the potential health effects of coexisting thorium (an α-particle emitter) and its decoy chain. High concentrations of thoron daughters have been observed in thorium mining (1).

Bibliography

1. Albert, R.E.: Thorium, Its industrial Hygiene Aspects. New York: Academic Press, 1966.
2. Ball, R.A. and Van Gelder, G.: Chronic toxicity of gadolinium oxide for mice following exposure by inhalation. Arch Environ Health *13:*601-608, 1966.
3. Brady, G.S. and Clauser, H.R.: Materials Handbook, 11th ed. New York: McGraw-Hill Book Company, 1977.
4. Cochran, K.W., Doull, J., Mazur, M., and Dubois, K.P.: Acute toxicity of zirconium, columbium, strontium, lanthanum, cesium, tantalum, and yttrium. Industr Hyg Occ Med *1:*637-650, 1950.
5. Grace, J.G., Davidson, F.C., and Feavel, J.B.: Comparative toxicity of stable rare earth compounds, Arch Environ Health *5:*437-444, 1962.
6. Grace, J.G., Davidson, F.C., and Feavel, J.B.: Comparative toxicity of stable rare earth compound. III. Acute toxicity of intravenous injections of chlorides and chelates in dogs. Arch Environ Health *8:*555-564, 1964.
7. Haley, T.J.: Pharmacology and toxicology of lutetium chloride. J Pharm Sci *53:* 1186, 1964.
8. Haley, T.J.: Pharmacology and toxicology of europium chloride. J Pharm Sci *54:* 643, 1965.
9. Haley, T.J.: Pharmacology and toxicology of the rare earth elements. J Pharm Sci *54:*663, 1965.
10. Heuck, F. and Hoschek, R.: Cerpneumoconiosis. Am J Roentg *104:*777-783, 1968.
11. Knight, A.L.: The Rare Earths in Occupational Medicine. Ed. by Carl Zenz. Chicago: Year Book Medical Publishers, Inc., 1975.
12. Kolthoff, I.M. and Elving, P.J.: Treatise on Analytical Chemistry, Part II, Vol. 8. The Rare Earths. New York: Interscience Publishers, Inc., 1963.
13. Nappee, J., Bobrie, J. and Lambard, D.: Pneumoconiose an cerium. Arch Mal Prof *33:*13, 1972.
14. Parkes, W.R.: Occupational Lung Disorders. London: Butterworths and Company, Ltd., 1974.
15. Patty, F.A., ed. Industrial Hygiene and Toxicology, 2nd ed. New York: Interscience Publishers, Inc., 1962.
16. Schepers, G.W.H., Delahart, A.B., and Redlin A.: Experimental studies of the effects of

rare. AMA Arch Industr Health *12*:297-300, 1955.
17. Schepers, G.W.H.: The biological action of rare earths: 1. The experimental pulmonary histopathology produced by a blend having a relatively high oxide content. AMA Arch Industr Health *12*: 301-305, 1955.
18. Tabershaw, I.R., Utidjian, H.M.D., and Kawahara, B.L.: Chemical Hazards, p 131-443. In Occupational Diseases by U.S. Department of Health, Education, and Welfare, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health. Washington, DC: U.S. Government Printing Office, 1977.