TOXICOLOGY
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ASBESTOS

NATURE OF MATERIAL (1)

The word asbestos, which means inconsumable, is generally used to describe several fibrous magnesium silicates (mineral silicates) which are different in their chemical composition and physical properties. The most important types of fibers are chrysolite, amosite, crocidolite, anthophyllite, actinolite and tremolite. Chrysolite belongs to the serpentine group while the others belong to the amphibole group. These terms denote the different types of asbestos according to the chemical and physical characteristics of each type. The chemical formula of chrysolite, which forms the bulk of commercial asbestos, is $3MgO \cdot 2SiO_2 \cdot 2H_2O$. Asbestos fibers are highly resistant to heat and acids. They have great tensile strength and large surface areas.

WHERE FOUND IN NATURAL STATE (2)

Total world production of all fibers in 1954 amounted to slightly more than 1,500,000 tons. Approximately 95% of the fibers produced were of the chrysolite variety (long, silky and soft fibers); 3% crocidolite and 2% amosite (short, stiff and brittle fibers). Deposits of various types of this mineral are found in many countries, but the largest mines are located in Canada and South Africa. The chrysolite variety comes from Canada while the crocidolite and amosite varieties come from Africa.

WHERE AND HOW USED IN INDUSTRY

Asbestos is widely used in industry because of its filamented structure and because of its resistance to physical and chemical agents. Asbestos is used in the manufacture of blankets, clothing, threads, rope, tape, braided tubing, brake lining and brake blocks, wallpaper, wallboard, shingles, firebricks. floor covering and plastics. Asbestos is mixed with cements and plastics. It is used as insulation material for houses, pipes, boilers, ranges, wire, heaters, ironing boards, heating pads, automobile and machinery parts. (2) Recently an automobile mechanic was reported to have acquired asbestosis while undercoating vehicles (3).

NATURE AND MECHANISM OF TOXICITY

There are two theories regarding the pathogenesis of asbestosis; the mechanical and chemical. The generally accepted theory of the production of asbestosis is the mechanical one. As the result of experimental work on the production of asbestosis in animals, Vorwald and associates (1) concluded that typical peribronchiolar fibrosis was produced when the particle length of the inhaled asbestos dust lay between 20 and 50 micra. Also, it has been shown that these fibers are less than one micron in diameter. These are the most active fibers in the production of asbestosis. They can reach the terminal bronchioles but generally not the alveoli. The bronchiole which is continually expanding, contracting, elongating, shortening is thus mechanically irritated. The primary site is the bronchiole and fibrosis spreads from there to involve the alveoli. A foreign body inflammatory reaction follows. Gardner states the mechanical theory as follows:(4)

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> We have come to the conclusion that inhaled asbestos fibers are irritating not because they are silicates but because they are stiff fibers which mechanically irritate the lungs. Unlike the free silicas, these minerals will not stimulate fibroblasts in any part of the body; only those in the lungs are affected. It was inferred that these organs were affected because the movements of respiration are so much more rapid and continuous than those of other viscera. Then it was discovered that if asbestos was ground very finely so that few of the fibers were longer than 2 microns in length, the irritating property of the asbestos was practically destroyed. Inhalation experiments with such fine chrysolite asbestos were carried out over a period of several years. No fibrosis has developed in spite of the fact that an average atmospheric concentration of 125 million particles per cubic foot of air has been maintained. In contrast, in a previously reported experiment, one third this concentration of long-fiber asbestos dust produced well marked fibrosis after about two years.

A decrease in particle size would be expected to accelerate tissue reaction if the effect of asbestos were chemical. In the case of silica, for example, as the size of silica particles decreases, the cellular reaction becomes more vigorous, and constitutional symptoms may follow exposure to ultramicroscopic particles. With fibrous asbestos particles, however, this is not the case, and the reverse is true. Also, the histology of early asbestosis does not suggest chemical injury. Even under extreme conditions, there is no preliminary phase of tissue necrosis with infiltration of leukocytes as occurs with high concentrations of fine quartz. Also, serpentine which has the same chemical formula as chrysolite asbestos but is nonfibrous does not produce proliferative fibrosis. The question arises though why fiberglass, which may be fairly similar in size, does not produce a disease state. The difference is probably the elasticity of fiberglass (1).

There are some questions which arise in regard to the acceptability of the mechanical theory as an explanation for the pathogenesis of asbestosis.

Knox and Beattie (5) noted that the time interval between the first exposure to asbestos dust and the appearance of asbestosis in human autopsy specimens was not less than 12 years. It appears that this long interval between the first exposure and the appearance of typical fibrotic changes indicates that the mechanism for the production of human asbestosis differs from that shown to be responsible for the experimental type as described by Vorwald and associates (1). For, if the mere presence of asbestos particles within a critical size range was the essential factor, it would be difficult to explain why so many persons escape any asbestotic change even when exposed for more than 30 years.

There is general agreement that soon after inhalation the majority of the asbestos fibers become included in the asbestos bodies. The experiments of Vorwald and his co-workers (1) suggested that these latter structures are inert but the bodies do not remain as intact structures indefinitely. With the passage of years they become "weathered," eroded, segmented and finally fragmented (6). It is thus possible that the fibrotic changes in the lung of humans is related to the process of disintegration of the asbestos body.

Knox and Beattie (6) offer several comments in support of the chemical theory as opposed to the mechanical theory in the production of asbestosis. Their study dealt with the mineral content of the lungs of some 27 workers who had had exposures from 5 - 33 years in the asbestos textile industry. (Time interval between the last exposure to dust and death - survival time - was from less than one year to 21 years.

1. There was an indication that the mineral material found in the lungs increased in amount as the exposure time lengthened. The amount so accumulated varied considerably from person to person. As the survival time increased, the mineral content of the lung tended to decline but again at a variable rate.

2. The severity of the asbestotic lesions in the lungs found at death was related not to the mineral content but to the sum of the exposure and survival times.

3. The number of particles with a greatest length in excess of 26 micra disappeared almost completely from the lung parenchyma when the survival time was more than eight years. This supports Gloyne's (7) opinion that in the long-standing cases of asbestosis the number and size of both the asbestos fibers and the asbestos bodies seen in histological preparations were less than in those cases more recently exposed to asbestos dust.

4. Excluding the cases of severe asbestosis, the particle counts in the two ranges (1) below five micra and (2) between 5 and 15 micra showed no significant change as the combined exposure and survival time increased. It would appear, therefore over a long period of time either that there was no movement of asbestos or asbestos-derived particles from the lungs or that the rate at which small particles were produced from larger ones was almost equal to the rate at which they were removed from the lungs. Since it appears that the mineral content of the lung tends to decline with increasing survival time, the latter alternative is the more probable.

5. In the cases of severe asbestosis, the significantly high counts in the small particle range indicates either a much more rapid breakdown of larger particles or a fall in the rate at which the small particles are removed. And while it seems that the rise in the small particle counts is quite probably due to the reduced rate of removal (in these cases, both the hilar, pleural and subpleural tissues contained much mineral material), there is no conclusive evidence that this is so.

6. The association of high counts in the small particle ranges with severe asbestosis suggests that the latter is not due to the mere presence within the lung of particles with greatest lengths within a critical size range of 20-50 micra.

7. A rise in the numbers of small mineral particles derived presumably from the breakdown of asbestos bodies is associated with severe fibrotic changes in the lung parenchyma. This implies that either these particles or some other product of the breakdown of the bodies can exert a fibrogenic effect on lung tissue.

8. If these products are removed as rapidly as they are formed, then either no asbestosis develops or a minimal degree of change occurs. A reduced rate of removal of these products may be due to partial blockage of the drainage routes from the lung - either toward the lung hilus or toward the pleural surface. Any patholo-

gical process which would cause any inflammatory change in the hilum or in the lymph nodes into which the pleural lympatics drain might cause a further reduction in the drainage rate and might precipitate the onset of severe fibrotic changes. Cardiac decompensation too might be a factor in the precipitation of these changes.

Pathology (8) - The important pathological findings involve the lungs. Gross: Generally there is much pleural thickening especially of the lower lobes with adhesions to the lower chest wall and diaphragm. The lower lobes are firm and indurated while the upper lobes may be emphysematons. Bronchiectasis is not an uncommon finding. There is often a honeycomb appearance of the lung. On palpation the lungs are usually firm, tough and airless. Areas of dense fibrosis show the grey-black mottling.

Microscopic: Early there is thickening of the bronchiolar walls with fibroblastic proliferation. With progression fibrosis is more marked and alveolar structure disappears as dense fibrous tissue develops. Although fibrosis may appear grossly to have escaped the apices, much may be seen on microscopic examination. Asbestos bodies are found in profusion in and around the densely fibrous areas; the tendency is to occur in radially arranged clumps. In addition to the dense fibrosis, inflammatory catarrhal changes may be observed, with desquamation of alveolar and bronchiolar epithelium and thickening of the alveolar and bronchiolar walls. Here asbestos bodies tend to be fewer in number. Foreign body giant cells, distinct from tuberculosis giant cells, may be present in the connective tissue. They are somewhat larger than the latter; their cytoplasm has a stippled and pigmented appearance in contrast with the structureless, caseating appearance of the tuberculous giant cell.

Asbestos Bodies: Highly characteristic golden yellow bodies are found in the sputum and fibrosed lungs of asbestos workers. They vary in size and shape, characteristically having bulbous enlargements at the extremities with a regularly or irregularly segmented body, resembling dumbbells; when fractured, they are club-shaped. The appearance of fully formed bodies are like beads on a necklace; the beads vary in size, and represent the irregularly segmented body. The golden-yellow material covering each fiber contains an iron substance which gives a prussian blue reaction. When stained with ammonium sulfide, the central core of the fiber stains lightly against a deeper stained body. The bodies have been observed to vary in length from 20 to over 200 microns. An asbestos fiber forms the central core of each body. The asbestos fiber is coated with a protein precipitate material and foreign body giant cells. The yellowish-brown color is the result of the deposition of iron salts, possibly iron silicate, on the surface of the asbestos body. The bodies have also been found in the feces, spleen and upper abdominal lymph glands. The bodies may be found in the lung tissue either singly or in clumps and may occur similarly in the sputum. The bodies tend to be scanty if there is little bronchial secretion; when they are more abundant in the sputum, they may occur in radially arranged clumps; such an occurrence indicates disintegration of lung tissue by either simple suppurative bronchopneumonia or secondary tuberculous infection. Their presence in sputum does not signify asbestosis, only the inhalation of asbestos.

Asbestos bodies may persist in the sputum for years despite short periods of exposure. In one instance a patient was exposed to asbestos dust for one year, yet the bodies were present in the sputum 14 years later. In another case exposure was for 10 weeks and the bodies were still present in the sputum 5 years later (8).

Asbestosis and Cancer: - Hueper (9), from the National Cancer Institute, feels rather strongly that asbestosis predisposes to lung cancer. In 1955 he quoted 127 cases of asbestos carcinoma of the lung as being on record (United States, 21; Canada, 6; Great Britain, 88; Germany, 12), and an incidence from 7.5% to 50% of carcinoma in autopsied asbestosis cases. In order to rule out any nonspecific irritant as a cause, he stated that silicosis has a normal or less than average association with pulmonary carcinoma.

Isselbacher's (1) survey of the literature in 1953 summarized several reports whose combined deaths from asbestosis total 603. Of these, 83 died from carcinoma of the lung, for an incidence of 13.8%. This incidence is considerably greater than the average autopsy incidence of carcinoma of the lung from 1935 - 1949, of 24.25 per 100,000 population as quoted by Cohart (11).

One further point made by Isselbacher deserves comment, as it may afford some help in determining if asbestosis and lung cancer are related. He pointed out that 80% of asbestosis carcinomas arise in the lower lobes. This is consistant with the primary locations of uncomplicated lung carcinoma which vary from 53% to 57% in the upper lobes and 26% to 35% in the lower lobes.

He points out one other factor to keep in mind and that is the association of lung cancer and cigarette smoking. About three-fourths of the cases studied gave a long history of cigarette smoking.

Keal (12) reports on 30 deaths (15 men and 15 women) out of 42 cases of asbestosis studied. There were 14 who died with lung cancer (10 men and 4 women). The women were all non-smokers. Nine women and 1 man died with ovarian or peritoneal cancer. This appears to be more than a chance association, and spread from undiagnosed lung cancer seems unlikely. He feels that there may be a relationship between abdominal neoplasms and asbestosis as well as lung cancer and asbestosis. Eisenstadt (13), reports on 3 cases of asbestosis which presented clinically as pleurisy. There was no x-ray evidence of lung involvement. 2 of the cases terminated in death from primary pleural mesothelioma.

In a survey of an asbestos plant by Dr. Mancuso (14), there was found to be an increase in the incidence of cases of lung cancer and primary cancer of the peritoneum (mesothelioma), together with an increase in abdominal cancer and cancer of the brain. The brain lesions may have been secondaries to the lung cancer. Asbestos bodies have been found in every organ in the body, and it has been suggested by other workers that the asbestos fibers or bodies may pass through the diaphragm to the peritoneal cavity.

Wagner et al (15) report 33 cases of diffuse pleural mesothelioma and all but one were exposed to crocidolite asbestos (Cape blue).

Not all authors have accepted this alledged association without reservation. In 1958 Braun and Truan (16) reported on an extensive survey of workers in the asbestos mines in Quebec, Canada. The medical records of 6,091 persons who had at least 5 years of exposure were reviewed. They concluded: 1) on the basis of what are believed to be complete and reliable data, it seems fair to conclude that the asbestos miners in the Province of Quebec do not have a significantly higher death rate from lung cancer than do comparable segments of the general population; 2) the death rate from lung cancer in the areas contiguous to the asbestos operations is comparable to that in areas widely scattered throughout the Province of Quebec and is lower than in some urbanized areas within the Province.

Clinical Picture - The average time lapse from the initial exposure to asbestos dust to the development of asbestosis is 9 years according to Egbert and Geiger(17), although this figure varies according to different authors and much shorter exposure times have been recorded. In many cases the worker has left his exposure in industry for several years before the onset of symptoms. The nature of the work and the duration and the degree of asbestos dust inhaled appear to influence the onset and severity of the disease (17). Even with clinical and radiological signs present, symptoms may be absent.

There is no typical clinical picture for asbestosis. The disease is insidious in its onset and slowly progressive with continued inhalation of the fiber. Some investigators (10) feel that the fibrosis is a progressive phenomenon even after exposure has ceased, although there are others who take the opposite view (1). There is a gradual increase in cough and expectoration, there may be chest pain, some anorexia and weight loss, then slowly increasing dyspnea. Cyanosis and clubbing of the fingers are rare findings seen only in the far advanced cases. Death may occur from heart failure due to corpulmonale or it may be caused by other complications.

Asbestos corns form a characteristic skin lesion. An asbestos fiber penetrates the skin producing a hyperkeratotic reaction around it. No asbestos bodies are found in the corn. They form on the hands, arms, and legs (8).

It has been shown by Smith (2) that asbestos workers are not predisposed to develop more intercurrent pulmonary infections than are found in other workers. However, when an acute pneumonitis develops in the presence of an established asbestotic fibrosis, the infection is slow to heal, relapses are frequent, and the patient may be more susceptible to subsequent pulmonary infections. Smith (2) cites a personal communication with Parrot who found that in two towns in the Province of Quebec where asbestos is mined and processed, the incidence of tuberculosis among asbestos workers was lower than among the general population of these mining towns.

Physical Findings (8) - There may be limited chest expansion, especially at the bases where the fibrosis begins. The percussion note may be impaired especially at the bases. There may be decreased breath sounds at the bases with harsh breath sounds and prolonged expiration over the upper lung fields, indicative of compensatory emphysema. Adventitious breath sounds are almost characteristic. Fine, dry crackling rales may be heard over the bases and in the axillary areas. Pleural friction rubs due to associated pleurisy are not uncommon. These physical findings will usually only be found in the more advanced cases.

Pathologic Physiology - Pulmonary function studies as reported by Gregoire and cited by Smith (18) have shown that the chief physiological problem is that of a "tight" lung. Expansion of the lung is difficult with decreased inspiratory capacity and decreased lung volume related to pleural adhesions and pulmonary fibrosis. Accordingly, the vital capacity and maximum breathing capacity are lowered. Forced expiratory volume is normal. Arterial oxygen saturation of the blood is diminished in some cases. This is usually considered to be predominantly a diffusing defect (2).

Thompson et al (19), however, feel that the apparent decrease in diffusion is due as much to a reduction in lung volume as it is to membrane permeability based

on the single breath CO method. It is agreed though that there is little or no functional emphysema in asbestosis. Pulmonary function studies are of importance in the proper diagnosis of pulmonary fibrosis and the estimation of pulmonary disability.

X-Ray Findings (20) - It has been suggested repeatedly that a negative period exists when the disease may be present to a significant degree clinically, without being manifest roentgenologically. This obviously has a bearing on the important and very difficult problem of the diagnosis of asbestosis in its early stage.

The roentgenographic changes may be divided broadly into pleural changes and parenchymal lung changes. Frequently a combination of both occurs. Hurwitz (20) feels the pleural changes far outnumber the parenchymal changes. The pleural changes may be nonspecific in the form of uni- or bilateral, parietal or interlobar, thickenings of varying extent. Obliteration of the costophrenic sulci as well as diaphragmatic and pleuropericardial adhesions also occur, statistically, more frequently among asbestos workers than in other groups.

A localized recent basal pleuritis may be observed but not frank or copious pleural effusion. The veiling and lack of radiolucency in lung areas where pleural pathology exists evidently appears, in many cases, to be due mainly to pleural fibrosis, rather than to underlying pulmonary fibrosis. As a result of extensive pleural thickening, the cardiac outline and the outline of the diaphragm are not sharply defined. When pleuritic adhesions are present, distortion and irregularity of contour in the form of "peaking" and "tenting" are noted. On fluoroscopy, restricted diaphragmatic mobility and diminished chest movement may be seen.

A more specific pleural pathology has recently come to light in the form of added calcification and the deposition of typical pneumoconiotic plaques. This has been noted as a regularly recurring feature in old asbestos workers with varying periods of service. Calcific plaque formation may be minimal or extensive, linear or occurring in irregular patches; it is usually bilateral and more or less symmetric. The plaques are often distributed along the parietal pleura, particularly in the middle and lower zones, but it is worth noting that extensive areas of calcification may be found along the anterior aspect and that both the diaphragmatic and mediastinal pleura are commonly involved. The asbestotic plaques, which, though not common, are usually seen in the upper zones peripherally. It may be emphasized that in pure asbestosis, in contradistinction to silicosis, associated "egg shell" lymph node calcification is singularly absent.

The parenchymal lung change presents as a classic pattern of simple uncomplicated diffuse pulmonary fibrosis. There may be merely a homogeneous clouding and haze over the lung fields, particularly over the lower lobes, producing a ground glass appearance. When very mild this can present great difficulty in diagnosis. A more definite stage is one which shows a fine striated, fibrillar change in the lung structure, causing progressive reduction of pulmonary radiolucency with blurring and masking of the vascular lung markings. Eventually, an advanced stage of diffuse lung induration is reached with marked pulmonary hypoventilation which gives an unmistakable picture. A few cases may present with localized areas of homogeneous, compact, pneumonic consolidation and fibrosis. These areas may occur in any part of the lung.

The diffuse interstitial fibrosis must be differentiated from scleroderma, rheumatoid arthritis and Hamman-Rich syndrome. Usually these nonoccupational diseases do not have pleural changes.

It should be emphasized that the parenchymal changes may occur alone but usually occur with the pleural changes. THE FINE DIFFUSE PUNCTATE MOTTLING STANDS OUT IN DEFINITE CONTRAST TO THE COARSE NODULAR MOTTLING SEEN IN SILICOSIS.

Many cases with x-ray evidence of advanced asbestosis have been known to carry on their usual work and live fairly comfortable lives for several years. On the other hand no case of definite disability has been seen unless there was the typical x-ray pattern.

In an x-ray survey of 708 employees in a milling operation, Smith (2) reports that the majority (91%) had normal films. Twenty-nine per cent of the 708 had 10 or more years of service; two men had worked more than 40 years in the dust. Conclusions of this survey: 10 or more years of exposure were necessary to produce x-ray changes; no cases of asbestosis were found in men who had worked less than 20 years in the dust; and of all workers exposed to the fibers, very few develop asbestosis.

Diagnosis

The presence of asbestos bodies in sputum indicates merely exposure to asbestos dust; it cannot alone justify a diagnosis of pulmonary asbestosis. A diagnosis of a diseased condition of the lungs depends upon the cumulative findings of:

1. exposure to asbestos dust
2. clinical evidence of pulmonary fibrosis
3. radiological evidence of fine, diffuse, pulmonary fibrosis
4. asbestos bodies in sputum, feces or lung tissue.

THERAPY OF INTOXICATION

As might be guessed by this time, there is no specific therapy for asbestosis. Treatment is symptomatic. If early or moderately advanced asbestosis is suspected, the worker should be removed from further exposure.

EFFECTIVE PREVENTIVE AND CONTROL MEASURES

Postman (21), feels that the best measures to control asbestos dust are proper engineering of machines and methods used to keep the dust enclosed; along with this, adequate exhausting of the contained dust and adequate ventilation where required. He also feels that approved respiratory equipment should be provided and that it be required to be worn when necessary.

LATEST MAC (22)

Asbestos dust ——— 5 million particles per cubic foot of air.

B I B L I O G R A P H Y

1. Vorwald, A. J.; Durkan, T. M. and Pratt, P. C.: Experimental Studies of Asbestosis, AMA Arch. Indust. Hyg. and Occup. Med., 3:1-43, Jan. 1951.

2. Smith, K. W.: Pulmonary Disability in Asbestos Workers, AMA Arch. Ind. Health, 12:198-203, 1955.

3. Brugsch, H. G. and Bauley, H.: Asbestosis in a Worker Engaged in Automobile Undercoating, New England Journal of Medicine, 265:379, Aug. 24, 1961.

4. Gardner, L. V.: Recent Developments in Relation to Silicosis, Ind. Med. and Surg., 9:45, 1940.

5. Knox, J. F. and Beattie, J.: Mineral Content of the Lungs After Exposure to Asbestos Dust, AMA Arch. Ind. Hyg. and Occup. Med., 10:23-29, July, 1954.

6. Knox, J. F. and Beattie, J.: Distribution of Mineral Particles and Fibers in the Lung After Exposure to Asbestos Dust, AMA Arch. Ind. Hyg. and Occup. Med., 10:30-36, July, 1954.

7. Gloyne, S. R.: Pneumoconiosis: Histological Survey of Necropsy Material in 1205 Cases, Lancet, 1:810-814, 1951.

8. Ellman, P.: Pulmonary Asbestosis: Its Clinical, Radiological and Pathological Features and Associated Risk of Tuberculosis Infection, Journ. Ind. Hyg., 15:165-183, 1933.

9. Hueper, W. C.: Silicosis, Asbestosis and Cancer of the Lung (Editorial), Am. Journ. Clinical Path., 25:1388, 1955.

10. Isselbacher, K. J.; Klaus, H. and Hardy, H. L.: Asbestosis and Bronchiogenic Carcinoma: Report of One Autopsied Case and Review of Available Literature, Am. J. Med., 15:721, 1953.

11. Cohart, E. M.: Socio-Economic Distribution of Cancer of the Lung in New Haven, Cancer, 8:1127, 1955.

12. Keal, E. E.: Asbestosis and Abdominal Neoplasms, Lancet, 2:1211-6, 3 Dec.1960.

13. Eisenstadt, H. B.: Pleural Asbestosis, American Practitioner, 13:573-8, Sep. 1962.

14. Mancuso, T. F.: Former Chief of Dept. Public Health, Columbus, Ohio, (Seminar) May, 1961.

15. Wagner, J. C.; Sleggs, C. A. and Marchand, P.: Diffuse Pleural Mesothelioma and Asbestos Exposure in the Northwestern Cape Province, Brit. Journ. Ind. Med., 17:260, Oct. 1960.

16. Braun, D. C. and Truan, T. D.: An Epidemiological Study of Lung Cancer in Asbestos Miners, AMA Arch. Indust. Health, 17:634-53, June, 1958.

17. Egbert, D. S. and Geiger, A. J.: Pulmonary Asbestosis and Carcinoma; Report of Case With Necropsy Findings, Am. Rev. Tuberc. 34:143-150, 1936.

18. Gregoire, F.: Pulmonary Function Studies in Men Exposed for Ten or More Years to Inhalation of Asbestos Fibers, read before the Seventh Saranac Symposium, 1952 (unpublished) cited by Smith, K. W.: Pulmonary Disability in Asbestos Workers, AMA Arch. Ind. Health, 12:198-203, 1955.

19. Thomson, J. L.; McGrath, M. W.: Smitker, W. J. and Shepherd, J. M.: Some Anomalies in the Measurement of Pulmonary Diffusion in Asbestosis and Chronic Bronchitis with Emphysema, Cl. Sci., 21:1, Aug. 1961.

20. Hurwitz, M.: Roentgenologic Aspects of Asbestosis, Am. J. Roent. 85:256-62, Feb. 1961.

21. Postman, B. F.: Dust Control in the Asbestos Textile Industry, Am. Ind. Hyg. Assoc. J. 23:67, Jan. - Feb. 1962.

22. American Conference of Governmental Industrial Hygienists: Threshold Limit Values for 1961, Arch. Envir. Health, 3:125, Oct. 1961.

COAL DUST AND CARBON DUST

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Soot and similar forms of carbon when stored in the lungs in small or moderate amounts is so called nondisabling anthracosis. Or the term "coal miner's lung" or "black lung" dates back to observations made during autopsies in the 1830's (1,2). In addition to heavy exposure to coal dust, many coal miners, particularly those mining anthracite coal, are exposed to much silica dust. In such exposed individuals, the accumulation in the lungs of two types of dust, silica and coal, results in the development of anthracosilicosis. Many hard coal miners develop this disease with all the characteristics of silicosis plus the results of the deposits of coal dust (3).

For many years until the recent time, attention was focused on the role of silica as the injurious agent in the dust to which miners are exposed; that is to say, it was believed that disability was solely the result of the fibrogenic effects of finely divided silica only and that coal dust was definitely harmless (2). Recently a modification of this concept has definitely become necessary since the cases of pneumoconiosis have been reported among coal trimmers in South Wales, whose only exposure consisted of loading coal into ships. With other evidences, it is now conclusively said that coal dust per se does contribute to the pathophysiology of pulmonary diseases in coal miners (1, 4).

The British have recognized coal workers' pneumoconiosis as a discrete entity and have concentrated their efforts to elicit the etiology of the disease in a centralized Pneumoconiosis Research Unit. In other countries, including the United States, the tendency has been to consider all pneumoconioses as variations of silicosis, until very recently (1, 5). Hence, reports of the incidence and natural history of the disease are virtually nonexistent outside of the British literature, except that a few have reported radiographic change in U. S. miners resembling those in British coal miners (12, 13, 14). Authors in the U. S. writing on this problem continue to use the term anthracosilicosis (10, 11).

In South Wales the Pneumoconiosis Research Unit adopted a disease classification consisting of 3 categories of simple pneumoconiosis and 4 categories of complicated disease or progressive massive fibrosis. These categories are established by the radiologic appearance of the lungs, and are analogous to the radiologic categories of the pneumoconioses, in general, adopted by the I.L.O. They are listed at the end of this paper.

Clinical Pathology

In Wales, the Cardiff group and Gough (6) particularly, has shown that coal dust stored in large quantities stimulates the production of a fine loose mesh of reticulum fibers. With massive storage of coal dust in the lungs in addition to this, soft nodules of stored coal dust and many scattered strands of coarse collagen fibrosis are produced. The nodular accumulations of coal dust, and the coarse fibrosis, collapse tiny pulmonary capillaries and exert marked pressure upon the adjacent bronchioles causing atrophy of their smooth muscle. Since the afflicted bronchioles are unable to enlongate with inspiration and contract on expiration, they tend to become fixed in an elongated distended position thus forming rosettes about the coal dust foci. For the most part, the alveoli remain normal and breathlessness does not develop unless bronchospasm and/or accumulations of mucus result in the development of a superimposed obstructive emphysema. Then the characteristic disabling symptoms of obstructive emphysema occur. In uncomplicated cases with widespread bronchial dilatation, there is increased residual air remaining in the

dilated bronchioles and possibly in the alveoli (focal emphysema). As a result the oxygen in the inspired air is diluted somewhat. However, the reserve capacity of the lung is so great that unless obstructive emphysema supervenes, no significant disability is present.

Sometimes, when the disease is advanced, the upper lobes of the lungs develop irregular dense masses of fibrous tissue. These masses may vary from 1-2 or 3cm in diameter. In time they tend to coalesce and form massive fibrosis causing marked breathlessness. About such dense fibrous masses, which are usually tuberculous in origin, areas of bullous emphysema develop.

The clinical picture is strictly one of progressive emphysema. There are first complaints of shortness of breath and reduced exercise tolerance, then chronic cough often accompanied by wheezing and production of black sputum (2, 7). In time, increased susceptibility to infection leads to bouts of pneumonitis with their accompanying sequellae of bronchiectasis, etc. Patients with advanced P.M.F show progressive weight loss, elevated erythrocyte sedimentation rates and, often, polycythemia, in addition to respiratory insufficiency (8). Cor pulmonale develops in about one out of five cases of coal workers' pneumoconiosis (2). Death may be due to pulmonary infection or congestive failure.

As is the case in silicosis, the disease is of serious significance to its victims only when it reaches the Progressive Massive Fibrosis stage. However, P.M.F. only develops upon a foundation of simple pneumoconiosis, making early detection and removal of victims from exposure to dust the only effective treatment (8

Gross Pathology: The lung is voluminous and crepitation may be elicited. If massive fibrosis has developed, emphysematous bullae are present. Cut section shows a dark surface with much focal and generalized emphysema. Innumerable minute black nodules are visible and soft on palpation. In some cases where fibrotic thickening is evident, these small dark foci can be palpated as discrete nodules although not fimr and round as silicotic nodules.

Microscopic pathology: The dust foci are composed of dense masses of coal dust laden phagocytes with some free particles of dust packed about small bronchioles and their arterioles. A delicate reticulum of loose fibers is present but only occasional coarse collagen fibers. The small amount of fibrosis is diffuse, rather than in the compact concentric arrangement characteristic of silicosis. Actually, the radial fibers may expand to noninvolved areas. The surrounding air spaces are dilated and many bronchioles are dilated resulting in focal areas of emphysema. In the upper lobe when massive fibrosis occurs, sections show dense fibrous tissue destroying all normal lung architecture. Most cases of massive fibrosis develop because of tuberculosis, but identification of the tuberculous infection is difficult in many cases (2, 3).

Difference of pathology caused by silicate dust and that caused by coal dust: If, as above mentioned, the coal dust by itself is responsible for the development of pneumoconiosis, the question may come up - how it is different from silicosis. Following are from two reports dealing with this:

> Anderson et al (9) studied a group of coal miners who had been hand loaders during their entire mining lives and a group who had spent most of their working time as motormen. Hand loaders, of all the men underground, are exposed primarily to coal dust. The motormen were exposed to dust from the haulage way and to dust of their own making from the application of sand to the rails for purposes of traction.

The results are summarized as follows:
The group of hand loaders contained significantly more men over the age of 60 years, although there is no difference between the two groups with regard to mean age. The group of loaders had significantly greater number of men working 35 years or more. More of the loaders with pneumoconiosis had a normal maximum breathing capacity (MBC 90% or more of predicted) than did the motormen with pneumoconiosis and the complaint of dyspnea than loaders with pneumoconiosis and a similar complaint. There was a marked and signifiaant difference between the two groups when considering the presence of pinhead or nodular densities in those with radiographic evidence of pneumoconiosis. The loaders had predominantly pinhead densities and the motormen predominantly nodular densities. In spite of these radiographic differences, the two parent groups and the two subgroups with pneumoconiosis did not differ with respect to cessation of work because of dyspnea, maximum breathing capacity less than 60% of normal, or EKG evidence of right ventricular hypertrophy.

Nakamura et al has studied the difference between metal miners silicosis and coal miners' pneumoconiosis in Japan (15).

a). Morphological differences
In silicosis, the chemical action of free silica is more prevalent, while in coal workers' pneumoconiosis (CWP) the mechanical action of the dust is predominant.

		Silicosis	CWP
1.	Shape of nodule	round, not radiating	Irregular, radiating to the surrounding
2.	Confluence	uncommon	frequent
3.	Tendency of fibrosis	strong; chemical action	poor; mechanical action
4.	Restrictive force to bronchial wall	intensive; less deformative bronchitis	poor; deformative bronchitis
5.	Vascular changes	intensive	poor

6. In silicotic massive fibrosis each nodule is rather easily distinguishable, but in CWP the nodule mostly appears as diffuse fibrous consolidation and each nodule cannot be distinguished. The progressive massive fibrosis comes mostly from organization of inflammatory exudate, and tuberculous inflammation is the most important form.
7. In silicosis, even if the distribution of nodules is dense, there are many cases in which destruction in the remaining lung tissue is not obvious. On the contrary, in CWP, not only focal emphysema but also emphysematous changes are remarkable.

b). Functional Differences

	Silicosis	CWP
1. RV/TLC x 100	slight increase	considerable increase
2. 1" VC/VC x 100	slight decrease	considerable decrease
3. viscous resistance	slight increase	considerable increase
4. static compliance	considerable decrease	slight decrease

Namely, in silicotic cases the lungs are inflated slightly, and, moreover, they become very stiff and difficult to dilate, but the resistance to ventilation is minimal, showing a slight ventilatcry impairment. The CWP cases do not differ

much from those of chronic pulmonary emphysema with pleural adhesion, showing severe ventilatory impairment.

c). The difference of silico-tuberculosis in metal miners and coal miners:
Compared with metal miners, among coal miners in Japan there are very few cases of complicated tuberculosis. In coal miners the tempo of progression of tuberculosis is very conspicuous, and many convalescent cases are observed even if the grade develops to moderately advanced tuberculosis.

Silicotuberculosis in metal miners is exceedingly drug-resistant and the effect of chemotherapy is hardly expected in moderately advanced tuberculosis. When the disease gets worse, the main change observed in coal miners' lung is the exacerbation of the existing tuberculous lesion, while in metal miners' cases such other changes as the formation of cavity, the reactivation of once healed foci and new dissemination of the disease are observed.

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Another question comes to our mind: if the pure carbon is capable of pulmonary fibrosis, since coal dust contains some amount of silica dust which, though of very little amount, may be yet partly responsible for the development of pulmonary fibrosis.

This problem does not seem to be settled today and a considerable literature on carbon pneumoconiosis has accumulated in the past 30 years but closer scrutiny reveals only very few cases in which the dust was pure carbon or "nearly pure" carbon (16, 17). The conclusions drawn from these cases are oddly contradictory. F. Koelsch (18) find the evidence that lung fibrosis can develop without silica unconvincing. He thinks that pneumoconiosis, caused by pure graphite without any admixture of silica or silicates, may possibly be produced experimentally but hardly occurs in practice. Meiklejohn (17) on the other hand says "it emerges that pneumoconiosis of the coalworkers' type, simple and complicated, can be caused in workmen by dust in which silica constitutes only a trace". Similarly, Gough and Heppleston (19) find "it may be concluded that free silica is not necessary for the development of the pure dust lesion in coal workers...".

Case reports of pure carbon pneumoconiosis are collected from various types of industries such as carbon stick workers, synthetic graphite mill and carbon black factory workers; mixing and grinding lamp black with other grades of carbon produced from gas and oil cokes, mixing carbon black in rubber, and turning and grinding synthetic graphite bars, etc.

W. Koelsch (20) described a condition of "pure carbon lung" which he found in electrode workers who had handled a pure form of carbon with very little silica contamination. He called it an advanced stage of carbon pneumoconiosis and not silicosis. Radiologically there were nodulation and conglomerate shadows with massive fibrosis. With so low a silicic acid content in the dust he was unable to explain the radiological findings, which were similar to soot workers' "silicosis" of the 2nd and 3rd degrees.

Meiklejohn (17) studied the radiological changes in a group of carbon black workers and found the reticulation of simple pneumoconiosis: in a second group handling carbon with a small amount of mineral impurity, one man showed the radiological appearances of pneumoconiosis with fibrosis. Vaccarrezza (21) described lung changes in a man who had been shovelling charcoal for several years and Watson (22) described changes in the lungs of a carbon electrode worker. In all these papers, excepting that of Watson, the evidence is entirely radiological; histological examination could not be made as the workers were alive and had not undergone surgery to the lungs.

Miller and Ramsdem reported a case which was discovered in a routine post-mortem examination (23). The man had worked in the carbon black store of a rubber works for a continuous period of 21 years, followed by 11 years in the calendar department of the same factory. At the age of 65 years the man was retired on the grounds of age and indifferent health; he collapsed and died soon afterwards. The medical history of severe cough with expectoration suggested that he may have had pulmonary tuberculosis in earlier life and some supporting evidence of this infection was found in that his wife contracted this disease after marriage and subsequently died from tuberculosis.

The appearances of massive fibrosis in the upper lobes of the lungs suggested that the combined action of carbon black and tuberculosis had produced an "infective" type of pneumoconiosis; in the lower lobes there was far less fibrosis and the appearances were those of simple pneumoconiosis. In addition to the fibrosis the lungs showed nodules of black dust with severe perifocal emphysema. Electron microscopy of the lung dust showed two distinct components, and they were similar to samples of channel and thermal blacks which were the main types of carbon used in the factory.

Classification according to the "International Classification of Persistent Radiological Opacities in the Lung Fields Provoked by the Inhalation of Mineral Dusts" from the "Classification of Radiographs of the Pneumoconioses" published by the International Labor Office in 1958 (Geneva Classification 1958).

Depending on the size of the small opacities, three types are listed:
p: predominance of punctiform opacities up to 1.5mm in diameter
m: predominance of micronodular opacities 1.5-3.0mm in diameter
n: predominance of nodular opacities 3-10mm in diameter

The number of small opacities are classified in three categories:
Cat. 1: a small number of opacities in an area equivalent to at least two anterior rib spaces and not greater than one-third of the lung field.
Cat. 2: opacities more numerous and diffuse than in Cat. 1 distributed over most of the lung field.
Cat. 3: very numerous profuse opacities covering the whole or very nearly the whole of the lung field.

The size and number of large opacities are divided into three categories:
Cat. A: an opacity having the longest diameter of between 1-5cm or several opacities each greater than 1cm, the sum of whose longest diameter does not exceed 5cm.
Cat. B: one or more opacities larger or more numerous than those in Cat. A whose combined area does not exceed half of the lung field.
Cat. C: one or more large opacities whose combined area exceeds half of the lung field.
Cases in which coalescence was suspected but not definite as in Category A below were designated as AX.

Comment on this Classification by Some Authors:

The difference between "small opacities" (simple pneumoconiosis) and "large opacities" (progressive massive fibrosis - PMF) is well established pathologically and differences between the two have also been established from the point of view of pulmonary function (25) and the expectation of life (26). The categories of the "small opacities" have also been shown to be related to the risk of developing PMF (27) and the amount of dust in the lungs (28). The classification of large opacities of PMF is usefully related to mortality and an even closer relationship

with mortality was found by measuring the area of the "large opacities (29).

REFERENCES

1. Drinker, Philip and Theodore Hatch: Industrial Dust, ed. II, McGraw Hill Book Co., N. Y., 1954.
2. Wyatt, John P.: Morphogenesis of pneumoconiosis occurring in southern Illinois bituminous workers. AMA Arch. Ind. Health 21:445-56, May, 1960.
3. Johnston and Miller:
4. Cochrane, A. L. et al: The prevalence of coalworkers' pneumoconiosis: Its measurement and significance. Brit J. Ind. Med. 13:231-50, 1956.
5. Roy, K. B.: Pneumoconiosis in central Indian coal miners. Brit. J. Ind. Med. 13:184-86, 1956.
6. Gough, J.: Pneumoconiosis in coal trimmers. J. Path. Bact. 51:277, 1940.
7. James, W. R. L and Arthur J. Thomas: Cardiac hypertrophy in coalworkers' pneumoconiosis. Brit. J. Ind. Med. 13:24-29, 1956.
8. Cochrane, A. L. et al: Factors influencing the radiological progression rate of progressive massive fibrosis. Brit. J. Ind. Med. 13:177-83, 1956.
9. Anderson, H. W. et al: A comparison of coal miners exposed to coal dust and those exposed to silica dust. AMA Arch. Environ. Health 1:540, 1960.
10. Davis, W. C. and Snow, W. T.: Anthrcosilicosis presenting as a solitary pulmonary lesion. J. Thoracic Surg. 36:185, 1958.
11. Theodos, P. A. et al: Studies in the clinical evaluation of disability in anthracosilicosis. Dis. Chest 17:249, 1950.
12. Levine, M. D. and Hunter, M. B.: Clinical study of pneumoconiosis of coal workers in Ohio River Valley. JAMA 163:1, 1957.
13. Reed, E. S. et al: Radiology 71:661, 1958.
14. Martin, J. E., Jr.: AMA Arch. Ind. Health 15:494, 1957.
15. Nakamura, T. et al: A comparative study of the metal miners' silicosis and coal workers' pneumoconiosis. Tohoku J. Exper. Med. 73:309-34, 1961.
16. Hollmann, R.: Z. Tuberk. 52:394, 1928.
17. Meiklejohn, A.: In reports, 12th International Congress on Occupational Health, Helsinki, 1957, v. 3, p. 335.
18. Koelsch, F.: Zbl. Arbeitsmed. 8:1, 1958.
19. Gough, J. and Heppleston, A. G.: A symposium on industrial pulmonary diseases. eds. E. J. King and C. M. Fletcher, p. 27. Churchill, London.
20. Koelsch, W.: Beitr. Silikose Forsch. (1951) 10:162.
21 Vaccarrezza, R. F.: Proc. 5th Int. Congr. on Diseases of the Chest, Tokyo, 1958, Abstr. of papers, p. 163.
22. Gough, J.: In Modern Trends in Pathology, ed. D. H. Collins, p. 285, Butterworth, London.
23. Miller, A. A. and Ramsden, F.: Brit. J. Ind. Med. 18:103, 1961.
24. Lister, W. B.: Carbon pneumoconiosis in a synthetic graphite worker. Brit. J. Ind. Med. 18:114, 1961.
25. Gilson, J. C. and Hugh-Jones, P.: Spec. Rep. Ser. Med. Res. Coun., London, no. 290, H.M.S.O., 1955.
26. Carpenter R. G. et al: Brit. J. Ind. Med. 13:102, 1956.
27. Cochrane, A. L. et al: Brit. Med. J., i, 1193.
28. Rivers, D. et al: Brit. J. Ind. Med. 17:87.
29. Cochrane, F. et al: The prognostic value of radiological classification in cases of progressive massive fibrosis. Tubercule 42:64, March, 1961.

Aluminum, Aluminum Dust, Bauxite, Shaver's Disease

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General Discussion:

Unfortunately, there still remains a good deal of discussion and dissention about the various aspects of the peucoconioses associated with exposure to Aluminum dust, etc. As a general statement at this time it can be said that there does exis a cause-effect relationship between exposure to bauxite, bauxite fumes, exposure to fumes from the mixtures of bauxite-coke-ferric hydroxide, etc. and a generalized diffuse form of interstitial, fibrotic pneumonitis leading to replacement of lung tissue by scar tissue, the formation of emphysematous bullae, and diffusion defects with subsequent cor pulmonale.

The situation is not clear cut at all in reference to exposure to pure aluminu however, as shall be seen in the discussion below.

ALUMINUM: Chemical symbol Al, valence +3
Melting point 658 degrees centograde
Atomic weight 26.97
Boiling point 1800 degrees C.
Density 2.70
MAC: Aluminum oxide dust 50 million particles/cubic foot air
Fume: 15 mgm/cubic meter
Common form: Al_2O_3 amphoteric

BAUXITE: Aluminum oxide 50%; Silica (free) (0.5%-.02%); $FeOH_3$ 9-10%

Occurrence and Usage

Aluminum has a relatively large amount of activity and thus is quite common in its occurrence, not in metallic form, but in compounds in rocks vegetation, animals. Oxygen and silicon only are more prevalent. Usually found as silicate or oxide, but may be in form of phosphate or sulfate. Bauxite, the most common ore containing aluminum (50-60% hydroxide) also contains contaminants of titanium, ferric hydroxide, and silica. Roughly four pounds of bauxite are used to manufactu one pound of pure aluminum, or two pounds of alumina. (3)

The production and use of aluminum is quite large and varied. Production in 1951 was over a million tons. There are at least 3500 uses for the metal, and it is commonly employed as an alloy: "duraluminum", an alloy of copper, magnesium, manganese; "magnalium", magnesium; and aluminum bronze of copper, tin and iron. Aluminum stearate is used as a stabilizer in various greases and oils, the aluminum salts are used as mordants in the textile industry, the alums have wide uses, and "corundum" is an effective popular abrasive compound.

Metabolism (See pathological discussions below).

Aluminum combines with both acids and bases, forming salts, and aluminates. The ion is rather small with a 3 charge, therefore strongly attracts negative groups, so that aluminum chloride and hydroxide behave as co-valent compounds (3).

The principle site of entrance is the GI tract primarily due to ingestion of various salts, etc., and through therapeutic regimentation. Small quantities can apparently be absorbed from the respiratory tract, the skin, or from intramuscular injections. Daily normal absorption is thought to be about 100 microgram/day. There appears to be little renal excretion of ingested aluminum suggesting poor absorption Tissue levels vary from 0.004 to 0.5 mgm/100 gm tissue, and it is assumed that the human body may contain 50 to 150 mgm of aluminum.

Injected aluminum is gradually transported and deposited in various tissues and organs where it remains for as long as 1 year or more. Generally, there appear to be no injurious effects, except a recently reported case of encephalopathy and respiratory failure associated with high tissue aluminum (McLaughlin, 1962). Experimental studies in rabbits indicate acute and lethal poisoning by injection of very large doses of salts either subcutaneously or peritoneally. Intravenous compo must be injected in solutions of 1% or less since precipitation occurs otherwise in the blood. Metabolic difficulties have occurred in patients treated for upper GI diseases with large amounts of aluminum salts, with alteration of absorption and changes in the acid-base balance.

Klosterkoter, Christie and others have studied the effects of inhalation of dust particles and have demonstrated acute "catarrhal", and inflammatory changes in the alveoli, bronchioles, etc., with the formation of alveolar edema, lipoid pneumonia, focal emphysema, abscesses, etc. (see below. Formation of progressive fibrosis or hyaline nodules presumably did not occur; and most of the effects appeared to be acute. Particles are phagocytosed, and collected in lymphoid tissue

Kidney, spleen, thyroid, brain, and liver contain the highest amount of absorl aluminum; excretion is primarily via the bile, GI tract, and urine.

Industrial Exposure and Manufacturing Techniques

Basically the exposure takes two different forms; the exposure to high concentrations of relatively pure aluminum oxide powder, or aluminum, used in the manufacturing of aluminum compounds such as duraluminum or other alloys of aluminum bronze products; and exposure to impure aluminum powder or fumes such as occurs in the use of bauxite to produce corundum compounds or more pure aluminum compounds The pathology results from the action of the combined Aluminum amorphous, fine sili in all probability in the latter; and presumably from the aluminum itself in the former.

One method of preparation involves the heating of bauxite or aluminum oxide in large crucibles using graphite rods as electrodes. The molten metal collects below (1000 degrees centigrade). If proper ventilation is not provided massive exposure to fumes can occur as the vats are opened for the addition of raw material and most of the cases of bauxite (Shaver's) lung reported in the literature appear to have occurred following such a type of exposure. A similar technique is utilize in the prepara tion of the abrasive corundum. It should be noted that the silica particles inhaled are of a very fine order in fume state (see above).

Another common method of exposure is to the dust produced by punching machines which are used to pound aluminum scrap into fine particles for future use in paints etc. Some workers are reported as appearing like "living statues".

Toxicity:

Acute:

Systemic: generally result from overtreatment by aluminum salts for GI disorders affecting the GI tract, metabolism, etc., absorption of minerals, vitamin precursors, etc. In large doses, they may act as irritants and produce nausea, vomiting, etc. These are presumably caused from the liberation of acids from the various salts.

Respiratory: no well documented acute respiratory toxicity has been demonstra other than exposures to high concentrations of dust in animals producing acute inflamation of the tracheo bronchial tree, and pneumonitis similar to lipoid pneumo Human exposures to amazingly high concent rations can occur without symptoms.

Skin toxicity: some aluminum salts can produce localized irritation occurring as the anion is liberated by hydrolysis.

Chronic toxicity:

Systemic: whether or not true "aluminum lung" can be classified under this heading is yet debatable. One case of central nervous system disease concurrent with development of respiratory disease is reported in the recent literature (McLaughlin). Other studies concerned with long term therapy of aluminum salts, exposure to cooking utilsils, etc. apparently have been negative.

Respiratory: Again here the differentiation must be made between the types of exposure to aluminum compounds before considering the effects on the lung.

ALUMINUM LUNG: This apparently is now becoming a more accepted disease entity although several of the previously reported cases raise some doubts as to the purit of exposure to pure aluminum. However, several other cases in the literature seem to be relatively well documented. (McLaughlin, 1962, Swensson, 1962). Earlier reports from the German literature dating back to the 1940's should probably be excluded, but Swensson's report from Sweden includes a survey of earlier investigations, and a report on workers in an aluminum bronze mill where five of 8 workers on the punch presses developed signs and symptoms of pulmonary disease manifesting itself by cough, sparse sputum, decrease in pulmonary functions, dyspnea on exertic spontaneous pneumothorax, and cor pulmonale. Swensson felt that there was no correlation between duration of exp osure and the progression of the disease which could be repid ending in 1-2 years. Analysis of the dusts revealed no other contaminant dusts, and comparison of these workers with those performing similar jobs in a gold-bronze factory revealed no pathology in the latter. One is referred to the literature for further information and discussion. (Mitchell, Johnstone)

BAUXITE LUNG: is a well known entity with symptoms, signs very similar to the above. It occurs from exposure to impure aluminum fumes, primarily, and of note are the formation of pleural and interstitial fibrotic-lesions, unlike silicosis however, with development of destructive, bullous, sub-pleural emphysematious blebs which frequently are a cause of death. The disease is essentially not a granulomatous or nodular type. The lungs become heavy-greyish-black, and the pleur adhesions are marked. Alveoln edema and exudate occurs, and with the progression of interstitial fibrosis, etc., diffusion block and cor pulmonale occur. Birefringent particles were noted by some of the earlier pathologists, but the diseas is now fairly well controlled dur to changes in manufacturing techniques. Again, however, this is thought by many to represent an atypical reaction to silica, not aluminum. The occurrence of tuberculosis is not at all like that in other forms of silicosis, however. (Riddell) The disease may occur within 3 months of the fir exposure. (Spencer, Pathology of Lung)

ALUMINUM DUST THERAPY FOR SILICOSIS: For the last thirty years a great deal of consideration has been given to the possible beneficial effects of combining exposure to silica dust with a moderate exposure to aluminum dust in order to prevent the development of silicosis, and to improve the disease and prevent its progression in workers who have developed it. At present there is still conflicting evidence in the literature, some enthusiastically supporting the regimen, others being more cautious. Much of the previous lack of concern of utilizing aluminum was based on the poorly-documented literature regarding the possible toxicity of aluminum itself, and the still prevalent opinion that it appears to be relatively harmless particularly in the concentrations used for exposure as a protective measure. Whether or not this will be re-evaluated remains to be seen. It should also be kept in mind that the good results may also be in part due to a more careful approach to exposure to silica dust on the part of the workers, and a change in the environmental conditions therefore.

One method of exposure consists of six minute inhalation of McIntyre aluminum powder once a week approximately 50 times per year. This apparently reduced the incidence and provided some protection (Hannon), and had no demonstrable inherent toxicity in itself.

Koechel in another study of 289 foundry workers receiving Al therapy for a six year period, of 1,600 mgm per year also felt that it was a valuable adjunct, in reducing the progression of the disease, and the incidence. Perry also has agreed to the value of such therapy in ceramic workers using a similar technique.

Dworski and others report laboratory confirmation of these observations by use of inhalation techniques, either concommitant or alternating, or injection of aluminum agents. Presumably this results from the coating of quartz particles by alumimum. The relative incidence was reduced in animals, and the formation of silicotic nodules and other characteristic lesions ameliorated or obviated. Although prior existing febrous nodules did not disappear, further progression of development was limited.

Attempts to use injection techniques on humans have not been successful due to problems of precipitation, etc.

On the other side of the fence, Brown and Fairhall, and VanWinkle apparently feel that these studies have been inadequately controlled, the time element is not sufficient to come up with accurate data following exposure, some miners have shown x-ray progresion despite this type of therapy, and the effect on the incidenc of tuberculosis is unknown.

One might postulate however, that if bauxite lung is actually a type of silicosis in conjunction with aluminum exposure, it may represent the histological changes which can occur with such concomitant exposure, yet indicate the still continuing tendency for progressive fibrosis, etc. to occur.

Several other factos should be considered in evaluating the effect of aluminum therapy, etc. First the control over the environmental conditions, and the changes that might occur therein with the institution of such a program; the placebo effect of aluminum dust inhalations coupled with the already present knowledge

that many workers demonstrating relatively far-advanced x-ray changes of silicosis are relatively symptom-free until they are advised of their disease(and the access to compensation); the great individual differences in susceptibility to diseases of this type; and the ever present possibility of low-virulent form of atypical tuberculosis or other infection as a predisposing or concurrent factor. Allergenic types of reactions in some of these cases must also be considered, but this is unlikely. Lastly, the natural incidence of "attack rate" of progressive, massive fibrosis and the difficulties in consistent, reliable x-ray interpretation varying with techniques, etc., must be considered. (Cochrane, Spink, Wise, Gross, etc.)

Bibliography

1. Pulmonary Effects of Inhalation of Aluminum by Rats and Hamsters. Christie: Am. Ind. Hyg. J., Jan., 1963, Vol. 24, #1.

2. Bauxite Lung, Pneumoconioses, etc. Spencer, Pathology of the Lung, 1962.

3. Al Dust Pneumoconiosis, Clinical Study. Swensson, A.: Int. Arch. fur Gewerbe and Hygiene, 19, 1962, April (in English)

4. Pulmonary Fibrosis and Encephalopathy Assoc. With Exposure to Al Dust McLaughlin, Brit. J. Ind. Med., 19, #4, Oct. 1962.

5. Pulmonary Effects of Titanium Dioxide in Rats. Christie: Am. Ind. Hyg. Assoc. J. 24, #1, Jan., 1963.

6. Hard Metal Disease, Bech, A. O. Brit. J. Ind. Med., 19: 239, 1962.

7. Dust and Fibrosis in Lungs of Coal Workers from Wigan Area of Lancanshire Spink: Brit. J. Ind. Med., 20:118, 1963.

8. Fibrogenicity of Some Respirable Dusts Measure in Mice. Rivers, D. Brit. J. Ind. Med., 20, #1, Jan., 1963.

9. Pneumoconiosis: Requirements for Lymphatic Dust Transport. Gross, Paul: Int Arch. fur Gewerbepath and Hygiene 19:660, 1962, Nov.

10. Effect of Radiographic Technique on Readings of Categories of Simple Pneumoconiosis: Wise, M. E. Brit. J. Ind. Med. 20:145, 1963.

11. Response of Lung to Physical Irritants. Gross, Paul Arch. Envir. Health, Volv. 6, #1, 1963. (Symposium on Respiratory Diseases, etc.)

12. Attack Rate of Progressive Massice Fibrosis. Cochrane, Vrit. J. Ind. Med. 19:52, 1962.