Lung Disease Caused by Inorganic and Organic Dust*

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For the purposes of this conference, emphasis was placed on what is new and what is important with respect to a selected number of occupational diseases of the chest. Discussion was developed around features of typical and unusual example of coal dust pneumoconiosis, silicosis, siderosis, asbestosis, reactions to fibrous silicates and plastic, berylliosis, aluminosis, farmer's lung, lipid pneumonia and hair spray thesaurus. A summary of the main topics follows:

Coal Pneumoconiosis

(a) Whereas the presence of silica is an important factor in aggravating and modifying the lung lesions found in coal miners, coal dust with insignificant amounts of silica and even other carbonaceous dusts, e.g. those derived from graphite and carbon arc electrodes, also can cause significant pulmonary disease.

(b) Focal emphysema due to abnormal permanent distension of respiratory bronchioles and alveolar ducts is a specific, but not an exclusive reaction to coal dust.

(c) Other forms of emphysema may supervene, e.g. hypertrophic vesicular type if there is associated severe silica exposure; centrilobular emphysema if there is infective bronchitis.

(d) Progressive occlusion of pulmonary blood vessels is a major disabling process in coal dust pneumoconiosis. In the absence of advanced emphysema, this is the basis for much of the disability and may explain discrepancies between physiologically determined emphysema and the grade of function impairment. The increased transradiancy caused by pulmonary devascularization may also be misdiagnosed as emphysema.

(e) “Progressive massive fibrosis” seldom is a fibrosis proper, but represents pulmonary detelectasia and occupation of air spaces by coal dust. Tuberculous infection may be a factor in the genesis of “progressive massive fibrosis,” possibly due to bronchostenosis following bronchial infection. This is suggested by results of experimental studies, but the clinical cases seldom yield positive sputa. In most of these cases, significant regional ischemia follows, leading to noninflammatory necrosis, liquefaction of the lesion, excavation and discharge of the contents into the sputum. This may follow years after the coal miner has left his occupation.

(f) In a small proportion of coal miners, systemic rheumatoid arthritis is associated with conglomerate multilaminated pulmonary nodule formation. These lesions may represent an autoimmune response, be a variant of systemic collagen disease or be the result of local inflammatory action of an infectious agent augmented by the retained dust.

(g) Tuberculosis is not a serious problem in coal workers exposed to dust with a low silica content. As the silica content rises, tuberculosis becomes increasingly more prevalent and less tractable. In some communities, tuberculosis accounts for up to 15 per cent of deaths in coal workers. The atypical Mycobacterial infections, however, have not yet presented a significant problem in coal workers.

(h) In some localities, there is increasing evidence of lung cancer in coal miners, which cannot be explained by associated cigarette smoking.


**Moderator.
(i) The main cause of death in coal workers, who die from their coal pneumoconiosis, is congestive cardiac failure due to cor pulmonale.

(j) Intermittent positive pressure breathing has proved beneficial for the relief of pulmonary insufficiency caused by coal pneumoconiosis. Since bronchiolar dilatation rather than bronchilo-spasm is the problem in most instances, the routine use of bronchodilator drugs is to be deprecated. If there is associated silicosis, bronchiolar spasm may be a factor. If vascular stenosis has reached an advanced stage, the IPPB is likely to prove of little enduring value.

Silicosis

(a) The importance of widespread small artery cicatrical occlusion is being recognized increasingly as an important factor in the genesis of disability in silicosis. Blood vessels may be incarcerated in silicotic nodules and the resultant regional ischemia produces functional impairment quite out of proportion to the space occupying nature of the nodule. These lesions are too small to cast radiographic shadows, and the normal vascular markings of the lung gradually disappear, simulating emphysema. Thus, an apparent discrepancy between the degree of radiographic change and disability arises.

(b) Destructive emphysema also is an important component of silicosis. In this process, the alveolar septa break down, causing confluence of adjacent air spaces. This results in functional impairment, both through absolute curtailment of the respiratory surface and by the interruption of the capillary circulation through the alveolar surfaces, which thus may remain aerated, but are unperfused. The latter feature may account for some of the physiologic diagnoses of alveolo-capillary block syndrome.

(c) Bronchitis and bronchiolitis are important early features of the response to inhaled silica dust. This bronchitis tends to be relatively nonproductive of sputum and the latter may be tenacious due to denatured mucoproteins. Purulent sputum seldom is found. Cigarette smoking augments the adverse effects of the bronchitis and bronchiolitis in silicotics and should be countermanded as a first step in the management of attendant disability. Some of the "sago grains" expectorated by silicotics actually consist of silicotic nodules which have developed within and ulcerated through the bronchial mucosa.

(d) If the silica dust is deposited mainly in intrapulmonary lymphoid centers, a relatively mild disease follows in which extensive nodulation may remain unattended by disability or curtailment of life span.

(e) The progression of silicosis may be independent of continued exposure. The lung is soon saturated with silica and additional exposure to silica dust does not materially augment the amount of retained silica. It is this early deposit of silica which causes the main disease. For this reason, removal of silicotic subjects from working areas does not necessarily improve their chances of survival and progression of the disease may follow years later. Unless a satisfactory financial solution is at hand for such victims of past exposures, it may, therefore, be more humane to permit the silicotic to continue working at a remunerative skill instead of causing him to become an economic derelict through well-intentioned, but belated efforts to segregate him from a harmful environment.

(f) Silica exposure potentiates the injurious action of numerous other dusts and vice versa. It is particularly important to avoid dual exposures to silica and beryllium, asbestos and coal dust.

(g) Several dozen synthetic, submicron, amorphous silica dusts have recently been introduced. Rash generalizations about their toxicity should be avoided. Some of these agents have proved virtually innocuous to multiple species of laboratory animals and have been well tolerated by human subjects over the past two decades. At the other extreme are submicron amorphous silicas which rapidly impair the lung through the mechanisms of emphysema, bronchiolitis or vascular destruction. Between these extremes many nuances of
pathogenicity exist. It is not yet possible to predict with certainty from the physicochemical characteristics of these siliceous agents what their pathogenic potentials may be, but some guides do exist.

(h) Exposure of silica to various degrees of heat causes its recrystallization into the more toxic isomers, tridymite and cristobalite. Extreme heat, however, changes quartz into relatively noninjurious vitreous silica. These isomers can be identified by x-ray diffraction techniques only. Both tridymite and cristobalite are significantly more injurious than is quartz dust and the lung response is more diffuse. This principle largely explains the occurrence of disabling pneumoconiosis after exposure to flux calcined diatomite, but not to raw diatomite dust, even though the latter is almost 100 per cent SiO₂. Tridymite and cristobalite also have been significant factors in the genesis of unusual varieties of silicosis in the ceramic industry, grey iron and steel foundries, and probably account for the pathology of Shaver's disease, rather than does the associated aluminum exposure.

(i) While many theories of silicosis have been considered, the cardinal fact in pathogenesis appears to be the propensity of the quartz particle surface to denature the protein of the lung phagocytes. These killed phagocytes autolyze and release the particles which are rephagocytosed by other cells which carry them a little distance farther. As soon as these new phagocytes have digested the layer of denatured protein derived from the original phagocyte and adhering to the silica particle, the surface of the latter is again released so that the second phagocyte is killed. This process carries on ad infinitum. The detritus of these killed cells attracts fibrocytes which facilitate the deposition of fibrous laminae around the particles. Since the latter are constantly being carried further afield by new cohorts of phagocytes, the siliceous nodule continues to grow peripherally.

(j) The capacity of silica to activate tuberculosis is well known. It is now clear that in many instances the infectious agent is not one of the virulent tubercle bacilli, but relatively avirulent atypical Mycobacteria. In laboratory experiments, and in human subjects, silica has proved capable of potentiating latent pathogenicity of attenuated bovine bacilli, BCG vaccine, and skotochromogenic and photochromogenic atypical avirulent Mycobacteria. Silica may also collaborate with Histoplasma capsulatum in this manner. These infectious agents are not rendered more virulent. Disease occurs only where dust is deposited and on explantation, the Mycobacteria once more revert to avirulence.

(k) Reasonable success has been obtained through chemotherapy of tuberculosis, provided the treatment is continued for protracted periods. Recrudescence is likely when the drugs are withdrawn because of clinical improvement. This is due to the fact that it is the silica in the lung tissue which potentiates the infection. Local excision of tuberculous lesions in silicotic subjects is entirely logical for this reason and is the more likely to be successful because capillaries have been sealed off.

(l) Lung cancer, formerly thought not to be unduly prevalent in silicotic subjects, may be on the increase. This may be due to associated cigarette smoking, or due to the fact that along with silica other mineral dusts may be inhaled or may be attributed to greater longevity. Cancer often develops in silicotic scar tissue. Such neoplasms initially spread slowly due to the extensive closure of lymph channels in the silicotic lung. This is favorable for surgery.

(m) Aluminum dust remains the only effective prophylactic against silicosis where dust suppression cannot be achieved. Aluminum also will partially halt the progression of silicosis. It cannot eliminate the nodules or restore the blocked circulation or disrupted alveolar surfaces, but it can curtail the extension of these processes in response to silica which is constantly being mobilized in the lung by the action of phagocytes. Certain organic compounds, e.g. polyvinyl pyridine, nitrous oxide, are currently
under study for their potential antifibrotic potentialities but are not yet available for clinical trial.

Asbestosis

(a) This condition is on the increase in proportion to the expansion of the industry. The novel uses of asbestos renders it likely that asbestosis may occur in the most unexpected circumstances.

(b) The pathology of asbestosis is that of a progressive interstitial fibrosis with emphasis on perivenous and subpleural localization of the main lesions. The lung damage is most severe where the greatest movement occurs, e.g. adjacent to the heart, supradiaphragmatically and at the lung apices. Lymph nodes remain unaffected. Sequelae are due to the shrinkage of collagen with secondary stenosis of trapped structures (bronchioles and veins) and dispersion of structures in between the fibrosed zones (bronchiectasis, compensatory emphysema). Initially, alveolar capillaries are not involved, so that at first, normal gas exchange takes place despite thickening of the septa. The complications are cor pulmonale and lung cancer. Neoplasia occurs in two forms, viz. alveolar and bronchial carcinoma and pleural mesothelioma. The latter is particularly common in crocidolite workers and has been mainly reported from South Africa. Bronchitis and secondary infection may occur terminally, but it initially is not important. Tuberculosis is not facilitated in the asbestotic lung.

(c) Asbestosis only follows exposure to dust containing a high proportion of fibers longer than 20 micra. If asbestos is ball-milled to a smaller particle size, no disease can be produced in experimental animals. There is a prolonged interval between exposure and the onset of serious disease. The latent period is particularly impressive, and the probability of disease appears to be a function of the duration and intensity of exposure plus elapsed time. Pulmonary fibrosis, vascular stenosis and bronchial disease have been induced experimentally, but neoplasia has not yet resulted. The carcinogen, 3,4 benzpyrene, has been demonstrated in certain types of asbestos mineral.

(d) Prevention of exposure is the only remedy. Aluminum prophylaxis is of no value. It is particularly disastrous to expose persons who are developing asbestosis, to quartz dust since the arteriolar damage, destructive emphysema, bronchiolitis and lymphoid tissue involvement characteristic of silicosis may then become superimposed.

Fibrous Minerals

(a) A number of these produce lung disease of variable severity. It is their fibrous nature rather than their chemical composition which induces the tissue reaction. Thus, substances such as mica, brucite, rock wool, fiberglass, fibrous potassium titanite can cause interstitial fibrosis and bronchial distortion.

(b) In general, these fibrous minerals do not activate pulmonary tuberculosis. Volcanic glass, however, does have this property, although it does not, by itself, cause lung disease.

Siderosis

(a) Iron welders ordinarily develop a completely non-disabling and partly reversible pneumoconiosis in which the distinctive lesions merely comprise focal dextrolectasis of the lung with the accumulation of ferrous pigment in koniophore cells.

(b) If arc welding is done in confined spaces, there may be sequential disablement by inhaled ozone or by nitrous dioxide caused by the passage of the electric spark through the air. Such individuals develop bronchiolitis which may progress to stenosis.

(c) Increasingly, too, ferrous welding rods are coated with fluxes which may contain injurious ingredients, e.g. silica, cadmium, etc. Welding may also be done on materials which have toxic properties. Some welders also are being recruited to weld exotic metals under conditions of such military secrecy that they may be unknowingly exposed to harmful metal fumes, e.g. beryllium.

(d) The siderosis described in foundry workers seldom is a pure metal dust disease. The heat of molten iron may convert
siliceous molding sand into cristobalite or tridymite. Since the latter two isomers of quartz cause atypical silicosis, besides being considerably more active as pulmonary pathogens than are equivalent amounts of quartz dust, there may be serious atypical silicosis as well as siderosis. Progressive occlusion of pulmonary blood vessels with sequential fatal cor pulmonale is the main disability, but tuberculosis contributes an excessive quota of deaths in certain foundries.

(e) Hematite ore dust may partially retard the development of silicosis. The massive fibrosis in hematite workers may be due to superimposed tuberculous infection, but need not be and can represent detelec-tasia with selective entrapment of the hematite in the lung segment. Tuberculosis does not appear to be unduly prevalent in hematite workers. Lung cancer has been reported in excessive numbers in workers dominantly engaged in hematite mining in certain areas. The possibility of associated radon, nickel or arsenical exposure is under study.

(f) Magnetite miners develop siderosis, but in these men the disabling factor is the associated silica exposure, the combined lesion being siderosilicosis.

(g) The concept of endogenous ferrous pneumoconiosis is a misnomer since the iron is not a dust at any stage in this syndrome.

(h) Ferrosilicon workers may develop a distinctive clinical syndrome, characterized by pulmonary lesions and systemic reactions.

Berylliosis

(a) This occupational chest disease appears to be well under control. The few new cases which are still being diagnosed received their exposure many years ago, before effective industrial hygiene had been instituted. The use of beryllium has greatly increased in connection with military and space technology programs. Such excellent protective measures now are in use that occupational exposure of individuals is highly unlikely.

(b) Re-examination of a large number of the key cases of berylliosis has revealed that a number of these were examples of Boeck's sarcoidosis and others were instances of other varieties of chronic pulmonary disease, including other pneumoconioses such as silicosis or asbestosis.

(c) Chronic pulmonary berylliosis is primarily an alveolar septal cellular granuloma with associated septal epithelization and capillary occlusion. Fibrosis is uncommon unless there are other pathogenic processes, but elastic tissue is readily destroyed so that emphysema is a common sequel. The lymphoid tissue is not involved and the early radiographic appearance of large hilar shadow either indicates that the diagnosis is in error, the case being sarcoidosis, or there has been heavy associated silica exposure with silicotic hilar adenopathy. Large hilar x-ray shadows which appear at a later stage may be due to distended pulmonary blood vessels. Cor pulmonale has proved to be the main cause of death.

(d) There is no enhanced susceptibility to tuberculosis. This is supported by the low incidence of tuberculosis in spite of the fact that a number of persons with berylliosis were originally hospitalized for protracted periods in tuberculosis sanatoriums. This point has been verified experimentally.

(e) Six cases of lung cancer have been reported in the group of approximately 7,000 who were originally exposed to beryllium compounds. This yields an incidence of over 80 per 100,000, which is about four times greater than the current national incidence of lung cancer of about 20 per 100,000. Lung cancer has been induced in rats and monkeys by inhalation exposure to BeO, BeF₂, BeHPO₄ and ZnMnBeSO₄, and bone sarcoma has resulted in rabbits after intravenous administration of ZnMn BeSO₄.

(f) Favorable results have been attained by corticosteroid therapy, but many cases of chronic berylliosis also have undergone spontaneous remission. This is due to the cellular nature of the beryllotic lesion. Fail-
ures have been due to mistaken diagnoses or complicating pulmonary fibrosis. Chelating agents have proved disappointing.

(g) Beryllium persists in the lung for protracted periods, being redeposited and accumulating there from storage depots in the liver or bone. This has been proved experimentally and may afford an explanation for the often delayed onset of chronic berylliosis. The pulmonary accumulation of Be also is accompanied by elevation of the serum alkaline phosphatase level. Although the inhaled and absorbed beryllium is widely dispersed through numerous body tissues, no berylliotic lesions have developed in tissues other than the lungs. Kidney stones have been reported in a few cases and have been thought to be due to hypercalciuria. No nephro-calcinosis has been noted in experimental animals.

Aluminosis

(a) Although this disease process is, in theory, a possibility, there are growing indications that many of the diagnoses have been made in error. The original examples of the chronic pulmonary disease were reported under war-time conditions in German employees of pyrotechnical and airplane propeller factories where crude exposures to finely powdered aluminum occurred. Isolated descriptions have come from several other countries, e.g. Sweden and England; and the disease which occurred at Niagara Falls in bauxite electric smelter workers was diagnosed as aluminosis.

(b) These cases have lacked two main diagnostic criteria. First, the pulmonary aluminum levels have generally been within the normal range and second, in many examples there was abundant silica, sufficient to have caused the disease. In some cases, there was a possibility of stearin, lipid or other metallic exposures which could have caused the pulmonary fibrosis. Epidemiologically, too, the few described cases do not match the lack of evidence of toxicity, despite extensive human contact with aluminum. In various parts of the world, aluminum metallic powder has been administered safely as a prophylactic against silicosis. Over 10 million such treatments already are on record. Metallic aluminum also has proved inert in exhaustive inhalation exposure experiments with animals.

(c) It has, however, been shown experimentally that a few crystalline forms of aluminum are cytotoxic and fibrogenic. Where a possibility exists that exposure to such agents may occur, proper precautions should be instituted. There is not currently any extensive use of these compounds and this possibility should no more create a fear complex toward all aluminum than that we should become afraid to breathe oxygen because over exposure to oxygen may cause alveolar injury or retrolental fibroplasia of babies or may kill fish. Aluminum is truly one of the safe industrial agents.

Plastics

(a) The plastics are mostly inert when fully polymerized. These substances can be inhaled, if sufficiently pulverized and will occasionally induce transient thesauroses similar to that which characterizes exposures to other inert substances (e.g. iron, barium, tin). These thesauroses are likely to be less readily diagnosable since the plastics are radiotranslucent. However, there is a growing trend to introduce fillers of various types. As long as these remain calcium sulfate or calcium carbonate, the original fillers, the picture will not change since these substances are inert and soluble in body fluids. The introduction of Fiberglas, a fibrous silicate, has not significantly altered the pulmonary responses. If metallic ingredients are used as fillers, punctate pulmonary radio-opacities may follow. Regrettably, some of the plastics are now being fortified by substances such as quartz or asbestos. A number of examples of lung disease have been attributed to such agents and the plastics per se have undeservedly acquired a bad reputation.

(b) Some of the chemicals which enter into the process of manufacture of plastics
may be biologically active and yield pulmonary reactions if inhaled. Sensitization may also occur, and organic isocyanate is a characteristic example. Plastics may also yield injurious thermal decomposition products when heated. The temperature of pyrolysis is critical for each plastic, and no general rule can be laid down. Thus, some plastics break down at temperatures less than 100°C while others remain relatively stable at temperatures two or three times as high.

**Farmer’s Lung**

(a) Two conditions require differentiation, viz., fungal infection and nitrogen dioxide damage. There are many synonyms for these conditions which do not occur exclusively in farmers. Histoplasmosis has in recent years been added to the list of mycoses which may favor the rural populations, but histoplasmosis has also been reported in urban dwellers and school children.

(b) The mycoses may be due to any of a large range of fungi which occur on vegetable matter handled by the farmer. The lesions consist primarily of focal inflammations and granulomatosis, and the disease is more a diagnostic than a health problem since the lesions regress in most cases. Because many farmers engage in some industrial activities (e.g., welding, tunnelling, blasting, spray painting, etc.), diagnosis of the mycosis may initially be missed, especially if the onset is insidious rather than dramatic by virtue of associated symptoms.

(c) Nitrogen dioxide lung disease, popularly known as silo filler’s disease, is but one of the innumerable examples of chemical-induced tissue reactions. Historically it was interesting because of the unexpected source of the exposure (silos). Nitrogen dioxide exposures also occur in other industrial situations, one of which, namely electric arc welding, has already been discussed. Nor are farmers the only victims. The urban relatives or friends of the farmer may be unwittingly injured when visiting and helping on the farm and may develop their full disease after their return to their city job.

(d) The main lesion in silo filler’s disease is bronchiolitis obliterans. The essential physiologic disturbance is due to focal dextelectasia. Secondary infection may aggravate the process. The prospects for complete recovery are discouraging, particularly since there is no satisfactory or specific therapy. However, intermittent positive pressure breathing, corticosteroids, antibiotics, and bronchodilator drugs may alleviate some suffering and abort impairment or halt progression caused by complicating infection and bronchospasm.

**Lipid Pneumonitis**

(a) This condition has been reported from a number of textile industries in which exposure to oils, used to lubricate fast moving textile fibers, occurs. The condition has acquired the layman’s appellation of yarn plant disability. Since the synthetic textile industry is new and constantly exploiting unusual chemical substances or technical procedures, there are theoretic possibilities for the occasional release of injurious agents. The lubricants used in the textile industry consist mainly of mineral oil with addition of animal and vegetable oils in various proportions plus antibacterial, antifungal, dispersant or other chemicals. Although manufacturers of textile yarns take precautions against inhalation of these substances, there are numerous opportunities for accidental exposure.

(b) The symptoms of this condition are progressive exertional dyspnea, cough and intermittent pyrexia. Pathologically, the main processes include alveolar septal cellular infiltration, destructive emphysema with ultimate cystic degeneration of the lung, and hyperplasia of bronchiolar epithelium. There are no indications of accompanying infective pneumonitis, but the possibility of intercurrent infection cannot be overlooked. The adjuvant role of cigarette smoking still needs to be resolved.
(c) Since affected employees improve on removal from the offending environment and relapse when returned to their jobs, early detection and transfer to another activity are, at present, the only remedies. Failing this, the condition is likely to be progressive and ultimately disabling. There are no conclusive early radiologic signs, and periodic assessment of lung function is probably the only way the surreptitious reduction of the respiratory surface may be detected soon enough to abort a disabling stage.

**Hair Spray Thesaurus**

(a) Recent clinical and pathologic reports have suggested the possibility of disabling and even fatal lung disease caused by inhaled ingredients of cosmetic hair sprays. The more serious cases have been observed either in women who have grossly abused the use of these toilet articles, subjecting themselves to multiple daily exposures, or in beauticians who are professionally exposed to hair spray vapors.

(b) The theory of this condition is plausible, but there remains considerable doubt concerning the validity of the claimed cases. In most of the published examples, the more permissible diagnosis would have been Boeck's sarcoidosis, and in the remainder other lung disease could account for the pathologic changes. No ingredient of hair sprays has as yet been demonstrated in necropsy or biopsy material. Periodic acid-Schiff-positive particles have been mistakenly identified by some authors as representative of polyvinyl pyrrolidone, one of the better known ingredients of hair sprays. Unfortunately, P.V.P. is not stainable by the periodic acid-Schiff method and periodic acid-Schiff-positive particles may be found in a variety of lung diseases, being glycoproteins of a nonspecific nature.

(c) It has been claimed that cessation of exposure alleviates the symptoms and causes regression of radiologic signs. Since sarcoidosis undergoes spontaneous regression in comparable manner, this criterion does not yet serve to differentiate thesaurus. So many millions of women have been exposed to hair sprays that more lung trouble should have already been recorded if the ingredients of these cosmetics are significantly injurious. The high prevalence of sarcoidosis in the United States renders likely the chance occurrence of this condition in persons exposed to hair sprays. However, the possibility of a potentiating capacity of hair spray ingredients on the sarcoidotic process needs to be considered. Idiosyncratic reactions may, of course, occur, but no allergy has as yet been proved. The hair spray ingredients have been subjected to extensive laboratory tests involving multiple mammalian species. Research on experimental animals, conducted by officials of the Food and Drug Administration, indicates that ordinary use of current types of hair sprays poses no safety problem for human subjects.

**CONCLUSION**

The ever-increasing complexity of the industrial environment indicates need for constant vigilance. Since not all environmental pollutants can, at present, be subjected to prior laboratory exploration, clinical science must remain an important source of guidance concerning industrial safety. Inhalants vary greatly in their potency and with respect to their specific effects. The factors of individual susceptibility and associated nonindustrial disease also come into play in many instances. Imprecise diagnosis, and the too ready acceptance of new industrial pulmonary entities, can hamper the prevention of environmental lung disease as much as do carelessness or ignorance.

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