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OCCUPATIONAL DISEASE DIAGNOSIS

34463

by

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I am happy to have a few minutes to discuss the occupational diseases with a group of practicing physicians. Curiously enough, such opportunities are relatively infrequent, since these diseases tend to be reserved, almost exclusively, for industrial health meetings. And few medical practitioners attend such meetings, because the emphasis, there, tends to be on the industrial environment and its control, rather than upon clinical medicine. But the fact remains that when a worker gets sick, he first consults his own doctor. And so this doctor is really in the front line when it comes to the need to recognize an occupational disease, clinically, and to make a correct diagnosis.

To the medical profession, the occupational diseases are always somewhat baffling because they have their origins in environmental conditions which are unfamiliar. Unlike the community environment, where the medical problems have always been largely epidemological in character, the industrial environment—being man-made—presents problems in fields somewhat further removed from the physicians conventional training and experience; fields such as industrial toxicology or radiation, for example.

There are literally thousands of potentially toxic chemicals which are either being produced in industry, or are being used in the production of other goods—with new ones being added all the time, by our research chemists. Aside from skin contact, workers are exposed to many of these substances in the form of dusts, gases, fumes, vapors or mists, which become disseminated into the air of the workroom. While inhalation is by far the most important source of injury to health from exposure to toxic chemicals, skin absorption and even ingestion may play important roles under certain circumstances.

Less familiar, perhaps, are a variety of other abnormalities in the working environment which are equally serious, as potential health hazards. Aside from dangerous machinery, there are abnormal temperatures and humidities; infra-red and ultra-violet light; compressed air in tunnel construction; continuous vibration in the use of pneumatic tools; excessive noise, even in the supersonic ranges; radiation, as in radium dial painting operations, or the use of the X-ray or fluoroscope, as industrial inspection devices; inadequate or improper illumination with glare and so forth. The industrial environment is, indeed, as complex and as fluid as modern technological research and development itself.

For the individual worker, health hazards will vary from industry to industry; from plant to plant, from workroom to workroom, and often from one process to another in a single workroom. And since labor is highly mobile, workers tend to go from one industry to another and from one type of work to another, in various parts of the country. Accurate evaluation of their occupational exposures, particularly on any long-time basis, may therefore present difficulties.

For some reason, the occupational diseases have always occupied a place somewhat removed from the rest of clinical medicine. The fact of their so-called "Common etiology"—the occupation—has, perhaps, carried with it a subtle implication that they represent a cohesive group, in which there is a relatively limited number of fairly clear-cut clinical entities; and that these are, on the whole, characterized by distinguishing ear-marks which suggest particular occupations. Actually, the occupational diseases range over much of the entire field of clinical medicine, since they reflect all of the physiological, biochemical and metabolic changes which develop in the body in response to working conditions which are inimical to health—including many compensatory responses initiated by the body for purposes of self-preservation.

Nor does the individual clinical picture necessarily suggest the existence of an occupational etiology. Far less does it point to any specific occupation, as the etiological factor. This is, in part, due to the fact that many of the same toxic chemicals and the same abnormal environmental conditions are to be found in greatly diverse industries and occupations. More important, however, is the fact that many occupational diseases are indistinguishable, clinically, from similar diseases which are non-occupational in origin. Only the etiology is different. But its recognition may provide the only opportunity for saving the patient's life.

Aplastic anemia or leukemia, for example, are the same hematological entities whether they are idiopathic, in origin, or have been contracted in a factory workroom as a result of exposure to benzol or excessive radiation. Epitheliomata of the bladder, produced by exposure to

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beta naphthylamine in the manufacture of aniline dyes, cannot be differentiated from non-occupational epitheliomata of the bladder, either clinically, on cystoscopic examination, or on microscopic section. Even their slow clinical course is the same. Asthma and dermatitis venenata, whether of occupational origin or not, are clinically the same. Only the precise antigen responsible may be one which is characteristic of a particular occupation—as in the case of the paraphenylene diamine dyes to which fur workers are exposed.

Some of the irritant gases present similar difficulties in differential diagnosis. Ammonia gas, for example, is so highly irritating, few persons would voluntarily remain in its presence long enough to inhale a toxic dose. But an accidental break in a pipeline could subject workers to sufficient absorption to produce a pneumonitis, pneumonia or even edema of the lungs. These conditions are not pathognomonic for ammonia gas. Only an occupational history will reveal what happened and provide necessary guidance for the management of the case.

The nitrous fumes, from welding operations—especially in enclosed spaces, as in the holds of ships—are more insidious because they are less obviously irritating. As a result, relatively large amounts may be inhaled without warning. However, after an interval of eight, ten or even twelve hours, their caustic action in the lungs may result in death from pulmonary edema. The long latent period tends to obscure causal relation, unless one is familiar with this type of situation and inquires into the occupational exposure. Standard procedure for saving a worker's life is to put him to bed immediately following a known exposure to nitrous fumes, even in the complete absence of any clinical manifestations of injury to health.

In carbon tetrachloride poisoning one is usually dealing with a toxic hepatitis, a nephrosis or a combination of both. There is nothing in the clinical picture, however, which specifically points to carbon tetrachloride as the etiological agent, or indeed suggests that one is dealing with some occupational disease. If the patient is jaundiced when he first consults his physician, obstructive, catarrhal or infectious jaundice immediately come to mind. The possibility of a toxic hepatitis is usually the last to be considered, and is often not considered at all. In the early stages, however, there may be no jaundice and the patient comes to his physician complaining only of vague gastro-intestinal symptoms. In the absence of an occupational history of exposure to a hepatotoxic chemical, the patient may be given a cathartic and dismissed. By the time jaundice develops, it may be too late to save his life. This has occurred.

In exposure to carbon tetrachloride, one is particularly impressed with the great differences in individual susceptibility which exist. A drink of alcohol may make the difference between life and death. These marked differences in individual susceptibility are not well understood. They are by no means confined to the occupational diseases, but pervade the whole of clinical medicine. In a poliomyelitis epidemic, for example, almost everyone is exposed but relatively few contract the disease. Nevertheless, physicians are prone to assume that if no one else in a plant is sick, his patient's illness cannot be due to his occupation. This is contrary to all experience. Of two workers having an identical exposure to benzol, at a work bench, one may die of an aplastic anemia and the other may be unaffected.

Among the pneumoconioses, silicosis is perhaps the most familiar. And physicians are becoming increasingly adept at recognizing the X-ray shadows of first, second and third stage silicosis. Less familiar, perhaps, are the pneumoconioses produced, under appropriate conditions of exposure, by other types of dust such as asbestos, talc, carborundum or mica. The extent to which there may be fundamental differences in pathological response to dust inhalation is also not sufficiently appreciated. For example, asbestosis and the inhalation of certain of the chromate dusts appear to play etiological roles in the production of lung cancer, whereas silica dust does not. Iron dust will produce characteristic X-ray shadows of "Siderosis" without, apparently injuring the lungs at all. Pulmonary granulomatosis, produced by the inhalation of beryllium, indicates a totally different mechanism at work. Whatever the pulmonary pathology, however; and no matter how characteristic the X-ray shadows may be, it is pretty well accepted at the present time that the X-ray pictures are never pathognamonic. The resemblance between third stage silicosis and miliary tuberculosis may be truly striking; beryllium granulomatosis may be readily mistaken for Boeck's sarcoid; "More fibrosis than usual," or pleural calcifications are particularly difficult to interpret, without a history of exposure.

And so, here again an investigation of the occupational history of the patient is indispensable. To be of real value, however, this occupational history must be carried beyond the patient's present job, to include the whole of his working life insofar as possible. For the pneumoconioses are chronic diseases which may take many years to develop. Occupational cancer, or lead poisoning are in the same category. In addition, it is important to appreciate the fact that a particular job classification does not necessarily provide precise information as to the nature of the occupational exposure. To learn that one's patient is a "foundryman", for example, means little unless one knows whether he is a "Moulder" who handles sand; whether he pours molten metals which are toxic; whether he is a sandblaster, or operates an X-ray machine

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to detect flaws in finished castings. Accurate and complete occupational histories of patients are often difficult to obtain because of the technical complexities inherent in the subject, and the failure of patients to present the whole story. Even a well-informed chemist, who contracts an occupational disease in his laboratory, will not necessarily, when asked, give a complete list of all of the substances which he handles though, unlike most workers, he knows exactly what they are. He tends rather to be selective, listing only those of which he is suspicious. Memory failure for occupations, years back, obviously further complicates the problem. But if one persists, a useful occupational history is usually forthcoming.

When it is discovered that a patient has been working in a dusty atmosphere, there is a tendency to focus attention solely upon X-ray evidences of a pneumoconiosis, forgetting that many dusts never reach the lungs at all—being larger than five microns in size; forgetting that such dusts may, nevertheless be highly irritating to the nose and throat, or to the upper respiratory passages; and forgetting further that it is the toxicological properties of a substance, rather than the portal of entry, which tends to determine the site of injury in the body. Thus, inhalation of beta naphthylamine dust can cause cancer of the bladder, but never cancer of the lungs. Similarly, lead, whether inhaled as a dust or as fumes, reaches the alveoli of the lungs. But it does not produce lung pathology. Instead, it is carried away in the blood stream and causes lead poisoning, a systemic disease. All of the industrial solvents enter the body by inhalation, but their toxicological effects are elsewhere. Carbon tetrachloride has a predilection for the liver and kidneys; benzol for the hematopoetic system; carbon disulphide for the nervous system, etc. Zinc fumes cause a deposition of fine particles of zinc oxide on the mucous membranes of the upper respiratory passages to which there is an anaphylactic reaction, commonly referred to as "Zinc chills".

Skin contact with toxic chemicals may, similarly, produce systemic disease with or without a local dermatitis, when there is skin absorption. Tetraethyl lead, unlike the inorganic lead compounds, is readily absorbed through the skin and has a predilection for the central nervous system. Nitrobenzene on the skin can produce a dangerous cyanosis with methemoglobinemia. Where there is exposure to a combination of chemical substances, regardless of precise portals of entry, the principle of synergism enters to further complicate the clinical picture.

Among the gases, carbon monoxide is always good for a full day's session as soon as someone raises the question of "Chronic carbon monoxide poisoning". Actually, whether or not there is a clinical entity such as "chronic" carbon monoxide poisoning is entirely a matter of definition. That varying degrees of anoxia may be present in persons, exposed to concentrations of this gas which are insufficient to produce acute asphyxia, is well known to all students of the subject. In industry, cases of acute asphyxia are relatively rare. More often, workers are exposed to relatively low concentrations for long periods of time. The typical picture, as one sees it in garage workers, for example, is that of an extremely intense and throbbing occipital headache, usually associated with dizziness, nausea, nervous instability, psychological susceptibility, insomnia and gastro-intestinal symptoms. There are two striking points about the headache: 1) Clinically, it immediately suggests a brain tumor; and 2) It continues for a great many hours after the carbon monoxide has obviously been eliminated from the body. It is an important cause of absenteeism among garage workers. And yet, it is this continuation of the headache—even into the following day—which always causes doubt to be thrown upon carbon monoxide as a possible cause. But when one considers the pathology this seemingly puzzling situation becomes pertectly clear. Trephine operations on animals exposed to carbon monoxide gas have demonstrated the presence of edema of the brain associated with increased intracranial pressure. This immediately explains the clinical similarity between the carbon monoxide headache and brain tumor. On the other hand, while carbon monoxide is rapidly eliminated from the body—usually within the first hour or two—edema of the brain takes many more hours to subside. And the headache continues during all this long period. Incidentally, quantitative determinations of carbon monoxide in blood are often carried out hours after exposure, when the patient finally reaches a hospital. Obviously, these can be of little value, since practically all of the gas has long disappeared.

Another point not sufficiently appreciated, is that a worker with a 40% oxygen displacement due to carbon monoxide is suffering from a far greater degree of anoxia for practical purposes, than is an individual with a 60% hemoglobin, and a corresponding oxygen lack, due to anemia, for example. This is because the oxygen-dissociation curve with carbon monoxide is such that what oxygen is present is far less readily available. A garage worker may collapse on sudden exertion under such circumstances, while the patient with the corresponding anemia still has a considerable ready reserve of oxygen, at his immediate disposal.

I will not attempt to discuss lead poisoning, excepting to point out that most of the difficulties in diagnosis arise from failure to differentiate between lead absorption and lead poisoning; and failure to visualize the medical findings in terms of a constantly shifting metabolic balance between absorption, storage and excretion. These difficulties are peculiarly characteristic of a whole group of occupational diseases which develop as a result of exposure to cumulative poisons. In an effort to be brief, one might say that diagnosis rests upon three pillars: 1) Evidence of *significant* exposure; 2) A characteristic clinical picture and 3) Laboratory data; particularly quantitative data as to the lead content of the urine and the blood, and as to the hematological picture. Sound clinical medicine requires that the findings in ***all three categories must be interpreted together.*** The laboratory data cannot be interpreted without the others.

"Evidence of *significant* exposure" stresses the need for accurate information as to dosage. Dosage in industry is quite as important as in a doctor's prescription. The fact that a person works with a toxic chemical, or that he has been exposed to radiation, for example, does not *per se* indicate that his health has been injured thereby. The question is always, "How much?" And frequently the only way in which this can be answered is by a technical evaluation of the industrial environment. This may require dust counts, chemical air analyses, radiation or noise measurements; or the application of a variety of other measuring sticks to the particular problem at hand. These findings can then be compared with accepted safe standards—the so-called Maximum Allowable Concentrations (M.A.C.)—always, however, taking into account individual differences in susceptibility among people. The practicing physician is obviously not equipped to make such tests. But, in New York State, he can always call upon the Division of Industrial Hygiene, in the Department of Labor, for assistance. The services of its pro-

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fessional staff of physicians, chemists and engineers are always at his disposal without charge.

In these days, when everyone is psychiatrically-minded, there is an increasing tendency to refer workers, showing personality changes, to a psychiatrist, without stopping to consider the possibility of a toxic etiology, possibly occupational. There are a number of industrial chemicals which are capable of producing psychoneuroses, psychoses and even neurological conditions, which cannot always be distinguished from those which are non-occupational in origin. Least serious, perhaps, are some of the less toxic solvents which are nevertheless narcotic in their effects. Workers exposed to trichlorethylene, for example, may under certain circumstances become drowsy, irritable and restless; and they may complain of vague gastro-intestinal disturbances, which are not easy to verify on physical examination. In the manufacture of rayon, workers exposed to toxic concentrations of carbon disulphide have developed mild to serious psychoneuroses and psychoses which for a long time were not recognized as being due to this exposure, and many were confined to psychiatric hospitals. A characteristic Parkinsonian syndrome may develop in manganese poisoning. In the manufacture of fur-felt hats, workers are exposed to low concentrations of mercury for long periods of time. Here, instead of the severe renal damage, with possible uremia, which one sees in a patient who has swallowed some bichloride of mercury tablets, we find an intention tremor and remarkably complicated personality changes. The Mad Hatter in Alice in Wonderland is a true case of industrial mercury poisoning! And so, it is highly important at this time to caution against jumping to conclusions that what the patient needs is a psychiatrist.

In conclusion, I would say that most patients are workers. And few workers, nowadays, succeed in escaping the hazards to health which modern technology has put in their path. Toxic chemicals are to be found not only in industry, but they are used in the home and in many hobbies as well. Carbon tetrachloride is a popular cleaning fluid with the housewife, benzol is a common constituent of rubber cements; and potentially toxic moth proofing materials and insecticides are in common use by almost everyone. For that reason, a history of exposure is of the essence. And one must never fail to consider the possibility of an occupational etiology in every differential diagnosis.

I wish to stress again the fact that ascertaining the occupational etiology in a given case, where it exists, may be the only means of saving the patient's life, since no amount of treatment will be effective unless he can be immediately removed from further exposure. But beyond that, I would like to direct your attention to the fact that recognition of the occupational etiology, contributes to proper reporting of occupational diseases, thereby making more accurate the occupational disease statistics available. Very few people realize that we have no reliable data at the present time as to the statistical incidence of any of the occupational diseases, principally because physicians fail to recognize them. With the best intentions in the world, a physician will not report a case of "Aplastic anemia" if it does not occur to him that it is occupational in origin. Practicing physicians, therefore, have a great contribution to make, as individuals, in the matter of prevention, in that they can provide public health agencies with accurate morbidity and mortality statistics which are the building stones of all public health programs.

FATAL EXPOSURE TO METHYLENE CHLORIDE VAPOR

From the November 1952 issue

BIBLIOGRAPHY

1. Fairhall, Lawrence T.: Industrial toxicology. Williams & Wilkins Co., Baltimore, 1949, p. 295.
2. E. I du Pont de Nemours & Co., Electrochemicals Dept.: Chlorine Products Bull. S 6-748.
3. Browning, Ethel: Toxicity of industrial organic solvents Medical Research Council, London, 1937, p. 128.
4. Threshold limit values for 1951 adopted at the meeting of the American Conference of Governmental Industrial Hygienists in Atlantic City, N. J., in April, 1951. Arch. Indust. Hyg. & Occup. Med. *4*, 198, 1951.
5. Heppel, L. A., Neal, P. A., Perrin, T. L., Orr, M. L., and Porterfield, V. T.: Toxicology of dichloromethane (methylene chloride) I. Studies on effects of daily inhalation. J. Ind. Hyg. & Toxicol., *26*, 8, 1944.
6. Heppel, L. A. and Neal, P. A.: Toxicology of dichloromethane (methylene chloride) II. Its effect upon running activity in the male rat. J. Ind. Hyg. & Toxicol., *26*, 17, 1944.
7. Svirbely, J. L., Highman, B., Alford, W. C., and von Oettingen, W. F.: The toxicity and narcotic action of monochloro-mono-bromo methane with special reference to in organic and volatile bromide in blood, urine and brain. J. Ind. Hyg. & Toxicol., *29*, 182, 1947.
8. Lehmann, K. B., and Flury, F.: Toxicologie und Hygiene der technischan Losungsmittel. Julius Springer, Berlin, 1938. Quoted in 5.
9. Henderson, Y., and Haggard, H. W.,: Noxious gases and the principles of respiration influencing their action. Second edition. Reinhold Publishing Co., New York, 1943, p. 201.
10. Same as 9, p. 205.
11. By courtesy of the Chief Medical Examiner of the City of New York.
12. Same as 9, p. 180.

INDUSTRIAL HYGIENE PUBLICATIONS

Studies in *Dermatitis*
Studies in the Fur Industry
Studies in Lead Poisoning
Studies in Tunneling
Studies in Silicosis
Studies in Rock Drilling
Methyl *Bromide*
Industrial Air Analysis
Cyanide Poisoning
Benzol Poisoning
Talc Miners and Drillers

GOOD-BYE

In retiring from the Division of Industrial Hygiene, I am also retiring as Editor of the "Monthly Review", a publication which I have had the pleasure of editing since it appeared in 1932 as "Industrial Hygiene". The Director of the Division of Industrial Hygiene will edit subsequent issues beginning with January, 1953.

I wish to take this opportunity to thank the many readers who have been kind enough to tell us of their appreciation of this publication, and to say good-bye to my friends.

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Update on asbestos-associated pulmonary disease

This review presents the historic, epidemiologic, scientific, and clinical aspects of asbestos-associated pulmonary diseases which are steadily continuing to increase. Only by applying concerted efforts in the understanding of the various occupational and biological aspects of asbestos exposure will the physician be able to provide improved surveillance, diagnosis, and management of these diseases.

The purpose of this review is to acquaint physicians with the historic, epidemiologic, scientific, and clinical aspects of asbestos-associated pulmonary diseases. As we enter the 1980s, these diseases will continue to increase in incidence and prevalence and will assume an even greater role in the daily practice of medicine.

Asbestos, derived from the Greek word *asbestos* meaning inextinguishable,' describes a group of fibrous silicates used in a number of industrial and domestic products. As implied by the Greek description, asbestos is virtually indestructible, being resistant to heat and chemical reactions. These properties give asbestos its unique physical and biological characteristics.

The major varieties of asbestos in order of their decreasing commercial importance are chrysotile, crocidolite, amosite, and anthophyllite.[2-6] Chrysotile comprises 90% of the asbestos used commercially.[2-6] Mineralogically, asbestos is divided into two classes: serpentine and amphibole. The former is a sheet silicate whereas the latter is built of double panes of tetrahedra. Chrysotile is the principal member of the serpentine family while amosite, crocidolite, and anthophyllite asbestos make up the major components of the amphibole family.[2]

Asbestos has a long and venerable history. It was initially employed by the ancient Egyptians for the making of pottery and noncombustible lamp wicks and for other products requiring fireproof components.[2-6] With the invention of the steam engine and the need for fire-resistant insulating materials, asbestos was first utilized commercially in the late 19th century.[2-6] Since that time, commercial use of asbestos has steadily increased and the resulting exposure of industrial workers has caused increasing numbers of asbestos-related pulmonary diseases. Only in the past 14 years, however, (following the work of Selikoff and co-workers[7]) has medical and public interest been aroused by the overwhelming incidence of pulmonary diseases secondary to occupational exposure to asbestos or asbestos-containing products.[8]

Epidemiological studies

Epidemiological evidence strongly supports an association between long-term and short-term asbestos exposure and diseases such as asbestosis, bronchogenic carcinoma, gastrointestinal cancer, and mesothelioma.[9-33] Differences in respiratory cancer mortality rates between exposed groups suggest that crocidolite asbestos may be more carcinogenic than chrysotile asbestos,[9] although these differences are difficult to identify in most studies.

It has been suggested that the presence of retained asbestos in lung tissues constitutes a continuing exposure. These in situ, or residential, exposures are of concern for cancer as well as asbestosis. In this type of exposure model the direct dose as well as the time in situ are determinants of the disease response. In the mortality follow-up study of the Paterson, NJ, amosite asbestos factory workers, Seidman and associates[10] found that work exposure to amosite asbestos for as short a period as one month was associated with an increased cancer risk. The risk of cancer increased with longer direct exposure (eg, two months, three months, or six months) and the length of time after onset of work. With very brief direct exposure, cancer risk was increased only after 25 to 35 years, emphasizing that with lighter (or brief) direct exposure, prolonged follow-up is necessary to evaluate asbestos-associated health effects. In addition to duration and level of exposure, the age at initial exposure also appears to be a major determinant of the disease response. Heavy direct (and prolonged) asbestos exposures in older men appear to result in a very large increase in mortality in a relatively brief period of time, five to 14 years after initial exposure as inferred by onset of work.

Cigarette smokers who experience long-term exposure to asbestos have a marked increase in lung cancer incidence (10 to 92 fold) compared with the unexposed nonsmoking population.[3,20,21,26] Even nonsmokers chronically exposed to asbestos experience a slightly increased risk for developing rare tumors such as malignant mesothelioma,[3,21] although recent information suggests that the cessation of smoking, after a number of years, will reduce the risk of lung cancer.[7]

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Interestingly, no correlation has been demonstrated between severity of asbestosis and cigarette smoking in asbestos-exposed individuals.[33]

In 1968, the possibility that asbestos-associated disease might be an important problem of shipyard workers was suggested, although it was not until recently that these risks were examined in the US.[12] Mapping the distribution of lung cancer mortality rates from 1950 to 1969 among males revealed an unexpected pattern.[13] The counties with the highest rates were clustered along the coastal areas of the South—Texas, Louisiana, and Florida—and in a series of counties along the southeast Atlantic. A subsequent case-control study of lung cancer diagnosed among residents of coastal Georgia revealed a significantly increased risk associated with employment in area shipyards in World War II.[14] The results of the Georgia study and reports from other studies in Europe and the United States[15] prompted the initiation of a series of lung cancer case-control studies in high mortality coastal areas,[16] including coastal Texas.[17] Results from this series of epidemiologic studies should help evaluate the contribution of shipyard asbestos exposures to respiratory cancer in the United States.

Biological properties

Asbestos gains entry into the airways via inhalation through either the nose or mouth. Fibers larger than 100 μ in length are usually filtered out by the nasal passages. Initial processing of the uncoated inhaled fibers occurs through interaction of the fibers with the human free alveolar macrophages (FAMs) in the alveolar ducts and alveoli. The FAMs are metabolically active phagocytic cells which are responsible for defending the lungs against inhaled foreign or injurious compounds.[34-36] Since asbestos is virtually indestructible, it poses a unique problem for the FAMs in their attempt to phagocytize and destroy these fibers. FAMs detoxify asbestos fibers by coating them with cell membrane components, acid mucopolysaccharides, hemosiderin, and other cellular components, thus converting them to asbestos bodies.[37-41] The asbestos bodies are less pointed than the uncoated asbestos fibers and their capacity to injure the alveolar walls during expiratory and inspiratory respiratory movements is decreased. In addition to phagocytosis of asbestos by FAMs, another valuable lung mechanism for removing foreign particulates is the mucociliary transport. This latter mechanism functions by means of the rhythmic beating of the cilia of the respiratory epithelial cells which carries foreign material cephalad where it is either expectorated or swallowed.

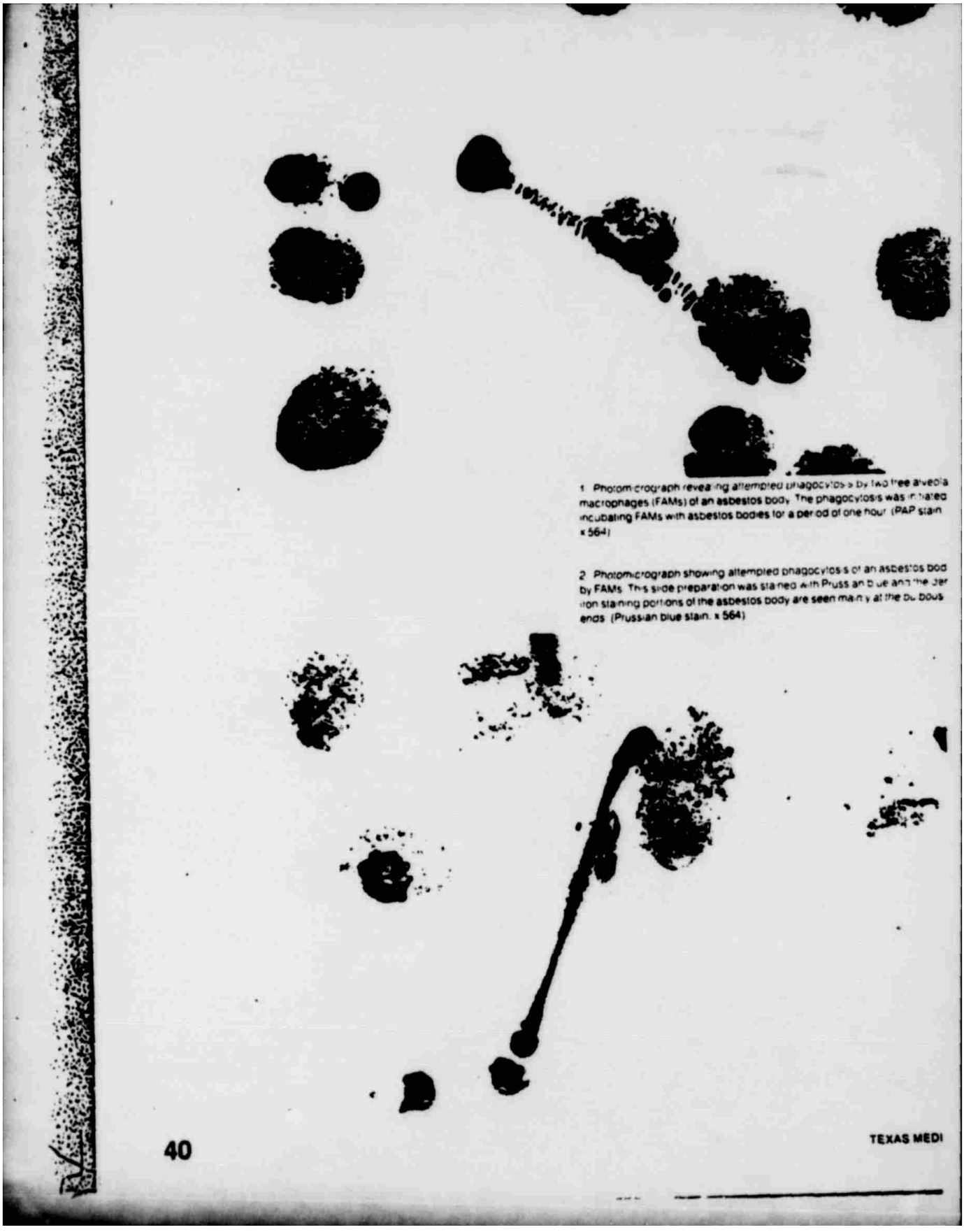
In vitro studies have demonstrated that uncoated asbestos fibers are cytotoxic to either animal[7,42] or human[39] lung cells. Human studies employing cultured FAMs have demonstrated a dose- and time-dependent effect of amosite asbestos on cell viability.[39] In contrast, studies employing asbestos bodies obtained from necropsy lung specimens of former asbestos workers have demonstrated that coated asbestos fibers are relatively nontoxic compared with naked fibers.[43] This thought that asbestos bodies are relatively inert was first expressed by Vorwald and associates in 1951,[44] following intratracheal injection of human lung asbestos bodies into guinea pigs. Figs 1–4 depict the phagocytosis of asbestos bodies and fibers by cultured FAMs.

The exact mechanisms for the synergistic interaction between components of cigarette smoke and asbestos fibers in production of human lung cancer have not been established. Some investigators have suggested that carcinogenic oils, trace metals, or unknown carcinogens are present on the surface of asbestos fibers and are responsible for these synergistic effects.[45-47] Existing evidence also supports the theory that the cocarcinogenic properties of asbestos are a function of physical rather than chemical characteristics.[27-28] According to this theory, asbestos acts as a storage depot for cigarette tars in the lungs of cigarette smokers.

Recent studies have demonstrated that uncoated asbestos fibers are capable of adsorbing components of cigarette smoke and transferring these compounds into artificial membranes[50,51] or cultured human cells.[48,52] Once they are transferred from the surface of asbestos fibers into cells, these compounds subsequently undergo metabolism by a membrane-bound nonoxygenase enzyme system.[48,52] This enzyme system, referred to as aryl hydrocarbon hydroxylase (AHH), is responsible for metabolism of components of cigarette smoke to active intermediate forms which are much more potent mutagens and carcinogens than the parent molecules. Because of these properties, AHH has been implicated in the etiology of lung cancer.[1,62]

Studies utilizing cultured human FAMs have demonstrated asbestos is capable of exerting a synergistic effect on AHH induction by binding components of cigarette smoke.[52] A recent report has also documented increased AHH levels in cells obtained from noncancer and lung cancer patients occupationally exposed to asbestos.[63] In this series, those individuals with asbestos exposure and histologically confirmed lung cancer demonstrated the highest AHH levels of any individuals studied. Thus, it has been hypothesized that as-

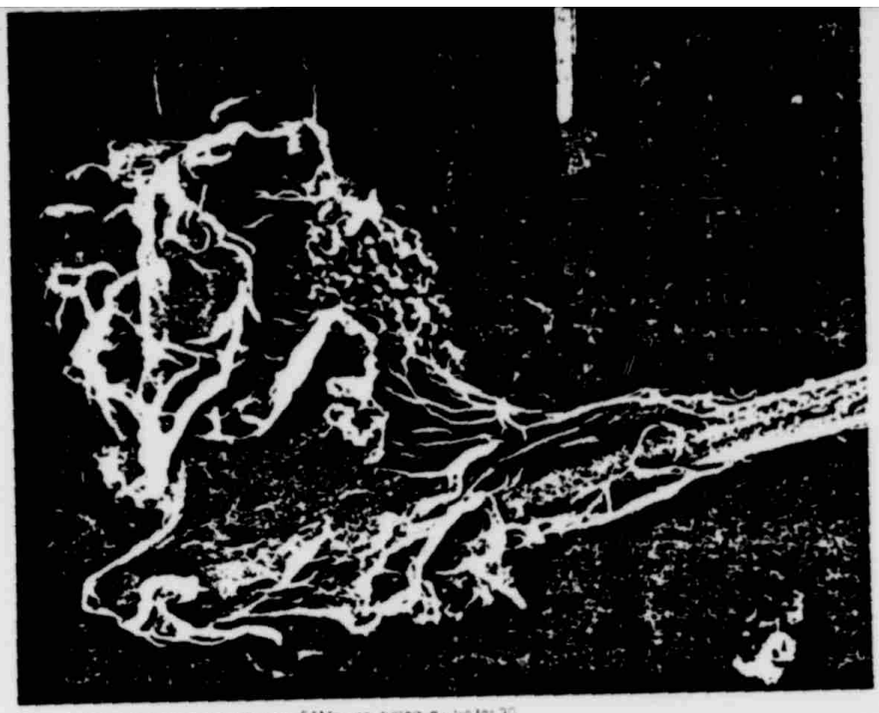
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1 Photomicrograph revealing attempted phagocytosis by two free alveolar macrophages (FAMs) of an asbestos body. The phagocytosis was initiated incubating FAMs with asbestos bodies for a period of one hour. (PAP stain x 564)

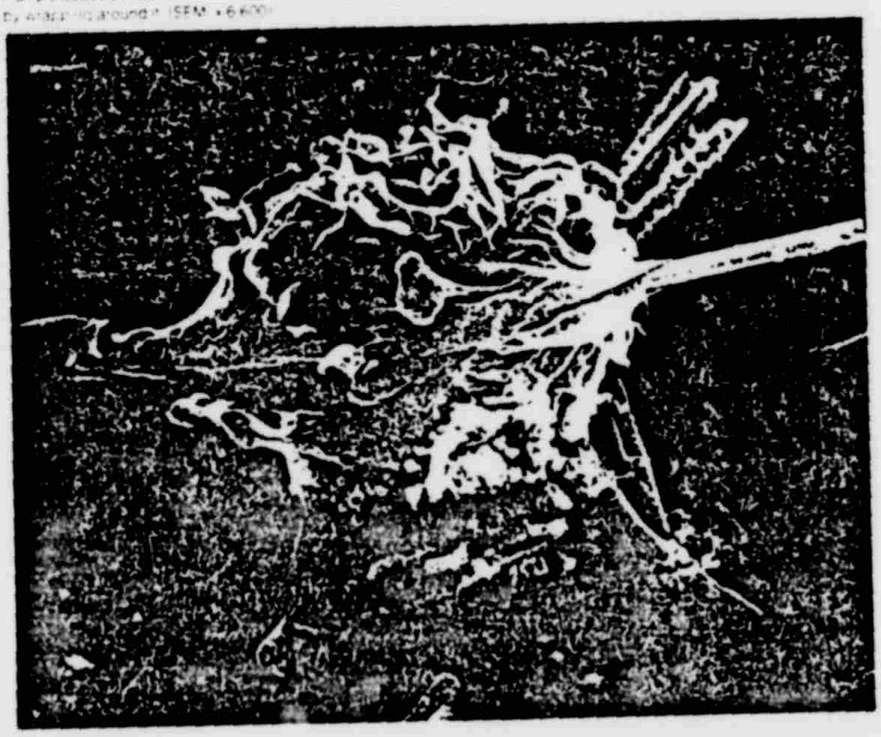
2 Photomicrograph showing attempted phagocytosis of an asbestos body by FAMs. This slide preparation was stained with Prussian blue and the iron staining portions of the asbestos body are seen mainly at the bulbous ends. (Prussian blue stain. x 564)

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3. Human free alveolar macrophages (FAMs) incubated in vitro for 30 minutes with amosite asbestos. The FAM has extended a cellular membrane covering one end of the asbestos fiber and encircling its length (SEM, ×6,600)

4. Human free alveolar macrophage (FAM) displaying phagocytosis of multiple asbestos fibers. The cellular membrane has covered the upper fiber by wrapping around it (SEM, ×6,600)



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5 Sources of occupational exposure to asbestos

1 Shipbuilding or Renovation—lagger, sailmaker-lagger, mason, painter, electrical fitter, sprayer, asbestos storeman, welder, shipfitter, plumber, driller, caulker, boilermaker, steamfitter
2 Manufacturer or Distribution of Asbestos-Containing Products (Asbestos cement products, friction materials, insulation products, paper products, textiles, milling, etc)—spinner, weaver, bag opener, cutter of dried products, carder, blender, bagger, packer, pelletizer, card loader, crusher, dryer operator, foreman, laborer, maintenance worker, mill operator, truck driver, heavy equipment operator, driller, putty manufacturing, cardboard manufacturing, automobile makers, welding rod manufacturing, munitions manufacturing, plaster makers, rubber workers
3 Construction Sites Which Utilize Asbestos or Asbestos-Containing Materials—lagger, painter, insulation worker, spray insulator, carpenter, mason, tile layer, demolition worker, heating equipment worker, plumber, welder, electrician, janitorial worker, sheet metal worker, and various other laborers exposed at construction sites
4 Automobile Repairs—brake repairman, body repairman, mechanics, service station attendants
5 Miscellaneous—repairmen, maintenance men, engineers, office workers, laboratory technicians, shipping personnel, sailors, longshoremen, dock workers, railroad workers, laundry and dry cleaning personnel, residents near asbestos processing and textile mills, persons living on or near roads where asbestos is transported, inhabitants of houses with asbestos insulation, persons living in homes with asbestos workers (spouses, etc)

Modified from references 3, 4, 74, 75

6 Asbestos containing products

1 Building Materials—pipes for gas, water and sewage, cement sheets for interior and exterior walls, reinforced asphalt or vinyl floor tiles, linoleum, panels, partitions, clapboard, asphalt siding and shingles, putties, ceiling board, millboard, stucco, plaster, artificial wood, sound proofing, facing of acoustical tile, asbestos cements, paint, roof coating and felt, caulking
2 Electrical—transformers, insulating tape, condensers, cables, spark plugs, conduits, electrical wire insulation, switch boxes, circuit breakers
3 Friction Materials—gaskets, clutch plates, brakelinings, conveyor belting, seals, bearing packing
4 Insulation—insulation blocks and board, pipe covering, insulation jackets, boiler and pipe covering, sprayed on structural heat insulation, pot holders, ironing board covers, table pads, stove mats, auto mufflers, automobile firewall and hood linings, glove linings
5 Miscellaneous—fire hoses, filter pads, filter paper, artificial snow, filler in rubber goods, cloth, sheets, blankets, draperies, yarn, cord, curtains, rope, twine, ribbon, welding electrodes, gas mask filters, filter cloths, catalyst supports for sulfuric acid production, steam, acid, and water proof bearings and packing, cardboard, paper products, boat hulls, airplane wings, wicks for lamps and oil burners, prison cell padding, clay for pottery and sculpture, life jackets, fireproof safety clothing, automobile undercoatings, asbestos reinforced hard standings in parking lots, asbestos asphalt, military helmet liners, piano padding, plastics, rocket reentry nose cones, frying pan handles, motion picture screens, mail bags. For others see reference 75

Modified from references 3, 4, 74, 75

bestos might exert harmful biological effects on human lung cells by mediating cytotoxicity as well as providing a vehicle for the storage, transportation, and potentiation of components of cigarette smoke in the human respiratory tract.[46 57 67]

The above studies suggest that the coating of raw asbestos fibers by FAMs renders the fibers less cytotoxic. In an individual who is exposed to large quantities of asbestos over a prolonged period of time the pulmonary defense mechanisms become overburdened and cannot function efficiently. When this occurs, increased numbers of the uncoated, more cytotoxic fibers begin to accumulate in the lung tissues. The alveolar tissue response to an overwhelming number of uncoated fibers is one of inflammation, cell death, and fibrosis. Once these asbestos fibers make their way into interstitial lung tissues, they are relatively indestructible and most will remain indefinitely. They then provide a focus for continuous irritation and cell damage. In those individuals who are cigarette smokers, asbestos would also provide continuous prolonged exposure of lung cells to cigarette tars which are adsorbed to the fiber surface. The subsequent interactions between asbestos and cigarette tar components (in smokers) provide the stimulus for the development of lung cancer 15 to 20 years following initial exposure.

Role of the primary physician

The most important role of the physician in control of asbestos-related diseases is the early detection of those individuals who are at risk secondary to occupational exposure. Fig 5 describes the major occupational sources of asbestos exposure. If the physician is familiar with these sources, he or she will have a much greater opportunity of establishing an early diagnosis of asbestos-associated pulmonary disease. Occupations which provide the most significant exposure are asbestos mill workers, asbestos textile workers, insulation workers, sprayers using asbestos insulation slurries, laggers installing asbestos insulation, openers of bags of asbestos, demolition workers at sites where asbestos insulation or products exist, and ship refitting workers.[4] Listed in Fig 6 are commonly used asbestos-containing products which should be considered when taking an occupational history. Other factors to be considered in determining the degree of individual occupational asbestos exposure are provided in Fig 7.

Following documentation of significant asbestos exposure in an individual, the physician should alert the patient to possible complications secondary to his exposure. The most common example would be emphasizing the greatly increased risk of lung cancer in those individuals who are chronically exposed to asbestos and who also smoke cigarettes. With this in mind, the physician should advise immediate cessation of smoking.

Clinical diagnosis of asbestosis

Clinical diagnosis of asbestosis may be made in one of two ways: searching for evidence of asbestosis in the presence of known exposure, and suspecting exposure in the presence of known disease.

In an asbestos-exposed worker, the extent of exposure is evaluated by considering the factors in Figs 5–7. It must be remembered that there is a latent period of 10 to 20 years or

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longer between exposure and overt disease, so that acute changes in a recently exposed worker are probably not asbestos-related. In workers with adequate exposure and time since exposure, a definitive diagnosis of asbestosis rests on chest roentgenographic findings of either the usual lower lobe reticulonodular change or pleural plaques. Support for a diagnosis of asbestosis can be obtained by finding ferruginous bodies in expectorated sputum,[64] an altered diffusion capacity for carbon monoxide, or a restrictive process with loss of lung volume by pulmonary function testing.[3,4] In the presence of an appropriate exposure history and radiograph consistent with asbestosis, further data are seldom necessary. However, if tissue proof of asbestosis is mandatory for medicolegal purposes, bronchoscopy with transbronchial biopsy is usually adequate to show pathologic changes as well as the presence of coated asbestos fibers (asbestos bodies).

Occasionally, the physician will be faced with a patient with apparent asbestos-related thoracic disease such as in Fig 8, but no definitive exposure history. In that case a careful review of possible occult exposure such as from Fig 6 is warranted. If the diagnosis is still uncertain, the sputum should be examined for ferruginous bodies, and if clinically or legally indicated, a tissue sample can be obtained and evaluated by light microscopic and electron probe analysis to determine the amount of asbestos present. Quantitation of "normal" and "abnormal" amounts of asbestos in lung tissue is a new procedure at Baylor College of Medicine and holds promise in helping to define asbestos-related disease in its occult presentations.

Diagnosis by sputum cytology

The practicing physician should be aware of sputum cytology procedures which are helpful in detecting ferruginous bodies (iron-coated asbestos or other type fibers) in the sputum of individuals chronically exposed to asbestos. A patient may have insufficient interstitial pulmonary fibrosis to be documented by chest roentgenograms or pulmonary function testings and yet sputum cytology specimens from the individuals can be screened for and reveal ferruginous bodies.[64-67] This screening procedure is not only helpful for detecting and documenting that the individual has had sufficient exposure to asbestos, but it is also beneficial in detecting premalignant atypias in the cells of the respiratory tract.

In addition to detection of ferruginous bodies in sputum, methods have been devised for the isolation and concentration of ferruginous bodies from lung and other tissues by a digestion technique.[68,69] Indeed, the number of ferruginous bodies in lung tissue has been shown to correlate with the degree of pulmonary interstitial fibrosis in two separate studies,[68,70] although other factors, such as infection or abnormal host response may be involved in the progression from moderate to severe interstitial fibrosis.[70,71] Furthermore, there is a statistically significant correlation between the concentration of pulmonary ferruginous bodies and the likelihood that a given sputum specimen from the same individual will contain ferruginous bodies (Roggli VL, Greenberg SD, McLarty J, *et al*, *unpublished observations*).

Sophisticated electron microscopic techniques are now

7 Factors predominantly in asbestos exposure*

1 Exposure before 1950
2 Constant exposure to high levels
3 Long-term exposure
4 Lack of use of protective inhalation devices
5 Occupations receiving high asbestos exposure
  a Asbestos mill workers
  b Asbestos textile factory workers
  c Sprayers using asbestos insulation
  d Asbestos insulation laggers
  e Asbestos bag openers
  f Demolition workers
  g Ship refitters

* Adapted from Asbestos-Related Diseases by Preger LP, Ara OT, Kolin P, et al, copyright © Grune & Stratton, 1968. Reprinted with permission of Grune & Stratton.

8 Radiographic manifestations of asbestosis

A Pulmonary parenchyma
  1 Reticulonodular infiltrates (predominantly lower lobe)
  2 Mass lesions (bronchogenic carcinoma)
B Pleural
  1 Plaques
  2 Effusion
  3 Mesothelioma

available which allow the determination of the chemical composition of the fibrous cores of individual ferruginous bodies isolated from tissues by the digestion-concentration technique. Although the theoretical and technical aspects of the electron microprobe or energy dispersive x-ray analysis (EDXA) are beyond the scope of this review, they have been thoroughly discussed elsewhere.[72] EDXA, in combination with selected area electron diffraction (SAED), is a powerful tool which the pathologist can use to obtain chemical and crystallographic information not only about ferruginous body cores from asbestos workers or the general population, but about other inorganic particulates, as well.

By utilizing the new advanced diagnostic techniques, sputum samples and or bronchial washings can be used to document occult asbestos exposure by identification of asbestos fiber cores in ferruginous bodies. At this point, the distinction should be made between the method of verification of asbestos exposure just described and the diagnosis of asbestosis which requires radiographic assessment as discussed in detail in the section on clinical diagnosis of asbestosis.

Case report

With the recent increase in environmentally related diseases knowledge of the latent [illegible]

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Such an example is the following case report in which the patient had been chronically exposed to asbestos but because of an incomplete occupational history the clinical diagnosis of asbestosis was long overlooked.

The patient was a 73-year-old black man with a history of cigarette smoking who had been seen at the Ben Taub General Hospital in Houston a number of times for various pulmonary complaints. His pulmonary symptoms were first documented in 1969, and his last admission was in 1976, when he complained of fever (105 F), dyspnea, and cough. The patient had been admitted one month earlier with similar symptoms and was found to have pneumonia. Clinically, an "insulinoma" was suspected. The patient stated that he awoke the day of his final admission and was "unable to breathe." He further stated that his coughing had increased and that he had begun to bring up a thick, purulent, brown sputum. He also complained of intermittent chest pains.

During the patient's hospitalization one week earlier, a bronchoscopy had been performed and the bronchial washings demonstrated the presence of ferruginous bodies. Subsequent questioning of the patient revealed that for 20 years (1945–1965) he had been employed as an insulator, working with asbestos.

Upon the patient's final admission, the physical examination revealed dullness to percussion over the right chest, posteriorly, and increased fremitus over the right and left midchest, posteriorly. He also had decreased breath sounds and diffuse rales and rhonchi over the right chest wall. Tachycardia was present. The chest roentgenogram showed bilateral interstitial infiltrates, predominantly in the lower lobes, which resolved somewhat following antibiotic treatment (Fig 9). His peripheral white blood cell count showed a leukocytosis of 30,000, with 15% to 25% eosinophils. An electrocardiogram showed arteriosclerotic cardiovascular disease, suggesting an old myocardial infarct.

Three days following his admission, the patient clinically appeared to be improving. He was in "good spirits" and in no distress. His sputum production had decreased although rales and rhonchi were still present. However, he suddenly began gasping for breath and sustained a cardiac arrest. Resuscitative efforts were unsuccessful.

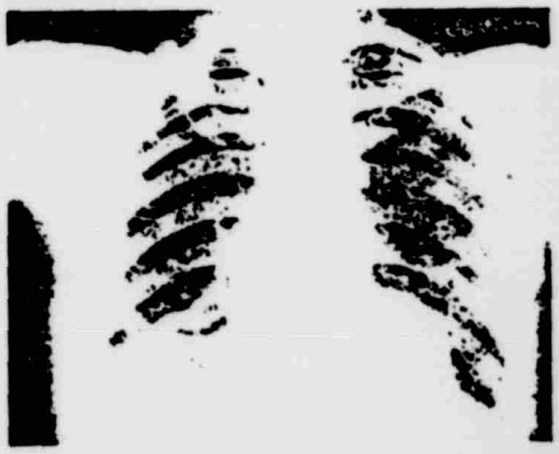
The major findings noted at necropsy were acute bilateral bronchopneumonia with abscess formation. Clinically, the pneumonia had been thought to be staphylococcal on the basis of sputum cultures; however, at necropsy, cultures of the lung grew *E coli*. Severe interstitial fibrosis of the lungs was also present and the combination of the pneumonia with the interstitial fibrosis was thought to be the cause of death. Microscopic examination of the lungs revealed diffuse interstitial fibrosis (DIF) and numerous ferruginous bodies consistent with asbestosis. Other necropsy findings included severe panlobular emphysema, severe and diffuse arteriosclerotic occlusive vascular disease, arteriosclerotic disease of the heart, and bilateral moderate nephrosclerosis.

Determination of ferruginous body (FB) counts by digestion of 5 gm of the lower lobe of the lung in 5.25% sodium hypochlorite solution (commercial Clorox bleach) demonstrated 10,120 FB/gm lung (wet formalin-fixed weight). For comparison, the counts from an adult autopsy population with no known occupational exposure to asbestos range from 0 to 20 FB/gm, with FBs identified in over 90% of samples from the "general population." EDXA studies on 11 FB isolated from this patient's lungs demonstrated an asbestos core with a composition of amosite or crocidolite, and SAED studies on three cores showed a crystallographic pattern of the type seen in amphibole asbestos (Fig 10). Blood cultures obtained at the time of necropsy were negative.

Summary

This review contains a classic example of a patient with heavy exposure to asbestos whose occupational history was ignored because of other clinical problems which were assumed to be responsible for his lung disease. It is emphasized that many patients will not reveal an occupational

9 Chest roentgenogram demonstrating the bilateral lobe interstitial fibrosis of asbestosis, with superimposed alveolar filling defects of bronchopneumonia



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asbestos exposure to their physician, either because they are not aware of it or do not understand its significance to their health and present illness. It is, therefore, the responsibility of the attending physician to carefully question each patient to insure that his occupation has not been associated with exposure to asbestos. Such concerted efforts by the primary physician in screening of patients occupationally exposed to asbestos are extremely important for early detection of asbestos-associated lung diseases. Only by understanding the various occupational, epidemiological, biological, and clinical aspects of asbestos exposure will the primary care physician be able to provide improved surveillance, diagnosis, and management of these diseases.

REFERENCES

1 Gurainik DB, Friend JH (eds). Webster's New World Dictionary of the American Language. College edition. New York, The World Publishing Co, 1968, p 85.

2 Harrington JS. The biological effects of mineral fibers, especially asbestos, as seen from in vitro and in vivo studies. Ann Ant Pathol 21: 155–198, 1976.

3 Selikoff IJ, Lee DH. Asbestos and Disease. New York, Academic Press, Inc, 1978.

4 Preger LP, Arai DT, Kotin P, et al. Asbestos-Related Diseases. New York, Grune and Stratton, 1968.

5 Becklake MR. Asbestos-related diseases of the lung and other organs: their epidemiology and implications for clinical practice. Am Rev Resp Dis 114: 187–227, 1976.

6 Levine RJ. Asbestos: An Information Resource. DHEW Pub No (NIH) 78–1681. US Dept of Health, Education and Welfare, 1978.

7 Selikoff IJ, Hammond EC, Churg J. Asbestos exposure, smoking and neoplasia. JAMA 204: 104–110, 1968.

8 Selikoff IJ, Hammond EC (eds). Health Hazards of Asbestos Exposure. Ann NY Acad Sci 1979, vol 330.

9 Henderson VL, Enterline PE. Asbestos exposure: factors associated with excess cancer and respiratory disease mortality, pp 117–126, in Selikoff IJ, Hammond EC (eds). Health Hazards of Asbestos Exposure. Ann NY Acad Sci 1979, vol 330.

10 Seidman H, Selikoff IJ, Hammond EC. Short-term asbestos work exposure and long-term observations, pp 61–89, in Selikoff IJ, Hammond EC (eds). Health Hazards of Asbestos Exposure. Ann NY Acad Sci 1979, vol 330.

11 Hammond EC, Selikoff IJ, Seidman H. Asbestos exposure, cigarette smoking and death rates, pp 473–490, in Selikoff IJ, Hammond EC (eds). Health Hazards of Asbestos Exposure. Ann NY Acad Sci 1979, vol 330.

12 Selikoff IJ, Lilis R, Nicholson WJ. Asbestos disease in United States shipyards, pp 295–311, in Selikoff IJ, Hammond EC (eds). Health Hazards of Asbestos Exposure. Ann NY Acad Sci 1979, vol 330.

13 Mason TJ, McKay FW, Hoover R, et al. Atlas of Cancer Mortality for US Counties: 1950–69. DHEW Pub (NIH) 75–780. US Dept of Health, Education and Welfare. US Government Printing Office, Washington, DC, 1975.

14 Biot WJ, Harrington JM, Toledo A, et al. Lung cancer after employment in shipyards during World War II. N Engl J Med 299: 620–624, 1978.

15 Evaluation of the carcinogenic risk chemicals to man. International Agency for Research on Cancer. Asbestos. IARC, Lyon, France, 1977.

16 Biot WJ, Fraumeni JF Jr. Lung cancer mortality in the United States shipyard correlations, pp 313–315, in Selikoff IJ, Hammond EC (eds). Health Effects of Asbestos Exposure. Ann NY Acad Sci 1979, vol 330.

17 Buffler PA. Personal communications, 1980.

18 Hammond EC, Selikoff IJ. Relation of cigarette smoking to risk of asbestos associated diseases among insulation workers in the United States, in Bogovski P, Gilson JC, Timbrell V (eds). Biological Effects of Asbestos. Lyon, International Agency for Research on Cancer, pp 312–317, 1973.

19 Berry G, Newhouse ML, Turok M. Combined effects of asbestos exposure and smoking on mortality from lung cancer in factory workers. Lancet 2: 476–478, 1972.

20 Higginson J. Importance of environmental factors in cancer in environmental pollution and carcinogenic risks. Lyon, IARC, Scientific Publication No 13, pp 15–23, 1976.

21 Fears TR. Cancer Mortality and Asbestos Deposits. Am J Epidemiol 104: 523–526, 1976.

22 Kogan FM, Guseinikova NA, Guleuskaya MR. On the causes of death in patients with asbestos. Gigiena Truda i Professional'nye Zabolevaniya 15: 43–46, 1971.

23 Fletcher DE. A mortality study of shipyard workers with pleural plaques. Br J Ind Med 29: 142–145, 1972.

24 Enterline P, DeCoufle P, Henderson V. Mortality in relation to occupational exposure in the asbestos industry. J Occup Med 14: 897–903, 1972.

25 McDonald JC. Cancer in chrysotile mines and mills, in Bogovski P, Gilson JC, Timbrell V (eds). Biological Effects of Asbestos. Lyon, IARC, pp 189–194, 1973.

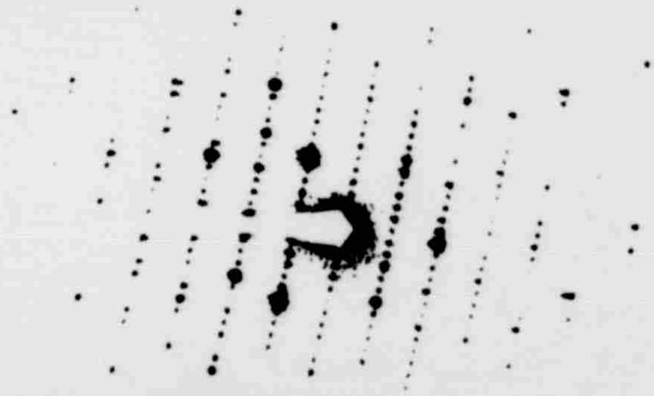
26 Meurman LO, Kiviluoto, Hakama M. Mortality and morbidity among the working population of anthophyllite asbestos miners in Finland. Br J Ind Med 31: 105–112, 1974.

27 Boucot KR, Weiss W, Seidman H, et al. The Philadelphia Pulmonary Neoplasm Research Project. Basic Risk Factors of Lung Cancer in Older Men. Amer J Epidemiol 95: 4–16, 1972.

28 Waller RE. The combined effects of smoking and occupational or urban factors in relation to lung cancer. Ann Occup Hyg 15: 67–73, 1972.

29 Selikoff IJ, Hammond EC, Seidman H. Cancer risk of insulation workers in the United States, in Bogovski P, Gilson JC, Timbrell V (eds). Biological Effects of Asbestos. International Agency for Research on Cancer, Sci Pub No 8, Lyon, France, 1973, pp 209–216.

30 Rom WN, Palmer PES. The spectrum of asbestos-related diseases. West J Med 121: 10–21, 1974.



10 A selected area electron diffraction (SAED) pattern obtained from an asbestos body core from 73-year-old black man (see case report). This pattern is typical of amphibole asbestos. EXMA of the same core showed a chemical composition consistent with either an amosite or crocidolite fiber.

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31 McDonald AD, McDonald JC. Mesothelioma after crocidolite exposure during gas mask manufacture. Environ Res 17: 340–346, 1978.
32 Churg AM, Warnock ML. Numbers of asbestos bodies in urban patients with lung cancer and gastrointestinal cancer and in matched controls. Chest 76: 143–149, 1979.
33 Samet JM, Epler GR, Gaensler EA, et al. Absence of synergism between exposure to asbestos and cigarette smoking in asbestosis. Amer Rev Respir Dis 120: 75–82, 1979.
34 Allison AC. Experimental methods: cells and tissue culture: effects of asbestos particles on macrophages, mesothelial cells and fibroblasts. In Bogovski P, Gilson JC, Timbrell V (eds): Biological Effects of Asbestos. International Agency for Research on Cancer, Sci Pub No 8. Lyon, France, 1973, pp 89–93.
35 Dourmashkin RR, Dougherty RM. Phagocytosis of crystalline particles by cells grown in tissue culture. Exp Cell Res 25: 480–484, 1961.
36 McLemore T, Corson M, Mace M, et al. Phagocytosis of asbestos fibers by human pulmonary alveolar macrophages. Cancer Lett 6: 183–192, 1979.
37 Davis JM. Electron microscope studies of asbestosis in man and animals. Ann NY Acad Sci 132: 98–111, 1965.
38 Governa M, Rosanda C. A histochemical study of the asbestos body coating. Br J Ind Med 29: 154–159, 1972.
39 Kannerstein M, Churg J, McGaughey WTE, et al. Pathogenic effects of asbestos. Arch Pathol Lab Med 101: 623–628, 1977.
40 Suzuki Y, Churg J. Structure and development of the asbestos body. Am J Pathol 55: 79–107, 1969.
41 Mace ML Jr, McLemore TL, Poggi VL, et al. Scanning electron microscopic examination of human asbestos bodies. Cancer Lett 9: 95–104, 1980.
42 Tucker RW, Frank AL. Asbestos cytotoxicity in a long term macrophage-like cell culture. Nature 264: 44–46, 1976.
43 McLemore TL, Mace ML Jr, Poggi VL, et al. Asbestos body phagocytosis by human free alveolar macrophages. Cancer Lett 9: 85–93, 1980.
44 Vorwald AJ, Durkan TM, Pratt PC. Experimental studies of asbestosis. Arch Indust Hyg Occ Med 3: 1–43, 1951.
45 Dixon JR, Lowe DB, Richards DE, et al. The role of trace metals in chemical carcinogenesis: asbestos cancers. Cancer Res 30: 1068–1074, 1970.
46 Harrington JS. Chemical studies of asbestos. Ann NY Acad Sci 132: 31–47, 1965.
47 Harrington JS, Roe FJC. Studies of carcinogenesis of asbestos fibers in the rat peritoneal cavity. Ann NY Acad Sci 132: 439–450, 1965.
48 McLemore TL, Jenkins WT, Arnott MS, et al. Aryl hydrocarbon hydroxylase induction in mitogen-stimulated lymphocytes by benzanthracene or cigarette tars adsorbed to asbestos fibers. Cancer Lett 7: 171–177, 1979.
49 McCullagh SF. The biological effects of asbestos. Med J Australia 2: 45–49, 1974.
50 Lakowicz JR, McNamara M, Stenson L. Particle-mediated membrane uptake of chemical carcinogens studied by fluorescence spectroscopy. Science 199: 305–307, 1978.
51 Lakowicz J, Hylden JL. Asbestos-mediated membrane uptake of benzo(a) pyrene observed by fluorescence spectroscopy. Nature 275: 446–448, 1978.
52 McLemore TL, Carson MA, Marshall MV, et al. Asbestos-mediated induction of aryl hydrocarbon hydroxylase in human pulmonary alveolar macrophages. J Clin Invest, submitted 1980.
53 Busbee DL, McLemore TL, Martin RR, et al. High AHH inducibility is positively correlated with occurrence of lung cancer. In Bjorseth A, Dennis A (eds): Polynuclear aromatic hydrocarbons: chemistry and biological effects. Columbus, Ohio, Battelle Press, 1980, pp 917–934.
54 Coomes ML, Mason WA, Mulsson I, et al. Aryl hydrocarbon hydroxylase and 16 alpha-hydroxylase in cultured human lymphocytes. Biochem Genet 14: 671–685, 1976.
55 Emery AE, Danford N, Anand R, et al. Aryl-hydrocarbon-hydroxylase inducibility in patients with lung cancer. Lancet 3: 470–472, 1978.
56 Gahmberg CG, Sekki A, Kosunen TU, et al. Induction of aryl hydrocarbon hydroxylase activity and pulmonary carcinoma. Int J Cancer 23: 302–305, 1979.
57 Guigis HA, Lynch HT, Mate T, et al. Aryl hydrocarbon hydroxylase activity in lymphocytes from lung cancer and normal controls. Oncology 33: 105–109, 1976.
58 Kellermann G, Shaw CR, Luyten-Kellermann M. Aryl hydrocarbon hydroxylase inducibility and bronchogenic carcinoma. N Eng J Med 289: 934–937, 1973.
59 Kellermann G, Luyten-Kellermann M, Jett J, et al. Aryl hydrocarbon hydroxylase in man and lung cancer: Human genetic variation in response of medical environmental agents: pharmacogenetics and energetics. Human Genetics (Suppl 1): 161–168, 1978.
60 McLemore TL, Martin RR, Springer RR, et al. Aryl hydrocarbon hydroxylase activity in pulmonary alveolar macrophages and lymphocytes from lunger cancer and noncancer patients: a correlation with family histories of cancer. Biochem Genet 17: 795–806, 1979.
61 McLemore TL, Martin RR, Wray NP, et al. Reassessment of the relationship between aryl hydrocarbon hydroxylase and lung cancer. Cancer, in press, 1980.
62 McLemore TL, Martin RR. Pulmonary carcinogenesis: aryl hydrocarbon hydroxylase. In Livingston RB (ed): Lung Cancer Vol 1: Advances in Research and Treatment. The Hague, The Netherlands, Martinus Nijhoff, in press, 1980.
63 Snodgrass DR, McLemore TL, Busbee DL, et al. Aryl hydroxylase activity in pulmonary macrophages and blood lymphocytes from asbestos-exposed cigarette smokers with and without lung cancer. Chest, in press, 1980.
64 Farley ML, Greenberg SD, Shuford EH, et al. Ferruginous bodies in sputa of former asbestos workers. Acta Cytol (Baltimore) 21: 693–700, 1977.
65 Greenberg SD, Hurst GA, Mallage WT, et al. Sputum cytopathological findings in former asbestos workers. Tex Med 72: 39–43, 1976.
66 Greenberg SD, Hurst GA, Mallage WT, et al. Tyler asbestos workers program. Ann NY Acad Sci 271: 353–364, 1976.
67 Greenberg SD, Hurst GA, Christianson SC, et al. Pulmonary cytopathology of former asbestos workers: report of the first year. Amer J Clin Pathol 66: 815–822, 1976.
68 Smith MJ, Naylor B. A method for extracting ferruginous bodies from sputum and pulmonary tissue. Amer J Clin Pathol 58: 250–254, 1972.
69 Roggli VL, Greenberg SD, Seltzman LH, et al. Pulmonary fibrosis, carcinoma, and ferruginous body counts in amosite asbestos workers: a study of six cases. Amer J Clin Pathol 73: 496–503, 1980.
70 Ashcroft T, Heppleston AG. The optical and electron microscopic determination of pulmonary asbestos fibre concentration and its relation to the human pathological reaction. J Clin Pathol 26: 224–234, 1973.
71 Merchant JA, Klouda PT, Soutar CA, et al. The HL-A system in asbestos workers. Br Med J 1: 189–191, 1975.
72 Marshall AT. Electron probe x-ray microanalysis. In Hayat MA (ed): Principles and Techniques of Scanning Electron Microscopy. New York, Van Nostrand Reinhold Co, vol 4, 1975, pp 103–173.
73 Dohrer VA, Beegle RG, Miller WT. Asbestos exposure and multiple primary tumors. Amer Rev Resp Dis 112: 181–199, 1975.
74 Hueper WC. Occupational and nonoccupational exposures to asbestos. Ann NY Acad Sci 132: 184–195, 1965.
75 Rosato DV. Asbestos: Its Industrial Applications. New York, Reinhold Pub, 1959.

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TOXIC GOITER DURING PREGNANCY

To the Editor:—*I should like information concerning any detrimental effect of propylthiouracil on the fetus when the medicament is used to treat toxic goiter during pregnancy.*

C. Lawrence Holt, M.D., Portland, Maine.

Answer.—When antithyroid drugs of any type have been used for long periods of time during the last half of pregnancy, a goiter is occasionally induced in the fetus. These goiters usually disappear spontaneously and, so far as is known, have never caused any difficulty or permanent disturbance in thyroid function. They are nevertheless undesirable; in the event that the mother's thyroid should enlarge during pregnancy serious consideration should be given to other forms of therapy, because when the mother's thyroid enlarges the fetus's is more apt to show the same reaction. Hypothyroidism should be watched for closely and prevented by simultaneous administration of antithyroid drugs and desiccated thyroid in the event that symptoms or signs of hypothyroidism develop. Small doses of iodine may also be used.

QUINIDINE AND PREGNANCY

To the Editor:—*A 28-year-old patient, para 1, gravida 3, suffers from sporadic attacks of paroxysmal tachycardia. She is completely relieved in one hour after taking 6 grains (about 0.4 gm.) of quinidine orally for one dose. The attack otherwise continues for as long as 15 hours and is refractory to all other forms of treatment that I know of. Has this drug any oxytocic effect on a three-month pregnancy? If so, what should be used in its place? When the patient tried the drug nothing happened to her pregnancy.*

Nerio W. Pioppi, M.D., Southbridge, Mass.

Answer.—Unless a person is overly sensitive to quinidine, the drug used in the dosage indicated for relief of paroxysmal tachycardia is not contraindicated in pregnancy. Since in this particular patient only one dose is necessary to relieve the tachycardia, there is no hazard in its use. Quinidine sulfate in the dosage mentioned has no oxytocic effect. It must be emphasized, however, that the drug should not be used in large amounts and repeated doses in pregnancy.

RESUSCITATION

To the Editor:—*Can you tell me if movement of the muscles would result if electroshock therapy, as used in psychiatric treatment, were applied to a corpse shortly after death? Might this have value for resuscitation?*

William H. Kupper, M.D., San Pedro, Calif.

Answer.—The skeletal muscles of the body usually retain their electrical excitability for a brief period after the heart has stopped beating. Persistent electrical excitability of the skeletal muscles would not necessarily indicate that the heart was still susceptible to resuscitation. Absence of electrical excitability of the skeletal muscles would indicate that any attempts at cardiac resuscitation would be fruitless.

ASBESTOSIS

To the Editor:—*A 50-year-old white man worked at covering pipe with asbestos insulation from 1940 to 1945. What would be the possibility of pulmonary fibrosis evident on roentgenograms in 1952 being due to asbestosis, when films had been normal for this in 1949?*

B. E. Morgan, M.D., Wilson, N. C.

Answer.—The cause of the 1952 pulmonary fibrosis in this case must be sought among other sources than the 1940-1945 occupation. Little evidence exists of progression of asbestosis after cessation of exposure to asbestos fibers. If exposure over the comparatively brief period of five or six years had been sufficient to produce pulmonary fibrosis, it would have had to be extremely severe, much more so than would be experienced by a laborer engaged in covering pipe with asbestos insulation. In the event that exposure over this period had been of such magnitude as to cause fibrosis, it would certainly have mani-

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Answer.—A daily dose of 0.13 gm. of codeine sulfate orally should not affect a person mentally to such an extent that he would be incapable of making a will, especially if, as is presumed to be the case, the total daily dose were divided into several smaller doses. The toxic effects of codeine include nausea, vomiting, skin eruptions, constipation, respiratory depression, and convulsions. Some of these effects may occur with doses of only 30 to 60 mg. The incidence of toxic effects is, however, low, and serious poisoning with codeine is rare. Eddy (Pharmacology of the Opium Alkaloids, *Pub. Health Rep.* suppl. no. 165, Washington, D. C., U. S. Government Printing Office, 1941) states that no fatal cases of poisoning with codeine have been recorded. Codeine does cause pupillary constriction, and true addiction to codeine does occur.

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M.D., California.

Answer.—The urethral secretion that the patient describes is probably prostatic or Cowper's gland fluid. It has no clinical significance and might cease after marriage. On the basis of the information presented, the patient can be reassured that he has no cause to worry. He is evidently in need of sex education.

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To the Editor:—*Has the injection of ganglions with cortisone or corticotropin (ACTH) proved efficacious?*

William A. Meadows, M.D., Lockport, Ill.

Answer.—Ganglions that have been aspirated so that most of their gelatinous or mucinous-like content has been removed and then treated by injection with hydrocortisone and application of a pressure dressing have in many instances been cured. There is not yet enough clinical evidence to determine the approximate percentage of success from this method. Corticotropin

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THE CAUSE OF POSTURAL PROTEINURIA

A FEW weeks ago we said that the mechanism of postural proteinuria was still unknown.[15] An important contribution has since been made by Greiner and Henry.[16] These workers criticise the view[17] that the proteinuria is directly due to increased pressure in the inferior vena cava and renal veins, and refer to an experimental study[18] in which increase of caval pressure to 150–220 mm. saline, maintained for thirty minutes, caused no proteinuria.

Carefully controlled observations in six young men with postural proteinuria indicated that the most important ætiological factor is pooling of blood in the extremities. Advantage was taken of the fact that postural proteinuria is particularly liable to occur in hot conditions,[17] and all the observations were made at a temperature of 122°F. Lordosis in the supine position produced proteinuria once only, whereas venous-occlusion cuffs applied at a pressure of 80 mm. Hg to all four limbs resulted in proteinuria in all the subjects. Proteinuria, which regularly occurred after tilting the subjects to a 70° head-up position, was prevented by compression of the legs, which effectively inhibited peripheral pooling of blood.

Greiner and Henry point out that their observations explain the facts that postural proteinuria is commoner in hot conditions producing peripheral vasodilatation, and in motionless standing[17] which is particularly liable to cause pooling of blood in the legs. They suggest that deviation of blood from the heart and lungs causes arterial vasoconstriction which is proportionately greater in the renal arterial system. The erect lordotic posture greatly reduces the renal plasma flow,[19] but this fall is no greater in cases of postural proteinuria than in non-proteinuric controls.

LUNG CANCER IN ASBESTOSIS

THE causes of cancer of the lung are probably mainly exogenous,[20] but each of the definitely known carcinogenic substances—e.g., ores in Schneeberg and Joachimstal mines, bichromates—accounts for only a minute proportion of all cases. Doll[21] now confirms suggestive evidence that lung cancer is an occupational hazard of asbestos workers. Examination of the cause of death in 105 persons who had been employed in one asbestos works showed that 18 had had lung cancer, associated in 15 cases with asbestosis. The mortality of 113 men who had worked for at least twenty years in places exposed to asbestos dust was compared with the mortality experience of the whole male population. There were 39 deaths in the first group, whereas 15·4 were expected: the excess was due to deaths from lung cancer (11, compared with 0·8 expected) and from other respiratory and cardiovascular diseases (22, compared with 7·6 expected). The average risk among men employed for twenty or more years has been of the order of ten times that experienced by the general population. This risk has become progressively less since the precautions introduced as a result of the Asbestos Industry Regulations, 1931, to prevent dust dissemination in the works became effective.

Gloyne[22] found in his series of 1205 specimens of lungs with dust diseases, including 121 of asbestosis, that the rates for primary neoplasm of the lung in male and female asbestos workers were 20% and 10% respectively. Barnett[23] found 31 deaths with carcinoma of lung in 235 deaths associated with asbestosis during the years 1924–46, with a distribution of 17·2% male and 8·4% female deaths. Adjustments for length of exposure to the dust and age at death would scarcely account for the discrepancy in the figures between the two sexes. The same discrepancy exists in the figures for all cases of carcinoma of the lung: Kennaway and Kennaway[24] showed that the rates of female to male deaths in England and Wales had changed from 1 : 1·9 in 1921 to 1 : 4·0 in 1945; between 1935 and 1945 the increase was 256% for males and 176% for females. If the causes of cancer in the lung are the same for both sexes (as in asbestosis and possibly in smoking), can the sex discrepancy be related to the baffling fact that, while the total "amount" of tumour in both sexes is approximately equal, 40% of the cancer deaths in females are from carcinoma of organs peculiar to the female,[25] leaving correspondingly smaller numbers for other sites? If so, what internal factor determines this organ selectivity?

Unlike asbestosis, the main causes of dust diseases in the lungs are not associated with an increase in carcinoma of the lungs; and Kennaway and Kennaway[26] showed that bronchial carcinoma is less common in coal-workers than in the general population. James[27] has confirmed this very neatly by comparing a series of South Wales coalminers with a series of non-miners in the same area, obtaining figures of 3·3% for the former and 5·4% for the latter; but he points out that the relatively low incidence of tumour in the miners may be partly due to dust disease causing death before the average cancer age. The dust diseases generally act on the connective tissues, and there is no satisfactory explanation of why the asbestos fibres should affect the epithelium as well.

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IMPROVED techniques of electro-encephalography (E.E.G.) have confirmed some earlier correlations of electrical with clinical activity, such as that of bilateral 3-per-second wave-and-spike patterns with petit mal; have led to the modification of some, such as that of square-topped waves and a sharp down peak with psychomotor epilepsy; and have cast renewed doubt on others, such as the identification of the cortical spike focus with the site of origin of an epileptic discharge.[28]

Gibbs and his colleagues[29,30] have described valuable information about the natural history of E.E.G. abnormalities which has important clinical implications. By following changes in E.E.G. patterns as infants and children develop, they have obtained a "longitudinal section" of electrical brain activity to supplement the brief "cross-sectional" view of isolated E.E.G. recordings. They point out that the immature brain tends to react to various possibly epileptogenic traumata with a generalised electrical abnormality. Moreover the pattern of reaction differs at different stages of maturation. In infancy "hypsarhythmia" (continuous slow-wave high-voltage discharge with diffuse spiking) is common;

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DMS

TOXIC GOITER DURING PREGNANCY

To the Editor:—*I should like information concerning any detrimental effect of propylthiouracil on the fetus when the medicament is used to treat toxic goiter during pregnancy.*

C. Lawrence Holt, M.D., Portland, Maine.

Answer.—When antithyroid drugs of any type have been used for long periods of time during the last half of pregnancy, a goiter is occasionally induced in the fetus. These goiters usually disappear spontaneously and, so far as is known, have never caused any difficulty or permanent disturbance in thyroid function. They are nevertheless undesirable; in the event that the mother's thyroid should enlarge during pregnancy serious consideration should be given to other forms of therapy, because when the mother's thyroid enlarges the fetus's is more apt to show the same reaction. Hypothyroidism should be watched for closely and prevented by simultaneous administration of antithyroid drugs and desiccated thyroid in the event that symptoms or signs of hypothyroidism develop. Small doses of iodine may also be used.

QUINIDINE AND PREGNANCY

To the Editor:—*A 28-year-old patient, para 1, gravida 3, suffers from sporadic attacks of paroxysmal tachycardia. She is completely relieved in one hour after taking 6 grains (about 0.4 gm.) of quinidine orally for one dose. The attack otherwise continues for as long as 15 hours and is refractory to all other forms of treatment that I know of. Has this drug any oxytocic effect on a three-month pregnancy? If so, what should be used in its place? When the patient tried the drug nothing happened to her pregnancy.*

Nerio W. Pioppi, M.D., Southbridge, Mass.

Answer.—Unless a person is overly sensitive to quinidine, the drug used in the dosage indicated for relief of paroxysmal tachycardia is not contraindicated in pregnancy. Since in this particular patient only one dose is necessary to relieve the tachycardia, there is no hazard in its use. Quinidine sulfate in the dosage mentioned has no oxytocic effect. It must be emphasized, however, that the drug should not be used in large amounts and repeated doses in pregnancy.

RESUSCITATION

To the Editor:—*Can you tell me if movement of the muscles would result if electroshock therapy, as used in psychiatric treatment, were applied to a corpse shortly after death? Might this have value for resuscitation?*

William H. Kupper, M.D., San Pedro, Calif.

Answer.—The skeletal muscles of the body usually retain their electrical excitability for a brief period after the heart has stopped beating. Persistent electrical excitability of the skeletal muscles would not necessarily indicate that the heart was still susceptible to resuscitation. Absence of electrical excitability of the skeletal muscles would indicate that any attempts at cardiac resuscitation would be fruitless.

ASBESTOSIS

To the Editor:—*A 50-year-old white man worked at covering pipe with asbestos insulation from 1940 to 1945. What would be the possibility of pulmonary fibrosis evident on roentgenograms in 1952 being due to asbestosis, when films had been normal for this in 1949?*

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Answer.—The cause of the 1952 pulmonary fibrosis in this case must be sought among other sources than the 1940-1945 occupation. Little evidence exists of progression of asbestosis after cessation of exposure to asbestos fibers. If exposure over the comparatively brief period of five or six years had been sufficient to produce pulmonary fibrosis, it would have had to be extremely severe, much more so than would be experienced by a laborer engaged in covering pipe with asbestos insulation. In the event that exposure over this period had been of such magnitude as to cause fibrosis, it would certainly have mani-

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