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Research on Health Effects of Asbestos

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ASBESTOS AS A CURIOUS MATERIAL was known several centuries B.C., especially for its ability to withstand flame. The physical and chemical properties of asbestos together with its fibrous structure made it a unique material with a wide range of potential industrial applications. It was not until the end of the last century, however, that it gained importance as an industrial resource. The study of the use of asbestos in a number of technological areas and its contribution to new products is the precursor of the special science of industrial mineral fiber technology. Asbestos is essential in today's industrial technology including national defense, aerospace, and civilian consumer use.

Asbestos is a general term applied to a group of fibrous crystalline hydrated silicate minerals. Although a number of different types of asbestos minerals exist, only four or five are of commercial importance. Each differs somewhat from the others in chemical composition, physical properties such as ability to withstand heat and chemical erosion, crystalline structure, fiber dimension, and degree of fiber harshness and brittleness.

The worldwide production of asbestos has greatly expanded since the turn of the century, the over-all consumption in this country leveling off for the period 1958 to 1963 at around 750,000 short tons annually. Of this tonnage, approximately 93% was chrysotile, 3.5% crocidolite, 2.5% amosite, and 1% anthophylite and tremolite.

Even though asbestos has been in industrial use for well over 50 years, much is unknown regarding its health effects and safe levels of exposure.

It has been known since the early nineteen hundred's that excessive exposure to asbestos gives rise to the disabling pulmonary disease "asbestosis." More recently, evidence has been developed that the incidence of respiratory tract and other malignancies in asbestos workers is excessive. A major problem in studying the health effects of asbestos is the long latent period of 20 or more years from initial exposure to the onset of disease. Also in the mid-nineteen thirties and earlier, there was little dust control and the workers were often exposed to massive levels of dust from asbestos and other associated materials in the manufacture of asbestos products. Thus, the causative agents of the resultant disease are essentially unknown. Included in these potential sources of causative agents, either alone or in combination, are asbestos fibers themselves, materials associated with the fibers in the ores such as trace minerals and polycyclic aromatic oils, materials added during processing such as metals, tars and pitches, and concomitant external exposures to tobacco smoke or other air pollutants.

A salient point is that in subsequent years when heavy dust exposures were reduced, disease also diminished. This definitely indicates that with sufficient knowledge of the agent(s) responsible for the disease, along with dose-response data, safe levels of exposure can be established.

Research to elucidate the importance of the asbestos minerals as hazards to health fall into two broad categories: *first*, studies to provide answers

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The recommendations in this report resulted from a meeting sponsored by the Occupational Health Program of the Public Health Service's National Center for Urban and Industrial Health, on December 7 and 8, 1966, under the Chairmanship of Murray C. Brown, M.D. Copies of this paper may be obtained from the Occupational Health Program, National Center for Urban and Industrial Health, USPHS, DHEW, Cincinnati, Ohio.

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to urgent questions involving public policy and control efforts; and *second,* long-term studies to provide more information as to the physical and chemical factors of fibrous materials as related to their interaction with animals and man so that safe working and living environments can be assured. Consider, for example, the program to evaluate reports of the presence, to some extent, of asbestos bodies in the lungs of a third or more of the American population.

Before public policy regarding the production and use of asbestos can be stated and implemented, we need answers to many questions: do these asbestos bodies truly represent responses to asbestos fibers, or are other fibers also involved? Where do these fibers come from, and what is their potential significance in terms of health? Is there an increasing incidence of mesothelial tumors in our population and is this in any way related to asbestos minerals? Do fibrous minerals play a major or minor role in the causation of lung cancer? Are certain forms of asbestos or other fibers more important in these relationships, and what co-factors are important?

These pressing questions cannot be definitively answered on the basis of present data. A strong supported long-term program is needed to provide the information regarding the pathogenesis of asbestosis and the other effects that appear associated with the inhalation of asbestos dust. More precise data on the physical and chemical characterization of the asbestos minerals which lead to their being inhaled and retained in the body, in their carrying with them other chemicals, in their migration, may open up unsuspected avenues of biological research.

Objectives

Research directed to answering the following questions is needed in order to safeguard the workers' health, yet permit the benefit of asbestos in today's industrial technology. The information gained will also have direct application in furthering the safe use of the many new synthetic fibers being introduced into industry as the result of the rapidly expanding science of industrial fiber technology.

1. What is the nature and pattern of disease in workers exposed to the different types of asbestos fibers and how do they relate to the magnitude and duration of exposure?

The answers to the above are basic to defining related health problems and setting up research on a rational basis for their solution. They should provide data evidencing etiologic factors involved and their interrelationship, the dose-response relationship of the agent(s) to the disease, the criteria for establishing safe levels of exposure, and the basis for establishing medical and environmental surveillance wherever asbestos is encountered and handled. It will also provide useful information for evaluating possible risks from inhaled fibers in those not occupationally exposed.

2. How are the diseases and other manifestations observed in workers exposed to asbestiform fibers characterized clinically and pathologically, and do they differ when exposure involves one type of asbestos or another?

Far more information is needed on the pathogenesis of asbestos and on other responses to asbestos fibers in man. This information should be based on careful serial studies and correlations of clinical, physiologic, radiographic, and histologic changes. Results of these studies would relate to the prevention of asbestos-related disease and would give useful information on the biologic response to other respirable fibers. The findings would supplement current criteria for diagnosis, prognosis, and management of disease, continued employability, fair adjudication of compensation claims, and effective rehabilitation. They would also provide information important in maintaining surveillanee programs for asbestos workers and in improving control measures.

3. What are the factors in the pathogenesis of the diseases associated with the inhalation of asbestos minerals and what are the primary etiologic factors involved? Although in many instances it is the predominant ingredient, generally and with only few exceptions, asbestos is formulated with other materials in the preparation of asbestos products. Even in the mining and milling of asbestos, recent studies have shown that these operations are associated with exposures to potentially injurious agents (such as trace minerals of nickel, cobalt, manganese, zirconium, and titanium), polycyclic aromatic compounds from some ores, and metals abraded from processing equipment due to the harshness of the fibers. These same injurious agents may be carried in degrees in the milled fiber and subsequently in increased degrees as processing of the fiber continues.

In the past, studies related resulting diseases to fiber exposure only. Thus, the etiologic agents resulting in the diseases observed in past studies are generally unknown. They may have been one or more of the fibrous forms of asbestos, trace minerals in the ore, polycyclic aromatic com-

pounds associated with the ore, additives in processing (such as metals, coal tars and pitch), smoking, other air pollutants, or some combination of these factors. A fresh look into both the clinical and animal research of the past and a new approach to current research to further define related agents in the light of our more recent information is indicated.

4. What chemical and physical characteristics of asbestos fibers relate to their respirability, mobility, clearance, and immobilization in the body and how do the types of asbestos differ in these respects?

Most of the research relating to the respirability and retention, mobility, and clearance of materials from the lungs has been done on particulates which have random movements since they are generally spherical. Fibers, however, having a much greater length-to-diameter ratio, have direction and orientation in their movement and many behave quite differently than particulates. Fibers that are harsh and rigid may have tissue penetration potential. Through this mechanism they may, as carriers, transport toxic agents to other tissue sites and, thus, have a causal relationship heretofore not evident. The behavior of fibers in lungs and other tissues must be understood and related to the respective physical and chemical characteristics of fibers so that patterns of response can be described and predicted.

5. How can asbestos fibers *in vivo* and *in vitro* be differentiated as to type and how can they be distinguished from non-asbestos fibers?

Respirable fibers are ubiquitous. They may be either natural or synthetic and from animal, vegetable, or mineral origin. Modern technology is introducing increasing numbers of synthetic fibers into industrial use.

It has been known for some time that asbestos fibers in the lungs give rise to asbestos bodies. Recently, similar-type bodies have been found in the lungs of a large percentage of individuals coming to autopsy in general urban hospitals. This finding, even though the number found in any individual may be relatively small, has given concern as to its significance as well as to the identification of the causative fibers and their environmental source. Methods must be developed for isolating, identifying, and quantitating fibrous materials in the lungs and other tissues and in the associated ferruginous bodies.

6. What levels of exposure to the etiologic agents associated with asbestos-related diseases can be regarded as safe?

Defining safe exposure levels is the prime objective of the research. When safe levels are determined, necessary measures can be taken to keep exposures within the recommended limits.

7. How can exposures be prevented?

The aerodynamic properties of fibers will differ depending upon the specific physical and chemical properties of the fibers. Their behavior in air is much less understood than that of particulates spherical in shape. Information on the behavior of fibers is needed for the design of ventilation control equipment and the design of process equipment to minimize the dispersion of fibers into the air.

8. What environmental and medical surveillance procedures are recommended where asbestos fibers are encountered or handled?

Surveillance of the working population at risk to detect early changes before damages to health have occurred is an essential part of any occupational health program in industry. Environmental monitoring of exposure levels as well as continuing information on the health status of the working force is an important segment of a surveillance program. The continued development and expanded application of surveillance procedures will assure the use of asbestos with minimum risk to health.

Projects

The answers to the above questions can come only from widely-based interrelated research directed to the health response of the worker in his specific environment. The research, although directed specifically to the asbestos worker and his environment, should result in findings applicable in the understanding of a wide range of allied occupational diseases, especially those relating to fiber exposures. This research on health effects of asbestos should encompass, as a minimum, projects as outlined below.

1. *Epidemiology:* (a) Longitudinal studies of groups of workers in different employment categories with contrasting exposures to different types of asbestos fibers by magnitude and duration, singly and in combination with other associated materials capable of producing injury or eliciting a synergistic response to establish interrelationships between health patterns of the workers and environmental exposures.

(b) Studies of the relation between exposure to asbestos minerals and clinical symptoms, pulmo-

nary changes demonstrable by pulmonary function and work tests, and chest roentgenographic shadows suggestive of asbestosis.

(c) Studies of records of morbidity and morality patterns and trends in groups of workers with contrasting exposures to asbestos and other associated materials; also a search for common genetic or hereditary patterns relating to the disease.

(d) Analysis of selected postmortem tissues of workers with work histories in industries having contrasting exposures to different types of asbestos and other associated materials during and after periods of massive dust exposure. Also, studies must be conducted on workers in these categories who died from an exposure-associated disease as well as those who showed no obvious indication of associated disease.

(e) Sputum study of asbestos workers to correlate and quantitate magnitude and duration of exposures with the occurrence of asbestos bodies.

(f) Study of contrasting population groups with respect to geographical areas, air pollution, employment patterns, etc., for presence of pulmonary ferruginous bodies ("asbestos bodies") to determine if these correlate with disease patterns observed.

(g) Study of ecological factors that may have a bearing on the disease or be interrelated with causative agents, including community exposures.

2. *Clinical and human pathology:* **(a)** Comprehensive study of selected individuals with different patterns and progression of disease with respect to: (1) impaired pulmonary vascular circulation, both by tests of function and by angiography; (2) pleural thickening in relation to reduced function, physical signs, altered roentgenographic patterns, and pleural tumors; (3) impact of viral infections on persons with asbestos exposures; (4) sites of pulmonary fiber depositions and injury; (5) immunochemical changes; (6) the nature of the emphysema so often associated with asbestosis; (7) the role of chronic bronchitis and other causes of pulmonary obstructive disease in altering the prognosis of asbestosis; (8) correlation between roentgenographic evidence of disease and the capacity of the cardiopulmonary system to fulfill its required function.

(b) Establishment of a mesothelioma case registry, including uniform criteria for diagnosis and epidemiologic follow-up of reported cases.

(c) Development of a uniform classification for reading chest roentgenograms of persons exposed to asbestos and other fibers; correlation of roentgenologic patterns with clinical, physiologic, and histologic changes.

(d) Study to detect individuals who may be hypersusceptible, either on an acquired or a genetic basis.

3. *Animal experimentation and tissue culture:* **(a)** Determination of respirability, sites of retention, mobility, penetration, and migration to other tissue, and clearance of pulmonary fibers in relation to their chemical and physical properties.

(b) Study of mechanism of formation and meaning of ferruginous bodies arising from respired pulmonary fibers from different sources.

(c) Study of the chemical and physical characteristics of various types of asbestos fibers, singly and in combination with other associated injurious materials and their capacity to give rise to different forms of cancer; evaluate additive, enhancing, or inhibiting action of fibers and carcinogens from cigarette smoke and other sources.

(d) Study of potential of pulmonary fibers as carriers of carcinogenic and other agents from lungs to other tissue sites.

(e) Development of dose-response data as an aid to developing safe exposure levels.

(f) Investigation into the effects of asbestos and other fibers, and of associated injurious materials, on cellular physiology, enzyme suppression, and genetic pattern.

(g) Study of immunochemical changes, biochemical tests, etc., that may further characterize the exposure-response pattern and serve as predictive tests.

4. *Chemical and physical characteristics:* **(a)** Study of the positive identification of individual fibers, both *in vivo* and *in vitro;* the nature and quantity of other contaminants such as minerals, metals, and oils associated with the fibers including mechanism of association.

(b) Study of solubility of fibers and associated contaminants in tissue fluids particularly as related to blood and urine levels of associated materials.

(c) Study of sources and identification of respirable fibers responsible for ferruginous bodies seen in lungs and general population of non-asbestos workers.

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