Medical Research Division

Esso Research and Engineering Company

SUMMARY OF

THE

CONFERENCE ON "BIOLOGICAL EFFECTS OF ASBESTOS"

October 19-20-21, 1964

On October 19, 20, and 21, 1964, the Section of Biological and Medical Sciences of The New York Academy of Sciences sponsored a three-day Conference on "Biological Effects of Asbestos" in New York City.

The first two papers in this Conference dealt with the occurrence in chemistry of asbestos. At the moment the total production of asbestos amounts to about three million tons per year, having increased markedly since World War II. Of this, about 95% is chrysotile, 3.5% is crocidolite, and 2.5% is amosite, with very small quantities of the three remaining types, namely tremolite, actinolite, and anthophyllite. Of the total asbestos mined, about 85% comes from Canada, Russia, South Africa, and Southern Rhodesia, with 11 other countries producing the remaining 15%. The greatest use of asbestos is in the manufacture of asbestos cement products which constitutes over 1,200,000 tons per year. The characteristic of asbestos is that it is a silicate, frequently an iron-containing silicate, which can be broken down into long fibers and is very resistant to corrosive actions and heat. The individual fibers, particularly of chrysotile, or white asbestos, are tubular in nature, having a hollow center. The crystal structure of the various types of asbestos vary somewhat, and the second most important asbestos is crocidolite, or blue asbestos.

The following four papers discussed the detection of asbestos dust in the tissues of animals, including ways of incinerating the tissues in order to bring out the asbestos fibers. In the paper by Skidmore and Wagner on "Asbestos Dust Deposition and Retention in Animals," the animals were exposed to 25 to 30 mg/m^3 of the various asbestos dusts and then killed on the first, the twenty-ninth, and the fifty-ninth day after exposure. The exposure period lasted for six weeks, seven hours a day, five days a week.

The next paper by J. Mills, of the University of Reading, England, discussed this experimental asbestosis with four types of fibers. The animals used in these experiments were guinea pigs, and they were exposed to chrysotile, crocidolite, amosite, and anthophyllite. The duration of exposure varied from 3 to 78 days, and the animals were killed at intervals from 3 to 420 days after the first exposure to dust. The same long-term results were obtained whether the total exposure was 3 days or 78 days. The dusts spread widely throughout the lungs, and it was pointed out by the author that it is extremely difficult to control the spread of asbestos dust throughout the laboratory since asbestos fibers were found in the control group not specifically exposed to asbestos. Extensive fibrotic changes in the guinea pig lung were found with all four types of dust, and it is believed that the guinea pig lung is extremely sensitive to these fibrotic changes.

The next paper described "Electron-Microscope Studies of Asbestosis in Man and Animals" and was given by J. G. M. Davis of the University of Cambridge, England. He demonstrated that the coating material around asbestos fibers which go to make up the asbestos bodies consists of a fine granular material that is probably ferritin. Actually this material is laid down in two layers over the asbestos fiber.

In the paper by Pernis, Vigliani, and Selikoff entitled "Rheumatoid Factor in Serum of Individuals Exposed to Asbestos," they found that 20% of patients with asbestosis will have an increase in the titer of the rheumatoid factor. This is a higher-than-normal frequency. They have found that the rheumatoid factor is present in many diseases and is not specific to asbestosis. They believe that the fibrosis of the lungs is responsible for the increase in the rheumatoid factor and not the dust itself. In the second paper by Vigliani and Pernis entitled "Observations on the Pathogenesis of Asbestosis," they studied the effect of asbestos fibers on cultures of macrophages and fibroblasts. They found that guinea pig macrophages in vitro are not killed by asbestos dust, such as occurs with silica dust. Further, they found that fibroblasts in vitro will pick up asbestos easily and increase the production of collagen to about three times normal. Such does not occur when cultures of fibroblasts are incubated with silica dusts.

The next several papers dealt with the occurrence of asbestosis in various areas of the world. The first report was from Great Britain and essentially brought up to date the inspector factory's report on asbestosis. The paper by Selikoff, Churg, and Hammond from The Mount Sinai Hospital in New York entitled "Asbestosis Among Insulation Workers in the United States" was conducted among members of an insulators union in the New York-New Jersey area. Of 1,117 of these union members who were examined, constituting about 90% of all the union members, it was found that the incidence of asbestosis increased with the duration of exposure to asbestos. Thus, 10.4% of men with 0-9 years of service had grade 1 asbestosis; 44.1% of men with 10-19 years of exposure had both grade 1 and grade 2 asbestosis; 72.8% of men with 20-29 years of exposure had grades 1, 2, and 3 asbestosis; 87.1% of men with 30-39 years of exposure had grades 1, 2, and 3 asbestosis; and 94.2% of men with 40 or more years of exposure had all 3 grades of asbestosis. As would be anticipated, the severity of the disease increased with the number of years of exposure. Among 307 deaths which occurred in the period January 1, 1943, to August 31, 1964, cancer in the lung occurred in 53, mesotheliomas in 9, carcinoma of the gastrointestinal tract in 35, and other neoplasms in 27, with 17 deaths being due to asbestosis, apparently without carcinoma. One hundred sixty-six of the deaths were due to all other causes.

A paper by J. G. Thomson entitled "Asbestos and the Urban Dweller" suggests that the families of asbestos workers may develop asbestosis as the result of brushing the fibers off their clothing and also that those who live in the vicinity of an asbestos factory, even though not working in the factory, may develop asbestosis and/or tumors of the lung. It would appear, therefore, that very minor exposures to asbestos may result in pulmonary changes but that these do not occur until long after the initial exposure, perhaps in the vicinity of 40 years.

The next series of papers dealt with methods for collecting and measuring asbestos dust in the atmosphere. Although the details of the methods used will be of value, it will probably be necessary to await the publication of the proceedings of this meeting in order to get the full details of each of the methods that have been used.

The paper by E. L. Schall of the New Jersey State Department of Health on the "Present Threshold Limit Value in the U.S.A for Asbestos Dust" concluded that the present level of 5 million particles per cubic foot seems to represent an adequate level.

In the paper by D. W. Hills of Turner Brothers Asbestos-Co., Ltd., in England on the "Economics of Dust Control," he demonstrated various types of ventilation equipment used in the asbestos processing industry and indicated that in his own plant the cost of such control equipment was about $1,500,000 and the annual operating cost $250,000.

The next several papers discuss the radiological and clinical diagnosis of asbestosis. Perhaps of greatest importance was the paper by I. J. Selikoff of The Mount Sinai Hospital who indicated that plaques of pleural calcification seen on roentgenograms of the lungs may be evidence of asbestosis exposures. These plaques have been missed in the past in a great number of these men, but now when you go back over the X-rays it is possible to pick out these calcified plaques of the pleura. They are convinced that these are practically diagnostic signs of asbestos exposure. As with asbestosis, the percentage of people who demonstrate such calcified plaques of the pleura increases with the duration of their exposure and this, of course, is taken as additional evidence that they are related to asbestos exposures. Presumably the minimum exposure for the development of pleural calcifications has been found to be 12 years, and the usual exposure is 20 or more years.

This series of radiological-pathological papers was followed by three papers dealing with lung function studies in people exposed to asbestos and in the presence of asbestosis.

There next followed a series of papers on the carcinogenicity of asbestos fibers and their products in experimental animals. J. S. Harington and F. J. C. Roe of the Royal Cancer Hospital, London, England, gave a paper on "Studies of Carcinogenesis of Asbestos Fibers and Their Natural Oils." They pointed out that asbestos does contain a great many other materials which may be of significance. For instance, chrysotile contains 5,000 ppm of nickel and 1,000 ppm of chromium. It could well be that these metal impurities in asbestos are important in the production of pulmonary tumors, since it is known that both nickel and chromium are pulmonary carcinogens. Furthermore, it is possible to extract from asbestos fibers a hydrocarbon oil using various solvents. The amount of such oils vary from 0.03 to 1%, and at the present time these oils are being tested for their carcinogenicity by being painted on the skins of mice. Apparently crocidolite contains more oil than amosite although there may be a considerable amount of variation in different samples of the same type of asbestos.

Next followed a series of three papers by Dr. W. E. Smith and his associates of Fairleigh Dickinson University in Madison, New Jersey. This is the same Dr. Smith that used to be at New York University and did the work on our high boiling carcinogenic oils. The first paper discussed the preparation of asbestos fibers for placing in the lung. The second paper by Dr. Smith

himself discussed the results from intrapleural injections of these various asbestos fibers with extensive granulomatous and fibrous pleural adhesions resulting. Several of the hamsters which had been injected intrapleurally developed tumors, and these tumors were transplanted serially into other animals, suggesting therefore that they are malignant. In addition to hamsters, rats were also given biweekly intratracheal injections of four types of asbestos, but no tumors have yet been produced although pneumonia and fibrosis have resulted. In the third paper by this group, asbestos was given with benzo(a)pyrene to see if the asbestos served as a cocarcinogen rather than as a carcinogen. Briefly, in 3 of 5 hamsters treated with benzo(a)pyrene alone tumors developed, whereas 15 tumors were found in 7 of 7 hamsters treated with benzo(a)pyrene plus chrysotile. There were no tumors in 6 hamsters treated with chrysotile alone, in 8 treated with a suspending medium (Tween 60), or in 10 untreated controls. It would appear from this work that perhaps the asbestos is acting more as a cocarcinogen rather than as a carcinogen in these experimental animals. Additional work will be needed in order to clarify this point.

Dr. Buchanan of the Ministry of Labor of London gave the next paper dealing with "Asbestos and Primary Intrathoracic Carcinoma." Again, this was somewhat of a summary of the death certificates of asbestos workers in Great Britain. A Dr. Peacock, prior to this paper, also gave an unscheduled paper dealing with tumors in fowl as a result of the injection of asbestos fibers into the air sac of the fowl. Asbestos was injected into chickens and left for approximately four years, with the production of tumors following such injections.

The next paper by E. C. Hammond, I. J. Selikoff, and J. Churg, of The Mount Sinai Hospital, dealt with "Neoplasia Among Insulation Workers in the United States With Special Reference to Intra-Abdominal Neoplasia." The point made in this paper was that the incidence of mesothelioma of the peritoneum and also G.I. cancers including stomach, colon, and rectum, were higher than would have been anticipated in the general population. They are not prepared to say that these G.I. tumors are the result of asbestos exposure but feel that this needs further investigation. These epidemiological studies, which constituted a series of five papers, suggest that there is a relationship between asbestos exposure and various types of cancer, particularly pleural mesotheliomas. It is interesting that in mesothelioma patients, either the pleura or the peritoneum, asbestosis is not a necessary requirement before the production of tumors, even though asbestos fibers can be demonstrated in the lungs of such patients.

An interesting paper was given by J. C. Wagner of the Medical Research Council Pneumoconiosis Research Unit entitled "Epidemiology of Diffuse Mesothelial Tumours: Evidence of An Association From Studies in South Africa and the United Kingdom." In these studies they found that the average latent period from the first exposure to the production of mesothelioma was 44 years. Of 120 tumors (mesothelioma) that have been observed in South Africa, 110 occurred in the crocidolite mine area and others in manufacturing areas, but no such tumors have occurred in the amosite or chrysotile mine areas. Again it was emphasized that mesotheliomas can occur without asbestosis being present. The five types of industry that this individual indicated ought to be studied for

possible asbestosis and/or pulmonary cancer and mesotheliomas are (1) the asbestos industry itself, (2) the shipbuilding industry, (3) railway workshops, (4) insulators, and (5) construction workers. There is a suggestion from some of these studies that the severely exposed asbestos worker, that is, the man actually working with asbestos, may develop asbestosis and die from this before he has an opportunity to develop a mesothelial tumor, whereas the foreman whose exposure is presumably quite light does not develop asbestosis but may in subsequent years go on to develop mesotheliomas.

Of 30 cases of mesothelioma studied by Churg, Moolten, and Rosen in a paper entitled "Histological Characteristics of Mesothelioma Associated With Asbestos," 19 had a known exposure to asbestos, whereas 11 had no known exposure or the exposure history was not known. Yet in a fair number of these people asbestos fibers were found in the lungs when carefully examined.

Ian Webster of the Pneumoconiosis Research Unit, Johannesburg, South Africa, gave a paper on "Mesothelial Tumors in South Africa: Pathology and Experimental Pathology." Of 125 mesotheliomas that they have observed, 117 have been pleural and 8 have been peritoneal. Dr. Webster emphasized that other factors have not yet been excluded in the production of these mesothelial tumors. In a paper by Dr. Hourihane of the London Hospital Medical School entitled "A Biopsy Series of Mesotheliomata and Attempts to Identify Asbestos Within Some of the Tumours," he discussed some 63 pleural and 11 peritoneal mesotheliomas. Of 30 cases that were carefully examined for the presence of asbestos fibers or asbestos bodies, 23 showed the presence of these.

In the course of these discussions a doctor from some town in Texas, whose name I did not get but presumably whose discussion will appear in the proceedings of the Conference, indicated that he has seen 10 cases of pulmonary cancer in asbestos workers, all of whom have been employed in his local oil refining industry. He gave a clinical discussion of these cases.

Dr. Kenneth W. Smith of the Johns-Manville Corporation, Manville, New Jersey, gave a paper on "Trends in the Health of the Asbestos Worker." Essentially his paper was defensive and apparently trying to protect the asbestos industry in the United States from the accusation of having produced pulmonary or mesothelial tumors. Basically I thought his paper was very poor, did not contribute very much to the discussion, and was inserted essentially to try to confuse people, although I am sure it failed in this objective.

The three concluding papers attempted to summarize the general tenor of the discussion. The first was given by J. C. Wagner of the Pneumoconiosis Research Unit of England and emphasized the production of asbestosis in asbestos workers and the experimental work that is now being done in an attempt to duplicate this disease in experimental animals. The paper by J. C. Gilson of the Medical Research Council Pneumoconiosis Research Unit, Wales, entitled "Problems and Perspectives: The Changing Hazards of Exposure to Asbestos Dust," was perhaps a very neat summary of the whole conference held in New York. He emphasized that there has been approximately a 100-fold reduction of dust in

the asbestos industry, but emphasized that this has occurred only in some segments of the industry, namely the larger companies who are in a position to expend large sums of money for dust control. In some industries which are not in a position to spend the amount of money required, there has been essentially very little, if any, reduction in the dust concentrations in the atmosphere. The importance of this is, of course, that if we are to eliminate asbestosis and/or pulmonary tumors and mesotheliomas in asbestos workers, it will be necessary to institute controls in the total industry rather than in just segments of the industry. As evidence of the effect of this dust reduction, he indicated that there has been a 50-fold reduction in the incidence of asbestosis. Finally he made a very important summary statement of the meeting which went as follows:

> "The striking feature of this conference is the new evidence showing that not only is there a high risk of bronchial carcinoma in those with asbestosis but that other types of tumour occur in the lungs and elsewhere in those exposed to the dust, and that these tumours develop in the absence of asbestosis in the lungs and sometimes after a small exposure but always with a long or very long delay. The evidence in man indicates that the type of fibre to which the individual is exposed - a long neglected aspect of this whole problem - is of great importance in the development of these tumours."

He emphasized that from the practical standpoint it may be very important to settle this last question as to whether or not all types of asbestos fibers can produce lung tumors and/or mesotheliomas. For instance, if it is found that certain asbestos fibers will not do this, then there may be sufficient justification to limit the use of those asbestos fibers which do produce these pulmonary tumors and asbestosis.

All in all, I would say that this three-day conference clearly suggests that exposure to asbestos is a most serious situation, and I would certainly agree with Dr. Gilson when he says that it is very important to "eliminate all unnecessary exposure to asbestos dust in the future." Until the evidence is quite clear and everyone agrees that additional work needs to be done, it would seem important for us in the petroleum industry to do epidemiological studies on the insulators who work in the petroleum industry and, in addition, to institute additional dust control measures in an attempt to fulfill the suggestion by Dr. Gilson that all unnecessary exposure to asbestos dust be eliminated. Certainly this appears to be a problem that cannot be taken lightly, and certainly it would seem that very careful control of exposures to asbestos throughout refinery operations should be instituted. This would include not only the insulators themselves but also those who are tearing down old units where insulation may be present around pipes and asbestos dust exposures may develop.

Again, in my mind there is no question, nor was there at this Conference, about the elimination of asbestos from industry. The approach will

have to be that of control of the dust exposures by whatever means seem necessary in order to eliminate the asbestosis, the bronchial carcinomas, and the mesotheliomas which seem to be related to asbestos exposures. The evidence which is accumulating indicates that this is a far more serious problem then we had ever thought in the past, and therefore control measures are going to have to be more fully developed than they were in the past.

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10/29/64