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cc: C. A. D'Alonzo, M.D.
J. W. Clayton, Jr.

November 2, 1964

MEMORANDUM

TO: J. A. Zapp, Jr.

FROM: G. J. Stopps

TRIP REPORT

Conference on Biological Effects of Asbestos
held Monday, Tuesday and Wednesday, October 19, 20 and 21, 1964
under the auspices of the New York Academy of Sciences,
the Section of Biological and Medical Sciences

Although this was a well-conducted and well-attended meeting there being some three to four hundred persons present at almost every session, there was also a feeling that there were several ghosts present at the banquet of information presented. No doubt this feeling largely stemmed from the fact that out of some 53 papers given, only two of them were given by people connected with the asbestos industry in the United States and Canada, whereas there were seven given by representatives of the asbestos industry in Britain and a further three or four papers were given by persons connected with the asbestos industry in South Africa.

From the point of view of the Du Pont Company as a whole, the main interest of the meetings was in drawing attention to the fact that asbestosis and complications of asbestosis have now been found in persons who would not in the ordinary way come to mind as being exposed to asbestos; that is to say, they do not work in asbestos mines, asbestos mills, or asbestos textile factories. Underlining this relatively wide exposure of persons to asbestos was the work of I. J. Selikoff, from the Mt. Sinai Hospital, New York, who has been studying the workers in the insulation trades in New York City. The investigation reported concerned 1522 members of the International Association of Heat and Frost Insulators and Asbestos Workers in the New York-New Jersey metropolitan area. The study included every individual who was a member of this union on December 31, 1942, or who joined by December 31, 1962. Two hundred sixty-four men were dead on January 1, 1963, and 43 have died since. Each death was studied. One thousand two hundred fifty-eight men were still alive and 1117 of these were examined. This represents 89.9% of the population at risk. Clinical, radiological and pulmonary function examinations were also made of these men. X-ray ranking of the degree of asbestosis present in four grades ranging from 0 to 3 indicated that in those having 0 to 9 years of exposure to asbestos, 89.6% had no asbestosis present, while 36% had grade 1. Whereas with 40 or more years of exposure, 94.2% had grade 2 asbestosis and only 5.8% had none. In an analysis of 307 consecutive

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deaths among asbestos insulation workers, 53 were found to have carcinomas of the lung, 9 had mesotheliomas of the pleura, 35 had carcinomas of the gastrointestinal tract, and 27 had neoplasms at other sites; 17 of them had asbestosis confirmed at autopsy. The conclusion of this paper was that pulmonary asbestosis was a significant risk of insulation workers in the United States; and it will be noted from the above figures that this paper touched upon the point developed later by other workers at the Mt. Sinai Hospital that the risk of carcinoma, either of the respiratory tract or of the gastrointestinal tract, appears to be significantly greater amongst the insulation workers than amongst the general population.

At a later session E. C. Hammond of the Mt. Sinai Hospital group further underlined the unusual occurrence of carcinomata amongst the insulation workers. First of all he noted that in a prospective study of 255 consecutive deaths amongst this group of insulation workers carried out over the years 1943-1962 that the total number of deaths were increased (observed 255, expected 204) as were deaths caused by cancer of lung and pleura (observed 45, expected 7), and stomach and colon (observed 29, expected 10). Dr. Hammond then updated his information to include a total of 307 consecutive deaths from January 1, 1943, to August 30, 1964. This updating of his statistics did not materially affect the standings but did serve to underline the fact that deaths due to intra-abdominal neoplasms were also greatly increased over what might have been expected if the death rates of the general population had prevailed. Dr. Hammond pointed out that for a variety of reasons the accuracy of diagnoses of gastrointestinal tract neoplasms is often insecure. In two-fifths of the 49 such deaths, analysis of all of the available data showed the diagnosis to be presumptive only. This was especially true of stomach cancer (8 out of 13) and generalized abdominal cancer (6 of 7). Therefore it is possible that peritoneal mesothelioma may be even more common than the 5 out of 307 deaths recorded. In addition to the neoplasia amongst the recorded deaths, there were three men alive with known neoplasms (1 lung cancer, 1 pleural, and 1 peritoneal mesothelioma), as well as one apparently cured of tongue cancer, one of cancer of the colon, and three following successful resection of localized lung cancer found in this survey. In questions at the end of this paper, Dr. Hammond brought out that the group of workers had presumably not been more intensively studied from the pathological point of view than any other similar group of workers in another industry since until the publication of the results there had not been any particular cause for concern that the asbestos insulation workers were showing an abnormal incidence of neoplasia.

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A report from Turner Brothers Asbestos Company, Ltd., Rochdale, England, and presented by Dr. J. F. Knox, showed a somewhat more optimistic story when suitable dust prevention regulations were introduced and enforced in the asbestos industry. In a mortality study of workers in an asbestos factory carried out prior to the enforcement of the British Asbestos Industry Regulations excess mortality amongst workers employed for 20 years and upwards was observed. Lung cancer in association with asbestosis was responsible for a considerable proportion of this excess. A study of a group of workers from the same factory exposed since the regulations went into effect shows a reduction in mortality rate without an excess of lung cancer. Dr. Hammond had pointed out in his paper that the extreme rarity of pleural mesothelioma in the general population meant the finding of even a very few cases in a particular study in industry was highly significant.

Dr. P. C. Elmes of Belfast, Ireland, tackled the problem of mesothelioma from another point of view. He had studied 42 cases of pleural mesothelioma found in his department in Belfast over the past 14 years; the population at risk being about three-quarters of a million people. A positive history of exposure to asbestos at work was obtained in 32 of the cases compared with only 9 of 42 matched controls. Asbestos bodies were found in the lungs of 88% of patients with mesothelioma of the pleura, 20% of patients with carcinoma of the bronchus and 20.5% of patients dying of non-malignant disease. The frequency of finding of asbestos bodies in the lung is higher (27%) in men dying of non-malignant disease between 60 and 69 years of age who went into industry between 1905 and 1915 than in the 50 to 59 age group who started work between 1915 and 1925. Between 1906 and 1923 over 1000 tons a year of boiler composition were imported into Belfast compared with 600 tons a year at other times. This boiler composition was an insulating material containing a considerable proportion of asbestos fiber. Dr. Elmes pointed out that the latent period for the development of pleural malignancy after exposure may be up to forty years so that increasing numbers of cases arising from exposure can be expected for many years to come.

Dr. Wagner, of the M.R.C. Pneumoconiosis Research Unit, Glamorgan, Wales, British Isles, noted that an association between asbestos and pulmonary malignancy was now generally accepted. More recent investigation had shown that there was an increased incidence of pleural and peritoneal mesotheliomas occurring in people occupationally or environmentally exposed to asbestos dust. In some of these cases the exposure has been extremely slight and not sufficient to produce the histological features of asbestosis. The only pathological evidence of exposure has been the presence of asbestos bodies or fibers in the air spaces. In South Africa more than 100 cases of this tumor have been confirmed histologically.

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Nearly all of these cases have been confined to one asbestos mining area. The majority of these people were not employed in the asbestos manufacturing industry. Chemical investigations have shown that oils containing carcinogenic hydrocarbons are present naturally in this particular type of asbestos.

Another study taking much the same approach as that reported by Dr. Elmes of Belfast was reported by Muriel Newhouse of the London School of Hygiene and Tropical Medicine. Dr. Newhouse reported on a series of patients attending a large hospital in the east end of London. Dr. Newhouse's patients were divided into two groups; the first consisted of 83 patients in whom the diagnosis of mesothelioma had been confirmed at autopsy or by biopsy. In all but seven the past occupational and domestic histories were obtained. In 21 patients the tumor was peritoneal in origin and in 62 it was pleural. The earliest recorded death was 1917 but only ten of the series died before 1950; 55% of the males and 42% of the females died under the age of 55. The interval between the first exposure and development of terminal illness ranged between 16 and 55 years, the mean was 37. The second group consisted of 76 patients at the same hospital, matched by sex and date of birth with those traced in the first series; 52.6% of those suffering from mesothelioma had been exposed to asbestos as compared to 11.8% of the control group. Three main types of exposure were recognized: work in factories manufacturing asbestos textiles, insulating materials and other products, employment as laggers or insulators, and exposure to dust brought home by relatives working with asbestos. Eighteen of those employed in factory work or whose relatives were working with asbestos were employed in one factory. This factory opened in 1913 and was until recent years a heavy user of crocidolite. All those whose records could be traced worked with this type of asbestos. Amongst the 36 patients with mesotheliomata with no positive occupational history and no relatives living at home working with asbestos, there were 11 who lived within half a mile of an asbestos factory. Five of the control series also lived in the same area. The difference in the proportion of patients in the two series was statistically significant.

Dr. Ian Webster, of the Pneumoconiosis Research Unit, Johannesburg, South Africa, pointed out in his paper that although animal experiments have succeeded in showing the growth of a mesothelioma-like tumor in animals in which the asbestos was inoculated directly into the pleura, it had not been possible to produce carcinomata by exposing the animals to an asbestos dust cloud.

A further study of pleural mesothelial tumors from autopsy records was given by W. Glyn Owen, of Liverpool, England. Seventeen cases were selected as good examples of diffuse mesotheliomas. Sixteen of these were pleural and one was peritoneal. Evidence of asbestos exposure was obtained in 14 (82%) of the 17 mesothelioma

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cases. None of a similar number of subjects with cancers of other sites were known to have handled asbestos. Of those giving an occupational history of asbestos exposure, five were laggers employed by firms of insulation engineers and two were boiler makers (shipbuilding), two patients were employed by sackware manufacturers and had handled old sacks which had contained asbestos. Only two of the 17 patients had worked in asbestos factories, and one patient gave a history of close environmental exposure having worked in the offices of concrete manufacturers using asbestos cement.

Dr. William D. Buchanan, Ministry of Labour, London, pointed out that earlier studies of the British Vital Statistics records indicated an apparent association between the presence of asbestosis and the finding of a thoracic tumor; although such an association had been postulated some years before 1947, it was believed that the study reported in that year was the first occasion when these findings had been related to a sizable group. The proportions so affected appear to be increasing in more recent studies. Up to the end of 1963, 584 death certificates recording the presence of asbestosis have been obtained and annual totals of such certificates were currently increasing. The proportion also recording a thoracic tumor has also in both sexes continued to increase disproportionately to the total number so that currently over 50% of the males dying with asbestosis present have also a neoplasm. Even when viewed against the steadily rising incidence of lung cancer in the population as a whole, Dr. Buchanan felt that there was little doubt that this increase was a real one.

Dr. Bader presented an interesting series of 17 cases of employees actively working in an asbestos factory ten years ago at which time the plant in which the men were employed discontinued operation. The men have been followed since that time with serial clinical, radiological and pulmonary function investigations. During the baseline studies, pulmonary function examinations, when abnormal, revealed the classic findings of the alveolar capillary block syndrome, uniform decrease in lung volumes, well-preserved maximum breathing capacity, decreased arterial oxygen saturation (especially on exercise), normal pCO_2 values, and decreased diffusing capacity. Hyperventilation at rest and exercise occurred in more than half the cases, and dead space ventilation and alveolar ventilation were increased. The most sensitive index of impaired function was arterial oxygen saturation. Slight reduction at rest was found in six, and reduction below 92% was found in half of the workmen on exercise. The post-employment serial evaluations were made in terms of x-ray progression, development or worsening of dyspnea on exertion and further measurements of pulmonary function. Follow-up observations were limited by complications of the disease being studied. Of the 17 men studied ten years ago, 8 men are now dead; 2 of lung cancer, 1 of pleural mesothelioma, 2 of gastric carcinoma, and 2 of pulmonary asbestosis (core pulmonale),

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and 1 of myocardial infarction. Nine of the original workmen are still alive, one following the resection of a lung or lung cancer.

Two papers were presented by workers from Britain discussing the value of routine lung function studies. In the first, Ross Hunt, of British Belting and Asbestos, Ltd., Yorkshire, England, gave the results of routine lung function studies on 813 employees in an asbestos processing factory. Routine work in this field of lung function was started in July 1960 in an asbestos textile plant in the north of England. The aim was to create a set of normal figures for lung compartment values, gas transfer factor coefficients, 90% mixing indices, ventilation on exercise, and forced breathing capacities. The subjects used in these tests were volunteers of both sexes in varying age and stature groups from departments other than those processing asbestos. These results were then analysed statistically and the regression formulae obtained applied to the results of men and women working in those occupations exposed to asbestos. Pulmonary function tests were also used as a screen to prevent people with lung impairment from taking up work in departments where asbestos dust was prevalent. Some difficulties were encountered in the beginning both in subject response and sampling technique. But these were overcome and this paper deals in the main with the technique and results obtained over the past three years. The evidence points to a significant decrease in gas transfer and vital capacity before any radiological or clinical signs are evident.

The other paper given by M. L. Thomson and W. J. Smither, from the London School of Hygiene and Tropical Medicine and from Cape Insulation and Asbestos Products, Ltd., London, England, indicated that inspiratory capacity and vital capacity were the best discriminates of asbestosis amongst the many pulmonary function tests used.

It would appear from the concensus at this meeting that the risk of persons not normally thought of as engaged in work with asbestos, and certainly not thought of as being in the asbestos industry, is greater than was originally thought. This fact should be borne in mind and embraces not only the person's occupation but also his hobbies - for instance, a do-it-yourself worker at home can have a material exposure to asbestos during home insulation. Since the prognosis for a diagnosed pleural mesothelioma is extremely poor, varying from a few weeks to one year, it is important that no persons within the company should be exposed to asbestos whether as frank asbestos fiber or asbestos contained in such materials as insulation, lagging, asbestos cement, etc. It is also of course important to present this type of information in perspective and not to cause undue alarm since there is no reason to believe that good industrial hygiene practice such as the use of masks when cutting asbestos or using powdered or fibrous asbestos products is not completely effective in preventing later disease. It is whether

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or not asbestos fiber penetrates through the respiratory passages that matters and not the classification of the man's occupation.

For persons who would like more information on this topic, the abstracts of the Conference on the Biological Effects of Asbestos are available from the writer and it is expected that the proceedings of the conference will be published within the year.

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