

THIRD INTERNATIONAL CONFERENCE

on PNEUMOCOCCUS

Held in JOHANNESBURG - 23.4.69. - 2.5.69.

REPORT

ON

STUDY

OF

MEDICAL PAPERS

1969

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Third International Conference on Pneumoconiosis -

Johannesburg - 23.8.63. - 2.9.63.

Purpose of the Conference :

- (1) To bring together recognised experts in the various disciplines(industrial medicine, clinical medicine, scientists, engineers and administrative officials actively engaged on research and the administration of compensation legislation etc.,) with a view to pooling, on an international basis, knowledge, experience and ideas.
- (2) To review the present state of research and preventive and control measures and
- (3) To determine further research necessary.

Membership of the Conference was closed and limited to persons who received personal invitations from the Secretary for Mines or from the Organising Committee. The invited membership numbered approximately 230, some 60 members coming from the United Kingdom, the United States of America, Canada, France, Italy, Belgium, Switzerland, Finland, West Germany, Australia, Japan and Rhodesia. No list of delegates was issued, but many prominent personalities were present. The Conference was held under the patronage of the Ministry of Mines of the Republic of South Africa and the Honourable the Minister of Mines, Dr.Carel de Wet, was the patron of the Conference. Dr.de Wet was the former South African Ambassador in London and has, in addition to the above portfolio, those for Health and for Planning and Development. The Conference was jointly financed by the Department of Mines of the Republic of South Africa, the Asbestos Mining Industry of South Africa, the Chamber of Mines of South Africa and the Mining Unions. Accommodation for the Conference and other facilities were provided by the South African Institute for Medical Research. English was the only official language of the Conference.

Pre-prints were available for most of the papers presented at the Conference and this proved invaluable in allowing full attention to be paid to the speaker without having to struggle to keep up with hastily scribbled notes. The pre-prints were published in a paper-back volume with tables and photographs. A list of the medical papers on asbestos with the page number in the pre-print volume

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is attached to this report. Dr. Holmes will review the papers on Dust Sampling etc., and I will attempt to evaluate the 'medical' papers.

The first half of the opening day of the Conference was accounted by the Registration procedures and a guided tour of the Pneumoconiosis Research Unit. We were shown the Library facilities by Miss Williams, who has produced a very comprehensive bibliography of all papers dealing with the subject of Asbestosis and its complications published in the years 1960 - 68 inclusive. This bibliography is available on request from the P.R.U. Other areas of interest which were seen were the new A.E.I. electron microscope which has just been installed and the Dust Corridor.

The papers of a purely medical nature presented at the Conference can probably be sub-divided into :

- (a) Basic Research and Animal experiments.
- (b) Ferruginous bodies.
- (c) Pathology (a. Asbestosis. b. Pleural plaques. c. Mesothelioma)
- (d) Epidemiology
- (e) Radiology.
- (f) Lung Function.

(a) BASIC RESEARCH AND ANIMAL EXPERIMENTS:

The work of Morgan and Holmes is now well known. Their report to the conference on the use of radioactive tracer methods in the study of the biological effects of asbestos has been previously described. A possible explanation for the increased association between crocidolite exposure and mesothelioma may be that by this technique it can be shown that over half the administered crocidolite is retained after 4 months, whereas chrysotile has previously been demonstrated to show significantly greater solubility than crocidolite or amosite. This paper was essentially similar to that presented in Dresden in April, 1968.

The papers by Langer and F.D. Pooley et al both dealt with the problem of identification of the mineral core of 'asbestos bodies' and the significance of the bodies studied by these researchers. Langer described his technique for isolating asbestos bodies by means of low temperature ashing of tissue, individual

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micromanipulation onto appropriate substrates and then subsequent analysis utilising the electron microprobe analyser. The instrument incorporates a scanning electron microscope and x-ray spectrometers which together permit detection and spatial display of sample current, secondary electrons, back-scattered electrons and x-ray emission. The electron probe used is the the Applied Research Laboratories EMX model. After calibration of the spectrometers with metal and oxide standards, analyses of known asbestos mineral types were made. Langer states that the results indicate that it is possible to uniquely identify each asbestos variety by single fibre electron microprobe microchemical analysis.

Asbestos bodies were studied from a workman exposed to amosite, a workman exposed to chrysotile and from seven cases, from 'individuals in the general population not known to be exposed to asbestos'. The seven cases from the general population were chosen 'on the basis of particle abundance'. 1,315 analysis were performed on 16 asbestos bodies from this group. Only one clearly possessed the characteristics of an amosite fibre core, 15 were possibly nucleated on chrysotile but some discrepancies were found to exist as two separate bodies possessed characteristics of crocidolite but were somewhat atypical. No clear evidence of unaltered chrysotile or anthophyllite fibres was seen. Langer states that his results indicate that amosite remains intact in lung for at least 10 years; large bundles of chrysotile may also stay intact for long periods but chrysotile has a tendency to split into very fine fibrils and specimen selection therefore (the larger bodies in a population of asbestos bodies) may introduce bias. Although 15 of the 16 bodies described above were possibly nucleated onto chrysotile, 'chemical interaction in vivo would have to have occurred to explain our findings'. The possible occurrence of 'double' (Schaumann - asbestos) body coatings on atypical bodies from the general population may be one of the factors affecting analysis as well.

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Poolley et al found the alkaline digestive technique developed by Gold to be very satisfactory in removing practically all of the lung tissue from a sample. Any fibres or bodies present are left in their 'original state', concentrated together for examination after having been sparsely distributed throughout the tissue. This technique makes the specimens obtained unsuitable for further study by electron diffraction. Poolley has devised a secondary ashing procedure to remove contaminants. The ashing of thin histological sections varying from 30 to 35 microns in thickness is the only other technique suitable for preparing fibres and bodies for examination with an electron microscope. An advantage of the alkaline digestive technique is that mounting of the extracted material for electron microscope examination is easily performed as the extract is generally in the form of a suspension in distilled water. Poolley also discusses a method for determining the contents of the completely encapsulated, shunt-like asbestos body. A sub-division of bodies has been achieved by a process whereby the extracted KCH bodies are sandwiched between two non-interacting films of plastic to which they adhere. When the films are separated, the bodies are split in two, generally along the line of the fibre core. The sub-divided body is then generally suitable for examination and its contents can be determined.

Wagner discussed his work on the induction of tumours by the inoculation of various kinds of asbestos dust and found that with all types of asbestos an appreciable portion of animals developed mesotheliomas. There was no difference in effect between the natural and oil-extracted forms of crocidolite. Amosite required a longer induction period than chrysotile or crocidolite before tumours were produced. Wagner concluded that when different doses were applied, the risk of developing a mesothelioma at a given age could be taken as proportional to the dose. Samples of chrysotile from seven different Canadian mines all produced mesotheliomas when inhaled. Timbrell has postulated that the early fibres of chrysotile when inhaled are intercepted at bronchial and bronchiolar bifurcations where they can be dealt with by the normal lung clearance mechanisms. The straight needlelike and more rigid crocidolite and amosite fibres are able to penetrate the depths of the lungs, where

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they are retained and can exert their action. Although this applies to both amosite and crocidolite, only crocidolite thus far appears to produce mesothelioma. Amosite's long induction period as described in experimental animals by Langer, may be the answer to its apparently minimal mesothelioma producing effect.

(2) FERRUGINOUS BODIES

Four papers were read on the subject of asbestos bodies, generally referred to by one and all as ferruginous bodies. Carl Gross started the ball rolling by describing experiments designed to demonstrate the origin of ferruginous bodies from various organic and inorganic fibrous materials. Data was recently published in the New England Journal of Medicine in an article by Gaensler which demonstrated that in 26 autopsies where 'asbestos bodies' were found in persons with no known occupational exposure to asbestos, in every instance chrysotile asbestos could be definitely excluded by electron diffraction. Glass fibre was also specifically excluded as the central core. This statement was challenged by Langer, who felt that some of the fibres shown on the slides projected, were definitely amphiboles - this form of asbestos had not been excluded and Gross' x-ray diffraction patterns were challenged.

A further challenge to Gross came from Goldstein, who was unable to produce ferruginous bodies with anything other than asbestos or glass. He used the following substances in his experiments :

A. Of Mineral Origin:

1. Chrysotile, Amosite, Crocidolite and anthophyllite supplied by the U.I.CC.
2. Fibre-glass, prepared from ground-up fibre-glass filter paper.
3. Sillimanite.
4. Brucite.

B. Of Vegetable Origin:

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5. Manila Rope. \ These were prepared by grinding in a Glen Creston mixer mill under standard conditions
6. Barboe. \ and suspending the resultant powder in saline immediately prior to use.

C. Of Animal Origin:

7. Tendon.
8. Aorta.

Dr. Goldstein found that 4.4% of deceased mine-workers had ferruginous bodies in their lungs and 'most cases occurred in asbestos workers'. Lung neoplasms occurred more frequently in the cases with ferruginous bodies. The failure to produce ferruginous bodies in experimental animals with anything other than asbestos or glass fibre suggests that there may be an optimal diameter necessary for their formation.

Selikoff analysed the occurrence of Asbestos bodies in the New York City population in two years, 1934- and 1967. They are studying 3,000 consecutive autopsies (1966-68) in 3 large New York City hospitals. The results of 1,975 cases have been analysed thus far, asbestos bodies being found in 942 (47.7%). In 772, they were few in number (1-4); in 170, they were more numerous (5 or more). The analysis of the lifetime occupational histories completed thus far in 856 cases suggests that 'asbestos bodies are not randomly distributed among the general population of New York City'. Broadly considered, 40% of housewives showed asbestos bodies - 50% of 'white collar' males.

50% of 'blue collar' males (manual work) except those who had any history, however brief, of ever having done shipyard or construction work (all trades - carpenters, electricians, plumbers, labourers etc.,) where the incidence was 70%. when housewives or white collar workers were positive, they generally had few asbestos bodies; when men who had worked in the construction industry were positive, often many bodies were present. Selikoff draws the following tentative conclusions from the above information :

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1. While asbestos bodies are commonly present in the lungs of adults in New York City, their occurrence is not a random event, but to an important extent occupationally related.
2. The construction and shipbuilding industries are rich potential sources of direct and indirect occupational asbestos exposure and, especially if possible neighbourhood and family contacts are considered, could be responsible for a large proportion of the asbestos bodies found in routine autopsies.

When comparing the incidence of asbestos bodies in the lungs of individuals examined at Autopsy at the Mount Sinai Hospital in 1934 and 1967, there was no significant difference in the percentage of cases having asbestos bodies in these two years. 53 of 100 were positive in 1934 and 60 of 100 in 1967. For individuals 30 years of age or more, 50 of 81 (62%) were positive in 1934 as against 57 of 93 in 1967 (61%). The amount of asbestos used in the construction industry in 1935 and that used in 1967 remains fairly constant at 60% of the total import. The growth in asbestos consumption, 1920 - 1965 has been largely in products in which asbestos is 'locked-in', as floor tiles, roofing felts, asbestos cement products. If the construction industry is the major source for the asbestos fibres in asbestos bodies found in urban areas, then the findings in 1934 and 1967 should be similar because the amount of friable asbestos products used has not changed. Selikoff states 'If it will be confirmed that urban populations 35 - 45 years ago had asbestos bodies in their lungs as often as such populations do now, and if appropriate pathological studies will demonstrate that mesothelioma was indeed uncommon until recently, there will perhaps be less reason to expect that the current finding of asbestos bodies in the lungs of the general population is a harbinger of future disaster, that we face a widespread epidemic of mesothelioma'. Shipyard and construction work appear to be in most urgent need of engineering and hygiene precautions.

In their paper on 'The Detection of Asbestos in Tissues', Pooley et al discuss the results of the multi-centre survey of asbestos bodies which they initiated in October, 1966 to estimate

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the frequency with which asbestos bodies are found in the lungs post-mortem in different geographical areas. The areas were intended to cover the range from unpolluted rural areas, through urban areas of varying degrees of industrialisation, to towns and areas where the prevalence was known to be very high. The centres chosen and the results are shown in Table 1 :

<u>CENTRE</u>			<u>Number</u> <u>Collected.</u>	<u>Number</u> <u>Examined.</u>	<u>Number</u> <u>Positive</u>
Glasgow	..	..	200	163	39.(24%)
Belfast	..	..	198	148	29.(20%)
Cardiff.	..	..	-	-	-
Dorchester	..	..	200	161	13.(8%)
Dublin	..	..	59	25	0.(0%)
Finland	..	..	200	156	62.(39%)
Galway	..	..	125	71	1.(1%)
London(1)	..	..	200	54	3.(17%)
Dresden	..	..	199	137	26.(19%)
London(2)	..	..	200	159	34.(25%)
Liverpool	..	..	200	157	24.(15%)
Mottinham	..	..	200	151	11.(7%)

The authors feels that when this study is completed and fully analysed it will become clear how differences in the frequency of detection of asbestos bodies at post-mortem in different geographical areas can vary according to general levels of air pollution with asbestos. These authors also reviewed tissue from lungs available in the Whittington Hospital, London from cases dying in the years 1936(123), 1946(100), 1956(100), and 1966(100). They attempted to see if the numbers of asbestos bodies in these lungs varied in the selected years and to relate this variation to estimates of the quantity of asbestos in use. In contrast to Selikoff's findings, in this study no asbestos bodies were found in those dying in 1936 or in the females dying in 1946. The overall percentages of positive cases rise steadily to 20% in 1966, a figure which compares with the number of positive cases for London and the industrial cities in the multi-centre survey. The authors produced a mathematical formula which showed that the risk (and hence the number of positive cases) increased with the cumulative amount of asbestos imported.

Mourman et al attempted to discover whether

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the high incidence of lung cancer in Finland is in some way associated with the frequent occurrence of asbestos bodies in the lungs of adult Finns, bearing in mind that tobacco smoking must also be taken into consideration. They noted that tobacco consumption in Finland as compared to some other European countries was high, that it has been so for a long time in sharp contrast to the other northern countries and that only the United Kingdom consumes more tobacco than Finland. Fifty consecutive lung cancer cases coming to autopsy during the years 1966 and early 1967 served as the basis for this study. The next autopsy case of the same sex and age (to within 5 years) without lung cancer was taken as a control pair. The mean age of the 50 lung cancer cases and their control pairs was 63 years. There were 46 men and 4 women in each group. Asbestos bodies were found in the lungs of 40 (80%) of the lung cancer group and of 32 (64%) of the control group. There is no significant statistical association between the occurrence of asbestos bodies in the lungs and cancer of the lung. On the other hand, this study seems to give some support to the view that combined exposure to tobacco smoke and asbestos dust could cause a rise in the incidence of lung cancer. A synergism of asbestos dust and tobacco smoke has not yet been established, but data available at present show that such a possibility must be taken seriously into consideration.

(c) PATHOLOGY :

(a) Asbestosis :

Development of asbestosis differs from that of silicosis in that the areas of fibrosis in the lung show, when carefully examined, according to Dr. Webster, that the fibres and ferruginous bodies are to be found in groups and they have no direct relationship with the areas of interstitial fibrosis. These bodies and fibres are in fact still in the alveolar spaces and the appearance of marked fibrosis, in addition to the fibrosis of the alveolar walls, consists largely of ^{alveolar} spaces in which a desquamative alveolitis has become organised by connective tissue.

After exposing Vervet monkeys to different types of

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asbestos dust, Dr. Webster concludes that the fibrosis found in cases of asbestosis appears to be of different types which he itemised. This relatively simple investigation may be of great benefit to pathologists involved in the post-mortem or biopsy diagnosis of pulmonary fibrosis attributed to asbestos exposure.

(b) Pleural Plaques :

Professor Thompson discussed the pathological development of pleural plaques. Professor Thompson states that one of the striking features of these plaques is that they are not associated with pleural adhesions and what he lacks is an explanation of their pathogenesis by a means which does not involve the likelihood of pleural adhesions developing. Pleural plaques are found only on the parietal pleura and only in very special parts of it. They are not found at the apex or the costophrenic angles and are sited anteriorly only exceptionally. They are found in the parietal pleura over the ribs and not over the inter-costal regions except possibly where there are vertebral bodies and their transverse processes. They are seen on the tendinous portion of the diaphragm and not on the muscular portion. They are relatively rare over the pericardium and are seen most frequently over the lower ribs posteriorly and laterally. Calcification occurs in the centre of the plaque. The sole significance of calcification is that the plaques have been there for some time and that the collagen in the centre is degenerated and devoid of nuclei. Routine chest x-rays will demonstrate only 8 to 15% of these plaques. Thompson considers that the growth of these plaques comes from the deepest portion furthest from the pleura and that mesothelial cells are not evident on the surface or elsewhere. After examining biopsy specimens of such plaques where the process is at an earlier stage of development, it is clear that the pleural mesothelial cells take no part in the formation of the plaque and merely cover it passively. Thompson feels that the plaque in fact is not a pleural plaque but an extra -

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pleural plaque and as the mesothelial cells take no part in its formation, suggestions that these plaques are the benign counterparts of malignant mesotheliomas, are untenable. Thompson suggests that some of the asbestos fibres, before they have had time to change to asbestos bodies, move downwards and laterally from gravity and the movements of the lung. They would tend to move downwards in the erect posture occupied by most human beings for 2/3rds of the day and laterally for the remaining 1/3rd during sleep. Dr. Thompson stresses that this gravitational downward and lateral movement of sharp asbestos fibres in the lung is possible because of the coincidence of three variables: the sharp asbestos fibres, the soft easily punctured structure of the lung, and the constant motion of the lung. This downward and lateral movement explains why pulmonary asbestosis, unlike other pneumoconioses is more marked towards the bases. Thompson also feels that this explains why mesothelioma of the pleura is seen most frequently to-day in subjects with a slight or limited asbestosis as there is no marked fibrosis to impede the downward movement of the fibres and their emergence from the lung to the pleura. He also feels that it explains why mesotheliomas of the peritoneum and possibly carcinomas of the ovary in females are seen more frequently in people with slight asbestosis.

The proposed pathogenesis of pleural plaques is that some fibres by this means can leave the lung. Most pass through soft tissues such as inter-costal muscles and the muscular portion of the diaphragm, but others are held up by the hard tissue of the ribs or the dense fibrous tissue of the tendinous portion of the diaphragm or of the pericardium. The localisation of pleural plaques at these sites especially posteriorly and laterally is thus explained according to Professor Thompson.

(c) The Pathology of Mesothelioma

There were three papers dealing with this subject. The paper by Gluckman was heckled and openly criticised. It was an ill-conceived attempt to dispute the work of the leading experts in this field and in addition to being non-factual

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to a large extent, was of no scientific value.

Professor Thompson attempted to show that the diagnosis of malignant mesothelioma was not as difficult as the literature led one to believe. He felt that malignant mesothelioma was no longer rare but that until it is diagnosed with confidence by the ordinary pathologist as a routine procedure, we will not be able to talk about its increase as we do not know its present frequency. In his paper on the subject, he discussed the findings of 17 autopsy cases, all recent, and mainly diagnosed during life, as well as over 50 positive biopsies, which included 10 of the autopsy cases. Professor Thompson's argument is based upon the rigid adherence to the currently acceptable criteria and he feels that by following these criteria there is little doubt that nothing but malignant mesotheliomas will be diagnosed. He questions what proportion of true malignant mesotheliomas are excluded in so doing. The presence of blood-spread secondary deposits no longer exclude the diagnosis of mesothelioma. Professor Thompson suggests that pleural and peritoneal mesotheliomas behave differently and that only peritoneal mesotheliomas usually conform to the old criteria and have absent or limited secondary deposits. Professor Thompson believes that malignant mesothelioma of the pleura has a range of malignancy as well as an average malignancy. While there are cases with virtually no secondaries, there are examples with extensive spread. He suggested a simple morphological classification into encephaloid mesothelioma and scirrhous mesothelioma. The encephaloid type is the one that is usually illustrated in naked eye photographs with the lung encased in a bulky, soft tumour mass. It is a very distinctive type but is the less common of the two. The more common scirrhous type in the pleura is harder and less bulky. Professor Thompson concludes by stating that in any individual case the absence of a history of exposure to asbestos, the failure to demonstrate pulmonary asbestosis or to demonstrate asbestos bodies in the lung, should not be regarded as in any way invalidating the diagnosis. He goes on to say 'we do not know that asbestos

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is the only carcinogen concerned, and it may well be that, exceptionally, the usual response to the presence of asbestos fibres in the lung is lacking and asbestos bodies are not formed.

In two cases described by him efforts were made to demonstrate asbestos bodies by basal smears and by multiple sections from the lung bases and elsewhere without success.

The third paper on Mesothelioma and asbestos by Ashcroft and Heppleston, was a reiteration of the paper which was presented at the Dresden Conference, and this work has been previously described. The summary to this paper reads as follows :-

'The association between mesothelioma, asbestos bodies in the lung and occupational exposure to asbestos inhalation is confirmed from an English ship-building area.

The matched case-controls showed a surprisingly high incidence of exposure to asbestos, though much less than in the cases of mesothelioma.

The survey of routine necropsies reveals that industrial exposure to asbestos largely accounts for the presence of asbestos bodies in the lungs of unselected cases. Accordingly the risk to the urban population as a whole from general atmospheric contamination by asbestos may well be less than was suggested by earlier pathological surveys without occupational histories, but the extent to which asbestos fibres are involved has yet to be determined.

Wide variations occur in the numbers of fibres and bodies from different cases of mesothelioma. The ratio of fibres to bodies is also variable, though fibres, many of them small, tend to predominate. '

(d) PAPERS ON EPIDEMIOLOGY :

The paper by Dr. Newhouse was exactly the same

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as that which she read at the President Conference and she presented no new material. The essence of her findings is that both in men with short exposure as well as in those with long exposure there was a statistically significant excess of deaths from cancer of the lung and pleura and other cancers after a period of at least sixteen years had elapsed from first exposure. Excess of deaths from respiratory diseases occurred only in men with a long exposure.

Dr. Newhouse stated that study of the autopsy reports and histological material from 84 subjects revealed 5 additional pleural and 10 peritoneal mesotheliomas. She thinks that these findings suggest that the excess deaths from other cancers was due to the occurrence of peritoneal mesothelioma which have not been identified at the time of death.

Dr. Gilson summarised the present position in the United Kingdom making special reference to the mesothelioma register which is being maintained at the Brompton Hospital in Dr. J. F. Wilson's Department, with support from the International Agency for Research on Cancer.

550 cases of mesotheliomas of pleura and peritoneum are provisionally registered in the United Kingdom, 20 were diagnosed before 1955. In the years 1955 to 1959, 40 were added, with an average of 8 per annum and between 1960 and 1964, 135 were registered, giving an average of 27 per annum. The annual figures for 1965, '66, '67 and '68, are 42, 32, 59 and 60 respectively.

Scottish cases registered between the years 1950 to 1967 number 85. There are 43 cases with information on dates incomplete and there are 28 cases as yet alive.

Dr. Gilson next referred to the epidemiological studies in dockyard workers in Great Britain and especially to the work of Surgeon-Commander P. G. Harries at Devonport and the publication by Sheers and Templeton in 1968 of the results of a survey of a 10% sample of the 15,040 employees at Devonport

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background.

Dr. Wiers concluded that there were 63 men (4.5%) in whom there was evidence of changes probably due to exposure to asbestos dust. In about 5 out of 6 cases the effects were limited to pleural thickening. Often there was little or no disability.

Dr. Gilson finally discussed a survey of pleural thickening in Chest Clinics which was organised with the help of the British Tuberculosis Association. This survey showed that there was a slight but unimpressive excess of positive histories of exposure to asbestos among the cases of pleural thickening. Further analyses are now in progress using the medical histories to see if there is a group with pleural changes for which there is no adequate medical history, and whether in this sub-group there is a relation to past exposure to asbestos.

Dr. Selikoff reviewed his findings in the members of the Asbestos Workers Union in the New York area and delved deeply into the composition of insulation materials and the quantities of asbestos used in insulation materials in the United States in the years 1920 to 1965. He also analysed the use of asbestos insulation by construction type in 1969 and showed that by far the greatest amount was used in marine construction work and in power process construction work, i.e. power plant and boiler rooms. The use of asbestos by insulation workmen in the United States in 1969 was analysed according to the volume used. (expressed as a percentage of the total) which in the case of asbestos workers was 35%, and the application (which was expressed as a percentage of time) indicating that insulation workers spent 43% of their time in the application of asbestos insulation. Fibrous glass was the other major material involved with 45% of the volume total being applied for 40% of the time.

Of the 632 members of the Union, on December 31st, 1942, 380 were dead by December 31st, 1968. 1 in 5 deaths was caused by lung cancer. Despite the recent rise in prominence of mesothelioma, this remains the most important asbestos-associated

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neoplasm among insulation workers.

Dr. Selikoff then went on to describe the special relationship which appeared to exist between cigarette smoking and cancer among asbestos insulation workers. According to him lung cancer death rates were seven times expected.

Twenty-two of the 380 deaths were due to mesothelioma, 6 pleural and 16 peritoneal. Peritoneal mesothelioma does not seem to be related to cigarette smoking. In the three cases of pleural mesothelioma for which they have recorded smoking histories, all had smoked cigarettes.

Dr. Selikoff stated that they have continued to see more deaths due to cancer of the stomach and colon than expected. He goes on to state however, that the ratio is only three times expected, and with so few deaths, they are not yet certain of the relationship. Selikoff is concerned that the incidence of cancer of the pancreas and oropharyngeal cancer among asbestos workers will be increased. Thirty deaths of the 380 were due to respiratory insufficiency with cor pulmonale.

Dr. Selikoff has analysed the importation and use of crocidolite into the United States and finds that very little crocidolite entered until World War II. The asbestos used in the United States was almost entirely chrysotile. The largest asbestos manufacturer in the United States first used crocidolite in 1929 for sheet packing, not insulation. According to Selikoff, this company never used crocidolite for the manufacture of insulation at any time between 1929 and 1968, employing it only in two product lines mainly asbestos cement pipes and packings. During these same years, 1929 - 1940, more than 267,000 tons of chrysotile were used for insulation purposes. Selikoff concludes therefore, that crocidolite exposure of United States insulation workers before 1930 and probably before 1940 is unlikely to have occurred to any significant extent.

The 22 cases of mesothelioma which have been seen in the years 1947 - 1968, all occurred in insulation workers who

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began work before 1930.

Selikoff argues that if a long-latent period is required for asbestos induced mesothelioma, then in his series, crocidolite exposure alone cannot easily explain the mesotheliomas seen among insulation workers in the United States. The moral which Selikoff draws from this is that these findings should engender caution in relying on other asbestos varieties always to be significantly less likely to cause mesothelioma. The relative mesothelioma hazard for each fibre variety is still to be defined in humans. At this time Selikoff's data suggests that it would be prudent to regard all fibre varieties as potentially hazardous, and to utilise appropriate industrial hygiene measures for all.

A number of short papers on the currently available results of epidemiological surveys in various countries then followed.

The paper by Avfil on the results of asbestos exposure in France contributed little and must be discounted for lack of adequately presented factual information.

Kiviluoto and Neuman, in a brief report on the results of asbestos exposure in Finland, once again were unable to find a single case of pleural or peritoneal mesothelioma in their series and also did not find a higher incidence of gastrointestinal cancer in their series.

Professor Vigliani reviewing the results of his studies in Italy, did not relate any new findings and presented essentially the same facts and figures as those which he gave to the Dresden Conference.

McDonald et al attempted to carry out a retrospective survey on the cases of mesothelioma which they were able to trace by writing to the members of the Canadian Association of Pathologists or the Quebec Association of Laboratory Physicians. They found 165 cases, 111 were pleural, 47 peritoneal, 3 pleural and peritoneal and 4 pericardial. The diagnosis was supported

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by autopsy in two thirds of the cases and by biopsy in the remainder. More cases were found in 1966 and 1967 than in previous years.

During the 8 complete years 1960 to 1967 the average annual incidence was 1 per million of population. The rate was appreciably higher in Quebec (1.5) than in Ontario (0.8) or in the rest of Canada (0.9), - 1966 and 1967 again accounting for much of the difference. There was no difference in the sex distribution under the age of 50 but thereafter males were always in considerable excess.

Men employed in asbestos textile manufacture, the installation of brake-linings or as insulators, were responsible for most of the excess of cases over controls. Mine or mill workers made little contribution to the difference and only one person, a hardware storeman, had worked with asbestos-cement products. The time between first exposure and death for the 19 cases in the definite or probable class ranged from 16 to 50 years; 4 men who worked on the job for less than 4 years had intervals of 18, 26, 29 and 33 years.

Excluding 5 cases and 1 mine and mill worker in each control who lived in mining towns, only 3 men and 2 women had ever lived within 20 miles of an asbestos mine. One of the 5 was a case, 3 were in control group A and one in control group B.

The possibility of contact as a result of some other member of the family bringing home dusty clothes from an occupation involving the use of asbestos was also examined. Again excluding 6 men already themselves occupationally exposed, there was one case in a female with 'definite' home exposure and one male in control group B with 'probable' home exposure. In addition there were 26 persons with a 'possible' home exposure; 10 were cases, 9 were in control group A and 7 in control group B.

In both males and females, persons in the primary lung cancer group had smoked considerably more than those in either

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the case or secondary lung cancer groups. The 19 men with definite or probable occupational exposure to asbestos showed no great differences in smoking habits from the cases without occupational exposure.

McDonald et al conclude that primary malignant mesothelial tumours are very rare in Canada and it is somewhat doubtful whether there has been any true increase in incidence since 1959. An association between these tumours and definite or probable occupational exposure to asbestos was clearly demonstrated by only a minority of male cases and no female cases had any such exposure. Lesser degrees of occupational exposure, indirect household contact and residence in asbestos mining areas were no more frequently reported for cases than controls. The excess in occupational exposure was in the manufacture and industrial application of asbestos rather than in mining or milling. These authors suggest either that chrysotile is less associated with mesothelial tumours than other forms of asbestos or that something in addition to asbestos is necessary. If there is an additional factor, their findings imply that it is not cigarette smoking.

The paper by Dr. McMulty on his Australian experiences is now clearly academic as the asbestos mine in Wittenoom, Western Australia, has been shut down. His follow-up survey of the men who worked at the mine and in the mill is of interest as it bears out the association between asbestos exposure and lung cancer. Since June 1958, 103 men who worked at Wittenoom have developed pneumoconiosis. 41 were mill workers, 29 were underground workers, 6 were both underground and mill workers and 24 were men with other significant mining experience. 3 men were excluded because of lack of clinical detail.

It would appear that although working conditions were poor and dusty from the beginning, these did not cause significant lung disease while the production of fibre remained low. Continued poor conditions and increasing production created a situation where pulmonary disease began to appear after relatively short periods

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of exposure.

The average length of exposure in the mill for development of disease was 5.25 years, with a range between 1 and 14; and of the underground workers 6.6 years, ranging from 3 to 13 - the average age being 40 and 45 years respectively.

Pleural plaques have not been found among workers or the townspeople. 6 men in this series developed bilateral pleural effusions, 3 obviously due to deep vein thrombosis with lung infarction, but there was no explanation for the other 3, and the subsequent raised adherent diaphragms made the diagnosis of lung disease difficult.

As with the chest x-rays, the pathology has almost invariably been that of silicosis, with typical nodulation and massive fibrosis with interstitial fibrosis and asbestos bodies.

To date, 2 men have developed lung cancer; both were heavy smokers.

Pleural mesothelioma occurred in a man who worked in the mill between 1947 and 1949, the tumour appearing in 1960.

A particularly bad feature was the persistent use of mine tailings for road surfacing, which exposed townspeople and children to loose dust containing fibre.

In South Africa asbestos is both mined and finds its way into factories where manufactured products are produced. According to Dr. Webster, little is known about the factories and works using asbestos but a considerable amount of information has been accumulated on the results of asbestos exposure in the mines and mills. In South Africa the high proportion of pulmonary tuberculosis in the patients with moderate degrees of asbestosis presents problems to the epidemiologist and the mine medical officer. The South African Asbestos Tumour Reference Panel has defined the criteria on which a mesothelioma can be diagnosed and, up to the end of 1968, 179 such tumours have been classified

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as 'definite mesothelioma'.

A study of the age distribution showed that all age groups from 20 to 90 years may develop mesothelioma.

Dr. Webster feels that the histological features of a pleural biopsy specimen are sufficiently characteristic for the diagnosis of mesothelioma of the pleura and even exfoliative cytological examination of the pleural fluid will give an indication of the diagnosis in almost all patients.

Of 174 cases, in 100 the diagnosis was made on a specimen of needle biopsy of the pleura only; and in a further 27 cases the positive pleural biopsy was confirmed by autopsy. In 34 cases the specimens examined were from autopsy examination only. In 13 cases an open thoracotomy was performed. Therefore, in 74 of the 174 cases of mesothelioma the Panel were able to satisfy the most stringent criteria for diagnosis.

Of the 61 autopsy cases, asbestosis was found in 25. In 14 cases there was no evidence of asbestosis or of bodies on histological examination. Ferruginous bodies were found in the histological sections of the lungs of 7 cases in which there was no evidence of an interstitial fibrosis. In 15 patients there was no report on the presence or absence of asbestosis.

Dr. Webster feels that because in 14 cases no evidence could be found of asbestosis, this in itself might be indicative that there was not a direct relationship between asbestos exposure and the development of a mesothelioma of the pleura. A study of the environmental and occupational histories of these 14 cases of mesothelioma is of great interest and, indeed, confirms the lack of a direct relationship.

Of the 148 cases in which the history was known, in 24 there was no evidence of asbestos exposure at all. There was no doubt that most of these patients had had an association with the Northern Cape and that a more detailed study of this area

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may give a possible indication of the pathogenesis of the disease.

Dr. Webster lists three cases where the exposure was due to amosite. These cases are not discussed in any further detail. In the discussion which follows the report, Harrison noted that production of amosite has taken place for long enough in time, and that production was as large in quantity as for North-West Cape blue asbestos, and that where amosite to be associated with mesothelioma this association would by now have been more definite.

Dr. Webster was careful to point out that other minerals were to be found in abundance in the North-West Cape and mentioned iron and manganese specifically. He suggested that the part played by asbestos in the development of a mesothelioma and indeed, of other tumours of the respiratory tract, may be indirect and may well cause the direct carcinogen to be retained in contact with the lower respiratory tract for a longer period than when the carcinogen is inhaled by itself.

The direct carcinogen may not be a single substance, and the cases from the Northern Cape suggest that another mineral, such as manganese or iron may play a part. Such an association may well be considered in those cases of mesothelioma occurring in shipyards and dockyards and in the insulation industry. This hypothesis has been previously stated by Dr. Stumpius.

(e) RADIOLOGY OF ASBESTOSIS :

The section on radiology was disappointing. Although the two papers by Solomon on the radiology of asbestosis and the radiological features of diffuse mesothelioma were good examples of the use of commonsense and powers of observation, they contributed little, in my opinion, to the problem of the earliest changes which one would associate with asbestos exposure or, if you like, early asbestosis. Dr. Solomon considered first of all pleural changes, and, secondly, the appearance of non-calcified pleural changes as opposed to calcified pleural plaques. In established cases of asbestosis fine fibrosis was described in 5 cases, nodular changes were

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described and in 7 cases a bilateral solid fibrosis on x-ray producing a homogeneous opacification was observed. Broad linear bands or strands of fibrosis producing coarse patterns and a striking resemblance to fibro-cavitating lesions of tuberculosis were noted in 2 cases as the predominant lesion. Massive fibrosis was seen in some instances. Dr. Solomon felt that pleural effusions, non-specific pleural reactions, accentuation of the fissures, lamellar pleural thickening and non-calcified pleural plaques should be regarded as significant changes in patients who have a history of asbestos exposure. These changes may occur with little histological evidence of asbestotic fibrosis in the lungs. Calcification of the pleura is a late manifestation of asbestos exposure.

In asbestosis, combined pleural and lung lesions occur commonly and should alert the clinician to the diagnosis.

Modular, pneumonitic and massive fibrotic changes often occur in combination. Fine and coarse linear fibrosis usually accompany punctiform and nodular patterns. The x-ray changes bear a direct relationship to the degree of fibrosis of the lung determined histologically.

Kiviluoto thinks that the type of asbestos plays a relevant part in the x-ray appearance of asbestosis as well as the degree, or the duration of exposure and the elapsed time from the first exposure. He describes the results of a study of the chest x-ray films of 431 workers employed by an anthophyllite asbestos mining company. The group studied consisted of former workers only, and the mean elapsed time from first exposure was about 20 years.

For an incidence study of hyaline and calcified pleural plaques among people not known to have been exposed to asbestos, the findings of 3,818 consecutive chest x-ray examinations in a private clinic were coded. 180 of the total of 410 cases were radiologically normal, whereas 230 had pleural and/or pulmonary pathology. Pathological changes not attributable to asbestos were considered to be normal.

No asbestosis was discernible in 56 cases and thus in

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about 24% of the pathological cases, only pleural changes were observed. In addition, it should be mentioned that in 10% of cases with lung cancer, the pulmonary fibrosis was 'slight' or 'very slight'.

The diffuse pleural thickening correlates with the severity of lung changes but Dr. Kivimäki emphasised that about 35% of cases with lung changes of even grade III showed no pleural thickening. In a series of 100,000 x-ray examinations in Finland, pleural thickening was the most common radiological finding after cardiac enlargement, aortic sclerosis, and pulmonary emphysema.

Hyaline and calcified pleural plaques may be a much more specific radiological feature.

Dr. Kivimäki states that in practice it transpires that a correct radiological interpretation of pleural lesions is a first step towards diagnosis in many cases of pneumoconiosis, where a routine clinical examination has not led to any suspicion of this disease.

Professor Bohlig discussed the problem of asbestosis in relation to the International classification of radiographs in pneumoconiosis and described the new UICC/Cincinnati classification which he proposed should be adopted in future for the classification of chest x-rays in pneumoconiosis.

(f) LUNG FUNCTION

Dr. Margaret Becklake presented a most elegant paper relating x-ray changes in Quebec asbestos workers to lung function tests.

In 1966 an epidemiological survey of Quebec asbestos workers was started to assess the effect of exposure to chrysotile dust on the health of the workers. Dust exposure is being evaluated from dust counts and job classification. Health has been evaluated from their most recent chest x-ray, from lung function tests and from a respiratory symptom questionnaire.

On the 31st October, 1966, 6,180 men were employed by the constituent companies of the Quebec asbestos mining industry.

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An age-stratified random sample of 1,027 men was selected for lung function tests and 665 were tested the following summer. In this original sample only 71 men (8%) were considered to have radiographic evidence of asbestosis, (only 5 being placed in categories 2 or 3), although the sample was weighted for the older men with presumably longer exposure and more dust disease. A second field study was carried out in 1968 to include all men 60 years and over not previously tested. In Dr. Becklake's report the combined result of these 2 field surveys was considered and the age distribution of the 1,073 subjects was investigated. The most recent chest x-ray of each subject was assessed in detail by an international panel of 6 readers. The UICC/Cincinnati classification was used.

Dr. Becklake itemised the lung function tests and the measurements which were made in sequence. These tests included studies both at rest and during exercise and the carbon-monoxide diffusing capacity was measured both by means of the single breath technique and the steady-state method.

The characteristic restriction of all sub-divisions of lung volume was present only when radiological changes were definitive. The first lung volume measurement to be significantly affected was the vital capacity. Both the forced expiratory volume 0.75 seconds, and the forced expiratory volume 0.1 second, tended to fall in unison with the fall in vital capacity, a finding in keeping with the view that expiratory flow rates are volume-dependent. The ratio of FEV₁ to FVC expressed as a percentage was essentially unchanged at all radiological categories, being even greater than control in the established cases of asbestosis. These findings underline the fact that obstruction to the airways is not a feature of this disease and that, when fibrosis is advanced airway calibre may even be increased.

Dr. Becklake measured the CO extraction which was reduced at rest with category 1 changes. However, because resting ventilation was increased, the diffusion of carbon-monoxide remained little affected until x-ray changes were advanced.

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The same general pattern was seen on effort, thus a reduced carbon monoxide extraction percent in spite of a low effect by an increase in ventilation, and the steady-state diffusing capacity for carbon-monoxide itself was not definitely affected before category 1'1. These findings are in keeping with previous reports that impairment of gas exchange may be seen on effort at an earlier radiological stage than impairment of gas exchange at rest.

It is of great interest that the two function measurements which most closely paralleled the radiological development of asbestosis were vital capacity and ventilation at 200 kg. per minute.

It is of interest that these two tests (vital capacity and exercise ventilation) are technically easy to carry out. They are thus potentially suitable for widespread application on a longitudinal basis.

Dr. Becklake's findings are not incompatible with the view that impairment of gas exchange reflected in the 100 may be one of the earliest functional changes in asbestosis, preceding even x-ray changes. However, it does appear that there are compensatory mechanisms which can make this change apparent at a later stage than the changes in vital capacity which she describes.

SUMMARY AND CONCLUSIONS :

In this report I have attempted to review very briefly, important papers which were produced at the International Conference on Pneumoconiosis held in Johannesburg between the 23rd April and 2nd May, 1969.

I attempted to be brief but inevitably in a task such as this I found myself repeating largely what the individual authors had stated.

For this approach I make no apology as I feel that I do not detract from the value of my appraisal of the authors findings.

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For me this Conference proved extremely useful. In fact, more useful than my visit to Dresden. I was able to meet many of the leading names in my field of Industrial medicine and I was indeed able, on two occasions, to contribute to the discussion.

The visit to the Cape Blue Asbestos Mine at Durban was, for me, one of the highlights of this journey to South Africa and I can only say that all of us who saw this mine were extremely impressed by the vigorous action which the owners have taken to introduce the most up-to-date dust control methods.

Dr. Wagner, during the Conference, paid a spontaneous tribute to the South African Asbestos Mining Industry for the role which they played in the organisation of the Conference and for the hard work which they had put into their factories and mills to make them safer places for men to work.

The scientific content of this meeting was of a high level and produced, I think, some significant new lines of thought. The tendency of many of the speakers concerning the role of asbestos bodies in the general population was to consider these as an index of occupational exposure rather than environmental exposure. Indeed, many went as far as to say that their work had revealed that where asbestos bodies were numerous an occupational history was almost invariably obtainable.

There still remains a great deal of speculation as to the role of the various types of asbestos in the causation of mesothelioma of the pleura and peritoneum. Once again it appears to be emerging that the consensus of opinion is now in favour of the theory that not all mesotheliomata are associated with asbestos. Asbestos may even have an indirect role to play in the causation of both lung cancer and mesothelioma, merely acting as the vehicle for some other carcinogen such as tobacco

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smoke, iron, manganese or some other trace element.

The world-wide interest in the problem of asbestosis and its complications was highlighted by the large number of epidemiological surveys recorded. Some workers appear to be better equipped than others for carrying out their surveys and it is to be hoped that the less informed will take note and make every effort to improve their recording of data and their statistical analysis of the data they record, in order to help to clarify the anomalies which still exist with regard to the geographical distribution of asbestosis and its complications.

If I have any regrets with regard to this visit to South Africa then they are that I was unable to cross the border to Rhodesia to see the mining conditions there and that I was not invited to see any asbestos works or mines within the Republic of South Africa or the Republic of Swaziland.

I hope that if the occasion should arise in the future to pay a visit to any asbestos mining country again, an opportunity will be afforded me to visit the various facets of the industry in that country.



H.C. LEWENSOHN,
M.P. B.Ch. D.I.H.

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