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| Mr. John Waddell | Mr. J.A.E. Clogg,<br>T. & N. Ltd. |

Ref:- JW/PM
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Your Ref:-

15th November, 1965

Wyers Memorial Lecture
by Dr. J C. Gilson, 22nd October, 1965

I had a copy of the script of this Lecture sent to you last week, and now I want to add some comments. I am also sending a copy of the Lecture to Mr. A.N. Marshall.

First, this must be treated as confidential at present. It is a Xerox copy of Dr. Gilson's own script, lent to Dr. Knox as a matter of courtesy; it will eventually be published in the Proceedings of the Royal College of Surgeons.

After reading it you will agree, I am sure, that this Lecture is of first class importance. It is the best and most balanced review of the whole subject of the health risks of asbestos that I have seen, and it is, of course, right up to date. You will note that it contains several complimentary references to T.B.A., to Dr. Knox, to the Asbestosis Research Council and to its researchers, Dr. Holt and Dr. Davis. The Bamblin referred to is the Manager of our Engineering Design Department, who has given several public lectures (with permission) on dust control in asbestos textile factories.

Dr. Gilson is, of course, the head of the Pneumoconiosis Research Unit at Cardiff and Dr. Wagner, late of South Africa, is now on his staff. Dr. Gilson has visited Rochdale several times at our invitation and knows the work that we and the A.R.C. have done and are doing; he is a man of very high standing and international reputation in this field and is a good friend to T.B.A

I think you may wish to circulate this Lecture - and perhaps some of these covering comments - to the Head Office Directors.

Continued .....

I regret that when this note is typed I shall be away, so my secretary will initial it for me.

p. p. John Waddell.

Mr. J.A.E. Clogg

Mr. J. Waddell,
Turner Brothers Asbestos
Co. Ltd.

16th November 1965

Wyers Memorial Lecture by
Dr. J. C. Gilson, 22nd October 1965

Thank you very much for your letter of 15th November and I am obliged for your comments.

On a brief preliminary reading one cannot but agree with your remarks and I look forward to an early opportunity of studying this lecture more closely.

Arrangements have been made to effect the requisite circulation and this will include Mr. Soothill.

JAEC/MHC

J.A.E. CLOGG

CONFIDENTIAL

22nd December 1965

Mr. A.D.N. Jones,

Mr. W. P. Howard, UKAEA

I attach copy of the Wyers Memorial Lecture by Dr. J. C. Gilson on the subject of "Asbestos - Recent Studies on its Biological Effects". This document is, at this stage, confidential. I thought you would be interested in reading it, and after Mr. Jones has sent it on to Mr. Howard, I should be glad if the latter will return it, in due course, to me.

JAEC/MHC
Enc.

J.A.E. CLOGG

WEBB MEMORIAL LECTURE

by

Dr. J. C. Gilson 22nd October 1965

Given before the Autumn Meeting of
the Association of
Industrial Medical Officers

at

The Royal College of Surgeons, London

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References to local (Rochdale) situation
on Page 6, 7, 8. Sections marked.

JCC/BBl. 20th October, 1965.

THE WYERS MEMORIAL LECTURE

"Asbestos - Recent Studies on its Biological Effects"

by

J. C. Gilson, F.R.C.P.

Pneumoconiosis Research Unit of the Medical Research Council,
Llandough Hospital, Penarth. Glamorgan.

This, the ninth of the series of lectures to renew the memory of Hubert Wyers, is a review of recent evidence about the biological effects and health hazards of asbestos. I much appreciate the honour of being asked to give it and I am sure it is an appropriate subject because Wyers obtained his Glasgow M.D. in 1946 for a thesis entitled, "That legislative measures have proved generally effective in the control of asbestosis".

Hubert Wyers was a man of wide interests and unusually deeply versed in the classics and philosophy. This is clear from his contributions to the 'Transactions' of the Association of which he was the first editor. Also, from the opening remarks of the other lecturers in this series by those who knew him well. I have wondered whether his interest was sparked off by my father who was his headmaster and taught classics at King Edward's School, Birmingham.

Wyers's thesis shows a deep interest in the individual and is full of shrewd observations and comparisons between different occupational diseases. It also contains not a few speculations of which one seems a very suitable starting point for this lecture. He said (p.93), "It is well-known that the short, dusty fibres of the amber coloured amosite are the most pernicious of all, the blue asbestos occupies an intermediate position, both as regards wear on machines and effects on the lungs, and the white asbestos is least harmful both to steel and to the human respiratory mechanism".

His comment is interesting for two reasons : the first, at the time it was made it was unsupported (as far as I can ascertain) by any epidemiological or experimental evidence; and secondly, it was in a sense far ahead of its time because it is only within the last few years that serious medical attention has been directed to the possible differences in the biological action of different types of fibre.

TYPES OF FIBRE AND PRODUCTION

There are four main types of fibre of commercial interest. They are

all fibrous silicates but differ in composition. Chrysotile, softest of the fibres, is a magnesium silicate with only a small amount of iron and is mined extensively in Canada, Southern Africa, and Southern Rhodesia. There is also a very large production from the U.S.S.R. Crocidolite and amosite are chemically similar and both contain iron in the place of magnesium. Crocidolite is a striking blue colour and amosite is brown. Crocidolite comes from a long range of hills in the North-West Cape and also in a small amount from North-West Australia. Amosite only comes from the Transvaal. Anthophyllite is of considerably less commercial interest than the other three types; it is a magnesium silicate but differs from chrysotile in being less soluble. It is mined principally in Finland and in Italy. Table 1 shows the world production of the four main types in 1962. The production of all types has been rising steeply since the war and much greater use can now be made of the short fibres to strengthen and increase the abrasion resistance in many building and other products. The mineral is now constantly around us in the ceilings, floors, walls; in the brake-shoes and clutch linings of our cars. It is reported that there are at least 3,000 separate uses for the mineral ( [illegible] ).

RECENT DEVELOPMENTS IN THE EXPERIMENTAL APPROACH

I will start by reviewing some of the recent experimental work and then discuss some of the new information on health hazards associated with asbestos.

Inhalation of fibres

The health hazard is primarily, though not exclusively, to the lungs and pleura. Earlier workers were puzzled by the presence of fibres of 100 μ or longer in the lungs of men or experimentally-exposed animals, and suggested that fibres gained access to the lungs by different means from that of other dusts. It is no longer necessary to postulate this. The falling speed of a particle is the most important parameter influencing its entry into the lungs. My colleague, Dr. V.Timbrell, has recently shown (Timbrell, 1965) that the falling speed of airborne fibres is related to their diameter squared but not closely to their length. The very long fibres may have a slow falling speed provided they are very thin. This is shown by using an aerosol spectrometer which collects particles according to their falling speed. Fig. 1 shows a record from this instrument. The small spherical particles of wax are about 10 μ in diameter and unit density, and have the same falling speed as the fine asbestos fibres several hundred μ long. The fibres are only about 3 μ in diameter.

These findings are very relevant to the parameter of the airborne dust which should be measured to assess its inhalability and toxicity. In the past too much attention has been paid to length, too little to diameter and aerodynamic behaviour.

Experimental asbestosis

The new work in experimental asbestosis - after an interval of many years - is producing some interesting results. It is now possible to carry out quantitative inhalation experiments in animals. By this means Wagner and his colleagues (1963, 1966) have shown that chrysotile produces less fibrosis than amosite or crocidolite for the same dose by inhalation and this appears to be due to the much more rapid elimination of the chrysotile (Fig. II). The reason for this more rapid elimination is not yet clear but it may be related to solubility. These findings in experimental asbestosis accord with the observations on man by Nagelschmidt (1965) and others that lungs with severe asbestosis often contain very little mineral compared with other types of pneumoconiosis.

The importance of particle length on the development of fibrosis is still not solved but work by Wagner (1957, 1963, 1965), Holt ~~and Hills~~ (1963), and Davis (1964) in several animals species has shown that fibrosis of the lung is produced by fine particles or very short fibres. Fibres may still be relatively more fibrogenic for a given mass than the more compact particles (Klosterkotter, 1965) but critical experiments to test this in lungs have not yet been achieved. We need experiments of the type King and Nagelschmidt developed to study the effects of mass, surface area, and number in experimental silicosis (Zaidi et al, 1956).

How the asbestos produced fibrosis is still uncertain; it appears to be less toxic to the phagocytes in tissue culture than quartz. Fernis (1965) suggests that it may be a direct stimulus to the fibro-blasts. Its action on the phagosomes in the phagocytes, which have been shown to be damaged by silica (Allison et al, 1966), is now being investigated.

The nature of the asbestos body - a term now agreed internationally to be more appropriate than the asbestosis body (U.I.C.C. 1965) - has been elegantly investigated by Davis (1964) with the electron microscope, but its importance, if any, in the pathogenesis of the fibrosis remains obscure. Ferritin - an iron

protein complex with about 20% iron - is probably an important constituent of the bodies. It is possible that the fixation of iron in the tissues in this way may contribute to the appearance of the chest radiograph. (Rossiter et al, 1965) Recent work at our Unit in other types of pneumoconiosis has shown a close relation between iron content of the lung and the category of simple pneumoconiosis in the radiograph. Although asbestos bodies now seem of less interest in the development of fibrosis, they have become of much greater interest as an epidemiological index of exposure.

Experimental carcinogenesis

At the time of the earlier work on experimental asbestosis the association between asbestos exposure and cancer had not been well established. Little attention was, therefore, paid to asbestos as an experimental carcinogen. The position is now very different. Many investigations are in progress following the preliminary report by Wagner and his colleagues (1962) that they are able to produce mesothelial tumours by intra-pleural inoculation of asbestos.

The earlier work has been fully confirmed by Wagner (1964) in standard and specific pathogen-free strains of rats. Twenty mg. of asbestos injected into the pleura has produced mesothelial tumours in a high proportion of animals. This is so for chrysotile, amosite, and crocidolite, both natural and after extraction of its natural oil by a single solvent. The investigation - a survival experiment - is not yet complete so we do not yet know whether there are significant differences in the number of tumours produced by the different types of fibre. So far amosite has produced the least. The yield of the tumours has been unexpectly high and further experiments are now in progress to investigate the effects of smaller intra-pleural doses and the effects of the dust inhalation.

Under animal experimental conditions asbestos, therefore, appears to be a powerful carcinogen. How it acts is not yet known. It is relatively insoluble, contains iron, and has absorbed on it natural oils and waxes (Harington, 1962). It also takes up oil readily from jute bags while in transport and from other sources (Harington and Rae, 1965). It is not yet at all clear whether these oils are of any biological or medical importance, nor is it yet clear whether the iron is an important factor. Wagner's animal experiments, so far, perhaps make this unlikely as the iron content of the chrysotile is only

about one-tenth that of crocidolite or amosite.

We may expect a great increase in experimental work on the carcinogenic effects of asbestos. To help in this work the producers of all the main types of asbestos have generously agreed to help the International Union Against Cancer (U.I.C.C.) to assemble at the Pneumoconiosis Research Unit in Johannesburg standard samples of the main types of asbestos, for use for biological testing in any part of the world. These standard samples will remove one of the variables which at present makes comparison between the results of different laboratories difficult. They will also provide standards against which to compare materials used in different parts of the industry.

HEALTH HAZARDS OF ASBESTOS

Asbestosis - present position in the U.K.

In his summary Wyers (p.137) concluded, "Legislation has been generally effective in controlling asbestosis but not entirely". I propose to look at some of the recent evidence on this, but at the outset it is necessary to emphasise how incomplete it is. We have no reliable figures for the prevalence of asbestosis in the country, nor do we even know the numbers of workers continuously exposed to asbestos; still less those intermittently or casually exposed.

Wyers reported a study of deaths from asbestosis in a factory. Dr. W. J. Smither has kindly provided me with recent figures for the same factory. Table 2 shows that between the two periods 1931-46 and 1957-64 there has been no striking change in the years of exposure or duration of illness in the deaths with this disease. There has been a marked increase in the age at death. This is in part apparently due to a very striking change in the importance of tuberculosis, which was present in 31% of Wyers's group, but only 4% of the more recent group. The absolute numbers of cases have little significance without a knowledge of the populations exposed. It looks as though Wyers was too optimistic, but it has to be remembered that the second period includes the results of the War when long hours, the black-out, and the difficulties of maintenance must have markedly increased the dose of dust.

Information about new cases of asbestosis diagnosed by the Ministry of Pensions and National Insurance Panels also shows that asbestosis is still a real problem (McVittie, 1965) and that the steps taken after the Merewether and

Price report in 1930 have not been fully effective. Table 3 shows that cases of asbestosis are still occurring in those who entered the industry after 1933 and, indeed, even after 1950. It also shows that it is occurring in occupations not included in those scheduled.

Table 4 shows the contrast between the general downward trend of the number of new cases receiving compensation for most types of pneumoconiosis, except asbestosis where there is an upward trend during the last 6 years (H.M.S.O. 1965). There are, of course, many factors affecting such figures, but they indicate a need for further action and investigation.

That action can be very effective is shown (Table 5) by comparing the prevalence of asbestosis by years of exposure found by Merewether and Price reported recently for the same factory (subject to some reservations about population selection). The striking improvement is impressive and has been achieved by a very impressive technical improvement in dust control as those who have visited the factory know. The magnitude of the problem is emphasised by Camblin (1959), that the dust extraction of the Cards requires about four times the power needed to drive them and that the cost of dust control is about 7% of the wage bill.

I think the history of the efforts to control the health hazard associated with asbestos in this country, when looked at nationally, demonstrates well the failure to provide a continuity of research effort. Merewether and Price in their classical work proved the existence of a serious problem and this led at once to improvements of dust control which have been very effective in some textile factories. It also led to a scheme to protect the individual employer and employee by a system of medical examinations, but it failed to use the results of the medical examinations and the dust assessments to see what was happening in the industry as a whole. Let us ensure that we do better now that renewed efforts are being made. We need a properly integrated scheme in which information about groups of individuals and their dust exposure is analysed to provide a continuing check on changing conditions in the industry. Our National Coal Board has already gone a long way to achieving such an integrated scheme of research and supervision in their dust problem (Rogan et al, 1965). There is an even greater need for it in the asbestos industry where there are still many more unknowns - for example, the means of detecting early damage to the lungs; the importance of type of fibre; and the relation of dosage to both the development of fibrosis and tumours.

Stimulated by Dr. J. Knox - who will long be remembered for his initiative here - the three biggest asbestos companies in this country made an excellent start by establishing their Asbestosis Research Council. Real progress has been achieved in exchanging information on dust control and recently on standardising dust sampling. Let us hope the research work they and others are now doing will shortly lead to improved methods of medical supervision by making the most use of lung function tests and radiograph. We shall also need a system of recording and follow-up. Only in this way shall we get early proof of the effectiveness or failure of preventive measures. The investigation of the individual is no substitute for studying the group.

Asbestos exposure and cancer

Bronchial tumours

An association between asbestosis and bronchial carcinoma was first suggested in 1934 by Lynch and Smith in U.S.A.; and shortly afterwards by Gloyne in this country. The evidence supporting this view gradually accumulated in the period reports from Merewether. The pattern of change over the years can be well seen Table 6 from Buchanan (1965).

Proof of an association between exposure to asbestos and lung cancer came in 1955 in Doll's study of the mortality of a defined population of men in scheduled jobs in the textile factory (Doll, 1955).

This study has now been extended in time and scope by Knox, Doll, and Hill (1965). Dr. Knox has kindly allowed me to give you the figures up to June 1964. Table 7 shows that for men followed up in excess of 20 years and who worked before and after 1933, there has been a marked secular fall in the excess lung cancer risk. In those entering the scheduled areas after 1933, men show no excess lung cancer risk in the groups followed for 10 and 20 years respectively. In the women there has been one death from lung cancer in which the post mortem did not show evidence of asbestosis.

The findings of this follow-up are very encouraging but some caution is needed. The follow-up period is still not very long for many in the group, and it is known that the latent period for other types of tumour associated with asbestos exposure is very long. Also it is not yet clear whether the excess bronchial carcinoma rate is always accompanied by asbestosis. This raises the problem of how you define asbestosis. Suggestions for an international agreement on this by a group of pulmonary pathologists have recently been published (U.I.C.C., 196

Reports from the U.S.A. (Mancuso, 1965; Selikoff et al, 1964) may indicate that an excess mortality from bronchial carcinoma may exist in the absence of asbestosis in some groups of asbestos-exposed workers.

The problem is at present unsolved and must await further follow-up of the type pioneered by Dr. Knox and Dr. Doll. We need ... comparable studies in other asbestos-exposed workers, for we have to be aware of assuming that the findings in one part of the industry apply to the whole until ... know much more than we do at present.

Diffuse mesothelial tumours

I now propose to review briefly the evidence on the association between diffuse mesothelial tumours and exposure to asbestos. The evidence on this subject is accumulating so rapidly that my comments may be out of date by the time they are published. Hubert Wyers would have been very interested to learn that in retrospect one of the most significant observations in his thesis was, and I quote (p.102), "an endothelioma of the pleura is described in the present series, the first to be recorded in association with asbestosis as far as the writer is aware".

The picture of this case in his thesis shows the lung encased and tightly pressed by the surrounding tumour. The similarity of appearance to the first case reported from South Africa by Wagner, Sleggs, and Marchand (1960) 14 years later is striking. Hubert Wyers was more than 10 years ahead of his time though we now know that earlier cases were in the records in the Pathology Departments. (Dr. Wagner has in the last 3 years collected as complete a list as possible of all previous and recent cases of these tumours in the U.K., and this case in Hubert Wyers's thesis is apparently not recorded elsewhere.)

Recent discoveries in this branch of industrial pulmonary disease read like a detective story, and part of it has been written elsewhere (Wagner, 1964).

The observation which set off the recent research was made by Dr. C. A. Sleggs, working in a large hospital in Kimberley. Around 1955 he noticed that there were a number of cases of pleural effusion in his beds which did not respond to anti-tuberculous chemotherapy; also, these cases came to him from the West but rarely from the East, although he was situated in the middle of the area he was serving. This led him to think these must be odd cases. A number of them were transferred to Johannesburg where biopsy of the pleura was made.

Within a short period 16 cases had been diagnosed as diffuse mesothelial tumours, but information on the underlying lung was not available. On the basis of an earlier single case of mesothelial tumour where asbestos bodies were found in the lungs, Wagner suggested that asbestos might be responsible for these other cases. This initially seemed very unlikely as their occupations did not fit.

However, very detailed industrial and residential histories of the survivors and their relatives revealed that many of the people had lived near but not necessarily worked in the asbestos mines and mills in the North West Cape, which is to the West of Kimberley. By 1959, at the time of the Pneumoconiosis Conference in Johannesburg, an association with asbestos had been established in 32 of 35 cases.

Later, surveys were made in other asbestos-producing areas in South Africa to see if these cases occurred there also. Fig. IV shows the distribution of cases in South Africa up to 1962. The majority of the cases have shown an association with the crocidolite mining area, but there were other cases from industry where the exposures may have included other types of asbestos. In the Transvaal, where amosite has been mined since the '20s, no cases have yet been reported (Sluis Cremer, 1964a and 1964b); nor have any yet been reported from Swaziland where chrysotile is mined, though in appreciable amounts only since shortly before the war. In Shabani in Southern Rhodesia where there has also been a large chrysotile mine for many years, with a medical service since the late 1920s, no cases of mesothelial tumours of the pleura have yet been reported (Walker, 1965).

The asbestos mining areas of South Africa are, of course, not places where technically satisfactory long-term epidemiological studies are possible on account of mobility of labour and lack of records, but despite an intensive and maintained search over 5 years, no cases have yet been discovered associated with the amosite or chrysotile mining areas. Therefore, present evidence for South African mining areas strongly suggests that the type of fibre is an important factor in explaining the high incidence of diffuse mesothelial tumours in the crocidolite mining area.

In the United Kingdom, up to 1962, no intensive search for cases had been made although a few cases were known (Wagner et al, 1960). In the last three years there have been many reports in the U.K. (Hourihane, 1964; Entickmap

and Smither, 1964; Fowler et al, 1966; Owen, 1964; Elmes et al, 1965; Hinson, 1965; and Steel and Boyd, 1965), of groups of cases largely from the pathological records in many centres, confirming the association of diffuse mesothelial tumours of the pleura and peritoneum and exposure to asbestos. The evidence has been based either on asbestos bodies in the lung and/or a history of contact with asbestos dust.

The records at The London Hospital started by the late Professor H. M. Turnbull and carried on by Professor Dorothy Russell and Professor I. Doniach have provided the largest single group. Dr. D. O'B. Hourihane (1964) has analysed these cases back to 1917 and has shown a highly significant association between diffuse mesothelial tumours of the pleura and the presence of asbestos bodies in the lungs.

The occupational and residential histories of these cases were investigated by Dr. Molly Newhouse (1965). Fig. V derived from her paper shows several interesting findings. First, the equal sex ratio of the cases, quite unlike bronchial carcinoma; second, the increasing number of cases recently. This is almost certainly a real increase of incidence as these tumours have been indexed in the records of the Pathology Department at the London for so long. Thirdly, of the group found on a retrospective survey of residence and occupation to have had an association with asbestos dust, over a third (11 out of 31) had contact with asbestos only outside industry, either living near a factory or through dusty clothes, etc., brought home from work. Three control groups in this survey showed significantly low exposure to asbestos and a difference in the area of residence.

In this investigation nearly a third of the cases gave no history of exposure to asbestos (though a proportion of this third had asbestos bodies in the lungs). There are many possible explanations for this; it was a retrospective study so that information about many of the cases was slender. In the more recent series where the records have been more complete the association between the tumours and exposure to asbestos has been even closer but, of course, once an association has been demonstrated material collected in this way may be biassed, because individuals with a history of working with asbestos and who develop symptoms suggestive of pleural effusion may be referred to those with experience of these cases.

These investigations in U.K. have rapidly confirmed the findings in South Africa of an association between asbestos exposure and diffuse mesothelial tumours. They have shown there has been an important hazard, but it must be remembered the average latent period from first exposure to the development of the tumour is about 40 years, and this makes it very difficult to assess the present hazard. They have as yet added little to the quantitative assessment of the risk as between one type of fibre and another, on account of mixed exposures in most cases. But taking the whole picture they have confirmed rather than contradicted the findings in South Africa. Where the proportion of chrysotile used has probably been high, the number of mesothelial tumours seems to be low, but this may be partly due to differences in past dustiness. The groups collected in U.K. have also confirmed that these tumours occur in the absence of asbestosis in some cases. Fig. VI summarises for U.K. the distribution of known cases up to 1964, but the pattern is changing as the search is extended and intensified. The association with the ports is in part related to the use of the material for lagging in ships.

In other countries the association between diffuse mesothelial tumours of the pleura and exposure to asbestos has been confirmed. In many cases the details of exposure are not known (Vander Schoot, 1958; Koenig, 1960; Frankel and de Jager, 1961). In Canada (Cartier, 1962) and in U.S.A. (Mancuso, 1963 and 1964) exposure was probably to chrysotile only, though details of occupational histories were not available. In other instances (Selikoff et al, 1965) exposure to crocidolite was thought unlikely. In North-West Australia, cases associated with crocidolite exposure have been reported (McNulty, 1962).

Table 8 summarises the number of known tumours in South Africa, U.K., and North America at the present.

The recent discoveries concerning these tumours raise many questions which cannot yet be adequately answered - for example :

(1) Are asbestos bodies commonly present in the lungs of the general population?

Table 9

The answer is apparently more commonly than most people would have suspected a few years ago! In consecutive autopsies in hospitals over age of about 50, the prevalence has varied from about 5 to 50% (Thomsen et al, 1963 and 1965; Hourihane, 1964; Elmes et al, 1965; Cauna et al, 1965; Heurman,

1965). The methods for search have varied so that valid quantitative comparisons between one city or one country and another are not yet possible. More work on this problem is needed.

(2) Are the bodies really asbestos bodies?

The pathologists seem generally agreed that the answer is probably yes in most instances, but there is an urgent need for positive identification of the type of fibres in a representative sample using x-ray diffraction and other methods.

(3) What is the medical significance of asbestos bodies in the lungs in consecutive autopsies?

The answer is that nobody yet knows. They are evidence of past exposure but whether the presence of sparse bodies in the lung carries with them any important excess morbidity or mortality, only future research will reveal.

(4) What is the relation between pleural plaques and mesothelial tumours?

There are two aspects to this question. First, do mesothelial tumours develop on the site of pleural plaques? Second, is there a high incidence of mesothelial tumours where the incidence of plaques is high? The answer to the first part is that occasionally it may be difficult to differentiate histologically between the fibrotic plaques and the fibro-sarcoma-like variety of the mesothelial tumour, but in general there is no clear evidence of the plaques being a procursor of the tumours.

Evidence is conflicting on the second part. In Finland, many plaques have been reported by Kiviluoto (1965) and also at post mortem (Neuman, 1965), but the incidence of mesothelial tumours is very low. In South Africa plaques were common in the survey of the population in the North West Cape where the mesothelial tumours incidence was high, but plaques were also common in the survey in the Transvaal area where no mesothelial tumours have yet been reported (Sluis Cremer, 1965).

(5) Is there an important difference in the risk associated with different types of fibre for equal exposures? What steps are being made to establish this quantitatively?

The answer here is that in South Africa a continuous search is being maintained to detect any cases of mesothelial tumour coming from the amosite and chrysotile areas; so far none has been discovered (Sluis-Cremer, personal communication). In Canada a start has been made to investigate systematically

this and other problems associated with chrysotile mining. But there are other countries in the world where a search might be valuable. For example, in Cyprus, where chrysotile only has been mined since classical times. Also, perhaps Czechoslovakia where only Russian chrysotile may have been used, and where no mesothelial tumours have been discovered in surveys of asbestos workers (Pachner, 1965). The International Union against Cancer (U.I.C.C.) is helping in this work following the report of its Working Party on Asbestos and Cancer in 1964. A small international committee has been established to help those with opportunities for contributing to any aspects of this whole problem, to meet and co-ordinate their investigations.

Conclusion

In Fig. VII I have attempted to show diagrammatically a summary of the health hazards associated with asbestos related to time and world production of the mineral. This indicates the long interval between the start of the industry and the recognition of asbestosis; then an interval before the excess bronchial carcinoma risk was detected and only quite recently the discovery of a related hazard of the pleural and peritoneal tumours. The very rapid expansion of the industry since the War is impressive and we must remember that the mesothelial tumours now being detected relate to output and conditions as they existed about 30 to 40 years ago.

I have said enough to prove that this invaluable mineral, for which there are no substitutes for some of its uses, has health hazards greater than were recognised at the time Wyers was writing, or indeed when Sutherland was contributing an earlier lecture in this series (1960).

I think Wyers was wrong in his conclusion about the effectiveness of legislative measures in eliminating asbestosis. He was right about the differences in the effect of the fibres, but probably got amosite and crocidolite in the wrong order. He was a long way ahead of his time in drawing attention to the case of endothelioma.

There are many difficult scientific, administrative, and technical problems ahead. We are fortunate in this country in having perhaps more diversity of skilled people interested in the asbestos problem than anywhere in the world, and who are keen to pool their knowledge to solve the problems. This was clear at the New York Academy of Sciences Symposium on 'The biological

effects of asbestos', held last autumn, where about half the contributions were from U.K. The 'Proceedings' of this Symposium, to be published next month, contain much of the evidence briefly referred to in this lecture.

There are many other aspects of the new work which I have had to omit - for example, studies of lung function; classification of the radiological appearances; and methods of dust sampling.

I should like to end by recording the excellent co-operation we have had from Industry and the Unions in our research in this interesting, difficult, and important problem. No request for help or information has been refused. The views in this lecture are, of course, my own, but I have been greatly assisted by discussion with my colleagues at the Pneumoconiosis Research Unit, and particularly Dr. J. C. Wagner; members of the Asbestosis Research Council; and members of the Pneumoconiosis Panels of the Ministry of Pensions and National Insurance; and many people in other countries with whom contact has been made possible through the International Union against Cancer.

"Asbestos - Recent Studies on its Biological Effects"

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Table 1.

## TYPES OF ASBESTOS

| | Production 1962 000 tons* | Colour | Composition (%) Si | Mg | Fe | Sources |
|---|---|---|---|---|---|---|
| Chrysotile | 1,700 | White | 40 | 38 | 2 | Canada; S. Africa; S. Rhodesia; U. S. A.; Italy; Cyprus; |
| Crocidolite | 132 | Blue | 50 | - | 40 | S. Africa (Cape); Australia; |
| Amosite | 75 | Brown | 50 | - | 40 | S. Africa (Transvaal); |
| Anthophyllite | 11 | White | 58 | 29 | 6 | Finland; Italy; |

* excluding U. S. S. R.

Table 2.

SECULAR CHANGES IN DEATHS WITH ASBESTOSIS IN A FACTORY

| | ALL CASES | | | | CASES WITH T. B. | | | |
|---|---|---|---|---|---|---|---|---|
| | 1931-46 | | 1957-64 | | 1931-46 | | 1957-64 | |
| No | 115 | | 71 | | 36 | | 4* | |
| | ♂ | ♀ | ♂ | ♀ | ♂ | ♀ | ♂ | ♀ |
| Average exposure (years) | 16.5 | 7.3 | 15.1 | 8.2 | 10.5 | 6.4 | 25.3 | 10 |
| Average duration of disease | 6.4 | 6.4 | 7.3 | 7.2 | 5.8 | 6 | 9.3 | 14 |
| Age at death (mean) | 46.5 | 37.5 | 56.0 | 57.7 | 34.4 | 34.9 | 57.3 | 42 |

* Healed T. B. in 3 cases.

Table 3.

# ASBESTOSIS

## CASES DIAGNOSED 1955-1963*

## ANALYSED BY PRINCIPAL OCCUPATION AND DATE OF ENTRY IN INDUSTRY

| | -1933 | 1933-1950 | 1950- | Total (%) |
|---|---|---|---|---|
| Opening ) Disintegrating ) | 3 | 35 | 3 | 41 (16.6) |
| Insulating | | | | |
| ó Laggers | 41 | 31 | - | 102 (41) |
| ó Sprayers | 1 | 8 | 4 | |
| Mattress | 2 | 1 | 2 | |
| ó Others | 3 | 9 | - | |
| Textile | | | | |
| Carding ) Spinning ) Weaving ) | 16 | 30 | 7 | 53 (21.5) |
| ó Slab and Pipe Making | 3 | 15 | 2 | 20 (8) |
| Brake lining | 3 | 1 | - | 4 (1.6) |
| ó Miscellaneous | 10 | 17 | - | 27 (11) |
| | | | | 247 |

* 4 M.P.N.I. Panels - London, Manchester, Newcastle, Sheffield.

ó Not in "Scheduled" Occupations.

Table 4.

U.K. Pneumoconiosis
New Cases Diagnosed under the
Industrial Injuries Act 1946

| Type | 1959 | 1960 | 1961 | 1962 | 1963 | 1964 |
|---|---|---|---|---|---|---|
| Coal Mining | 3523 | 3279 | 2768 | 2171 | 2268 | 1215 |
| Byssinosis | 466 | 403 | 388 | 381 | 354 | 271 |
| Asbestosis | 37 | 29 | 43 | 52 | 67 | 83 |
| Pottery | 89 | 50 | 68 | 99 | 76 | 65 |
| Foundry and Steel Dressing | 177 | 118 | 135 | 105 | 110 | 95 |
| Slate | 35 | 43 | 33 | 47 | 38 | 69 |
| Refractories | 22 | 16 | 28 | 24 | 24 | 13 |
| Building, etc. | 45 | 33 | 49 | 44 | 42 | 48 |
| Others | 113 | 86 | 99 | 67 | 63 | 60 |
| Total | 4507 | 4057 | 3611 | 2990 | 3042 | 1919 |

Table 5.

## SECULAR CHANGES IN PREVALENCE OF ASBESTOSIS IN A FACTORY

| Years' Exposure | 1929 | | 1960 | |
|---|---|---|---|---|
| | No. | % Asb: | No. | % Asb: |
| 10-14 | 84 | 32 | 225 | 0.4 |
| 15-19 | 28 | 54 | 140 | 0.7 |
| 20-24 | 21 | 81 | 33 | 3.0 |

(From Bamblin W. P. Ann. occup. Hyg. 1960)

Table C.

Incidence of Asbestosis and Asbestosis and Lung Cancer 1924 - 1962

| Period | Males | | | Females | | |
|---|---|---|---|---|---|---|
| | All Asbestosis | Asbestosis and Cancer of Lung | % with Cancer of Lung | All Asbestosis | Asbestosis and Cancer of Lung | % with Cancer of Lung |
| 1924 - 1930 | 13 | - | Nil | 7 | - | Nil |
| 1931 - 1940 | 66 | 12 | 18.2 | 82 | 5 | 6.1 |
| 1941 - 1950 | 92 | 20 | 21.8 | 44 | 4 | 9.1 |
| 1951 - 1960 | 149 | 46 | 30.9 | 43 | 13 | 30.2 |
| 1961 - 1962 | 49 | 22 | 44.9 | 11 | 2 | 18.2 |

Table 5.

MORTALITY FROM CANCER OF LUNG AND PLEURA IN WORKERS IN "SCHEDULED AREAS" IN AN ASBESTOS TEXTILE FACTORY

| No. | Sex | Exposure at 1/6/33 | 30/6/64 | Lung Canc: Obs: | Exp: |
|---|---|---|---|---|---|
| 57 | M | > 10 yr. | >20 yr. | 15 | 1.06 |
| 45 | M | 5-10 yr. | | 5 | 1.01 |
| 16 | M | < 5 yr. | | 1 | 0.27 |
| 104 | M | None | | 1 | 0.78 |
| 489 | M | None | >10 yr. | 6 | 5.78 |
| 190 | F | None | | 1 | 0.15 |

(From Knox, Doll, and Hill, 1964)

Table 8.

## ASBESTOS EXPOSURE AND MESOTHELIOMAS

| Country | No. of Cases | Type of Exposure |
|---|---|---|
| SOUTH AFRICA<br>1956-1962 | 120 | Crocidolite |
| UNITED KINGDOM<br>1962-1964 | 160 | Mixed dust |
| UNITED STATES OF AMERICA<br>1963-1965 | 16 | Chrysotile |
| CANADA<br>1952-1964 | 6 | Chrysotile |

Table 9.

## UNSOLVED PROBLEMS

(1) Are asbestos bodies and fibres common in the lungs of the general population?

(2) Are these bodies really asbestos bodies?

(3) What is the medical significance of asbestos bodies in the lungs in consecutive autopsies?

(4) What is the relation between pleural plaques and mesothelial tumours?

(5) Is there, for equal exposures, an important difference in the risk of mesothelial tumours for different types of fibre? What steps are being taken to investigate this problem?

Fig. 11

DUST ELIMINATION RATES

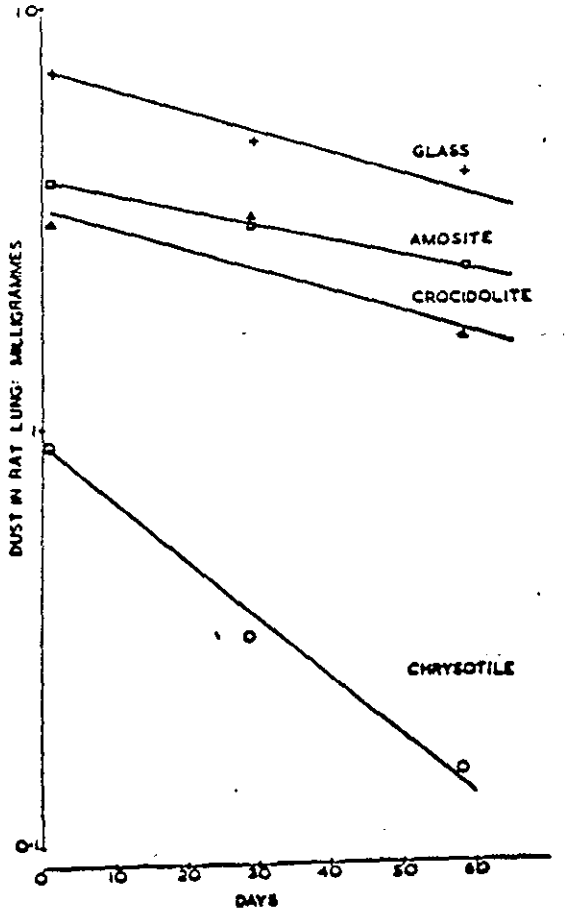
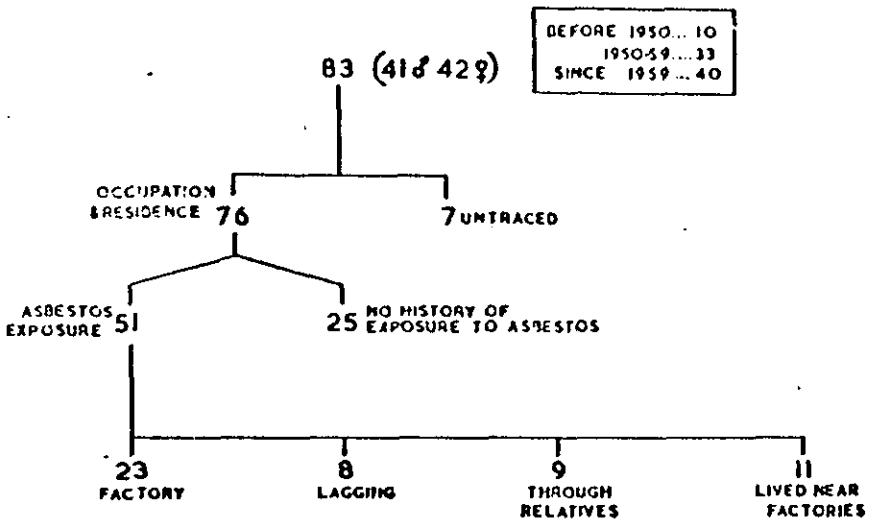


Fig. III

Fig. V

DIFFUSE MESOTHELIAL TUMOURS AT THE LONDON HOSPITAL OVER 30 YEARS




(10 ONLY WORKED IN SCHEDULED JOBS (1931))

(FROM HOURIHANE & NEWHOUSE 1964-5)

Fig VI

MESOTHELIOMAS IN GREAT BRITAIN

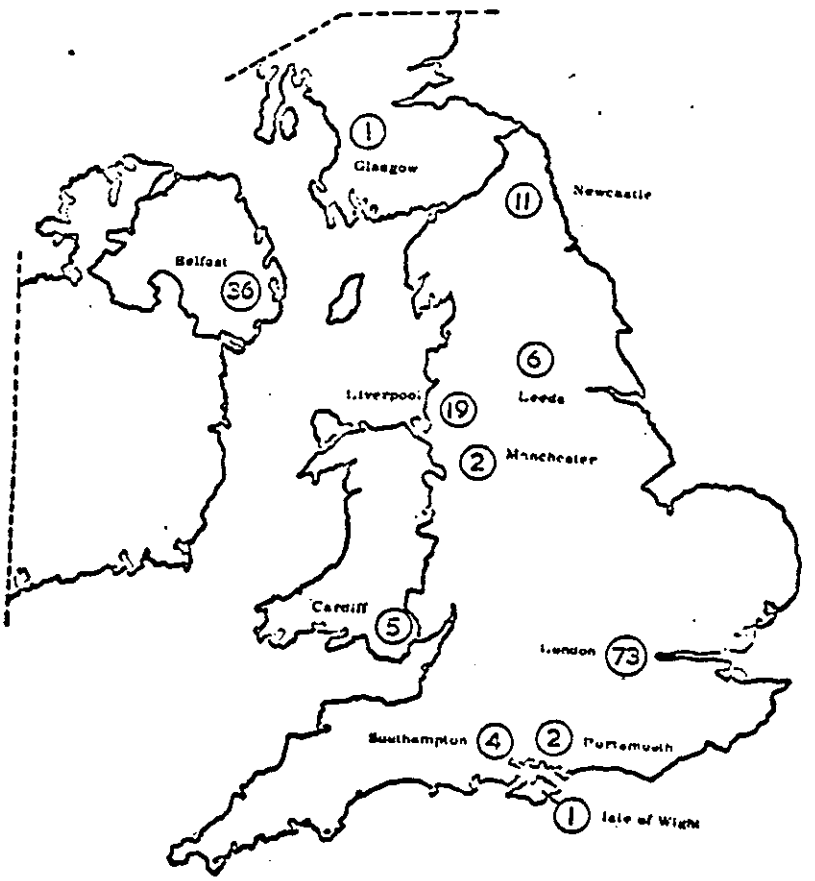
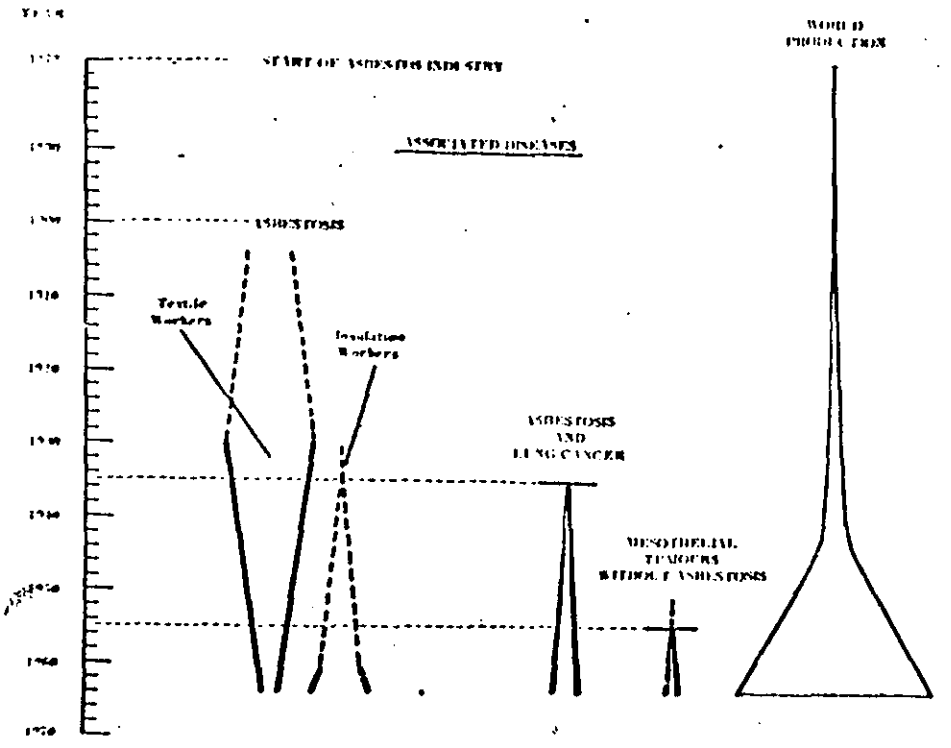


Fig. VII


ASBESTOSIS
Textile Workers
Insulation Workers
ASBESTOSIS AND LUNG CANCER
MESOTHELIAL TUMOURS WITHOUT ASBESTOSIS