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EPIDEMIOLOGY OF DIFFUSE MESOTHELIAL TUMORS:
EVIDENCE OF AN ASSOCIATION FROM STUDIES IN
SOUTH AFRICA AND THE UNITED KINGDOM

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The first South African case of diffuse mesothelioma of the pleura with asbestos bodies in the lung was diagnosed at the Pneumoconiosis Research Unit in Johannesburg in 1956. Earlier than this C. A. Sleggs, Superintendent of the West-End Tuberculosis Hospital in Kimberley, had observed an increasing number of cases admitted to his hospital with the diagnosis of pleural tuberculosis, who did not respond to antituberculous therapy. These cases subsequently died from pleural malignancy which, Sleggs was informed, was secondary to some other internal neoplasm. He was puzzled by this, as the incidence of malignancy among his patients was in general surprisingly low. A few months after the original case, a number of patients from Kimberley were transferred to Johannesburg for investigation, and specimens taken at thoracotomy showed histological features similar to those seen in the original mesothelioma. Paul Marchand, a thoracic surgeon, went down to Kimberley to biopsy the remainder of Sleggs' cases and within a year 16 cases of diffuse mesothelioma had been diagnosed histologically.

In trying to explain this mysterious epidemic we suggested that asbestos might play some part in the etiology. The grounds for this were extremely flimsy; asbestos bodies had been found in the lungs of the first case, and large crocidolite asbestos desposits were 200 miles west of Kimberley at the nearest point. At first, this hypothesis received little support since none of the original cases had been referred from the asbestos fields. Their occupations were housewives, shepherds, farmers, lawyers, and insurance agents. None of them admitted to mining asbestos. In the meanwhile, other cases were occurring both in Kimberley and elsewhere in South Africa. From one of these, Marchand established that although he was not a miner, his father had been manager of a small asbestos mine, and he had played around the mine and on the dumps as a boy. Sleggs and Marchand then requested all the surviving patients and relatives of the others, and obtained detailed life histories. By 1959, they had been able to establish an association with the Cape Asbestos fields or the industrial use of asbestos in 32 of 33 patients with histologically proven pleural mesotheliomas. The majority of these patients had not actually worked with asbestos but had lived in the vicinity of the mines and mills, and some had left the asbestos fields as young children, or in their teens. The average

period between first exposure and development of the tumors was 40 years.

As a consequence of this the investigation was intensified, with the support of the South African Government, the asbestos producers, and the South African Cancer Association. The findings of the epidemiological surveys of this area have been presented by G. K. Sluis-Cremer and C. P. Theron. Ian Webster, who has been in charge of the Pathology Division of this Unit throughout these investigations, will describe some of the problems of diagnosis and the experimental work.

At the end of 1961 we had diagnosed a total of 87 pleural and two peritoneal mesotheliomas. In only two cases had it not been possible to establish a history of exposure to asbestos dust and only in one of the cases was there no definite exposure to crocidolite. This was a man who had made fireproof clothing while serving in the South African Air Force during the last war. The youngest case diagnosed, aged 21, gave a history of a very brief exposure as an infant when he was taken to a "cobbing" site by his mother from the age of six weeks until he was weaned. Of the 87 cases, 12 had had industrial exposure and the rest came from the region of the Cape Asbestos fields. More than half of these people had not been employed by the asbestos industry. A few of them had had occupational exposure — two men had been road workers in an area where before 1940 many of the roads were surfaced with material from the asbestos dumps, and one man had worked in a railway yard where the same material had been used as ballast for the rails. Another man had been employed digging wells in the vicinity of the asbestos mines.

The remainder of the people had had environmental exposure due to living in the vicinity of the mills and dumps in an arid, windswept region. An example of this was a woman who was born in a town on the asbestos fields in 1900. She left there at the age of five, and was in good health until she was 55 when she developed a pleural effusion. She died from a pleural mesothelioma eighteen months later. Detailed questioning on her childhood revealed that she attended an Infants School near to an asbestos dump. The children used to enjoy sliding down this on their way home. Two of her playmates at this school have subsequently died of the same condition.

Even among those working in the asbestos mines, the actual exposure seems to have been slight — a number of them cobbled under relatively dust-free conditions. In these cases, there was no evidence of asbestosis in the lungs, but only a few asbestos bodies and fibers in the air spaces. Therefore, the association appeared to be with exposure to asbestos dust rather than a sequelae of asbestosis.

A puzzling feature of the South African investigations is that although the country produces approximately the same amount of crocidolite, amosite and chrysotile (if Swaziland is included), no case of mesothelioma has been reported from either of the other areas in spite of an intensive investiga-

tion. This is particularly true of the mining area, crocidolite mining and milling and exposure seems to be the most significant factor.

There are two possible explanations. The first started in 1890, when the annual production was about 30 years more than 40 years. The second is that the aromatic hydrocarbons are a significant factor.

Webster has diagnosed well over 100. The first case was 10 years ago, at a time when the annual production was more than 80,000 tons, which was subsequently milled to produce asbestos.

When I came to the investigations at the Unit, in order to see and mesotheliomas and long-established and long-established conducted in cooperation Gloyne's first observation, workers, the Inspector, W. D. Buchanan Annal.

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tion. This is particularly remarkable because on the edge of the amosite mining area, crocidolite also occurs, sometimes in the same seams. The mining and milling methods are similar and the chance of environmental exposure seems to be the same.

There are two possible explanations for this. Firstly, crocidolite mining started in 1890, whereas the other two areas were only mined to a significant extent 30 years later. Nevertheless they have been operational for more than 40 years. Secondly, Harington's discovery of the polycyclic aromatic hydrocarbons adsorbed onto the crocidolite fiber. This may be the significant factor.

Webster has diagnosed further cases since 1961, and the total is now well over 100. The most disturbing fact of this investigation is that 40 years ago, at a time when most of these cases had their initial exposure, the annual production of crocidolite was less than 10,000 tons a year. Today more than 80,000 tons are produced and a large proportion of this is intensively milled to produce short clean fibers.

When I came to the United Kingdom it was decided to continue these investigations at the Medical Research Council's Pneumoconiosis Research Unit, in order to see whether this association between asbestos exposure and mesotheliomas could be confirmed in Britain — a country with a large and long-established asbestos industry. The investigations are being conducted in cooperation with the industry and the Ministries concerned. Since Gloyne's first observations in 1935 of pulmonary malignancy in asbestos workers, the Inspectorate of Factories has been concerned with this problem. W. D. Buchanan has reported their findings up to date earlier in this *Annal*.

To find out if cases of mesothelioma were occurring among people who had been exposed to asbestos, we approached the problem through those thoracic surgery and pathology departments who had published accounts of these tumors. We asked people to cooperate in finding out how many of their cases had been associated with asbestos dust exposure. The evidence for this could be established in the following ways:

- examination of lung tissue, if available, for the presence of asbestos bodies and fibers.
- in the case of living patients by examining the sputa for asbestos bodies and fibers.
- by obtaining detailed occupational and environmental histories from the patients or their relatives.

The excellence of their response you can read in the papers from London, Belfast and Liverpool. Unfortunately, all those concerned in this investigation were not present at the Conference, although we were uncommonly well represented. I will, therefore, add briefly an account of the findings in Cardiff, Newcastle and Portsmouth. Some of these reports are of a

preliminary nature and the investigations in Britain are far from completed. However, we have been able to show evidence of asbestos exposure in at least as many cases of mesothelioma of the pleura and peritoneum as have been diagnosed in South Africa.

The South African finding has been confirmed that the association is with asbestos exposure, and not necessarily with asbestosis. In a number of cases the actual exposure has been slight, in one case three months of boiler lagging, and the latent period between initial exposure and diagnosis of tumor is again about 40 years.

At Sully Hospital near Cardiff, Roger Seal has diagnosed six cases of pleural mesothelioma. The histories of these patients have been followed in detail by members of Professor A. L. Cochrane's Epidemiological Unit, and in five of the six cases, there has been a definite history of asbestos exposure.

In Newcastle-upon-Tyne, T. Ashcroft of Professor A. G. Heppleston's Department, has found 13 histologically diagnosed cases, and evidence of asbestos exposure in 11. In Portsmouth, R. D. Clay has found evidence of asbestos exposure in two out of his three cases.

Of Britain's main ship-building areas — Belfast, Tyneside, Merseyside, and Clydeside — we have not yet investigated Clydeside but two cases have been referred by P. D. Stewart at Dunbarton. The most disturbing fact is that during the investigation new cases in increasing numbers have been reported from all these areas.

In Britain, it has not been possible to obtain positive, clear evidence implicating a single type of asbestos as in South Africa, since the majority of cases have been exposed where several types of asbestos were used. However, definite evidence of crocidolite exposure has been established in a majority of cases, and no indisputable case of pure chrysotile exposure has yet been discovered.

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