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# SOME PATHOLOGICAL ASPECTS OF ASBESTOSIS IN THE UNION OF SOUTH AFRICA.

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There are considerable deposits of asbestos in the Union of South Africa[1]. Dr. Sleggs has dealt with the Griqualand West deposits which are said to be the largest in the world. In the Transvaal, amosite asbestos is mined on an extensive scale in the Lydenburg District, and on a smaller scale near Pietersburg. The large chrysotile mines are outside the Union, in Southern Rhodesia and Swaziland. Chrysotile is mined to a lesser extent in the Transvaal in the region of Carolina. The first map shows the localities of the various mines, and the different asbestos deposits[2].

Asbestos minerals are fibrous silicates. The fibre has a similar composition to the ore in which it is found. Crocidolite and amosite both occur in banded iron stone and they have a similar composition. In some of the Transvaal deposits they occur in the same seam[3]. These two minerals have a high iron content and contain little magnesium. The reverse of this is true for chrysotile, which occurs in serpentine.

In the Transvaal the larger mines are mined on the adit principle. Conditions in the mines are damp and very little dust is produced. The ore is then cobbed, and dried in the sun before milling. This dry milling is the major factor in the production of the dust.

The study of Asbestosis in South Africa started in 1926 when Simson[4] studied the Pathology and Slade[5] the clinical investigation. Both were concerned with Chrysotile Miners. Slade demonstrated that asbestosis was far more common among the mill workers than the miners and that exposure to asbestos dust predisposed to acute respiratory infections.

In this Unit work on asbestosis started in 1954. The main problem was to ascertain, whether the pulmonary lesions and complications following the inhalation of crocidolite and amosite dusts, were the same as those associated with exposure to chrysotile. Material from asbestos miners and experimental animals has been studied. Some of the investigations undertaken will be described briefly and the more significant results discussed.

A) Autopsy and Biopsy Material. The autopsy material received

What is a biopsy?

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at the Pneumoconiosis Bureau has been limited, as the asbestos mines have only been registered from 1953. The first cases received from the Transvaal Mines were during 1954, but no cases were received from the Cape Fields until 1958. In addition, evidence of asbestosis has been found in lung biopsies. The disease was unsuspected in the majority of these cases.

The following table shows an analysis of the material received between 1954 and 1958. (Table 1 attached.)

The most interesting feature of the table is that of a total of 68 Bantu and Coloured autopsy specimens submitted to the Pneumoconiosis Bureau in which there was evidence of asbestosis, 38 were not from the asbestos mines. Almost all of these were gold miners in whom we have not been able to obtain a history of exposure to asbestos dust. Asbestosis was a major factor in the cause of death of 16 of the cases. 22 showed evidence of active tuberculosis. This figure is similar to that given by Gloyne[6] in England but it is considerably higher than Lynch's[7] findings in the United States. In 11 cases there was evidence of either a lobar or confluent broncho pneumonia. The latter was the more common finding, and in some of these cases it may well have been a terminal phenomenon. Definite evidence of cor pulmonale was only observed in 5 cases. The finding of silicosis in 9 cases may have been due to gold mining, for it should be noted that 7 of the cases with silicotic lesions had had service on the gold mines. The question of malignant neoplasia and haemorrhagic pleural effusion is an extremely interesting one in regard to the mesotheliomas, which will be discussed later in the paper.

The macroscopic lesions of asbestosis observed are similar to those described by Gloyne[8], except that, whereas Gloyne[8] described the most marked lesions as occurring in the lower lobes, in this series there was a tendency for such lesions to occur in the upper lobes. In some cases large areas of apical fibrosis were also seen.

The microscopic appearance of sections from the lungs of cases both from the amosite and crocidolite mines are identical to those described by Gloyne[8] and Lynch[7], the lesion being essentially one of an interstital fibrosis. In the early cases this is seen to be peribronchiolar in distribution. Later the lesion becomes diffuse with alveolar wall thickening and peribronchiolar and perivascular fibrosis. In marked cases of asbestosis large areas of fibrosis are seen. Asbestos bodies, and fragments of asbestos fibres are seen in both the interstitial tissue and in the air spces at all stages of the disease. In addition a large amount of iron pigment is present which is probably derived from the ore. Curved and circular bodies are commonly found in sections from the lungs of crocidolite miners.

Pleural fibrosis was a common finding in the cases of Gloyne[8] and Lynch[7]. Similar features have been observed in our cases

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from both the amosite and crocidolite mines. The changes varied from a thin veiling of the visceral pleura to a dense cartilage-like layer of tissue involving both pleurae. In none of the cases examined have asbestos bodies or fibres been found beyond the elastic lamina of the visceral pleura, although aggregations of asbestos bodies, fibres and dust particles are common in the peripheral lung tissue.

These findings agree with those of Lynch [7], but Gloyne [8], states that he has observed small stumpy asbestos bodies in the pleural tissue. Gloyne [8], described the appearance of horn-like pleural plaques. Although these have been observed in the radiological investigation of workers on the Cape Asbestos fields, we have only encountered one such case in the autopsy material so far submitted. Several of these plaques have been observed in the biopsy material. Plaques occur both on the visceral and parietal pleurae, and consist of dense hyalina fibrous tissue in which foci of calcification are found. Tuberculous pleurisy has been a common finding in autopsy material, and was observed in three cases biopsied because a mesothelioma was suspected.

In two autopsy cases from Kuruman, both right lungs were atelectatic and covered by an organizing haemorrhagic exudate. The visceral pleurae were about 0.5 cms. in thickness. Histologically these pleurae were shown to consist of loosely woven fibrous tissue in which numerous proliferating fibroblasts and a moderate number of atypical mesothelial cells were seen. There was evidence of asbestosis in both these cases.

The most interesting and significant of the pleural changes have been the presence of diffuse mesotheliomas. The clinical and radiological presentation of these cases has been described by Drs. Sleggs and Hurwitz[9].

Mesotheliomas.

The origin and nature of diffuse mesotheliomas of the pleura and the multipotentialities of the mesothelial cells have been clarified in the papers of Klemperer and Rabin [10], Stout and Murray [11], Miller and Wynn [12]. In 1957 Smart and Hinson[13] published a comprehensive review of the subject. One case, from a chrysotile factory is reported by Doll [14]. This is the only case of mesothelioma associated with asbestosis that I have been able to find in the literature.

In South Africa these tumours are rare. Higginson and Oettle[15] did not observe a single case in their survey of malignant tumours occurring in the non-European population of the Witwatersrand. With the exception of the present series, no neoplasms of this nature have been observed in the Pathology Department of the South African Institute for Medical Research during the last five years. During this period more than 100,000 biopsy and post mortem specimens were received from widespread regions in Southern Africa.

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The first case of a diffuse pleural mesothelioma was received in February 1956. The patient was a Bantu gold miner with a clinical diagnosis of tuberculous pleurisy and empyema. At the autopsy examination the large gelatinous tumour (shown in the next figure 3) was found in the right thoracic cavity. No other primary source of the tumour was found. Histological sections (figures 5 and 6) show the features of a papillary mesothelioma similar in appearance to those described recently by Godwin 16 and McGaughey 17. In addition asbestos bodies were found abutting on the pleural elastic lamina (figure 7) and there was a slight degree of asbestosis in the lungs. Although no history of exposure to asbestos dust has been received in this case, it was subsequently discovered that he was born in the Kuruman District.

During the last three years, in addition to the cases described by Dr. Sleggs 9, we have received a further 9 cases in three of which a definite association with the Kuruman District has been established. In a further case from Kuruman, with a long mining history, neoplastic cells have been observed in the pleural fluid, with confirmatory radiological and clinical findings but a biopsy has been refused. One of the additional cases was of particular interest. This was a middle aged Bantu male with a marked haemorrhagic pleural effusion. He gave a history of loading crocidolite asbestos into trucks at a mine in the Kuruman District for one year, "many years ago". At thorocotomy the right lung was found to be bound down by a thick white fibrous tissue. The parietal pleura was about 0.5 cms. in thickness and white in colour. Sections from both these pleural layers (figures 8 and 9) showed the presence of fibrosed pleural tissue in which evidence of a mesothelioma are seen. Fragments of asbestos bodies and dust were seen in the interstitial tissue immediately below the pleural elastic lamina (figure 10). Further asbestos bodies were observed in the air spaces.

The following two figures show the cases of mesothelioma that have been diagnosed and the patients association with the Kuruman District. In the first of these charts (figure 11) I have divided the cases into 4 groups. The first group consists of 20 cases of mesotheliomas histologically confirmed (11 of which have been described by Dr. Sleggs 9). In the second group there are two cases in whom Dr. Sleggs performed needle biopsies of the pleura. The histology was suggestive, but there was insufficient material for a definite diagnosis. The third group consists of four cases which are believed to have been biopsied elsewhere in the Union. Although these cases have been included, the diagnosis has not been confirmed. In the fourth group there are three cases with atypical cells in the pleural fluid on which no biopsy material is available.

The second of these diagrams (figure 12) demonstrates the association of these cases with the Kuruman district. It can

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be seen that 14 of the histologically confirmed cases were either born or spent part of their early youth in the Kuruman District. No history has been obtained from remaining six of these cases. The majority of these cases were diagnosed on pleural biopsies. In two cases we have evidence of subsequent metastases being found at autopsy.

The histological features of these cases were remarkably similar to those illustrated by McCaughery [17]. There is usually a mixed pattern of a tubular-papillary appearance with small cellular areas. Clefts lined by a layer of flattened mesothelial cells, surrounded by proliferating fibrous tissue are seen. In one case the tumour was highly cellular and consisted of pleomorphic spindle cells. Examples of these tumours are shown in the next three photo micrographs (figures 13, 14, 15)

The possible association of these cases of diffuse pleural mesotheliomas with asbestosis has not been proved, but I feel that there is sufficient evidence to warrant a fuller investigation of the problem.

If exposure to asbestos dust is a factor in the development of these tumours, similar cases should have been expected in the Lydenburg District, as the native rock, ore and fibre are almost identical in both areas. As can be seen from the map (figure 16) two adeno-carcinomas have been received from this area, but as yet there is no evidence of mesotheliomas. This may be due to the fact that almost all the material received has been from men actually employed at the mines. Dr. Sleggs' findings suggest that the tumours develop 20 to 35 years after exposure to the dust. Therefore it is felt that before asbestos can be incriminated, a survey must be made of the Sekukiniland Reserve from where most of the Bantu labourers who have previously worked in these asbestos mines were recruited. Two autopsy specimens have been received from one mission hospital in the area. In addition asbestos bodies have been found in the sputa of 12 cases from this and neighbouring hospitals.

As a possible aid to the diagnosis of these tumours Dr. Harington, of this Unit, is investigating electrophoretic and chromatographic methods of separating hyaluronic acid from pleural fluid. Initially an attempt is being made to confirm the findings of Meyer and Chaffe [18], who state that hyaluronic acid is present in excess, in the pleural fluids of cases of mesotheliomas.

B) Animal Experiments. In dusting experiments we have exposed monkeys, guinea pigs and rabbits to chrysotile and amosite. At present similar animals are being exposed to dust collected from a crocidolite mill.

The method of dusting has been described by Webster [19]. These experiments are preliminary investigations as only small numbers of animals were used. 16 Guinea pigs, 4 rabbits and three Vervat monkeys being exposed to a dust concentration of an average

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of 37,000 particles/per cc. in the case of the chrysotile dust and 20,000 particles per c.c with the amosite. A further 12 guinea pigs were exposed to the chrysotile for a period of 2 years. In both these experiments the guinea pigs were killed at monthly intervals. The results of the chrysotile experiment were described at the 1957 Conference at Munster [20]. It was shown that a very fine chrysotile dust with the majority of particles (87.5%) less than 1 micron produced marked pulmonary fibrosis in guinea pigs after 22 months.

Initially these results appear contrary to the finding of Gardner [21], and Vorwald [22] in their experiment with Ball Milled chrysotile dust. However the concentration of dust was approximately 10 times as much as in their experiments. In addition the particle counts in this experiment were done with thermal precipitators and subsequent examination of the dust showed the presence of approximately 6% of long fibres.

The amosite dust used was a comparatively coarse fibred dust and is that used commercially for the making of asbestos cement. This dust was difficult to suspend in the air in suitable concentration. The method of dusting was modified and a concentration of approximately 30,000 particles/cc. obtained. It was found that the large particles rapidly settled and that the thermal precipitator counts were similar to those obtained with the chrysotile. The percentage of large fibres being about 8%. This dust produced similar lesions in guinea pigs as was previously described in the chrysotile experiment, but the exposure to this dust was only continued for 14 months. The histological appearance of sections from the lungs of this animal were similar to those seen in the guinea pig exposed to chrysotile for the same period. Asbestos bodies were observed in the sections from the animal exposed to amosite.

Rabbits showed only slight lesions after an 18 month exposure to chrysotile. Two of the rabbits exposed to amosite for 14 months died 4 to 7 months after this exposure with evidence of cor pulmonale and right ventricular hypertrophy. Slight diffuse fibrotic lesions were present in their lungs which were more marked in the latter animal. The Vervet monkeys proved to be the most susceptible animals to both these dusts. The three animals exposed to chrysotile died within eighteen months all showing evidence of congestive cardiac failure and apparent right ventricular hypertrophy. There was a slight generalised interstitial fibrosis of the lungs in these cases when compared to human cases of asbestosis.

One of the monkeys exposed to amosite dust died of lobar pneumonia after seven months exposure. The second animal died after 14 months. The third animal was removed from the dust room after 14 months and died 6 months later with evidence of congestive cardiac failure. At autopsy of this last case the right ventricle appeared to be markedly hypertrophied and microscopic examination of the lungs revealed a moderate interstitial fibrosis of the lungs with numerous asbestos bodies in the interstitial tissue and

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air spaces . These lesions were more marked than those seen in the animal which had died after 14 months exposure.

These experiments are far from conclusive, but the results suggest that similar lesions are caused in experimental animals by both chrysotile and amosite. No opinion can be expressed at this time in regard to the fibrogenic properties of crocidolite.

## CONCLUSIONS.

In conclusion it would appear from the examination of human material and preliminary animal experiments with chrysotile and amosite that the lesions caused by exposure to amosite and crocidolite dust are essentially similar to those caused by chrysotile.

The problem requiring most urgent investigations is the high incidence of mesotheliomas on the Cape Asbestos fields, where a very serious hazard may exist.

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What is a biopsy? Exam of a live person!

TABLE 1.

ASBESTOS CASES 1954 - 1958.

| Place of Exposure | Total with evidence of Asbestosis | | Death due to Asbestosis | Other Lesions: Tuberculosis | Pneumonia | Pulmonary Neoplasm | Cor Pulmonale | Haemorrhagic Pleural Effusion. | Silicosis |
|---|---|---|---|---|---|---|---|---|---|
| Non-Eur. Autopsies Transvaal Mine | 18 | | 3 | 9 | 4 | 1 | 1 | 1 | 2 |
| Cape Mines | 12 | 68 | 5 | 2 | 3 | 0 | 2 | 4 | 0 |
| Unknown | 38 | | 8 | 11 | 4 | 2 | 2 | 3 | 4 |
| European Autopsies Transvaal Mine | 2 | | 0 | 0 | 0 | 1 | 1 | 0 | 1 |
| Swaziland Mine | 1 | 5 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Unknown | 2 | | 1 | 1 | 0 | 1 | 1 | 0 | 1 |
| Non-Eur. Biopsies Cape Mines | 4 | | | 2 | 0 | 1 | 0 | 3 | 0 |
| Unknown | 5 | 9 | | 0 | 0 | 0 | 0 | 0 | 0 |
| European Biopsies Cape Mines | 1 | | | 0 | 0 | 0 | 0 | 0 | 0 |
| Industrial | 2 | 3 | | 0 | 0 | 0 | 0 | 0 | 0 |
| Total. | 85 | | 17 | 25 | 11 | 6 | 7 | 11 | 14 |

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TABLE 11.

MESOTHELIOMAS.

| | Total | Autopsy | Biopsy | Association with Kuruman District. |
|---|---|---|---|---|
| Histologically Confirmed. | 20 | 3 | 17 | 14 |
| Histologically Suggestive | 2 | - | 2 | 2 |
| Histology Examined Elsewhere | 4 | - | 4 | 4 |
| Atypical Cells in Pleural Fluid - No Biopsy. | 3 | - | - | 3 |

TABLE 111

ANALYSIS OF MESOTHELIOMA CASES FROM KURUMAN DISTRICT.

| | Total | European Male | European Female | Non-European Male | Non-European Female | Definite Mining Transport Hist. | Born in Kuruman District | Childhood in Kuruman District |
|---|---|---|---|---|---|---|---|---|
| Histologically Confirmed | 14 | 4 | 4 | 4 | 2 | 2 | 7 | 5 |
| Histologically Suggestive | 2 | 1 | | 1 | | 2 | | |
| Histology Examined Elsewhere | 4 | 3 | | 1 | | 1M.2 T. | | |
| Atypical Cells in Pleural Fluid - No Biopsy. | 3 | 1 | | 2 | | 1 | 1 | 1 |

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