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ASBESTOSIS BODIES IN THE SPUTUM: A STUDY OF SPECIMENS FROM FIFTY WORKERS IN AN ASBESTOS MILL.

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The following communication is based on the examination of the sputum of fifty workers in an asbestos mill, some of whom had also been exposed to asbestos dust in other occupations. The atmosphere of the mill was at times so overcharged with dust that it was impossible to distinguish large objects at a distance even of 15 or 20 feet. Since concentration of dust is one of the main factors in the production of pulmonary changes, under the working conditions of the mill any reaction would be likely to occur rapidly. The cases examined comprised five europeans and forty-five natives; it is among the latter that the greatest exposure to dust occurs.

The examinations were carried out in the South African Institute for Medical Research from material supplied by Dr C. F. Slade, and as the mine was several hundred miles distant, specimens were sometimes not received until after a lapse of two or three days. In spite of this it was possible to demonstrate that the asbestosis bodies were intracellular in practically every case. A difficulty was encountered in the collection of specimens from natives. The ideal time for collection is in the morning, when, as a result of the overnight action of the ciliated epithelium of the bronchi, mucus from the lower respiratory tract has been brought up. In this mucus dust cells can usually be demonstrated, but in a few of the specimens, without dust cells, there were enormous numbers of asbestos fibres and crystals, the latter presumably derived from the lode which accompanies the fibre. This was apparently due to native boys filling the sputum receptacles in the evening just after coming on the shift, at a time

when the mouth and nasopharynx were loaded with dust. Fortunately it was possible to duplicate these samples, and a satisfactory specimen was obtained in all but two cases.

Technique.

Two series of films were made from each sample. In the first thick films of the mucoid portion were made and dried in a paraffin oven at 54° C. These were fixed with saturated mercuric chloride solution, one set being stained with hæmatoxylin and eosin, the other for tubercle bacilli. The second series was made from the centrifuged deposit after digestion with antiformin, as recommended by Stewart (1929). We found however that it was as easy to demonstrate asbestosis bodies in the direct films as in the antiformin treated specimens, and the former method had the advantage of showing both the cytology of the specimens and the intracellular development of the asbestosis bodies.

Results of sputum examination.

Burton Wood and Gloyne (1930) describe the sputum in pulmonary asbestosis as "thick and mucoid—frequently so thick as to resemble semi-coagulated egg albumen. In the latest stages small nummules of pus appear." In practically all our specimens there was a mucoid element, usually thin and watery, occasionally very thick. Pus cells were present in all specimens, but only a few contained obvious pus. The colour varied from grey to brown according to the amount of free asbestos and lode dust present. The free dust sometimes separated out as a deposit on standing. In all films asbestos fibres, small crystals of various types and colours, and amorphous debris both brownish and black were present, some of it intracellular. Pus cells, dust cells and epithelial squames were present in all specimens which contained bodies, but their proportions varied. Always the bodies were seen to be lying within dust cells. Many of the asbestos masses present were disintegrating into their constituent fibres.

Asbestosis bodies were present in 48 of the 50 cases examined. They show great variety in size and shape. Some are long and thin, much longer than the normal diameter of a dust cell, so that the ends are bent and tend to project on either side, where they are covered by cytoplasmic prolongations. The extremities show a bulbous enlargement and commencing segmentation is often seen. The colour is greenish- or golden-yellow. In the middle portion of the more slender bodies the fibre forming the core is very thinly coated with the golden-yellow material. Many of the bodies are sharply angled, suggesting incipient fracture. Should complete separation take place at this point it will give rise to two bodies of "crustacean" type, with bulbous heads, segmented bodies and tapering tails.

Analysis of cases.

The age of the workers ranged from 17 to 50, two-thirds of them falling within the 30 to 45 age-period. All but 10 had worked in the asbestos mill (or consecutively in mill and mine) for periods ranging from 3 to 9 years. In the others the period of service ranged from 7 months to 2 years. 18 of them had also worked underground in the gold mines. Cough was present in every case, dyspnœa in all but 10 and loss of weight in all but 21. These symptoms naturally varied in severity, but they showed fairly close parallelism in individual cases. Examination of the sputum for tubercle bacilli was negative in every instance.

As already mentioned asbestosis bodies were present in 48 out of the 50 cases examined. In 9 the antiformin method was negative when direct smears gave a positive result; in 11 the converse obtained. The two cases which gave negative results with both methods had been employed in the asbestos mill for 7 months and 2 years respectively. The shortest exposure to be followed by the appearance of the bodies was five months, and another case was positive after four months in the mill and three months underground. We are informed, however, that the atmospheric conditions in the mine are not such as are likely to be associated with asbestosis.

Simson (1929) has recorded the presence of asbestosis bodies in a human lung from a case with a history of only two months' exposure to dust, and Stewart (1930) in the lungs of guinea-pigs after three to five months' exposure in an asbestos factory. The bodies in Simson's case were well formed, and it would appear that the time necessary for their development must be even less than this.

Discussion.

It is obvious that the presence of asbestosis bodies in the sputum does not necessarily imply the existence of pulmonary fibrosis, although we are of the opinion that they indicate a reaction on the part of the alveolar epithelium. McCrae (1913) has shown that in silicosis most of the inhaled particles which reach the alveoli are of a size comparable with that of ordinary bacteria. In the case of asbestos dust the fibres which ultimately go to form the core of the asbestosis bodies (Burton Wood and Gloyne, 1930) may be 60 μ or more in length, and must therefore enter the alveoli lengthwise. Here they become phagocyted by dust cells (Simson, 1928) and we are of the opinion that it is in these or in similar phagocytes elsewhere that the changes which go to the formation of the bodies take place. There are several observations which seem to support this view. In carefully prepared direct films of sputum the bodies are always intracellular, and we have noted appearances which we would interpret as stages in their development. Briefly these are as follows. The fibre becomes coated with a pale greenish-yellow or golden-yellow substance giving the prussian blue reaction. This coating may be uniform except at the extremities, where there is a bulbous enlargement. The deposited material increases in amount and with the increase segmentation appears in most of the bodies. Later this segmentation becomes deeper, and even complete

fracture of the fibre may occur with formation of the "crustacean" type of body. The latter may continue developing, the tail again becoming slightly bulbous. We believe that the alveolar phagocyte and not merely the body fluid is the source of the material which goes to form the asbestosis body.

Asbestos fibre is not the only inorganic substance which, in the lung, becomes coated with material giving the prussian blue reaction. Mavrogordato (1922) has observed in the case of experimental quartzite inhalation that there may be associated with this substance intracellular yellow or red granules and sometimes yellowish plates, some of which give the iron reaction. In some of the dust cells in specimens which we have examined, both in silicosis and in asbestosis, we have noted granules such as Mavrogordato has described. Simson (1929) has observed, after 3 months, similar iron-reacting material around asbestos fibres injected subcutaneously, and Stewart (1930) has been able to produce typical iron-reacting asbestosis bodies by the subcutaneous inoculation of a suspension of asbestos dust.

Summary.

The inhalation of asbestos dust in high concentrations leads to the appearance of asbestosis bodies in the sputum in a large percentage of the workers exposed thereto. They were present in 48 out of 50 workers examined.

Asbestosis bodies were as easily demonstrated by direct thick films as by the antiformin method.

The sputum was always mucoid in character when there were no bronchial complications. It may resemble egg albumen. In none of the sputa were tubercle bacilli demonstrated.

Study of the intracellular asbestosis bodies in these cases suggests that they are formed by the deposition on the asbestos fibre of an iron-containing substance elaborated by the cell.

We wish to tender our acknowledgments to Dr Slade for the opportunity of carrying out this work, for the collection of the material and for the clinical data which he supplied.

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EXPERIMENTAL LIVER NECROSIS FROM SHALE OIL.

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(Plates I. and II.)

Davidson (1923, 1925) observed that carcinogenic tar caused liver necrosis in rabbits. The carcinogenic action of shale oil and its derivatives is widely recognised (Scott, 1923; Southam and Wilson, 1928; Leitch, 1922; Twort, C. C. and J. M., 1929 and Roussy, 1929). It appears that its action on the liver has hitherto escaped notice. No liver lesions were observed in man (Scott, 1930).

Experimental Procedure.

The oil used was shale oil No. 8(2), the carcinogenic action of which was described by C. C. and J. M. Twort in 1929. Dr C. C. Twort also sent a sample of the non-carcinogenic residue No. 8(2) CHR5, an oily substance having similar physical properties to the original oil.

In the preliminary experiment on six rabbits, each animal received a daily dose of 5 c.c. of undiluted oil per vaginam for three days. Within the week two of the rabbits had died from acute liver necrosis: the remainder were killed at the end of a fortnight. A fresh series of thirty-one rabbits was then used to investigate this liver damage. With one exception, each of the new rabbits received the oil intraperitoneally. In the longer experiments, additional doses were administered intrapleurally or subcutaneously. The dosage ranged from 1 c.c. to 10 c.c. and the experiments lasted from three days to several months. In the longer experiments the oil was diluted from 1/2 to 1/20 with liquid paraffin (*B.P.*). In order to exclude, as far as possible, vitiation of the experiments by naturally occurring disease twenty of the rabbits were subjected to laparotomy and biopsy of the liver at the commencement or during the course of the treatment. This procedure was adopted both in the long experiments and in the controls. In addition three rabbits were used to control the effects of laparotomy followed by the intraperitoneal administration of liquid paraffin alone.

Twelve mice, four guinea-pigs and eight rats were also given oil.

Dilution of the oil and the effects of its subjection to heating were also tested. The non-carcinogenic residue of the oil was administered intraperitoneally in single doses of 10 c.c. to each of six rabbits and in 3 c.c. doses to each of four rats. Twelve rabbits received an intraperitoneal dose of a 10 per cent. solution of scharlach R in olive oil, six had doses of 10 c.c. and six, of 5 c.c.

1. *Findings in rabbits.*

One of the three control rabbits given liquid paraffin at laparotomy was killed three weeks later and the other two at the end of seven