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THE PRESENCE OF THE ASBESTOS FIBRE IN THE LESIONS OF ASBESTOS WORKERS.

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The use of asbestos as a trade product has produced a new variety of pulmonary fibrosis. The clinical and radiological features of this disease have been well described by Burton Wood [1] and the morbid anatomy by Cooke [2] and Stuart McDonald [3]. A short investigation of the condition has been made by the writer, as recorded below, with a view to detecting, if possible, the presence of asbestos in the body during life.

The Raw Asbestos Fibre.—The raw asbestos is found in various parts of the world, and differs somewhat in composition in different places. The variety chiefly used in this investigation has been blue fibrous asbestos known as Cape asbestos. This raw material when ground up in a mortar with a little water or saline solution, yields a fine bluish white, almost powdery, deposit. As the asbestos does not take up aniline dyes and does not show up well unstained, under the microscope, the dark-ground illumination technique was adopted for practically all examinations. The fibres stain faintly with both the Fontana silver and the prussian blue methods, but neither is adequate for purposes of identification. When examined by dark-ground illumination powdered asbestos is seen to consist of fibres of varying length mixed up with a varying amount of particulate matter of irregular shape and often of reddish colour, which presumably represents minute particles of ore. The asbestos fibres are straight and highly refractive, and they vary in length, according to the thoroughness with which the raw asbestos has been ground, from fibres extending across the whole field of the microscope to fibres the length of an anthrax bacillus or even shorter. In the raw asbestos the fibres are held together in thick straight bundles, but when ground up the large bundles are split into smaller and smaller bundles until eventually fine individual fibres are obtained. The broken-off ends of the bundle can also be seen like bundles of freshly cut reeds. No branching has been observed, but frequently small particles of ore will stick in the fibres, giving at first sight a very rough resemblance to a filament of mould with gonidia. When individual fibres are examined carefully they are often found to have an extremely fine saw-like edge rather suggestive of the marks on a freshly cut plank. This saw-like edge does not always extend the whole length of the fibre. Occasionally, the free edge of the fibre will vibrate like the end of a fine steel spring, whilst split ends and notches in the fibres may be found. The fibres show the ends broken off at varying angles, quite unlike the ends of bacilli or fungi generally. Indeed, the appearance of the preparation under dark-ground illumination gives the impression of sharp brittle metallic wire broken up at all sorts of angles and in all lengths. But the chief characteristic of a single asbestos fibre when viewed by this method is its marked refractivity. The whole fibre appears to be brightly illuminated like the filament in an electric bulb.

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and when very thin the fibre has a bluish luminosity, whereas bacteria, cells, crystals, &c., generally show only a refractive edge with the rest of the structure in darkness. Finally, the asbestos fibre will withstand the heat of a Bunsen flame and is not destroyed when placed in concentrated sulphuric acid.

To summarise, therefore, raw asbestos may be ground up into a fine powder, calcined in a crucible, and mounted on a slide as a wet preparation with concentrated sulphuric acid without showing any signs of destruction. When examined by means of the dark-ground illumination method with a $\frac{1}{12}$-in. objective, a film thus prepared shows bundles of fibres and individual fibres of varying lengths. The fibres are highly refractile; they are straight and rigid like steel wire and have often a very fine saw-like edge, whilst the ends are broken at different angles and occasionally split, and the finest of them have a bluish tinge.

With these appearances in mind attention was next directed to the finding of asbestos in persons exposed to the risks of the trade.

Asbestos Corns.—The first and most obvious site for the fibres is the "asbestos corns" in the skin to which the workers are liable. Fine asbestos fibres penetrate the superficial layer of the epidermis like thistle thorns and produce a minute corn of hypertrophied epidermis around them. These fine asbestos fibres may be so ubiquitous that they even penetrate the stockings of girl operatives and produce corns on the legs. The asbestos fibres can be readily removed from the corns with a fine needle and when examined by dark-ground illumination they show the characteristic appearances of the fibres noted above.

Asbestos Fibres in Upper Respiratory Tract and in Sputum.—The next step is the demonstration of the asbestos fibres in the upper respiratory tract and in the sputum. Here the task is not so simple, because it is essential to eliminate any foreign bodies which may resemble an asbestos fibre. Accordingly, nose swabs, mouth washes and sputa from asbestos workers were dealt with by the following technique:—

(1) Digestion with 10 per cent. antiformin solution (in normal saline) which was filtered through an L3 Chamberland candle before use in order to remove any minute foreign bodies.

(2) Centrifugation of the digested material.

(3) Calcining of centrifuged deposit in crucible to destroy all cellular debris, &c.

(4) Preparing a wet preparation of the calcined deposit in concentrated sulphuric acid (a control film of which should be examined to eliminate the possibility of foreign bodies in the acid) and examining with $\frac{1}{12}$-in. objective by dark-ground illumination.

By this means asbestos fibres were demonstrated in the mouth and nose of two operatives who had been at work in the factory within a few days of examination. The finding of the fibres in the sputum was more difficult. These two operatives had no sputum, and it was necessary to fall back on cases which for medical reasons had been out of the factory for some time. Sputum from six cases in all were examined. In three

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asbestos fibres were identified, in three none was found. It is advisable always to put up a control slide of raw asbestos for comparison.

Asbestos Fibres in the Lung.—Paraffin sections of the lung of a case of pulmonary asbestosis were cut and mounted on a slide in the usual way. The lung tissue was then deliberately destroyed by the addition of concentrated sulphuric acid and the acid in turn replaced by water. The section was then covered with a thin cover glass and examined by dark-ground illumination. Typical asbestos fibres were found. They were also present in the expressed juice of the lung in this case.

Asbestos Fibres in Animal Tissues.—Finally, as a confirmation of the method, a suspension of ground up asbestos fibres in sterile saline made from freshly re-distilled water was inoculated intraperitoneally into the guinea-pig. A lymphocytic response was produced in half an hour, and the asbestos fibres were readily demonstrated in wet films by means of dark-ground illumination.

A guinea-pig was also inoculated, subcutaneously, with a suspension of asbestos in saline solution. When killed twelve days later it was found that the asbestos was collected together in bluish-grey masses lying in the fascial planes between the muscles of the groin at the site of inoculation. These masses were surrounded with a small quantity of soft gelatinous adhesions but there was no sign of suppuration. Sections of these adhesions showed them to consist of granulation tissue densely impregnated with asbestos fibres. The fibres were lying in all directions, many of them being in small bundles like minute wisps of hay. No "curious bodies" were seen, but a few of the fibres appeared to be slightly bulbous at their extremities. The granulation tissue also contained large numbers of foreign body giant cells, many of which appeared to have phagocyted small asbestos fibres. These foreign body giant cells were a very prominent feature of all the sections.

The cellular reaction to asbestos in living tissues will be dealt with in a later communication.

The So-called "Curious Bodies."—The golden bodies occurring in the lungs of cases of pulmonary asbestosis have been described by Cooke, McDonald, Simson [4] and Stewart [5]. No "curious bodies" were found in raw asbestos or in asbestos corns, nose swabs, mouth washes or sputum of workers. They were found, however, post mortem, in great profusion in the lungs of the case referred to above. It occurred to the writer that they might be derived from the kieselguhr with which the asbestos is mixed at a certain stage of manufacture in some factories. Kieselguhr is a whitish or greyish powder which consists of fossil diatoms. These diatoms occur in many shapes—star-like, slipper-shaped, elongated, segmented forms, and so on, and a comparison between these and the "curious bodies" suggested that the latter might possibly be fossil diatoms from kieselguhr which had become shrunken and distorted by pressure and by the action of tissue juices in the lungs. This view proved on further investigation to be erroneous.

The point was settled by the following experiment. A wet preparation of "curious bodies" in expressed lung juice was placed on the stage of the

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[2] Cooke, W
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[5] Stewart,

dark-ground illumination microscope and the position of a readily recognisable group of these bodies noted. Concentrated sulphuric acid was then very gently run under the cover slip, the "curious bodies" being kept under observation all the time. Slowly these bodies began to dissolve and in the middle of their structure was a number of typical asbestos fibres. At the end of half-an-hour practically all the material of which the "curious bodies" were composed had disappeared, leaving only a faint ghost-like outline of the bodies with highly refractive asbestos fibres within them. There were several of these bodies in this particular group and the asbestos fibres lay at different angles within them. Dr. D. S. Page, who confirmed this observation with me, made the suggestion that along the length of the fibres and in the angles formed between them there is laid down the material—possibly blood-pigment—which ultimately gives to the "curious bodies" their characteristic shape. At all events, it seems clear that whatever other material enters into their composition their basic scaffolding is the asbestos fibre. The writer would therefore suggest that "asbestos bodies" would be a more accurate description of the appearances seen than "curious bodies."

Conclusions.

(1) Asbestos fibres can be demonstrated in the corns from which the workers suffer, in the upper respiratory tract, in sputum in the lung, post mortem, and in animal tissues.

(2) The so-called "curious bodies" are derived from asbestos fibres. It is suggested that asbestos bodies would be a better name for them than "curious bodies."

(3) In view of the marked prominence of foreign body giant cells in the sections from the guinea pig, it is important that tubercle bacilli should be demonstrated in sections of the human lung in cases of pulmonary asbestosis before assuming that tuberculosis is present as a complicating factor.

I am greatly indebted to Dr. W. Burton Wood, Dr. C. Leonard Williams, and Dr. W. L. Yell for kindly sending me cases and material for this study, and to Mr. A. W. Smart, Chief Laboratory Assistant, for practical help.

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Haemolysis.

Considerable haemolysis has been reported in several earlier bubble oxygenators, but the method per se need not be traumatic.

It is important to use a non-wetable material such as polyethylene. Undoubtedly a flexible system holds advantages over the rigid systems. Furthermore, it is important to break the foam effectively at the top of the oxygenator column, and no free fall of the blood should be allowed. In addition, fairly large tubes should be used in order to minimize turbulence.

One and a half liters of freshly drawn citrated human blood has been recirculated 100 times through the apparatus at flows up to 4 liters per minute. The haemolysis at the end of the experiments varied between 20 and 70 mg per 100 ml of plasma, the greatest amount of haemolysis occurring with the highest blood flows.

Table 1.

Results of recirculation with one liter of human citrated blood 100 times through the machine at a flow rate of 1.5 l/minute, using carbogen for oxygenation.

	Haemolysis mg/100 ml plasma	Leucocyte count	Fibrinogen %
Before	0	2720	0.29
After 100 passages	22	2610	0.29

Table 1 shows the amount of haemolysis, white blood cell count and fibrinogen analysis before and after one liter of human citrated blood had been recirculated at a flow of 1.5 liter per minute one hundred times.

Oxygenating capacity.

The oxygenating capacity has been tested in vitro by one passage of venous blood through the system.

In the model which we use in animal experiments, the capacity is limited to 1500 ml per minute with a total extracorporeal blood volume of about 1200 ml. It can easily be altered by increasing the diameter of the oxygenating columns.

Table 2.

Results of eight dog perfusions of 30—43 minutes' duration (mean values).

Flow rate	65 ml pr. kg
Venous O_2-saturation	57 % (33—68)
Arterial O_2-saturation	96 % (93—99)
Arterial CO_2 pressure	25.5 mm Hg.
Free haemoglobin ...	42 mg/100 ml plasma (terminal values)

Perfusion experiments.

Table 2 shows the results of eight experimental perfusions of dogs weighing from 10 to 18 kilograms. During the perfusions, cardiac venous blood was aspirated from the opened right ventricle and returned to the venous reservoir.

The present design is not to be considered as final. Work is still in progress to improve the system further.

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ASBESTOSIS WITH PLEURAL CALCIFICATION AMONG INSULATION WORKERS

By J. FROST, J. GEORG and P. FLEMMING MØLLER

Pulmonary disease due to the inhalation of asbestos dust has been known for the last fifty years. The first case was described by Murray (1906). In Scandinavia, cases were reported from Norway and Finland by Wolff (1910), Schrumpf (1911), Wegelius (1916) and Noro (1946).

From the Clinic for Occupational Diseases (Chief: *J. Frost*) and the Radiological Department (Former Chief: Professor *P. Flemming Møller*), Rigshospitalet, University of Copenhagen, Denmark.

In Denmark, asbestos does not occur in the natural state, and comparatively few people are engaged in the processing of imported asbestos. Ive (1950) reported one case of asbestosis, and Frost (1950) three cases. These cases occurred in factories making insulation products, brake linings, and flooring material; the last case was a lagger in a shipyard.

The discovery of these cases led to closer supervision of factories of this kind. Lagging work, etc., is usually undertaken by small firms. In Copen-

hagen, employees of such firms have their own union, so it was found most convenient to carry out examinations through the Union. As there were no statistics about occupational hazards in this trade, the Union was interested in having its members examined.

After consultation with the Union officials, we began examinations in 1953 by selecting workers who had been in the trade for twenty years or more. The Copenhagen Union of Insulation Workers had about a hundred members during the thirties. These men often change from one firm to another and are employed on all kinds of insulation work. Before 1930 or so, lagging material chiefly consisted of kieselguhr and magnesia, mostly mixed with asbestos, or of asbestos ropes, or, in the case of boilers, mattresses filled with asbestos flock.

Since about 1935 the use of rock wool and glass-wool has gradually come to the fore in the insulation of hot-water pipes, etc. A special process for the insulation of ships' walls, *i.e.*, spraying with powdered asbestos, has been used to a certain extent.

The Union urged all the workers who had been in the trade for more than twenty years to submit themselves for examination: 31 attended; 3 did not. The occupational history was recorded, and a detailed clinical examination was carried out with X-ray of the chest (frontal, lateral and oblique positions).

The average age of the subjects was 52 years, ranging from 41 to 70; the period of exposure averaged 27 years, ranging from 20 to 45 years. Six of them complained of shortness of breath, which they considered abnormal for their age. All of them were working full time.

RESULTS

Roentgenographic examinations revealed abnormalities in 22 cases. 9 cases showed definite signs of pulmonary asbestosis, varying in degree - usually a fine mottling or nodulation. In no less than 19 cases abnormalities of the pleura were found. These changes ranged from obliterated sinuses and pleural adhesions to extensive thickening of the pleura with calcification.

The pleural abnormalities were bilateral in 12 cases; unilateral in 7. Calcification of the pleura was bilateral in 8 cases; unilateral in 3.

Parenchymatous lesions of the lungs alone were found in 3 cases, and in 6 cases combined with pleural lesions, 3 of which were calcifications.

In a few cases the abnormalities of the pleura were so widespread that no definite diagnosis could be made regarding the conditions of the lungs.

COMMENTS

It was a surprise to find 22 subjects with abnormalities of the chest out of a total of 31 examined. Only one of these stated that he had suffered from any lung disease, *i.e.*, pleurisy with effusion 18 years previously.

While it is generally observed that asbestosis of the lungs is accompanied by pleural thickening and adhesions, we have only been able to find one reference to pleural calcification in this connection. (Jacob & Bohlig, 1955).

Calcification of the pleura is a rather rare finding in radiological examinations of the chest. The incidence among unselected cases is estimated by Patch & Perry (1952) to be less than 0.2 per cent. Floyd & Hepburn (1939) found 23 in 15,000 examinations, and Kristiansen (1944) 15 in 10,000. In selected groups, con-



Fig. 1.
Insulation worker, age 70 years, exposure 45 years. Bilateral pleural calcification.

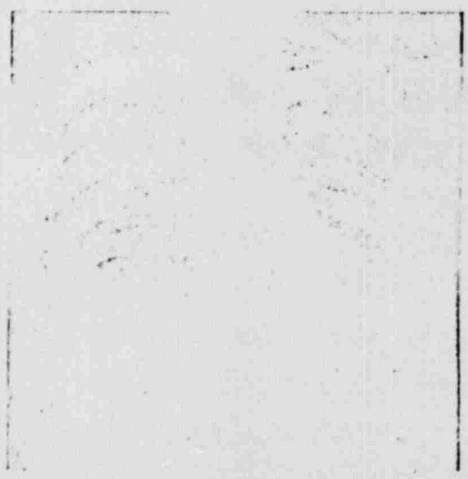


Fig. 2.
Insulation worker, age 57 years, exposure 38 years. Extensive pleural calcification over lower two-thirds of the lungs.

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taining many ex-servicemen, Ulrich (1930) found 16 out of 5,700 (etiology: bullet wounds, 5 cases; pleurisy, 5 cases; tuberculosis, 1 case; pneumonia, 1 case; unknown, 4 cases), and Behrendt (1930) found 12 out of 966 subjects (etiology: bullet wounds, 5 cases; tuberculosis, 7 cases). Head (1934) considers tuberculous pleuritis and hemothorax the only causes definitely known to produce calcification of the pleura.

Patch & Perry point out that calcification is usually unilateral, but bilateral in the so-called idiopathic cases (approximately 20 per cent of all cases).

A special investigation of workers exposed to dust was carried out by Smith (1952). She found 35 cases of pleural calcification out of 8,779 subjects examined. Only four groups showed a definitely higher incidence of calcification than that among the average population, *viz.*, workers exposed to the dust in making bakelite insulators, (1.5 per cent), calcimine (1.7 per cent), mica (1.6 per cent) and tremolite talc (6.3 per cent). Tremolite talc is a calcium magnesium silicate, which structurally resembles asbestos. It is known to cause pneumoconiosis. Calcimine is composed of whiting, clay, talc, silica, mica and asbestos. Four cases of pneumoconiosis were found in this group. Mica is a complex silicate of potassium, aluminium, magnesium, calcium and fluorine. Bakelite was mixed with talc and mica. No case of pneumoconiosis was found among the workers exposed to mica or bakelite. No pleural calcification was found among 261 asbestos workers. Smith suggests that it is the combined exposure to calcium and magnesium, together with a dust producing pleural irritation, which provokes the calcifications.

None of the workers examined by us have been working with asbestos alone; all of them have been exposed to kieselguhr, magnesium, rockwool and glass-wool too. The last three substances do not cause pneumoconiosis. Exposure to kieselguhr is known to involve a risk, as several cases of pneumoconiosis seemingly caused by this substance have been reported. According to Luton, Champeix, Ravet & Valland (1956) it is primarily a question of the alpha-quartz content. Exposure to the amorphous form of kieselguhr involves considerably less risk than does exposure to the flux-calcinated substance, nearly all of the silica of which may be in the form of alpha-quartz. The kieselguhr used in this country is not known to be flux-calcinated, and sample-analysis has not revealed the presence of alpha-quartz.

In our cases the workers have been exposed to asbestos, which is known to produce pneumoconiosis with pleural affection, and to kieselguhr, magnesia, rock-wool and glass-wool. Our findings thus give some support to Smith's contention that the incidence of pleural calcification may be connected with exposure to mixed dust; but it should be emphasized that our subjects have not been exposed to calcium.

While smaller pleural thickenings and adhesions are a rather common finding in chest X-rays of persons not known to have had any lung disease previously or to have been exposed to dust at their jobs, the findings of pronounced bilateral pleural changes in the present series definitely point towards an occupational origin. The diagnosis of asbestosis may be made with confidence when these pleural changes are found together with parenchymatous lesions of the lungs. The occurrence of similar pleural changes without any definite changes of the lung proper may also, with reasonable certainty, be accepted as evidence of asbestosis in subjects known to have worked with insulating material of the sort used by the workers examined here.

SUMMARY

31 workers engaged for 20 years or more in different kinds of insulation works were examined for occupational lung disease. They had been exposed to dust containing asbestos, kieselguhr, magnesia, glass-wool and rock-wool. 9 were found to have definite signs of pulmonary asbestosis. 19 showed abnormalities of the pleura, 12 of these being bilateral. In 11 cases calcification of the pleura was found, being bilateral in 5 of them.

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