INDUSTRIAL MEDICINE

AND

HYGIENE

Edited by

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to be observed the first is the patient's reaction to the effort of undressing and dressing; this constitutes a simple exercise-tolerance test; secondly come the general build, somatic type, chest configuration and nature and range of respiratory movements. The development of the soft tissues of the chest wall and, particularly in the female, the size and conformation of the breasts, should be recorded, for these items are often important in the interpretation of the radiograph.

Percussion, auscultation and percussion.—By reason of the insidious onset and the paucity of physical signs, pneumoconiosis has been described as a silent disease. Percussion and auscultation frequently, in the presence of well-established changes, suggest no abnormality, yet on the other hand, in another group of cases, one may discover the whole range of abnormal physical signs. Even when massive shadows appear radiographically, precise areas of dullness can seldom be mapped out by percussion, while, despite the evidence of morbid-anatomical changes, clinical signs of pleurisy and bronchitis are the exception rather than the rule.

Cyanosis

Classically, cyanosis and clubbing of the fingers are regarded as regular accompaniments of chronic pulmonary disease, and so one would expect evidence of these in pneumoconiosis. Slight cyanosis is very difficult to define, even by the most careful inspection, and quite often it is present only in the imagination of the physician. It can definitely be asserted that easily recognizable cyanosis, except when associated with serious cardiac embarrassment as in cor pulmonale, is seldom observed in pneumoconiosis. Asbestosis, however, is exceptional, for in this variety of chronic pulmonary fibrosis, unmistakable cyanosis of the malar regions, lips and lobes of the ears is not uncommon, while drumstick clubbing of both fingers and toes is almost pathognomonic of the disease, in workmen employed in certain processes in the manufacture of asbestos textiles.

Diagnosis of clubbed fingers

Clubbing of the fingers, too, except as just mentioned, is a rare manifestation (Fig. 13*a*).

Any enlargement of the terminal phalanx is, by many people, mistakenly regarded as clubbing. In many artisans, who, in the course of work, are required to apply pressure with the tips of the thumb and fingers, the pulp of the terminal phalanx often becomes considerably broadened and thickened. This spatulate appearance is not clubbing.

Clubbing generally appears first in the thumb and index finger and later involves the others. When present in asbestosis it usually affects both hands symmetrically. The first changes are observed at the root of the nail, where thickening occurs and the overlying skin becomes shiny and injected. In this area the circulation is impaired and, in advanced cases the defect may actually impart a dusky blue coloration.

Manufacture of artificial graphite

Artificial graphite is prepared by crushing, grinding and calcining of gas and oil cokes, and is used in the manufacture of shaped carbon blocks and electrodes for use in electric furnaces in the production of aluminium metal This material is a very pure form of carbon, and the silica content seldom exceeds 1 per cent of the total weight. It has been proved, and accepted for purposes of industrial disablement benefit, that labourers employed in the milling operations suffer from pneumoconiosis similar to that found among workers in natural graphite.

In Great Britain, soot, lamp-black or "nearly pure carbon" is manufactured commercially by the incomplete combustion of gas and tar oils and petroleum distillates Mineral impurity constitutes only a trace. The chief use of this product is as a reinforcing filler in rubber-compounding. In addition to producing rigidity in the vulcanized rubber, the carbon increases the tensile strength and the resistance to abrasion.

No definite evidence of pneumoconiosis, in either the lamp-black or the rubber industry, has so far been recorded in Great Britain, but Brauss and Gärtner (1951) have recorded the occurrence of cases in Germany.

A similar product—gas-black—is manufactured in America by burning natural gas, which is 95 per cent methane. This work, it is reported, does not cause any pulmonary disease.

Recently the writer has observed a few cases of simple pneumoconiosis among a group of workmen in the north of England who were engaged for many years (30 to 50) in the manufacture of soot (no silica impurity).

Cause of coal and graphite pneumoconiosis

These observations are important in relation to the aetiology of pneumoconiosis of coal-workers The problem is whether these cases of pneumoconiosis are due to the small amount of silica within the coal or graphite or are due to the carbon itself. That there is no simple answer to this question will be realized, if one recalls that the pathological changes in the lungs may be determined, not only by the quality of the dust, chemical and physical, but also by mere quantity of fine particles, while both factors may be further influenced by associated infection

ASBESTOSIS

Asbestos, meaning unconsumable, is a collective term applied to a group of silicate materials, which, while differing widely in chemical composition, resemble each other in certain valuable physical properties. They are finely fibrous in structure, and so can be split readily to microscopic size without loss of identity. Single fibres have been noted up to 43 inches and down to 0·000003 inch in length. The fibrous structure, which, in varying degree, is associated with flexibility, enables it to be spun into yarn and then woven

into textiles. The following are the special qualities of the material which make it of use in industry: (1) resistance to fire and heat, (2) low heat-conductivity, (3) high electrical resistance and (4) inertness to chemical action.

Varieties of asbestos

The several varieties of asbestos fall into two main groups: (1) chrysotile, or serpentine asbestos, and (2) amphibole asbestos, which includes (*a*) amosite, (*b*) crocidolite and (*c*) tremolite

Chrysotile

Chrysotile asbestos, which constitutes 90 per cent of world production, is a hydrated magnesium silicate. The fibres are short (usually a fraction of an inch), very fine and of a silky sheen. Thetford (Quebec) is the chief source of supply; lesser quantities are obtained in Southern Rhodesia, the U.S.S.R., and elsewhere

Amphibole

Amosite contains iron from which it derives a dirty brown colour. Deposits of this variety of asbestos occur almost entirely in South Africa. Normally the fibres are several inches long and of poor spinning quality. Accordingly, its main use is for the manufacture of heat-insulating blocks, and as a binding material in the composition used in the production of asbestos cement sheets, which are nowadays so extensively used in the fabrication of modern houses and other buildings

Crocidolite, or blue asbestos, occurs mainly in the Cape Province of South Africa, and in the industry it is usually designated "Cape Blue". It is extensively used when resistance to chemical action is required.

Tremolite asbestos is obtained from Italy It is white and the fibres may exceed a yard in length Because of undue brittleness, it is not suitable for the manufacture of cloth, and so is chiefly employed for insulation purposes, such as the lagging of boilers and steam pipes.

Mining and manufacture of asbestos

Mining

The mineral is obtained either in open quarries or in shallow mines, and the normal operations are drilling, blasting, breaking and sorting When freed from waste rock, the asbestos is dried and successively crushed to a fine powder. Foreign matter is removed by screening, and particles of iron are extracted by passing the material over powerful electric magnets. The crude fibre is then graded according to length of fibre, and is packed for despatch to the manufactories.

Manufacture

Asbestos textile manufacture is similar to that of other fibres, such as

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cotton, wool and flax. First the fibres are opened in a Crighton machine, then follow in succession carding, spinning and weaving. All these operations, unless carefully controlled, produce considerable amounts of fine thistledown dust, which is wafted far and wide throughout the factory premises and even into neighbouring buildings, including adjacent offices. Water, or even wetting agents, so useful in the control of dust, are of no value because asbestos is practically unwettable.

The cloth is used for the manufacture of fire-protective clothing: suits, helmets and gloves, and safety curtains. It is sewn into covers which, when filled with crude fibre, form mattresses or pads for the insulation of heating boilers, tanks and pipes. In the form of tape, it is very easy of application for the protection of domestic pipes against either frost or heat loss. Bonded with bitumen it is moulded into slabs for use as panelling, or cut and shaped into brake-linings, gaskets and other forms of packing for machines. In the manufacture of cement roofing-tiles, flat or corrugated sheeting, rain-pipes and other building materials, asbestos is introduced into the "mix" as a binder. During World War II, small quantities were incorporated into the cotton-wool filters of gas-masks.

Waste asbestos boarding is often crushed and used as a filler in paint manufacture. The importance of this reference is that very frequently the workmen in these processes do not know the danger, which is aggravated by an almost entire lack of safety precautions.

The main centres of asbestos textile manufacture in Great Britain are at Rochdale, Leeds, Cleckheaton, Barking and Glasgow.

History of asbestosis

In 1906, Montague Murray reported the case of an asbestos-worker, who had died in the Charing Cross Hospital in 1900 of "typical fibroid phthisis". The man, a card-room worker aged 34 years, had stated that 10 of his work-mates had died at about the age of 30 years. Sporadic cases continued to be recorded, and finally in 1928 Seiler reported on a case, which seemed definitely to establish the relationship between the inhalation of asbestos dust and disabling and fatal pulmonary fibrosis.

Therefore the Home Office instituted an official inquiry into the asbestos manufacturing industries throughout Great Britain, and the report by Merewether and Price remains the authoritative account of the disease (*See* Merewether, 1930.) The occupational origin was proved, and accordingly asbestosis was recognized as a compensatable disease under the Workmen's Compensation (Silicosis and Asbestosis) Act of 1930. In addition all workmen employed in certain scheduled occupations were required to pass an initial examination, and thereafter, at yearly intervals—since extended to 2 years—to submit to periodical medical examination. Any workman found at such examination to be suffering from asbestosis was immediately suspended permanently from all further work in the processes

Pathology and morbid anatomy of asbestosis

In crushing operations, fiberizing and disintegrating, in opening, spinning, weaving and the filling of asbestos mattresses, production of fine thistledown dust occurs. This consists of fine needles or spicules of asbestos, which are inhaled by the workmen. Most of the dust inhaled never reaches the lungs, but is arrested in the upper respiratory tract and trachea, from which it is rejected in the nasal mucus and sputum. Whereas only the minute particles of silica gain entrance and are retained within the lungs, much larger particles of asbestos, when inhaled, because of their physical form, are mechanically trapped. Fibres up to 200 microns have been detected in the air passages, but dangerous fibres measure up to 20 microns. In the lung no local necrosis results, nor is there any leucocytic reaction. As a result of mechanical irritation the pulmonary epithelial cells are desquamated, and fibroblasts appear round bronchioles and alveoli, in interlobular septa and in the subpleural tissue. Finally, collagenous fibres appear around the distal ramifications of the bronchial tree.

Gardner and Cummings (1931) have shown, by animal-inoculation experiments, that the chief site of asbestos-dust localization is the respiratory bronchiole.

They describe the early lesion, in the guinea-pig exposed to inhalation of asbestos dust, as follows:

> "The asbestos dust is carried by the inspired air only to the distal respiratory bronchioles . . . The mononuclear phagocytes from the adjacent connective tissues enter the lumen of the air passages and engulf the particles. The phagocytes with their contained fragments of dust are frequently pushed aside into the alveoli which pouch out of the sides of the bronchioles, where many of them remain indefinitely. More dust entering the lung is held up by the partial obstruction created, and further reaction is largely proximal to the point of original localization."

At 60 days the authors describe the dust-cells of the terminal bronchioles as being increased, and the lumina of some of the lateral alveoli completely blocked with mononuclear phagocytes and giant cells. At the end of 2 months small asbestosis bodies appear. After 90 days' exposure it was found that the amount of cellular reaction had not kept pace with the number and size of the asbestosis bodies. Hyperplasia of the lymphoid tissues was now visible. At the end of a year the walls of the bronchioles proximal to the alveolar ducts were thickened from excessive local accumulation of phagocytes, but definite proliferation of fibroblasts was not noted until after 550 days. This was confined to the walls of the air spaces adjacent to the deposits of dust phagocytes. At the end of a further 100 days a true fibrosis developed, contracting the air spaces, which now appeared to be filled with compact masses of dust cells and phagocytes, fibres and bodies. After 2 years the mischief had reached the periphery of the lung, and sub-pleural greyish-white nodules were uniformly distributed over the surface.

King, Clegg and Rae (1946) have recorded the results of experiments in rabbits exposed to the intratracheal injection of asbestos fibres of varying length. In

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animals treated with long fibres (15 microns) a nodular reticulinosis developed, comparable with the experimental silicotic nodule, whereas in animals treated with short fibres (2–5 microns) a diffuse reticulinosis appeared. The addition of powdered aluminium did not afford any benefit in either group.

Post-mortem appearances

Macroscopical findings

The morbid appearances to the naked eye are very similar to those described above for silicosis (*see* p. 23). No specific change occurs in the air passages. The pleural changes, however, are more marked than in any other variety of pneumoconiosis. Generally the pleura is everywhere thickened, and in advanced long-standing cases the lungs appear encased in a glistening yellow sheath like a plastic material. All over the pleura is puckered and raised in folds, and it insinuates itself universally into fissures and sulci. Not infrequently the whole space between the visceral and parietal pleura is completely obliterated by massive tough sessile adhesions. These changes, as is shown on page 115, dominate the radiographic appearances.

The asbestosis lung is firm and airless, and when it is cut with a knife the fibrotic character is immediately apparent. The characteristic lesion presents

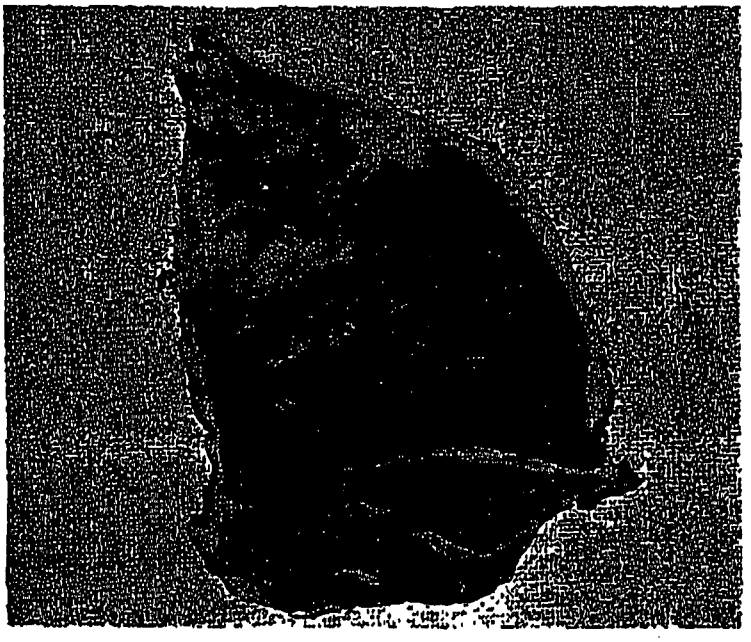

FIG. 19.—Female aged 35 years. Asbestos spinner 5 years. Post-mortem section of lung showing blue-black polygonal areas of asbestosis and thickened pleura. At the lower pole a squamous carcinoma surrounds an abscess cavity. (*By courtesy of Dr H. Wyers*)

as blue-black polygonal areas $\frac{1}{8}$–$\frac{1}{4}$ inch in diameter. These are distributed over the whole of the cut surface, but are most evident in the lower lobes. This may be due to confluence or simply to the greater bulk of the base of the lung. Anatomically it will be observed that these polygonal fibrosed areas conform to the size and shape of the pulmonary lobules, which they have, in fact, replaced.

All these changes may be considerably modified according to the terminal illness: broncho-pneumonia, tuberculosis, bronchial carcinoma or congestive heart failure.

Other organs do not show any characteristic changes, they are not involved in the disease save indirectly and in relation to complications and sequelae

Microscopical appearances

Asbestos fibres (natural and altered), plugs of mucus and desquamated epithelium may be observed in the main air-passages In the terminal bronchioles and alveolar ducts, these changes are more advanced and associated with the presence of large mononuclear phagocytes. The alveoli and lymphatic vessels are blocked with dust and phagocytes Connective tissue surrounds the bronchioles, alveolar ducts, air-sacs and blood vessels, and penetrates into the interlobular septa and beneath the pleura. In the most advanced stage, all appearances of lung structure are obliterated by fibrous tissue.

The asbestosis body

Curious bodies in the lungs were first described by Stuart McDonald in 1927. They are now recognized as a feature of exposure to the inhalation of asbestos fibres, and they have been identified in the lungs, pleura, sputum and faeces. It is now accepted that they are formed from the original fibre by the following process:

(1) deposition of some material around the fibre so as to thicken it; (2) fissure or cracking of this material giving rise to the appearance of segments; (3) fragmentation, or the separating off from the asbestosis body of fractured portions of the deposited material. Gloyne (1932) summarizes the variety of appearances as follows.

(1) Marked variation in length (24–60 microns) and breadth (12–24 μ). Gardner and Cummings (1931) record their being as long as 250 μ in experimental animals The short forms are sometimes seen within phagocytes.

(2) Golden yellow colour: Gardner and Cummings have pointed out the resemblance of this colour to the haemosiderin deposits found in areas of tissue in which haemorrhage has occurred.

(3) Homogeneous structure when viewed by ordinary transmitted light.

(4) By cutting down the light, a suggestion of a central fibre can often be seen. This fibre may also sometimes be seen projecting beyond the body.

(5) No differentiation with polarized light.

(6) Tendency to be arranged in irregular clumps and clusters

FIG. 20.—Ast

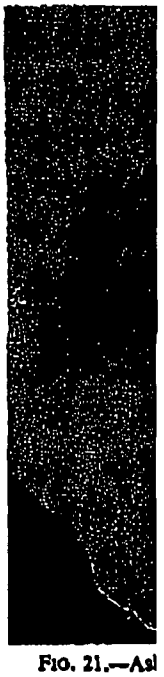

FIG. 21.—Ast

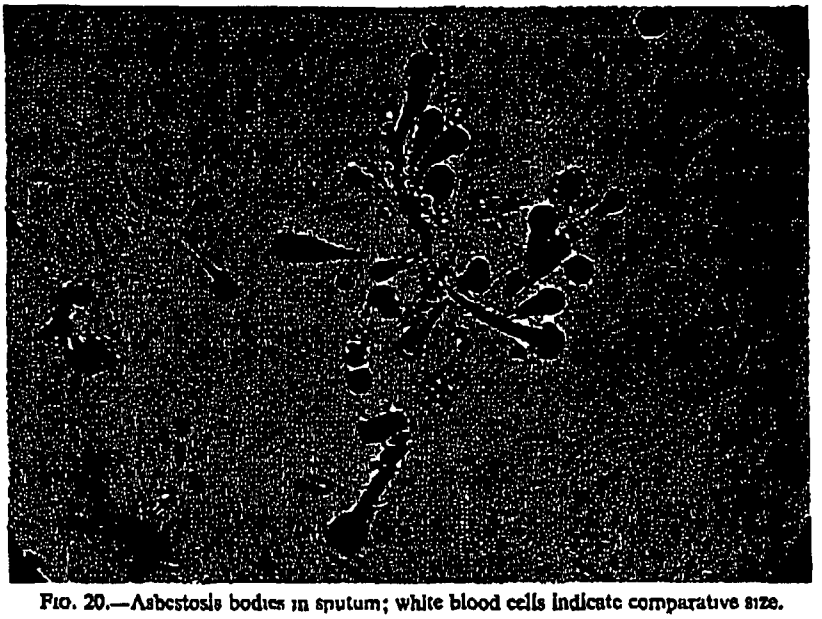

FIG. 20.—Asbestosis bodies in sputum; white blood cells indicate comparative size.

FIG. 21.—Asbestosis bodies in sputum; white blood cells indicate comparative size.

(7) Very early forms unsegmented (" sausage-shaped ").

(8) Later forms crenated, segmented, or resembling a series of oval discs, or beads strung together in a necklace form. Sometimes, later, a short length of fibre is seen between the segments.

(9) Bulbous or pointed extremities (or one bulbous and one pointed suggesting " heads and tails "). Simson and Struchan (1931) have noted sharply angled forms suggesting incipient fracture, and believe that the tapering tail forms may be the broken ends of this fracture

(10) Generally quite straight, occasionally curved, very rarely S-shaped During examination in a wet preparation, slight pressure on the cover slip will sometimes cause them to bend owing to the elasticity of the central fibre. This proneness to bend under stress and strain may explain the curved forms often seen in sections of tissue, as suggested by Gardner and Cummings.

(11) Forms seen " end-on " look like knobs or door-handles. Small secondary knobs and bosses sometimes seen thereon.

Histological technique.—Gloyne (1933) describes the following technique for the identification of these bodies:

After digestion of the sputum with equal quantities of concentrated antiformin and centrifugation, the antiformin is pipetted off, and the deposit covered with a small quantity of a 5 per cent solution of ammonium sulphide The asbestosis bodies are then coloured black. This colour can be removed with hydrochloric acid.

Sections.—In the case of sections the following technique has been found useful:

After removal of the paraffin wax with xylol and alcohol in the usual way, the section is washed with water and then flooded with ammonium sulphide, which is allowed to remain for several minutes. The section is next washed and counter-stained with an aqueous solution of neutral red, dehydrated, and mounted in balsam. This method of staining also shows the presence of a large amount of iron in the sections. Unfortunately the black colour is slowly removed by the mounting fluid, and the sections will only keep for a few weeks.

Staining with haematoxylin—Haematoxylin, which also has an affinity for iron, can be made to colour asbestosis bodies, but it is rather a deposition of stain than a true staining reaction. The technique is as follows.

After digestion of the sputum with equal quantities of concentrated antiformin and after centrifugation, the antiformin is pipetted off and replaced by a 5 per cent solution of Ehrlich's haematoxylin. Blueing of the haematoxylin immediately takes place owing to the remains of the alkaline antiformin. The mixture is well shaken and allowed to stand for ½–1 hour, and then centrifuged again and the deposit mounted as a wet preparation By this means the asbestosis bodies become a dark-brown or black colour, according to the length of time they have been exposed to the haematoxylin.

Although these haematoxylin-coloured bodies give the impression of having the haematoxylin deposited on them rather than having actually taken up the stain, after washing over-night they still retain sufficient stain to give a dark-brown effect under transmitted light.

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Clinical aspects

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Diagnosis of asbestosis

While the methods of diagnosis follow those for the pneumoconioses in general—namely, occupational history and clinical and radiographic investigation—the relative value of these items is unusual and so merits comment.

Occupational history

Reference is made on page 107 to the authoritative contributions made to our knowledge of asbestosis by Merewether and others 20 years ago. At that time the industry was comparatively new, factory conditions were not good, and neither employers nor workers realized the dangers of the material and the processes. The type of workman was poor and the labour turn-over was heavy. The great majority of cases, when diagnosed, were in the advanced stages of the disease, and the symptoms, clinical signs and radiographic changes were correspondingly severe. Furthermore, by present standards the technical quality of x-ray films was unsatisfactory, with the result that radiographic interpretation was not always reliable. Meanwhile, conditions have substantially altered for the better, and patients present themselves for diagnosis at a much earlier stage—indeed, sometimes before the disease has had time to develop. Despite increased knowledge and experience of the disease and the higher standard of radiology, a firm diagnosis in the earliest stages is still often extremely difficult.

Another matter worthy of note is that, in the spinning, weaving and asbestos-mattress sections of the industry, the workers are predominantly females, but doctors outside the immediate locality of the factory seldom associate dust disease of the lungs with women, particularly young girls This is further complicated by the fact that the disease may not become manifest until the woman has married and left work, and her occupation is then designated as "housewife". Pregnancy—especially in the later months—is sometimes the circumstance which aggravates any dyspnoea and leads to investigation of the cause. Furthermore, early radiographic changes in asbestosis are usually most marked in the lower halves of the lung fields, and the female breasts, when engorged in pregnancy and occasionally during menstruation, may obscure these changes when present, or simulate them when they do not exist.

However, by reason of the great publicity which the disease has attracted in the main centres of the industry, the workman usually announces the diagnosis to the doctor, who himself is equally aware of the local scourge. Nevertheless, even without this guidance, any doctor should be aware of the possibility, provided that he has investigated the occupational history in the manner described.

Clinical aspects of asbestosis

Dyspnoea is the single universal complaint, and it is all the more conspicuous because frequently it is quite out of proportion to the clinical signs

in the lungs Considerable emphasis has often been laid on the showers of persistent fine crepitations, which are particularly audible over the bases of the lungs. These adventitious sounds are intrapulmonary, but they do not necessarily indicate disease, for they can be detected within a few weeks of commencing work and without any accompanying departure from health. The most probable explanation of their occurrence is that they are due to obstruction of the bronchioles by asbestos fibres, and this is supported by the simultaneous appearance of altered fibres in the sputum. The presence of true asbestosis bodies in the sputum is not diagnostic of the disease; these bodies merely indicate that asbestos fibres have been inhaled and retained sufficiently long in the lung to acquire the characteristic changes. Stewart (1933), however, has expressed the opinion that clumps of fibres may denote disease associated with breaking-down of lung tissue. This observation is analogous to the occurrence of elastic tissue in the sputum in tuberculosis, and of persistent " black spit " in the late stages of massive fibrosis in silicosis and pneumoconiosis of coal-workers.

In advanced cases all the clinical signs of lung fibrosis may be detected, and they are usually associated with evidence of cardiac distress. Apart from dyspnoea, two features are impressive: (1) an earthy cyanosis and (2) the sudden appearance of an extraordinary degree of drum-stick clubbing

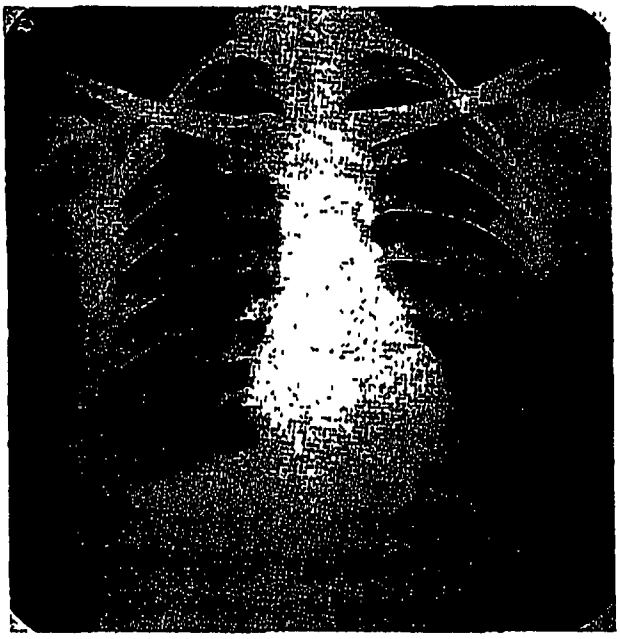

FIG. 22 Normal chest radiograph Female, aged 24 years; married. Note obscuration of basal lung fields by heavy breast shadows.

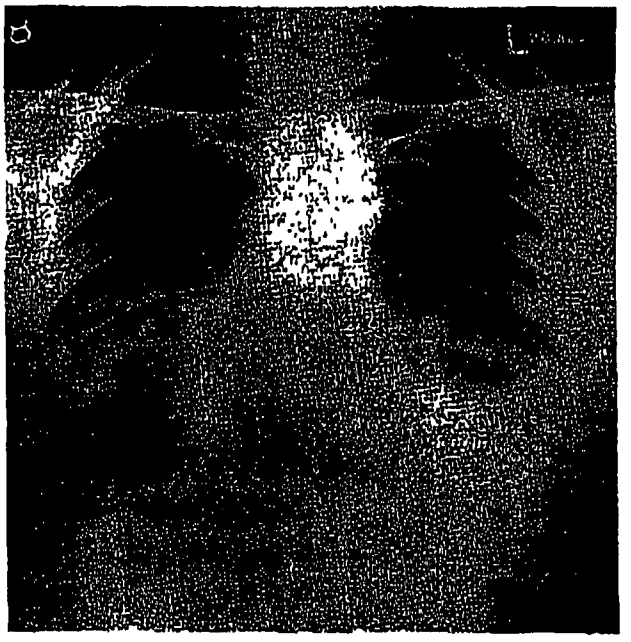

FIG 23.—Male aged 49 years (1953). 1926–38, asbestos millboard cutter; 1938–43, timekeeper and gatekeeper; 1943 *et seq.*, despatch clerk. Typical radiographic appearances of advanced asbestosis; clubbing of fingers (*see* Fig. 13). At present working regularly. (*By courtesy of Dr. H. Wyers.*)

of the fingers and sometimes of the toes. Out of Wyers' series of 53 consecutive cases, clubbing of the fingers was present in 29 cases (Wyers, 1949).

Complications of asbestosis.—Pulmonary tuberculosis occurs as a complication, but there does not seem to be the same close relationship to asbestosis as exists in silicosis. An excess mortality from cancer of the lung and other organs has been recorded by several observers. Wyers, the medical officer to a large asbestos manufacturing company, stated in 1949 (*see* Table V) that he had collected details of 115 deaths from asbestosis, and that of these cases 11 males and 6 females showed pulmonary cancer, whilst cancer of other organs was present in 3 males and 4 females (in the pancreas, colon, stomach and ovary). Despite the frequency of clubbing of the fingers, frank infective bronchiectasis is unusual. Congestive heart failure and bronchopneumonia are common terminal conditions.

Radiological appearances in asbestosis

Often the first fact which impresses the reader is the smallness of the chest, as if the lungs were shrunken from apex to base. The next feature is a general haziness of the lung fields; this has been described as veiling or a

ground-glass appearance. While there is no orderly progression of changes, the next stage is characterized by fine mottling or stippling, localized or general, and particularly conspicuous in the lower halves of the lung fields. This mottling may later become coarser, thus producing a granular pattern. Thereafter the whole picture is dominated by the sclerotic pleurisy described on page 109 The costo-phrenic and cardio-phrenic angles are obscured, and the outlines of the cupolae of the diaphragm and of the cardiac shadow appear shaggy, because of opacities, which, as so aptly described by Wyers, resemble teased-out cotton-wool. In some cases a very characteristic appearance is presented by the horizontal fissure, which is thickened and presents a lenticular rather than a fine linear shadow. It is also often considerably depressed in level, especially laterally, so that instead of appearing horizontal it is oblique, with the convexity directed upwards and outwards.

Differential diagnosis

It cannot be said that the condition requires to be differentiated from any other condition. If the investigation follows the routine which is outlined, almost complete accuracy should be achieved. It may be said, however, that, in the early diagnosis of asbestosis, as a supplement to the occupational history, the clinical features are a more reliable guide than radiographic changes and, indeed, often precede them.

Incidence of asbestosis

In Great Britain the risk of contracting the disease occurs in the asbestos manufacturing industries, and to a small extent in heat-insulation work, pipe and boiler covering (lagging) and the other incidental processes, such as stripping the old composition. The risk varies, of course, with the dustiness of the process and, in the absence of efficient dust suppressing and collecting devices, the most dusty operations are (1) preparatory processes of crushing, opening, sieving, mixing and blending, (2) sack filling and emptying and all handling of loose asbestos, (3) carding and card cleaning and grinding, (4) cloth weaving, (5) mattress making, and (6) cleaning dust settling or filtering chambers In recent years considerable advances have been made in controlling the dust at the source of production. Thus, whereas in 1929 cases were identified after 7 years' exposure—some even after a much shorter period—the corresponding figure now is 10 years.

Prevention

There is no specific method of prevention, except the suppression and control of dust. In this connexion as long ago as 1930, the Asbestos Industry collaborated wholeheartedly with the Factory Department (then of the Home Office and now of the Ministry of Labour and National Service) in devising methods of localized exhaust ventilation for application to operations and machines (for example, cloth looms), the necessity for which had never been

envisaged before. In this connexion the dictum of the Committee that " For practical purposes the conditions arising from flyer spinning carried on without exhaust under good conditions may . . . be taken as the 'dust datum' "* was agreed, and this level of dust production was accepted as the basis on which to assess the dustiness (and hence the necessary protective measures) of other processes. Nothing has emerged to suggest departure from this practical standard. It should be remembered that ring spinning is more dusty than flyer spinning, and therefore local exhaust ventilation should be applied to ring spinning. Doubling, plaiting and braiding may be linked with flyer spinning in this connexion. At one time prohibition of the industry was advocated—a completely futile and absurd attitude, as is proved by the present importance and development of the manufactures A substantial measure of control has been achieved by mechanization and by enclosure of machines with Perspex panels.

As a means of safeguarding the health of workmen in dangerous processes, the statutory system of initial and periodical medical examinations by the Pneumoconiosis Medical Panels is in operation. This medical supervision is supplemented at most large factories by the work of the firm's own factory medical officer.

OTHER SILICATES CAUSING PNEUMOCONIOSIS

Apart from asbestos, silicates do not constitute a serious cause of pneumoconiosis among workmen. One important reason, of course, is that the population at risk (excluding the clay industries, bricks and tiles) is small. Sporadic cases, however, have been reported, and certain relevant facts are worthy of note.

Silicate minerals exist in two forms: (1) fibrous, which includes (*a*) asbestos, (*b*) talc, (*c*) sillimanite, and (*d*) sericite; (2) non-fibrous, including (*a*) mica, (*b*) china and ball clays, and (*c*) Fuller's earth.

Talc and French chalk

Talc is hydrated magnesium silicate, and in its compact form is known as steatite or soapstone, which is familiar as the chalk used by tailors for marking cloth. The purest talc deposits occur in association with dolomite and marble, and the chief sources of supply are the United States of America and Manchuria. Talc exists in fibrous and plate forms, and the special qualities which make it valuable in industry are low conductivity to heat and electricity and resistance to fire: hence its use in insulation. About 90 per cent of the talc production is marketed in ground form, as a white powder, which is used as a filler for paints, distemper, paper and soaps. Popularly it is best known as toilet powder and as a dusting agent (French chalk) in the manufacture and handling of rubber.

* Report on Conferences between Employers and Inspectors concerning Methods for Suppressing Dust in Asbestos Textile Factories, H.M. Stationery Office, 1931.

compounds, at least, must be added to the list of substances which may cause cancer of the respiratory tract.

Association of pulmonary cancer with silicosis and asbestosis

Between 1930 and 1940 there were several papers calling attention to a suspected association between lung cancer and silicosis, the inference being that silica might, directly or indirectly, play some aetiological part in producing the malignant disease. Such an association has not been borne out by further inquiry.

The relation between asbestosis and lung cancer is, however, quite different. This subject is dealt with in Chapter I of this volume

New and unknown industrial carcinogens

In the future there may be new and increased usage of certain materials now known to be carcinogenic. This is true at the present time for radioactive materials, especially isotopes, and for x-rays. Furthermore, as our knowledge of the aetiology of malignant disease of the respiratory tract increases, it is to be expected that other materials which are now encountered in the industrial environment, as well, perhaps, as some in the domestic environment, will prove to have carcinogenic properties. New uses for some of the rarer metals are continually being found and the toxicology of many of these is incompletely known.

Substances carcinogenic to animals.—Some substances, not yet known to produce cancer in human beings, have been shown to induce malignant changes in animals. Beryllium is one of these, intravenous injections having been reported, both in Great Britain (Barnes, 1949) and in America (Gardner and Heslington, 1946; Dutra and Largent, 1950), as causing sarcoma of bones. Animal experiments have also shown that selenium is carcinogenic for certain species, although no human case attributed to its industrial exposure is known.

Mineral oils.—Uncertainty exists about exposure to mists of mineral oils, encountered by garage workers and in other occupations. Kennaway and Kennaway (1936) note that spinners and piecers of cotton, who are exposed to fine droplets of mineral oil, have a very low ratio (31) for lung cancer, but a rather high ratio (148) for laryngeal cancer. Hueper (1951) mentions *iso*-propyl oil, as requiring further study in regard to cancer of the nasal sinuses and lungs, in the manufacture of *iso*-propyl alcohol. Santo (1949) summarizes available knowledge concerning the reaction of the lungs to the instillation of various types of oil. He says that mineral oils may produce not only acute lipoid pneumonia but chronic granulomatous infiltrations or paraffinomas. He presents 2 cases of bronchial carcinoma in patients who had been taking liquid paraffin daily by the mouth over a period of years. In 1 case organizing lipoid pneumonia was present throughout the affected area, and in the other the carcinoma appeared to have arisen in such an

there was 1 milligram per gramme of nickel in the lung even 8 years after cessation of exposure. If Løken's results were correct, there must have been some 1·2 grammes of nickel in the lungs—a wellnigh incredible figure—completely out of harmony with Barnes and Denz's conception of non-retention unless there was very great difference, as seems likely, in the physical form and states of the nickel.

ASBESTOS

The association of what appears to be purely mechanical trauma with a later development of neoplastic change has a long history both in the experience of myriads of medical observers and in that of theorists who invoked it in the exposition of a theory of cancer. If such an association is looked at askance it is not because it is denied that it can occur, but rather that it is too facile and even sterile an explanation. Of the tens of millions of mechanical traumas occurring daily, the number which can be later recognized as having possibly initiated a neoplastic process *in situ* is minute. Most pathologists would sum the matter up by saying that if trauma is followed by the development of a tumour at the site of the original trauma, then that site was not normal at the outset.

Co-carcinogenesis

The classical experimental basis for the effect of the super-imposition of trauma on an abnormal site is the *Deelman phenomenon.* Deelman showed in 1923 that if a tarred area of animal skin is injured by wounding or other physical effect, tumour formation might be hastened and its location thereby determined. This observation was later confirmed by other workers who used pure carcinogens and laid the foundation of what is now called co-carcinogenesis. Co-carcinogenesis may be defined as the augmentation of the action of a carcinogen by some suitable additional treatment which shows itself in increased numbers of induced tumours and/or shortening of the induction time. In general the term co-carcinogenesis is applied to an effect produced by local application of an agent to a tissue (Berenblum, 1947). A co-carcinogen is not itself a carcinogen although Anderson (1948) appears to think otherwise, regarding co-carcinogenesis as a synergy between subliminal doses of two or more carcinogens. Such mechanical irritation as strongly brushing the skin, and foreign body fibrosis, have been shown to be effective as co-carcinogens. Heat, cold, radioactive radiations, croton oil and resin, all possess co-carcinogenic power.

The precise nature of co-carcinogenesis is difficult to understand except as an expression of certain experimental facts. The significant matter from our present viewpoint is that for a co-carcinogen to produce its effects it must be applied after a preparation of the tissue has taken place by a carcinogen, or even after an overt carcinogenic response has regressed.

Although the whole conception of co-carcinogenesis has arisen from

experimental work on mouse and rabbit skin, some such idea must be evoked by a problem such as that of asbestosis and cancer, until some more experimental evidence of direct carcinogenesis by asbestos or a decomposition product of it can be obtained. If such an idea is feasible, then we must also assume a pre-neoplastic preparedness in the organ in which the co-carcinogen (asbestos or the fibrous tissue in the peribronchiolar reaction) later induces a further development into true neoplastic growth. The preparedness of the tissue if it is to be regarded as more than a form of words is brought about by something independent of the asbestosis, and this must be regarded as an endogenous factor. But some special property must also attach to the asbestosis for the alleged cancer induction in this condition is not apparently found in the long-standing cases of silicosis.

We will first consider the evidence that asbestosis leads in a proportion of cases to cancer of the lung. As long ago as 1938 the suspicion arose that asbestos workers might be more than normally prone to lung cancer.

Nordmann (1938) analysed six cases of lung cancer and showed that the range of exposure periods was 7 21 years, and the range of intervals between entering the industry and death was 15 to 21 years The malignant disease in some cases occurred years after leaving the industry. Half of these cases were comparatively young, 35–41 years of age at death. In one remarkable case a 71-year old woman had worked in asbestos for only 19 months. Later in the same year he referred to a further seven cases of associated asbestosis and lung cancer, including Gloyne's (1936) finding of six cases of carcinoma of the lung in 50 necropsy cases of asbestosis.

In the 1947 Annual Report of the Chief Inspector of Factories, Merewether tabulated the age incidence among 235 deaths caused by asbestosis: in 13·2 per cent of these cancer of the lung was present, and it is especially important to note that 4·8 per cent of the age-group 25–34 years and 5·6 per cent of the age-group 35–44 years had this condition. It will be seen that the over-all figure is closely in agreement with Gloyne's findings.

In a further report* carrying this analysis up to the end of 1954, he found that amongst 344 deaths, in 55, or 16·0 per cent, cancer of the lung was present.

In their series of papers on asbestosis Lynch and Cannon (1948) give an analysis of the post-mortem examination of 40 cases of asbestosis among which 3 cases of carcinoma of the lung were found associated with medium or advanced grades of asbestosis, which, according to these authors, is seven times the general incidence in the United States.

In a more recent study of the clinical picture and pathology of asbestosis, Behrens (1952) estimated that of 309 cases of asbestosis reported in the literature there were 44 cases of carcinoma of the lung (14·2 per cent) whereas in a series of 2,204 cases of silicosis only 32 such tumours were found (1·4 per cent).

* Annual Report Chief Inspector of Factories for 1954, pp. 190–193

[redacted]

The discrepancy between the two incidences in Switzerland is of the same order as that found in the smaller series by Lynch and Cannon in the United States.

Suggestive as these and other data are, Stoll, Bass and Angrist (1951) were dissatisfied with the statistical weight one could put upon available figures at that time which included, in addition to those of Lynch and Cannon, a series of 235 cases of asbestosis with 31 carcinomas of the lung (13·2 per cent) which is again almost identical with the finding of Behrens. They refer also to another series of 115 cases with 14·8 per cent lung tumours.

Describing the case of a worker who had been engaged for only 6 years covering pipes with asbestos and who had refused to take precautions by wearing a respirator, they point out that except for weakness and persistent cough nothing noteworthy was found until malignant cells were found in the bone marrow. Radiographs of the chest showed numerous large discrete oval shadows which were interpreted rather as metastatic deposits than primary tumours. Post-mortem examination showed asbestosis with scattered large nodules and metastases in kidneys, brain and liver. Histological examination confirmed the presence of asbestosis bodies and anaplastic carcinoma of the lung, with numerous metastases. There appeared to be some doubt about the primary focus of malignancy in this case, and the authors inclined toward a multiple origin. Whether this case is relevant to the problem of asbestosis cancer is open to question, but the authors were led to suggest that asbestos must itself be regarded as a direct carcinogen in respect of its composition as a silicate.

A less compromising attitude is taken by Werber (1952) who states categorically that in 7-17 per cent of cases of asbestosis after a latent period of about 1½–20 years, as a result of epithelial metaplasia, carcinoma becomes established in the lung. Werber then reports what appears to be a clear-cut case successfully operated on. The patient was a man of 58 years who, after years of work in asbestos with complaint of irritant cough, showed, in a mass radiographic investigation, a well-marked dense round shadow in the right lower lung field associated with bilateral finely granular shadows in the middle and lower fields, more marked on the right side.

Lobectomy of the right lower lobe confirmed the presence of a non-keratinizing squamous cell carcinoma. Nearly the whole of the lower lobe was occupied by an almost certainly bronchogenic (postero-lateral segment) tumour. Asbestosis bodies were found in the lung and in an excised hilus lymph node. Recovery was uneventful and x-ray examination showed later expansion of the upper and middle lobes.

A suggestive case is also described by Cureton (1948) of a young woman of 37 years who 15 years before had left asbestos work after 7 years in the industry. Necropsy showed a predominantly squamous-celled bronchial carcinoma accompanied by asbestos bodies and fibrosis in both lungs. This author is cautious about the relation between the neoplasm and the asbestosis

but points out that the woman was very young for a squamous growth.

As in the case of most other occupational tumours, it is commoner to find workers without the neoplastic reaction than with it, even after all the apparently necessary and sufficient conditions for its development have been found to exist. Many such cases have been amply described. We give one or two from the Continental literature.

Having worked for 22 years consecutively applying insulating (asbestos) material to articles, a man aged 40 years was killed in a street accident, never having complained of respiratory troubles. Franchini and Canepa (1949) performed the post-mortem and found a fracture of the base of the skull as the immediate cause of death. The lungs were massively and extensively fibrosed mainly in the middle and lower lobes, with lymphocytic infiltrations and thickened elastic tissue; many asbestosis bodies were found occupying the lungs and lymph nodes. No mention of neoplastic change is made. It is specially interesting that, as in so many other cases, the massive pulmonary changes should have been unaccompanied by complaint.

This is of importance because if after a period of exposure to asbestos dust a certain measure of fibrosis is developed and thereafter the industry is left, we may picture a static non-symptomatic, non-progressive fibrosis, but a continuing process of cancerization in a certain number of cases Whether the preceding fibrosis is necessary for the subsequent neoplastic process or whether the latter is conceivable without the former, it is not as yet possible to say.

The entry of any particles or fibres into the lung, even when they are soluble in water, produces a phagocytic response from the septal cells in the alveolar walls and giant cells with many nuclei soon develop. In the case of a soluble compound the ultimate degeneration of the dust cell permits the second stage of the absorption of the compound. This is readily shown experimentally with any of the common laboratory animals. The lung presents a temporary barrier to soluble particles; in the case of insoluble particles the barrier is more permanent, depending on the size of the particles. The smaller particles may be taken up by phagocytic cells arising from various sources and disposed of in lymph glands, in the interstitial tissue of the lung and even to some extent in organs from which they can be excreted Everything depends upon the size.

Phagocytic cells may, however, be completely frustrated both by the nature and size of particles. In such cases they surround the foreign material and a process of local fibrosis sets in, the foreign unattackable material remaining more or less *in situ*.

A small particle (2–3 micrograms) will ultimately enter the alveoli and the fibrous reaction will start from the alveolar walls and lymphatics, if it cannot otherwise be disposed of. If the particle is big (10–15 micrograms) and cannot therefore proceed into the ultimate air passages, it is held up and the reaction occurs more proximally in the bronchiolar tree

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In respect of the basic features of the body's reaction to asbestos fibres there is nothing to choose between them and particles of silica. The particular differences, which are undoubtedly observed, arise from different physical form; difference in solubility; difference in size, and the possible difference in carcinogenic properties.

The term asbestos is vague and industrially may refer to any of a series of complex silicates. It belongs to a group of crystalline magnesium silicates, which include talc (steatite) $Mg_3H_2(SiO_3)_4$, Meerschaum $Mg_2H_2(SiO_3)_3.H_2O$, possessing varying degrees of resistance to heat and to chemical agents. It is best as recommended by Spencer (1937) to preface the word asbestos with the particular mineral from which it is derived, for example serpentine asbestos and amphibole asbestos (hornblende). Unfortunately, more words than one are used in this industry for the same natural product.

The common forms, with country of main origin, used in the various industries with which our present theme is concerned are:

(1) *Serpentine asbestos* (*Canadian*) (chrysotile*; amiant). Chrysotile is the most used of the fibrous silicates. Empirical formula: $H_4Mg_3Si_2O_9$ $(= 3MgO.H_4(SiO_3)_2)$.

As mined the following is the analytical composition of an average sample of the naturally found mineral (serpentine: hydrous magnesium silicate):

	per cent
SiO_2	43
Al_2O_3	0·52
$FeO\ Fe_2O_3$	1·0
MgO	41·36
H_2O	13·79

(2) *Amphiboles* Empirical formulae:

$H_2Ca_2Mg_5(SiO_3)_8$	Tremolite (Italian)
$H_2Ca_2(MgFe)_5(SiO_3)_8$	Asbestos (amphibole asbestos)
$CaMg_3(SiO_3)_4$	Actinolite
$H_2Na_2Fe''Fe_2'''(SiO_3)_6$	Crocidolite (Blue asbestos—South Africa, Australia)

(3) *Amosite asbestos* (*South Africa*) (ferro-anthophyllite). Empirical formula: $H_2(MgFe)_7(SiO_3)_8$.

Their commercial value is due to the long fine, infusible, non-conducting fibres in which these silicates exist and can be worked and it is this character which motivates the characteristic changes in the lungs when inhaled over considerable periods. In the mining of serpentine and of the asbestos from it as a mass of fine, silky crystals in Canada, Cartier (1949) found that he could divide the 3,242 workers of whom 40 per cent had been in the mines for 10–40 years into two groups, one exposed to the dust of serpentine, which remained free from asbestosis and the other, exposed in grinding,

* Not to be confused with chrysolite which is an isomorphous mixture of Mg_2SiO_4 (forsterite) and Fe_2SiO_4 (fayalite).

screening, suction and bagging to the dust of the dried separated fibrous silicate, in which all the cases of asbestosis developed. Among the 22 cases of asbestosis found by radiography and confirmed post-mortem, there was no mention of any cases of cancer of the lungs. More clinical and occupational data on these cases would have been desirable. On the basis of the findings elsewhere, 1 or 2 cases of lung cancer would have been expected. On the experimental side Cartier implies that his clinical data are confirmed by exposure of animals to the two kinds of dust.

Cartier makes two statements of considerable interest as to the severity of asbestosis among his miners.

(1) During his 3 years of clinical observation (more than 10,000 complete medical examinations) no worker has died of uncomplicated asbestosis under the age of 60 years, even after 20-30 years' severe exposure to asbestos dust; nor has he seen among asbestosis cases as severe cyanosis or dyspnoea as that seen in asthmatics, lung cancer or advanced tuberculous cases. From this he concludes that pure asbestosis is not as severe a disease as it is considered in Great Britain and elsewhere where manufacturing processes are carried out with the separated asbestos.

(2) Pure asbestosis, often even radiologically very advanced, is found among workers who show no clinical signs, no diminution of respiratory function and can without discomfort carry out their habitual tasks.

The claim by Cartier amounts to this, that asbestosis as usually described is really a mixed disease, complicated by cardiopathies and even tuberculosis, and that " pure " asbestosis as seen by him is by no means a severe condition. Having been in close association with such notable authorities as Gardner and Vorwald, these statements cannot be ignored because of relatively short experience of the industry. It may be that Cartier considers a life of 60 years amply sufficient for the relatively few cases who develop the disease severely enough to die from it. He does not, however, in this paper give the populations at risk so that we cannot calculate essential data It may be relevant to his thesis that the population around the Thetford mines is almost entirely pependent upon them for their " gagne-pain ".

Cartier's second statement is, however, borne out by the case of Franchini and Canepa. It will be recalled that whereas the general view in Great Britain is that the symptomatic picture is more severe in asbestosis than in silicosis, the reverse view is held in America. The long period of absence of symptoms has been known for many years, but the diminution in vital capacity is demonstrable even when the worker is perhaps unwilling to admit any respiratory abnormality. As was pointed out over 20 years ago by Merewether and Price (1930) and Merewether (1930), the worker is inclined to attribute his discomforts to causes other than his work.

A more normal case history is that given by Luton, Champeix and Faure (1951) who describe what is stated to be the first case of asbestosis reported in France. This was a man aged 62 years who, having worked for 11 years

in an asbestos cloth factory ($2{\cdot}25$–$4{\cdot}0 \times 10^8$ particles (1–2 μ) per litre of air) complained of dyspnoea on exertion and was somewhat cyanosed. Radiographically the fibrotic condition progressed in the middle and lower lobes until he died 7 years later. Necropsy findings were of the classical kind: diffuse fibrosis, thickened pleurae, no nodulation, many asbestosis bodies with giant cells and many mineral particles in the lungs.

Dust particles were found also in the vessels of the liver, kidney and spleen. No mention is made of metaplasia or neoplastic changes. These authors discount the possibility of a chemical influence of asbestos particles on the pulmonary tissues.

We have been at some pains, but without success, to elicit any statement or evidence in the literature of asbestosis which could be interpreted as more than a verbal attribution of the effects of asbestos particles to irritation. For the fibrotic effects there does not seem any reason to seek causes other than sharp "insoluble" foreign bodies larger than a critical size. The work of King, Clegg and Rae (1946) in which they pursued the mechanical action theory of Gardner, presented a reasonably full picture of the response of the lungs of rabbits to insufflation of small ($2{\cdot}5$ μ) and large (15 μ) asbestos fibres. Gardner and his school had emphasized that, as we have already mentioned, with asbestos particles size is everything, small particles being innocuous, big particles hazardous, and that this distinguishes their effects from those of silica and quartz which are entirely the result of small particles. Nevertheless, King, Clegg and Rae did find some effect from the inhalation of small ($2{\cdot}5$ μ) particles of asbestos, which might be described as a diffuse fibrous tissue reaction affecting mainly the interstitial tissue and alveolar walls with hyperplasia of the bronchial nodes and some nodular areas of giant-cell reaction. Phagocytosis of these small particles was probably easy enough to restrict the reaction to the locations mentioned. With larger fibres (15 μ), the foreign body giant-cell processes were apparently overlapped by a more permanent reaction, nodular in distribution, which fixed the asbestos particles *in situ*.

King, Clegg and Rae make the significant comment that these nodular, somewhat acellular, areas of intra-alveolar connective tissue were strictly comparable to, if less intense than, those produced by quartz, which means that the lung does not distinguish them.

In respect of small particles they suggested that if fibres $< 2{\cdot}5$ μ in size were insufflated, they would be completely removed from the alveolar wall and fail to produce interstitial fibrosis. It seems possible that in the case of Luton and his colleagues the smaller particles were phagocytosed and discharged into the circulation in the way probably envisaged by King and his co-workers, since they report having found dust particles in the vessels of the liver, kidney and spleen.

Summing up the many years of research of Gardner and his co-workers on the effects on animals' lungs of asbestos particles administered by

inhalation, intratracheal insufflation, intravenously or intraperitoneally. Vorwald, Durkan and Pratt (1951) recall that ordinary industrial (asbestos) dust and, especially, long fibre asbestos dust from which the small fibres had been separated, produced characteristic peribronchiolar fibrosis which remained static on discontinuance of exposure, whereas to particles of 3 μ and less there was no tissue reaction (King, Clegg and Rae, 1946). On substituting Brucite (native magnesium hydroxide containing only 0·9 per cent silica as silicate—Brucite is a crystalline compound easily split into thin sheets and has a flexibility comparable to that of asbestos fibre), for the asbestos peribronchiolar fibrosis is similarly established, but dust of glass fibre which is not flexible and, of course, cannot be split does not, on long inhalation, lead to fibrosis.

The dependence of the fibrosis on physical form was, however, settled by the failure to induce fibrosis by long inhalation of asbestos which, having been fused and ground, no longer retained its original structure.

The Gardner school held that the combination of size, physical form and immobilization in a rhythmically moving organ is the determinant of the pathogenic effect. Effects somewhat similar to this pulmonary fibrosis can be obtained by injection of asbestos fibres into the peritoneum.

But at no stage in all these impressive researches was any clue obtained which might have offered any support to the possibility that asbestos could act as a carcinogen. There is no reliable criterion by which one can anticipate carcinogenicity and, as is well known, relatively minute changes in the structure of a chemical carcinogen are sufficient to diminish or eliminate carcinogenic action.

If asbestos is indeed to be regarded as a carcinogen, the need is felt to demonstrate some property which can be regarded as something more than inertness. The simplest such property is solubility. Solubility confers some activity on a compound as, for example, in the case of silica, the solubility of which in aqueous conditions is sufficient to found a chemical theory of silicosis.

Asbestos has, however, not given much evidence of a solubility which might be significant.

In analysing the working environment for asbestos dust Sundius and Bygden (1938) made the curious remark that only amphibole asbestos could be recognized in their analyses, in spite of the fact that the asbestos commonly used in industry contains mainly chrysotile and to a considerably lesser extent amphibole asbestos. This statement, if confirmed, might mean that chrysotile is dissolved in the analytical process. In fact, chrysotile is the least resistant of asbestos types to chemical and physical agents: it is decomposed by hydrochloric and sulphuric acids, it loses water at red heat and its fibres can be fused in the bunsen flame. (Crocidolite--blue asbestos—is also fusible to a black magnetic glass but is resistant to chemical agents).

Assuming that chrysotile might be capable of exerting some chemical

effect by virtue of these and perhaps other related properties, the mind turns to the asbestos body which, lying in the lung tissues for long periods, might have some significance other than that usually attributed to them of being a structure in which the enclosed asbestos fibre can lie innocuous. In the experiments of Gardner and his school the injection of isolated asbestos bodies did not produce fibrotic reactions. But this need not deter us.

Cooke (1930), who, with MacDonald, discovered the asbestosis body, made the following comment: "they consist of central nuclei of asbestos spicules upon which colloidal aggregates of blood proteins, plus, possibly, soluble fractions of asbestos, and, in the case of chrysotile workers, iron salt, have been absorbed and moulded by currents in the bronchi and alveoli".

In recent work Champeix and Bouteville (1950) examined asbestosis bodies in the electron microscope at magnifications of 25,000. It may be recalled that Champeix was associated with the view opposing a chemical factor in the aetiology of asbestosis (Luton and his colleagues).

Electron microscopy

The procedure to examine an object as delicate as an asbestosis body in the electron microscope presents much difficulty, and the interpretation of the photographs obtained should be correspondingly cautious.

Champeix and Bouteville treated expectorated material as follows:

Alkaline digestion of the diluted sputum with NaOH (equal volumes). After 10 minutes' warming in a porcelain dish, allowed to cool.

Homogenized fluid divided among several centrifuge tubes and centrifuged cautiously to avoid disintegration of the asbestos bodies.

Decanted and residues spread on several slides.

To examine in the optical microscope, mount in Canada balsam

To examine in the electron microscope the smear allowed to dry and with a micro-manipulator a single asbestosis body is lifted on to the collodion membrane of the object carrier. This operation is difficult and delicate and the hazard of fracture of the asbestos body is great.

As regards the general morphology of the asbestosis body, the electron microscope confirms in greater detail and without deformation the findings with the optical method—the central, needled fibre ($\frac{1}{2}$–1 μ thick, length always > 10 μ) surrounded by an amorphous, somewhat opaque rounded envelope (2–3 μ thick) in parts appearing as if burst and giving a general *impression of a colloidal, proteinous gel: the extremities ovoid, ellipsoid,* fusiform or sometimes angular.

Two observations suggested solution of the asbestos fibre: (1) there were no fibres less than 10 μ in length in any asbestosis body; (2) removal of the colloidal envelope of the asbestosis body by means of the micro-manipulator shows the central fibre with one edge semi-transparent as if it were being dissolved away.

These facts lead the authors to some dubiety on whether the fibrosis is

due to a maintained mechanical irritation produced by the insoluble amphibole, or to a chemical effect brought about by the dissolving silicate. It may be recalled that Alden and Howell (1944) stated that amosite needles are capable, where embedded in epithelial tissue in the skin, of eliciting a non-inflammatory epithelial proliferation. This statement was made from observations on amosite workers who developed hyperkeratotic epithelial thickening after penetration by a small splinter-like fibre. X-ray examination and biopsy show no evidence of a foreign body in these " corns ".

Solubility of asbestosis bodies

More work is required on this problem especially quantitative studies of the solubility of asbestos types in a variety of conditions, together with an identification of the products after solution. The question is not one of explaining fibrosis of the lung by a chemical process, for this is almost decisively negatived by the undoubted fact that the smallest particles of asbestos have not in fact produced a fibrosis in the experience of most investigators. The question is rather one of finding a product of solution which, by entering the modified squamous epithelium of the lung, or by changing its environment, can lead to de-differentiation or to tumour formation. The majority of pulmonary tumours in men are anaplastic or undifferentiated or (epidermoid) squamous epitheliomata and they constitute a type of new growth in the lung which has hitherto eluded the experimentalist. Probably the only claim to have induced a true cancer in the lungs of mice was that made by Nordmann and Sorge (1941) who exposed 100 mice to undefined asbestos dust and stated that 20 per cent of the animals developed cancer. There is considerable doubt, however, whether the evidence presented is really acceptable.

In fact, cancer of the lung (truly so called—not adenomas as found and induced in mice) has not hitherto been produced by inhalation of any material W E Smith (1952) in a very forceful consideration of the experimental aspects of cancer of the lung concludes " that we are singularly ill-equipped for the experimental study of one of the chief problems of human cancer ".

Until this charge is successfully answered we may for practical purposes regard asbestos or a derivative of asbestos as a probable co-carcinogen in that proportion of cases of diffuse fibrosis of the lung in which the necessary preparedness of the lung has been brought about, probably endogenously Such a view has, at least, the merit of less sterility than the common panacea for carcinogenic dilemmas, irritation

AROMATIC AMINES

Of the few identifiable chemical agents which may without doubt be accepted as standing in the line of causality of particular types of human neoplastic disease, certain aromatic amino intermediates in the dyestuffs industry occupy the most interesting and, from the point of view of the experimentalist, the most fruitful position. Not only have they been repeatedly reported in

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