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PNEUMONOCOONIOSIS

WITH SPECIAL REFERENCE TO THE SILICO-ANTHRACOSIS OF COAL MINERS

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At the International Congress on Silicosis, Johannesburg, 1930, the definition of silicosis finally accepted was as follows: "A pathological condition of the lungs due to the inhalation of silicon dioxide." This definition has been challenged, in recent years, especially by the observations of W. R. Jones of the Royal School of Mines, London, who associates "silicosis" with sericite (1933); and it is quite certain that grave pathological effects follow the inhalation of certain mineral particles—for example, asbestos dust—in which the silica is not free but combined as a silicate.

In this paper no attempt will be made to discuss the problems raised in this controversy, which is still unsettled, but, instead, the issue will be avoided by adopting the following less stringent definition of silicosis as "a pathological condition of the lungs due to the inhalation of silica, whether free or combined, in such a state as to be capable of setting up its characteristic pathogenic effects." At the International Congress above referred to E. L. Middleton expressed the view that

"while it appears to be true that free silica tends to produce its characteristic effects whether alone or in admixture with other dusts, it seems equally true that its action is influenced to a greater or less extent by such dusts. When the accompanying dusts happen to be silicates which are capable themselves of producing effects, the resulting changes in the lung tissues, the influence on function, and the reactions to infections, become extremely complicated."

This is true; and it may therefore be justifiable to attempt a simplification of the problem presented by the inhalation of mixed dusts, the fact being that the dust inhaled by the industrial worker is practically never pure but always mixed.

Active Dusts and Inert Dusts

The first broad differentiation which it seems necessary to make is that between (a) dusts which are chemically active, and (b) dusts which are inert, when inhaled into the respiratory tract.

(a) *Chemically active dusts* must necessarily be soluble, to a greater or less extent, in the body fluids; and it is upon this solubility that their activity depends. This activity, manifested in the situations to which the dust particles are carried in phagocytes along the lymph stream, causes lesions of two types, "toxic" and "sclerotic," both of which have been reproduced experimentally by Gye, Purdy, and Kettle in this country, and by Gardner in America. The toxic lesions depend on local necrosis and cell death, and appear to favour the pullulation of tubercle bacilli. The sclerotic lesions take the form of the nodular and diffuse fibrosis so characteristic of silicosis.

(b) *Inert dusts* are insoluble in the body fluids, and therefore cannot exert any chemical action in the lung tissues. They may, however, if they accumulate to any marked extent, exert the mechanical action characteristic of foreign bodies, and thus lead to a certain amount of diffuse fibrosis around the dust deposits. Certain chemically inert dusts, too, may have physical effects; there being, for instance, much reason to think that the carbon accumulations in silico-anthracotic lungs are capable of adsorbing toxic substances; an action to which the writer attributes the relatively low incidence of clinically active tuberculosis in silicotic coal miners.

A state of pneumoconiosis may depend either upon the inhalation of chemically active dust particles alone, of inert dust particles alone, or of active and inert particles breathed in together or in succession the one to the other.

The lung tissue, after death, presents to the investigator a record of the mineral particles breathed in during life; is, in fact, a kind of palimpsest of the individual's industrial history. This statement, however, while true as a generality, must be made with one reservation, especially in view of the recent observations of E. King in Toronto (1934). If, as we believe, the activity of a dust depends upon its gradual solubility, the examination of lung residues is likely to bring to light a larger proportion of the inert and insoluble minerals than of the chemically active and relatively soluble minerals to which the more important pathological lesions are actually due.

This fact has not been sufficiently stressed in the past, either by the present writer or by other workers on pneumoconiosis. The persistence of a given substance in the lung tissue and its preponderating excess in lung residues does not, in itself, constitute a proof of its aetiological importance. If, for instance, sericite were proved to be insoluble, or almost insoluble, in the body fluids, its mere presence in the lungs would be no argument in favour of its role in the production of lung fibrosis. Like the inert coal dust, it might accumulate in the lung tissues and always be visible in sections, yet be chemically harmless, in contrast to silica, which is known to be sufficiently soluble to set up pathological changes in the situations to which it has been carried in the lungs and lymphatic glands.

This problem of the relative solubility of the mineral constituents of inhaled dusts in relation to their pathogenic properties is one which calls for further careful study by chemists and pathologists working together.

These remarks are made without prejudice to the sericite *v.* silica controversy. Jones, indeed, suggests, in his original publication (1933) that sericite fibres are soluble in the body fluids; "silicate minerals less stable than

quartz" he calls them, "and which, because of their physical form, expose far greater surface to volume for any chemical action than do the more compact grains of quartz." His views on this point, however, are not universally accepted, and require the confirmation of careful biochemical investigation.

The accumulation of stone dust in the lungs has, however, a very definite significance, as proof that the individual has been exposed to high concentrations of the dusts found, and as evidence that some factor has interfered with the normal power of the lungs to free themselves from the dusts inhaled during life.

Classification of the Pneumoconioses

With these preliminary remarks it is now possible to pass to a simple classification of the effects of inhaled dusts.

Type 1.—Dust retention and accumulation determined by the operation of a chemically active dust inhaled into the lungs; resulting in nodular fibrosis and, in *x*-ray films, bilateral symmetrical mottling.

Examples: silicosis; asbestosis.

Type 2.—Retention and accumulation of an inert dust, determined by lymphatic blockage through previous or simultaneous inhalation of a chemically active dust; resulting in nodular and diffuse fibrosis, dust accumulations, and, in *x*-ray films, bilateral symmetrical mottling and irregular diffuse shadows.

Examples: silico-anthracosis; silico-siderosis.

Type 3.—Accumulation of an inert dust through excess of entry over elimination; resulting in black anthracotic but usually well-aerated lungs without much fibrosis and, in *x*-ray films, nil or partial small mottling.

Examples: the anthracosis of coal trimmers and screeners.

Type 4.—Localized dust retention in areas of obstructed lymph flow due to old tuberculous foci or other lesions; resulting in extensive, sharply localized accumulations of dust in fibrotic "india-rubber-like" areas of non-symmetrical distribution, and, in *x*-ray films, "cricket-ball" or "pseudoneoplasm-like" shadows.

Examples: the fibrotic aggregations of inert dust occasionally present in individual cases in all types of pneumoconiosis, but especially frequent in silico-anthracotic persons, in coal trimmers, and in screeners.

It will be seen that Types 1 and 2 depend on the inhalation of chemically active dust, alone or mixed with inert particles. In both these types, therefore, there is a liability to the toxic and sclerotic effects of siliceous dust and, in Type 2, the physical effects of accumulation of an inert dust in excessive quantity as well.

It seems to me that insufficient attention is being paid to the conditions which are here included under Type 2; and that the risk to working efficiency and health may be greatly accentuated through the inhalation of finely divided particles, even of a chemically inert dust, when there has occurred the lymph stasis which is known to follow exposure to siliceous dust. The point in the development of silicotic fibrosis at which lymph stasis may occur to a sufficient extent to lead to retention of another type of dust has not yet been determined, but it probably falls far short of what might be expected to produce recognizable silicosis were siliceous dust alone in question. In cases investigated by myself there had occurred a vast and dangerous accumulation of coal dust in lungs of which the total silica in the ash, as determined by chemical analysis, was only about twelve to fourteen times the normal, whereas in advanced cases of silicosis the percentage may be from thirty to fifty times the normal, taking the normal as about 1 per cent.

This risk may be great in the case of persons who, after a period of work in a "hard heading" or in some other job involving exposure to the dust of hard stone, return to work in a normally inert dust, as, for instance, to work as hewers at the coal face. A case of this kind was recorded by me in 1927.

Silicosis and "Miners' Phthisis"

Until recent years the occurrence of any form of silicosis in the coal-mining industry was either denied or ignored, for the simple reason that silicosis was associated, in the minds of medical investigators, with "miners' phthisis," the tuberculous wasting disease which so frequently supervenes as a last phase in the silicotic gold miner or other worker in quartz or quartzite dust, through the toxic and "tuberculophile" action of the products of solution of siliceous particles in the lungs.

It was true in the past, and is still true to a great extent, that coal miners, as a class, exhibit no striking evidence of a marked liability to "miners' phthisis," a liability which is so extremely well marked in the statistical records of other workers exposed to the inhalation of siliceous dust. Coal miners, however, in common with others exposed to siliceous dust, exhibit a great deal of what I have ventured to call "miners' dyspnoea," the stage of silicosis in which the sclerotic and mechanical effects of the disease are often extreme, but, in the case of the collier, with a diminished tendency to pass on into the terminal stage of "miners' phthisis."

Silico-anthracosis

I find the explanation of this relative exemption from terminal phthisis not in the absence of silicosis but in the presence of an added factor, absent or minimal in the typically "silicosis-producing" industries. This added factor I believe to be coal dust, in large quantity and exceedingly fine division, present along with the siliceous dust in and around tuberculous foci. With C. Weatherall (1933) I have shown experimentally the power of coal dust to adsorb the active principle of tuberculin *in vitro*, and it seems probable that a similar adsorption may take place *in vivo* in colliers.

It is dangerous, however, to generalize about an industry which includes such a wide variety of occupations, each with its special liability to, or security from, exposure to stone dust. In the coal-mining industry are included certain tasks, such as "sinking," "boring," and work with compressed-air drills in "hard headings," which are just as dangerous, where the stone happens to be rich in silica, as the work of a metalliferous miner on the Rand. It is among such "stone-drilling" workers that the worst cases of silico-anthracosis arise.

Exposure to Different Dusts

While the great majority of underground workers in the coalfields are engaged in "getting" coal at the face and thus encounter coal dust rather than stone dust in their normal work, they are frequently exposed to fine stone dust in the work of ripping roof or repairing, which often falls to their lot, and, while there is some tendency to specialization, many of them take a turn at work in "hard headings" from time to time; and there is a considerable amount of change from one type of work to another. There is also the stone dust used for "dusting" as a precaution against explosions to be reckoned with; usually an inert shale dust, but sometimes, perhaps, chosen without sufficient regard to its constituents. It is therefore difficult or impossible to draw any sharp line between "hard-heading" workers and other colliers of long service in the industry. Silico-anthracosis, in fact, may occur in all types of colliers exposed to both stone dust and coal dust, but is commonest in those who work with mechanical drills in hard stone.

Work of the screens is probably the safest type of employment in the coalfield, so far as exposure to stone dust is concerned, as it is carried out above ground and the workers breathe coal dust only; but it is staffed either by youngsters just entering the industry and destined

to pass on as soon as possible to the better wages of underground work or by old men who are unfit to go underground and who seek this extremely dusty but otherwise less strenuous job as a favourable alternative to work at the "face." Such workers, engaged in a very dusty occupation but breathing a dust which is, for the most part, inert, might be expected, if pneumonoconicotic, to exemplify, perhaps, in an extreme degree the pure anthracosis depending on excess of inhalation over elimination of coal dust.

In this category, again, there are the "coal trimmers" at the docks, men who work intermittently in distributing the coal in the holds of ships. These men work in an atmosphere charged with dense clouds of fine coal dust almost entirely free from stone particles, and afford, in this respect, a sharp contrast to the "hard-heading" workers, both in the type of dust inhaled, the mineral content of their lungs, and the pathological and histological characters of the highly anthracotic pulmonary tissue found at post-mortem examination.

It may be stated as a generality to which, of course, there are exceptions, that the liability to "miners' dyspnoea" and "miners' phthisis," the frequency of radiological evidence of "lung fibrosis," the presence and extent of nodular and diffuse fibrosis at post-mortem examination, and of a high percentage of total silica in the dried lung on chemical analysis, vary directly with the degree of exposure to stone dust during the life of the individual worker.

The "sinkers," "borers," and "hard-heading" workers, breathing in much stone dust and relatively little coal dust, are liable to exhibit advanced silicosis after a relatively short period of work, and may show a marked tendency to phthisis, just as do metalliferous miners. At the other extreme are the coal trimmers, with little or no risk of silicosis, though it is possible that they may prove to suffer, to some extent, from a form of diffuse lung fibrosis, of "foreign body" type, from excess of anthracotic accumulation. In between come the great body of coal miners whose risk depends upon varying degrees of exposure to stone dust of varying type according to the kind of work undertaken from time to time and the quality of the rock worked in their mine. It is upon this numerous intermediate body of colliers that the statistics relating to coal miners are based. Few now deny the silicosis risk run by "hard-heading" workers in coal mines, but the relative exemption of colliers in general from "miners' phthisis" as evidenced by the absence of a high tuberculosis mortality in late middle-age in the coal-mining industry, has led to the belief that there is no real silicosis in coal miners other than "hard-heading" workers.

It must be stressed, in this connexion, that the effect of silicosis is to produce "miners' dyspnoea," not "miners' phthisis." Silicosis creates a liability to "miners' phthisis" by acting as an adjuvant to tuberculous infective processes, but is not, in itself, a form of tuberculosis.

It is my contention that, in the silicosis of coal miners, while the classical state of "miners' dyspnoea" is very marked, and is expressed in the death returns as a high bronchitis mortality, the terminal effect of a high tuberculosis mortality is much diminished through the operation of coal dust as an adsorbent for the toxic products of tuberculous foci in the lungs. It is not suggested that the silicosis of coal miners is unaccompanied by the liability to tuberculosis noted in silicosis elsewhere. What is suggested is that this "tuberculophile" effect is neutralized through the detoxicating effects of the coal dust inhaled, in large quantity, throughout the life of the collier. The studies of Dr. Enid M. Williams on the lung conditions of old and retired coal miners (1933) show

clearly that a benign type of tuberculosis is very common amongst the dyspnoeic but far from "phthisical" subjects observed by her.

In the direction of prophylaxis, the point which must be emphasized, first and last, is that the element of serious risk lies in exposure to stone dust, a risk inseparable from coal mining as from all industries which involve the getting of minerals from underground seams in rock containing silica in sufficient quantity and in a dangerous form; a risk which may be greatly diminished by adequate precautions.

Compressed-air Drills

Stone dust is thrown into the atmosphere in the course of compressed-air drilling, after "shot-firing," and in such jobs as repairing, ripping, and other work in stone. While there has been a great improvement in the ventilation and general hygiene of coal mines in the last fifty years, one factor has been added to an ever-increasing extent—the use of compressed-air drills. This must necessarily imply, in the absence of very special precautions, that there is more and finer rock dust in the air.

Tatham, writing in 1902 about the marked liability of colliers in South Wales and Lancashire to non-tuberculous diseases of the lungs, evidenced by a mortality of 76 per cent. more than that of "occupied males" generally, pointed out that these diseases have very considerably increased in fatality since 1881. In the Registrar-General's *Decennial Supplement*, England and Wales, 1921, Part II, Occupational Mortality, etc., it is shown that the mortality from both tuberculous and non-tuberculous respiratory diseases had increased in 1921–3 as compared with 1910–12. It is added that "from causes from which the mortality of miners was especially low in 1910–12, such as phthisis, their advantage is now much less, while causes showing heavy mortality for miners in the earlier period, such as bronchitis at ages over 45, show a still heavier mortality." While the report adds that bronchitis is one of the diseases which have always been a source of high mortality in the areas in question, this does not explain why it should be still higher at a time of general advance in preventive medicine. It is true that the war period had intervened; but this can hardly suffice to explain the difference. To me it suggests itself that the increase may be a further extension of the tendency noted earlier by Tatham, and that the explanation lies in the steady increase in machine drilling of rock which has been taking place since these instruments were introduced into industry during the making of the Simplon Tunnel. E. Williams, writing on this subject, points out that "in the old days—for example, more than twenty years ago, all the boring was done by hand, and this work, in hard quartz rock or sandstone, was slow. At the present time, following the introduction of various patterns of compressed-air drills, the boring is done much more quickly. There is consequently a much greater amount of dust produced in the drilling process." The same author expresses the opinion that the production of silicosis is, in some places, more noticeable among the relatively young than among the old men, as the former have had more stone dust to breathe owing to more modern drills being in use at the present time.

The risk of drilling can be greatly diminished by the use of efficient dust-catching devices, such as the "Hay" and the "Trewill" dust traps now so popular in the South Wales minefield; but there is a need for further research aimed at the provision of dust-free air for the miners working at ripping, repairing, and other jobs in which much dust is produced apart from the use of drills. Careful studies are needed, too, as to the time necessary for the subsidence of the finest, and therefore the most dangerous, dust particles after "shot-firing,"

and for the regulating of the time of return to work accordingly. And it should be added that the new suggestions as to the danger of certain minutely fragmenting fibrous silicates, on which stress has been laid by W. R. Jones (1933), serves to emphasize the importance of a careful scrutiny of the stone dusts so successfully used for "stone dusting" as a precaution against explosions. It may well be that the importance given, in the past, to the presence or absence of "free silica" may have blinded us to the existence of other dangerous elements capable, equally with or in greater degree than free silica itself, of producing silicosis.

PERSISTENCE OF TETANUS ANTITOXIN IN MAN FOLLOWING ACTIVE IMMUNIZATION

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During the past two years we have determined the antitoxin content in the blood serum of a group of adults at various intervals after subcutaneous injections of tetanus toxoid. From the beginning of this study subjects 1 to 16 have been given tetanus toxoid, supplied through the kindness of the Pasteur Institute, Paris, and subjects 17 to 29 have been injected with a similar toxoid, prepared at the Connaught Laboratories, University of Toronto.

Persistence of Antitoxin Two Years after Three Doses of Tetanus Toxoid

Serum was obtained from thirteen persons about two years after the last dose of the primary series of injections of tetanus toxoid. Of twelve persons in whom comparison was possible, as may be noted by Table I, the residual

TABLE I.—*Tetanus Antitoxin Response to the Injection of
Tetanus Toxoid*

Subject Number	Following Primary Series			Following Fourth Dose	
	Maximum Response	After 12-15 Months	After 2 Years	After 1 Week	After 1 Month
Units per c.cm. of Serum					
1	0.1	0.01	0.01	5.0	2.5
3	>0.1	>0.01 <0.01	0.025	1.25	2.5
4	>0.1 <0.5	>0.1 <1.0	0.25	5.0	—
7	>0.1	—	0.05	>5.0 <10.0	>5.0 <10.0
9	>0.1	>0.01 <0.1	0.1	2.5	2.5
10	0.25	0.01	0.01	>0.1 <0.5	>5.0
13	>0.25 <0.5	>0.01 <0.1	>0.125 <0.25	—	—
15	0.1	>0.01 <0.1	0.05	5.0	10.0
18	>0.1 <0.25	>0.01 <0.1	0.025	2.5	>2.5 <5.0
20	0.01	>0.001 <0.01	>0.01 <0.05	>1.25 <2.5	>1.25 <2.5
21	0.005	<0.001	<0.001	0.01	0.025
25	>0.01 <0.1	>0.01 <0.25	0.025	1.25	>1.0 <2.5
29	0.25	>0.01 <0.1	0.025	5.0	>2.5 <5.0

The symbols > and < represent "more than" and "less than" respectively

antitoxin showed no evidence of having fallen below that shown twelve to fifteen months after the last dose. Three of the group (subjects 4, 9, and 13) retained at least 0.1

unit of tetanus antitoxin per c.cm. In view of the limitation to accurate interpretation of the tests, the apparent increases in antitoxin titre shown by three of the group (subjects 3, 9, and 20) during the second year cannot be accepted without reserve. If subclinical infection by *Cl. tetani* were a possible explanation of such a delayed antitoxin increase, acting in this instance as a *secondary* stimulus, it is probable, as may be observed later in this paper, that a higher residual titre would be found than is shown here. It is therefore considered that the apparent increase in antitoxin titre over this period is probably not significant.

Antitoxin Response to Reinjection of Tetanus Toxoid after Two Years' Interval

A fourth dose of toxoid was given to the same group of twelve persons who had been given an initial series of three doses two years previously, and serum was obtained at intervals of a week and a month thereafter. Within a week an increase in antitoxin titre occurred in the order of ten to five hundred times more than the residual level shown two years after the primary series. After a month five (subjects 3, 10, 15, 18, and 21) showed a further increase in antitoxin titre, four showed no appreciable change, two showed a definite fall, and one serum was not tested. The most striking feature of the response is the fact that eleven persons developed tetanus antitoxin in amounts of between 0.1 and 10 units per c.cm. Subject 21, whose titre did not rise above 0.025 unit, has shown a poor antitoxin response throughout. Nevertheless, the increase shown here is similar in trend to that of the other members of the group. The rapid increase of antitoxin titre and the fact that after a month the antitoxin level so induced does not rapidly fall confirm our previously recorded observations.

Persistence of Antitoxin One Year after Reinjection of Tetanus Toxoid

A fourth subcutaneous dose of 1 c.cm. of tetanus toxoid given to fourteen persons about a year after a primary series of three doses has been shown to occasion a rapid increase of antitoxin within a week, thirteen of the group attaining or exceeding an antitoxin titre of 0.1 to 0.25 unit per c.cm., which level was maintained after a month.¹ A year later the sera of ten of this group (Table II) were available. One (subject 5) had retained approximately the same antitoxin titre as was found a month after the fourth dose, whereas in the others the titre had definitely fallen. Nine persons retained antitoxin in amounts varying from 0.1 to 0.75 unit per c.cm., these residual levels in general being substantially in excess of those found a year after the initial doses.

Comment

It is recognized that the development of antitoxin and an immunity to diphtheria may follow subclinical infection with the diphtheria bacillus. Should the presence of *Cl. tetani* in the human digestive tract as shown by Bauer² be capable of inducing a similar immunity to tetanus in men as has been shown by Tenbroeck³ in experimental animals, it would be expected that active immunity so acquired might be indicated by the presence of measurable amounts of antitoxin in the serum. There is no convincing evidence in the sera of sixty-five normal adults which have been investigated that would indicate the prevalence of this type of immunity in Toronto. However, it is possible to induce the development of tetanus antitoxin by the subcutaneous injection of tetanus toxoid, but as yet it is not possible to state definitely at what level this antitoxin must be maintained in the blood stream to confer immunity upon human beings.