Observations

ON

THE PNEUMONOCONIOSES*

BY

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Although dust diseases of the lung have been recognized in this country for many years, for most of our exact knowledge of the pathology of the condition we have to consult South African experience, because, for reasons into which I need not enter here, an intensive study of pneumoconiosis has been carried out in Johannesburg for the last twenty years in a way which has not been approached in any other part of the world. But South African workers have had to consider only one form of pneumoconiosis—that due to the presence in the atmosphere of the Rand mines of crystalline silica in a high degree of concentration. In this country we have to deal with various trades and industries in which a comparable atmospheric pollution occurs. But this is only part of our problem. In many industries the workers are exposed to dusty atmospheres into the composition of which silica does not enter at all, or only in a minor degree, and such questions are constantly arising as: Is silica the only form of dust capable of producing pneumoconiosis? Must the silicon be present as silica, the dioxide of silicon, or is it dangerous when in the form of a silicate? Is the action of silica modified by the presence of other dusts, and, if so, is this modification merely a matter of dilution, or do the adulterant dusts specifically inhibit or alter the action of the silica? What action on the lung, if any, have non-siliceous dusts if inhaled over a considerable period of time?

It might be supposed that these and similar questions are capable of being answered by ordinary human and medical experience, but, if only for the sake of argument, I am prepared to adopt a rather extreme attitude, and to assert that our human and medical experience in these matters is so conflicting and so poorly substantiated by definite facts as to be worth very little. I am not very impressed by the accuracy of the mortality statistics which represent the scientific data on which many generalizations about pneumoconiosis have been based, and until we have at our disposal a mass of statistics composed of the correlated observations of the clinician, the radiologist, and the pathologist, we shall be wise in approaching the problems with unprejudiced minds. I do not wish to labour the point, but to take only one instance, the work of Cummins and Sladden¹—of which no doubt we shall hear more later—dangerously disturbs the doctrine of the immunity of the coal miner to silicosis, and all that that implies. If we are to answer the questions formulated above we must build up our own statistics, and must supplement our observations on the human being by recourse to experimental animals.

ACTION OF SILICA ON THE LUNGS

We know a good deal about the action of silica on the lungs. Largely owing to the labours of South African workers the characteristic silica lesion is now well recognized, and we may adopt silicosis as our paradigm of a pneumoconiosis. It is, I think, generally agreed that silica is soluble in the tissue fluids, and that its action is, broadly speaking, chemical and not physical. There is, however, still some doubt concerning the exact method of the production of the

characteristic nodule and its distribution in the lung. Strachan and Simson² lay great stress on the localization of silica-containing phagocytes in the pulmonary lymphadenoid tissue, and I gather that Dr. Gardner³, whose experience of the dusting chamber is unrivalled, supports this view. It may be so, and my experience of both human and experimental material is so much less than theirs that I hesitate to register more than a tentative difference of opinion. But my experimental material suggests to me that the nodule can form apart from lymphoid tissue and without the intervention of the fibroblast. Some of my preparations seem to me to lend a good deal of support to the view, which I put forward as a working hypothesis, that collagen may be deposited around and in the neighbourhood of silica-containing phagocytes by a process of gelation of an intercellular colloidal sol.

However this may be, we are all agreed that the continued presence of crystalline silica in the lung is followed by the gradual development of a characteristic fibrosis. Does any other dust produce a similar change? In recent years abundant evidence has accumulated showing that asbestos does, though the fibrosis in the asbestos lung differs in type and distribution from that induced by silica. These differences are probably due to the size of the asbestos particles and their transport in the lung; the process seems to be essentially the same in both cases, and the silicate asbestos provides us with an example of a dust other than crystalline silica which is capable of producing pulmonary lesions. But this is the only one we have. Other silicates, kaolin for instance, are held to be entirely innocuous, as are also the non-siliceous dusts. But as a pathologist I must confess that I have been amazed at the way in which the industrial worker can tolerate the presence of ounces, if not pounds, of foreign material in his lungs without apparently feeling any ill effects. In the post-mortem room one is constantly being asked the question: Why did the patient die? My immediate reaction is usually to reply: "I don't know, but can you tell me how he could possibly have survived long enough to develop this extraordinary condition?" It is true that the body can compensate in a marvellous way for the most remarkable structural derangements, but nevertheless I have found it difficult to believe, when examining the lungs of, say, a haematite miner, that they came from the body of a man who had suffered from no occupational incapacity.

ACTION OF SILICA MODIFIED BY OTHER DUSTS

Another question, which is as important as it is difficult, is the modification of the silica reaction by other dusts. In one group of cases the inhalation of silica combined with an alkali has been thought to cause an unduly rapid development of fibrosis, an acute silicosis, due to the increased solubility of the silica. I am doubtful myself whether the alkalinity of the tissues can be sufficiently increased to affect the solubility of silica without the production of an acute inflammatory reaction, and in such cases of acute silicosis as I have actually examined the condition present was an acute tuberculosis, enhanced, no doubt, by the silica present.

The opposite side of the picture—the influence on silica of other dusts in the direction of weakening or inhibiting its action—is of far greater practical and theoretical importance. The recognition of this possibility rests partly on statistical evidence, partly on experimental observations. I have already questioned the doctrine that coal dust protects the coal miner against the deposit of silica in his lungs. Even more unconvincing is the claim that atmospheres containing over 80 per cent. silica are harmless to workers in the refractory industries because of the presence of less than

* Read in opening a discussion in the Section of Pathology at the Centenary Meeting of the British Medical Association, London, 1932.

10 per cent. of alumina in the dust. Experimentally A. Mavrogordato,⁴ H. M. Carleton,⁵ and F. Haynes⁶ have studied the early pulmonary reactions in experimental animals following moderate exposures to dusty atmospheres, and have obtained evidence of the protective action of adulterant dusts. My criticism of these experiments is that they have not been continued to the end point, and unequivocal lesions have not been produced in an adequate number of control animals. And in respect to the statistical evidence, I may say quite frankly that I find it difficult to believe. I should like to be able to do so, because it would be of immense value to us industrially if we could neutralize one dust with another, but I am not convinced of the reliability of the data on which the mortality and morbidity tables are based.

RELATION BETWEEN SILICOSIS AND TUBERCULOSIS

So far I have only considered the simple effect of dust on the lung; a much more important aspect of pneumoconiosis is the influence of inhaled dusts on pulmonary infections, particularly tuberculosis. There is abundant evidence, both clinical and experimental, that silica in the tissues enhances the proliferative power of the tubercle bacillus, and while silica alone may produce such extensive pulmonary fibrosis as to cause death from cardiac failure, it is chiefly dreaded because of its association with tuberculosis. A rapidly progressing tuberculosis may supervene upon a recognized silicosis, or silicosis and tuberculosis, each modified by the other, may develop in the lung more or less simultaneously; and there can be no doubt that a latent tuberculosis may lighten up in the presence of silica dust.

Exactly how the silica influences the bacillus is not known. It is not merely a question of fibrosis, for there is nothing to suggest that a fibrotic lung is peculiarly susceptible to tuberculosis, and, in fact, in many individuals the infective element is recognizable long before the characteristic fibrosis has developed. There is, however, much evidence to show that, as it dissolves, silica combines with protoplasm and converts it into a particularly favourable pabulum for the growth of the bacillus.

A reaction of this kind has not been demonstrated satisfactorily *in vitro*, nor is it always apparent *in vivo*. In experimental animals the proliferation of tubercle bacilli in silicotic tissues is often very unequal, and I have been struck by the extreme variations in the bacillary content of the lesions met with in different cases of human tuberculo-silicosis. In some lungs which I have examined tubercle bacilli are present in enormous numbers; in others, with a very similar histology, they are extraordinarily scanty or absent altogether. This kind of thing is, of course, familiar to all of us in uncomplicated cases of tuberculosis, and the number of bacilli demonstrable in lesions by ordinary methods is no criterion of the rapidity or severity of the infection. Bacteriolysis is only one of the factors in the immunity reaction to the tubercle bacillus, and in the absence of adequate means of coping with the endotoxins liberated by bacterial destruction it does far more harm than good. But the growth of tubercle bacilli in the tissues can be studied with some degree of accuracy in an animal like the mouse, which is naturally highly resistant to tuberculosis, for errors due to variations in the susceptibility of individuals are reduced to a minimum. In these animals it can be shown with reasonable constancy that tubercle bacilli grow with far greater readiness in tissues saturated with silica than in normal tissues, or in lesions produced by other substances. Nevertheless, even in the mouse this phenomenon is not something entirely new; it is only a modification of a normal process, for tubercle bacilli do grow in the uninjured tissues of the animal, and in lesions not due to silica. All we can do at

present is to suggest that silica in some way alters the tissues so as to make them less resistant to the organism. The result of this alteration may be to determine a fulminating infection, or it may just swing the balance slightly in favour of the organism and convert an obsolescent or latent infection into a slowly progressing one.

INFECTIVE SILICOSIS

It is important to realize that the combination of silica and the tubercle bacillus in the lung does not necessarily imply an acute and dramatic pulmonary tuberculosis. In South Africa a condition known as infective silicosis is well recognized. It is, as I understand it, a slowly progressing lesion in which necrosis and fibrosis proceed side by side with a preponderance of the latter. Although the organism has not been demonstrated in many of the cases, it is believed that the tubercle bacillus is the chief infecting agent, and it is suggested that the chronicity of the lesion is due partly to the damaging effect of the silica on the organism as well as on the tissues, and partly to the limitation of the advancing lesion by fibrosis. I do not think this explanation is likely to be true, for all the evidence suggests that the influence of silica on the tubercle bacillus is invariably favourable to its proliferation, and I find it difficult to visualize a continuous process of encapsulation in a progressive lesion. I would rather suggest that infective silicosis is an example of a chronic tuberculosis in an individual whose resistance, naturally high, is so modified by the presence of silica that a low-grade progressing infection results, accompanied by the excessive fibrosis one might expect in such a process.

My experience of human pneumoconiosis is relatively small, but I am becoming more and more impressed by the importance of the infective element in this disease as we see it in England, and the difficulty of the differential diagnosis between infective or tuberculo-silicosis and chronic fibrous tuberculosis. I have received for examination lungs from several cases of silicosis, but in very few of them have I found what I regard as pure silicotic lesions. On the other hand, I have constantly found fibro-caseous tuberculosis, often, it is true, with a nodular distribution, but differing only in the greater extent of the lesions from the chronic tuberculosis encountered in ordinary hospital work. Some of these lungs contain a high content of silica, and I do not doubt that they are examples of something more than simple, uncomplicated tuberculosis. But I find it extremely difficult to determine in many cases whether or not silica has played any part in the production of the lesions. South African workers have been fortunate in that their pneumoconiosis has been concentrated in a small area, and it has been relatively easy for them to adopt uniform standards in their clinical and pathological diagnosis. We are not so happily situated in this country, and it is all the more necessary that we should make every effort to come to agreement about the nature and classification of the various pulmonary lesions we may encounter. Until we can arrive at satisfactory pathological standards we shall not be in a position to take our part in that correlation of the clinical, radiological, and pathological observations which seems to me to be necessary.

RELATION OF OTHER DUSTS TO TUBERCULOSIS

Until a few years ago it was believed that crystalline silica was the only dust which had any aetiological relation to pulmonary tuberculosis. Recently, however, it has become clear that asbestos acts in much the same way, and the question arises whether other dusts may not do likewise. I believe that this question can be answered with a fair degree of certainty by a relatively simple experimental test.⁷ I have found that dusts which are recognized as innocuous when inhaled into the lungs are also

inert when inoculated into the subcutaneous tissues of an animal such as the mouse. Silica and certain silicates, on the other hand, are active irritants, and produce recognizable tissue reactions. Furthermore, the intravenous inoculation of tubercle bacilli into animals prepared by previous subcutaneous injections of dusts results in the settlement and proliferation of bacilli in the active dust lesions to a demonstrably greater degree than occurs in the deposits of the inert dusts. So far as I can see, this method provides a reliable means of determining whether or not any particular substance has the power of enhancing the growth of tubercle bacilli in the body. It should also, I think, enable us to form some idea whether a dust is itself capable of producing lesions in the lung. So far as our knowledge goes at present, inhaled dusts are dangerous only when they become soluble in the body and act as tissue poisons; large amounts of inert dusts cause no pulmonary disability because they are incapable of producing anything more than a minor tissue reaction. It may very well be that the action of a dust on the tissues is considerably modified by the way in which it is presented to them. Dust which is slowly picked up from the surface of the lung by phagocytosis may act very differently from dust which is injected directly into the tissues; nevertheless, its final and fundamental action must be the same. And it seems reasonable to suppose that a substance which produces an active reaction in the subcutaneous tissues will be capable of causing lesions in the lung itself.

This simple method, however, will not solve some of

the more complicated problems with which we are faced. It will not, for example, help us in the study of the action of combined dusts in the lung, nor will it help us to determine the exact degree to which infection enters into the production of pneumoconiosis. For these and other problems we must revert to direct observation on the lung itself. It does not necessarily follow, however, that our investigations should be bound by the limitations of the dusting chamber; there are other ways in which particulate matter may be presented to the lung than in the inspired air. R. Hilton and I⁸ have recently described a method of introducing dust into the lung by direct intratracheal injection. It is not necessary to recapitulate the advantages of this method over the inhalation technique, but so far our results have been so promising as to suggest that we have now a means of investigating experimentally in any ordinary laboratory many of the problems of pneumoconiosis which so urgently demand solution.

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RADIOLOGY IN DISEASES OF THE LUNGS*

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It has always appeared to me that the great value of these Annual Meetings lies in the fact that they afford an opportunity to review the work of the past and to see if recent work has anything of value for us. With this thought in my mind I feel that the advantage of a combined discussion between clinician and radiologist is inestimable. It ought to show us team work at its best; and what is good for us is, I would suggest, good also for our patient. For example, the radiologist is asked to give an opinion on the *x*-ray appearances, as indicating or contraindicating the production of artificial pneumothorax. This is a question that he is perfectly qualified to answer, but the matter does not end here. The clinician is the sole judge of the clinical fitness of the patient.

The value of radiology in the diagnosis of lung disease has now taken its place as one of supreme importance; indeed, it is difficult to imagine any clinician giving a lecture without illustrating it with radiograms. I know when we have a class at Brompton, and it comes to the turn of myself or my co-workers in the *x*-ray department to give a lecture, it is an extremely difficult matter to find suitable pictures, our clinical colleagues having taken them all. A. Salusbury MacNalty, in his recent illuminating report, well presents the attitude of to-day in relation to radiography of the chest. He says: "From a former tendency to disparage chest radiograms, the pendulum has swung too far in the other direction. Some enthusiasts diagnose pulmonary tuberculosis solely on *x*-ray evidence, and ignore the results of orthodox physical examination. This attitude is as mistaken as would be that of the clinician of to-day who, when diagnosing pulmonary disease, neglected to take into account the *x*-ray picture."

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PULMONARY TUBERCULOSIS

With regard to the value of *x*-ray examination in the diagnosis of pulmonary tuberculosis, I think I am not overstating the case in putting it as follows:

1. Definite infiltration can be demonstrated upon an *x*-ray film at quite an early stage of the disease, and frequently before definite physical signs are present.

2. Consistently negative *x*-ray evidence, extending over a period of some months, may be taken as conclusive proof of the non-existence of pulmonary tuberculosis.

3. In cases in which physical signs are present it may be assumed that the initial stage has passed, and, in such cases, the *x*-ray picture will as a rule show much more extensive disease than can be demonstrated by physical examination.

As to the incidence of pulmonary tuberculosis, I think there is still some cleavage in our ranks, more especially in relation to the part played by the mediastinal glands. Leaving out the epoch-making researches of Stanley Griffith on the question of bovine tuberculosis, I should like to find some agreement among us on the important question of lung tuberculosis in the infant and in the adult. I should like to make confession of what a long period of work at Brompton Hospital has led me to believe. I believe that the tubercle bacillus gains an entrance into the lung by "aspiration" in the vast majority of cases, and it is also my belief that, in the adult, any further invasion is of the nature of a "reinfection" (that is, exogenous). Against this view is that of many deep thinkers, past and present, who regard pulmonary tuberculosis much as they regard another of the infective granulomata, syphilis—namely, that one stage of the disease follows another in regular sequence, and that, even after a prolonged period of apparent inactivity, further manifestations may reveal themselves. To take this view is, I suggest, to disregard much of the work that has been done of late years upon the allergic state—the acquired reaction peculiar to the previously infected person.

In the infant the incidence of pulmonary tuberculosis would seem to depend upon the initial dosage and the