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THE PLACE OF ALUMINIUM IN THE PROPHYLAXIS AND THERAPY OF SILICOSIS.

By J. F. MURRAY, M.D. (S.A. Institute for Medical Research)

It is an honour to me to speak to the members of this association. I say this in all sincerity because there is no doubt that, while medical science has contributed a very great deal to a knowledge of silicosis, the main factor in its diminishing incidence on the mines is the engineer's and ventilation officer's success in reducing dust concentrations in the working environment of the miner. But while the engineer and members of associations such as this have made immense strides in controlling dust, there is a minimum beyond which it is probably impossible to go. Silicosis will, therefore, remain with us though in greatly reduced incidence, severity and rapidity of progress. It is the problem of the medical man to seek further measures which will prevent the onset, or delay the progress, of the disease. In common with many other workers in various parts of the world, numerous members of the staff of this Institute have worked on this problem over the last 25 years. It is my purpose this morning to attempt to show you briefly the work which is at present in progress and to outline to you the problems we are seeking to solve.

Before doing so, it might not be amiss for me briefly to outline the anatomical background of silicosis. As you already know the causative agent is free silica (SiO_2) which is inhaled with the inspired air into the lungs. The particulate matter in the air varies very considerably in size but that which is most important so far as silicosis is concerned is the size below 10μ and particularly that below 5μ. The smaller the silica particles the more dangerous they are and all particles below 2μ are <u>really</u> dangerous particles.

Let us briefly follow the course of the inhaled air. It passes through the mouth, larynx and trachea (or windpipe) to the bronchi, which constantly dividing, diminish into smaller and smaller air passages until at a diameter of 0.5mm. they become known as respiratory bronchioles. These small airways open into a group of airsacs called alveoli. At the point at which the bronchioles end and the airsacs begin the cells lining the air passages change in type. Those lining the bronchioles are tall and palisided. Their free border next to the air stream is covered with constantly moving fine cilia which, moving in a layer of mucus, tend always to sweep foreign material up from the depths of the lung to the mouth whence it can be swallowed or expectorated. The cells lining the airsacs are flattened and lie more or less edge to edge like paving stones. Some of these flattened cells are capable, if properly stimulated, e.g. by dust, of becoming rounded and motile. In this condition, they engulf any foreign material, such as dust, which they encounter and carry it up to the bronchioles. As these phagocytes, as the

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motile scavenging cells are called, reach the ciliated epithelium of the bronchi, they may take one of two routes. They may continue up the bronchial passages in the layer of mucus towards the mouth or they may penetrate the wall of the bronchiole and enter the tissue just outside the wall.

With this brief superficial survey of the lung structure, let us now consider the fate of an inhaled particle of dust. If the particle is large, e.g. 200μ or so, it will almost certainly be arrested by the protective mechanisms of the nose and throat and will never enter the windpipe or bronchi. If it is a smaller particle of 10μ or less it may continue in the air stream to the depths of the lung and, if it strikes no bronchial or airsac (alveolar) surface, be returned in the expired air and so lost to the body without having had any effect whatever. Or the particle may, at some point in its passage down the bronchi, be caught in the mucus covering the bronchial walls. In this case, it will be slowly brought up the bronchial tree in the layer of mucus and eventually expectorated in the sputum. Such a particle may, of course, penetrate the bronchial wall or be taken up by a phagocyte but we will not pursue this possibility further. Finally, the particle, particularly if it is a very small one, may successfully negotiate the whole length of the bronchial tree and enter the ultimate airsacs. Here it will eventually be taken up by an alveolar phagocyte which, as already stated, will carry it and many like it, to the bronchial tree. The phagocyte, with its load of dust particles, may continue up the mucus layer of the bronchi and eventually be expectorated or it may penetrate the bronchiolar wall and enter the connective tissue. At this point in the tissues, just outside the bronchiolar wall, where the bronchioles and the airsacs meet, the alveolar phagocytes, with their loads of dust particles, tend to congregate. As the silica particles increase in number at this point, they call forth a response on the part of the tissues which leads to the formation of a nodule of dense fibrous tissue, not unlike scar tissue. (Fig. 1) This is the primary lesion of silicosis in the lung and this is the point, at the junction of bronchiole and airsac, where it always initially occurs. As time passes and as the concentration of silica dust increases, the nodule grows larger. (Fig. 2) Eventually it compresses and may completely close the lumen of the bronchiole so that the airsacs distal to it collapse. As the nodule grows larger, it tends to coalesce with other neighbouring growing nodules and to form an area of confluent or massive silicosis with closing off of still more bronchioles and collapse of still more airspaces. (Fig.3) Some of the dust, however, does not remain in the nodule but migrates, according to its position in the lung, in phagocytes, to the pleural (covering) surface of the lung or to the lymph glands at the root of the lung. In these situations the dust again causes a tissue reaction with fibrosis (hardening) of the tissues and various other complications.

So much for the way in which the dust reaches the lungs and the sites in which it causes its harmful effects.

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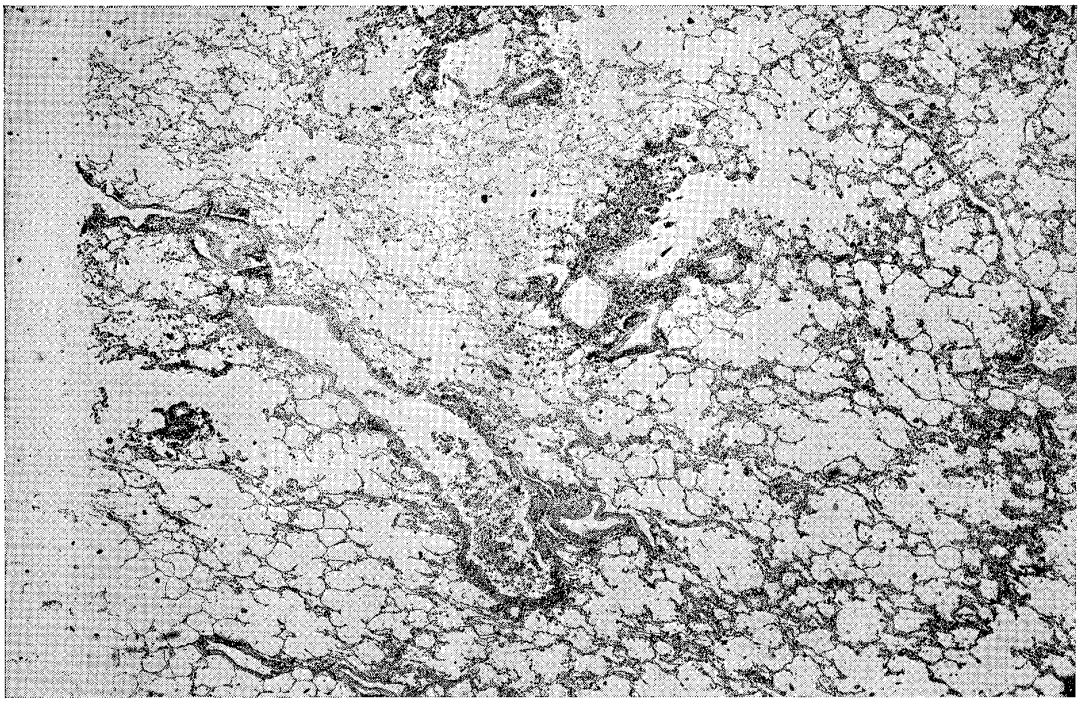

FIGURE 1. Earliest reaction to the accumulation of silicosis dust in the tissues at the entrance to the primary unit of the lung.
A small collection of dust cells is seen in the walls and supporting tissue of the respiratory bronchiole and its continuation as the alveolar duct. As yet there is no sign of nodule formation. Examined under polarized light, birefringent mineral particles are always present, and are usually found to be numerous in this type of lesion.
Magnification of the order of 25×.

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Mode of action of silica

Many theories have been postulated in attempts to explain the mode of action of silica in the tissues. Obviously the action must be complex and cannot be explained on a simple physical or chemical basis. The environmental conditions in which the silica particles find themselves in the pulmonary alveoli are extremely complex and are subject to numerous variations. The dust itself varies in size, age, constitution and many other factors. Brief mention may, however, be made of some of the theories. (a)Mechanical trauma. This theory fails to explain the effect which silica dust has on the lung tissues and is subject to numerous criticisms. (b) Chemical. In its broadest sense, this theory has much to be said for it. The noxious substance is a specific chemical entity which tends to be slowly dissolved in biological fluids. The lung environment in which the silica slowly dissolves is biochemically complex and could clearly be affected by the release of an extraneous chemical substance. But while this is true in its broad sense, the exact mechanism by which such an effect might be exercised is obscure. It is postulated, that in the solution of silica, silicic ions are slowly given out and that these call forth the tissue reaction. On the other hand, it has been suggested that the silica slowly forms a colloid and that it is the colloid which damages the surrounding tissues. (c) Exchange of bases. During their presence in the lung, the silica particles slowly "weather" by giving up basic ions and taking in OH ions. As a result, the tissues become alkalinised and the mineral particles hydrated and thereby, according to Policard, inert. It is suggested that it is this molecular exchange which leads to the tissue reaction. (d) Electrical potential. Heffernan maintains that the silica dust exercises its effect on the tissues by reason of the electro-chemical energy existing at the freshly fractured surfaces of the particles. These fresh surfaces, according to Heffernan, are ionised and it is this factor which leads to silicosis. (e) Piezoelectric force. Recently it has been stated that the activity of mineral particles in producing fibrosis of the lung is related to their piezo-electric properties and that it is the exercise of this force which leads to silicosis in the presence of silica dust. By placing animals in strong electro-magnetic fields and thus deforming the crystals already placed in their tissues, the degree of fibrosis was increased as a result of the piezo-electric force released.

Whichever is the correct theory, the action and reaction is exceedingly complex if for no other reason than that it occurs in a biological environment. Such being the case, it is not easy to devise experiments which will elucidate the mechanism of silicosis. In test-tube experiments, one factor at a time can be carefully varied by a known degree. But in living tissues, it is very difficult and sometimes impossible to control all other factors while varying the one under investigation.

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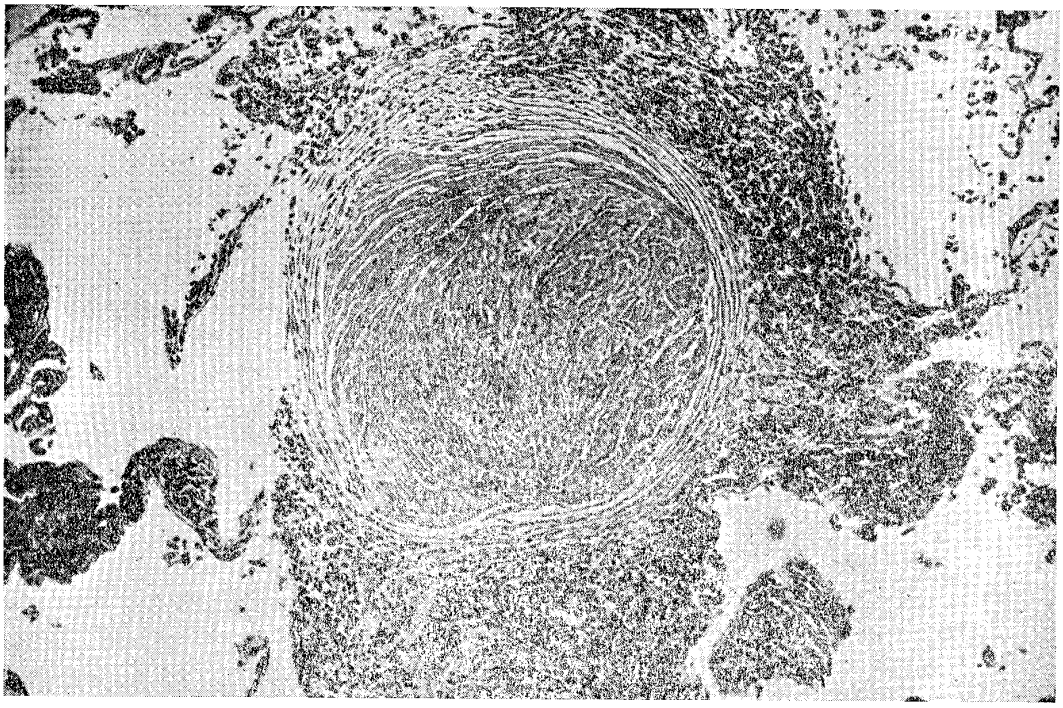

FIGURE 2. The fully formed single small simple silicotic nodule.
The fibrotic islet is fairly sharply delimited from the surrounding area of pigmented dust-laden cells.

Magnification of the order of 300×.

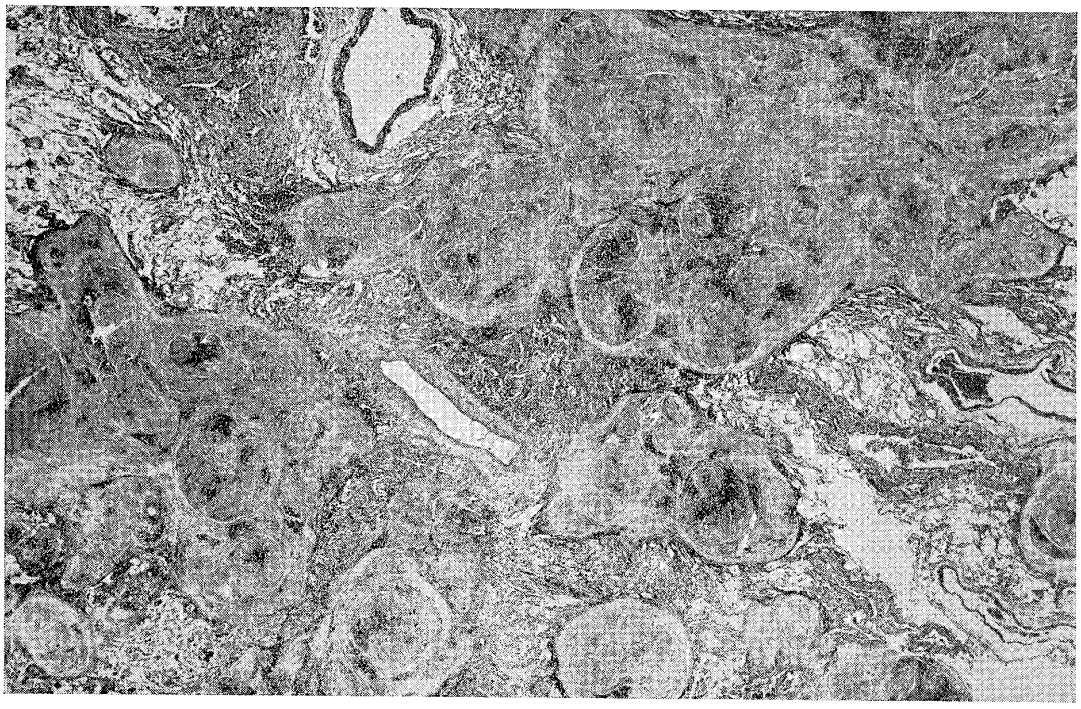

FIGURE 3. Silicotic massive fibrosis of non-infective type.
This section shows numerous contiguous composite nodules which macroscopically formed a single massive area of fibrosis of non-infective type. The alveolar tissue is collapsed.

Magnification of the order of 100×.

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Aluminium in preventing silicosis.

Acting, however, on the assumption that the chemical solubility of silica was in some way associated with its harmful effects a group of Canadian workers commenced a search for some non-toxic substance which would depress its solubility. At last they hit upon aluminium. By an odd chance, Gardner, working independently, and by other methods, reached the same conclusion at almost the same time. It would appear that the aluminium forms a monomolecular layer around the silica particles which either by depressing their solubility, or by satisfying the unsatisfied ions of their freshly fractured surfaces, or by neutralising their electrical potential, or by some other method, prevents the occurrence of the usual fibrotic tissue reaction. The original investigations were carried out with animals but from laboratory animals to man is but a step, albeit a large one, and inhalation of aluminium dust is now employed in many parts of Canada and the United States in an effort to prevent the onset or stay the progress of silicosis in miners and other workers exposed to silica dust.

The methods of administering the aluminium dust are numerous but in all of them the essential object is to get the dust into the lung alveoli where it can come into contact with inhaled silica particles and inhibit their action on the tissues.

Present experiments.

At the Institute here we are trying to obtain further information on this vital subject. A series of dust chambers has been constructed in which animals can be exposed to dust clouds day after day and the effect upon their lungs observed. To this end, some animals are being exposed to pure silica dust and others to mine dust. In relation to mine dust an important point arises. It is contended that old dust, i.e. settled dust which has had a chance to weather, or at least to lose the electrical potential of its freshly fractured surfaces by contact with other particles, is less dangerous than newly formed silica dust. The late Dr. Simson of this Institute, after 20 years' experience in which he observed numerous animals into which he had injected suspensions of "old" mine dusts was of the opinion that they were just as active as fresh dust. This, however, may be a question of either quantity or environment. It may be that freshly fractured dust, particle for particle, is more active than old dust when inhaled into the lungs though no difference can be noted when relatively large amounts are injected into the veins. In an effort to learn more about this important point, we are, in conjunction with Professor Walker of the Mechanical Engineering Department of the University and with members of the Ventilation Department of the Chamber of Mines, seeking to devise a means of exposing animals to inhalation of freshly fractured dust in order that their reaction may be compared with those exposed to resuspended "old" dust. Finally, animals are being exposed to aluminium and to silica so that we may observe the beneficial effects or otherwise of the aluminium inhalations. A control group of animals is, of course, being exposed to aluminium alone so that any noxious effects of the substance may be noted. In the chambers, therefore, groups of animals will be exposed to:

/(a) Pure ...

(a) Pure aluminium

(b) Aluminium + silica dust

(c) Pure silica dust

(d) Mine dust

(e) Freshly fractured mine dust.

In conclusion let me say that in the conduct of these experiments I am happy to acknowledge the very great help we have received from many members of your association who assist us in technical ways too numerous to mention. In particular, I would like to mention your Chairman, Mr. Campbell-Pitt; also Mr. Rees of the Chamber of Mines with many members of his staff, and Mr. Barenbrug, of the New Consolidated Goldfields, all of whom have given us invaluable help and without whom the work simply could not have been undertaken.

VOTE OF THANKS TO DR. MURRAY

By A.W.T. Barenbrug

From the address which Dr. Murray has given us this morning and from the exhibits he so kindly has shown us, we must conclude that a great stride has been made towards the prevention of silicosis in our mines. Dr. Murray has told us this morning that the very bad cases of silicosis as shown by the three worst lung-specimens seldom occur these days. I think the achievements must be very gratifying to the industry, and the organisers of dust-prevention can indeed be very proud of their work.

Nevertheless silicosis still occurs and far from resting upon our laurels it is still the duty of every ventilation officer and every person connected with silicosis prevention to assist in removing silicosis from our mines altogether, either directly by removing or causing to remove any form of dust from our mines, or indirectly through research.

Dust conditions in our mines have reached such a state of perfection that it will be difficult to improve upon them without involving the industry in heavy expenditure or cumbersome regulations. However, we know as yet far too little about the reason why the dust in the mines is so dangerous. Research in silicosis may tell us one day why that is the case, and once knowing "why" it may not be difficult to find the correct solution to the problem. The work that Dr. Murray is carrying out is therefore most important. From the extremely interesting talk so ably presented we are convinced that this research work is in expert hands and I cannot thank him better than wishing him, on behalf of you all, success in his work.

Seconding of Vote of Thanks to Dr. Murray

By S.R. Robson

The maintenance of health and prevention of silicosis is the ultimate aim of the Ventilation Officer, the control of dust and ventilation being an intermediate but necessary step towards this aim. Dr. Murray has therefore dealt with a side of the dust problem which is of vital interest to us and of which ventilation men ought to have an intelligent understanding.

I must congratulate Dr. Murray on his very clear and lucid explanation of the processes with which the lungs deal with silicosis-producing dust particles. The experiments being carried out at the S.A.I.M.R. are of great interest, and we appreciate the opportunity of getting an inside view of the work being done on the medical side of silicosis prevention. We trust that co-operation between the medical and ventilation sides on the problem of silicosis will lead to the complete elimination of this disease. The exhibits of lungs in various stages of silicosis which Dr. Murray has demonstrated to us may then well become mere museum pieces.

I have great pleasure on your behalf in supporting the vote of thanks to Dr. Murray for his very interesting and instructive address.

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