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THE BREATHING OF PNEUMOCONIOSIS-PRODUCING DUSTS*

Pneumoconiosis-producing dusts must be insoluble or have a very slow solubility. Dusts which cause long termed cumulative effects act in three ways: by stimulating the growth of fibrous tissue (quartz), by producing mechanical injuries (asbestos, talc) and by accumulating of large quantities of particles in the lymphatic system and throughout the lung.

Another kind of risk from dust accumulating in the lungs arises from radioactive materials, particularly from solid products of radioactive decay of radon. An association between the normal content of radon in the atmosphere and lung carcinoma in the general population cannot be dismissed as impossible when varying susceptibility is taken into account.

Pneumoconiosis-producing dusts are those which cause slowly developing conditions of the lung to the accumulation of solid particles in that organ over a period of years. Dusts must therefore be insoluble, or have a very low solubility, like quartz, or else be changed to an insoluble substance after deposition in the lungs. Even quartz has sufficient solubility when dispersed into fine, colloidal particles, to come into a different category and produce rapid effects if inhaled in large enough quantities (1).

Dusts which cause long-term, cumulative effects act in three ways. The first method, shown above all by quartz, is stimulation of the growth of fibrous tissue. Secondly, is the production of mechanical injury by the lodgement of fibres in the fine bronchioles, as with asbestos and talc. Finally comes the accumulation of inert dust, such as coal, first in the lymphatic system and finally throughout the lung.

The sizes of dust particles contributing to these effects depends on the mechanism by which they are brought about. Access to the alveoli is essential for silicosis so that particles greater than five microns have little significance. Too great a speed of solution makes the initiation of fibrous growth impossible which certainly cuts out particles finer

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than 0.01 microns. Within the five hundredfold size range, 0.01–5 microns, fibrogenic dusts are active. The most effective size depends upon the distribution of sizes in the inhaled dust and is likely to be in the region of 0.5 microns.

Asbestosis is caused by fibres which are short enough to reach the finer bronchioles and long enough to pierce their walls (2, 3). The contraction and expansion of the bronchioles during respiration enables the end of the fibres to work in: if the fibres cleave longitudinally in the manner characteristic of asbestos, with a tendency for the ends to open out in a brushlike manner, it seems that the peribronchiolar fibrosis typical in this disease can be produced by the mechanical stimulus. The fibres must be more than about 10 microns and less than about 1000 microns in length. Materials forming fibres which break clean like glass do not cause asbestosis, presumably because the fibres can work in and out of the walls of the bronchioles quite freely, without becoming anchored in the tissue by the spreading of the ends. Carcinoma of the lung may follow asbestosis.

Inert dusts, like coal, have to penetrate beyond the ciliated epithelium when inhaled if any accumulation is to be possible; hence. like quartz, particles much over five microns diameter cannot be significant. There is, in fact, some difference in the theoretical limiting sizes depending on the density of the particles. Coal is less dense than quartz in a ratio of at least 1.4 : 2.5, i. e. 1 : 1.8. If five microns is taken as the limiting size for quartz, that for coal is therefore

$$5 \times 1.8 = 6.7 \text{ microns, or greater.}$$

The qualification is made since coal dust particles are often loose aggregates whose density is below that of the compact material which is 1.4 gram/cm^3. Shape, also, may have an appreciable influence (4).

Coal dust deposited in the alveoli is phagocyted, either to the ciliated epithelium, which excretes it, or to the lymphatics where it accumulates in the lymph nodes. After exposure to dust for some time, or due to high concentration, lymphatic drainage may be inadequate so that coal dust foci form in respiratory tissue. No fibrous growth takes place in these: they are simply tightly packed stores of coal dust which has been collected by phagocytes. This stage of disease is not progressive, but if coal dust accumulates beyond a certain point localised areas of fibrous tissue may appear; these coalesce and constitute a serious, progressive condition. It is suspected that this development is associated with the presence of tubercular infection (5).

Of the lower limit of particle size for coal and inert dust pneumoconiosis nothing is known, but, since they are diseases due to bulk of dust, it is probable that the larger particles reaching the alveoli are the most nuisance. The most offensive sizes would therefore seem to be

about three to eight microns diameter though, as in the case of quartz, the size frequency in the inhaled dust must be taken into account; great numbers of small particles may exceed in bulk a few large ones.

When a dust of normal size distribution is inhaled which contains about 1000 particles per cm^3 in the 0.2–5 micron range, quite a high concentration, about 500 per cm^3 will reach the alveoli. A man at work might breathe 20 times a minute inhaling 8000 cm^3 each time, hence each respiration will deliver to the alveoli $8000 \times 500 = 4.10^6$ particles. Now there are about 52.10^6 alveoli so that, on the average, a given alveolus will get a particle only about once in thirteen respirations, or rather more than one a minute. This calculation shows that dust particles which are deposited in the alveoli are likely to arrive at a rate which is well within the capacity of the phagocytes to cope with, unless the concentration is extremely high. Fine fumes, containing a million or so particles per cm^3 below 0.5 microns in size, would deliver about a hundred particles to each alveolus per respiration which could not be cleared so quickly; the clearance of the alveoli by phagocytes would then be dependent upon adequate periods during which clean air was inhaled, between the exposures to dust or fume.

A miner working in a atmosphere containing 600–700 particles per cm^3 between 0.2 and 60 microns in size, as in the British coal mines, inhales about 75 grams of dust in a year. Most of it deposits on the ciliated epithelium of the bronchial tubes and is excreted, but not more than 10 grams a year hat access to the lung alveoli. Phagocytes take up this dust and the bulk is transported to the ciliated epithelium and cleared away, but it is probable that about half a gram a year fails to take this route and is conveyed, instead, to the pulmonary lymph glands where it accumulates. It is not known why this small proportion of either inert dusts or fibrogenic dusts should find their way to the lymphatics. The calculation in the preceding paragraph may perhaps contain a hint as to the reason. It is conceivable that the route to the respiratory bronchioles is normally followed as long as the rate of arrival of particles in an alveolus is not too great; exposure to peak concentrations may be the signal for the diversion of some dust to the lymph vessels. The magnitude of such a peak concentration might be high in terms of the number of microorganisms usually found floating in the atmosphere but quite low in relation to common figures for industrial dust.

The accumulation of coal dust at the rate of about half a gram a year causes an early stage of coal miners' pneumoconiosis, demonstrable only by x–rays, in about ten years. Quartz administered at the same rate would usually be lethal in a shorter period. Advanced pneumoconiosis from inert dust, with loss of working capacity, might require from 20 to 40 years to develop at this rate of administration.

The possible significance of small amounts of quartz in an inert dust is worth considering. A given small amount of quartz inhaled on its

own over a long period might cause lesions only in lymph tissue; but when diluted with a considerable bulk of inert dust accumulation in respiratory tissue is encouraged and silicotic nodules develop therein with more serious consequences (7, 8).

Another kind of risk from dust accumulating in the lungs arises from radioactive materials. Substances emitting β or γ radiations, which have ranges in tissue of a few centimetres or metres, respectively, are much less effective in terms of the biological effects produced than emitters of α-particles. The range of α-particles is less than 50 microns in human tissue so that an α-emitting dust particle deposited in lung tissue can produce serious damage in the cells immediately adjacent to it within all its ionising power is concentrated. The ionising power of an equivalent β emitter is spread over a sphere whose radius is about 500 times greater so that the local effects are much less.

Very small quantities of dust from luminous paint containing radium are known to produce symptoms in human beings (9), but these cannot be classed as pneumoconiosis since, although the radium is absorbed in the lungs, it is not stored there. Accumulation of radioactive dust in the human lungs has not yet been clearly established as an industrial risk but it may be a factor in the development of lung carcinoma following inhalation of radon.

Radon is a gas which changes by radioactive decay into a series of solids emitting α-particles. A gas molecule is thus transformed into a molecule with the physical properties of a solid. This means that the molecules of the decay products condense on one another, when they collide, or on any surface they encounter. A dust in an atmosphere containing radon becomes radioactive because its particles collect the radon decay products which are termed the active deposit. In an atmosphere free from dust the decay molecules coagulate with atmospheric ions and can be filtered out. Ions are removed by the lungs during normal respiration, as is shown by the decrease in the ion count in the air of occupied rooms.

Hence it is certain that people breathing air in radioactive equilibrium with radon will collect in their lungs most of the solid radioactive products in the air inhaled, whether it is dusty or not. The decay series from radon passes through four short lived elements with an effective half life of about 40 minutes to give radium D which is a β emitter with a half life of 22 years and is an isotope of lead.The chemical behaviour of this substance, as regards elimination from the lung, is thus the same as lead. It has been suggested by *Fine* (10) that metallic lead particles are retained in the lung like quartz and may be fibrogenic. The quantity of lead aquired from radon inhalation must be extremely small but the α-irradiation, with a half life of 40 minutes, during its formation and also the subsequent accumulation of the longlived β-emitter cannot be disregarded as possible causes of lung carcinoma.

The ordinary atmosphere often gives over 1000 radon disintegrations per minute per cubic metre while the air in uranium mines has been observed to give ten million. The safe level of radon in industrial atmospheres and laboratories is under discussion and a concentration giving about 22,000 disintegrations per minute per m^3 has been suggested as an upper limit (11) one tenth of this, corresponding to 10^{-11} curies/litre, is claimed to be desirable and attainable in the United States.

It is interesting to observe how close maximum permissible concentration of radon has come to the normal atmospheric content and an association between atmospheric radon and lung carcinoma in the general population cannot be dismissed as impossible when varying susceptibility is taken into account.

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SADRŽAJ

UDISANJE PRAŠINA, KOJE UZROKUJU PNEUMOKONIOZE

Prašine, koje uzrokuju pneumokonioze, treba da budu netopljive ili vrlo slabo topljive. Takve prašine djeluju na tri načina: 1. stimuliraju rast fibroznog tkiva (kvarc), 2. mehanički ozljeđuju stijenke bronhiola (azbest) i 3. nagomilavaju se u velikim količinama u limfnom sistemu i čitavim plućima (inertne prašine). Najdjelotvornija veličina čestica zavisi od raspodjele veličina čestica prašina, koje udišemo, ali je najvjerojatnije, da je negdje u području oko 0.5 mikrona.

Rudar, radeći u atmosferi, koja sadržava 600–700 čestica na 1 cm^3 veličine 0,2–60 mikrona, udiše oko 75 g prašine na godinu, ali samo oko 10 g na godinu uđe u plućne alveole. Najveći dio te prašine prihvate fagociti i transportiraju do cilijarnog epitela, otkuda se ta prašina izbacuje. Međutim, mali dio te prašine ne ide tim

putom, nego odlazi u limfni sistem. Autor misli, da se to skretanje u limfni sistem može rastumačiti pomoću brzine, kojom čestice dolaze u alveole. Ako je brzina malena, kapacitet fagocita će biti dovoljan da se svaka čestica transportira do cilijarnog epitela; ako je brzina ulaženja čestica u alveole velika (ekspozicija vrlo visokim koncentracijama prašine), opterećenje fagocita je preveliko, pa jedan dio prašine odlazi u limfne žile.

Naročitu vrstu opasnosti predstavljaju radioaktivne prašine, a naročito raspadni produkti radona. Autor misli, da ne treba odbaciti hipotezu, da postoji neka veza između normalnog sadržaja radona u atmosferi i raširenosti plućnog karcinoma, naročito ako se uzme u obzir različita osjetljivost pojedinaca.

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