THE EXPERIMENTAL PRODUCTION OF RADIOGRAPHIC SHADOWS BY THE INHALATION OF INDUSTRIAL DUSTS

PART II : ZIRCON (ZrSiO_4)

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(RECEIVED FOR PUBLICATION FEBRUARY 2, 1951)

A preliminary report on the toxicology of zircon (Harding, 1948) gave some details of the properties and uses of this substance and suggested that it was extremely inert within the animal body. At the time of the publication of this preliminary report an experiment was almost completed during which rats were exposed to a fairly high concentration (7–25,000 particles per cc. of air) of zircon dust in a chamber. The period of exposure lasted just over three months, and the animals were killed at intervals up to six months thereafter. To our surprise we were unable to find any zircon in the lungs of these animals either by radiography or microscopically. Since it seemed possible that there had been an error which we were unable to identify, we repeated the experiment on two further occasions. Again no zircon, or only very small amounts, could be found in the lungs. The animals were exposed in a chamber with a dust feed of the type described by Lloyd Davies (1946): working with identical techniques before, between, and after these experiments we found no difficulty in demonstrating dust in the lungs of rats exposed to other dusts (e.g., iron oxide, manganese dioxide, beryllium oxide, silica, graphite, talc, cobalt metal) of similar particle size and in similar concentrations.

Because of the difficulty we had experienced in demonstrating appreciable quantities of zircon in these animals, we set up a fourth experiment in which the concentration of dust in the chamber was increased considerably and the period of exposure was also lengthened. It is this fourth experiment that forms the basis of this paper.

Experimental

Twelve rats, aged about 3 months, weighing 109–135 g. each, were exposed to a very high concentration of

zircon dust for six hours daily, five days a week for 144 days, and then for eight and a half hours daily, five days a week for 20 days. Atmospheric dust counts with a thermal precipitator were frequently too high to be counted, but when they could be determined they varied between 37,000 and 130,000 particles per cc. of air, usually near the higher figure; 80% of the particles were below 1μ , and 30% below 0.2μ : only rare particles over 5μ were encountered in the counts. One rat died during the experiment and the others were sacrificed at intervals up to seven months after exposure to the dust. The animals were killed and their lungs preserved in an inflated state according to the technique previously described (Lloyd Davies and Harding, 1949). The lungs were later radiographed and sections made from them for microscopic examination. Sections were stained by haematoxylin and eosin, iron haematoxylin and van Gieson, and by Wilder's modification of Foot's reticulin stain.

Results

The radiographs were examined by Dr. J. L. A. Grout who reported that they showed a fine pin-point mottling all over both lung fields. Although generalized, the mottling was more intense at the mid-zones and towards the apices, with a nodular character similar to that seen in well-established cases of silicosis in the human being (Fig. 1). He also examined films obtained after intratracheal injections of a suspension of zircon (Fig. 2), and reported that the radiographs showed mottling in both lung fields, coarser than in the preceding films, and suggesting the coalescence of several of the affected areas. The morbid anatomy after injection of zircon was described in a previous paper (Harding, 1948). A radiograph of normal lungs is given for comparison (Fig. 3).

One rat died of bronchopneumonia, and a few of those that lived longest showed early bronchiectatic

FIG. 1

FIG. 1.—Rat 542. Inhalation of zircon dust during seven and a half months: killed six months later. Enlarged positive print of radiograph.

FIG. 2.—Rat 104. Intratracheal injection of suspension of zircon on October 6, 1946: killed July 18, 1947. Enlarged positive print of radiograph.

FIG. 3.—Normal rat. Enlarged positive print of radiograph.

FIG. 4.—Rat 542. See legend Fig. 1. Haematoxylin and eosin $\times 25$.

FIG. 4

FIG. 2

FIG. 3

FIG. 5

FIG. 6

FIG. 7

FIG. 5.—Rat 537. Inhalation of zircon during seven and a half months : killed six months later. Haematoxylin and eosin $\times 65$.

FIG. 6.—Rat 537. Haematoxylin and eosin $\times 190$.

FIG. 7.—Rat 538. Inhalation of zircon during seven and a half months : killed six and a half months later. Haematoxylin and eosin $\times 500$.

changes, which are found at a similar age in our stock rats : apart from these findings the lungs of all the animals were essentially similar. After fixation the lungs seemed slightly whiter and slightly more opaque than normal, but no abnormality was discernible on the cut surfaces. Microscopically small aggregates of cells densely packed with fine crystals were located at lymphatic junctions throughout the lungs, but most often just beyond the ends of the bronchioles or alongside small blood vessels (Figs. 4, 5). Pleural aggregates were rare, and the so-called "pleural drift" played no evident part in the localization. Around the dust-filled cells there were often a few cells that appeared to be small histiocytes, but the majority of the cells were so filled with crystals that no structural details could be seen (Fig. 6). In one or two areas the quantity of dust was much less, and it could then be seen that the cells were very large histiocytes (Fig. 7). No evidence of collagen formation could be found associated with these cellular aggregates, and we were unable to satisfy ourselves that there was any increase in reticulin fibrils. There was a suggestion of dilatation of alveoli in relation to the dust deposits but no genuine emphysema.

Discussion

Although we have not succeeded in getting very large quantities of zircon dust into the lungs of rats, the results show clearly that, like iron oxide (Harding, Grout, and Lloyd Davies, 1947), zircon can produce radiological shadows in these lungs in the complete absence of fibrosis. If zircon should come to be used at all extensively in industry, this is a fact of which radiologists should be aware.

From the evidence presented here and in a previous paper (Harding, 1948) it seems certain that zircon is harmless when inhaled by the rat or when a suspension is injected intratracheally, intravenously, or intraperitoneally into various laboratory animals. We have no explanation for the difficulty we found in getting appreciable quantities of zircon, as compared with other dusts, to reach and/or to be retained in the lungs of rats exposed to fairly high atmospheric concentrations : zircon powder is very heavy compared with most of the dusts with which we have had experience, but theoretical arguments are against mere "heaviness" of the particles playing a prominent role, and it seems unlikely that unusually efficient removal of particles can be responsible. Since we are unable to explain our findings, which might be due to some error in technique that we cannot trace, we do not wish to place much emphasis on them for the moment.

We realize that a failure to demonstrate any toxic reaction in animals, especially perhaps in rats, may

not be a sure indication of what may occur in man, in whom it seems likely that recurrent respiratory infections may increase greatly what would otherwise be very slight reactions to many dusts. Nevertheless, the complete absence of any reaction except phagocytosis is at least proof that zircon is much less dangerous than silica, for which it is proposed as a substitute in industry. If our findings that less zircon than several other dusts is retained in the lungs of rats when equivalent concentrations are breathed by them is confirmed, it would not imply that this would necessarily occur in man. If it were true it would be important, since, whatever the mechanism of production of damage in the lungs by various dusts, the extent of the damage will depend on the number of particles of appropriate size that are there present.

If these animal experiments are applicable to man, the replacement of silica by zircon wherever this is possible would reduce the risk of pneumoconiosis very considerably, both because zircon is less toxic, and possibly not toxic at all (Harding, 1948), and also because it is just possible that less of it might be inhaled into the lungs. Substitution of a safe material for a dangerous one is a basic method of prevention of industrial disease. The Foundries (Parting Materials) Special Regulations 1950 S.I. 1700 prohibit the use of silica as a parting powder: zircon is among the permitted substances so long as silica is not added to it. Zircon could, however, be substituted for silica in many other operations, e.g., in paints and washes, and even if its physical characters require the evolution of modifications of industrial techniques, the use of zircon appears to be one method, and on the basis

of this note a profitable method, of eliminating silicosis. To condemn the use of zircon because methods and techniques for using silica are not immediately and totally applicable to it, would be wrong.

Summary

Dense radiological shadows are produced by aggregates of phagocytes containing zircon.

Apart from phagocytosis, and possibly slight small cell accumulation, there is no evident reaction to the presence of zircon in the lungs of rats.

Since zircon is far less toxic than silica (and possibly completely inert), and since animal experiments suggest that it is less readily inhaled into and/or retained in the lungs than the latter, it could provide a desirable substitute for silica.

We could not have proceeded without the help and advice of Dr. J. L. A. Grout, radiologist to the United Sheffield Hospitals. The photomicrographs were made by Mr. A. W. Collins, F.I.M.L.T., and the radiographs by Mr. A. L. Watson, M.S.R. The animals were cared for by Miss E. Wilkinson and Miss E. Parker.

The zircon used was given by Messrs. Colin Stewart Ltd., Winsford, Cheshire.

A small part of the expenses of this investigation was met by a grant from the Sheffield University Research Fund.

The dusting of the rats was done in the Research Department (Pharmacology Division) of Boots' Pure Drug Co., Ltd., Nottingham.

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