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Preliminary Observations of the Effect of Inhalation of PVC in Man and Experimental Animals

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Attention has been focussed, both in man and experimental animals, on the effects of inhalation of the gas monomer, vinyl chloride. Recently, note is being taken of the possible effects of the inhalation of the polymer in man. The particles in question are those produced commercially as paste polymer or dispersion polymer or having an average diameter of 0.15 μm, and accounting for more than 10% of the production in Britain. There are now strict regulations for the control of the monomer gas, but the particles are regarded as nuisance dust and their emission is not covered by specific legislation.

Our studies on rats, where both inhalation and implantation methods of exposure have been used, and examination of tissue from human cases exposed to paste polymers, indicate that these small particles can only be regarded as evidence of exposure, and on present evidence there is no indication of causation of significant pulmonary disease. Techniques have been developed by which these particles can be demonstrated in ordinary histological preparations and by transmission electron microscopy.

The finer particles of PVC known in the United States as dispersion polymer, are usually less than 0.5 μm in diameter. During the last five years we have conducted a number of preliminary investigations using this material, and have also observed these small particles in the lungs of men exposed to this type of PVC, and have recovered these particles from the lungs and livers of human cases using maceration techniques. A second series of experiments has been started but no results are available.

The recognition of PVC in tissue has been greatly facilitated by a staining method developed by Wilson (*1*). Normally processed histological sections are stained with a Sudanophilic dye, which stains the particles a bright red. As the tissue has been processed and all lipid removed, only the PVC and some other related plastics will stain. The particles can also be recognized under the transmission electron microscope, and the morphological appearances supported by the confirmation of the presence of chloride when examined by x-ray microanalysis.

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Animal Experiments

Experiment 1

The experimental animals were caesarean-derived, barrier-maintained rats of the I.C.I. Alderley Park Wistar strain. Six-week old rats were randomized, with equal numbers of each sex, and inoculated intrapleurally by using a previously described technique (*2*). Forty-eight animals received 20 mg of PVC dispersion polymer into the right pleural cavity. The control animals were inoculated in a similar manner (Table 1). The rats were allowed to live out their lives and all are now dead.

Between 12 and 18 months after inoculation, nine of the animals receiving the PVC died. Of these, five had tumors of the liver and one had a tumor originating from the site of inoculation. None of the other animals injected with PVC, nor any of the control animals, had a tumor of this type. These tumors were shown to pathologists in Britain and the United States. It was generally agreed that they were poorly differentiated sarcomas, and in three of the animals, the possibility of Kupffer cell origin was considered. As no other animals devel-

Table 1. Intrapleural inoculation (rats 6 weeks old).

No. rats	Treatment
48 rats	20 mg PVC in saline
24 control rats	20 mg UICC crocidolite in saline
24 control rats	20 mg Min-U-Sil (quartz) in saline
24 control rats	saline

oped these tumors, two further experiments have been started. In the first, dispersion polymer from three British manufacturers was used, and in the second, freshly produced dispersion polymer from two sources has been inoculated, as well as similar material from which all evidence of detergent or vinyl chloride monomer has been removed. These investigations are still in progress, but in the first of these studies, the animals have passed the 18 month period without any occurrence of the tumors.

Inhalation Studies

A group of 48 rats, 24 of each sex, of the same stock as used in the previous experiments were exposed in an inhalation chamber to PVC dust, the apparatus and methods being the same as previously described (*3*). The animals were exposed to dispersion polymer, at a concentration of 12 mg/m^3 for 7 hr/day, 5 days/week, for 5 months. There were also 48 nonexposed controls. The cumulative dose of the exposed rats was 8552 mg/m^3 (Table 2). Six rats from each group were killed at the end of the exposure, and a further six a year after the start of the exposure. The remaining animals were allowed to survive until they died of natural causes.

Table 2. Inhalation study.

No. of rats	Exposure
48 rats 6 weeks old	22 weeks, 12 mg/m^3; cumulative dose 8552 mg/m^3 -hr
48 control rats	None

The PVC particles were present in the macrophages within the alveoli arising directly from the respiratory bronchioles immediately after the exposure. The distribution of these accumulations was widespread but less than a third of the primary units were involved. Occasional dust particles were observed in sections from the bronchopulmonary lymph glands, the Kupffer cells in the liver and in the spleen. At the end of a year, the dust was still present in the spleen and around some foci of macrophages there was evidence of a slight proliferation of reticulin fibers. This early dust reticulination did not show evidence of progression in any of the other animals, some of which survived for more than two years after the initial exposure.

Experience with Human Tissue

We have had the opportunity of examining a limited amount of human tissue. This included three cases of accepted angiosarcoma of the liver, a man with severe hepatic fibrosis who underwent a subsequent porto-caval shunt and material from people who had been employed in a PVC factory. These people had either had pulmonary biopsies or had died of diseases unconnected with their occupations. In all but one case we found small amounts of PVC in the lung tissue. In two of three angiosarcomas, particles of PVC were found after the maceration of the liver tissue.

At this stage of the investigation, these particles can only be regarded as evidence of exposure to dispersion polymer.

REFERENCES

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