

THE CHEMICAL ENVIRONMENT

1967. A. J. C. 20: 1-12.

See, T. S. G. Carter, M.D., *Washington, J.S.* (1967). The pathologic effects of intratracheal injections of asbestos fibres in mice: induction of tumors in subcutaneous tissues and induction of mesotheliomas. *Int. J. Cancer* 2, 625-634.

Exposure to asbestos dust in industry and mining has been associated with cancer of the pleura (mesothelioma) for some time (IARC Bull. 1956, 2, 110). The carcinogenic properties of asbestos fibres were investigated in rats (Cotton, J. *Neoplasia*, 1958, 62, 561) and hamsters (IARC Bull. 1967, 2, 514-517) by subcutaneous or intrapleural injection, with production of malignant tumors at the sites of application. Certain forms of asbestos contain appreciable quantities of mineral oil and it is not clear whether the malignancy is due to the asbestos itself or to contamination by mineral oils (IARC 1965, 4, 516).

In an attempt to resolve this problem, fibres of crocidolite, amosite and chrysotile were injected subcutaneously into groups of 20 mice. Fibres of the first two types were also injected after their natural and contaminating oils had been extracted. In each case 10 mg fibre suspended in 0.1 ml saline was administered followed after a 5-day interval by a second dose. Injections were given on the right flank.

Both local sarcomas and mesotheliomas (tumors of serous membranes) were produced. Treated crocidolite induced two sarcomas and four mesotheliomas, while amosite induced two sarcomas and four mesotheliomas. One mesothelioma was induced by extracted crocidolite, while the extracted amosite induced one sarcoma only. Chrysotile also induced just one sarcoma. Other pathological findings of importance included a non-malignant mesothelial proliferation in serous membranes of thorax and abdomen associated with deposition of asbestos fibres and a mild to moderate inflammatory cell infiltration. In particular, no thick fibrous bands were discovered at the site of subcutaneous injection although a foreign-body reaction with fibres both inside and outside the macrophages was observed.

The experiments confirm earlier reports on the carcinogenicity of asbestos fibres, but fail to establish the extent to which mineral oil contamination is responsible for the carcinogenic process.

The appearance of sarcomata at the site of local injection without the production of extensive fibrosis and fibroblastic proliferation would tend to indicate a 'true' carcinogenic effect. This effect is however 'weak' since the number of tumors induced is small (about 10%) and the induction period is long (over 65 wks). There is a striking difference between the mild connective tissue changes produced by asbestos and the extensive necrosis and collagenization produced by repeated injection of food colorings capable of inducing sarcoma and wrongly classed as 'weak' carcinogens (Crasso & Goldberg, IARC Bull. 1966, 5, 212 & 213). This indicates that by a careful study of the tissue reaction a distinction can be made between 'weak' but 'true' carcinogens and substances that induce local sarcoma as a result of repeated trauma and regeneration by virtue of non-specific physico-chemical factors.

PLAINTIFF'S
EXHIBIT

DOW-273

It is well known that to investigate the role of the lysosomes in the cellular activity of various substances, a suitable model has been used in the form of cells which are on stress micrographs by severely limiting the lysosomal membrane with release of powerful hydrolytic enzymes.

Our in vitro work (Allison et al. *Nature*, Lond. 1967, 215, 194) indicated that under certain conditions, release of lysosomal enzymes inhibited cell division, an effect indicative of direct involvement of nuclear DNA, while Allison & Paton (1965, 207, 1170) have shown in vitro that release of lysosomal enzymes by photosensitization techniques can effect a break in the chromosomes of human diploid cells. The ingested asbestos fibres may induce a less severe degree of lysosomal damage than silica. The leakage of hydrolytic enzymes may not be sufficient to bring about cell death but may affect the genetic apparatus and lead to uncontrolled cell proliferation.]

1942. OZONE AND IONIZING RADIATION - A DANGER TO HEALTH

Tonings, T.S. (1967). Toxicity of ozone in comparison with ionizing radiation. *Strahlentherapie* 145, 469.

In an earlier paper, this author and his colleagues commented on the similarities between the toxic effects of radiation and those produced by exposure to high concentrations of ozone (Singer et al. 1966, 3, 195). The need for further investigation of the possible deleterious effect of ozone at the low concentrations generally encountered in commercial usage has led to the present report.

Ozone is used as an air freshener in concentrations which are considered to be harmless or even favourable to man. The natural occurrence of ozone is no more a guarantee of its safety, however, than is that of ionizing radiation, and in recent years the acceptable limit for ozone in factory atmospheres has been reduced in the U.S. and U.K. to 0.1 ppm. The present author has found that mortality was increased in mice that had been exposed to concentrations of ozone as low as 0.05 ppm for 1 hr prior to treatment with sublethal doses of X-rays. Comparison of the deleterious effects of ozone and ionizing radiation, particularly on animal and plant cells and on foetal development, supports the view that ozone is a radiomimetic substance.

[In view of the fact that natural ozone levels may be as high as 0.04 ppm, these findings surely justify a critical attitude to commercial ozonizers.]

1943. PEROXYACETYL NITRATE - SOME FIGURES FOR LETHALITY

Campbell, E.S., Clarke, G.L., Turk, L.O. & Plata, R.L. (1967). The atmospheric contaminant peroxyacetyl nitrate. Acute inhalation toxicity in mice. *Archs envir. Hlth* 15, 739.

The acute local toxicity of peroxyacetyl nitrate (PAN) expressed as the median lethal concentration (LC₅₀) for mice exposed for 2 hr at