TRICHLOROETHYLENE (Group 3)

A. Evidence for carcinogenicity to humans (*inadequate*)

Three cohort studies have been reported, two of which showed no excess of cancer[1,2]; the third[3], in an extended and updated version[4], showed slightly increased incidences of cancer of the bladder (3 observed, 0.8 expected) and prostate (4 observed, 2.4 expected) and of lymphoma (2 observed, 0.3 expected). Two case-control studies of lymphoma have been reported: one on Hodgkin's lymphoma, in which three of 25 cases and none of 50 controls had had exposure to trichloroethylene[5], and the other on Hodgkin's and non-Hodgkin's lymphomas combined in which seven of 169 cases and three of 338 controls had been exposed[6]. Four studies of liver cancer have indicated no clear association with exposure to trichloroethylene[7-10]. A few more cases than controls were exposed in two of the studies, especially when the two studies were analysed together[7,9]. In a proportionate mortality study of polishers and platers with potential exposure to trichloroethylene, but also to chromates (see p. 165) and nickel (see p. 264), there were excesses of oesophageal and primary liver cancers. There were also slight excesses of cancers of the buccal cavity and pharynx, pancreas and larynx and of lymphoma (Hodgkin's and non-Hodgkin's lymphomas combined, 13 observed, 9.3 expected)[11].

Exposure to trichloroethylene may occur to some extent in laundry and dry-cleaning work, although exposure to tetrachloroethylene (see p. 355) probably predominates. Decaffeinated coffee, which is often extracted with trichloroethylene, appeared to be a risk factor for pancreatic cancer in one study, as did dry-cleaning[12].

The inconsistent relationship between liver cancer and dry-cleaning is considered in the summary on tetrachloroethylene. Even if there is some consistency among several studies with regard to an association between lymphatic malignancies and exposure to trichloroethylene, the small numbers involved do not permit any definite conclusion to be drawn about a causal association.

B. Evidence for carcinogenicity to animals (*limited*)

Trichloroethylene was tested for carcinogenicity by oral administration in mice in one experiment and in rats in two experiments. In mice, it produced hepatocellular carcinomas and lung tumours in both males and females. One study in rats was considered to be inadequate, and the other showed equivocal evidence of carcinogenicity[3]. Inhalation studies with trichloroethylene have been conducted in mice, rats and hamsters[13,14]. In one study in female mice, it caused lung tumours[13], but it gave negative results in the other study in mice and in rats and hamsters. Administration by skin painting and by subcutaneous injection to mice also gave negative results[15]. In inhalation experiments using two strains of mice, trichloroethylene increased the incidences of liver tumours in males of one strain and in males and females of the other strain, and of lung tumours in males of one strain and in females of the other. In rats, a low incidence of adenocarcinomas of the renal tubules was observed following exposure to trichloroethylene by inhalation[16]. In mice, oral administration of trichloroethylene containing epichlorohydrin (see p. 202) as a stabilizer induced

forestomach carcinomas but no liver or lung carcinoma[17]. Pure trichloroethylene was tested by oral administration in mice and rats. Hepatocellular carcinomas were induced in male and female mice; none were induced in female rats, and the experiment in male rats was considered inadequate[18]. A study by oral administration was conducted in four strains of rats, but it was inadequate because of toxicity and poor survival[19].

C. Other relevant data

Oral administration of trichloroethylene to mice induced hepatic peroxisome proliferation; however, no such effect was observed in rats[20].

No adequate data were available on the genetic and related effects of trichloroethylene in humans.

Many commercial preparations of trichloroethylene contain stabilizers which are known to be mutagenic. As a rule, the purities of the preparations tested are not given. Trichloroethylene induced micronuclei, somatic mutation (in the spot test), sperm anomalies and DNA strand breaks in the kidney and liver, but not lung, of mice treated *in vivo*; it did not induce dominant lethal mutations. It induced sister chromatid exchanges and unscheduled DNA synthesis in human lymphocytes *in vitro*. It induced transformation of mouse and rat cells but not of Syrian hamster cells; it did not induce sister chromatid exchanges in Chinese hamster cells *in vitro* or unscheduled DNA synthesis in rat hepatocytes. It was mutagenic to plant cells and induced mutation, gene conversion and mitotic recombination in *Saccharomyces cerevisiae* both *in vivo* and in host-mediated assays, but mutation was not induced in *Schizosaccharomyces pombe in vitro* or in a host-mediated assay. It was mutagenic to bacteria when tested as a gas but not when tested as a liquid, except in one study using a mouse-liver metabolic system[21].

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