DDT (Group 2B)

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

Alveolar-cell carcinoma of the lung has been reported in five patients with granulomatous disease of the lungs associated with the inhalation of DDT powder[1]. In four studies[2-5], tissue levels of DDT were reported to be higher in cancer patients than in subjects who died from other causes; no significant difference was found in four other studies[2,6-8], one of which was confined to cancer of the breast and included some living patients[7]. Serum DDT levels appeared to be elevated in another study of nine cancer patients[9], but the study is difficult to interpret. In two case-control studies of soft-tissue sarcoma[10,11] and in three of malignant lymphoma[12-14], relative risks for the association of these diseases with exposure to DDT were 1.2, 1.3, 1.6, 1.5 and 1.8, respectively. Some of the men in these studies had also been exposed to chlorophenoxy herbicides (see p. 156) and chlorophenols (see p. 154), for which there were higher relative risks. Excesses of leukaemia (particularly chronic lymphocytic leukaemia) were noted in two studies[15,16]. A case-control study of colon cancer[17] showed no increased relative risk for exposure to DDT. A small excess of deaths from cancer (3 observed, 1.0 expected) was found in forestry foremen exposed to DDT, 2,4-D and 2,4,5-T[18]. In two other cohort studies of men involved in the manufacture of DDT, there was no increase in mortality from cancer overall[19,20] (standardized mortality ratio [SMR], 68 and 95, respectively), although in one[20], mortality from respiratory cancer was increased slightly (SMR, 156; 95% confidence interval, 74-286). An increase in lung cancer mortality was also observed in agricultural workers who had used DDT and a variety of other pesticides and herbicides (180 [140-240])[21], but a small case-control study of lung cancer deaths in orchardists showed no excess[22]. Studies of pesticide applicators, who use DDT as well as a number of other pesticides, showed excesses of lung cancer[23,24]. In one of these studies, the risk for lung cancer increased with duration of holding a licence to nearly three fold among those licensed for 20 or more years[24]. Exposure to multiple pesticides in these studies prevents a clear evaluation of the cancer risk associated with DDT alone.

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

DDT has been tested for carcinogenicity by oral administration in mice, rats, hamsters, dogs and monkeys and by subcutaneous injection in mice. After oral administration to mice, it caused benign and malignant liver neoplasms, lymphomas and lung neoplasms[2,25]; oral administration to rats caused liver neoplasms[26,27]. Three feeding studies with hamsters gave negative results[2,28,29], and feeding studies with dogs and monkeys were inconclusive[2]. Following subcutaneous injection to mice, it produced liver tumours, lymphomas and lung tumours[25]. Oral administration of DDT enhanced the incidence of liver neoplasms induced in mice by oral administration of *N*-nitrosodiethylamine[30], and the incidences of liver preneoplastic lesions induced in rats by oral administration of 3'-methyl-4-(dimethylamino)-azobenzene[31] and of liver tumours induced in rats by oral administration of *N*-nitrosodiethylamine[32]. Feeding of DDT to rats also accelerated the development of mammary-gland tumours induced by 2-acetamidophenanthrene[33].

C. Other relevant data

In a single study, it was reported that workers exposed to DDT and other pesticides showed increases in chromatid-type aberrations, but not in chromosomal aberrations, in peripheral lymphocytes[34].

Conflicting results were obtained for the induction of dominant lethal mutations in mice and rats. DDT induced chromosomal aberrations in bone-marrow cells of mice, but not of rats, and chromosomal aberrations in spermatocytes of mice treated *in vivo*; it did not induce micronuclei in bone-marrow cells of treated mice. In human cells *in vitro*, it did not induce chromosomal aberrations, mutation or unscheduled DNA synthesis. It did not induce mutation, DNA strand breaks or unscheduled DNA synthesis in cultured rodent cells; conflicting results were obtained for chromosomal aberrations in Chinese hamster cells. DDT inhibited intercellular communication in human and rodent cell systems. It did not induce sex-linked recessive lethal mutations in *Drosophila*, but conflicting results were obtained with regard to aneuploidy; it caused dominant lethal mutations. It did not induce mutation in fungi, either after direct exposure or in a host-mediated assay. DDT was not mutagenic to bacteria and did not induce breakage of plasmid DNA[34].

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