LEAD AND LEAD COMPOUNDS: LEAD AND INORGANIC LEAD COMPOUNDS (Group 2B) ORGANOLEAD COMPOUNDS (Group 3)

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

Three epidemiological studies of workers exposed to lead and lead compounds were reviewed previously[1]: one on smelters and battery workers in the USA, one on workers exposed to tetraethyllead in the USA, and one on copper smelters in the USA; data on the first of these populations have been updated[2]. A study on battery workers in the UK[3] is now available, and studies of a US lead smelter[4] and of a Swedish copper smelter[5] have also been reported. A statistically significant excess of cancers of the digestive system (21 observed, 12.6 expected) was found in the study of battery workers in the UK, spanning 1925-1976, although the excess was confined to the years 1963-1966[3]. Significant excesses of stomach cancer (34 observed, 20.2 expected) and of respiratory cancers (116 observed, 93.5 expected) were seen in the study of US battery plant workers[2], although there was a downward trend in standardized mortality ratio by number of years of employment; in the lead production facilities, the excesses noted for stomach and respiratory cancers were not significant[2]. A nonsignificant excess of respiratory cancer (41 observed, 36.9 expected) was reported in one of the studies of smelters[4], with 28 observed and 25.7 expected in the group with high exposure to lead. Excesses were also noted in this study for kidney cancer (6 observed, 2.9 expected) and bladder cancer (6 observed, 4.2 expected)[4]. A small study of workers at a Swedish smelter[5] with long-term exposure to lead demonstrated a nonsignificant excess of lung cancers (8 observed, 5 expected). Two cases of kidney cancer in lead smelter workers have also been reported[6,7].

The excesses of respiratory cancer in these studies were relatively small, showed no clear-cut trend with length or degree of exposure, and could have been confounded by factors such as smoking or exposure to arsenic (see p. 100).

A study of workers manufacturing tetraethyllead revealed excesses of respiratory cancer (15 observed, 11.2 expected) and brain cancer (3 observed, 1.6 expected)[8].

B. Evidence for carcinogenicity to animals (*sufficient* for inorganic lead compounds; *inadequate* for organolead compounds)

Lead acetate and lead subacetate were tested for carcinogenicity by oral, subcutaneous and intraperitoneal administration in rats, lead phosphate was tested by subcutaneous and intraperitoneal administration in rats, and lead subacetate was tested by oral administration in mice. Renal tumours were produced in animals of each species by each route of administration. Rats given lead acetate or lead subacetate orally developed gliomas. Lead subacetate also produced an increased incidence of lung adenomas in mice after its intraperitoneal administration[1]. Oral administration of lead dimethyldithiocarbamate (ledate) increased the incidence of reticulum-cell sarcomas in male mice of one strain[9] but was not carcinogenic to mice or rats in another experiment[10].

Synergistic effects were reported[1,11-14] in the kidneys of rats given lead acetate and *N*-nitroso-*N*-(hydroxyethyl)ethylamine, *N*-(4′-fluoro-4-biphenyl)acetamide or 2-(nitroso-ethylamine)ethanol orally and in the lungs of hamsters given lead oxide with benzo-[*a*]pyrene intratracheally. Lead subacetate given in the diet enhanced the incidences of liver and kidney tumours induced in rats by 2-acetylaminofluorene given in the diet[1].

The lead compounds tested for carcinogenicity in animals are almost all soluble salts that were selected on the basis of ease of administration. Metallic lead, lead oxide and lead tetraalkyls have not been tested adequately.

C. Other relevant data

Studies of chromosomal aberrations in people exposed to lead have given conflicting results: positive reports have been published concerning workers in lead-battery industries and lead smelters, but other studies of workers under comparable conditions have given negative results. Increased incidences of sister chromatid exchanges have been reported in the peripheral blood lymphocytes of workers exposed to lead but not in those of children exposed to high levels of lead in the environment. An increased incidence of sperm abnormalities was seen in men exposed occupationally to lead[15].

Although a few studies in rodents treated with lead salts *in vivo* have shown small (but significant) increases in the frequency of chromosomal aberrations and micronuclei in bone-marrow cells, most studies showed no increase. Lead salts caused morphological sperm abnormalities in mice but not in rabbits. Sister chromatid exchanges and unscheduled DNA synthesis were not induced in cells of animals treated with lead salts *in vivo*. Lead salts did not induce chromosomal aberrations in human lymphocytes *in vitro*. Conflicting results have been obtained in assays for transformation in cultured rodent cells. Lead salts did not cause aneuploidy in *Drosophila*, mutation or gene conversion in yeast or mutation or DNA damage in bacteria[15].

Tetraethyl- and tetramethyllead did not induce mutation in bacteria[15].

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