

FLUORIDES (INORGANIC, USED IN DRINKING-WATER) (Group 3)

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

Only studies on water fluoridation and cancer were reviewed. Comparisons have been made of mortality from cancers at all sites and from particular types of cancer between areas with high concentrations of inorganic fluoride in drinking-water (either occurring naturally

or as a consequence of fluoridation) and areas with low concentrations, or before and after fluoridation; the areas or groups of areas most frequently studied are in Australia, Canada, China, England and Wales, New Zealand, Norway and the USA¹⁻⁶. When possible, confounding of fluoride concentration with relevant variables such as age, sex, race and ethnic composition of the populations was taken into account. Fluoridation of drinking-water was introduced in the USA in 1950¹, and thus the studies in the USA encompass periods of observation of 20 years or more. Studies of areas with different levels of naturally fluoridation cover longer periods of exposure^{1,6}. The studies have shown no consistent tendency for people living in areas with high concentrations of fluoride in the water to have higher cancer rates than those living in areas with low concentrations or for cancer mortality rates to increase following fluoridation.

In several studies, trends in cancer incidence or mortality in naturally or artificially fluoridated areas and in areas with low natural fluoride content and no artificially fluoridated water were evaluated according to individual cancer sites or groups of sites^{1,3,4,6}. Since a large number of comparisons was made, some would be expected by chance alone to show differences. However, no consistent difference has been seen, and there have been as many significant negative associations between fluoridated water supplies and cancer incidence or mortality as there have been positive associations.

Many studies, therefore, cover the range of doses of fluoride in drinking-water to which humans are exposed, and these are mutually consistent in not showing a positive association between exposure to fluoride and overall cancer rates or rates of different cancers. The Working Group noted that the studies involved were of the ecological or correlation type. The Group was therefore unable to classify the evidence for inorganic fluorides used in drinking-water as 'suggesting lack of carcinogenicity'.

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

Sodium fluoride was tested in three experiments in three different strains of mice by oral administration. The available data are insufficient to allow an evaluation to be made¹.

C. Other relevant data

Epidemiological studies have shown no association between the presence of fluorides in drinking-water and the incidence of Down's syndrome⁷.

Sodium fluoride did not induce DNA strand breaks in testicular cells of rats treated *in vivo* and did not cause chromosomal aberrations in bone-marrow or testicular cells or sister chromatid exchanges in bone-marrow cells of mice treated *in vivo*. It was reported to induce unscheduled DNA synthesis in cultured human cells, and conflicting results were obtained on the induction of chromosomal aberrations; it did not induce sister chromatid exchanges. It induced transformation, sister chromatid exchanges and chromosomal aberrations in Syrian hamster embryo cells *in vitro*. At high doses and low cell survival, sodium fluoride induced dose-related increases in mutations in cultured mouse lymphoma cells. It did not induce aneuploidy in *Drosophila*. It induced chromosomal aberrations in plants. It did not induce gene conversion in yeast and was not mutagenic to bacteria⁷.

Stannous fluoride, sodium monofluorophosphate and sodium silicofluoride did not induce sex-linked recessive lethal mutations in *Drosophila*, and sodium monofluorophosphate did not induce dominant lethal mutations in *Drosophila*⁷.

References

¹IARC Monographs, 27, 237-303, 1982

²Wang, B. (1981) The relationship between malignancy and fluorine content in the drinking water in Xilinkuolemeng, Nei Menggu (Chin.). *Zhonghua Zhongliu Zazhi*, 3, 19-21

³Neuberger, J.S. (1982) Fluoridation and cancer: an epidemiologic appraisal. *J. Kansas med. Soc.*, 83, 134-139

⁴Chilvers, C. (1982) Cancer mortality by site and fluoridation of water supplies. *J. Epidemiol. Commun. Health*, 36, 237-242

⁵Chilvers, C. (1983) Cancer mortality and fluoridation of water supplies in 35 US cities. *Int. J. Epidemiol.*, 12, 397-404

⁶Chilvers, C. & Conway, D. (1985) Cancer mortality in England in relation to levels of naturally occurring fluoride in water supplies. *J. Epidemiol. Commun. Health*, 39, 44-47

⁷IARC Monographs, Suppl. 6, 312-315, 1987