FLUORIDE EXPOSURE AND CHILDHOOD OSTEOSARCOMA

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Does fluoride increase the risk of osteosarcoma in young men? This case-control study by the New York Department of Health tested this hypothesis by comparing the estimated fluoride intake of 130 osteosarcoma victims with that of an equal number of presumed healthy sex- and age-matched surrogates. The authors report finding little difference, and concluded that fluoride does not increase the risk, and may even be protective. Differing conclusions are not uncommon in science, and especially in medical science since underlying causes are often exceedingly complex, subtle and heterogeneous. It is important, therefore, to examine this report's results, its test design, and the assumptions on which the test and the conclusions are based.

Several lines of investigation suggest that fluoride intake increases the risk of cancer in general and, in particular, the incidence of osteosarcoma in males. As the authors admit, in vivo studies show fluoride to be mutagenic, inducing chromosome aberrations, sister chromatid exchanges, cytotoxicity, and neoplastic transformation in cultured mammalian cells. The authors also agree that fluoride accumulates primarily in bones; and that children, who are actively forming bone, have a higher uptake of fluoride into bone than adults. Further, bone in knees, ankles, shoulders, and wrists, where childhood osteosarcoma most often occurs, shows a high response to fluoride.1

In 1990, a two-year carcinogenicity study by the National Toxicology Program (NTP) found a statistically significant, dose-related increase of osteosarcoma rates in male rats, but not in mice.2 That the so-called peer review members at the time quixotically chose to call this fluoride/osteosarcoma correlation “equivocal” (as reported by the authors of this present study) does not change the facts. This same study revealed a strong correlation of fluoride intake with nasal and oral cancer and precancerous lesions in test rats and mice. A coincidental Proctor and Gamble study reported an increased incidence of cancer in rats but this was discounted later on the basis of a concomitant viral contamination in the test rodents.3 Time trends for bone and joint cancer and osteosarcoma derived from the Surveillance, Epidemiology and End Results (SEER) data of the National Cancer Institute (NCI) revealed a positive association of osteosarcoma incidence and water fluoridation among males under 20 years of age.4 In 1993, an ecological study performed by the New Jersey Department of Health found a strong statistical association between fluoridation and osteosarcoma among young men.5 It would appear that the fluoride/osteosarcoma hypothesis is credible and convincing, if not yet “conclusive” to fluoridation proponents.

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* See Abstract on page 252.
Testing for the fluoride/osteosarcoma link is a daunting prospect. Osteosarcoma is quite rare, the incidence being only 2.9 cases per million people in the US. Test design always follows from assumptions made. The susceptibility of a cell to be cancer-prone may stem from a variety of subtle influences. In the case of xenobiotics (petrochemical compounds such as pesticides and various plastics), it is now known that exposure during embryonic tissue differentiation is far more toxic than later in life; yet the effects show up much later in life as an increased susceptibility to cancer of urogenital tissues such as the vagina, cervix, ovary, or testes.

Fluoride readily crosses the placenta. Maternal fluoride intake determines whether baby’s bones are fully fluoridated or not. It is likely that fluoride intake later in life will be more toxic to the child whose bones are already fully fluoridated than to one whose bones are not so fluoridated. Thus, one might well assume that exposure to fluoride during embryo life could be a factor in developing bone cancer later in life, regardless of whatever other factors may also play a role. Oncology researchers often make the distinction between cancer initiators and cancer promoters. Whether fluoride is considered a cancer initiator or a promoter, one’s test design must include the fluoride intake by the mother prior and during the time of her pregnancy. This factor is missing in this present study.

In testing the fluoride/osteosarcoma link, one must be able to calculate total fluoride intake at various stages of life preceding the onset of the cancer. This is more difficult than it might at first seem. In calculating total fluoride intake, the study included fluoride tablets used, mouth rinses, toothpaste used, dental treatments, and water fluoridation levels. Missing from this list are calculations of differences in water actually consumed based on differences in ambient temperature, individual work or athletic exercise that greatly increases water consumption, and dietary habits such as processed beverages versus “plain” water. It is not difficult to understand that commercially processed beverages made from fluoridated water are sold in unfluoridated communities. Likewise, it is not difficult to understand that some children drink more processed beverages than water from the tap. Thus, knowing the fluoride concentration of the tap water is not the same as knowing the fluoride intake from one’s drinking of fluids.

Further, it is well established that much of our US diet choices are canned or processed foods rather than fresh, unprocessed foods. Community water fluoridation adds fluoride not only to one’s drinking water but to foods processed with the fluoridated water. It is for this reason that processed foods of different brands can differ greatly in their fluoride content, and this difference is not recognized when making food purchase choices. It is likely that one family will routinely choose one brand while the next family always uses another brand. Estimating averages does not help since the “average” does not exist; one brand will be fluoridated and the other is not. Fluoride from processed foods comprise a major portion of one’s total...
fluoride intake, often equalling or exceeding that obtained from tap water. This calculation, too, is missing from the fluoride exposure variables listed in this study.

In the present study, something is odd about the case subjects. While it is routinely found that osteosarcoma is more common in young men than in young women, this study's list of 130 cases included only 42 males, or 32% of the total. Thus, the osteosarcoma cases used were not typical of the disease in question. Did the males go elsewhere for treatment? Did some male cases of osteosarcoma slip through undetected in the study's case selection method? Did the young women with osteosarcoma drink more fluoridated beverages and less unfluoridated water than the young men? From the information given, no clue is found. The authors seem unconcerned over this discrepancy.

Finally, one must question the case-control method of the study. In the case-control method, patients with the disease in question are compared to similar appearing, same-age people without the disease. In effect, patients susceptible to osteosarcoma were selected controls, i.e. those without evident osteosarcoma. Given the rarity of osteosarcoma, and the fact that the sources of fluoride exposure are so ubiquitous, it would be no problem to find an equal group of healthy people living in the same communities and using the same toothpaste as those with osteosarcoma.

The fact that the two groups' drinking water and toothpaste choices are the same does not invalidate the conclusion that fluoride was a factor in the development of osteosarcoma. The study's authors apparently assume that osteosarcoma victims require higher fluoride exposure than those without the disease. An equally plausible assumption is that variable individual susceptibility exists such that equal fluoride exposure will affect only those with the requisite susceptibility. Given the rarity of the disease, this seems more probable. The susceptibility for osteosarcoma may stem from early prenatal fluoride exposure or from factors not yet known. The later occurrence of the cancer may require only the level of fluoride exposure common to fluoridated communities. If this assumption was correct, as case-control study such as this comparing only post-natal fluoride exposure between osteosarcoma victims and controls would find no difference.

When polio "epidemics" were common, it was clear that only a small percentage of children in any given community developed clinically apparent poliomyelitis while well over 90% of the children showed an equal rise in polio antibodies. That is, despite equal exposure, only a few children were sufficiently susceptible to be stricken with polio. A similar scenario might well apply to the osteosarcoma problem. Since we often do not know all the factors that "cause" or "promote" a given cancer, we do not know what factors are important in selecting comparison groups. Case-control study designs are not appropriate for all illnesses and this, one might suspect, is one of them.
Conclusion

This present study, while being used to cast doubt on the relationship of fluoride to osteosarcoma, is flawed by: 1) disregard of prenatal fluoride exposure; 2) inadequate calculation of postnatal total fluoride intake; and 3) inappropriate choice of study design. Thus, the study carries little weight in negating the fluoride/osteoporosis connection or in any consideration of continuing fluoridation as a public policy.

References

3 As presented at the NTP peer review conference at Research Triangle Park, North Carolina, 1990, attended by the author.
7 Lee JR. Optimal fluoridation - the concept and its application to municipal water fluoridation. *Western Journal of Medicine* 122 431-436