

## Caution needed in fluoride and osteosarcoma study

Chester W. Douglass · Kaumudi Joshipura

Received: 3 January 2006 / Accepted: 12 January 2006  
© Springer 2006

This issue of *Cancer Causes and Controls* includes a paper with results from an analysis of a subset of participants in our ongoing study of fluoride and osteosarcoma. The paper, ‘‘Age-specific fluoride exposure in drinking water and osteosarcoma’’, presents a partial view of this ongoing study. We would like to advise the readers to be especially cautious when interpreting the findings of this paper for several reasons. The authors themselves have already raised a flag of caution in their final paragraph with the note that they are aware of additional findings from other incident cases that appear not to replicate the findings from the cases presented in their paper.

The Harvard School of Dental Medicine study of fluoride and osteosarcoma has been a 15-year collaboration among NIEHS, NCI, NIDCR, and Harvard. Two sets of cases have been collected each with their own control groups. The study started in 1992. The first set of cases was recruited from existing cases between 1989 and 1992, and the second set of cases was recruited from new incident cases between 1993 and 2000. The Bassin et al paper reports age-specific results among only the cases from 1989 to 1992. We are also finding some positive associations between fluoride and osteosarcoma in the overall (not age-specific) analysis of the first set of cases. However, our preliminary findings from the overall analysis of the second

set of cases (1993–2000) do not appear to replicate the overall findings from the first part of the study. Our findings currently being prepared for publication, do not suggest an overall association between fluoride and osteosarcoma. This seems particularly important since the cases had been accrued essentially from the same hospitals within the same orthopedic departments with the same providers, and the same pathology departments making the diagnosis of the osteosarcoma and also using similar methods of fluoride exposure.

In addition to fluoride intake history, many of the cases and controls that were accrued in the 1993–2000 time period agreed to provide bone specimens. The cases provided bone that was obtained proximal to the osteosarcoma lesion as well as from their contra lateral hip. The control group of non-osteosarcoma cancer patients provided bone specimens. Our preliminary analysis of the fluoride content of the bone specimens suggests that the fluoride level within the bone is not associated with excess risk of osteosarcoma. We are grateful to Dr. Bassin and her coauthors for mentioning at the end of their paper that we are not finding a positive association from the bone specimens in the second set of cases.

Obtaining and analyzing sufficient numbers of bone specimens has been a laborious and a time consuming effort by many people throughout the hospitals and research teams. The analysis of these specimens has included quality control procedures on laboratory techniques, pilot studies to test reliability, many runs of small batches of specimens, the double checking of specimen transport procedures, and the preparation of data sets for analysis.

We are now in the possession of the complete analytic data sets and are pursuing previously planned analysis and comparisons with the earlier set of collected cases. We

---

C. W. Douglass (✉) · K. Joshipura  
Harvard School of Dental Medicine, Boston, MA, USA;  
Harvard School of Public Health, Boston, MA, USA  
e-mail: chester\_douglass@hsdm.harvard.edu  
Tel.: +1-617-432-1456  
Fax: +1-617-432-0047

K. Joshipura  
University of Puerto Rico, Medical Sciences Campus, San Juan,  
Puerto Rico

have delayed publication of all the major findings until we found replication or lack of replication of the earlier positive findings. Our role model in this process has been Sir Richard Doll, whose first publication associating smoking with illness was rejected for publication until it could be replicated (New York Times, July 26, 2005). It was too important and too unexpected to be published on its own. Professor Doll did replicate his initial findings; we apparently have not and the bone specimens seem to corroborate the lack of an association between the fluoride content in drinking water and osteosarcoma in the new cases. Interestingly, the NIEHS replication of their own earlier study that found excess osteosarcoma in male rats was recently presented on the NIEHS web site [1]. The findings of their second study do not replicate their original widely quoted National Toxicology Program study [2]. Drinking water with very high fluoride content was not found to be associated with osteosarcoma in either male or female rats.

A parallel analysis of age-specific exposure to fluoride, especially during growth periods, is also being pursued by our study team in the second set of cases of our study. Accordingly, readers are cautioned not to generalize and over-interpret the results of the Bassin et al. paper and to await the publications from the full study, before making conclusions, and especially before influencing any related policy decisions.

## References

1. The National Toxicology Program (NTP). Supplemental 2-year study of sodium fluoride in male F344 rats (CAS No. 7681–49–4)
2. National Toxicology Program (1990) Toxicology and carcinogenesis of sodium fluoride in F344 TN rats and B 6C3FL mice. Technical Report Services 393, NIH Publication No. 90–2848