

## Final Report

Grant Number: 5 RO1 ES06000  
Project Title: Fluoride Exposure and Osteosarcoma  
Principal Investigator: Douglass, Chester W.  
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The **Fluoride Exposure and Osteosarcoma** project was funded by NIEHS to study the association of exposure between fluorides and the diet and osteosarcoma. Dr. Sheila McGuire (a Dental Public Health resident at Harvard School of Dental Medicine) and Dr. Mike McGuire (a former MGH resident in Orthopedic Surgery) collaborated with Dr. Chester Douglass, Principal Investigator, to obtain cooperation from hospitals across the nation for a case-control study of fluoride and osteosarcoma. Prevalent cases found in the patient records of 10 Orthopedic Surgery Departments across the nation were matched with two sets of hospital-based controls: 1) a non-Osteosarcoma tumor control, and 2) a non tumor control (usually trauma). Controls were matched on age, gender and distance of residence from the hospital.

Fluoride exposure was estimated first by using the CDC Fluoridation Census data and, second, due to many missing values in the Fluoridation Census, by the time consuming process of direct contact with officials in each state or town in which each case or control had ever lived. Telephone interviews were conducted with each case and control to collect information on risk factors and confounding factors. During the data analysis phase, it became apparent that it was difficult to estimate the actual amount of dietary fluoride consumed by study subjects. The retrospective nature of the interviews and the frequency of well water use and bottled water use made it difficult to construct a reliable estimate of fluoride exposure through water consumption. The analysis carried out for the International Conference of the American and European Musculoskeletal Tumor Society meeting on the 139 cases and 280 controls reported an Odds Ratio of 1.28 to 1.5 between fluoride and osteosarcoma that was not significantly different from 1.

The NCI then asked us to cooperate with them in conducting a prospective study on incident cases. The cooperation of the orthopedic departments in the 10 tertiary case hospitals was unusual. Since most were headed by former MGH orthopedic residents and were colleagues of Dr. Mike McGuire, cooperation to collect data from incident cases and controls was obtained. Interviews and specimen collection was carried out by Westat, a frequent collaborator of NCI. The study team from Harvard School of Dental Medicine participated in all phases of the study with Dr. Robert Hoover of NCI. Several bone specimens were collected, including tumor bone and normal bone from cases, tumor bone from non-Osteosarcoma tumor cases, and normal bone from controls. Toenails were also collected on all cases and controls. Data collection extended for five years. A total of 464 subjects were recruited for the study, 189 cases and 275 controls. Initial results using a variety of analyses show that all odds ratios are not significantly different from 1.

The bone specimens are being held by a contractor for NCI and are being analyzed by Professor Gary Whitford at the Medical College of Georgia. Bone specimens were obtained from 71% of cases and 64% of controls. The laboratory chosen for analyzing the fluoride content of the bone specimens has been visited and reliability tests have been conducted by the NCI. Pilot tests on bone specimens from the study were conducted in the fall of 2003. All the specimens to be analyzed were then grouped into appropriate batches for final analyses. For example, the controls for each case must be asked and analyzed in the same batch as their respective cases. This laboratory analysis process will be conducted in the first six to nine months of 2004, with data analysis to follow the succeeding months. Final report writing is planned for

2005. The study is expected to provide the nation with the best information to date regarding a possible relationship between fluoride in the diet and the risk of Osteosarcoma.

### Publications/Papers

Douglass, CW. Fluoride and Osteosarcoma. Paper delivered at the Annual Meeting of the Water Fluoridation and Health Society. London, UK. November 18, 2002.

McGuire SM, Joshi A, Joshipura KJ, Hunter D, Hoover R, DaSilva J, Douglass CW. Lifetime Exposure to Fluoride and Risk of Osteosarcoma. Paper delivered at the Annual International Conference of the American and European Musculoskeletal Tumor Society. Washington, DC 1998.

McGuire S, Douglass CW, Joshi A, Hunter D, DaSilva J. Fluoride exposure and Osteosarcoma. J Dent Res 74 (AADR Abstracts) 1995; 98.

Bassin EB, Association Between Fluoride in Drinking Water During Growth and Development and the Incidence of Osteosarcoma for Children and Adolescents. Doctoral Thesis, Harvard School of Dental Medicine, 2001.