

PROGRESS REPORT SUMMARY		NT NUMBER ES06000 - 03	
PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR Chester W. Douglass, DMD, PhD		PERIOD COVERED BY THIS REPORT	
APPLICANT ORGANIZATION Harvard School of Dental Medicine		FROM 9/30/94	THROUGH 9/29/95
TITLE OF PROJECT (Repeat title shown in item 1 on first page) Fluoride Exposure and Osteosarcoma			
(SEE INSTRUCTIONS)			

Final Data Collection Figures for Retrospective Aspect of the Study

The orthopedic department from ten hospitals nationwide participated in collecting data from retrospective cases of osteosarcoma and their matched controls. Telephone contact was possible for 673 participants, with 23 refusals. Telephone interviews were conducted and completed with 210 cases and 440 matched controls. Fluoride levels in the drinking water were ascertained for a participant's complete residential history for 164 cases and 346 controls. Fluoride levels were unobtainable for 140 participants (46 cases and 94 controls) for two reasons; 52 participants had lived overseas for a period of time during their life and 88 participants did not return a well water sample. To measure fluoride exposure, participants self-reported consumption of either municipal water and well water, or bottled water at each residential address. The CDC Fluoridation Census provided the fluoride levels in the municipal water. Well water samples were analyzed for fluoride content at Harvard School of dental Medicine. No attempt to gather the fluoride content of bottled water was made, assumptions will be made in the analyses.

Initial Analyses for the Retrospective Aspect of the Study

The following analyses assumed that the fluoride level in bottled water was 1.0 ppm. The average lifetime exposure of fluoride was 0.55 ppm in the population of cases and 0.53 in the population of controls (t-test=-0.49, p=0.62). For four matched-pairs analyses, the point estimates of the odds ratio (OR) was less than 1. The OR of disease (osteosarcoma) associated with an average lifetime exposure greater than 0.7 ppm fluoride was 0.904 (CI=0.583, 1.402). The OR associated with and average lifetime exposure greater than 1 ppm fluoride was 0.942 (CI=0.568, 1.562). The OR associated with exposure greater than 0.7 ppm of fluoride during the first fifteen years of life was 0.854 (CI=0.504, 1.448). The OR associated with exposure greater than 1.0 ppm of fluoride during the first fifteen years of life was 0.537 (CI=0.302, 0.956). However, if we look at the 19 cases and 27 controls who at some point in their life had lived at an address where the fluoride level was greater than 1.0 ppm, the point estimate of the OR was not less than 1. The OR for the matched analysis was 1.315 (CI=0.603, 2.869). In an unconditional analysis in which we assume bottled water to contain 0.0 ppm fluoride, and look at other exposures to fluoride of greater than 1 ppm at any time, the OR=2.75 (1.2, 6.4). Included in that analysis are 10 controls and 12 cases.

Questions Left Unanswered

Using fluoride levels in drinking water to measure fluoride exposure has its limitations due to other potential sources of fluoride exposure. Other common sources of fluoride

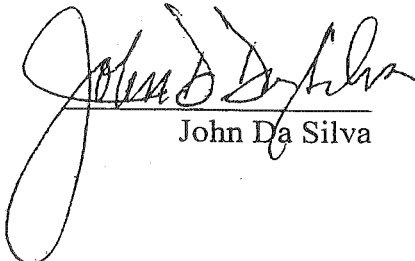
include, school-based fluoride programs, prescription fluoride tablets, fluoride drops, fluoridated toothpaste and mouth rinses. Data were collected on exposure to these other fluoride sources and are currently being analyzed. Due to the potential impact of these and other unknown sources of fluoride, it is important to obtain an objective measure of fluoride exposure such as fluoride bone burden. Therefore bone sample analysis is a component of the prospective aspect of the study. The importance of the prospective study is further magnified if one considers point estimates of OR using the assumption of 0 ppm fluoride in bottled water. All of those analyses have point estimates of the OR that are greater than one. However, all confidence intervals include one.

Update on the Prospective aspect of the Study

Working closely with NCI, the IRB approval has been received and data collection is underway at seven of the participating hospitals. Nineteen cases and twenty controls have been enrolled to date. The iliac crest bone biopsy and tumor sample harvest was completed for 15 of the cases. The Massachusetts General Hospital and Boston's Children's Hospital are two of the three remaining hospitals where data collection will begin soon. Initially, the Co-Investigators agreed to follow only the retrospective protocol in the prospective aspect of the study. They have now agreed to participate in the full protocol including the collection of the iliac crest bone biopsy from the case population.

Minority Supplement

During this past year Dr. Da Silva has been involved in closing out the outstanding cases and controls for the retrospective study. This involved following up on missing data and calling cases and controls who lived in homes supplied by well water, as well as measuring fluoride content of remaining well water samples. Dr. Da Silva assisted in the IRB process to ensure that IRB's collection at each site. In addition, he was responsible for overseeing the protocol for data collection at the Massachusetts General Hospital as well as Children's Hospital in Boston. Currently Dr. Da Silva is in the process of data analysis for the other sources of fluoride for the retrospective study. Data collection has begun for the prospective aspect of the study which includes data to support the analysis of Dr. Da Silva's minority supplement. Dr. Da Silva presented the preliminary findings of the retrospective aspect of the study in a meeting of the faculties of the Forsyth Dental center and Harvard School of Dental Medicine. Dr. Da Silva attended the American Dental Association's annual meeting and the American Academy of Implant Dentistry's Annual Meeting, both held in New Orleans. During this year Dr. Da Silva and Dr. Joshi applied for a grant from the Agency for Health Care Policy Research titled Clinical and Microbiological Outcomes of Oral Implant Treatments. He also worked with Dr. Douglass to respond to and RFP from HRSA entitled "An evaluation of the Ryan White Dental Reimbursement Program".



John Da Silva