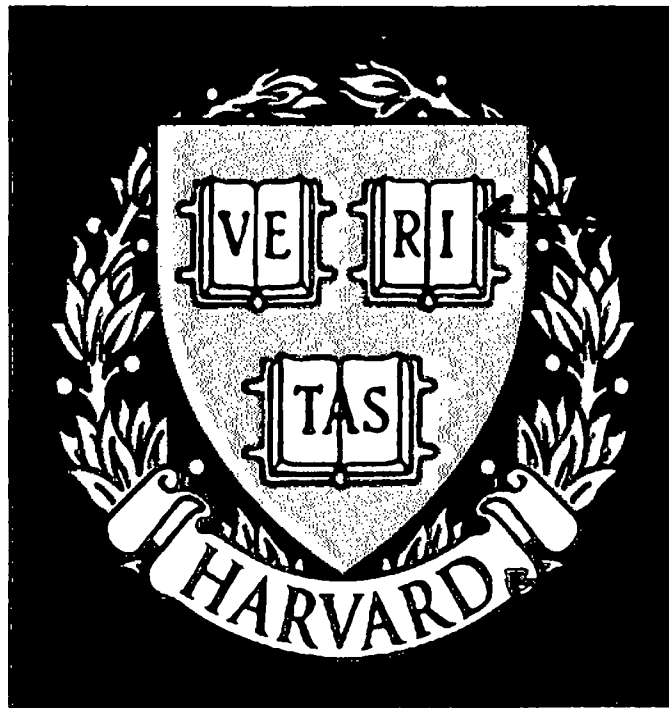
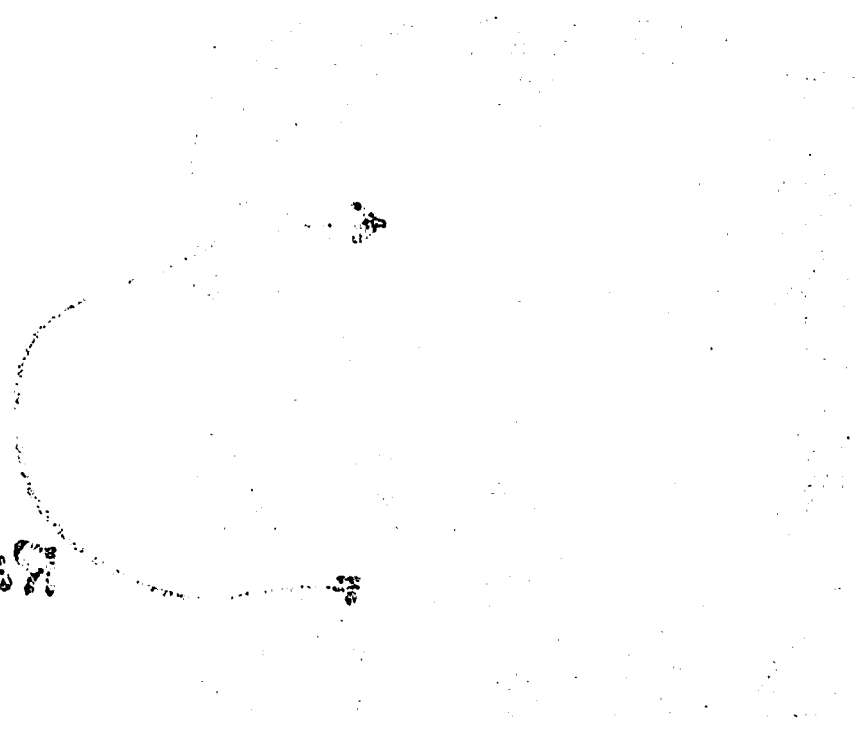


VERITAS
(Latin for “Truth”)



REALLY?

5. 11. 1952



Final Report

Grant Number: 5 RO1 ES06000
Project Title: Fluoride Exposure and Osteosarcoma
Principal Investigator: Douglass, Chester W.
Project Award Period: 09/30/92 - 06/30/99

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 an Orthopedic Surgery Research meeting reported an Odds Ratio of 1.2 to 1.4 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 419 subjects were recruited for the study, 139 cases and 280 controls.

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. 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

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.

Age-specific fluoride exposure in drinking water and osteosarcoma (United States)

Elise B. Bassin · David Wypij · Roger B. Davis ·
Murray A. Mittleman

Received: 24 July 2005 / Accepted: 7 November 2005
© Springer 2006

Abstract

Objective We explored age-specific and gender-specific effects of fluoride level in drinking water and the incidence of osteosarcoma.

Methods We used data from a matched case-control study conducted through 11 hospitals in the United States that included a complete residential history for each patient and type of drinking water (public, private well, bottled) used at each address. Our analysis was limited to cases less than 20 years old. We standardized fluoride exposure estimates based on CDC-recommended target levels that take climate into account. We categorized exposure into three groups (<30%, 30–99%, >99% of target) and used conditional logistic regression to estimate odds ratios.

Results Analysis is based on 103 cases under the age of 20 and 215 matched controls. For males, the unadjusted odds ratios for higher exposures were greater than 1.0 at each exposure age, reaching a peak of 4.07 (95% CI 1.43, 11.56) at age 7 years for the highest exposure. Adjusting for potential confounders produced similar results with an adjusted odds ratio for males of 5.46 (95% CI 1.50, 19.90) at age 7 years. This association was not apparent among females.

Conclusions Our exploratory analysis found an association between fluoride exposure in drinking water during childhood and the incidence of osteosarcoma among males but not consistently among females. Further research is required to confirm or refute this observation.

Keywords Osteosarcoma · Fluoride · Fluoridation · Case-control

E. B. Bassin
Department of Oral Health Policy and Epidemiology, Harvard
School of Dental Medicine, USA
e-mail: elise_bassin@post.harvard.edu

D. Wypij
Department of Pediatrics, Harvard Medical School, USA
and Clinical Research Program, Children's Hospital, USA

R. B. Davis · D. Wypij
Department of Biostatistics, Harvard School of Public Health,
USA

R. B. Davis (✉)
Division of General Medicine and Primary Care, Beth Israel
Deaconess Medical Center, 330 Brookline Avenue, Boston, MA
02215, USA

M. A. Mittleman
Department of Epidemiology, Harvard School of Public Health,
USA and Cardiovascular Epidemiology Research Unit,
Beth Israel Deaconess Medical Center, USA

Introduction

Osteosarcoma is a very rare primary malignant tumor of bone. Although uncommon, primary malignant bone tumors comprise the sixth most common group of malignant tumors in children and the third most common malignant tumor for adolescents, with an annual incidence rate of 5.6 per million for Caucasian children under 15 years old [1]. Osteosarcoma is the most common tumor of bone and for patients less than 20 years old more than 80% of these tumors tend to occur in the long bones of the appendicular skeleton which are undergoing rapid growth [2]. The incidence of osteosarcoma is slightly higher in males than females with an annual incidence rate of approximately 3.5 per million for males and 2.9 per million for females under the age of 24 years [3].

June 27, 2005

Ms. Janice Strother, NIEHS Ethics Coordinator
NH Room 269
MD NH-01
PO Box 12333
Research Triangle Park, NC 27709

Dear Ms. Strother:

During the past week we have had several conversations with NIEHS ethics staff about potential, serious misrepresentations of research results contained in a final report to NIEHS submitted by Dr. Chester Douglass, chairman of the Harvard University School of Dental Medicine's Department of Oral Health Policy and Epidemiology for grant number 5 R01 ES06000.

We are writing to request a formal investigation into this issue, based on the discrepancies described below.

The principle issue of concern is the serious contradiction between the conclusion in the grant report, where Dr. Douglass reports no evidence of a link between fluoride and osteosarcoma, and the findings of the grant-supported publications listed in support of this position that conclude exactly the opposite. By reporting the results of grant-supported publications in this way, it appears that Dr. Douglass may have violated Sec. 93.103 (b) of federal research rules concerning falsification of data and the reporting of research results.

Specifically, in the grant report, Dr. Douglass concludes that there is no evidence of a link between fluoride and osteosarcoma, and references work by Dr. Elise Bassin as one of only two publications supported by the grant that support this finding. The issue is that Dr. Bassin's findings, contained in her doctoral thesis at Harvard, do not support the finding that Douglass reported to NIEHS - but instead resoundingly contradict it. What makes this inconsistency more curious is that Douglass was the lead advisor on the Bassin doctoral thesis. Dr. Douglass personally signed off on Dr. Bassin's research.

In Douglass's grant report to NIEHS he presents only the following conclusions regarding fluoride and bone cancer: "The analysis carried out for the Orthopedic Surgery Research meeting reported an Odds Ratio of 1.2 to 1.4 between fluoride and Osteosarcoma that was not significantly different from 1."

The Bassin doctoral thesis was one of two grant-supported publications cited in support of this conclusion. However, the Bassin work does not support this finding. In contrast, the Bassin doctoral thesis found a strong, statistically significant association between fluoride levels in tap water during the mid-childhood growth spurt and

osteosarcoma in adolescent boys. This is even more noteworthy because the Bassin work is the most rigorous study of the link between bone cancer and fluoride in tap water ever conducted in the United States. Unlike the epidemiology studies that have found no relationship between fluoride in tap water and bone cancer, Bassin focused her analysis on the population of concern (males under 20 years of age) during the relevant period of growth and development. Her study also validated fluoride levels in the tap water consumed during that time period.

The following is just one of several passages from the Bassin thesis describing the link she observed between fluoride in tap water and bone cancer in boys:

"Among males, exposure to fluoride at or above the target level was associated with an increased risk of developing osteosarcoma. The association was most apparent between ages 5-10 with a peak at six to eight years of age. The odds ratio for the high exposure group was 5.16 at 7 years of age with a 95 percent confidence interval of 1.64 to 16.20." (Bassin page 75)

By inaccurately reporting the findings of the Bassin publication, it appears that Dr. Douglass violated Sec. 93.103 (b) of federal research guidelines by falsifying his final report for grant 5 R01 ES06000. Falsification is defined in Sec. 93.103 (b) as follows (emphasis added):

"Falsification is manipulating research materials, equipment, or processes, or changing or *omitting data or results such that the research is not accurately represented in the research record.*" [emphasis added]

This potential violation of ethical standards is made more serious by its enormous public health implications. Millions of boys drink fluoridated water every day, and any health risk as serious as bone cancer that is associated with fluoridation could have a devastating impact on hundreds of children each year. While Douglass might not agree with the conclusions of this work, that is not a justification for misrepresenting it in his final report to federal health officials and taxpayers.

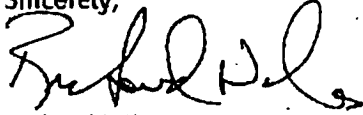
Adding to our concern is the fact that Douglass's misrepresentation of the Bassin findings appears to be part of a pattern.

In a presentation Douglass made to the Royal College of Physicians in London in November of 2002, Douglass concluded that case-control studies showed no association between fluoride exposure and osteosarcoma. This conclusion directly contradicts the findings of the Bassin doctorate that Douglass signed off on in 2001.

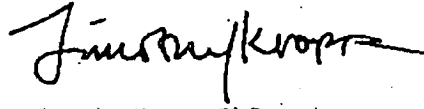
In January 2004, Douglass submitted his final grant report to NIEHS as written testimony to the National Research Council committee studying the toxic effects of fluoride. This appears to be an attempt to use the imprimatur of the NIEHS to influence the deliberations of a National Academy of Sciences committee by submitting an NIEHS grant report concluding that six years of research had found no evidence of a relationship between fluoride and osteosarcoma.

In sum, we are convinced that the evidence presented warrants a full investigation into the worrisome discrepancies in research reporting on the part of Dr. Douglass. We thank you for your attention to this important matter.

Sincerely,



Richard Wiles
Sr. Vice President



Timothy Kropp, PhD
Senior Scientist

Government Asked to Evaluate the Cancer-Causing Potential Of Fluoride in Tap Water

EWG Cites Compelling Body of Science Linking Fluoride to Rare Bone Cancer in Boys

WASHINGTON — Citing a strong body of peer-reviewed evidence, Environmental Working Group (EWG) today asked the National Toxicology Program (NTP) of the National Institutes of Health (NIH) to list fluoride in tap water in its authoritative Report on Carcinogens, based on its ability to cause a rare form of childhood bone cancer, osteosarcoma, in boys. The Report on Carcinogens lists only substances that are known or reasonably anticipated to cause cancer in humans.

In recent years, concerns have grown about the safety of fluoride in tap water. In 2002, the Environmental Protection Agency (EPA) commissioned a study by the National Research Council (NRC) on the overall safety of fluoride in tap water. The final report is expected by February 2006. The NRC, however, does not have the expertise or the mandate to determine the carcinogenicity of fluoride.

EWG recognizes the value of fluoride to dentistry, yet a substantial and growing body of peer-reviewed science strongly suggests that adding fluoride to tap water is not the safest way to achieve the dental health benefits of fluoridation.

Nationwide about 170 million people live in communities with fluoridated water. Adding fluoride to tap water can be a contentious issue. There are ongoing fights over fluoridation in Colorado, New Jersey, Oregon, Vermont, Washington, California, Massachusetts and Nebraska. States with recent battles over fluoridation include New Hampshire, Virginia, Florida, Arkansas and Tennessee.

Research dating back decades, much of it government funded, has long suggested that fluoride added to drinking water presents a unique cancer risk to the growing bones of young boys. New epidemiology provides strong evidence of a link between exposure to fluoride in tap water during the mid-childhood growth spurt between ages 6 and 10, and bone cancer in adolescence. Additional science strongly suggests that fluoride can cause genetic mutations in bone cells directly related to childhood bone cancer.

"We recognize the potential benefits of fluoride to dental health, but there is very compelling evidence that fluoride in tap water can cause bone cancer in boys," said EWG Senior Vice President Richard Wiles. "The government needs to assess the overall strength of the evidence and make a determination of fluoride's cancer-causing potential," Wiles added.

EWG's letter to the NTP and related materials can be found at <http://www.ewg.org/issues/fluoride/20050606/petition.php>

###

Environmental Working Group is a nonprofit research organization based in Washington, D.C., that uses the power of information to protect human health and the environment

Harvard Fluoride Findings Misrepresented?

Environmental Working Group (EWG) has obtained documents suggesting that the Chairman of the Department of Oral Health Policy and Epidemiology at the Harvard School of Dental Medicine falsified reporting to the National Institutes of Health. Dr. Chester Douglass has received several years of large federal grants to study the possible relationship between bone cancer in boys and drinking fluoridated water. Reporting on the findings of this funding, he told federal officials unequivocally that there was no relationship, but the grant-funded publication he cited found exactly the opposite. In fact, the research was done by a former doctoral student of Douglass's and was the *most rigorous* study of its kind to date.

Douglass has made the same assertion to the National Academy of Sciences panel now reviewing the safety of fluoridated drinking water. He is the publisher of a Colgate-funded fluoride journal.

EWG has filed an ethics complaint against Douglass with the National Institute of Environmental Health Sciences (NIEHS).

For Immediate Release: June 6, 2005

Contact: EWG Public Affairs, 202-667-6982



News Release

Harvard Medical School Office of Public Affairs

STATEMENT CONCERNING THE OUTCOME OF THE REVIEW INTO ALLEGATIONS OF RESEARCH MISCONDUCT INVOLVING FLUORIDE RESEARCH

BOSTON-August 15, 2006-The Harvard Medical School and School of Dental Medicine (HSDM) review of Chester Douglass, DMD, PhD, professor of oral health policy and epidemiology at HSDM, has concluded that Douglass did not intentionally omit, misrepresent, or suppress research findings of a graduate student surrounding federal grant work looking at potential links between fluoride in drinking water and osteosarcoma, a form of bone cancer.

An Inquiry Panel and the Standing Committee on Faculty Conduct, both comprised of senior faculty from a range of fields, each conducted reviews and found that Douglass did not commit research misconduct. The committees did not examine and took no position on the question of whether or not there is a correlation between fluoride in drinking water and osteosarcoma.

The U.S. Department of Health and Human Service's Office for Research Integrity (ORI) has oversight authority for misconduct reviews and processes that govern the handling of inquiries. The ORI has reviewed the record from the Harvard inquiry and has determined that further investigation is not warranted.

The review also looked at whether or not Douglass violated school and federal conflict of interest guidelines by serving as editor of the quarterly newsletter The Colgate Oral Care Report. The two review groups found that Douglass's editorship of the newsletter did not constitute a conflict of interest under school and federal guidelines.

CONTACTS:

John Lacey, 617-432-0442, public_affairs@hms.harvard.edu

October 11, 2006

Derek Bok, J.D.
President
Harvard University
Massachusetts Hall
Cambridge, MA 02138 USA

Dear President Bok:

I am writing to inform you of an apparent violation of federal rules by Harvard University during its investigation into charges that Dr. Chester Douglass, of the Harvard Medical School faculty, misrepresented or suppressed the findings of federally funded research into whether fluoride in tap water is associated with bone cancer in adolescent boys. The review also addressed whether Dr. Douglass's employment as a paid consultant for the toothpaste giant, Colgate, which has a clear pro-fluoride stance, was a conflict of interest.....

On top of all of this, it has recently come to light that Douglass donated one million dollars to the University's Dental School in 2001. Although giving one's employer a million dollars is a perfectly noble gesture, it heightens concern about the integrity and propriety of this entire proceeding.

If you as President stand behind your ethics investigation or inquiry, there is no reason not to release it to the public and let it stand in the light of public scrutiny.

We call on you to immediately release:

- * the full text of the final report and the minutes of all the meetings of the ethics panel that produced it, and;
- * the identities of all the panel members along with all information that you have on their potential conflicts of interest including but not limited to disclosure documents required for participation on the ethics review panel.

We look forward to your prompt release of the information.

Sincerely,

Richard Wiles
Sr. Vice President

Cc:

Mr. Chris B. Pascal,
Director

Office of Research Integrity
Department of Health and Human Services

Mr. John E. Dahlberg,
Director
Division of Investigative Oversight
Office of Research Integrity
Department of Health and Human Services

Mr. Christian C. Mahler
Research Integrity Team Leader
Office of the General Counsel
Office of Research Integrity
Department of Health and Human Services