FLUORIDE EXPOSURE AND CHILDHOOD OSTEOSARCOMA
A CASE-CONTROL STUDY*
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Objectives: This study tests the hypothesis that fluoride exposure in a nonoccupa-
tional setting is a risk factor for childhood osteosarcoma. Methods: A population
based case-control study was conducted among residents of New York State
excluding New York City. case subjects (n = 130) were diagnosed with osteo-
sarcoma between 1978 and 1988 at age 24 years or younger. Control subjects were
matched to case subjects on year of birth and sex. Exposure information was ob-
tained by a telephone interview with the subject, parent, or both. Results: Based on
the parents responses, total lifetime fluoride exposure was not significantly associ-
ated with osteosarcoma among all subjects combined or among females. However,
a significant protective trend was observed among males. Protective trends were
observed for fluoridated toothpaste, fluoride tablets, and dental fluoride treat-
ments among all subjects and among males. Based on the subjects' responses no sig-
nificant associations between fluoride exposure and osteosarcoma were observed.
Conclusions: Fluoride exposure does not increase the risk of osteosarcoma and
may be protective in males. The protective effect may not be directly due to
fluoride exposure but to other factors associated with good dental hygiene. There is
also biologic plausibility for a protective effect.

Key words: Fluoride intake; Osteosarcoma.

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WATER FLUORIDATION, BONE DENSITY AND HIP FRACTURES:
A REVIEW OF RECENT LITERATURE [Review]
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Abstract from Community Dentistry and Oral Epidemiology 23 (5) 309-316 1995

A review of recent scientific reports that investigated an association between
exposure to fluoride in drinking water and the incidence of hip fractures in the
aged found inconsistent results. Although some studies suggest that exposure to
fluoridated water is associated with an increased risk of hip fracture, others found
no association or a decreased risk of hip fracture associated with exposure to
fluoridated water. The inconsistent findings could in part be attributed to the
limitations of the ecological study design used in many of the studies. This design is
useful for formulating hypotheses but, to test these hypotheses, analytical studies
conducted among individuals are required. Recent studies conducted on individuals
found that exposure to high fluoride levels (3.5-4.0 mg/L) in the drinking water
was associated with reduced radial bone mass. Few individuals studies included
communities with low fluoride levels in their drinking water, so the effects on

* Critique on pages 237-240
bone from exposure to optimum levels of fluoride (ca. 1.0 mg/L) could not be
determined. The number of reported hip fractures in several studies was too small
to enable conclusions to be drawn about hip fracture risk. Osteoporosis is a major
contributor to fractures in the aged, so it is important in hip fracture studies to
collect data about the known risk factors for osteoporosis as well as history of
exposure to fluoride. This enables control of the effects of confounding factors in
the statistical analyses. Further research to determine a cause and effect relation-
ship between fluoridation and hip fracture incidence is warranted.

Key words: Bone density; Fluoridation; Hip fractures.

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[The "ecological" studies which reported an association between fluoridated water and
hip fractures were mostly of much larger populations. The authors of the Utah study of
5000 persons residing in fluoridated and nonfluoridated communities answered the
argument that "ecological" studies did not record exposure of individuals to fluoridated
water by pointing out that their fluoridated population "had a net migration of 0.2%, the
lowest in Utah. For this reason, we doubt that migration confounded our data." (Journal
of the American Medical Association 268 6 747 August 12 1992).]

PATTERNS OF FRACTURE AMONG THE UNITED STATES
ELDERLY: GEOGRAPHIC AND FLUORIDE EFFECTS

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Abstract from Annals of Epidemiology 6 (3) 209-216 1996

The purpose of this study was to examine whether geographic area or water
fluoride were related to the occurrence of fractures among the elderly in the
United States. We used a 5% sample of the white U.S. Medicare population, aged
65 to 89 years during the period 1986-1990, to identify fractures of the hip,
proximal humerus, distal forearm, and ankle. The association of geographic region
and fluoridation status with fracture rates was assessed using Poisson regression.
We found that rates of hip fracture were generally lower in the northern regions of
the United States and higher in the southern regions. For fractures of the distal
forearm and proximal humerus, lower rates were found in the Western states, and
higher rates in the East. No discernible geographic pattern was found for ankle
fractures. Adjustment for water fluoridation did not influence these results.
Independent of geographic effects, men in fluoridated areas had modestly higher
rates of fractures of the distal forearm and proximal humerus than did men in
nonfluoridated areas; no such differences were observed among women, nor for
fractures of the hip or ankle among either men or women. In conclusion, our data
suggest that fractures of the distal forearm and proximal humerus have etiologic
determinants distinct from those of fractures of the hip or ankle.

Key words: Fluoridation; Fractures; Geography.

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CIRCULATING TESTOSTERONE LEVELS IN SKELETAL FLUOROSIS PATIENTS
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Abstract from Journal of Toxicology - Clinical Toxicology 34 (2) 183-189 1996

Objective: The present study focuses on serum testosterone concentrations in patients with skeletal fluorosis, in order to assess the hormonal status in fluoride toxicity. Methods: Serum testosterones were compared for patients afflicted with skeletal fluorosis (n = 30) and healthy males consuming water containing less than 1 ppm fluoride (Control 1, n = 26) and a second category of controls (Control 2, n = 16): individuals living in the same house as the patients and consuming same water as patients but not exhibiting clinical manifestations of skeletal fluorosis. Results: Circulating serum testosterones in skeletal fluorosis patients were significantly lower than those of Control at p < 0.02. Testosterone concentrations of Control 2 were also lower than those of Control 1 at p < 0.05 but were higher than those of the patient group. Conclusion: Decreased testosterone concentrations in skeletal fluorosis patients and in males drinking the same water as the patients but with no clinical manifestations of the disease compared with those of normal, healthy males living in areas nonendemic for fluorosis suggest that fluoride toxicity may cause adverse effects on the reproductive system of males living in fluorosis endemic areas.

Key words: Endemic fluorosis; Fertility; Reproduction; Skeletal fluorosis; Testosterone. Reprints: A K Susheela, All India Institute of Medical Sciences, Department of Anatomy, Fluoride and Fluorosis Research Laboratories, New Delhi 110029, India.

FLUORIDE ION TOXICITY IN HUMAN KIDNEY COLLECTING DUCT CELLS
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Abstract from Anesthesiology 84 (2) 428-435 1996

Background: Several halogenated anesthetics induce a urinary concentrating defect, partly related to fluoride ion toxicity in collecting duct cells. The aim of this study was to investigate the effects of fluoride ion in human kidney cells. Methods: Immortalized human collecting duct cells were used. In a first set of experiments, the toxicity threshold concentration was determined by exposing cell cultures for 24 h to increasing concentrations of fluoride ion in the medium: 0, 1, 5, and 10 mM. The second set of experiments was a time-effect study in which cells were exposed to 5 mM fluoride for 2, 6, and 24 h. Assessment of toxicity was based on several endpoints: cell number, protein content, 3H-leucine incorporation in newly synthesized proteins, extracellularly released lactate dehydrogenase, Na-K-ATPase pump activity, and electron microscope studies.

Results: After 24 h of exposure, fluoride ion decreased cell number (-23%, P < 0.05), total protein content (-30%, P < 0.05), and 3H-leucine incorporation (-43%, P < 0.05) and increased lactate dehydrogenase release (+236%, P < 0.05) at a threshold concentration of 5 mM. Fluoride ion also inhibited Na-K-ATPase
activity at 5 mM (-58%, P < 0.05). Major morphologic alterations of mitochondria, including crystal formation, were detected from 1 mM fluoride concentration. Time-effect studies showed that, after only 6 h of exposure at 5 mM, fluoride decreased cell number (-13%, P < 0.05), 3H-leucine incorporation (-48%, P < 0.05), and Na-K-ATPase activity (-20%, P < 0.05) and increased lactate dehydrogenase release (+145%, p < 0.05). Crystal deposits in mitochondria again were a more sensitive marker of cell injury, detectable after only 2 h of exposure.

Conclusions: These results suggest that the mitochondrion is a target of fluoride toxicity in human collecting duct cells, and its alteration is partly responsible for the sodium and water disturbances observed in patients.

Key words: Collecting duct; Fluoride ions; Kidney; Mitochondria.

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EXPOSURE TO PARTICULATES AND FLUORIDES AND RESPIRATORY HEALTH OF WORKERS IN AN ALUMINUM PRODUCTION POTROOM WITH LIMITED CONTROL MEASURES

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Abstract from American Industrial Hygiene Association Journal 56 (10) 1008-1015 1995

Occupational exposure to air pollutants and health status of potroom workers of an aluminum reduction plant in a developing country were studied and compared with those in developed countries. In this plant, the pots were constructed and installed without recommended gas collecting hoods or segmented side doors, and the workers did not use any respiratory protection. These conditions, combined with manual material handling and poor housekeeping, gave rise to fugitive air pollution generation. All 213 male potroom workers and 148 male control subjects were studied using air sampling, urinary fluoride measurement, ventilatory function testing, and a questionnaire on respiratory symptoms. On average, breathing zone respirable and total particulates in the potroom were 0.98 and 1.82 mg/m³, respectively. Stationary air sampling showed 0.93 mg/m³ of total fluoride, 2.09 mg/m³ of respirable particulates, and 7.59 mg/m³ of total particulates. During an 8-hr shift, the average increase of urinary fluoride in the potroom workers (2.73 mg/L) was significantly higher than that in the control group (0.39 mg/L). Workers in the potroom reported significantly higher frequency of respiratory symptoms than the control group. Potroom workers, especially nonsmokers, showed significantly greater decrease in their ventilatory function parameters during the shift than those of the control group; however, there was no difference between the basic ventilatory function of the two groups. The exposure to airborne particulates and the consequent respiratory symptoms as well as the daily increase of urinary fluoride values were generally higher in this plant than in similar operations in developed countries. This may be attributable to the fact that both process flow and machinery are often imported and assembled without the application of adequate engineering controls or complete understanding of proper safe work practices.

Key words: Aluminum; Developing countries; Industrial fluorosis.

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THE RISK OF FLUOROSIS IN STUDENTS EXPOSED TO A HIGHER THAN OPTIMAL CONCENTRATION OF FLUORIDE IN WELL WATER

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Abstract from Journal of Public Health Dentistry 56 (1) 22-27 1996

Objectives: In December 1991 the residents of the community of Rigolet, Labrador, Canada, discovered that they were exposed to higher than 2.0 ppm fluoride in the drinking water from the new town well, which became operational in December 1983. In 1993 an investigation of the occurrence of fluorosis in children exposed to the high-fluoride water during different ages of life was carried out. Methods: A dental examination for fluorosis was conducted using Pendrys' Fluorosis Risk Index. Out of 84 students in Rigolet, 74 were examined and the parents of 60 students agreed to be interviewed. Out of the 60 students, 48 lived all of their first six years of life in Rigolet. Results: Of the 48 children with life-long residence, the odds ratio of fluorosis on enamel zones that began forming during the first year of life was 8.31 (95% CI=1.84, 38.59) for children exposed since birth or during the first year of life relative to those exposed after 1 year of age. The odds that a child had a maxillary central incisor with fluorosis were 5.69 (95% CI=1.34, 24.15) times higher if exposure occurred during the first year of life compared with exposure after 1 year of age. Only those exposed to the high-fluoride water during the first year of life developed fluorosis on the mandibular central incisors. Conclusions: Within the limitations of this small population study, age relative to the date when the new water well became operational was a significant risk factor in development of fluorosis. The first year of life was a significant period for developing fluorosis on the mandibular and maxillary central incisors.

Key words: Dental fluorosis; Fluoridation; Preventive dentistry.

CALL FOR PAPERS

Scientists and practitioners working in the field of endemic fluorosis and defluoridation of water are invited to present papers and to participate in the

2ND INTERNATIONAL WORKSHOP ON FLUOROSIS AND DEFLUORIDATION OF WATER
Addis Ababa, Ethiopia, November 19-22, 1997

arranged by the Technical University of Denmark and University of Addis Ababa in collaboration with the International Society for Fluoride Research, UNICEF and UNDP.

Provisional titles and 100-word abstracts for scientific and discussion papers should be submitted before March 31, 1997. A Selection Committee will review submissions and send guidelines for paper preparation to those accepted. Typed papers, preferably with disks, must be received before August 15, 1997. Send offers of papers, and requests for further information, to the International Organizing Committee. Registration fee US$200 (US$150 for authors). Authors of acceptable papers may apply for financial support to cover direct costs in connection with the workshop.

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