

HEALTH/BIOLOGICAL EFFECTS

Fluoride in drinking water and risk of hip fracture in the UK: a case-control study

Background: Although the benefits of water fluoridation for dental health are widely accepted, concerns remain about possible adverse effects, particularly effects on bone. Several investigators have suggested increased rates of hip fracture in places with high concentrations of fluoride in drinking water, but this finding has not been consistent, possibly because of unrecognised confounding effects.

Methods: We did a case-control study of men and women aged 50 years and older from the English county of Cleveland, and compared patients with hip fracture with community controls. Current addresses were ascertained for all participants; for those who agreed to an interview and who passed a mental test, more detailed information was obtained about lifetime residential history and exposure to other known and suspected risk factors for hip fracture. Exposures to fluoride in water were estimated from the residential histories and from information provided by water suppliers. Analysis was by logistic regression.

Findings: 914 cases and 1196 controls were identified, of whom 514 and 527, respectively, were interviewed. Among those interviewed, hip fracture was strongly associated with low body-mass index (p for trend <0.001) and physical inactivity (p for trend <0.001). Estimated average lifetime exposure to fluoride in drinking water ranged from 0.15 to 1.79 ppm. Current residence in Hartlepool was a good indicator for high lifetime exposure to fluoride. After adjustment for potential confounders, the odds ratio associated with an average lifetime exposure to fluoride \geq or \leq 0.9 ppm was 1.0 [95% CI 0.7-1.5].

Interpretation: There is a low risk of hip fracture for people ingesting fluoride in drinking water at concentrations of about 1 ppm. This low risk should not be a reason for withholding fluoridation of water supplies.

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Keywords: Bone fractures, Calcium, Epidemiology, Fluoride in water.

Source: Lancet 2000 Jan 22;355(9200):265-9 (Comment page 247-8).

Bone-fracture incidence rate in two Italian regions with different fluoride concentration levels in drinking water

The effect of the fluoride concentration in drinking water on the prevention of fractures related to osteoporosis has been questioned or contradicted in several recent studies. These studies have been mostly performed using water with artificially added fluoride, at the optimum level of about 1 mg/L.

In the present study authors have investigated the effect of equal or greater fluoride concentrations (mean 1.45 mg/L) naturally present in waters supplied

for human consumption to a population of 72.756 (Bracciano county), in comparison with a population of 126.189 (Avezzano county), supplied with low fluoride concentration water (mean 0.05 mg/L).

The incidence of fractures in the years 1990 and 1991 was evaluated in the two areas (Bracciano and Avezzano), which are located in central Italy and where population have a similar life style, economic and social level and employment structure. The incidence data were obtained from the registers of the public hospital taken as a reference in each district. The authors noticed a significantly greater rate of fracture incidence at several parts of the body, in particular femur fractures (relative risks for males 4.28 and for females 2.64), in the population of the district of Avezzano than in the population of Bracciano. The greater concentration of fluoride in waters distributed for human consumption in Bracciano district seems to have the effect of protecting its inhabitants against fractures.

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Keywords: Bone fractures, Fluoride in water, Italy.

Source: J Trace Elem Med Biol 1999 Dec;13(4):232-7.

Caries prevalence after cessation of water fluoridation in La Salud, Cuba

In the past, caries has usually increased after cessation of water fluoridation. More recently an opposite trend could be observed: DMFT remaining stable or even decreasing further. The aim of the present study, conducted in La Salud (Province of Habana) in March 1997, was to analyse the current caries trend under the special climatic and nutritional conditions of the subtropical sugar island Cuba, following the cessation, in 1990, of water fluoridation (0.8 ppm F).

Diagnostic evaluations were carried out using the same methods as in 1973 and 1982. Boys and girls aged 6-13 years (N = 414), lifelong residents in La Salud, were examined. Between 1973 and 1982 the mean DMFT had decreased by 71.4%, the mean DMFS by 73.3% and the percentage of caries-free children had increased from 26.3 to 61.6%. In 1997, following the cessation of drinking water fluoridation, in contrast to an expected rise in caries prevalence, DMFT and DMFS values remained at a low level for the 6- to 9-year-olds and appeared to decrease for the 10/11-year-olds (from 1.1 to 0.8) and DMFS (from 1.5 to 1.2). In the 12/13-year-olds, there was a significant decrease (DMFT from 2.1 to 1.1; DMFS from 3.1 to 1.5), while the percentage of caries-free children of this age group had increased from 4.8 (1973) and 33.3 (1982) up to 55.2%.

A possible explanation for this unexpected finding and for the good oral health status of the children in La Salud is the effect of the school mouthrinsing program, which has involved fortnightly mouthrinses with 0.2% NaF solutions (i.e. 15 times/year) since 1990.

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Keywords: Caries prevalence, Cuba, Water fluoridation, Cessation.

Source: *Caries Res* 2000;34:20-5.

The effects of a break in water fluoridation on the development of dental caries and fluorosis

Durham, NC, fluoridated since 1962, had an 11-month cessation of fluoridation between September, 1990, and August, 1991. The purpose of this study was to assess the effects of this break on the development of caries and fluorosis in children. Study participants were continuously-resident children in Kindergarten through Grade 5 in Durham's elementary schools. There were 1696 children, 81.4% of those eligible, for whom a questionnaire was completed and clinical data recorded. Age cohorts were defined by a child's age at the time that fluoridation ceased. Caries was recorded in children in the Birth Cohort through Cohort 3, and fluorosis for children in Cohorts 1 through 5. Caries was assessed in the primary first and second molars according to the decayed-filled index; fluorosis on the labial surfaces of the upper permanent central and lateral incisors was assessed by the Thylstrup-Fejerskov (TF) index. Mother's education was associated with caries; higher education of the mother had an odds ratio of 0.53 (95% CI 0.40, 0.76) for caries in the child. No cohort effects could be discerned for caries. Overall prevalence of fluorosis was 44%. Prevalence in Cohorts 1, 2, 3, 4, and 5 was 39.8%, 32.3%, 33.0%, 62.3%, and 57.1%, respectively. These cohort differences remained statistically significant in regression analysis. It was concluded that while the break had little effect on caries, dental fluorosis is sensitive to even small changes in fluoride exposure from drinking water, and this sensitivity is greater at 1 to 3 years of age than at 4 or 5 years.

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Keywords: Dental caries, Fluoridation, Dental fluorosis.

Source: *J Dent Res* 2000 Feb;79(2):761-9.

The prevalence and severity of enamel fluorosis in North American children

The question considered in this review is the extent to which changes in the prevalence or severity of enamel fluorosis have occurred over the last half-century. Emphasis is given to a review of those studies in which subjects are drinking water that is fluoride deficient and those in which subjects are drinking optimally fluoridated water, either adjusted or natural. Trends in fluorosis were examined using two definitions of fluorosis (definite and any signs) and three types of comparisons – comparisons of pooled estimates from all avail-

able studies that include data from different communities and time periods, comparisons of estimates from the same communities at different times, and comparisons of estimates from selected studies in the early years of fluorosis research with results of the US National Fluorosis Survey done by the National Institute of Dental Research.

A clear increase in fluorosis among populations drinking community water that contains less than 0.3 ppm fluoride was found. Results of the comparisons using studies with Dean's Index pooled at different time points, comparisons in the same communities over time, and comparisons of prevalence found in selected communities before fluoride was widely available with the National Fluorosis Survey all support this conclusion. An increase in the prevalence of fluorosis in those drinking optimally fluoridated water likely has occurred as well; however, evidence for such a trend is not as clear as for fluoride deficient communities because of mixed results depending on the type of comparison.

The majority of fluorosis cases continue to be mild and seem of little esthetic consequence for most of the public or dental profession. But a few cases of more severe fluorosis can be found now in some communities. Because the prevalence of fluorosis is now higher than 50 years ago, we can conclude that fluoride availability to the developing enamel during critical periods when enamel is at risk of fluorosis has increased in North American children.

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Keywords: Dental fluorosis, Epidemiology.

Source: J Public Health Dent 1999 Fall;59(4):239-46.

Paleopathology of skeletal fluorosis

Skeletal fluorosis is one of a range of conditions causing excessive ossification and joint ankylosis in skeletons. It is rarely considered, however, in differential diagnoses of palaeopathological lesions. This paper considers the identification of skeletal fluorosis in a skeletal sample from the island of Bahrain, Arabian Gulf, dating to ca. 250 BC-AD 250. Approximately 4% of 255 adult skeletons in the sample have hyperostotic lesions resulting in joint ankylosis primarily of the lumbar vertebrae, as well as the major joints. These lesions most frequently occur among males in the 50+ age group. Chemical analysis on a small series of bone and dental samples confirmed the presence of high levels of fluoride, while staining of the teeth is evidence of dental fluorosis. The level of dental fluorosis is comparable with a naturally occurring fluoride level in water of between 1-2 ppm. The prevalence of hyperostotic lesions, however, appears higher than expected, and two possible reasons are suggested: confusion between a diagnosis of diffuse idiopathic skeletal hyperostosis and skeletal fluorosis on partial or less severely affected skeletons; and the presence of predisposing factors for skeletal fluorosis on the island in the past.

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 Keywords: Fluoride, Prehistoric Arabia, Bahrain, Endemic fluorosis.
 Source: Am J Phys Anthropol 109(4):465-483, 1999.

DIETARY FLUORIDE

Total fluoride intake and implications for dietary fluoride supplementation

This paper reviews the history and validity of recommended "optimal" levels of systemic fluoride intake and the available information on levels of fluoride intake in young children from foods and beverages (including water), dentifrices, dietary fluoride supplements, mouthrinses, and gels.

Most of the studies emphasize the substantial variation in ingestion among individuals. Often, a substantial proportion of individuals received fluoride well beyond the mean exposure reported in the study. Limitations in the existing data make it difficult to determine the total distribution of fluoride intake from all sources. Therefore, hypothetical combinations of possible daily fluoride intake from the three main sources (diet, dentifrices, and supplements) are presented for those aged 6, 12, 24, and 36 months, with associated mean intake per kg body weight. Findings suggest that some children exceed the "optimal" level of fluoride intake from single sources alone, while others can from a combination of sources. Moreover, if current recommended "optimal" levels, which have been derived on an empirical basis, are actually lower than what has been quoted in the literature, then more children could be ingesting excessive amounts of fluoride, which could increase their risk of developing objectionable dental fluorosis. The variation and complexity of fluoride ingestion from all sources should be considered in the evaluation of recommendations for use of dietary fluoride supplements.

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 Keywords: Fluoride in food & dental, Fluoride supplements.
 Source: J Public Health Dent 1999 Fall;59(4):211-23.

Assessing fluoride levels of carbonated soft drinks

Background: Dental fluorosis occurs as a result of excessive total fluoride intake during tooth development. Some children may receive substantial intake from soft drinks, but few studies have reported fluoride levels in soft drinks. The authors examined the fluoride concentrations of 332 soft drinks.

Methods: Soft drinks were purchased from Iowa grocery stores. To identify production sites, the authors recorded product details and batch numbers. After

decarbonating the drinks, the authors assayed samples for fluoride content using a fluoride ion-specific electrode, and reported the results in parts per million, or ppm, using appropriate standards and duplicate assessments. Descriptive statistics were used to summarize the findings.

Results: The fluoride levels of the products ranged from 0.02 to 1.28 ppm, with a mean level of 0.72 ppm. Fluoride levels exceeded 0.60 ppm for 71 percent of the products. Results varied substantially by production site, even within the same company and for the same product. There were no substantial differences between flavors or between diet and regular soft drinks.

Conclusions: The majority of soft drinks had fluoride levels exceeding 0.60 ppm. Variation in fluoride levels probably is due largely to the different water sources used in production.

Clinical Implications: With no fluoride levels marked on the soft drink products or easily available from the manufacturers, it is not possible for clinicians or consumers to directly estimate fluoride ingestion from carbonated beverages. Therefore, to reduce the risk of dental fluorosis, dental and medical practitioners should be cautious about prescribing dietary fluoride supplements to preschool-aged children in nonfluoridated areas who consume large quantities of carbonated soft drinks.

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Keywords: Bottled drinks, Fluoride in water, food & dental.

Source: JADA 1999;130(11):1593-9.

The case for reducing the current Council on Dental Therapeutics fluoride supplementation schedule

The milder forms of dental fluorosis have increased in prevalence since the original epidemiologic surveys of the 1930s. Most studies of fluorosis have identified the use of supplements as a major risk factor. Fluorosis could be prevented, in part, by stopping the improper prescription of fluoride supplements in optimally fluoridated areas and by lowering the dosage currently recommended by the Council on Dental Therapeutics supplemental fluoride schedule.

At a 1991 workshop at the University of North Carolina, five alternatives to the present ADA Council on Dental Therapeutics schedule were suggested; however, no consensus on dosage was reached. Recently, the Federation Dentaire International adopted a dosage schedule of 0.25 mg F from birth to 3 years of age, 0.5 mg F from 3 to 5 years, and 1 mg F thereafter.

At a 1992 Canadian workshop it was proposed that supplements should not be started until age 3, should be given only to those "at high risk" of caries, and only 0.25 mg F should be prescribed from 3 to 5 years of age. Similarly, in some European countries supplements are not recommended until 3 years, at which time 0.5 mg F is prescribed, but only "for children at risk." Australia is

considering a dosage schedule starting with 0.25 mg F at 6 months, again only for those "particularly at risk of caries." Serious problems exist in limiting fluoride supplementation only to high-caries-risk children because they are not easily identifiable at a young age. Ideally, a dosage schedule should be based on body surface area or weight rather than simply age, and supplements should be in the form of lozenges for children over 2 years of age. A reduced fluoride supplement dosage schedule is proposed.

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Keywords: Dental fluorosis, Fluoride supplements.

Source: J Public Health Dent 1999 Fall;59(4):263-8.

The case for eliminating the use of dietary fluoride supplements for young children

Fluoride supplements have been used for years to prevent dental caries; nevertheless, there are three reasons why their use is inappropriate today among infants and young children in the United States. Evidence for the efficacy of fluoride supplements when used from birth or soon after is weak, supplements are a risk factor for dental fluorosis, and fluoride has little preeruptive effect in caries prevention. While there are many reports on the caries-preventive efficacy of supplements, few meet standards for acceptability as clinical trials, and those that do have tested chewable tablets or lozenges under supervision in school-aged children. North American children today are exposed to fluoride from many sources – drinking water, toothpaste, gels, rinses, and in processed foods and beverages. The additional cariostatic benefits that accrue from using supplements are marginal at best, while there is strong risk of fluorosis when young children use supplements.

Available evidence suggests that the public is more aware of the milder forms of fluorosis than was previously thought; thus, it is prudent for caries-preventive policies to aim to maximizing caries reductions while minimizing the risk of fluorosis. It is therefore concluded that the risks of using supplements in infants and young children outweigh the benefits. Because alternative forms of fluoride for high-risk individuals exist, fluoride supplements should no longer be used for young children in North America.

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Keywords: Dental fluorosis, Fluoride supplements.

Source: J Public Health Dent 1999 Fall;59(4):269-74.

BIOCHEMICAL EFFECTS**Competition between internal AlF_4^- and receptor-mediated stimulation of dorsal raphe neuron G-proteins coupled to calcium current inhibition**

Intracellular aluminum fluoride (AlF_4^-), placed in a patch pipette, activated a G-protein, resulting in a "tonic" inhibition of the Ca^{2+} current of isolated serotonergic neurons of the rat dorsal raphe nucleus. Serotonin (5-HT) also inhibits the Ca^{2+} current of these cells. After external bath application and quick removal of 5-HT to an AlF_4^- containing cell, there was a reversal or transient disinhibition (TD) of the inhibitory effect of AlF_4^- on Ca^{2+} current. A short prepolarization of the membrane potential to +70 mV, a condition that is known to reverse G-protein-mediated inhibition, reversed the inhibitory effect of AlF_4^- on Ca^{2+} current and brought the Ca^{2+} current to the same level as that seen at the peak of the TD current. With AlF_4^- in the pipette, the TD phenomenon could be eliminated by lowering pipette MgATP, or by totally chelating pipette Al^{3+} . In the presence of AlF_4^- , but with either lowered MgATP or extreme efforts to eliminate pipette Al^{3+} , the rate of recovery from 5-HT on wash was slowed, a condition opposite to that where a TD occurred. The putative complex of AlF_4^- -bound G-protein ($\text{G}\alpha\text{.GDP}\cdot\text{AlF}_4^-$) appeared to free G-beta-gamma-subunits, mimicking the effect on Ca^{2+} channels of the G.GTP complex. The ON-rate of the inhibition of Ca^{2+} current, after a depolarizing pulse, by beta-gamma-subunits released by AlF_4^- in the pipette was significantly slower than that of the agonist-activated G-protein. The OFF-rate of the AlF_4^- -mediated inhibition in response to a depolarizing pulse, a measure of the affinity of the free G-beta-gamma-subunit for the Ca^{2+} channel, was slightly slower than that of the agonist stimulated G-protein. In summary, AlF_4^- modified the OFF-rate kinetics of G-protein activation by agonists, but had little effect on the kinetics of the interaction of the beta-gamma-subunit with Ca^{2+} channels. Agonist application temporarily reversed the effects of AlF_4^- , making it a complementary tool to GTP-gamma-S for the study of G-protein interactions.

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Keywords: Aluminofluoride complexes, Brain, G protein.

Source: J Neurophysiol 2000 Mar;83(3):1273-1282.

ENVIRONMENTAL EFFECTS**Cancer incidence and cause-specific mortality among workers in two Norwegian aluminum reduction plants**

Background: Concern about the health hazards in the aluminum industry has initiated this study where we have investigated associations between exposure

to polycyclic aromatic hydrocarbons (PAH) and fluorides, and cancer incidence and cause-specific mortality among workers in two Norwegian aluminum plants in operation since 1954 and 1957, respectively.

Methods: The study was designed as a historical cohort study and comprised 5627 identified men employed for more than six months. Cancer incidence was investigated from start of employment to 1995, and cause-specific mortality was investigated from 1962 to 1995. The observed cases of cancers and observed deaths were compared with expected numbers calculated from national rates. Internal comparisons were made using Poisson regression with age and smoking included in the models. Historical exposure to PAH and fluoride had been estimated previously by use of statistical modeling on industrial hygiene measurements and process parameters. A job exposure matrix was used to investigate possible associations between cumulative exposures, and cancer incidence and cause-specific mortality. Smoking habits were identified for 92% of the cohort members.

Results: The study showed a significant excess risk for urinary bladder cancer among workers exposed to PAH, but no clear dose-response relationship. When using a 30-year lag period, a significant excess of bladder cancer in the highest exposure category ($> 2000 \text{ mug/m}^3\text{;year PAH}$) was shown (SIR 4.08). The data also suggested an association between exposure to PAH and pancreatic cancer, but no association with lung cancer was seen. The mortality analysis indicated an association between exposure to potroom emissions (fluorides) and mortality from chronic bronchitis, emphysema and asthma, but no associations with cardiovascular diseases.

Conclusions: The study findings are compatible with an excess risk for bladder cancer for aluminum plant workers exposed to PAH. The increased risk for cancer of the pancreas indicated, should be further evaluated in larger exposed populations.

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Keywords: Aluminum, Fluoride inhalation, Fluoride toxicity.

Source: Am J Ind Med 2000 Feb;37(2):175-183.

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