

## HEALTH/BIOLOGICAL EFFECTS

### Systematic review of water fluoridation

*Objective:* To review the safety and efficacy of fluoridation of drinking water.

*Design:* Search of 25 electronic databases and world wide web. Relevant journals hand searched; further information requested from authors. Inclusion criteria were a predefined hierarchy of evidence and objectives. Study validity was assessed with checklists. Two reviewers independently screened sources, extracted data, and assessed validity.

*Main outcome measures:* Decayed, missing, and filled primary/permanent teeth. Proportion of children without caries. Measure of effect was the difference in change in prevalence of caries from baseline to final examination in fluoridated compared with control areas. For potential adverse effects, all outcomes reported were used.

*Results:* 214 studies were included. The quality of studies was low to moderate. Water fluoridation was associated with an increased proportion of children without caries and a reduction in the number of teeth affected by caries. The range (median) of mean differences in the proportion of children without caries was -5.0% to 64% (14.6%). The range (median) of mean change in decayed, missing, and filled primary/permanent teeth was 0.5 to 4.4 (2.25) teeth. A dose-dependent increase in dental fluorosis was found. At a fluoride level of 1 ppm an estimated 12.5% (95% confidence interval 7.0% to 21.5%) of exposed people would have fluorosis that they would find aesthetically concerning.

*Conclusions:* The evidence of a beneficial reduction in caries should be considered together with the increased prevalence of dental fluorosis. There was no clear evidence of other potential adverse effects.

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Keywords: Dental fluorosis, Epidemiology, Fluoridation, Fluoride toxicity.

Source: BMJ 2000 Oct 7;321(7265):855-9.

### Association of silicofluoride treated water with elevated blood lead

Previous epidemiological studies have associated silicofluoride-treated community water with enhanced child blood lead parameters. Chronic, low-level dosage of silicofluoride (SiF) has never been adequately tested for health effects in humans. We report here on a statistical study of 151,225 venous blood lead (VBL) tests taken from children ages 0-6 inclusive, living in 105 communities of populations from 15,000 to 75,000. The tests are part of a sample collected by the New York State Department of Children's Health,

mostly from 1994-1998. Community fluoridation status was determined from the CDC 1992 Fluoridation Census. Covariates were assigned to each community using the 1990 U.S. Census. Blood lead measures were divided into groups based on race and age. Logistic regressions were carried out for each race/age group, as well as above and below the median of 7 covariates to test the relationship between known risk factors for lead uptake, exposure to SiF-treated water, and VBL >10  $\mu$ /dL.

*Results:* For every age/race group, there was a consistently significant association of SiF treated community water and elevated blood lead. Logistic regressions above and below the median value of seven covariates show an effect of silicofluoride on blood lead independent of those covariates. The highest likelihood of children having VBL > 10  $\mu$ /dL occurs when they are both exposed to SiF treated water and likely to be subject to another risk factor known to be associated with high blood lead (e.g., old housing). Results are consistent with prior analyses of surveys of children's blood lead in Massachusetts and NHANES III. These data contradict the null hypothesis that there is no difference between the toxic effects of SiF and sodium fluoride, pointing to the need for chemical studies and comprehensive animal testing of water treated with commercial grade silicofluorides.

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Keywords: Children, Fluoridation and blood-lead levels, Silicofluoride, Sodium silicofluoride.

Source: Neurotoxicology 2000 Dec;21(6):1091-100.

### **Community water fluoridation, bone mineral density, and fractures: prospective study of effects in older women**

*Objective:* To determine whether fluoridation influences bone mineral density and fractures in older women.

*Design:* Multicentre prospective study on risk factors for osteoporosis and fractures.

*Setting:* Four community based centres in the United States.

*Participants:* 9704 ambulatory women without bilateral hip replacements enrolled during 1986-8; 7129 provided information on exposure to fluoride. Main outcome measures: Bone mineral density of the lumbar spine, proximal femur, radius, and calcaneus plus incident fractures (fractures that occurred during the study) of vertebrae, hip, wrist, and humerus.

*Results:* Women were classified as exposed or not exposed or having unknown exposure to fluoride for each year from 1950 to 1994. Outcomes were compared in women with continuous exposure to fluoridated water for the past 20 years (n=3218) and women with no exposure during the past 20 years

(n=2563). In women with continuous exposure mean bone mineral density was 2.6% higher at the femoral neck (0.017 g/cm<sup>2</sup>, P<0.001), 2.5% higher at the lumbar spine (0.022 g/cm<sup>2</sup>, P<0.001), and 1.9% lower at the distal radius (0.007 g/cm<sup>2</sup>, P=0.002). In women with continuous exposure the multivariable adjusted risk of hip fracture was slightly reduced (risk ratio 0.69, 95% confidence interval 0.50 to 0.96, P=0.028) as was the risk of vertebral fracture (0.73, 0.55 to 0.97, P=0.033). There was a non-significant trend toward an increased risk of wrist fracture (1.32, 1.00 to 1.71, P=0.051) and no difference in risk of humerus fracture (0.85, 0.58 to 1.23, P=0.378).

*Conclusions:* Long term exposure to fluoridated drinking water does not increase the risk of fracture.

Authors: Phipps KR; Orwoll ES; Mason JD; Cauley JA.

For correspondence: School of Dentistry, Oregon Health Sciences University, 611 SW Campus Drive, Portland, OR 97201, USA.

Keywords: Bone fractures, Epidemiology, Fluoridation.

Source: BMJ 2000 Oct 7;321(7265):860-4.

### **Fluoride deposition in the aged human pineal gland**

The purpose was to discover whether fluoride (F) accumulates in the aged human pineal gland. The aims were to determine (a) F-concentrations of the pineal gland (wet), corresponding muscle (wet) and bone (ash); (b) calcium-concentration of the pineal. Pineal, muscle and bone were dissected from 11 aged cadavers and assayed for F using the HMDS-facilitated diffusion, F-ion-specific electrode method. Pineal calcium was determined using atomic absorption spectroscopy. Pineal and muscle contained 297±257 and 0.5±0.4 mg F/kg wet weight, respectively; bone contained 2,037±1,095 mg F/kg ash weight. The pineal contained 16,000±11,070 mg Ca/kg wet weight. There was a positive correlation between pineal F and pineal Ca ( $r = 0.73$ ,  $p < 0.02$ ) but no correlation between pineal F and bone F. By old age, the pineal gland has readily accumulated F and its F/Ca ratio is higher than bone.

Author: Luke J.

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Keywords: Fluoride in bone, Fluoride in pineal.

Source: Caries Res 2001 Mar-Apr;35(2):125-8.

### **Tooth-surface progression and reversal changes in fluoridated and no-longer-fluoridated communities over a 3-year period.**

*Objective:* To compare permanent tooth surface-specific progression/reversal changes between fluoridation-ended (F-E) and still-fluoridated (S-F) communities in British Columbia, Canada, over a 3-year period.

*Methods:* D1D2MFS examinations were contrasted for 2,964 schoolchildren in 1993/94 (grades 2, 3, 8 and 9) and 1996/97 (grades 5, 6, 11 and 12). Generalized Estimating Equation (GEE) models explored the relation between progression/reversal changes and fluoridation status, age, gender, socioeconomic status, and dietary/fluoride histories.

*Results:* Within a scenario of low levels of caries overall, few children had multiple surfaces progressing. At least one smooth surface progressed in 31.4% of subjects; at least one pit-and-fissure (PF) surface progressed in 43.1% of subjects. At least one smooth surface reverted in 89% of subjects who had reversible stages; at least one PF surface reverted in 23.8% of subjects who had reversible stages. GEE (smooth) indicated that odds ratios of progression were twice as large in the F-E site compared to the S-F site, and slightly increased in older participants and in participants exposed to more fluoride technologies. GEE (PF) also indicated that progression was slightly more common in the F-E site; more frequent snacking and lower parental educational attainment had modest associations with increased progression in PF surfaces. For the two types of surfaces, GEE models demonstrated that unerupted surfaces were less likely to progress than sound surfaces. No associations were found between reversals and independent variables.

*Conclusion:* Progressions were found to be weakly linked to socio-demographic factors; baseline surface statuses were better predictors of progression. Using the current definitions for disease transitions, F-E communities had more frequent progressions than a S-F community.

Authors: Maupog G, Shulman JD, Clark DC, Levy SM, Berkowitz J.

For correspondence: Center For Health Research, Portland, Oreg., USA.

Keywords: Dental caries, Fluoridation cessation.

Source: Caries Res 2001 Mar-Apr;35(2):95-105.

### **An attempt to explain why Tanzanian children drinking water containing 0.2 or 3.6 mg fluoride per liter exhibit a similar level of dental fluorosis**

The aim of this study was to identify factors that might explain the similar level of prevalence and severity of dental fluorosis in two neighboring areas in Tanzania: Kibosho; 0.2 mg fluoride/L, n = 96 and Arusha; 3.6 mg fluoride/L in drinking water, n = 80. Subjects aged 8-16 years were examined for dental fluorosis using the Thylstrup and Fejerskov Index (TFI). Based on the score on the upper left central incisor, the prevalence was not significantly different between the communities (TFI  $\geq$  1). The severity, however, was significantly higher in Arusha. The areas had different food habits, e.g., type of weaning food used, and the use of magadi, a fluoride containing salt. In Arusha, 99% of the children had been given lishe, which is a magadi-free weaning food. Conversely in Kibosho, 61% used lishe while 39% used the magadi-containing

weaning food kiborou. Magadi was used as food tenderizer in 'adult food' by 98% in Kibosho and 45% in Arusha. Residential area and use of magadi explained 5% of the variance in TFI scores in inter-area analyses. In intra-area analyses, weaning food in Kibosho and use of magadi in Arusha had a significant effect, but the total explained variance was only 5 and 4%, respectively. Apart from fluoride in the drinking water, other sources of fluoride such as use of magadi in weaning food (kiborou) and in the adult food may partly explain the high prevalence and severity of dental fluorosis in the community with 0.2 mg fluoride per liter in the drinking water.

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Keywords: Dental fluorosis, Fluoride in food, Fluoride in water.

Source: Clin Oral Investig 2000 Dec;4(4):238-44.

### **Calcium preventing locomotor behavioral and dental toxicities of fluoride by decreasing serum fluoride level in rats**

Spontaneous motor activity, rota-rod performance (motor co-ordination), body weight gain, food intake, activities of total cholinesterase (blood) and acetylcholinesterase (brain), and dental structure were determined in adult female rats treated with a very high dose of sodium fluoride (500 ppm in drinking water) alone and in combination with calcium carbonate (50 mg/kg body weight by oral intubation) for 60 days. The concentration of fluoride and calcium were measured in the serum of these animals. Administration of sodium fluoride with drinking water produced both behavioral and dental toxicities and not lethality in the present study. A suppression of spontaneous motor activity, a shortening of rota-rod endurance time, a decreased body weight gain and food intake, a suppression of total cholinesterase and acetylcholinesterase activities and dental lesion were observed in test animals. Serum fluoride concentration was raised markedly and that of calcium was decreased in these animals. The effects of sodium fluoride were prevented significantly when animals received calcium carbonate along with sodium fluoride. Serum fluoride content was decreased and that of calcium was restored to control level in these animals. These results indicate that calcium prevents not only fluoride-induced hypocalcemia but also the locomotor behavioral and dental toxicities of fluoride by decreasing bioavailability of fluoride.

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Keywords: Calcium, Fluoride toxicity, Rat study.

Source: Environ. Toxicol. Pharmacol. 2001 Mar;9(4):141-146.

### **Effect of long-term exposure to fluoride in drinking water on risks of bone fractures**

Findings on the risk of bone fractures associated with long-term fluoride exposure from drinking water have been contradictory. The purpose of this study was to determine the prevalence of bone fracture, including hip fracture, in six Chinese populations with water fluoride concentrations ranging from 0.25 to 7.97 parts per million (ppm). A total of 8266 male and female subjects  $\geq 50$  years of age were enrolled. Parameters evaluated included fluoride exposure, prevalence of bone fractures, demographics, medical history, physical activity, cigarette smoking, and alcohol consumption. The results confirmed that drinking water was the only major source of fluoride exposure in the study populations. A U-shaped pattern was detected for the relationship between the prevalence of bone fracture and water fluoride level. The prevalence of overall bone fracture was lowest in the population of 1.00-1.06 ppm fluoride in drinking water, which was significantly lower ( $p < 0.05$ ) than that of the groups exposed to water fluoride levels  $\geq 4.32$  and  $\leq 0.34$  ppm. The prevalence of hip fractures was highest in the group with the highest water fluoride (4.32-7.97 ppm). The value is significantly higher than the population with 1.00-1.06 ppm water fluoride, which had the lowest prevalence rate. It is concluded that long-term fluoride exposure from drinking water containing  $\geq 4.32$  ppm increases the risk of overall fractures as well as hip fractures. Water fluoride levels at 1.00-1.06 ppm decrease the risk of overall fractures relative to negligible fluoride in water; however, there does not appear to be similar protective benefits for the risk of hip fractures.

Authors: Li Y, Liang C, Slemenda CW, Ji R, Sun S, Cao J, Emsley CL, Ma F, Wu Y, Ying P, Zhang Y, Gao S, Zhang W, Katz BP, Niu S, Cao S, Johnston CC Jr.

For Correspondence: Center for Dental Research, Loma Linda University School of Dentistry, California 92350, USA.

Keywords: Bone fractures, Epidemiology, Fluoride in water.

Source: J Bone Miner Res 2001 May;16(5):932-9.

### **DIETARY FLUORIDE**

#### **Fluoride levels in breast milk and infant foods**

The aim of the present study is to determine the fluoride concentrations of breast milk, several milk formulations, cow's milk and yogurt shake in a nonfluoridated area, in order to estimate the fluoride intake of infants and evaluate fluoride supplementation suggestions. Breast milk samples were collected from 57 lactating mothers. Ten brands of milk formulations, 9 different brands of cow's milk and 3 brands of yogurt shake were purchased from the market. Fluoride concentrations of the samples were analyzed us-

ing a specific fluoride electrode. The average fluoride level was  $0.019 \pm 0.004$  ppm in breast milk,  $0.022 \pm 0.007$  ppm in cow's milk and  $0.022 \pm 0.003$  ppm in yogurt shake. Fluoride levels of milk formulations prepared by distilled water were ranging between 0.118 to 0.021 ppm. It is concluded that in non-fluoridated areas, fluoride intake of infants from the above sources is not very high and fluoride supplements may be prescribed.

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Keywords: Fluoride in breast milk, Fluoride in food.

Source: J Clin Pediatr Dent 2000 Summer;24(4):299-302.

## BIOCHEMICAL EFFECTS

### Compensatory hyperparathyroidism following high fluoride ingestion – A clinico - biochemical correlation

*Objective:* To evaluate the effect of varying ingestion of drinking water containing high fluorides and its effect on serum parathyroid hormone.

*Design:* Cross sectional clinical study.

*Setting:* S.M.S. Medical College, Jaipur.

*Subject:* 200 children were selected from four areas (50 from each area) consuming water containing 2.4, 4.6, 5.6 and 13.5 mg/l of fluoride. All children were in an age group of 6 to 12 years.

*Methods:* All children were graded for clinical, radiological and dental fluorosis and biochemical estimations were made for serum calcium, serum and urinary fluoride and serum parathyroid hormone.

*Results:* Serum calcium levels were well within normal range in the patients of all areas but an increase in serum parathyroid levels (S. PTH) was noted. The increased S. PTH was well correlated with increase in fluoride ingestion. The severity of clinical and skeletal fluorosis was observed to increase with increase in S. PTH concentration.

*Conclusion:* High Fluoride ingestion has a definite relationship with increased parathyroid hormone secretion, which may be responsible for maintaining serum calcium levels and may have a role in toxic manifestations of fluorosis.

Authors: Gupta SK, Khan TI, Gupta RC, Gupta AB, Gupta KC, Jain P, Gupta A.

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Keywords: Fluoride in water, Parathyroid hormone, Skeletal fluorosis.

Source: Indian Pediatr 2001 Feb 7;38(2):139-146.

**THIRD ANNOUNCEMENT: XXIVTH CONFERENCE OF THE  
INTERNATIONAL SOCIETY FOR FLUORIDE RESEARCH**

**September 4 - 7, 2001 – Otsu, Japan**

The 24<sup>th</sup> Conference of the International Society for Fluoride Research (ISFR) will be held at the Piazza Ohmi in scenic Otsu, Shiga, Japan, September 4-7, 2001. Reports (in English only) on environmental fluoride; effects of fluoride on humans, animals, and plants; dietary fluoride; and fluoride analysis will be included, along with a mini-symposium on the neurological and other biological impacts of fluoride. Members of the Conference Organizing Committee welcome your attendance and participation.

*Conference venue:* Piazza Ohmi, Nionohama 1-1-20,  
Otsu, Shiga 520-0801, Japan.

*Phone:* 81-77-527-3311 or 81-77-527-3315; Fax 81-77-527-3319  
(International access code is 81; 2-digit area code is 77 for Otsu).

*Registration:* Tuesday, September 4, 2001 1200-1800 at Hotel Piazza Ohmi.

*Opening ceremony:* Tuesday, September 4, 2001 1800-2000 at the  
Crystal Room, Hotel Piazza Ohmi. (Participants and guests).

*Poster and platform sessions:* Wednesday, September 5, 2001 0900-1515;  
Thursday, September 6, 2001 0930-1300; Friday, September 7, 2001  
0900-1545.

*Tour:* Thursday, September 6, 2001 1300-. (Participants and guests).

*General meeting:* Friday, September 7, 2001 1545-1645.

*Banquet:* Friday, September 7, 2001 1830 at the Hotel Biwako.

*Lodging:* (prices are per room per night, including tax and breakfast)  
Hotel Piazza Ohmi (single: ¥ 8,800; twin: ¥ 17,600);  
Hotel Blue Lake (single: ¥ 7,300; twin: ¥ 14,600).  
Both hotels are located within 20 minutes walking distance or 6 minutes by taxi from the Japan Railway (JR) Otsu Station.

*Access to Otsu, Japan:*

The best gate for coming to Otsu is via the Osaka (Kansai) International Airport KIX, followed by a JR rapid train (Kan-kuu Kaisoku) to JR Osaka Station, then change to Tokaido Line rapid train to Otsu Station. The travelling time on the Tokaido Line rapid train is 37 minutes. A faster but more expensive option from Osaka (Kansai) International Airport KIX is to take the JR limited express (Haruka)

to Shin-Osaka, and then change to Tokaido Line rapid train to Otsu Station.

Nagoya Airport NGO is the second choice for entering Japan to come to Otsu. Take the limousine or bus to the railway station to take the JR Shin-Kansen to Kyoto Station and then change to the Tokaido Line (Biwako Line) to Otsu station. The travelling time on the Tokaido Line is 9 minutes.

Tokyo (Narita) International Airport NRT has the biggest international connections. It is situated a long way from the domestic Tokyo (Haneda) Airport HND and it is best to go from Tokyo (Narita) International Airport NRT to JR Tokyo Station, then by JR Shin-Kansen to Kyoto Station. At Kyoto Station change to Tokaido Line (Biwako Line) which brings you to Otsu station in 9 minutes.

*Conference registration:* for participants and delegates,

¥ 35,000 after June 1, includes the welcome reception, program and abstract book, admission to the scientific sessions, lunches, and coffee breaks. The fee for students is ¥ 20,000. The guest fee, ¥ 20,000, includes the welcome reception, lunches, and special tours to be arranged. The fee for the banquet is separate and is ¥ 6,000.

*Registration fee:* This is payable in Japanese yen by bank transfer to:

Account name: The 24<sup>th</sup> ISFR

Account number: 190-942562

Bank: Shiga Bank (Seta Ekimae)

Address of bank: Oogaya, 1-12-9, Otsu, Shiga 520-2144, Japan.

*Further information and registration forms can be obtained from:*

The Chairman: Professor Dr. K. Yoshitake, or

The Secretary General: Dr. G. Yamamoto at:

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