GROUNDWATER ARSENIC AND FLUORIDE IN CENTRAL MEXICO

The occurrence, distribution, and origin of total inorganic arsenic (iAs), fluoride (F⁻) and other trace elements (Se, Sb, V, Cr, Mo, Re, Pb, Cu, Cd, Co, and Zn) are investigated by hydrogeologic, hydrochemical, and isotopic techniques in the Independence Basin (IB), with an area of 7000 km², a tributary of the continental Lerma-Chapala Basin in the central part of Mexico. Groundwater samples from 246 wells, in both granular and fractured aquifers, show high concentrations of iAs (0.025–0.120 mg/L) and F⁻ (1.5–16 mg/L in the northeastern part of the basin in an area of about 500 km². Thirty-three water samples from this area, where a regional drawdown cone has developed, indicate that the origin and hydrochemistry of iAs and F⁻ are associated with high concentrations of HCO₃⁻ and Na⁺, mainly from the dissolution of sodium feldspar and other minerals of the fractured aquifer in cryolite-ignimbrite rocks, with long periods of groundwater residence time up to 35,000 years. Dissolution of arsenic minerals is a secondary process for iAs enrichment in groundwater, whereas F⁻ is related to dissolution of fluorite along with high concentrations of Li⁺, Cl⁻, Cs⁺, and Br⁻ in thermal water. There are no correlations of iAs and F⁻ with heavy metalloids and elements forming oxides, nor with other trace elements in solution. Stable isotopes in 125 samples indicate the meteoric origin of the groundwater and variable altitude of the recharge, not affected by evaporation during recharge, including those with ages in the ranges of thousands of years of time residence in the aquifer. There is no evidence that the basin was closed during its geologic evolution. If criteria and policies for groundwater management are not established at the IB, the size of the areas impacted by high concentrations of iAs and F⁻ may increase with time, which would affect the health of the inhabitants and the environmental and economic sustainability of the basin.

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Keywords: Arsenic in groundwater; Groundwater fluoride; Independence Basin; Lerma-Chapala Basin; Guanajuato, Mexico.

ASSOCIATIONS OF FLUORIDE INTAKE WITH CHILDREN’S BONE MEASURES AT AGE 11

Background: Relationships between fluoride intake and bone health continue to be of interest, as previous studies show conflicting results. Objectives: The purpose is to report associations of fluoride intake with bone measures at age 11. Methods: Subjects have been participating in the ongoing Iowa Fluoride Study/Iowa Bone Development Study. Mothers were recruited postpartum during 1992–95 from eight Iowa hospitals, and detailed fluoride questionnaires were sent every 1.5–6 months. From these, combined fluoride intakes from water sources (home, childcare, filtered, bottled), other beverages, selected foods, dietary fluoride
supplements and dentifrices were estimated at individual points and cumulatively
(with area under the curve (AUC)). Subjects underwent dual-energy X-ray
absorptiometry (DXA) scans of proximal femur (hip), lumbar spine, and whole
body (Hologic QDR 4500A). DXA results (bone mineral content – BMC; bone
mineral density – BMD) were related to fluoride intake as revealed by bivariate
and multivariable analyses. Results: The mean fluoride intake estimated by AUC
was 0.68 mg (SD = ±0.27) per day from birth to 11 years. Associations
(Spearman) between daily fluoride intake (mg F/day) and DXA bone measures
were weak (r = 0.01 to 0.24 for girls and 0.04 to 0.24 for boys). In gender-
stratified, and body size-and Tanner stage-adjusted linear regression analyses,
associations between girls’ bone outcomes and fluoride intake for girls were
almost all negative; associations for boys were all positive and none was
statistically significant when using an a = 0.01 criterion. Conclusions:
Longitudinal fluoride intake at levels of intake typical in the United States is only
weakly associated with BMC or BMD in boys and girls at age 11. Additional
research is warranted to better understand possible gender-and age-specific effects
of fluoride intake on bone development.

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Keywords: Bone measures; Bone mineral content; Bone mineral density; Children’s bone measures; Dual-
energy X-ray absorptiometry (DXA); Fluoride intake.

**FLUORIDE RISK IN INFANT FORMULAS FOR DENTAL FLUOROSIS**

**ASSESSING A POTENTIAL RISK FACTOR FOR ENAMEL FLUOROSIS: A PRELIMINARY
EVALUATION OF FLUORIDE CONTENT IN INFANT FORMULAS**

**BACKGROUND:** The authors conducted a study to determine concentrations
of fluoride in infant formulas, and to estimate fluoride intake in infants consuming
predominantly formulas. The authors compared estimated fluoride ingestion with
the tolerable upper limit and adequate intake level for fluoride recommended by
the Institute of Medicine (IOM). METHODS: The authors analyzed fluoride
concentrations of powdered and liquid formula concentrates and ready-to-feed
formulas. They estimated the total fluoride ingested by infants by considering the
fluoride content measured in both the infant formula and various concentrations of
fluoridated water. They based consumption volumes on published
recommendations. The authors compared estimates for fluoride ingestion with the
upper tolerable limit and adequate intake level, which they calculated by using
published infant growth charts. RESULTS: Fluoride concentrations of the different
formulas were low and, if reconstituted with low-fluoride water, would not result
in ingestion of fluoride at levels exceeding the IOM’s upper tolerable limit. Some
infants aged between birth and 6 months who consume powdered and liquid
concentrate formulas reconstituted with water containing 1.0 part per million
fluoride likely will exceed the upper tolerable limit of fluoride. CONCLUSIONS:
When powdered or liquid concentrate infant formulas are the primary source of
nutrition, some infants are likely to exceed the recommended fluoride upper limit
if the formula is reconstituted with water containing 1.0 ppm fluoride. On the other
hand, when the fluoride concentration in water used to reconstitute infant formulas is below 0.4 ppm, it is likely that infants between 6 and 12 months of age will be exposed to fluoride at levels below IOM’s recommended adequate intake level.

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Keywords: Fluoride water concentration; Infant formulas; Institute of Medicine (IOM) adequate F intake; IOM tolerable upper F limit.

ALTITUDE AND DENTAL FLUOROSIS IN NIGERIA

THE PREVALENCE AND SEVERITY OF DENTAL FLUOROSIS IN THE HIGH AND LOW ALTITUDE PARTS OF CENTRAL PLATEAU, NIGERIA

OBJECTIVE: To compare the prevalence and severity of dental fluorosis in the high and low altitude parts of the Central Senatorial District of Plateau State.
BASIC RESEARCH DESIGN: The study was cross-sectional and descriptive.
SETTING: The community-based study was carried out in Central Plateau Nigeria, in 2005.
PARTICIPANTS: The study subjects were 12–15 year old life long residents selected using the multistage sampling technique. One Local Government Area each was randomly selected from the high and low altitude parts of the district and from each selected Local Government Area two health districts were randomly selected with probability proportional to size. From each of the selected Health Districts two major settlements were selected again with probability proportional to size. 12–15 year old life long residents of the selected settlements were studied. Each respondent completed an interviewer-administered questionnaire after which he/she was clinically examined to ascertain his/her fluorosis status. Samples of water were collected from water sources consumed by the respondents in each settlement.
MAIN OUTCOME MEASURES: The main outcome measures were presence and severity of dental fluorosis as measured by the Thylstrup and Fejerskov index. (TF score). RESULTS: One thousand one hundred children were studied, 554 (50.4%) from the high altitude part of the district and 546 (49.6%) from the low altitude part. Fluorosis prevalence was 12.9% in the district, but significantly higher (22.2%) in the high altitude areas compared to the low altitude ones (3.5%). The severest form of fluorosis in the district was TF 6 for tooth 14 and TF 5 for tooth 11.
CONCLUSION: The prevalence and severity of dental fluorosis is significantly higher in the high altitude parts of the district compared to the low altitude ones. Efforts are needed to further investigate and control the problem.

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Keywords: Children 12-15-years old; Dental fluorosis; Fluorosis status; Interview questionnaire; Plateau State, Nigeria.
Source: Community Dent Health 2009 Sep;26(3):138-42.
DENTAL FLUOROSIS AND CARIES IN JAMAICA

REEXAMINATION OF CARIES AND FLUOROSIS EXPERIENCE OF CHILDREN IN AN AREA OF JAMAICA WITH RELATIVELY HIGH FLUOROSIS PREVALENCE

The aim of this cross-sectional study was to reexamine in 2006 caries and fluorosis experience among 5- to 6- and 11- to 12-year-olds (n = 789) in St. Elizabeth, Jamaica, an area found to have a high prevalence of dental fluorosis in 1999. Mean (± SD) dmft/DMFT scores were 2.4 ± 3.1 (n = 275) and 2.2 ± 2.3 (n = 133), fluorosis prevalence (tooth surface index of dental fluorosis 10) of upper central incisors was 67% (n = 109) and 39% (n = 132) among 6- and 12-year-olds, respectively. Results indicate slightly reduced caries experience for 6-year-olds compared to 1999. Fluorosis prevalence was high, particularly in 6-year-olds. Thus, risks and benefits from use of fluoride from multiple sources should be monitored carefully.

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Keywords: Dental caries; Dental fluorosis prevalence; Dietary fluoride; Jamaica; Salt fluoridation.

ENAMEL FLUOROSIS AND DENTAL CARIES

THE ASSOCIATION BETWEEN ENAMEL FLUOROSIS AND DENTAL CARIES IN U.S. SCHOOLCHILDREN

BACKGROUND: The authors assessed the association between enamel fluorosis and dental caries to determine if there is any beneficial effect of enamel fluorosis in U.S. schoolchildren. METHODS: The authors used data from a National Institute of Dental Research survey of the oral health of U.S. children conducted in 1986 and 1987 to determine the prevalence of caries and mean decayed, missing or filled surfaces on permanent maxillary right first molars in children 7 to 17 years of age who had a history of a single residence. (To date, this is the only national oral health data set in the United States with detailed information on fluoride exposures.) They examined the association between enamel fluorosis and caries using logistic regression analysis, controlling potential confounders in communities with water at or above optimal fluoridation levels and in communities with nonfluoridated or suboptimally fluoridated water. RESULTS: Permanent maxillary right first molars with fluorosis consistently had lower levels of caries experience than did normal molars. Adjusted odds ratios for caries prevalence in molars with fluorosis were 0.71 (95 percent confidence interval [CI], 0.56–0.89) in communities with nonfluoridated or suboptimally fluoridated water and 0.89 (95 percent CI, 0.74–1.06 in communities with water at or above optimal fluoridation levels. CONCLUSION: This study's findings suggest that molars with fluorosis are more resistant to caries than are molars without fluorosis. CLINICAL IMPLICATIONS: The results highlight the need for those considering policies regarding reduction in fluoride exposure to take into consideration the caries-preventive benefits associated with milder forms of enamel fluorosis.

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Keywords: Dental caries; Enamel fluorosis; NIDR survey; US schoolchildren.
FLUORIDE TOOTHPASTE USAGE BY CHILDREN UNDER AGE SIX

HOW MUCH TOOTHPASTE SHOULD A CHILD UNDER THE AGE OF 6 YEARS USE?

AIM: To discuss current concepts in the use of fluoride and to determine how much fluoride is sufficient for caries prevention but also how much is too much. Use of fluoride by young children is a balance between maximizing caries efficacy and minimizing the risk of fluorosis. METHODS: Review of the current literature. This review considers the importance of amount, concentration and dose of fluoride applied from toothpaste and the implications for risk and benefit.

RESULTS: Dental fluorosis is dependent on local fluoride levels in the extra cellular fluid surrounding the tooth during its development. These fluoride levels are determined by the plasma concentration that in turn is a function of the daily intake of fluoride. Fluoride released from bone during remodelling may also contribute to fluoride levels in the tissue. There is evidence to suggest that the effects of fluoride resulting in fluorosis prior to eruption of the tooth are cumulative and dependent on the amount and duration of exposure rather than a specific window of vulnerability. In contrast to dilution of ingested fluoride in the large volume of plasma, dilution of toothpaste in oral fluids is relatively small. Hence, for a given dose of fluoride, higher fluoride levels can be achieved in the oral environment using small amounts of toothpaste with higher fluoride concentrations rather than larger amounts with lower fluoride concentrations.

CONCLUSION: It is concluded that for young children fluoride ingestion needs to be carefully controlled during the first six years of life, and the best balance between risk and efficacy might be achieved by using small amounts of high fluoride toothpaste under close supervision from parents.

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Keywords: Caries prevention; Dental fluorosis; High fluoride toothpaste; Parental supervision; Remodelling.

MECHANISMS OF DENTAL FLUOROSIS

THE IMPACT OF FLUORIDE ON AMELOBLASTS AND THE MECHANISMS OF ENAMEL FLUOROSIS

Intake of excess amounts of fluoride during tooth development cause enamel fluorosis, a developmental disturbance that makes enamel more porous. In mild fluorosis, there are white opaque striations across the enamel surface, whereas in more severe cases, the porous regions increase in size, with enamel pitting, and secondary discoloration of the enamel surface. The effects of fluoride on enamel formation suggest that fluoride affects the enamel-forming cells, the ameloblasts. Studies investigating the effects of fluoride on ameloblasts and the mechanisms of fluorosis are based on in vitro cultures as well as animal models. The use of these model systems requires a biologically relevant fluoride dose, and must be carefully interpreted in relation to human tooth formation. Based on these studies, we propose that fluoride can directly affect the ameloblasts, particularly at high fluoride levels, while at lower fluoride levels, the ameloblasts may respond to local effects of fluoride on the mineralizing matrix. A new working model is presented, focused on the assumption that fluoride increases the rate of mineral formation, resulting in a greater release of protons into the forming enamel matrix.
Abstracts
Fluoride 42(4)297–304
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Keywords: Ameloblasts; Amelogenin; Dental fluoride; Enamel Fluorosis; Mineralising matrix.

Editor’s note: Portions of this work were included in an invited presentation by Dr DenBesten at the XXVIIIth Conference of the International Society for Fluoride Research, August 7–11, 2008, Toronto, Canada (Abstract: Fluoride 2008;41(3):236). For related work on the effect of fluoride on apatite crystal formation in rat hard tissues, see M Kakei and co-workers (Ann Anat 2007;189:175-81; abstracted in Fluoride 2007;40/3:204).

FLUORIDE-INDUCED METABOLIC CHANGES

THE EFFECTS OF FLUORIDE ON CELL MIGRATION, CELL PROLIFERATION, AND CELL METABOLISM IN GH4C1 PITUITARY TUMOR CELLS

The consumption of drinking water rich in fluoride has toxic effects on the central nervous system. In cell biology research fluoride is currently used as a phosphatase inhibitor. The aim of the present study was to evaluate the effect of fluoride on different physiological processes in GH4C1 pituitary tumor cells. We used a range of fluoride concentrations from level below normal human serum concentrations (0.23 and 1.2 µmol/L) up to those observed in chronically exposed persons (10.7 µmol/L) and above (107 and 1072 µmol/L). Treatment with 10.7 µmol F/L resulted in a discrete induction of DNA synthesis, without a change in cell number. Cell migration, usually a response to growth factors, was increased in cells treated with 2.4 µmol F/L. At this fluoride concentration changes in the phosphorylation status of both cytoskeletal and cytosolic protein fractions, as well as in actin cytoskeletal arrangements were observed. The fluoride-treated GH4C1 cells had significantly less cellular protein than control cells, suggesting an effect of fluoride on hormone secretion and protein synthesis in this endocrine cell. The reduction of MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide] was significantly increased with a wide range of fluoride concentrations. With the highest fluoride concentration, 1072 µmol/L, all of the analyzed parameters were significantly reduced, suggesting that this dose is highly toxic to GH4C1 cells. Our results show, that biologically relevant concentrations of fluoride are capable of increasing cell migration in tumor cells, suggesting that exposure to fluoride could stimulate tumor invasion.

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Keywords: Cell metabolism; Cell migration; Cell proliferation; Fluoride and phosphatase; GH4C1 pituitary tumor cells; MTT metabolism.
Source: Toxicology Letters 2009;190:179-86.

Editor’s note: Fluoride, together with trace levels of aluminium, is currently used in biological research as a trigger of certain G-proteins that in turn are involved in the regulation of kinases. The biological function of various inositol derivatives and that of many proteins, including enzymes, depends directly on their phosphorylation status. Furthermore, it appears that the authors of the paper
did not consider the possibility that increased $^3$H-thymidine incorporation without increased cell proliferation might be an indication of increased DNA repair synthesis.

**HAEM BIOSYNTHESIS AND NEUROLOGICAL VARIABLES**

**FLUORIDE-INDUCED CHANGES IN HAEM BIOSYNTHESIS PATHWAY, NEUROLOGICAL VARIABLES AND TISSUE HISTOPATHOLOGY OF RATS**

Fluoride-induced changes in the haem biosynthesis pathway, oxidative stress, and neurological variables supplemented by histopathological observations are reported for the brain, kidneys, and liver of rats drinking 1, 10, 50, and 100 ppm fluoride water for a period of 12 weeks. Significant alterations in the haem synthesis pathway are indicated by inhibition of blood $\delta$-aminolevulinic acid dehydratase (ALAD) and $\delta$-aminolevulinic acid synthetase (ALAS), oxidative stress, depletion of reduced glutathione (GSH), and increase in oxidized glutathione (GSSG) and thiobarbituric acid reactive substances. These changes were accompanied by a fluoride dose-dependent decrease in the GSH:GSSG ratio and whole brain biogenic amine levels. Interestingly and most significantly, these changes were more pronounced at lower fluoride concentrations than at higher concentrations. The observed changes were supported by histological observations, which also revealed that toxic effects and damage to organs were more pronounced at high fluoride concentrations. They also support our earlier findings indicating the effect of decreased ionic mobility of fluoride ion at higher concentrations, leading to less pronounced toxicity.

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Keywords: Blood parameters; Fluoride effects on blood; Haem biosynthesis; Histopathological observations; Neurological disorders; Oxidative stress; Rat brain; Rat kidney; Rat liver.
Source: J Appl Toxicol 2009; accepted July 14; publ. online (www.interscience.wiley.com) DOI 10.1002/jat.1474

**Editor’s note:** A small discrepancy occurs in this report: in the Discussion section the authors state that the decrease in ALAS activity in the fluoride-treated groups was markedly dose-dependent, whereas in the Results section they aver it was not. The more pronounced changes at lower than at higher fluoride concentrations suggest the presence of hormesis (stimulatory) effects.

**FLUORIDE GENETICS IN MICE**

**GENETICS AND F METABOLISM IN MICE**

A/J and 129P3/J mouse strains have different susceptibilities to dental fluorosis, due to their genetic backgrounds. This study tested whether these differences are due to variations in water intake and/or F metabolism. A/J (susceptible to dental fluorosis) and 129P3/J mice (resistant) received drinking water containing 0, 10, or 50 ppm F. Weekly F intake, excretion and retention, and terminal plasma and femur F levels were determined. Dental fluorosis was evaluated clinically and by quantitative fluorescence (QF). Data were tested by two-way ANOVA. Although F intakes by the strains were similar, excretion by A/J mice was significantly higher due to greater urinary F excretion, which resulted in lower plasma and
femur F levels. Compared with 129P3/J mice given 50 ppm F, significantly higher QF scores were recorded for A/J mice. In conclusion, these strains differ with respect to several features of F metabolism, and amelogenesis in the 129P3/J strain seems to be unaffected by high F exposure.

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Keywords: A/J and 129P3/J mouse strains; Amelogenesis; Dental fluorosis; Fluoride metabolism; Genetic susceptibility/resistance; Inbred mouse strains.  

Editor’s note: For a related report (not cited by these authors) on environmental response gene differences with respect to dental fluorosis in humans, see JL Liu et al. Fluoride 2006;39(3):195-201.

MICRONUTRIENTS IN PARENTERAL NUTRITION

MICRONUTRIENTS IN PARENTERAL NUTRITION: BORON, SILICON, AND FLUORIDE

Boron may be beneficial for bone growth and maintenance, central nervous system function, and the inflammatory response, and silicon may be beneficial for bone maintenance and wound healing. Fluoride is not an essential element but amounts provided by contamination may be beneficial for bone strength. Fluoride toxicity may be a concern in parenteral nutrition. Further studies are warranted to determine whether there are optimal amounts of boron and silicon that should be delivered to typical and special population patients receiving parenteral nutrition. In addition, further studies are needed to determine whether providing the dietary guideline of adequate intake amounts of fluoride parenterally would prevent or treat parenteral nutrition osteopenia.

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Keywords: Bone strength; Boron; Fluoride in parenteral feeding; Osteopenia; Parenteral nutrition; Silicon.  

Editor’s note: Although the author cites the 1997 report of the Food and Nutrition Board of the Institute of Medicine in support of the view that 10 mg/day above the age of eight is a “tolerable upper limit” of fluoride ingestion to avoid crippling skeletal fluorosis in adults, he does not refer to the 2006 report of the US National Research Council on Fluoride in Drinking Water that documents evidence of other serious toxic effects of fluoride at considerably lower levels of intake.