

BIOCHEMICAL EFFECTS**Mechanisms of sodium fluoride-induced endothelial cell barrier dysfunction: role of MLC phosphorylation**

NaF, a potent G protein activator and Ser/Thr phosphatase inhibitor, significantly increased albumin permeability and decreased transcellular electrical resistance (TER), indicating endothelial cell (EC) barrier impairment. EC barrier dysfunction induced by NaF was accompanied by the development of actin stress fibers, intercellular gap formation, and significant time-dependent increases in myosin light chain (MLC) phosphorylation. However, despite rapid, albeit transient, activation of Ca^{2+} /calmodulin-dependent MLC kinase (MLCK), the specific MLCK inhibitor ML-7 failed to affect NaF-induced MLC phosphorylation, actin cytoskeletal rearrangement, and reductions in TER, suggesting a limited role of MLCK in NaF-induced EC activation. In contrast, strategies to reduce Rho (C3 exoenzyme or toxin B) or to inhibit Rho-associated kinase (Y-27632 or dominant/negative RhoK) dramatically reduced MLC phosphorylation and actin stress fiber formation and significantly attenuated NaF-induced EC barrier dysfunction. Consistent with this role for RhoK activity, NaF selectively inhibited myosin-specific phosphatase activity, whereas the total Ser/Thr phosphatase activity remained unchanged. These data strongly suggest that MLC phosphorylation, mediated primarily by RhoK, and not MLCK, participates in NaF-induced EC actin cytoskeletal changes and barrier dysfunction.

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Keywords: Endothelial cell barrier dysfunction, MLC phosphorylation.

Source: Am J Physiol Lung Cell Mol Physiol 2001 Dec;281(6):L1472-83.

Effects of selenium and fluoride on apoptosis and lipid peroxidation in human hepatocytes

Objective: To study the influence of selenium and fluoride on apoptosis and lipid peroxidation in human hepatocytes in vitro.

Methods: The apoptosis, cell cycle, GSH content and lipid peroxides (LPO) level in human hepatocytes, LPO level and LDH, AST and ALT activity in cell culture supernatants were investigated after hepatocytes were incubated with selenium and/or fluoride for around 12 hours periods in vitro.

Results: The percentage of hepatocyte apoptosis bodies (15.557 ± 2.056)%, the number of cells in S phase (4.823 ± 0.454)% and LPO level in liver tissue and supernatant [(2.884 ± 0.589) and (3.547 ± 0.561) nmol/L MDA/mg.prot, respectively], AST and LDH activity in supernatants (91.1 ± 36.4 and 140.4 ± 7.6 U/L, respectively) in the fluoride treated group was

higher than the control group [(10.313 ± 1.023)%, (3.253 ± 0.743)%, (1.473 ± 0.401) nmol/L MDA/mg.prot, (1.694 ± 0.443) nmol/L MDA/mg.prot, (54.5 ± 3.2) U/L and (126.4 ± 2.6) U/L, respectively], The GSH content in live tissue [(4.225 ± 0.781) microgram/mg.prot] is lower than control group [(7.595 ± 1.042) microgram/mg.prot]. Selenium treatment reduced these kinds of toxicity of fluoride through raising GSH content, reducing LPO level, LDH and AST activity and percentage of apoptosis bodies.

Conclusions: Selenium can be and antagonist to apoptosis and lipid peroxidation of hepatocytes induced by fluoride.

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Keywords: Apoptosis, Lipid peroxidation, Hepatotoxicity

Source: *Zhonghua Yu Fang Yi Xue Za Zhi* 2002 Jul;36(4):235-8. [Article in Chinese]

Fluoride plus aluminum: useful tools in laboratory investigations, but messengers of false information

Aluminofluoride complexes (AlF(x)) form spontaneously in aqueous solutions containing fluoride and traces of aluminum ions and appear to act as phosphate analogs. These complexes have become widely utilized in laboratory investigations of various guanine nucleotide-binding proteins. Reflecting on many laboratory studies, a new mechanism of fluoride and aluminum action on the cellular level is being suggested. The long-term synergistic effects of these ions in living environment and their hidden danger for human health are not yet fully recognized.

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Keywords: Aluminum fluoride complexes.

Source: *Physiol Res* 2002;51(6):557-64.

Note: For a related review by these authors, see *Fluoride* 1999;32:230-42.

Sodium fluoride-induced hypoproteinemia and hypoglycemia in parental and F(1)-generation rats and amelioration by vitamins

Oral administration of sodium fluoride (NaF; 40 mg/kg body weight) daily from day 6 of gestation to day 21 of lactation caused, compared with the distilled water control (group 2), significant reductions in body weight and feed consumption as well as concentration of glucose and protein in the serum of P- and F(1)-generation rats; however, sodium and potassium concentrations in the serum were significantly higher than those of the vehicle

control (group 2). Administration of either vitamins C (50 mg/kg body weight/day), D (2 ng/0.2 mL olive oil/animal/day) or a combination of vitamins C+D+E along with NaF caused significant amelioration in body weight and feed consumption, as well as glucose, protein, sodium and potassium concentrations in the serum of P- and F(1)-generation rats compared with the NaF-only treated group.

Withdrawal of NaF treatment during lactation caused significant amelioration in feed consumption (days 15-21 only), sodium, potassium, glucose and protein concentrations in the serum of both P- and F(1)-generation rats. Co-treatment with vitamin E (2 mg/0.2 mL olive oil/animal/day) caused significant amelioration in body weight (days 15 and 20 of gestation only), sodium, potassium, glucose (only in P-generation females) and protein (only in P-generation female) concentrations in the serum of rats than in NaF-treated rats alone. It is concluded that co-treatment with vitamins C, D and C+D+E were found more effective in ameliorating NaF-induced effects than vitamin E and withdrawal of NaF treatment during lactation.

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Keywords: Fluoride toxicity amelioration, Hypoglycemia, Hypoproteinemia.

Source: Food Chem Toxicol 2002 Dec;40(12):1781-8.

Note: For an abstract of a related report by these authors, see *Fluoride* 2002;35:131.

DIETARY FLUORIDE

Fluoride exposure of East African consumers using alkaline salt deposits known as magadi (trona) as a food preparation aid

The fluoride content of Tanzanian and Kenyan magadi has been estimated to be in the range 0.1-17.9 mg F⁻/g, which is comparable with that reported elsewhere, but indicating a considerable variation in levels. The median fluoride content of crystalline magadi harvested from the alkaline lakes was 2.1 mg/g, which was higher than the median of 1.4 mg/g for scooped magadi harvested from the surface soil. The highest median fluoride contents of 3.2 and 2.9 mg/g were found in magadi originating from Lake Magadi, Kenya, and Lake Natron, Tanzania, respectively. It was found that the fluoride content varied significantly even for magadi originating from the individual lake, e.g. the fluoride content in magadi from Lake Magadi was between 0.1 and 8.7 mg/g. In a lump of magadi originating from Lake Magadi, it was found that the fluoride content in 20 smaller part samples was subject to considerable variation indicating that the fluoride-bearing minerals were unevenly distributed in the lump.

Results show that the fluoride is mainly present in grains <1.0 mm that made up 25% of the magadi sample. When daily eating the popular meal makande as in Tanzania, the exposure to fluoride through magadi in 70% of cases was estimated to be <4 mg per adult/day, as recommended by the WHO. Thus, the health hazard from magadi-fluoride is estimated to be significant in cases where the magadi is heavily contaminated.

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Keywords: Fluoride in food, Magadi, East Africa.

Source: Food Addit Contam 2002 Aug;19(8):709-14.

The fluoride content of foods and beverages from negligibly and optimally fluoridated communities

In the spring of 1996, foods and beverages most commonly consumed by adolescents were analyzed for fluoride as part of a larger investigation. These foods were selected by interviewing 711 adolescents, 12-14 years of age, who were long-time residents of either an optimally or negligibly fluoridated community. The brand names of the identified foods and beverages most commonly purchased were determined by interviews with the parents. A total of 441 brand-name food and beverage items were purchased from both communities and were individually analyzed for fluoride. These analyses were done in order to estimate the fluoride content of various kinds of foods and beverages and to determine whether or not there was a significant difference between the two communities in the amount of fluoride ingested from these dietary sources. The food and beverage items were classified into dietary groups based on US Department of Agriculture (USDA) guidelines. Overall, the fluoride content of the sampled foods and beverages was low. In addition, there was no significant difference in the fluoride content of the same pre-packaged or ready-to-eat food or beverage items purchased in the two communities. However, a significant difference was found between the two communities in the fluoride content of fountain beverages and in cooked or reconstituted foods prepared using local water from the respective communities. Based on these results, we have estimated the mean daily, dietary fluoride intake for 3-5-year-old children who are more susceptible to developing dental fluorosis.

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Keywords: Fluoride in beverages, Fluoride in food.

Source: Community Dent Oral Epidemiol 2002 Oct;30(5):382-91.

Fluoride intake in Japanese children aged 3-5 years by the duplicate-diet technique

This study was conducted to determine the fluoride intakes in 94 pre-school children aged 3, 4 and 5 (n = 30, 30, 34, respectively) residing in Yokkaichi, Mie Prefecture (< 0.16 ppm F water supply). The parents duplicated all the diets that their children ingested on 3 separate days during a 1-year period. The acid-diffusible fluoride in the diet was isolated by the acid-diffusion technique and measured with a fluoride electrode. The mean daily fluoride intakes from diet alone by children aged 3, 4 and 5 were 0.30 mg (n = 29, SD 0.19), 0.28 mg (n = 30, SD 0.19) and 0.30 mg (n = 34, SD 0.19), respectively. The total estimated mean values from diet and dentifrice were 0.35 mg (n = 29, SD 0.22, range 0.13-1.00), 0.33 mg (n = 30, SD 0.19, range 0.13-0.86) and 0.39 mg (n = 34, SD 0.18, range 0.18-1.01), respectively. It was concluded that the mean (\pm SD) total fluoride from diet and dentifrice in 3- to 5-year-old Japanese children was 0.35 ± 0.19 mg/day (0.021 ± 0.012 mg/kg body weight).

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Keywords: Fluoride in food, Japanese food.

Source: *Caries Res* 2002 Nov-Dec;36(6):386-90.

Editorial comment: In West Germany, the total daily fluoride intake of children 3-6 years old was estimated to be 53 μ g/kg bw in a report published in *Caries Research* in 2001 and abstracted in *Fluoride* 2002;35:63. Note that, in the report above, the daily F intake of 3-5 year old children in Japan was only 21 μ g/kg bw.

Fluoride intake in children living in a high-fluoride area in Ethiopia - intake through beverages

Introduction: The present study was conducted in Wonji Shoa, a sugar estate in the Ethiopian Rift Valley. Drinking water in the area is provided either by the Awash River or by high-fluoride ground water wells. Defluoridation plants have been installed, but are not in regular use, and fluorosis, dental as well as skeletal, is endemic. The aim of this study was to assess daily fluoride intake from drinking water and beverages in children from neighbouring villages with varying fluoride concentration in the drinking water.

Subjects and Methods: Thirty families were selected from two of the plantation villages (A and K). The criterion for being included in the project was the presence in the household of at least one child, fully weaned and below the age of 5 years. For sampling of beverages, the duplicate portion tech-

nique was used. The fluoride concentration in the beverage samples was determined using standard methods, using a fluoride ion-selective electrode.

Results: Ten of the selected households in Village A fetched water from the Awash River (1.8 mg F⁻/L) while five relied upon water from a local well (2.1 mg F⁻/L). All 15 households in Village K used water from a local well with fluoride concentration of 14.4 mg/L. The mean daily fluoride intake from drinking water and beverages during the four days, varied from 1.2 to 1.5 mg and 5.9 to 8.8 mg in Village A and K, respectively. Low variety in types of beverages consumed was reported both during the study period and through the questionnaire. Only local water was used for beverage preparation. Children who consumed milk had a reduced fluoride intake. Tea, which was part of the children's diet, was not found to be a main source of fluoride.

Conclusion: An effective defluoridation of the drinking water or a change of water source would seem to be the only options for avoidance of dental and possibly skeletal fluorosis.

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Keywords: Ethiopia, Fluoride in beverages, Fluoride in village water.

Source: Int J Paediatr Dent 2003 Jan;13(1):27-34.

Fluoride concentrations in three types of commercially packed tea drinks in Taiwan

Tea is a popular drink around the world. It is also one of the major sources of fluoride intake. The objectives of this study were to assess fluoride concentrations in popular non-, semi-, and full-fermented tea drinks sold on the Taiwan market. Concentration differences among three types of commercially available tea drinks (tea leaf, tea bag, and packaged tea beverage) were explored. Several influential factors in intake concentrations were evaluated. The acute threshold intake (ATI) and allowable daily intake (ADI) of those tea drinks were also estimated. For each commercial type, samples from the most popular tea in one particular fermentation degree (non, semi, and full) were randomly purchased and analyzed for fluoride concentrations. Fluoride levels in different rounds of tea, in different containers, and with different ratios of water and tea leaf were also assessed. In total, 132 tea samples were analyzed. The mean fluoride concentrations in leaf tea without the first round, leaf tea with the first round, bagged tea, and packaged tea were 7.04, 7.79, 5.37, and 25.7 mg/L, respectively. Most of the intake concentrations in those samples exceeded 4 mg/L F, the lower bound of fluoride levels reported in the literatures to be associated with a lower IQ in children and a higher risk of bone fracture. Fluoride concentrations in

packaged tea were the highest among the three types of commercially available tea. For studied leaf and bagged tea, almost a constant amount of fluoride was infused from the same amount of tea leaf regardless of the water volume. Besides this, making tea with glass or pottery tea makers would not affect fluoride intake concentrations. Acute intoxication is unlikely to occur. However, tea lovers in high fluoride content areas shall consider limit their consumption of tea drinks to avoid potential chronic effects.

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Keywords: Fluoride in tea.

Source: J Expo Anal Environ Epidemiol 2003 Jan;13(1):66-73.

Fluoride in the environment and brick-tea-type fluorosis in Tibet

To explore whether endemic fluorosis in Tibet is related to local factors, an epidemiological survey of fluorosis was conducted in 3 districts in Tibet. The survey used the WHO and FAO established "Guideline for the study of dietary intake of chemical contaminants" and the Horowitz suggested criteria for children dental fluorosis examination. The fluoride in the local environment of the 3 selected districts was studied in detail. The possible fluoride sources examined indicated that only the brick-tea carried a high content of fluoride; water, other food materials, and fuel contents were insignificant. The children's daily fluoride intake was high: Naqu 8.03 mg, Lahsa 6.93 mg, and Dingri 7.68 mg. All the dietary fluoride came from the brick-tea processed foods: the buttered-tea and zamba, these two contributed 99.74%, 98.70% and 99.60% of their daily fluorine intake respectively. The dental fluorosis index indicated that Naqu and Dingri were severely epidemic and Lahsa moderately epidemic. The endemic fluorosis that occurs in Tibet was essentially due to heavy consumption of foodstuffs prepared with brick-tea. However, the high altitude, harsh living conditions, and poor nutritional status aggravated the fluorosis. Brick-tea type fluorosis is a new type of fluorosis recently discovered in China. Compared with the drinking water type and coal combustion type of fluorosis, it covers a more extensive area, is more covert, and is more difficult to control. Decreasing the fluorine content of brick-tea may be the most promising preventive measure.

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Keywords: Brick-tea, Tibet.

Source: Huan Jing Ke Xue 2002 Nov;23(6):97-100. [Article in Chinese]

Note: For the abstract of a related report prepared for presentation at the XXVth ISFR Conference, see *Fluoride* 2002;35:255.

Brick tea fluoride as a main source of adult fluorosis

An epidemiological survey was conducted in Naqu County, Tibet in September 2001 to investigate the manifestations of fluorosis in adults caused by the habitual consumption of brick tea. Profiles were obtained for the total daily fluoride intake, environmental fluoride levels and average urinary fluoride concentration, and a physical examination and a skeletal radiographic study were conducted. One hundred and eleven 30-78-year-old adults were enrolled. It was found that the fluoride level of water sources in Naqu County was 0.10 ± 0.03 mg/L; no evidence of fluoride air pollution was found, but the brick tea water processed foods--zamba and buttered tea--had fluoride contents of 4.52 ± 0.74 mg/kg and 3.21 ± 0.65 mg/L, respectively. The adult daily fluoride intake reached 12 mg, of which 99% originated from the brick tea-containing foods. The positive rate of clinical symptoms by physical examination was 89%; furthermore, 42 of the 111 subjects were diagnosed by X-ray. The positive examination rate was 83%. Although the osteosclerosis-type skeletal fluorosis (overall increased bone matrix density) affected 74%, arthropathy and arthritis affected a significant number of the patients, resulting in functional disability. The results suggest that this brick tea-type fluorosis had even more severe adverse effects on human health compared with both the water-type and coal combustion-type fluorosis that occurred in other areas of China.

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Keywords: Brick-tea, Tibet.

Source: Food Chem Toxicol 2003 Apr;41(4):535-42.

EFFECTS ON TEETH

Caries occurrence in a fluoridated and a non-fluoridated town in Finland: a retrospective study using longitudinal data from public dental records

The tap water of Kuopio, Finland, was fluoridated from 1959 to 1992. In the first decade of fluoridation, children in Kuopio had lower DMF values than children in Jyvaskyla, a nearby low-fluoride town, but later differences between the towns have been small and inconsistent. The present study aimed to gain further insight into caries occurrence in Kuopio and Jyvaskyla using longitudinal tooth-specific data from public health records on cohorts born in 1970/71 and 1980/81 (total n = 1,503). Survival analyses were used to summarize the tooth-specific times elapsed between eruption and the first filling (used as a proxy for dental caries). Generally, the first filling was

placed sooner after eruption in the 1970/71 cohort than in the 1980/81 cohort. The curves for the two towns were virtually identical except for the first molars of the 1970/71 cohort, for which the percentage of filled first molars was consistently lower in Jyvaskyla than in Kuopio. This study indicates that, among children and adolescents whose permanent teeth erupted in the mid-1970s or thereafter, even a longitudinal approach did not reveal a lower caries occurrence in the fluoridated than in the low-fluoride reference community. The main reason for the modest effect of water fluoridation in Finnish circumstances is probably the widespread use of other measures for caries prevention. The children have been exposed to such intense efforts to increase tooth resistance that the effect of water fluoridation does not show up any more. The results must not be extrapolated to countries with less intensive preventive dental care.,

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Keywords: Cessation of fluoridation, Dental caries, Finland, Kuopio.

Source: Caries Res 2002 Sep-Oct;36(5):308-14.

A randomised controlled trial of the effectiveness of providing free fluoride toothpaste from the age of 12 months on reducing caries in 5-6-year old children

Objective: To assess the impact of regularly supplying free fluoride toothpaste regularly to children, initially aged 12 months, and living in deprived areas of the north west of England on the level of caries in the deciduous dentition at 5-6 years of age. A further aim was to compare the effectiveness of a programme using a toothpaste containing 440 ppm F (Colgate 0-6 Gel) with one containing 1,450 ppm F (Colgate Great Regular Flavour) in reducing caries.

Design: Randomised controlled parallel group clinical trial. Clinical data were collected from test and control groups when the children were 5-6 years old.

Setting: A programme of posting toothpaste with dental health messages to the homes of children initially aged 12 months. Clinical examinations took place in primary schools.

Participants: 7,422 children born in 3-month birth cohorts living in high caries areas in nine health districts in north west England. Within each district children were randomly assigned to test or control groups.

Interventions: Toothpaste, containing either 440 ppm F or 1450 ppm F, and dental health literature posted at three monthly intervals to children in test groups until they were aged 5-6 years.

Main Outcome Measures: The dmft index, missing teeth and the prevalence of caries experience.

Results: An analysis of 3,731 children who were examined and remained in the programme showed the mean dmft to be 2.15 for the group who had received 1,450 ppm F toothpaste and 2.49 for the 440 ppm F group. The mean dmft for the control group was 2.57. This 16% reduction between the 1,450 ppm F and control group was statistically significant ($P < 0.05$). The difference between the 440 ppm F group and control was not significant. Further analyses to estimate the population effect of the programme also confirmed this relationship.

Conclusion: This study demonstrates that a programme distributing free toothpaste containing 1,450 ppm F provides a significant clinical benefit for high caries risk children living in deprived, non-fluoridated districts.

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Keywords: Dental caries, Free toothpaste.

Source: Community Dent Health 2002 Sep;19(3):131-6.

Blood lead level and dental caries in school-age children

The association between blood lead level and dental caries was evaluated in cross-sectional analyses of baseline data for 543 children 6-10 years old screened for enrollment in the Children's Amalgam Trial, a study designed to assess potential health effects of mercury in silver fillings. Approximately half of the children were recruited from an urban setting (Boston/Cambridge, MA, USA) and approximately half from a rural setting (Farmington, ME, USA). Mean blood lead level was significantly greater among the urban subgroup, as was the mean number of carious tooth surfaces. Blood lead level was positively associated with number of caries among urban children, even with adjustment for demographic and maternal factors and child dental practices. This association was stronger in primary than in permanent dentition and stronger for occlusal, lingual, and buccal tooth surfaces than for mesial or distal surfaces. In general, blood lead was not associated with caries in the rural subgroup. The difference between the strength of the associations in the urban and rural settings might reflect the presence of residual confounding in the former setting, the presence of greater variability in the latter setting in terms of important caries risk factors (e.g., fluoride exposure), or greater exposure misclassification in the rural setting. These findings add to the evidence supporting a weak association between children's lead exposure and caries prevalence. A biologic mechanism for lead cariogenicity has not been identified, however. Our data

are also consistent with residual confounding by factors associated with both elevated lead exposure and dental caries.

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Keywords: Blood lead, Dental caries, Lead.
Source: *Environ Health Perspect* 2002 Oct;110(10):A625-30.

An epidemiological profile of dental caries in 12-year-old children residing in cities with and without fluoridated water supply in the central western area of the State of Sao Paulo, Brazil

This study aimed to analyze the epidemiological profile of dental caries in the central western region of the State of Sao Paulo, Brazil, focusing on 12-year-old children by gender, comparing the DMFT index in fluoridated and non-fluoridated cities. The study used data from the Epidemiological Surveys in the State of Sao Paulo, 1998, pertaining to the 10th Regional Health Directorate, including 8 cities. The sample consisted of 485 schoolchildren, both boys and girls, distributed by city. In Pederneiras (a medium-sized city with a fluoridated water supply), DMFT was 7.06, higher than the Brazilian national mean for 1986. Boys showed a higher prevalence of dental caries than girls, showing a new trend for dental caries in the region. There was no statistically significant difference between DMFT in municipalities of the same size, regardless of the presence or absence of fluoride in the water supply, thus suggesting a "convergence" phenomenon, possibly due to the intake of other sources of fluoride and the presence of a "halo" effect. Prevalence of caries in the region was "high", with a DMFT of 4.82, thus failing to reach the goals set for the year 2000.

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Keywords: Brazil, Dental caries, Fluoridation.
Source: *Cad Saude Publica* 2002 Sep-Oct;18(5):1281-8. [Article in Portuguese].

Fluorosis development in seven age cohorts after an 11-month break in water fluoridation

This study used an 11-month break in water fluoridation to identify the time when developing incisors are most sensitive to fluorosis development. The study was based in Durham, NC, where an interruption to water fluoridation occurred between September, 1990, and August, 1991. A total of 1896 children were dentally examined. Fluorosis was measured by the TF

index, and parents or guardians completed a questionnaire on demographics and fluoride history. Age cohorts ranged from those born 5 years before the break, to those born 1 year after the resumption of fluoridation. Fluorosis prevalence for seven age cohorts whose birth years ranged from 1985-86 to 1991-92 was 57.1, 62.3, 33.0, 32.3, 39.8, 30.2, and 36.8%, respectively. Children aged from birth to 3 years at the break, and those born 1 year after it, had less fluorosis than those aged 4-5 years at the break.

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Keywords: Dental fluorosis, Fluoridation cessation.

Source: J Dent Res 2003 Jan;82(1):64-8.

Degree of fluorosis in areas of South Africa with differing levels of fluoride in drinking water

The purpose of this study was to study the relationship between degree of fluorosis and varying fluoride concentrations in the drinking water in a relatively dry region in South Africa. A strong positive association was found between drinking water fluoride levels and fluorosis but only up to a level of approximately 2.0 ppm for areas with a high average daily temperature (approximately 79 degrees F). The results indicate that the optimum drinking water fluoride concentration for a region with a high average daily temperature should be less than 1.00 ppm.

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Keywords: Dental fluorosis, Fluoride in drinking water, South Africa.

Source: Gen Dent 2002 Jul-Aug;50(4):352-6.

ENVIRONMENTAL FLUORIDE

Defluoridation of drinking water by boiling with brushite and calcite

Existing methods for defluoridating drinking water involve expensive high technology or are slow, inefficient and/or unhygienic. A new method is now suggested, encompassing brushite and calcite suspension followed by boiling. Our aim was to examine the efficiency of the method and the chemical reactions involved. Brushite, 0.3-0.5 g, and an equal weight of calcite were suspended in 1 litre water containing 5-20 ppm fluoride. The suspensions were boiled in an electric kettle, left to cool and the calcium salts to sediment. Solution ion concentrations were determined and sediments were

examined by X-ray diffraction. In distilled water initially containing 5, 10 and 20 ppm fluoride the concentration was reduced to 0.06, 0.4 and 5.9 ppm, respectively. Using Aarhus tap water which contained 2.6 mmol/L calcium the final concentrations were 1.2, 2.5 and 7.7 ppm, respectively, and runs without calcite gave results similar to those with calcite. Without boiling the fluoride concentration remained unaltered, as did the brushite and calcite salts, despite occasional agitation by hand. All solutions were supersaturated with respect to fluorapatite and hydroxyapatite and close to saturation with respect to brushite. Boiling produced well-crystallised apatite and traces of calcite, while boiling of brushite alone left a poorly crystallised apatite. We conclude that boiling a brushite/calcite suspension rapidly converts the two salts to apatite which incorporates fluoride if present in solution, and that this process may be exploited to defluoridate drinking water.

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Keywords: Brushite, Calcite, Defluoridation of water.

Source: Caries Res 2002 Sep-Oct;36(5):341-6.

Environmental impacts on health from continuous volcanic activity at Yasur (Tanna) and Ambrym, Vanuatu

Continuous low-level basaltic volcanic activity, from Yasur Volcano in Tanna, and Marum and Benbow vents on Ambrym, have occurred for as long as records have been kept in Vanuatu. The potential chronic health implications for the inhabitants of these two areas were investigated in a preliminary environmental sampling program. The focus was particularly on fluoride and other volcanic gas-derived chemical contamination in areas surrounding the volcanic centres. Little immediate contamination of the environment was evident for areas affected by volcanic ash and gas on Tanna, with water fluoride concentrations being elevated (to 0.42 mg/L only within a lake adjacent to the active volcanic cone. Selected re-sampling in April 2001 following the long active phase of Yasur, revealed higher F levels in surface waters (to 1.05 mg/L). Analysis of cow rib bone and teeth indicated a possible long-term accumulation of F in grazing animals, which probably consume F-bearing volcanic ash and gas hydrates on the surface of plant leaves. No human impacts (including stress and respiratory problems) were noted, probably due to the constant and familiar low-level activity, plus the coarse nature of most ash ejecta. Ambrym appears to be a more F-concentrated system than Tanna, with volcanic ash containing 281 total and 36.7-43.6 soluble mg F/ kg (cf. 178 total and 7.3-9.1 soluble mg F/ kg on Tanna), and water levels reaching up to 2.8 mg F/L in rainwater tanks. The drinking water F levels on Ambrym are higher than WHO recommended

levels, despite the being sampled during a substantial lull in eruptive activity, and signal potential for chronic dental and skeletal fluorosis.

Authors: Cronin SJ, Sharp DS.

For Correspondence: Institute of Natural Resources, Massey University, Private Bag 11 222, Palmerston North, New Zealand.

Keywords: Ambrym, Fluoride in water, Tanna, Volcanic activity, Yasur.

Source: Int J Environ Health Res 2002 Jun;12(2):109-23.

A map of natural fluoride in drinking water in Pakistan

Aim: The assessment of fluoride levels in domestic water supplies in Pakistan.

Method: Water samples were collected from sources supplying the majority of the population: taps in places where piped water supply was available, tube-wells, boreholes and wells in rural areas, and stream water where appropriate.

Results: Analysis of 987 water supplies showed that they are predominantly low in fluoride content, 84% containing less than 0.7 ppm of fluoride.

Conclusion: For the majority of the population in Pakistan there is a clear indication for use of alternate sources of fluoride to ensure optimal intake necessary for the control of dental caries.

Authors: Ayyaz AK, Whelton H, O'Mullane D.

For Correspondence: Shaikh Zayed Federal Postgraduate Medical Institute, Lahore, Pakistan. E-mail: ayyazk@brain.net.pk

Keywords: Fluoride in water, Pakistan.

Source: Int Dent J 2002 Aug;52(4):291-7.

Study on fluoride emission from soils at high temperature related to brick-making process

Characteristics of fluoride emission from 12 soils at temperatures of 400-1,100 degrees C related to the brick-making process were studied. The results obtained in this study indicate that fluoride emission as gaseous HF and SiF₄ was related to the firing temperature, soil total fluoride content, soil composition and calcium compounds added to soils. Soils began to release fluoride at temperatures between 500 and 700 degrees C. Marked increases of the average fluoride emission rate from 57.2% to 85.4% of soil total fluoride were noticed as the heating temperature was increased from 700 to 1,100 degrees C. It was found that the major proportion (over 50%) of the soil total fluoride was emitted from soils at approximate 800 degrees C. The amount of fluoride released into the atmosphere when heated depended on the total fluoride contents in the soils. Correlation analysis showed that the soil composition, such as cation exchange capacity, exchangeable calcium

and CaCO_3 , had some influence on fluoride emission below 900 degrees C, but had no influence at temperatures above 900 degrees C. Addition of four calcium compounds (CaO , CaCO_3 , Ca(OH)_2 , and CaSO_4) at 1.5% by weight raised the temperature at which fluoride began to be released to 700 degrees C. The greatest decrease in fluoride emission among the four calcium compound treatments was found with CaCO_3 .

Authors: Xie ZM, Wu WH, Xu JM.

For Correspondence: College of Environmental and Resource Science, Zhejiang University, Hangzhou 310029, PR China. E-mail: zhmxie@zju.edu.cn

Keywords: Brick-making, Fluoride in soil.

Source: Chemosphere 2003 Feb;50(6):763-9.

Study on the regeneration methods of the synthetic hydroxyapatite as a material for defluoridation of drinking water

The regeneration efficiencies of the synthetic hydroxyapatite saturated by fluoride using either sodium hydroxide method or surface coating method are studied and compared. Both static and dynamic conditions for surface coating regeneration method are also tested. The results showed that the regeneration efficiency of the synthetic hydroxyapatite saturated by fluoride treated by surface coating method is 46%-64%, more than two times of that of it treated by the traditional sodium hydroxide regeneration method.

Authors: Ying B, Li X, Cong Z.

For Correspondence: Institute of Environmental Health & Engineering, Chinese Academy of Preventive Medicine, Beijing 100050, China.

Keywords: Defluoridation, Hydroxyapatite.

Source: Wei Sheng Yan Jiu 2002 Apr;31(2):83-4. [Article in Chinese]

Fluoride toxicity to aquatic organisms: a review

Published data on the toxicity of fluoride (F^-) to algae, aquatic plants, invertebrates and fishes are reviewed. Aquatic organisms living in soft waters may be more adversely affected by fluoride pollution than those living in hard or seawaters because the bioavailability of fluoride ions is reduced with increasing water hardness. Fluoride can either inhibit or enhance the population growth of algae, depending upon fluoride concentration, exposure time and algal species. Aquatic plants seem to be effective in removing fluoride from contaminated water under laboratory and field conditions. In aquatic animals, fluoride tends to be accumulated in the exoskeleton of invertebrates and in the bone tissue of fishes. The toxic action of fluoride resides in the fact that fluoride ions act as enzymatic poisons, inhibiting enzyme activity and, ultimately, interrupting metabolic processes such as glycolysis and synthesis of proteins. Fluoride toxicity to aquatic inverte-

brates and fishes increases with increasing fluoride concentration, exposure time and water temperature, and decreases with increasing intraspecific body size and water content of calcium and chloride. Freshwater invertebrates and fishes, especially net-spinning caddisfly larvae and upstream-migrating adult salmons, appear to be more sensitive to fluoride toxicity than estuarine and marine animals. Because, in soft waters with low ionic content, a fluoride concentration as low as 0.5 mg F⁻/l can adversely affect invertebrates and fishes, safe levels below this fluoride/l concentration are recommended in order to protect freshwater animals from fluoride pollution.

Author: Camargo JA.

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Keywords: Aquatic organisms, Fluoride toxicity.

Source: Chemosphere 2003 Jan;50(3):251-64.

Safety threshold of fluorine in endemic fluorosis regions in China

Four endemic fluorosis regions in China and their environmental epidemiological characteristics were summarized in this paper. It shows that the epidemiology of endemic fluorosis is closely related to the geochemical parameters of the local environment. The food-web and dose-effect relationship of fluoride from the environment to the human body in different types of endemic fluorosis regions were studied. The safety threshold of fluoride in different regions was determined. The results have provided a scientific basis for environmental risk assessment of fluoride in China.

Author: Li Y, Wang W, Hou S.

For Correspondence: Institute of Geographic Sciences and Natural Resources Research, CAS, Beijing 100101, China.

Keywords: China, Endemic fluorosis, Safety threshold.

Source: Huan Jing Ke Xue 2002 Jul;23(4):118-22. [Article in Chinese]

Manufacture of hydroxyapatite as a defluoridator and the mechanism of defluoridation for drinking water

Hydroxyapatite as a defluoridator for drinking water is characterized by a large capacity of defluoridation, and easy and simple operation in application. The quality of drinking water is not changed, the sorbent is easy to be regenerated, and the second pollution does not occur after the treatment of drinking water with the sorbent. Hydroxyapatite method has advantage over the methods such as activated alumina, bone char and electro dialysis commonly used in defluorination of drinking water. It is for this reason that the

components, structural feature, synthesis and application of hydroxyapatite and its mechanism of defluoridation are summarized in this paper.

Authors: Li X, Zheng D, Ying B.

For Correspondence: College of Environment & Energy Engineering, Beijing Polytechnic University, Beijing 100022, China.

Keywords: Defluoridation, Hydroxyapatite.

Source: Wei Sheng Yan Jiu 2002 Apr;31(2):136-8. [Article in Chinese]

HEALTH/TOXIC EFFECTS IN ANIMALS

Toxic effects of various water pollutants on structural and functional parameters of hepatocytes

A prolonged intragastral intoxication of male and female rats by low doses of fluorine, zinc, chromium, arsenite, and combination of these compounds lead to developing cytolysis and hepatic-cellular insufficiency. These changes are more pronounced in female rats especially if chromium, arsenite and a combination of toxicants were used. They lead to developing hyper lipid peroxidation in male rats the most expressed by intoxication with arsenite and combined effect. Unlike to male rats LPO intensity in female rats was more pronounced and fixed by effect of all preparations. SOD activation was revealed to be in male rats by effect of chromium and especially zinc, in female rats by effect of fluorine and zinc. A distinctive inhibition of SOD activity determined to be by using arsenite and combination of toxicants. Activation of catalase especially in male rats was also revealed. Activation of membrane-destructive processes in the liver of experimental animals results in reducing pharmaco-metabolizing function of this organ.

Authors: Karimov Khla, Inoiatova FKH, Inoiatov FSH va "A".

For Correspondence: Tashkent State Second Medical Institute, Uzbekistan.

Keywords: Fluoride toxicity, Liver toxicity.

Source: Vopr Med Khim 2002 Mar-Apr;48(2):174-9. [Article in Russian].

Testicular toxicity in sodium fluoride treated rats: association with oxidative stress

This study examined the effect of sodium fluoride, a water pollutant important through the world, including India, on testicular steroidogenic and gametogenic activities in relation to testicular oxidative stress in rats. Sodium fluoride treatment at 20mg/kg/day for 29 days by oral gavage resulted in significant diminution in the relative wet weight of the testis, prostate, and seminal vesicle without alteration in the body weight gain. Testicular delta(5),3beta-hydroxysteroid dehydrogenase (HSD) and 17beta-HSD activities were decreased significantly along with significant diminution in plasma levels of testosterone in the fluoride-exposed group compared to the

control. Epididymal sperm count was decreased significantly in the fluoride-treated group and qualitative examination of testicular sections revealed fewer mature luminal spermatozoa in comparison to the control. The seminiferous tubules were dilated in treated animals. Fluoride treatment was associated with oxidative stress as indicated by an increased level of conjugated dienes in the testis, epididymis, and epididymal sperm pellet with respect to control. Peroxidase and catalase activities in the sperm pellet were decreased significantly in comparison to the control. The results of this experiment indicate that fluoride at a dose encountered in drinking water in contaminated areas exerts an adverse effect on the male reproductive system and this effect is associated with indicators of oxidative stress.

Authors: Ghosh D, Das Sarkar S, Maiti R, Jana D, Das UB.

For Correspondence: Department of Human Physiology with Community Health, Reproductive Endocrinology and Family Welfare Research Unit, Vidyasagar University, Midnapore 721 102, West Bengal, India. E-mail:debidasghosh@yahoo.com

Keywords: Fluoride toxicity, Oxidative stress, Testicular toxicity.

Source: *Reprod Toxicol* 2002 Jul-Aug;16(4):385-90.

Fluoride concentrations in thoroughbred horses in India

Fluoride possesses both essential and toxic potentials. A cross-sectional study recorded the fluoride concentrations in sera of thoroughbred horses 5 years of age from 4 localities in India. A total of 628 serum samples were analyzed for fluoride content using ion selective potentiometry. The mean serum fluoride was estimated as 0.018 ± 0.002 , 0.096 ± 0.004 , 0.16 ± 0.008 and 0.32 ± 0.02 ppm in horses from the eastern, central, western and southern parts of the country respectively. Although there were significant differences in fluoride concentration among horses from different zones, all were within the normal range for this species.

Authors: Dwivedi SK, Dey S.

For Correspondence: National Research Centre on Equine, Hisar, Haryana, India.

Keywords: Horses, India, Serum fluoride.

Source: *Vet Hum Toxicol* 2002 Oct;44(5):292-3.

Chronic fluoride toxicity decreases the number of nicotinic acetylcholine receptors in rat brain

In order to investigate the molecular mechanism(s) underlying brain dysfunction caused by chronic fluorosis, neuronal nicotinic acetylcholine receptors (nAChRs) in the brain of rats receiving either 30 or 100 ppm fluoride in their drinking water for 7 months were analyzed in the present study employing ligand binding and Western blotting. There was a significant reduction in the number of [³H]epibatidine binding sites in the brain of rats

exposed to 100 ppm of fluoride, but no alteration after exposure to 30 ppm. On the other hand, the number of [¹²⁵I]alpha-BTX binding sites was significantly decreased in the brains of rats exposed to both levels of fluoride. Western blotting revealed that the level of the nAChR alpha4 subunit protein in the brains of rats was significantly lowered by exposure to 100 ppm, but not 30 ppm fluoride; whereas the expression of the alpha7 subunit protein was significantly decreased by both levels of exposure. In contrast, there was no significant change in the level of the beta2 subunit protein in the brains of rats administered fluoride. Since nAChRs play major roles in cognitive processes such as learning and memory, the decrease in the number of nAChRs caused by fluoride toxicity may be an important factor in the mechanism of brain dysfunction in the disorder.

Authors: Long YG, Wang YN, Chen J, Jiang SF, Nordberg A, Guan ZZ.

For Correspondence: Department of Pathology, Guiyang Medical College, Guizhou, PR China.

Keywords: Acetylcholine receptors, Neurotoxicity.

Source: Neurotoxicol Teratol 2002 Nov-Dec;24(6):751-7.

Effects of selenium and zinc on rat renal apoptosis and change of cell cycle induced by fluoride

Objective: This study was conducted to study the effects of sodium fluoride (NaF) on rat renal apoptosis and proliferation, the antagonistic effect of selenium-zinc preparation (Se-Zn) to NaF.

Methods: Wistar rats were provided with distilled water containing NaF (50 mg/L) and administered by gavage with different dosed of Se-Zn for six months. Kidney cell apoptosis and the cell cycle of proliferation were detected by TUNEL (TdT-mediated dUTP Nick End Labelling) and flow cytometry.

Results: NaF caused rat renal apoptosis, reduce the cell number of G(2)/M period in cell cycle and decrease the relative content of DNA significantly. Se-Zn inhibited the effects of NaF on apoptosis and increased the cell number of G(2)/M period in cell cycle, but failed to increase relative content of DNA.

Conclusion: It was suggested that NaF could induce apoptosis and change the cell cycle in rat renal cells and Se-Zn could antagonize apoptosis and the changes of cell cycle induced by NaF.

Authors: Yu R, Xia T, Wang A, Chen X.

For Correspondence: Department of Environmental Health, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430030, China.

Keywords: Apoptosis, Renal damage, Selenium, Zinc.

Source: Zhonghua Yu Fang Yi Xue Za Zhi 2002 Jul;36(4):219-21. [Article in Chinese]

Studies on DNA damage and apoptosis in rat brain induced by fluoride

Objective: To explore the DNA damage effects and apoptosis in brain cells of rats induced by sodium fluoride.

Methods: SD rats were divided into two groups, i.e. control group and fluoride treated group, which were injected intraperitoneally with distilled water and sodium fluoride (20 mg/kg/d) respectively. On the hand, 5 mmol/L NaF were used in the *in vitro* study. Single Cell Gel Electrophoresis (SCGE or Comet Assay) was utilized to measured DNA damage and apoptosis was detected by the TUNEL method and Flow Cytometry (FCM).

Results: The DNA damage in pallium neurons in rats of the fluoride group was much more serious compared with those of the control group, with the Rdit value being 0.351 and 0.639 respectively ($P < 0.01$) *in vivo*, and 0.384 4 and 0.650 1 respectively ($P < 0.01$) *in vitro*. TUNEL positive cells were found in pallium, hippocampus and cerebellar granule cells in rats of fluoride group, whereas those in the control group were rare. It was demonstrated by FCM results that the percentages of apoptotic cells both in pallium and hippocampus were significantly higher ($P < 0.01$) in rats of fluoride group (27.12 ± 3.08 , 34.97 ± 5.46) than those in control group (4.63 ± 0.98 , 5.35 ± 0.79), ($P < 0.01$).

Conclusion: Sodium fluoride could induce DNA damage and apoptosis in rats brain.

Authors: Chen J, Chen X, Yang K, Xia T, Xie H.

For Correspondence: Department of Environmental Health, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430030, China.

Keywords: Apoptosis, DNA damage, Neurotoxicity.

Source: Zhonghua Yu Fang Yi Xue Za Zhi 2002 Jul;36(4):222-4. [Article in Chinese]

HEALTH/TOXIC EFFECTS IN HUMANS

Fluoride overfeed at a well site near an elementary school in Michigan

A fluoride overfeed occurred at a well site near an elementary school in Portage, Michigan. The incident resulted in a high concentration of fluoride (92 mg/L) in drinking water at the school. Seven students who drank water from the school fountain reportedly suffered nausea and vomiting. Toxicological evaluations were made by conducting a risk assessment. On the basis of the symptoms experienced by the students, it was concluded that the fluoride had irritated the stomach causing nausea and vomiting. This mild oral exposure to fluoride was, however, deemed too low to cause any long-term appreciable adverse health effects. Despite subsequent flushing, the concentration of the fluoride in the drinking water remained variable during the

first nine days after the incident. With several flushings over the 48 days after the incident, the concentration of fluoride was brought down to optimal levels. The electrical circuit that energized the fluoride system was modified to prevent another overfeed. In addition, operational changes were made to further minimize the impact of such an overfeed.

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Keywords: Acute fluoride toxicity, Fluoride overfeed, Fluoridation acute toxicity.

Source: J Environ Health 2002 Oct;65(3):16-21

Endemic fluorosis in Rajasthan

Chronic fluoride (F) toxicity in the form of osteo-dental fluorosis was observed in both sexes of children and adults from ten villages viz., Bhavanpura, Dovada, Genhuwara, Gokulpura, Hathai, Kahela, Mandav, Nalwara, Pratappura and Samota located in the vicinity of F mines of Dungarpur district (Rajasthan) where F concentration in drinking waters varied from 1.2 to 8.9 ppm. At 1.7 and 6.1 mean F concentrations, 70.6% and 100.0% of children (< 18 years) and 68.0% and 100.0% adults, respectively, were found to be affected with dental fluorosis of varying grades. No such sex difference was seen in prevalence of dental fluorosis. Both prevalence and severity of dental mottling were found to be increased with increasing of F concentration and were found maximum in the 17-22 years age group. At these same F concentrations, 7.4% and 37.7% adults (> 21 years) were showing evidence of skeletal fluorosis, respectively. Although, skeletal fluorosis was also found in children with low prevalence (5.2%) but at high F concentration (4.8 ppm). The prevalence of skeletal fluorosis was relatively higher in males and increased with higher F level and age.

Deformities such as crippling, kyphosis, invalidism and genu-varum were observed frequently in higher age group subjects (> 48 years) at a F concentration of 3.3 ppm. None of fluorotic individuals revealed evidence of genu-valgum syndrome and goitre (thyroidism). Radiological findings of other deformities in fluorotic subjects were also found. The distribution of F and endemic fluorosis in different districts of Rajasthan state have also been reviewed.

Authors: Choubisa SL, Choubisa L, Choubisa DK.

For Correspondence: P. G. Department of Zoology, S. B. P. Government College, M. L. Sukhadia University, General Hospital, Dunagrpur-314001, Rajasthan, India.

Keywords: Endemic fluorosis, Rajasthan.

Source: Indian J Environ Health 2001 Oct;43(4):177-89.

Note: For a related report by the first author, see *Fluoride* 2001;34:61-70.

Fluoride excretion in children after sevoflurane anaesthesia

Background: Defluorination of sevoflurane is catalysed by the hepatic enzyme cytochrome P450 2E1 (CYP2E1). Data about the ontogenesis (developmental variations in activity) of this enzyme suggest a low metabolism of sevoflurane during the first months of life.

Methods: To test this hypothesis, 45 children less than 48 months of age undergoing sevoflurane anaesthesia were enrolled in a prospective open clinical trial. The 24 h urine fluoride excretion was measured in five groups of children (A, <4 months; B, 4 to <8 months; C, 8-12 months; D, >12-24 months; and E, >24-48 months old). An index of sevoflurane metabolism (ISM) was calculated as the ratio of fluoride excretion, cumulative expiratory sevoflurane concentrations measured every minute during anaesthesia, and body surface area. ISM values were median (IQ 25-75%).

Results: ISM was lower in group A (n=9, 18.9 (11.2-29.5) than group C (n=11, 44.2 (37.5-53.5), $P<0.05$), group D (n=7, 52.6 (45.8-68.4), $P<0.01$) and group E (n=9, 53.6 (50.7-85), $P<0.001$). Median ISM expressed as a function of median age, exponentially increased with a rapid increase during the first months of life, followed by a slower increase after 10 months of age.

Conclusion: These results suggest that, in children less than 48 months, sevoflurane metabolism parallels postnatal development of CYP2E1.

Authors: Lejus C, Le Roux C, Legendre E, Renaudin M, Boiteau HL, Pinaud M.
For Correspondence: Department of Anaesthesiology, Hotel Dieu, C.H.U. Nantes, France. Societe d'Etude des Risques Toxiques, Nantes, France.

Keywords: Cytochrome P450 2E1, Fluoride excretion, Sevoflurane anaesthesia.
Source: Br J Anaesth 2002 Nov;89(5):693-6.

Note: For an abstract of a related report from this group, see *Fluoride* 2002;35:62.

Reversal of fluoride induced cell injury through elimination of fluoride and consumption of diet rich in essential nutrients and antioxidants

The objective of the present communication is to address the issues concerning reversal of fluoride induced cell injury and disease (i.e. fluorosis) through the elimination of fluoride and consumption of a diet containing essential nutrients and antioxidants. Humans afflicted with fluorosis, as a result of consuming fluoride contaminated water or food, have been investigated. Hospital based diagnostic procedure for early detection of fluorosis, through retrieval of history, clinical complaints, testing of blood, urine and drinking water for fluoride using ion selective electrode technology, along with X-ray of the forearm have been carried out. Confirmed cases of fluorosis were introduced to an intervention protocol consisting of (1) provision of

safe drinking water with fluoride levels less than 1 mg/L and (2) counseling on nutritional supplementation with focus on adequate intake of calcium, vitamins C, E and antioxidants. The patients were monitored at frequent intervals up to one year and the results are reported. With a standardized early diagnosis, elimination of fluoride intake and supplementation of a diet rich in essential nutrients and antioxidants, we have shown that the fluorosis can be reversed.

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Keywords: Amelioration of toxicity, Antioxidants, Reversal of fluoride toxicity, Treatment of fluorosis.

Source: Mol Cell Biochem 2002 May-Jun;234-235(1-2):335-40.

Human exposure to hydrogen fluoride induces acute neutrophilic, eicosanoid, and antioxidant changes in nasal lavage fluid

The development of asthma-like symptoms among aluminum potroom workers has been associated with exposure to fluorides. In the present study, the immediate nasal response in humans was examined subsequent to short-term hydrogen fluoride (HF) exposure. Ten healthy subjects were exposed to HF (3.3-3.9 mg/m³) for 1 h. Nasal lavage (NAL) was performed before, immediately after, and 1.5 h after the end of exposure. Control lavages were performed on the same subjects at the same time points but without HF exposure. At the end of HF exposure, 7 of 10 individuals reported upper airway symptoms. A significant increase was observed in the number of neutrophils and total cells, while there was a decrease in cell viability. The changes in neutrophil numbers correlated significantly with the reported airway symptoms. HF also induced a significant increase in tumor necrosis factor-alpha and the total protein content of NAL fluid. Among the eicosanoids, prostaglandin E(2), leukotriene B(4), and peptide leukotrienes were elevated after exposure. Of the antioxidants measured, the concentration of uric acid increased after exposure. In conclusion, exposure to HF induced immediate nasal inflammatory and antioxidant responses in healthy human volunteers. These findings may contribute to a further understanding of the way HF exerts damage to the airways and show that HF could represent an occupational hazard.

Authors: Lund K, Refsnes M, Ramis I, Dunster C, Boe J, Schwarze PE, Skovlund E, Kelly FJ, Kongerud J.

For Correspondence: Department of Respiratory Medicine, The National Hospital, University of Oslo, N-0027 Oslo, Norway.

Keywords: Aluminum potroom, Hydrogen fluoride toxicity, Neutrophils.

Source: Inhal Toxicol 2002 Feb;14(2):119-32.

Prolonged respiratory symptoms caused by thermal degradation products of freons

Objectives: The chlorofluorocarbons (CFC) used in refrigeration systems decompose on heating and produce substances that are highly irritating to the airways (eg, chlorine, carbonyl fluoride, and hydrogen fluoride). This study examined persistent respiratory symptoms among several workers exposed to thermal decomposition products of CFC.

Methods: Seven patients with respiratory symptoms caused by inadvertent exposure to thermal decomposition products of CFC in a restaurant kitchen or during refrigerator repair were studied with the use of spirometry, peak flow follow-up, and histamine challenge tests. Three patients also underwent bronchoscopy and bronchoalveolar lavage.

Results: In five of the cases, cough or dyspnea lasted longer than 1 month; for three of the five, the symptoms lasted more than 4 years. Three cases showed increased bronchial hyper-reactivity, and two of the three had increased diurnal peak flow variation. Three patients fulfilled the criteria for acute irritant-induced asthma or reactive airway dysfunction syndrome. One case exhibited bronchiolitis while, for the other six, the clinical picture was consistent with bronchitis.

Conclusions: The studied cases indicate that the thermal decomposition products of CFC used in refrigerators may cause irritant-induced airway diseases of long duration.

Authors: Pirila P, Espo T, Pfaffli P, Riihimaki V, Wolff H, Nordman H.

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Keywords: Fluoride pollution, Freons, Respiratory symptoms.

Source: Scand J Work Environ Health 2003 Feb;29(1):71-7.

Hemodialyzability of ionizable fluoride in hemodialysis session

The fluoride ion content in serum and in dialysate medium was determined by means of a fluoride ion-selective electrode in 29 patients undergoing hemodialysis treatment. An abnormally high serum fluoride of 65.9 ± 28.3 $\mu\text{g/L}$ at the beginning and 46.5 ± 26.7 $\mu\text{g/L}$ at the completion of the hemodialysis session was observed. Results showed that 60.0 ± 23.9 % of the serum fluoride at the beginning of the session was theoretically filterable, and 80.8 ± 42.4 % of this fraction was actually filtered throughout the hemodialysis session. The dialysis procedure is considered to be safe and adequate for serum fluoride removal. The high serum fluoride at the completion of the hemodialysis session was thought to originate from the fraction of unfilterable bound fluoride. To make further progress towards im-

provements in serum fluoride removal during HD, attention to the bound fraction of serum fluoride is required.

Authors: Usuda K, Kono K, Watanabe T, Dote T, Shimizu H, Tominaga M, Koizumi C, Nishiura H, Goto E, Nakaya H, Arisue M, Fukutomi A.

For Correspondence: Department of Hygiene and Public Health, Osaka Medical College, Takatsuki, Japan.

Keywords: Hemodialysis, Ionizable fluoride.

Source: Sci Total Environ 2002 Oct 7;297(1-3):183-91.

XXVTH ISFR CONFERENCE ABSTRACTS

(See *Fluoride* 2002;35:244-63 for other abstracts)

Water fluoride concentration and dental fluorosis prevalence in a north-western arid region of Mexico

In north-western Mexico, drinking water comes from underground wells and is characterized by a high content of fluoride. In this study, a quantitative assessment of dental fluorosis was made in 24 rural communities located in the arid north-western state of Chihuahua, Mexico. The assessment was done through a convenience sampling of the population. The Dean index of dental fluorosis was correlated with the fluoride concentration in drinking water.

Results show that 77% of the water samples exceed the maximum fluoride concentration limits (1.5 mg/L) established by both the Mexican and international regulations. 79.69% of the population presented dental fluorosis, 10.36% presented grade 0.5 in the Dean index, and only 7.97% did not present it at all. In those communities with fluoride concentrations over 6 mg/L, 84% of the population presented dental fluorosis, while the maximum prevalence was found in the 18-30 year age group.

It was observed that zones with a high fluoride concentration also presented a high level of dental fluorosis. This shows that the risk of dental damage related to fluorosis is closely related to the fluoride level in drinking water.

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Keywords: Chihuahua, Dental fluorosis, Fluoride in water, Mexico.

Arthritis in America

Data from Roholm's classical study on fluoride shows that arthritis occurs in first and second stage skeletal fluorosis (SF). He found remarkably large variations of times for the onset of the various stages of skeletal fluorosis. Analysis of his results shows that stage 1 SF occurred in 2.4 years, stage 2 SF occurred in 4.8 years, and stage 3 SF occurred in 11.2 years after an intake range of 0.2 – 0.35 mg F/kg body weight/day. Roholm pointed out that some fluoride compounds are more toxic than others. As fluosilicate water fluoridation compounds fall in this category, shorter onset times may occur for SF.

Literature searches show that many writers commented on the relationship of arthritis with skeletal fluorosis. This fact strongly points to equivalence of SF with arthritis.

The US Centers for Disease Control and Prevention (CDC) surveys in 1995 and 2001 show the high and increasing incidence of arthritis. 7- 8 million Americans experience substantial limitations due to arthritis.

All this evidence points to the high probability that millions of Americans are suffering from skeletal fluorosis. Most of these cases are in the pre-skeletal and first stage of skeletal fluorosis with some in stage 2.

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Keywords: Arthritis, Skeletal fluorosis, United States of America

Defluoridation of brick-tea with serpentine

The use of serpentine to control endemic fluorosis caused by drinking brick-tea was studied by examining the conditions which gave the optimal reduction in brick-tea fluoride levels together with factors that influenced the activation and regeneration of serpentine.

The factors tested for defluoridation efficacy, using an orthogonal design, were serpentine size, reaction time, pH, kinds of regenerating agents, concentration of regenerating agents, and regeneration time. A fluoride sensitive electrode was used to measure fluoride levels and an atomic absorption spectrometer for other chemical elements.

The defluoridation capacity of serpentine rock was 0.31 mg/g, and did not decrease with repeated use after regeneration. Defluoridation efficacy was not influenced by regeneration time or activation ($P>0.05$). Optimal conditions for defluoridation were: serpentine size 0.2-0.3 mm, pH 6-6.5, reaction time 20-25 minutes, regenerating agent ($KAl(SO_4)_2 \cdot 12H_2O$) concentration 5%. After defluoridation the tea still complied with the national standard on all infusion indices such as colour, nature, and content, and no toxic substances were present.

Serpentine could help control the endemic fluorosis caused by drinking brick-tea by decreasing the brick-tea fluoride levels.

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Keywords: Brick-tea, Defluoridation, Serpentine.

Fluoride effects on thyroid function

The past 30 years have witnessed dramatic changes in the concepts of thyroid hormone activity. The 1970s brought the recognition of the central role of triiodothyronine (T3) in mediating thyroid hormone action, establishing T3 as the "active" thyroid hormone. The same decade shattered the long-held belief that all thyroid hormones entered the cell by "diffusion" and brought first evidence that the uptake of T3 was energy-dependent. In the 1980s and 1990s the cloning of receptors and the discovery of G proteins further enabled investigators to undertake detailed analyses of the biochemical events which underlie the physiological and pathological action of thyroid hormones.

The laboratory discovery of fluoride as a "universal G protein activator" contributes greatly to the understanding of fluoride effects upon thyroid hormone activity and helped define the role of thyrotropin, the thyroid-stimulating-hormone (TSH), and its function in activating thyroid cancer cells. Fluoride directly imitates the effects of the TSH-receptor - the only G-protein-coupled-receptor known so far able to activate all G protein families - thus displaying unprecedented diversity indicative of complex multi-functioning signaling throughout the body.

When the new findings from the field of endocrinology are applied to the vast amount of historical data on fluoride as an effective anti-thyroid agent, a new picture of fluoride toxicity emerges, calling for an urgent re-assessment of our understanding of "fluorosis". The toxic effects of fluoride in humans are dependent upon the individual's thyroid status. Opposing effects are observed when fluoride is given to hypothyroid or hyperthyroid patients.

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