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REFLECTIONS ON THE BEIJING CONFERENCE

Tohru Murakami M D
Maebashi, Japan

I agree with the Editorial in the last journal (Vol. 27, No. 4, October 1994). The XXth Conference in Beijing was the most successful in the Society’s history. Over 200 Chinese researchers actively participated, and the size and enthusiasm of the gathering were beyond the expectations of many members, especially those from Western countries. While listening to the discussions, my thoughts returned to the late Professor Emeritus Fumiyoshi Yanagisawa M D, former Professor of Epidemiology at the Tokyo Medical and Dental University, who pioneered the study of poisonous effects of fluoride in Japan. Had he lived to see the Beijing Conference, he would surely have rejoiced, together with his Chinese colleagues, at the progress of that study in China.

Dr Yanagisawa founded the Japanese Society for Fluoride Research, and subsequently constantly enlightened Japanese people about fluoride toxicity, including that resulting from fluoridation of drinking water for prevention of tooth decay. For this purpose, he worked in collaboration with Chinese researchers, and sponsored over 15 of them on study tours to Japan, at his personal expense. A personal communication from Professor Wei Zan Dao, of Guiyang Medical College in China, informs me that the Chinese Society for Fluoride Research will hold its 10th Commemorative Conference in 1995. The outstanding progress in Chinese fluoride research is no doubt the result of hard work on the part of Chinese researchers. But I attribute it also to the strong foundation laid down by Dr Yanagisawa, and his efforts to promote fluoride research in China.

In Japan we are proud to have had a predecessor to Dr Yanagisawa. As early as 1958, Kazuo Samezina, a dental researcher at Kagoshima University, concluded in an article that fluoride in drinking water should be as low as possible because the Japanese daily diet contains ample fluoride. Professor Kanzi Soezima, who was a supervisor of Dr Samezina, also warned that more than 2 mg/day of fluoride is harmful. These reports were rather radical at that time, but can now be recognized as outstanding works because they foretold results that many people have only now come to realize are true. The profound works of the late Professor Soezima, introduced to China by Professor Yanagisawa, have had a great influence upon Chinese policy on fluoridation. For example, the maximum contaminant level of fluoride in drinking water recommended to the Chinese Government is 0.6 ppm, which is three fourths that of the Japanese and much less than the United States’ 4 ppm. We can easily understand how much they have suffered from endemic fluorosis and why they have considered fluoride an enemy of public health.

Dr Murakami is Secretary-General of the Japanese Society for Fluoride Research. Address: 1-5-16 Kamikoide-Machi, Maebashi-Shi, Gunma-Ken, 371 Japan.

(continued next page)
But, needless to say, it is not easy to achieve the new standard. As was explained in the last Editorial, we examined teeth of about 30 school children (aged from 5 to 12 years), who were chosen arbitrarily from about 120 school children who waited in line to welcome us. All of the examinees had dental fluorosis. Even young children aged 5-6 had chalky white teeth, including deciduous teeth. The teeth of some children of age 12 were badly discolored. I learned that in that village the water fluoride level of 4-5 ppm has been successfully reduced to 0.8-1.0 ppm for the last six years, and that new severe skeletal fluorosis has not been seen since. But, even with that lower concentration, children had obvious dental fluorosis. It would seem that the widely accepted “scientific” standard for water fluoridation is not reliable. Dental researchers from the World Health Organization were also there, but it seemed that they were not very interested in dental fluorosis, which did not make sense to me.

As was also reported in the earlier Editorial, we visited three villages around the city of Langfang, southeast of Beijing, in a tour for the foreign delegates. There was a slogan, written with six Chinese words, repeatedly displayed in the defluoridation plant in one of the villages. It may have “been Greek” to members from most Western countries, but we Japanese, who share some words with the Chinese people, could readily understand the meaning. The slogan said: “Improve water, reduce fluoride. It makes us happy.” This is exactly what should be achieved by fluoride study. As Professor A K Susheela, of the All-India Institute of Medical Sciences, stated in her thoughtful and articulate presentation: “the only way to prevent fluorosis is to not ingest fluoride.”

In many ways the conference in Beijing was very fruitful. I am really thankful to all those who worked on the meeting.

ANNOUNCEMENT
The XXIst Conference of the International Society for Fluoride Research will be held in Hungary in 1996. Inquiries should be sent to Dr Miklos Bély, Director, Department of Pathology, National Institute of Rheumatology, ORFI M4 POB 54, H-1525 Budapest, Hungary.

CORRECTION
In most printings of the last issue (Vol. 27 No. 4 1994) the sources of the abstracts on page 236 were inadvertently omitted. The correct headings were:

DENTAL TISSUE EFFECTS OF FLUORIDE
O Fejerskov, M J Larsen, A Richards and V Baelum
Aarhus, Denmark
Abstract from Advances in Dental Research 8 (1) 15-31 1994

ERUPTION OF DECIDUOUS TEETH: INFLUENCE OF UNDERNUTRITION AND ENVIRONMENTAL FLUORIDE
Venkata Ranga Rao Kodali, K A V R Krishnamachari and J Gowrinathasastry
Osmania, Hyderabad, India
Abstract from Ecology of Food and Nutrition 30 (2) 89-97 1993
ACID SECRETION AND FLUORIDE ABSORPTION
BY THE LIGATED STOMACH OF THE RAT
MUTUAL INFLUENCES OF FLUORIDE AND LUMINAL ACIDITY

K Gharzouli, A Senator, A Gharzouli, M Mustapha and S Abed
Sétif, Algeria

SUMMARY: The ligated stomach of the rat was used to study the net fluxes of acid and fluoride. Luminal 10 mM NaF decreased basal and histamine-stimulated acid secretion (-53%), but increased four times the loss of acid from the gastric lumen filled with 100 mM HCl. Two hours intravenous infusion of 5 mM NaF alone (20 μmoles F⁻·Kg⁻¹·h⁻¹) did not affect acid secretion, but the addition of 0.1 mM AlF₃ to the infused solution stimulated acid secretion (+28%).

The stimulation of acid secretion by histamine did not change absorption of fluoride. When the luminal concentration of acid was increased with 100 mM HCl, fluoride absorption was enhanced by 80% as compared with control. The increase of fluoride absorption was accompanied by a rise of fluoride concentration in the plasma (+43% - +53%). A positive correlation was observed between the percentage absorption of fluoride and its concentration in the plasma.

Key words: Acid secretion; Aluminium; Fluoride absorption; Ligated stomach; Plasma fluoride; Rat.

Introduction

Fluoride is likely transported by epithelial cells by passive diffusion of the undissociated fluorhydric acid.¹⁻⁴ In the stomach, the rate of absorption of fluoride is not proportional to the luminal concentration of NaF,⁵ and is inversely related to the luminal pH.⁴ Sodium fluoride present in the lumen of the cat stomach was reported to inhibit the histamine-stimulated acid secretion.⁶ However, NaF added to the serosal fluid of the isolated mouse distended stomach causes a dose-related stimulation of acid secretion, and did not interfere with histamine-stimulated secretion.⁷ A time-dependent secretagogue effect of oral administration of NaF to rats was also reported.⁸ The difference in experimental conditions employed by different workers (such as the difference between in vivo and in vitro preparations, the route and mode of administration of NaF, the species used) might have caused the discrepancy.

The aim of this study is an attempt to unify earlier reports by examining with a same model, the ligated stomach of the rat: 1) the effect of luminal and plasma fluoride on acid secretion, 2) the effect of luminal acid on fluoride absorption.

Materials and Methods

Male Wistar rats weighing between 200 and 240 g were purchased from Institut Pasteur (Alger, Algeria). The animals were fed on standard chow. Thirty-six hours prior to experiments, food was withdrawn and the animals were allowed free access to water.

Université Ferhat Abbas, Institut de Biologie, 19000 Sétif, Algeria.
The animals were anæsthetized with pentobarbital (36 mg.Kg\(^{-1}\)). After a median incision of the abdomen, the stomach was ligated at the level of the cardia and filled through the pylorus with a precisely measured volume (2 ml) of the test solution and immediately closed with a pyloric ligation. The abdomen was then sutured and the animal kept under a heating lamp. One hour later and before excising the stomach, a sample of blood was withdrawn from the posterior vena cava for fluoride determination in the plasma. The stomach was then rapidly exteriorized, cut proximally to the outside of the ligatures. The test solution was drained and completely recovered by washing with 5 ml of 0.9% NaCl. The recovered solution was weighed, centrifuged, and the supernatant stored for acid and fluoride determinations. The stomach was then freed from the mesenteric attachments, blotted dry and weighed.

To avoid the secretory reflex of the stomach to distension by the filling solution, all animals received a subcutaneous injection of atropine 5 mg.Kg\(^{-1}\) (Prolabo, France) 30 minutes prior to opening of the abdomen.

In order to study the effect of luminal acidity on fluoride absorption and simultaneously the effect of the halogen on acid secretion, 3 groups of rats were formed: 1) a basal group received an intravenous injection of 0.9% NaCl via the dorsal vein of the penis; 2) a histamine treated group received by the same way 3 mg base.Kg\(^{-1}\) of histamine-HCl (Merck, Darmstadt) just after filling the stomach; 3) an HCl treated group received intravenously 0.9% NaCl as the control and the stomach was filled with an isotonic test solution containing 100 mM HCl. In each group, the filling test solution was either 0.9% NaCl (control) or 10 mM NaF (+ NaCl to isotonicity).

In order to study the effect of circulating fluoride on acid secretion by the ligated stomach, an intravenous infusion (4 ml.Kg\(^{-1}\).h\(^{-1}\)) was initiated via a jugular vein one hour before the opening of the abdomen and was maintained during the incubation period. The infused solution in each group was one of the three following: 0.9% NaCl, 5 mM NaF, 5 mM NaF + 0.1 mM AlF\(_3\). The two latter solutions were made isotonic with NaCl. The stomach was filled with 0.9% NaCl.

Acid was determined by titration of the recovered fluid with 10 mM NaOH to the phenol red end point. Fluoride in the recovered solution and plasma was determined by direct potentiometric method\(^8\) using fluoride ion-selective electrode (Tacussel PF4-LM). All fluoride samples were stored in polyethylene flasks.

Net flux, expressed as µEq.h\(^{-1}\).g\(^{-1}\) fresh tissue, was calculated as the difference between the recovered and the injected amounts for fluoride and acid. Net absorption from the lumen was then expressed as a negative value and net secretion into the lumen as a positive value.

Calculated values of experimental groups were reported as mean ± s.e.m. The significance of the difference between means was determined by analysis of variance. Linear function was derived by the least-squares method.
Results

Acid and water net fluxes

In control conditions (see Table), basal acid secretion was 13.2 ± 0.8 μEq.h⁻¹.g⁻¹. Under histamine treatment (3 mg.Kg⁻¹), acid secretion was significantly increased to 47.1 ± 4.3 μEq.h⁻¹.g⁻¹ (P < 0.001). The final concentration of acid in the lumen was 2.6 times the basal value but without a significant change in secretion of water. A marked loss of acid was accompanied by a significant gain of water secretion in the lumen when the stomach was initially filled with 100 mM HCl (P < 0.05). The rate of acid disappearance from the lumen attained 17.4 ± 4.2 μEq.h⁻¹.g⁻¹.

When NaF (10 mM) was initially present in the lumen (see Table), acid secretion was reduced in the basal and histamine treated groups (P < 0.05). The final concentration of acid in basal and histamine treated groups was respectively 67% and 78.5% below the control value; whereas water secretion was significantly increased (P < 0.05). In the HCl treated group, the loss of acid from the lumen was increased four times in comparison with control (P < 0.001). The final concentration of H⁺ was reduced by 40% and water secretion was increased, but not to a significant level.

<table>
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<th>TABLE. Effect of intravenous injection of histamine 3 mg.Kg⁻¹ and luminal 100 mM HCl on net fluxes of water, acid and fluoride, and on plasma fluoride concentration.</th>
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<td>Treatment</td>
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<tr>
<td>Control:</td>
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<tr>
<td>Net water flux (ml)</td>
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<tr>
<td>H⁺ net flux (μEq)</td>
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<td>H⁺ concentration (μEq/ml)</td>
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<td>Luminal NaF (10 mM):</td>
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<td>Net water flux (ml)</td>
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<td>H⁺ net flux (μEq)</td>
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<td>H⁺ concentration (μEq/ml)</td>
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<td>F⁻ net flux (μEq)</td>
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<tr>
<td>Percentage absorption</td>
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<td>Plasma fluoride (μEq/l)</td>
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Fluxes are expressed per gram fresh tissue and per h. Secretion is indicated by positive values, absorption by negative values. Horizontal comparisons with basal group: <sup>a</sup>P < 0.05; <sup>b</sup>P < 0.001. Vertical comparisons with control: <sup>c</sup>P < 0.05; <sup>d</sup>P < 0.001.
Intravenous infusion of NaF alone (total infused amounts ranging from 8 to 9.6 μmoles) had no significant effect on acid secretion; but when fluoride was infused with AlF₃ 0.1 mM (total infused amounts ranging from 0.16 to 0.19 μmoles), acid secretion by the stomach was significantly increased from 11.3 ± 0.8 to 14.5 ± 1.2 μEq.h⁻¹.g⁻¹ (P<0.05) (Figure 1).

**FIGURE 1.** Secretion (panel A: μEq.h⁻¹.g⁻¹) and luminal concentration (panel B: μEq.ml⁻¹) of acid in the ligated stomach of the rat intravenously infused with 1) 0.9% NaCl, 2) 5 mM NaF, 3) 5 mM NaF + 0.1 mM AlF₃. Handle bar represents one s.e.m.; (1,2): n = 13; (3) n = 6. *: P < 0.05.

**Fluoride absorption**

Fluoride was absorbed by the ligated stomach when it was present in the lumen as 10 mM NaF (see Table). The stimulation of acid secretion by histamine (3.5 times the basal level) did not change significantly the rate of fluoride absorption. But when the stomach was filled with 100 mM HCl, the absorption of fluoride was significantly enhanced (P<0.001). In this latter condition, the percentage absorption of fluoride increased from 22.4 to 38.1%.

**Plasma fluoride**

The absorption of fluoride by the stomach was accompanied by a net increase of plasma fluoride (see Table). Plasma fluoride was significantly greater in the HCl treated group than that observed in the basal and histamine treated groups (P<0.001). The pooled data from basal, histamine and HCl treated groups showed
a positive correlation ($r = 0.77$) between plasma fluoride and the percentage absorption ranging from 16.5 to 45% (Figure 2).

![Graph showing the relationship between plasma fluoride and percentage absorption.](image)

**FIGURE 2.** Relation between plasma fluoride and the percentage absorption of fluoride by the ligated stomach of the rat. Symbols: ○ basal, ● histamine treated group, ■ HCl treated group. The straight line ($y = x + 12.8$) gave the best correlation ($r = 0.77$, $n = 27$).

**Discussion**

The role of luminal acidity on fluoride absorption and the effect of fluoride on acid secretion were simultaneously studied under histamine-stimulated acid secretion or under $H^+$ loss from the lumen of the ligated stomach. The loss of $H^+$ was induced by acidification of the lumen with 100 mM HCl. This procedure did not alter the permeability of the stomach to albumin.¹⁰
Luminal NaF (10 mM) decreased basal and histamine-stimulated acid secretion (respectively 53% and 72% below the control values). Simultaneously water secretion was increased by NaF under basal conditions and histamine treatment (respectively 69% and 75% above the control values). The gain of water in the lumen may explain partially the observed decrease of the final acid concentration. It has been shown that instillation of 5 mM NaF into the gastric cavity of cats produces a marked reduction of acid secretion in response to histamine. This effect was attributed to an inhibition of secretion by NaF.6

Exposure of the gastric mucosa to 100 mM HCl alone or with 10 mM NaF led to a loss of H+ and to a gain of water into the lumen. The loss of H+ induced by the combination of HCl and NaF was four times greater than that induced by HCl alone. The demonstration that instillation of 10 mM HCl into the main stomach was associated with an increase of HCO3- secretion by dog Heidenhain pouch11 provides at least a partial explanation for the loss of H+. Moreover, barrier-breaking agents, such as unionized forms of acetic and salicylic acids, are able to render the gastric mucosa more permeable to ions and larger molecules.12 At pH 2, all fluoride present will exist as HF (96.6%) and may behave as a barrier-breaking agent. It is very likely that, under conditions of increased permeability, H+ diffuses out from (and HCO3 into) the gastric lumen.

If we consider that fluoride is mainly transported as HF,1-4 we would then expect an increase of fluoride absorption whenever the luminal pH is rendered more acidic. Our results agree with this view since the absorption of fluoride was increased by a high concentration of HCl. This effect was also observed with the everted stomach incubated in a medium at pH 4.0 (unpublished data). The same dependence of fluoride permeation upon pH was reported for other epithelia.1-3 Although acid concentration in the lumen was raised by histamine, fluoride absorption did not change significantly. The lack of effect of histamine may be due 1) to similar levels of HF in basal and histamine treated groups, 2) to a back diffusion of the transported fluoride from the blood as was shown in vitro with the everted stomach preparation.5

Intravenous infusion of fluoride stimulated acid secretion only when aluminium was added to the perfusion solution. However, a stimulation of basal acid secretion was observed in the isolated mouse stomach with NaF present in the serosal medium,7 and in the rat drinking a water containing NaF for 60 days.8 It has been shown that NaF stimulates cyclic AMP formation in preparations of canine fundic and antral gastric mucosae.13 Aluminium has been shown to potentiate the effects of fluoride on the G proteins which regulate adenylate cyclase. Fluoride ions in the form of aluminium fluoride complex binds adjacent to GDP and apparently mimics the y-phosphate group of GTP.14 Similarly, aluminium potentiates the effect of fluoride to mobilize fibroblast intracellular stores of Ca2+,15 and to accelerate the influx of extracellular Ca2+ in endothelial cells.16 These findings suggest that fluoride with trace amounts of aluminium may act directly on protein G to
increase intracellular cyclic AMP and Ca$^{2+}$ responsible for the activation of H$^+$.K$^+$-ATPase located at the luminal membrane of the parietal cells. Another possible effect of NaF is to induce the release of histamine from the mast cells$^{17}$ which acts at parietal cell H$_2$-histamine receptor.

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FLUORIDE CONTENT OF DAIRY MILK FROM SUPERMARKET
A POSSIBLE CONTRIBUTING FACTOR TO DENTAL FLUOROSIS

Cuifeng Liu, a Leigh E Wyborny b and Jarvis T Chan b,c
Beijing, China and Houston, Texas, USA

SUMMARY: Fluoride analyses were carried out on 42 different types and brands of milk obtained from supermarkets. The average fluoride content of dairy milk is 0.030 ppm, with a range of 0.007 to 0.068. Soy milk contains as much as 0.491 ppm fluoride. Infant daily fluoride intake as low as 0.04 mg/kg body weight can result in fluorosis of the permanent dentition. Therefore, in view of the very large variation in milk fluoride content, it is suggested that daily consumption of milk with high fluoride content could be a contributing factor to increased prevalence of dental fluorosis. In view of results of the present study, monitoring of fluoride content in dairy milk available from supermarkets may be necessary.

Key words: Fluoride; Dairy milk; Dental fluorosis.

Introduction

The deciduous teeth undergo substantial mineralization during the first year of life, and fluoride provided during this period is reported to give significant protection against caries in deciduous teeth, when available from birth onwards. 1,2 During the first year of life, besides rapid bone growth, enamel formation in the primary teeth is being completed, and hard tissue formation has begun for the permanent central, lateral, canine and first molar teeth. When systemic fluoride is incorporated into the developing teeth, it is believed to increase the crystallinity of the enamel and possibly also to enhance the morphogenesis of the teeth by making the pits and fissures shallower. 3 Fluoride has therefore been widely used as a caries preventive agent both topically and systemically. 4,5

Milk is a universal food for newborn and growing mammals and contains all of the essential nutrients for their development and growth. Since purchased milk is consumed by a large percentage of children, the natural fluoride content in milk could conceivably play a significant role in enhancing the mineralization of deciduous teeth in children. 6,7 Milk has also been reported to be a useful vehicle to deliver fluoride to infants and young children for prevention of dental caries. 8,9 However, the dosage of fluoride to achieve optimum caries reduction appears to be extremely critical during the first year of life in order not to exceed levels which produce dental fluorosis.

According to the literature, the values for the fluoride content of cow's milk and milk formulas span a wide range, between 0.02-0.8 ppm. 10,11 It is the goal of this

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b Oral Biology Research Laboratory, Veteran Affairs Medical Center, Houston TX USA.
c (For correspondence) Department of Pharmacology, University of Texas Dental Branch, PO Box 20068, Houston, Texas 77225, USA.
study to determine the fluoride level in dairy milk available in the typical US supermarket.

Recent studies have reported an increase of enamel fluorosis in the population of US children.\textsuperscript{12} One of the suggested causes has been an increase of dietary fluoride intake by the children.\textsuperscript{13-15} Therefore, the second goal of this study is to determine if the variation of fluoride content of different types and brands of dairy milk available in supermarkets could be a contributing factor in enamel fluorosis in the child population.

**Materials and Methods**

Forty-two different types and brands of milk were purchased from supermarkets in the Houston, Texas, area. All samples were kept at 4°C in a refrigerator. Within five days, fluoride analysis of all the samples was carried out by the hexamethyldisiloxane-microdiffusion method reported by Taves.\textsuperscript{16} In order to facilitate the accuracy of fluoride determination, each milk sample was diluted 1:1, v:v, with an aqueous solution containing 0.19 ppm fluoride as sodium fluoride. This known amount of added fluoride was subtracted to provide the true fluoride content of the milk. The fluoride content of each milk sample recorded in this study represented the average value of quintuplicate analysis.

Fluoride measurements were performed with a Corning double junction reference electrode in conjunction with an Orion Research microprocessor pH/millivolt meter, Model 811. ANOVA and Tukey test were used to determine the significance of differences.

**Results**

The fluoride content of milk samples available from Houston supermarkets is rather low; however, it varies almost ten-fold, from 0.007 to 0.068 ppm (Table 1). Among the 42 different milk brands that were analysed for fluoride, 14 samples (33%) contained less than 0.02 ppm F; 20 samples (48%) contained 0.02 to 0.04 ppm F; and 8 samples (19%) contained more than 0.04 ppm F (Table 1).

Among the different types of milk, homogenized vitamin D milk contained the lowest fluoride content (0.018 ± 0.006 ppm), while the soy milk contained the highest fluoride content (0.491 ppm) (Table 2). The difference in fluoride content of these two types of milk was statistically significant (P<0.01). The fluoride content in protein fortified milk was also significantly greater than that in homogenized milk, (P<0.01).

Among the different brands of milk that were investigated, Oak Farms milk (0.042 ± 0.005 ppm) contained significantly (P < 0.05) more F than Borden milk (0.022 ± 0.005 ppm) (Table 3). With the exception of soy milk (a non-dairy soybean product) which has a fluoride content of 0.491 ppm, the average fluoride content of all the bovine milks that were analysed in this study was low (0.030 ± 0.02 ppm).
<table>
<thead>
<tr>
<th>MILK BRAND</th>
<th>F CONTENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apple-Tree; GA, P, H; vit D milk</td>
<td>0.019</td>
</tr>
<tr>
<td>Apple-Tree; lowfat milk; 2% milkfat; vit A &amp; D</td>
<td>0.043</td>
</tr>
<tr>
<td>Apple-Tree; GA, P; skim milk; vit A &amp; D</td>
<td>0.033</td>
</tr>
<tr>
<td>Borden; H; vit D milk</td>
<td>0.015</td>
</tr>
<tr>
<td>Borden; skim-milk; vit A &amp; D</td>
<td>0.013</td>
</tr>
<tr>
<td>Borden; Lite-line; GA, P, H; protein fortified; skim milk; vit A &amp; D</td>
<td>0.038</td>
</tr>
<tr>
<td>Borden; Hi-protein, 2% low fat; protein fortified; vit A &amp; D</td>
<td>0.039</td>
</tr>
<tr>
<td>Borden; Golden Churn, Cultured lowfat Buttermilk 1.5% milkfat</td>
<td>0.016</td>
</tr>
<tr>
<td>Borden; GA, P; Dutch chocolate milk; vit D</td>
<td>0.028</td>
</tr>
<tr>
<td>Borden; half and half</td>
<td>0.007</td>
</tr>
<tr>
<td>Dairy Ease; lactose reduced; nonfat milk; H; ultra-P; vit A &amp; D</td>
<td>0.040</td>
</tr>
<tr>
<td>Dairy Ease; lactose reduced, 1% lowfat milk; H; ultra-P; vit A &amp; D</td>
<td>0.026</td>
</tr>
<tr>
<td>Fiesta; GA, P, H; lowfat milk; vit A &amp; D</td>
<td>0.042</td>
</tr>
<tr>
<td>Fiesta; GA, P, H; vit D</td>
<td>0.013</td>
</tr>
<tr>
<td>Hygeia; H; vit D</td>
<td>0.022</td>
</tr>
<tr>
<td>Kroger; GA; vit D; 3.25% milkfat</td>
<td>0.016</td>
</tr>
<tr>
<td>Kroger; 2% milkfat, lowfat milk; vit A &amp; D</td>
<td>0.019</td>
</tr>
<tr>
<td>Kroger; GA, P, H; a blend of cream and milk; half and half; 10.5% milkfat</td>
<td>0.035</td>
</tr>
<tr>
<td>Lactaid; special digestible; lactose reduced; ultra-P; lowfat milk; vit A &amp; D</td>
<td>0.007</td>
</tr>
<tr>
<td>Lactaid; specially digestible; lactose reduced; H; ultra-P, lowfat milk, 1% milk; vit A &amp; D</td>
<td>0.015</td>
</tr>
<tr>
<td>Nestle; Quik chocolate milk; GA, P, H; vit D.</td>
<td>0.017</td>
</tr>
<tr>
<td>Nestle; Quik artificial flavor; GA, P, H; strawberry milk; vit D</td>
<td>0.019</td>
</tr>
<tr>
<td>Oak Farms; GA, P, H; vit D</td>
<td>0.035</td>
</tr>
<tr>
<td>Oak Farms; GA, P, H; vit A &amp; D; lowfat milk, 2% milkfat</td>
<td>0.031</td>
</tr>
<tr>
<td>Oak Farms; Cultured lowfat buttermilk, 1% milkfat</td>
<td>0.038</td>
</tr>
<tr>
<td>Oak Farms; Protein fortified skim milk; vit A &amp; D</td>
<td>0.040</td>
</tr>
<tr>
<td>Oak Farms; ultra-P; half and half</td>
<td>0.039</td>
</tr>
<tr>
<td>Oak Farms; chocolate milk</td>
<td>0.068</td>
</tr>
<tr>
<td>Olde Tyme; GA, H; ultra-P; Heavy whipping cream; 36% milkfat</td>
<td>0.027</td>
</tr>
<tr>
<td>Plum Flower; soy milk</td>
<td>0.491</td>
</tr>
<tr>
<td>Randall; GA, P; vit A &amp; D; 2% low milkfat</td>
<td>0.024</td>
</tr>
<tr>
<td>Schepps; GA, P, H; 2% lowfat milk; vit A &amp; D</td>
<td>0.033</td>
</tr>
<tr>
<td>Schepps; H; vit D</td>
<td>0.011</td>
</tr>
<tr>
<td>Schepps; cultured lowfat buttermilk; 1% milkfat</td>
<td>0.022</td>
</tr>
<tr>
<td>Schepps; protein fortified; skim milk; vit A &amp; D</td>
<td>0.050</td>
</tr>
<tr>
<td>Schepps; GA, P; half and half</td>
<td>0.063</td>
</tr>
<tr>
<td>Schepps; GA, P; chocolate milk</td>
<td>0.058</td>
</tr>
<tr>
<td>Sealtest; H; vit D</td>
<td>0.007</td>
</tr>
<tr>
<td>Sealtest; chocolate milk</td>
<td>0.038</td>
</tr>
<tr>
<td>Sealtest; cultured lowfat; buttermilk; 1% milkfat</td>
<td>0.032</td>
</tr>
<tr>
<td>Sealtest; ultra-P; half and half</td>
<td>0.050</td>
</tr>
<tr>
<td>Super Fresh; GA, P; vit D</td>
<td>0.027</td>
</tr>
</tbody>
</table>

GA = Grade A  
P = Pasteurized  
H = Homogenized
TABLE 2. RANGE AND MEAN FLUORIDE CONTENT OF DIFFERENT TYPES OF MILK IN PARTS PER MILLION

<table>
<thead>
<tr>
<th>MILK TYPE</th>
<th>RANGE</th>
<th>MEAN ± SEMa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Homogenized milk(9)</td>
<td>0.011 - 0.035</td>
<td>0.018 ± 0.006</td>
</tr>
<tr>
<td>Lactose reduced milk(4)</td>
<td>0.007 - 0.040</td>
<td>0.022 ± 0.007</td>
</tr>
<tr>
<td>Skim milk(6)</td>
<td>0.013 - 0.050</td>
<td>0.032 ± 0.005</td>
</tr>
<tr>
<td>Butter milk(4)</td>
<td>0.020 - 0.038</td>
<td>0.032 ± 0.005</td>
</tr>
<tr>
<td>Low fat milk(6)</td>
<td>0.024 - 0.043</td>
<td>0.035 ± 0.017</td>
</tr>
<tr>
<td>Half &amp; Half milk(5)</td>
<td>0.007 - 0.063</td>
<td>0.038 ± 0.009</td>
</tr>
<tr>
<td>Chocolate milk(5)</td>
<td>0.017 - 0.058</td>
<td>0.042 ± 0.009</td>
</tr>
<tr>
<td>Protein fortified milk(4)b</td>
<td>0.038 - 0.050</td>
<td>0.042 ± 0.003c</td>
</tr>
<tr>
<td>Strawberry milk(1)</td>
<td>0.019</td>
<td>0.019</td>
</tr>
<tr>
<td>Soy milk(1)</td>
<td>0.491</td>
<td>0.491</td>
</tr>
</tbody>
</table>

a Standard error of mean
b Three of these milks are also classified as skim milk
c Significantly differed from homogenized milk, P < 0.01

TABLE 3. RANGE AND MEAN FLUORIDE CONTENT OF DIFFERENT BRANDS OF MILK

<table>
<thead>
<tr>
<th>MILK BRAND (N)</th>
<th>RANGE</th>
<th>MEAN ± SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appletree (3)</td>
<td>0.019 - 0.043</td>
<td>0.032 ± 0.007</td>
</tr>
<tr>
<td>Borden (7)</td>
<td>0.007 - 0.039</td>
<td>0.022 ± 0.005</td>
</tr>
<tr>
<td>Dairy Ease (2)</td>
<td>0.026 - 0.042</td>
<td>0.030 ± 0.010</td>
</tr>
<tr>
<td>Fiesta (2)</td>
<td>0.013 - 0.042</td>
<td>0.028 ± 0.001</td>
</tr>
<tr>
<td>Hygeia (1)</td>
<td>0.022</td>
<td>0.022</td>
</tr>
<tr>
<td>Kroger (3)</td>
<td>0.016 - 0.035</td>
<td>0.023 ± 0.006</td>
</tr>
<tr>
<td>Lactaid (2)</td>
<td>0.007 - 0.015</td>
<td>0.010 ± 0.001</td>
</tr>
<tr>
<td>Nestle (2)</td>
<td>0.017 - 0.019</td>
<td>0.018 ± 0.001</td>
</tr>
<tr>
<td>Oak Farms (6)</td>
<td>0.031 - 0.068</td>
<td>0.042 ± 0.005</td>
</tr>
<tr>
<td>Olde Tyme (1)</td>
<td>0.027</td>
<td>0.027</td>
</tr>
<tr>
<td>Plum Flower, Soy Milk (1)</td>
<td>0.491</td>
<td>0.491</td>
</tr>
<tr>
<td>Randall (1)</td>
<td>0.024</td>
<td>0.024</td>
</tr>
<tr>
<td>Schepps (6)</td>
<td>0.011 - 0.058</td>
<td>0.040 ± 0.008</td>
</tr>
<tr>
<td>Sealfest (4)</td>
<td>0.007 - 0.050</td>
<td>0.032 ± 0.009</td>
</tr>
<tr>
<td>Super Fresh (1)</td>
<td>0.027</td>
<td>0.027</td>
</tr>
</tbody>
</table>

Discussion

The level of fluoride in milk has been a subject of disagreement for many years. With advances in analytical technology, the reported fluoride content has steadily declined. More recent studies have reported the level of ionic fluoride in bovine milk to range from 0.007 to 0.086 ppm, while those in human milk ranged from 0.009 to 0.065 ppm.14,17-20 Therefore, the fluoride content of cows' milk found in this study is within the range obtained by other laboratories.

However, unlike a previous report of 1978,20 the present study demonstrates large variation in fluoride content of different brands of milk, and even within the
same brand that is processed in a different geographical location. Thus, Borden milk processed in Columbus, Ohio, with a mean fluoride concentration of 0.022 ppm, contained the lowest level of fluoride; Oak Farms milk bottled in Dallas, Texas, with a mean fluoride concentration of 0.042 ppm, contained almost twice as much fluoride (Table 3). Such variation could be introduced by the difference in water fluoride content of the farms where these dairy cows are being raised and by the water fluoride level of factories where cows' milk was being processed.21,22

The fluoride content of milk may be influenced by the interaction between fluoride and milk, as well as by the wide variety of heat-treatment processes used for pasteurization.23,24 The variation in fluoride content between different brands and types of milk may be due to differences in the source of the "raw" milk, the heat-treatment, and the type of milk product.

On average, homogenized milk contained the lowest level of fluoride (0.018 ppm). This value is similar to values reported from other laboratories.20,22 The mean fluoride content of skim milk, buttermilk, low-fat milk, and "half & half" milk is slightly higher than that of homogenized milk and lactose-reduced milk. However, this difference is not statistically significant. Protein-fortified milk contains twice the amount of fluoride found in homogenized milk, and the difference is statistically significant at P<0.01. Five different brands of chocolate milk were also analyzed for fluoride: the values varied from 0.017 ppm (Nestle) to 0.058 ppm (Schepps), with a mean figure of 0.042 ppm. The above difference may due to variation in the fluoride content of water and/or cacao beans from which the chocolate was obtained.

Recently there has been growing concern about the increase in the prevalence of dental fluorosis in the US child population.12,15,25 It has been suggested that, apart from systemic fluoride supplementation,26,27 other potential contributing factors to dental fluorosis include fluoride in the water supply,15 canned juices,28 carbonated beverages,29 infant formulas,11,28 commercially prepared infant food,11,30 toothpaste used at an earlier age,31 and mouthrinses.15

Milk consumption in infancy and early childhood increases with the age and weight of the child. An infant may depend entirely on cows' milk for his or her daily source of caloric intake. Even though the average fluoride concentration in cows' milk is low, because of the very large variation in fluoride content of different brands of dairy milk, an individual dairy milk with an unusually high fluoride content could contribute significantly to the increase in prevalence of dental fluorosis in the US population. Although milk is known to interfere with the rate of fluoride absorption, a human study has demonstrated that 67 to 82% of total fluoride in milk is absorbed.32

A typical six-month old infant weighing about 7 kg consumes about 1.2 liters of fluid daily. If the fluid happens to be a certain brand of milk that contains 0.068 ppm fluoride, then the daily fluoride available from milk alone could be as much as 0.059 mg. In view of the estimation that, for infants, a daily intake of fluoride as low as 0.04 mg/kg body weight can result in dental fluorosis of the permanent dentition,33 a daily fluoride intake of 0.059 mg from milk will represent 21% of daily fluoride intake of the borderline (7 x 0.04 = 0.28 mg) for dental fluorosis. Even though consumption of milk alone is not likely to cause dental fluorosis, intake of
milk with high fluoride content together with fruit juices, beverages such as tea\textsuperscript{34} and baby food, especially those with meat containing considerably more fluoride than milk, the safety level of daily fluoride consumption could easily be exceeded by such combination of diet.

Furthermore, in infants who are allergic to cows’ milk, soy-based milk is often substituted, and this contains as much as 0.491 ppm fluoride (Table 1), easily exceeding the safety level for prevention of dental fluorosis. Health-care providers therefore need to take into consideration the fluoride level of the milk that is being consumed by their pediatric patients when prescribing fluoride supplementation. Results from the present investigation show that there is a need to monitor the fluoride content of milk available from supermarkets. Dairy companies should consider providing the public with information on fluoride content of all dairy products.

Acknowledgement

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WATER FLUORIDE IN THE MOLO DIVISION
OF NAKURU DISTRICT, KENYA

J K Gikunju,* J M Mbaria, W Mureithi, M N Kyule,
J J McDermott and T E Maitho
Nairobi, Kenya

SUMMARY: Water samples were collected from 40 households in four sublocations of the Molo division of the Rift Valley in Nakuru District of Kenya. The mean fluoride concentration was 0.28 ± 0.03 ppm. Of the samples collected, 62.5% were from streams/springs, 15.0% from tap water, 10.0% from borehole water, 10.0% from dam water, and 2.5% from rain water. Turi sublocation had 75% of the total number of boreholes in this study, and had the highest mean fluoride concentration (0.44 ± 0.06 ppm), whereas Kamara had the lowest mean fluoride concentration (0.19 ± 0.08 ppm). Kerisoi and Sachiagwan sublocation had mean fluoride concentrations of 0.21 ± 0.07 ppm and 0.32 ± 0.04 ppm, respectively. Borehole water had more fluoride (0.66 ppm) than any other water source, while rain water had the least amount of fluoride (0.07 ppm). The highest fluoride encountered in this study was 2.0 ppm while the lowest was 0.06 ppm.

Key words: Fluoride; Molo, Kenya; Water source.

Introduction

Kenya lies on the Eastern Coast of Africa and is bordered by the Indian Ocean and the Somali Republic on the east, by Ethiopia and Sudan on the north, by Uganda on the west, and by Tanzania on the south. Dental fluorosis has been endemic to eastern Africa and particularly in Kenya for many years,¹ and thus is an important public health problem. The sources of high fluoride are thought to be primarily from drinking water, particularly in the volcanic rock regions of the country.

Kenya has both surface and ground water sources. These sources, however, are limited in quantity and quality, and in many cases they are located far from the highly populated areas. Hence water has to be piped for long distances to the urban centres. Most of the rural population still continues to fetch water from rivers, springs, streams, and shallow wells, and to use it without any form of treatment. In most of the self-help water supply schemes, piped water is available but is untreated. All the urban centres have improved water supply systems, but in many cases they are not adequate to supply all the people. For this reason, the peripheral populations in these areas are in situations similar to those in the rural areas and have to depend on an unimproved water supply.

Materials and Methods

Molo subdivision is made up of 11 sublocations, of which four were selected using the random selection technique of Cannon and Roe.² The four selected sub-

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locations, namely Sachangwan, Kerisoi, Kamara, and Turi, had a total of 197 households of which 40 were selected by the same random technique. Water samples (Table 1) were obtained from the 40 households. The samples were collected in clean 500-mL polyethylene bottles, transported to the laboratory in a cool box, and then stored at -20°C while awaiting analysis, as in our earlier report on fluoride in borehole water around Nairobi.\(^3\) Prior to analysis each solution was adjusted to the same pH (5.0 to 5.5) with TISAB III (total ionic strength buffer, Orion \(\text{R} \ 940911\)).

<table>
<thead>
<tr>
<th>Sublocation</th>
<th>Total No</th>
<th>Tap</th>
<th>Stream</th>
<th>Dam</th>
<th>Borehole</th>
<th>Rain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sachangwan</td>
<td>7</td>
<td>4</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Kerisoi</td>
<td>13</td>
<td>1</td>
<td>8</td>
<td>3</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Kamara</td>
<td>10</td>
<td>0</td>
<td>9</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Turi</td>
<td>10</td>
<td>1</td>
<td>5</td>
<td>0</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>40</td>
<td>6</td>
<td>25</td>
<td>4</td>
<td>4</td>
<td>1</td>
</tr>
</tbody>
</table>

The pH and F levels were determined with a digital pH meter (Orion \(\text{R} \ 3020\)) and a F specific ion electrode (Orion \(\text{R} \ 96-09\)). Calibration of the F electrode was repeatedly checked with appropriate standards during the measurement.

Fluoride standard solutions (0.1, 1.0 and 10.0 ppm) were prepared by diluting a 100-ppm standard solution (Orion \(\text{R} \ 94-09-07\)) with deionised water.

Two parallel tubes were filled will 3.0 mL standard fluoride solution and 0.3 mL of TISAB III buffer was added to each tube before analysis.

A calibration curve was prepared from these standards.

The average relative millivolt value for each standard was plotted against the fluoride concentration on a 4-cycle semi-logarithmic paper. The difference between a ten-fold increase in fluoride concentration was between 54 and 60 relative millivolts.

**Results and Discussion**

Investigations of the fluoride content of African drinking waters have been reported by Ockerse from South Africa,\(^4\)\(^5\) by Williamson,\(^1\) by Manji and Kapila,\(^6\) by Gitonga and Nair,\(^7\) and by Karuiki et al\(^8\) from Kenya; and by Wilson\(^9\) from Nigeria. These studies are of special interest because they provide background information on fluoride levels in African water. Since the catchment basins in East Africa are composed primarily of basic volcanic rocks, fluoride is likely to be present in water in these areas.
TABLE 2.
Fluoride concentrations in water available for consumption in 4 sublocations in Molo

<table>
<thead>
<tr>
<th>Sublocation</th>
<th>Samples (n)</th>
<th>Mean F(ppm)</th>
<th>SD</th>
<th>Mean acreage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sachangwan</td>
<td>7</td>
<td>0.324</td>
<td>±0.04</td>
<td>17.9</td>
</tr>
<tr>
<td>Kerisoi</td>
<td>13</td>
<td>0.206</td>
<td>±0.08</td>
<td>8.18</td>
</tr>
<tr>
<td>Kamara</td>
<td>10</td>
<td>0.188</td>
<td>±0.08</td>
<td>4.5</td>
</tr>
<tr>
<td>Turi</td>
<td>10</td>
<td>0.443</td>
<td>±0.06</td>
<td>82.5</td>
</tr>
</tbody>
</table>

The mean fluoride concentrations from the four sublocations (Table 2) were significantly different (P<0.05) after statistical analysis by the Statview program. It is interesting that the mean acreage varies proportionally with the mean fluoride concentration for each sublocation. A regression test revealed that acreage and fluoride are highly related (p=0.0552). This observation may be due to difference in soil type or climatic variation. Kerisoi and Kamara sublocations are fairly wet as compared to Turi and Sachagwan. However, the relationship between acreage and fluoride cannot be explained entirely in this way. Turi sublocation has higher mean fluoride than other sublocations probably because it also contains three of the four borehole samples.

TABLE 3.
Mean fluoride concentrations for the various sources of water in Molo

<table>
<thead>
<tr>
<th>Water source</th>
<th>no of samples (%)</th>
<th>mean F(ppm)</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tap</td>
<td>6 (15)</td>
<td>0.327</td>
<td>±0.151</td>
</tr>
<tr>
<td>Stream</td>
<td>25 (62.5)</td>
<td>0.232</td>
<td>±0.101</td>
</tr>
<tr>
<td>Dam</td>
<td>4 (10)</td>
<td>0.199</td>
<td>±0.092</td>
</tr>
<tr>
<td>Borehole</td>
<td>4 (10)</td>
<td>0.657</td>
<td>±0.0901</td>
</tr>
<tr>
<td>Rain</td>
<td>1 (2.5)</td>
<td>0.07</td>
<td>-</td>
</tr>
</tbody>
</table>

Borehole water contains higher fluoride concentration than other sources of water (Table 3). After analysis of 1286 samples, Gitonga and Nair\(^7\) found that 61% of the samples had fluoride concentration above 1 ppm, while Gikunju \(et\ al\)\(^3\) reported 80% of their samples had more than 1 ppm fluoride. These studies involved borehole samples only. In the present study all sources of water were considered, and only 10% were borehole water and only 2.5% contained fluoride above 1 ppm.
Borehole water in this study contains more fluoride (0.66 ppm) than any other water source. However, only 10% of the households are exposed to the borehole water. Most households consume water from streams and springs. Apparently rain water also contains low amounts of fluoride, but only 2.5% of households depend on rain water.

Other households also use rain water but to a lesser degree. Perhaps some people are shy to indicate that they use rain water for domestic consumption, yet rain water is relatively safe according to our study.

Most of the households in Molo (62.5%) use streams or springs as their source of water, mainly because rural water development projects have not been initiated, possibly because the majority of the people settled in Molo fairly recently.

Acknowledgements

The authors are grateful for financial support given by the Norwegian Agency for International Development (NORAD), and the Canadian International Agency for Development (CIDA).

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5 Ockerse T. *Dental Caries: Clinical and Experimental Investigations*. Department of Public Health (South Africa), Pretoria 1949.
INTESTINAL EFFECTS OF SODIUM FLUORIDE
IN SWISS ALBINO MICE

H Sondhi, M L Gupta and G L Gupta
Bikaner, India

SUMMARY: Adult Swiss Albino mice (6-7 weeks old) were treated with sodium fluoride (NaF) until autopsy. The organo-somatic index, histology and biochemistry of the intestines were observed at commencement of treatment and on the 7th, 15th and 30th day. The crypt cells exhibited cytoplasmic degranulation and vacuolation. Hydropic degeneration in lamina propria and muscular tissue, increase in the number of goblet cells, broken tips of villi, nuclear pyknosis, and abnormal mitoses were observed. The organo-somatic index decreased significantly on days 7 and 15. Total protein and cholesterol values declined significantly, whereas those of glycogen and acid, and alkaline phosphatase activities, increased significantly on day 7 and to day 30. The results provide evidence of intestinal involvement in fluorosis.

Key words: Intestinal effects; Sodium fluoride; Swiss albino mice.

Introduction

Fluoride in drinking water is easily absorbed by the intestines\(^1\) and is quickly distributed throughout the body. Fluoride easily crosses membranes and enters tissues, thus affecting every phase of metabolism.\(^2\) Bones and teeth especially are the sink for fluoride, which accumulates in them and causes fluorosis.\(^3\) Only limited work has been done, however, on the toxicity of fluoride on soft tissues, viz liver,\(^4\) kidney,\(^5\) muscles,\(^6\) and testes\(^7\). The aim of the present study, therefore, was to examine the effects of NaF in the intestines of Swiss albino mice.

Material and Methods

Twenty adult healthy Swiss albino mice (6-7 weeks old) were selected from our mice colony and treated as follows. The animals were fed mice feed and given sodium fluoride in water (100 ppm \textit{ad libitum} until autopsy). Five mice were sacrificed by cervical dislocation on days 0, 7, 15, 30 from commencement of treatment. Three parameters were studied:

1. Organo-somatic index \(= \frac{\text{weight of the organ x 100}}{\text{total body weight}}\)

2. Histological study: a piece of intestine was fixed in Bouin’s fluid. After routine procedure 5-micron sections were cut and stained with haematoxylin and eosin.

3. Biochemical studies: the parameters estimated were total proteins,\(^8\) glycogen,\(^9\) cholesterol,\(^10\) and acid and alkaline phosphatase activities\(^11\).

Results and Discussion

The values of the organo-somatic index decreased significantly on day 7, continuing to day 15. The value increased by day 30, but it was still significantly lower than the 0-day value (Table 1). This decrease may be attributed to weight loss, degeneration of organs, and decreased protein levels. The functional sterility, with alterations in the structure, function, and metabolism of soft tissues in mice, rats, and rabbits administered different doses of fluoride has been observed.\(^12,13\)

Zoology Department, Dungar College, Bikaner 334 001, India.
<table>
<thead>
<tr>
<th></th>
<th>0 day</th>
<th>7 days</th>
<th>15 days</th>
<th>30 days</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>8.36 ± 0.060</td>
<td>7.05 ± 0.056</td>
<td>6.83 ± 0.048</td>
<td>7.77 ± 0.042</td>
</tr>
<tr>
<td></td>
<td>P&lt;0.001</td>
<td>P&lt;0.001</td>
<td>P&lt;0.001</td>
<td>P&lt;0.001</td>
</tr>
</tbody>
</table>

Histopathological changes observed in intestine included increased numbers of goblet cells in the villi and in the crypts, loosened muscular part, cytoplasmic degranulation and vacuolation, nuclear pyknosis, and abnormal mitoses. Lymphocytic infiltration was widespread in sub-mucosa and lamina propria. The lesions were observed by day 7 and continued up to day 30, being severe by day 15 (see Figures 1-4 below, photomicrographs of intestines).

1. 0-Day. Almost normal structure. x 640
2. 7-day. Increased goblet cells, loosened muscular part, cytoplasmic changes. x 640
3. 15-day. Broken villi tips (arrow), cell debris in lumen. x 320
4. 30-day. Lymphocytic infiltration, cytoplasmic changes, nuclear pyknosis, abnormal mitoses. x 640
Biochemically significant decreases were noted in the values of total proteins, cholesterol from day 7 up to day 30, and increases in glycogen and acid and alkaline phosphatase activities from day 7 to day 30. Their values were significantly higher than the 0-day values (Table 2).

**TABLE 2.** Changes in the values (mean ± S.E.) of biochemical parameters in intestine of Swiss albino mice after sodium fluoride treatment.

<table>
<thead>
<tr>
<th>Biochemical parameters</th>
<th>0-day</th>
<th>7 days</th>
<th>15 days</th>
<th>30 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total proteins (mg/gm tissue weight)</td>
<td>95.32 ± 1.23</td>
<td>91.23 ± 1.26</td>
<td>84.20 ± 1.85</td>
<td>79.45 ± 2.23</td>
</tr>
<tr>
<td>Glycogen (mg/gm tissue weight)</td>
<td>0.96 ± 0.011</td>
<td>1.16 ± 0.010</td>
<td>1.54 ± 0.012</td>
<td>1.83 ± 0.12</td>
</tr>
<tr>
<td>Cholesterol (mg/gm tissue weight)</td>
<td>3.13 ± 0.012</td>
<td>2.47 ± 0.011</td>
<td>2.23 ± 0.016</td>
<td>2.11 ± 0.015</td>
</tr>
<tr>
<td>Acid Phosphatase Activity (mg pi/gm/hr)</td>
<td>1.86 ± 0.032</td>
<td>2.36 ± 0.045</td>
<td>2.85 ± 0.036</td>
<td>3.13 ± 0.052</td>
</tr>
<tr>
<td>Alkaline Phosphatase Activity (mg pi/gm/hr)</td>
<td>22.36 ± 0.21</td>
<td>26.54 ± 0.23</td>
<td>30.36 ± 0.34</td>
<td>32.67 ± 0.27</td>
</tr>
</tbody>
</table>

Decreased total serum proteins in rabbits ingesting fluoride has been reported. Protein metabolism has also been shown to be affected by fluoride.

After NaF treatment, an increase in glycogen values of muscle and liver has been observed. This may be attributed to reduced utilization of glycogen due to alteration in the activity of some key enzymes of carbohydrate metabolism. The *in vitro* and *in vivo* oxidation of fatty acids has been reported to be inhibited by fluorides. The increase in acid and alkaline phosphatase activities following NaF treatment may be due to disruption of lysosomes. Elevated plasma alkaline phosphatase and calcium levels have been found in endemic fluorosis areas. Gastro-intestinal manifestations are major features of intolerance to fluorides.

**Acknowledgement**

The authors are grateful to the Head, Zoology Department, and to the Principal, Dungar College, Bikaner, India, for their constant encouragement and for providing facilities.

**References**


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REPORT OF THE SIXTH FLUORINE SYMPOSIUM IN POLAND

Anna Machoy-Mokrzynska
Szczecin, Poland

The successful Sixth Fluorine Symposium, organized by Professor Z Machoy, was held in Szczecin on September 15 1994. The conference was attended by over 50 persons from Poland and abroad. The program comprised nine submitted papers and 24 communications presented in the form of posters.

The first paper, “Influence of fluoride on energy metabolism in vitro and in vivo and related biological effects”, was presented by Professor M Guminska of Cracow. The author concentrated her attention on possible interactions of fluorine and magnesium, which appears in many enzymes and participates in the process of ATP formation (Mg-ATP). It was shown that the process of great significance for energy generation was glycolysis, while the enzyme sensitive to fluoride was pyruvate kinase which takes part in ATP formation.

Professor Z Machoy and Professor J Straszko, of Szczecin, in their paper “An attempt to establish the relationship between distribution of fluorine compounds from industrial emission and fluoride content in fallow deer bones”, dealt with their verification of the established Polish norms for permissible emission of fluorine compounds, and reported fluoride accumulation in bones of forest animals living in regions of Western Pomerania. Despite modification and modernization of many industrial technologies, as well as the decrease in phosphate fertilizer production, the animals living at large do accumulate more fluorine in bones that the control animals from other regions of Poland.

A continuation of studies on the effect of industrial emissions on forest animals was presented in the paper “Severe chronic fluoride intoxication in free ranging red deer (Cervus elaphus) from Northwestern Bohemia (Czech Republic)” by Dr H Kierdorf et al of Germany. The authors reported new results of their investigations into changes in dentition (dental fluorosis) in deer inhabiting the area of the Czech Republic contaminated by industrial emissions.

The paper submitted by Professor J Franke of Germany, “Neue aspekte zur bestimmung des nüchternserumfluorspiegel beim therapiemonitoring der osteoporose”, reported results of treating osteoporosis with various preparations containing fluorine compounds.

Assistant Professor K Opalko-Klucznik of Szczecin, in her paper “Enamel defects in children living in a fluoridated water area”, described the morphological changes and defects in children’s teeth caused by tap water fluoridation.

Dr H Minta from the Institute of Veterinary Science, Pulawy, in his communication “Fluorine and other toxic compounds and reproduction”, discussed the possible interactions of microelements, particularly between fluorine and selenium,
in the processes of embryo- and fetogenesis. Due to the possibility of teratogenic action, the small difference between an indispensable dose and a toxic one is of essential significance. It is hard, in the opinion of the author, to find out the margin of safety for doses of the two elements.

The next paper, "Adaptive mechanisms in chronic poisonings by fluorine compounds", was presented by Dr A Machoy-Mokrzynska of Szczecin. On examples of different species of plants and animals it was disclosed that, after protracted exposure to fluorine compounds, the organisms acquire certain protective (adaptive) mechanisms. The content of fluorine in the tissues keeps increasing to a certain point, reaches a peak, and gets stabilized at that level. Further exposures fail to cause any increase of fluorine in the tissues, but not infrequently a tendency to a decrease may be noticed.

Professor D Chlebna-Sokół of Łódź, in her paper "Usefulness of some biochemical indicators for evaluating the influence of excessive fluorine on children's skeletons during intensive development", reported extensions of previously published studies of children from the locality, where the drinking water had an excessive content of fluorine. The biochemical indices pertaining to the bones, and the anthropological investigations, appeared to be extremely useful for evaluating the negative influence of fluorine compounds on the overall growth process at the period of puberty.

The last communication at the plenary session was the paper by Professor E Czerwinski of Cracow, "Computerised x-ray image analysis in the diagnosis of fluorosis". The author provides a method of modern computer analysis of the radiological image, which facilitates a description of bone structure and specific features of fluorosis.

Twenty-four communications, derived from experimental studies, were presented in the poster session. They covered the following problems: analytic methods for determining fluoride in various materials, including milk and fodder mixtures for poultry and swine; the role of fluoride in the formation of urinary calculi; content of fluoride in serum, urine, nails, and bones; and the effects of fluoride on dentition, embryonal and individual development (in sheep, experimental rats, hamsters and chickens), on metabolism of chemical compounds (glucose, basic phospholipids, activities of enzymes) and on plants (gladiola, algae, vegetables, conifers).

A lively discussion followed the posters presentation. The problem that is almost always debated is, undoubtedly, the verification of analytical methods. Attention was focussed on the necessity of properly preparing biological material for fluoride determination, an area which often gives rise to reservations about findings.

The Sixth Fluorine Symposium in Szczecin was the summing-up of 15-year-long studies on fluorine metabolism in Poland. The Szczecin Centre has come to be the co-ordinator and organizer of meetings, attended by fluoride researchers in Poland and neighbouring countries (Germany, Czech Republic, Hungary) in order to present their results and exchange experiences. The publication of the
book, *Metabolism of Fluorine '94* (Szczecin, 1994), containing the papers and communications of this Symposium, was made possible by the sponsorship of the Ministry of Health and Social Welfare in Poland. The Introduction was written by the Editor of *Fluoride*, Dr John Colquhoun of Auckland, New Zealand.

**INTRODUCTION TO THE SIXTH FLUORINE SYMPOSIUM IN POLAND**

John Colquhoun  
Auckland, New Zealand

We of the international community of fluoride researchers warmly congratulate all participants in the Sixth Fluorine Symposium in Poland. Science, the pursuit of truth about our world and universe, is an international undertaking involving free and unimpeded exchanges of information and research findings. When human freedoms are curtailed, knowledge and truth suffer. The Polish people’s struggles for truth and freedom have become an inspiration to us all. True internationalism does not mean a lessening of national pride. The Polish nation has much to be proud of in many areas of human endeavour.

In far-away Aotearoa/New Zealand, our problems seem small in comparison with the stupendous experiences of the Polish people. But we do know something of the difficulties met in pursuing the goals of truth and freedom. We have rejected nuclear weapons, despite enormous pressures from a major superpower. We refuse to invest in nuclear power plants, despite commercial pressures to do so. To us, the happenings in Hiroshima and Nagasaki in Japan in 1945, and in Chernobyl in the Ukraine in 1986, are nightmares and terrible lessons for human kind.

The contributions of Polish researchers to our understanding of fluoride toxicity have been mighty. You have much to teach us, in New Zealand and elsewhere. A summary of your last Symposium, and some of the excellent Polish research reported then and later, have been, or will soon be, published in *Fluoride*. The works of Professor Z Machoy and his colleagues at the Pomeranian Medical Academy in Szczecin have added to world knowledge of fluoride effects, as have the works of Professor J Krechniak and his colleagues at the Medical Academy in Gdansk. Work which attracted particular interest worldwide was the research of Dr D Chlebna-Sokół of Łódź and Professor E Czerwinski of Cracow, reported to the last Symposium and later published in *Fluoride*. Their discovery, using computerized X-ray image analysis, of bone structure disturbances in male children who have dental fluorosis, was of great significance - following as it did American reports of a fluoride dose-related carcinogenic effect (osteosarcoma) on bones of males in animal experiments. The Polish authors suggested that the greater effect on boys reflected a greater influence of fluoride on mineralization in the earlier period of development, because boys develop later than girls. However, it has subsequently been pointed out that the greater effect of fluoride on boys’ bones could be because low fluoride concentrations can depress testosterone synthesis. The shutting off of
bone growth in boys, by the production of testosterone, takes longer than the shutting off in females, which involves oestrogen. Some American authors\textsuperscript{10,12} have attached great significance to the fact that osteosarcoma, a rare bone cancer, has increased dramatically among teenage boys in fluoridated areas of America but not in non-fluoridated areas.\textsuperscript{13,14} No doubt further research will throw more light on this intriguing question.

We look forward to receiving more interesting reports on the progress of Polish and European fluoride research, following this Sixth Fluorine Symposium.

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INORGANIC FLUORIDES
CANADIAN ENVIRONMENTAL PROTECTION ACT
(PRIORITY SUBSTANCES LIST ASSESSMENT REPORT)
GOVERNMENT OF CANADA 1993

Reviewed by Richard G Foulkes
Abbotsford, British Columbia, Canada

Summary of Report

Objectives

The publication, Inorganic Fluorides (Priority Substances List Assessment Report) 1993 was prepared by the Government of Canada pursuant to the Canadian Environment Protection Act (CEPA). This Act requires the Federal Ministers of the Environment and of Health to prepare and publish a Priority Substances List that identifies substances that may be harmful to the environment or constitute a danger to human health.

"Toxic" is defined in Section 11 of the Act: "... a substance is toxic if it is entering or may enter the environment in a quantity or concentration or under conditions (a) having or that may have an immediate or long-term harmful effect on the environment; (b) constituting or that may constitute a danger to the environment on which human life depends; or (c) constituting or that may constitute a danger in Canada to human life or health."

The Report states that "the assessment of whether 'inorganic fluorides' are 'toxic', was based on the determination of whether they enter or are likely to enter the Canadian environment in a concentration or quantities or under conditions that could lead to exposure of humans or other biota at levels that could cause adverse effects" (emphasis in the original).

Methodology

The Report states that the data used in the study were derived from studies of humans and laboratory animals exposed to different forms of inorganic fluoride compounds. Data regarding human health published after July 1993, and on the environment after April 1993, were not considered for inclusion.

With respect to the effects of fluoride on human health, it is stated: "neither dental fluorosis nor the beneficial effects of fluoride in the prevention of dental caries have been assessed in this report".

The principal inorganic fluorides assessed were: hydrogen fluoride (HF); calcium fluoride (CaF₂); sodium fluoride (NaF); and sulphur hexafluoride (SF₆).

Conclusions

The conclusions were: a) that inorganic fluorides are entering the environment in quantities or under conditions that may be harmful to the environment; b) there is insufficient information to conclude whether sulphur hexafluoride is entering the environment in quantities or under conditions that may constitute a danger to the environment on which human life depends (ie, global climate change); and c) that inorganic fluorides (ie, the fluoride ion derived from such inorganic substances) are not entering the environment in quantities or under conditions that may constitute a danger to human life or health.

Dr Richard G Foulkes, PO Box 278, Abbotsford BC, Canada V2S 4N9.
Discussion

The strong suit in this study is the concise review of the properties, production and uses of inorganic fluorides, and the review of the known effects of anthropogenic sources of fluoride on plants and other biota such as ungulates and aquatic species.

In a section entitled “Ecotoxicity”, the Report discusses a number of key studies, selected on the basis of “proper controls, measured toxicant concentrations, acceptable protocols and identification of the most sensitive biota”.

From these, those responsible for the study deduced that inorganic fluorides are entering the Canadian environment at concentrations that may cause long-term harmful effects to biota in aquatic and terrestrial ecosystems. For example, with regard to the effects on aquatic organisms, the authors extrapolate laboratory findings to the field, to yield estimated adverse effect thresholds (lethal, growth impairment, and decreased egg production) of 0.28 mg/L fluoride for fresh water species and 0.5 mg/L fluoride for marine species. These are exceeded by many anthropogenic sources.

With regard to the adverse effects of inorganic fluoride, especially air emissions, the authors review inorganic fluoride toxicity to plants and animals, especially herbivores. The white-tailed deer consuming contaminated browse, was used as a “model”. The authors concluded that inorganic fluorides from anthropogenic sources result in concentrations in some Canadian plants and air that may cause long-term adverse effects to biota in terrestrial ecosystems.

The weakness of this Report that could rob it of total credibility is the obvious protection of the Government-sanctioned process of adding inorganic fluoride to drinking water. In the preceding example of the effects thresholds for aquatic organisms, no mention is made that one of the anthropogenic sources discharging inorganic fluoride into Canadian water that exceed these, is effluent from fluoridated cities that may persist, in fresh water, for some distance.

In fact, the absence of an estimate of inorganic fluoride from this source, in the text and in the accompanying table (Table 1), is conspicuous.

Total inorganic fluoride emitted to the environment annually in Canada from anthropogenic sources is estimated to be 23,500 tonnes. The amount released to the water is estimated to be 13,500 tonnes, 80% of which is attributed to phosphate fertilizer production (11,000 tonnes). The authors give indirect evidence to enable the reader to calculate that approximately 10 million people in Canada are “fluoridated” and that the annual release of inorganic fluoride from this source is approximately 2000 tonnes. This puts this source in second place, behind phosphate fertilizer production, but ahead of chemical production (1362 tonnes), coal-fired power (555 tonnes), primary aluminum production (307 tonnes), and others that are identified.

In the Recommendations of the Report a request is made for information on the extent of releases from municipal drinking water fluoridation. With the authority of the Government of Canada and two Ministries, it is surprising that this information was not obtained during data collection.
The conclusion that "inorganic fluorides (i.e., fluoride ions) are not entering the environment in quantities or under conditions that may constitute a danger to human life or health" is derived from a somewhat tautological argument.

The Report presents a digest of previously published reviews and secondary sources that deal with the possible adverse effects of inorganic fluoride on human health. Like previous assessments of inorganic fluoride and human health to be found in recent literature, dental fluorosis is not considered an "adverse effect". In fact, this Report ignores this effect except with regard to its occurrence in herbivores and that it does occur at a lower intake in humans than that required for skeletal changes.

The Report presents (Table 3) an estimated intake of inorganic fluoride by the general population of Canada. This table shows intake by various age groups in micrograms per kilogram body weight per day (µg/kg bw/day). It includes breast-fed and formula-fed infants and all age groups exposed to "fluoridated" and "non-fluoridated" water. The table appears to have been prepared largely from studies reported by the Environmental Health Directorate in 1992. The Table is comprehensive in as much as it shows intake from ambient air, food, soil, water (both "fluoridated" and "non-fluoridated") and household products.

Those responsible for the Report state that "available information is considered inadequate ... to assess the carcinogenicity of inorganic fluoride in humans" and recognize that the dose-response trend in the occurrence of osteosarcoma in rat experiments cannot be dismissed. The authors also recognize that there is evidence that fluoride is genotoxic, based on the outcome of in vitro and in vivo studies, and that this may be an effect of fluoride that results from its inhibition of enzymes involved in DNA synthesis and/or repair.

The authors, also, show that they have reservations regarding the potential of adverse effects upon human reproduction, development, or the central nervous and immune systems, at levels required to produce skeletal effects.

Nevertheless, the authors opt to consider that effects on the skeleton are more relevant than others in assessing the toxicological effects of long-term exposure to inorganic fluorides.

The authors present data from a number of studies and conclude that potentially adverse effects associated with skeletal fluorosis are likely to be observed at intakes of greater than approximately 200 µg/kg bw/day fluoride. Based on the information that estimated daily intakes of inorganic fluoride range from approximately 0.5 to 160 µg/kg bw/day by various age groups in the population, the authors conclude that these are less than the level at which adverse effects on the skeleton are anticipated.

**Conclusion**

This assessment document is an interesting addition to the literature on inorganic fluoride. The sections devoted to the ecological effects of emissions in Canada from anthropogenic sources point to serious adverse effects on aquatic and terrestrial biota. These suggest, also, that there is a need for further study of sulphur hexafluoride and its possible role in global climate change.
Overall, the Report suffers from the obvious attempt to defend the current support of fluoridation of drinking water. The deliberate omissions in the study are evidence of this, in addition to the acceptance, in the section on human health, that the development of crippling skeletal fluorosis is the adverse effect for which a threshold should be determined.

If these omissions had been included in the Report, the quantity and concentration of emissions into the aquatic ecosystem from fluoridated communities would have been shown to exceed the effect thresholds for aquatic life.

In addition, consideration would have been given to the growing view, even of a spokesman from the Canadian Dental Association, that systemic fluoride does not prevent caries, but topical fluoride may have a "remineralization" effect on incipient caries.

Finally, if dental fluorosis, as a clinical entity, had been fully discussed, the Report would have to present the view that it represents a continuum developing in severity along with skeletal changes. If dental fluorosis, in humans, were to be accepted as an "adverse effect", as it is in herbivores, it could easily be shown that the intake of inorganic fluoride by children living in fluoridated areas of Canada easily exceeds the effects threshold.

This Report, in spite of some excellent sections on such aspects as ecotoxicity, lacks credibility as, once again, the politics of fluoridation have pre-empted objectivity and science.

Reference
WATER FLUORIDATION IN NEW ZEALAND:
AN ANALYSIS AND MONITORING REPORT
Public Health Commission Rangapu
Hauora Tumatanui, Wellington 1994

Reviewed by Bruce Spittle
Dunedin, New Zealand

In introducing this 128 page report, published in July 1994, Dr Gillian Durham, Chief Executive of the Public Health Commission (PHC), notes that fluoridation of public water supplies, as a means of promoting dental health, continues to be a contentious public health issue in New Zealand as well as other countries such as Australia and the United States. The PHC considered that it was time to review the evidence concerning the safety and effectiveness of fluoridation so that water supply authorities, and the communities they serve, could make informed decisions about fluoridation. Public submissions were invited on an initial draft entitled Fluoridation of Water Supplies: Draft Policy Statement released in May 1993. It had been prepared for the PHC by E Treasure, B Drummond, H Buchan, M Beasley, M Henaghan and B Nicholas. Dr Nicholas Wilson considered the 82 submisssions received on the draft and prepared the final report. He acknowledged that the review had been essentially written by only one person with experience in only particular areas, primarily public health medicine, epidemiology and clinical medicine, so that it was not possible to achieve the depth of analysis required in all the fields involved such as clinical dentistry, toxicology, environmental health, immunology, risk assessment, public health dentistry, risk perception psychology, sociology and public health ethics. It was also necessary, because of the vast literature on fluoride and health, to place some reliance on the quality of the previous reviews that had been conducted. It was acknowledged that there were limitations with some of these and that they in turn may have tended to place unwarranted weight on the findings of previous expert reviews. Emphasis was placed on several key reviews including Health Effects of Ingested Fluoride by the National Research Council in the USA, Review of Fluoride: Benefits and Risks by the US Public Health Service, and The Effectiveness of Water Fluoridation by the National Health and Medical Research Council of Australia. A total of 1592 listings and abstracts from the Medline database for the 1989-1993 time period were obtained. The books critical of fluoridation that were examined included Fluoridation: The Great Dilemma by Waldbott, Burgstahler and McKinney, and Fluoride: The Freedom Fight by Moolenburgh.

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The Executive Summary in the report reviews the health and non-health benefits and costs of water fluoridation. The report acknowledged that an unequivocal assurance that fluoridation was safe could no longer be given. An earlier 1957 New Zealand Report of the Commission of Inquiry on the Fluoridation of Public Water Supplies had found that fluoridation was a public health measure that was not merely beneficial but also safe, and that no harmful effects on health would follow the fluoridation of water supplies. In contrast the 1994 report found that it was possible that there was a small increased risk of hip fracture associated with water fluoridation and that the possibility of a similar increased risk of osteosarcoma in young men could not be ruled out. It was acknowledged that fluoridation encroached on the individual freedom of those who did not wish to consume fluoridated water with some people having to purchase bottled water or use expensive filters. Although fluoridation was seen to possibly degrade the spiritual value of water for some Maori, it appeared, from the limited evidence available, that if some access to “pure water” was maintained, Maori favoured fluoridation overall for its benefits to dental health. It was considered that aspects of the controversy over water fluoridation had probably led to some loss of public trust in public health authorities and dental professionals. It was estimated that the lifetime benefit for the average New Zealander drinking fluoridated water was the prevention of a total of 2.4 to 12.0 decayed, missing or filled teeth. Water fluoridation was seen to also contribute to equity of health outcomes with the benefit of dental caries prevention being greater for those in lower socioeconomic groups, Maori and children. Prevention occurred also of dental abscesses and more rarely serious infections such as infective endocarditis. At the present level of coverage of the population with 50% receiving fluoridated water, the net savings for New Zealand society were seen to be in the range of $1.4 to $14.3 million per year, representing between 58,000 and 267,000 decayed, missing or filled teeth in New Zealand per year.

Comparing the health benefits and costs was seen as difficult as the levels of risk involved were not all known. It was considered that, with the current state of knowledge, most health professionals put significant weight on the overall benefits of water fluoridation for improving oral health and achieving equity of health status outcomes. However it was seen that members of the public may have more concern for individual rights and the unknown risks. A high degree of informed public input into deciding about water fluoridation was seen to be critical for democratic reasons and the necessity for value judgements about possible but unknown risks. Achieving informed citizen participation was seen to be more likely with citizen's panels or mixed citizen/expert panels rather than referenda. A high
requirement for further information on the benefits and costs of fluoridation was seen to remain, to ensure a properly informed debate and to minimise the levels of uncertainty.

It is likely that supporters of fluoridation will find reassurance in the report and consider that an impartial and objective review of the evidence in 1994 vindicates the judgement and vision of those responsible for its introduction. Those with doubts about the safety, efficacy and ethical correctness of fluoridation may not be persuaded to change their minds. The reassurance that, apart from hip fracture, osteosarcoma and mottled enamel, there is no scientific basis for concern about other health effects from exposure to fluoridated water at the level of one part per million (ppm), may not be convincing. Critics are presented as being somewhat naive and gullible with Waldott described as admitting that he had no formal research training and that his studies were not double-blind but relied on personal intuition. This does not seem to be in accordance with the published literature where double-blind studies are described. It suggests a tendency to denigrate the stature of critics rather than to look objectively at the arguments presented. It is perhaps symbolic of the lack of familiarity with Waldott’s pioneering work that the first mention of his name in the report on page 6 is misspelt as “Walbott”. The claim by Mooenburgh’s group of a double blind test for intolerance to fluoridated water is doubted because no evidence was presented that the subjects could not distinguish between samples by taste. The finding by Susheela et al. that fluoride in water, at levels comparable to those used in fluoridation, may cause gastrointestinal symptoms is rejected because of the lack of a comparison group with very low fluoride levels and the high prevalence of other gastrointestinal diseases in India. No reference is made to an earlier paper by Susheela et al., where a comparison group using water with a lower fluoride level of 0.36±0.19 ppm, who were screened for ova, cysts and worms, was described. No reference is made to the scanning electron microscopic studies done in rabbits and humans. No critique is made of the arguments presented in Fluoride: The Aging Factor.

Thus Water Fluoridation in New Zealand may be seen as sound and scientific, or superficial and selective, depending in large part on the prior position of the reader. This reviewer inclines towards the latter view.

References


STUDIES ON FLUORIDE-ALUMINUM COMBINED TOXICOSIS

Z D Wei, F Li, L Zhou, X Chen and G Dai
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Abstracted from papers presented at the XXth Conference of the International Society for Fluoride Research, Beijing, China, September 5-9, 1994, and published in the Journal of Guiyang Medical College.

1. Environmental Sanitation and Epidemiology

In the Shuicheng area of Guizhou Province more than 1500 people were examined and screened for F-Al combined toxicosis. Blood and urine from patients and normal youths in the endemic area were collected and assayed for F and Al. X-ray pictures of the two groups were taken and analyzed, and an investigation of the environment was also conducted.

The results revealed that the patients belonged to families in which corn dried by burning coal mixed with kaolin was eaten. Among the people examined, 50 had osteomalacia, corresponding to an incidence of 3.95%. For the youths who were less than 20 years old, the morbidity was 6.13%.

The Al and F contents in the blood and urine of the patients were significantly higher than those of the control group. Al levels in blood and urine of sick children were significantly higher than those of normal children in the toxicosis area where the grain dried by burning the coal mixture absorbed large amounts of aluminum.

Biochemical tests on 84 patients and 47 normal people disclosed that the levels of lactic dehydrogenase (LDH) and creatine phosphate kinase (CPK) activities as well as the contents of Cu and P were increased (p < 0.001), but the alkaline phosphatase (ALP) level decreased.

The level of lipoxygenase (LPO) and antioxidation were measured on 12 sick children and 21 normal children in the toxicosis area as well as on 11 normal children in the control area. Glutathione peroxidase (GSH-Px) activity in the plasma of children in the toxicosis area was decreased. There were no significant differences between the toxicosis and control groups for plasma superoxide dismutase (SOD) activity, LPO content, GSH level, and red blood cell count (RBC).

The intelligence of 196 children (6.5-12 years old) was measured by a drawing test. It was found that the mean intelligence score of children in the toxicosis area was clearly lower than that of children in the control area.

F and Al levels in blood and urine from 100 osteomalacia patients in endemic areas of Guizhou and Hebei were also determined and were found to be significantly higher than in those of controls. Thus F-Al combined toxicosis is endemic in the severe fluorosis areas.
X-rays of 150 persons in the endemic areas were taken. The prevalence of abnormal radiology was 65%.

Elemental analysis of blood and urine from 68 youths in the endemic area revealed changes of Zn, Mo, Mn, and Fe levels were related to the levels of Ca, P, Mg, and Cu. For example, there was a negative relationship between Zn and Mo in the patient group, but a positive relationship between Zn and Mo in the control group.

2. Animal Toxicology

In experiments with male chickens, F and Al contents in the biomaterial were determined, and structural changes in the bones were assayed by a histomorphometric method with tetracycline as a tissue marker. A synergism was found between F and Al when the ratio of F and Al in diet was 2:1, but independent action was found when the ratio was 1:1.

In experiments with rabbits, Al-F combined toxicosis was related to the chemical forms of aluminum as well as F and could accelerate accumulation in bone. The accumulation of Al in bone from organic Al in food was accelerated by F in the diet, but inorganic Al in the diet had an antagonistic effect against F.

In experiments with rats, it was confirmed that F can increase Al absorption and accumulation. It was also found that dental fluorosis and damage to kidney function were related to F-Al combined toxicosis. These results indicated that Al has a contributing relationship to fluorosis.

Based on the foregoing experiments, therapeutic experiments with Al-F intoxicated rats were carried out. Boron and silicon reduced blood F levels in the control and Al groups. Boron, silicon, and zeolite significantly decreased bone Al, which therefore might have therapeutic value.

3. Clinical treatment and prevention

To cut off sources of F and Al intake, it is necessary for people not to do direct drying of food or grain by burning coal or coal mixed with kaolin. In order to set up models, the stoves of 70 families were improved with proper ventilation. Operations were also performed on three patients with osteomalacia. In the clinical work, health education was provided in many ways. A comprehensive plan for prevention and treatment based on decreasing total F and Al intake was prepared and submitted to the Government for approval.

Key words: Aluminium; Fluoride; Combined toxicosis.
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The following (to page 41) are abstracts of papers presented at the XXth Conference of the International Society for Fluoride Research, Beijing, China, September 5-9 1994.

THE CARTILAGE DAMAGE OF FLUOROSIS

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Beijing, China

A study of 260 cases of skeletal fluorosis demonstrated that the large joints of the extremities were severely damaged, especially the elbow, which was involved in 93% of the cases. In order to determine whether fluorosis damages cartilage, 20 young rabbits, and 10 young dogs were fed with sodium fluoride 20 mg/kg/day for periods up to 6 months. Radiographs and correlated HE-stained sections of the large joints of the extremities were made. Electromicroscopic examinations were also made of cartilage specimens of 5 young dogs.

Histologic study showed irregular calcareous deposits and globules in the matrix of the articular and epiphyseal cartilage. In the epiphyseal cartilage the way these were concentrated demonstrated that the disturbance occurred in the course of epiphyseal cartilage calcification. We also saw multiple dry necroses in the articular cartilage.

Electromicroscopic examination showed chondrocyte deformations, with cellular processes shortened or disappeared, calcareous deposits within the cytoplasm, increased glycogen deposition which almost filled the cell body, with organelles disappeared and myelin appearing in the cell. All the above changes indicate necrosis of the cell, demonstrating the direct damage to chondrocytes which is the origin of the damage to cartilage caused by fluorosis. We suggest that this pathologic change be called the “arthropathy of fluorosis.”

The radiographic changes of this arthropathy of fluorosis include: cyst formation, sclerosis of subarticular cartilage, and narrowing of the joint space, similar to general degenerative arthropathy. But the calcification and ossification of tendons and ligaments around the joints, and of synovia and ligaments within the joints, are characteristic changes of fluorosis and are rarely seen in degenerative arthropathy.

Key words: Arthropathy; Cartilage; Chondrocytes; Fluorosis.
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SERUM AND URINARY FLUORIDE CONCENTRATION IN FLUORIDE-EXPOSED WORKERS OF AN ALUMINIUM SMELTING FACTORY IN CHINA

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Osaka, Japan and Shenyang and Fushun, China

Measuring the fluoride (F) concentration of post-shift serum and urine is considered to be an appropriate way to evaluate F exposure in the work environment.

To define the relationship between F concentrations in the serum and urine of workers and the amount of gaseous F in the workplace, post-shift serum and urine samples of 200 F-exposed workers and 121 unexposed workers of an aluminium smelting factory were examined. For the measurement of gaseous F concentration in the air a volumetric method was used.

Average gaseous F concentration in each work environment was 1.89 mg/m³. Although serum F concentrations in unexposed workers increased with age, those in F-exposed workers did not change, and the levels of F in their serum and urine were more than twice as high as those in the control. The serum and urinary F of exposed workers were well correlated (r = +0.66).

From the present results the environmental exposure to gaseous F in an aluminium smelting factory could be monitored by determining the post-shift serum and urinary F concentrations.

Key words: Fluoride exposed workers; Serum fluoride; Urinary fluoride.

FLUORIDE METABOLISM AND KIDNEY FUNCTION: HEALTH CARE OF FLUORIDE EXPOSED WORKERS

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Osaka, Japan

The major pathway for fluoride (F) elimination from the human body is via the kidney. F concentration in urine has, therefore, been recognized as a good indicator of F body burden. When the renal function deteriorates, the ability to excrete F markedly decreases, possibly resulting in greater retention of F in the body.

In this study, the usefulness of measuring F concentration in serum, urine and hair, as indicators for health care of hydrofluoric acid (HF) workers, especially for persons with diminished kidney function, was investigated. F concentrations were measured in serum, urine and hair specimens of patients with chronic renal failure (CRF), HF workers and nonexposed healthy controls.

Post-shift serum, urinary and hair F concentrations in HF workers were higher (P < 0.001) than the control subjects. Although the serum and hair concentrations of patients with CRF were markedly higher (P < 0.001) than controls, their urinary contents of F remained normal. Serum F concentrations in HF workers with diminished renal function were strikingly higher than in other patients with CRF and HF workers. Their urinary levels of F, however, were within normal limits.

In conclusion, the monitoring of serum and hair F, and renal function tests other than urine analysis are necessary for the health care of F exposed persons, especially for those with impaired renal function.

Key words: Fluoride exposed workers; Fluoride metabolism; Kidney function.

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PLANNING, IMPLEMENTATION AND EVALUATION OF A FLUOROSIS CONTROL PROJECT

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Gujarat, India

Excess fluoride in drinking water results in a progressive, crippling, irreversible, untreatable health problem: fluorosis. The fluorosis problem has been reported in fifteen states of India.

Prevention is the only hope for control of this dreaded disease. The only way to prevent this disease is to provide water with a permissible level of fluoride forever. Planning, implementation and evaluation of such a water supply project should be based on sound epidemiological observations, and cost benefit and cost effective analyses.

Such a study was conducted in Mehsana district of Gujarat state, to tackle the problem of fluorosis in 550 villages. Two alternative technologies, surface water supply and defluoridation plants (Nalgonda technique), were evaluated. The results justified the need for such a fluorosis control programme, and strongly supported the surface water supply scheme for overall economic and health benefits.

Key words: Defluoridation; Fluorosis control and prevention; Surface water.
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DEFLUORIDATION OF DRINKING WATER BY CO-PRECIPITATION WITH Apatite

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Dental fluorosis is a major problem in some rural areas of China and other countries, where small flowthrough home water treatment units may be used to reduce the fluoride (F) concentration in drinking water to acceptable limits. However, such a system is often difficult to arrange where there is no piped water supply, gradual exhaustion of the absorbent agent is not easily detected, and bacterial contamination is possible. To overcome these problems a batch defluoridation method based on the precipitation of F as fluorapatite is now under development. In this two-step technique water is first saturated with the calcium phosphate mineral brushite, and subsequent seeding with a less-soluble calcium phosphate, hydroxyapatite, causes precipitation of fluorapatite. The method has been tested with water in the range 1-10 ppm F. Each cycle of the procedure can reduce the F concentration approx 2.5 ppm, and cycle effects are additive. Addition of calcium hydroxide during the brushite step improves F removal but results in a high residual pH. Computer simulations of the fluorapatite precipitation process suggest that any desired reduction in F may be achieved by adding sufficient calcium and phosphate and/or by raising the pH. Co-precipitation in a batch system promises to be a convenient low-technology method to defluoridate drinking water.

Key words: Apatite; Coprecipitation; Defluoridation.
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AN OUTBREAK OF FATAL FLUORIDE INTOXICATION IN A LONG-TERM HEMODIALYSIS UNIT

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Abstract from Annals of Internal Medicine 121 (5) 339-344 1994

Objective: To determine the cause of an outbreak of acute illness and death in a long-term hemodialysis unit.

Design: A retrospective cohort and case-control study of patients receiving hemodialysis and a laboratory study of a model deionization system to purify water for hemodialysis.

Setting: An outpatient hemodialysis unit of a university hospital.

Patients: 12 patients who became severely ill after hemodialysis treatment and 20 patients who did not become ill after receiving hemodialysis treatment in the same unit.

Measurements: Medical and dialysis unit records were reviewed to identify and characterize cases. Fluids for dialysis were tested for toxic substances, and fluoride was measured in patients’ serum. Resistivity and fluoride were measured in effluent from a model deionization system operated in the same way as the system associated with illness.

Results: During five consecutive hemodialysis shifts, 12 of 15 patients receiving dialysis treatment in one room became acutely ill, with severe pruritus, multiple nonspecific symptoms, and/or fatal ventricular fibrillation (3 patients). None of 17 patients treated in the adjacent room became ill (P < 0.0001). Death was associated with longer hemodialysis time and increased age compared with other patients who became ill. Serum concentrations of fluoride in the sick patients were markedly increased to as high as 716 μmol/L, and the source of fluoride was the temporary deionization system used to purify water for hemodialysis only in the affected room. Operation of a model deionization system showed how fluoride was adsorbed and then displaced in a massive efflux.

Conclusions: Because deionization systems are used widely in hemodialysis and can cause fatal fluoride intoxication, careful design and monitoring are essential.

Key words: Deionization systems; Fluoride poisoning; Hemodialysis; Hemodialysis units; Hospital; Water.

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ABNORMAL BONE MINERALIZATION AFTER FLUORIDE TREATMENT IN OSTEOPOROSIS: A SMALL-ANGLE X-RAY-SCATTERING STUDY

P Fratzl, P Roschger, J Eschberger, B Abendroth and K Klauschofer
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Sodium fluoride treatment of osteoporosis is known to stimulate bone formation and to increase bone mass, but recent clinical trials failed to prove its antifracture effectiveness. The formation of bone with abnormal structure and, therefore, increased fragility is discussed as a possible explanation. Until now, however, exact
THE ASSOCIATION BETWEEN WATER FLUORIDATION AND HIP FRACTURE AMONG WHITE WOMEN AND MEN AGED 65 YEARS AND OLDER. A NATIONAL ECOLOGIC STUDY
S J Jacobsen, J Goldberg, C Cooper and S A Lockwood
Milwaukee, Wisconsin

Abstract from Annals of Epidemiology 2 (5) 617-626 1992

For the past 45 years, there has been a great deal of debate regarding the health issues surrounding the fluoridation of public water supplies. In order to assess the association between fluoridation and hip fracture, we identified 129 counties across the United States considered to be exposed to public water fluoridation and 194 counties without exposure. Data from the Health Care Financing Administration and the Department of Veterans Affairs were used to calculate the incidence of hip fracture among white persons, aged 65 years or older, in fluoridated and non-fluoridated counties. There was a small statistically significant positive association between fracture rates and fluoridation. The relative risk (95% confidence interval) of fracture in fluoridated counties compared to nonfluoridated counties was 1.08 (1.06 to 1.10) for women and 1.17 (1.13 to 1.22) for men. As comparisons were made at the grouped level, it may be inappropriate at this time to draw inferences at the individual level. The relationship observed at the county level needs to be duplicated at the individual level with more precise measures of fluoride exposure.

Key words: Aged; Fluoridation; Hip fractures; Human; Men; USA; Women.
Reprints: S J Jacobsen, Medical College of Wisconsin, Milwaukee WI, USA.
FLUOR IN THE TREATMENT OF OSTEOPOROSIS: AN OVERVIEW OF THIRTY YEARS CLINICAL RESEARCH
J Dequeker and K Deleerck
Pellenberg, Belgium
Abstract from Schweizerische Medizinische Wochenschrift.
Journal Suisse de Medicine 123 (47) 2228-2234 1993

It has long been known that fluoride "hardens" mineralized tissues. Fluoride ingestion through drinking water in areas naturally rich in fluoride leads to osteosclerosis, known as endemic fluorosis. The first suggestion that fluoride be used in the treatment of osteoporosis was made in 1964. However, despite 30 years of research, the treatment remains controversial. Fluoride has a dual effect on osteoblasts. On the one hand, it increases the birthrate of osteoblasts at tissue level by a mitogenic effect on precursors of osteoblasts, while on the other hand it has a toxic effect on the individual cell with mineralization impairment and reduced apposition rate resembling osteomalacia. Fluoride has a positive effect on axial bone density, but the axial bone gain is not matched by similar changes in cortical bone. Furthermore, approximately one third of patients are non-responders. The effect of the addition of fluoride to the drinking water on fracture rate is not clear. It probably only has a small relative impact on total hip fracture rates. In two controlled fluoride therapy studies the incidence of vertebral fractures decreased, while in two other studies it increased. Experience teaches that denser bones are not necessarily better bones. The major side effects of fluor therapy are skeletal fluorosis, gastrointestinal intolerance, and painful lower extremity syndrome. Fluoride is the single most effective agent for increasing axial bone volume in the osteoporotic skeleton; however, its therapeutic window is narrow. The best candidates for fluoride therapy are patients with axial osteoporosis but with good peripheral bone density. They should have a good renal function and vitamin D status.

Key words: Fluoride; Fluoride therapeutic use; Osteoporosis.

THE EFFECT OF INVITRO FLUORIDE ION TREATMENT ON THE ULTRASONIC PROPERTIES OF CORTICAL BONE
W R Walsh, D P Labrador, H D Kim and N Guzelsu
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Abstract from Annals of Biomedical Engineering 22 (4) 404-415 1994

The mechanical properties of composites are influenced, in part, by the volume fraction, orientation, constituent mechanical properties, and interfacial bonding. Cortical bone tissue represents a short-fibered biological composite where the hydroxyapatite phase is embedded in an organic matrix composed of type I collagen.
and other noncollagenous proteins. Destructive mechanical testing has revealed that fluoride ion treatment significantly lowers the Z-axis tensile and compressive properties of cortical bone through a constituent interfacial debonding mechanism. The present ultrasonic data indicates that fluoride ion treatment significantly alters the longitudinal velocity in the Z-axis as well as the circumferential and radial axes of cortical bone. This suggests that the distribution of constituents and interfacial bonding amongst them may contribute to the anisotropic nature of bone tissue.

Key words: Anisotropy; Bone; Fluoride; Interfacial bonding; Ultrasound.
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NORMAL AGE-RELATED CHANGES IN FLUORIDE CONTENT OF VERTEBRAL TRABECULAR BONE - RELATION TO BONE QUALITY

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Abstract from Bone 15 (1) 21-26 1994

In several clinical osteoporosis studies, fluoride treatment has been shown to have a positive effect on bone mass but without a concomitant decrease in vertebral fracture rate. In contrast, some studies have shown that increases in spinal BMD are also paralleled by decreased vertebral fracture incidence. We have previously demonstrated, in a pig model, that 6-month treatment with fluoride increased bone mass but decreased bone quality. The aim of the present study was to elucidate whether normal age-related fluoride accumulation in human bone per se influences bone quality. From 73 normal individuals, aged 20-91 years (36 females, 37 males) two trabecular bone cylinders were obtained from the central part of L3. Biomechanical competence, ash density, and fluoride content were assessed in one cylinder, and trabecular bone volume was determined in the other. The results showed an age-related decrease in bone mass for both men and women. Bone strength normalized for bone mass (bone quality also identical with bone material strength) also showed an age-related decrease in men and women. Bone fluoride concentration increased significantly in both sexes (range 463-4000 ppm). Multiple regression analyses disclosed that fluoride by itself had no influence on bone quality, in this study with a limited number of cases, when the influence of sex and age were taken into account. It is concluded that normal age-related accumulation of fluoride in vertebral trabecular bone does not seem to affect the quality of bone. Whether this is also the case during fluoride therapy has to be assessed.

Key words: Age-related changes; Bone quality; Fluoride; Human; Vertebral trabecular bone.
Reprints: A Richards, Department of Oral Anatomy, Dental Pathology and Operative Dentistry, Royal Dental College, Aarhus, Denmark.
FLUORIDE THERAPY: EFFECT ON BONE MICROSTRUCTURE AND BIOMECHANICS
C Marcelli and P J Meunier
Montpellier, France
Abstract from Presse Medicale 23 (29) 1344-1348 1994

Fluoride, in the form prescribed as sodium or monophosphate fluoride for the treatment of vertebral osteoporosis, modifies the microscopic structure and biomechanical properties of bone tissue. For cancellous bone, the main effect of fluoride is a stimulation of bone formation leading to a hypertrophy of the remaining trabeculae. It may also have a beneficial effect by improving interconnections within the trabecular network. Although the mechanisms have yet to be fully understood, the process is probably dependant on the quality of the remaining network. The biomechanical properties of bone after fluoride therapy also are partly dependent on these modifications in the bone microstructure but also on fluoride's effect on bone minerals. When the concentration of fluoride becomes too high in bone, mineralization defects can occur causing major loss in mechanical resistance despite an increase in bone mass. Thus the beneficial effect of fluoride on wedge fractures of the spine in osteoporosis is probably the result of a balance between the effects of increased trabecular bone mass and modifications in bone mineralization. The respective intensities of these two phenomena also depend on the concentration of fluoride accumulated within the bone. This concentration is a function of the level of fluoride salt intake and its biodisposability during treatment.

Key words: Bone; Fluoride therapy.
Reprints: C Marcelli, Hop Lapeyronie, Service Rhumatologie, F-34295 Montpellier 5, France.

PHARMACOKINETIC PROFILE OF A NEW FLUORIDE PREPARATION: SUSTAINED-RELEASE MONOFLUOROPHOSPHATE
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Loma Linda, California, USA
Abstract from Calcified Tissue International 54 (1) 7-11 1994

The pharmacokinetic profiles of a sustained-release monofluorophosphate (MFP-SR) preparation (76 mg) and of plain MFP (76 mg) were compared in six osteoporotic females. These studies were performed in a randomized, crossover, double-blind design to select a preparation that would result in therapeutic serum levels while avoiding high serum peak values. Following a single dose of 76 mg MFP-SR, the serum fluoride levels remained within the accepted therapeutic range (5-10
μM/Liter) for 24 hours. In contrast, following a single dose of 76 mg plain MFP, serum fluoride levels exhibited a wide circadian fluctuation and serum levels approximately threefold higher than those of the MFP-SR preparation (9.5 ± 1.6 vs 3.5 ± 0.8 μM/Liter, P < 0.005). Compared with plain MFP, the sustained-release MFP had a significantly lower peak concentration (C\text{max} MFP-SR: 10.6 ± 3 vs C\text{max}MFP: 18.9 ± 5 μM/Liter, P < 0.005) and a significantly longer absorption lag time (T\text{max}MFP-SR 7.3 ± 1.6 vs T\text{max}MFP: 3.0 ± 0.6 h, P < 0.05). Twenty-four-hour urinary fluoride excretion after ingestion of plain or SR fluoride was significantly increased from pretreatment values documenting absorption with either MFP formulation. Our results show that the use of sustained-release MFP preparation that we tested prevents the development of high peak levels associated with the use of plain MFP preparations. Furthermore, a single dose of MFP-SR resulted in serum fluoride levels within the accepted range of 5-10 μM/Liter for 24 hours.

Key words: Monofluorophosphate; Osteoporotic females; Serum fluoride; Sustained-release.

Reprints: H Resch, Loma Linda University, Department of Medicine and Mineral Metabolism 151, Benton St 11201, Loma Linda, CA 92357 USA.

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PHARMACOKINETIC DIFFERENCES BETWEEN SODIUM FLUORIDE AND SODIUM MONOFLUOROPHOSPHATE AND COMPARATIVE BONE MASS INCREASING ACTIVITY OF BOTH COMPOUNDS IN THE RAT

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Rosario, Argentina

Abstract from Arzneimittelforschung 44 (6) 762-766 1994

After the administration of an oral dose of 80 μmol/L of NaF (CAS 7681-49-4) to rats, the area under the curve of total plasma fluoride equals 10,200 μmol.min/L. After an oral dose of 80 μmol of monofluorophosphate (MFP/CAS 10,163-15-2), two forms of fluoride appear in plasma: protein-bound MFP and diffusible fluoride. The areas under the curve of total (protein-bound + diffusible) and diffusible fluoride equal 22,200 and 8,850 μmol.min/L, respectively. The activity of MFP for increasing the bone mass of the rat was assessed with NaF as the standard. The animals were treated chronically for 100 days since weaning with food ad libitum and 5 mmol/L NaF, 5 or 2.5 mmol/L MFP solutions as the water supply. The effect obtained with 2.5 mmol/L MFP was similar to that produced by 5 mmol/L NaF, indicating a potency ratio MFP is twice as active as NaF.

Key words: Bone; Sodium fluoride, Sodium monofluorophosphate.

Reprints: A Rigalli, Laboratorio de Biologia Osea, Facultad de Medicina, Rosario, Argentina.
TOXIC EFFECTS OF CHRONIC FLUORIDE INGESTION ON THE UPPER GASTROINTESTINAL TRACT

T K Das, A K Susheela, I P Gupta, S Dasarathy and R K Tandon
New Delhi, India

Abstract from Journal of Clinical Gastroenterology 18 (3) 194-199 1994

In a prospective case controlled study, we evaluated the adverse effects of long-term fluoride ingestion on the gastrointestinal tract. Ten patients with otosclerosis who were receiving sodium fluoride 30 mg/day for a period of 3-12 months, and 10 age- and sex-matched healthy volunteers were included. They were all evaluated clinically and subjected to a real time ultrasound examination, upper gastrointestinal endoscopy, and biopsies from the gastric antrum and duodenum. The biopsies were subjected to a rapid urease test as well as light and electron microscopic examinations. Ionic fluoride was estimated in the serum, urine, and drinking water using an ION 85 Ion Analyzer. Seven subjects (70%) ingesting fluoride had abdominal pain, vomiting, and nausea. Petechiae, erosions, and erythema were seen on endoscopy in all the subjects, but not in the controls. Histological examination of the gastric antral biopsy showed chronic atrophic gastritis in all the subjects but in only one (10%) healthy volunteer. Scanning electron microscopic examination showed "cracked-clay" appearance, scanty microvilli, surface abrasions, and desquamated epithelium in the subjects ingesting fluoride, but not in the controls. We conclude that long-term fluoride ingestion is associated with a high incidence of dyspeptic symptoms as well as histological and electron microscopic abnormalities.

Key words: Fluoride; Gastrointestinal tract; Toxic effects.
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IN VITRO FLUORIDE TOXICITY IN HUMAN SPERMATOZOA

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Abstract from Reproductive Toxicology 8 (2) 155-159 1994

Effects of sodium fluoride (NaF) on washed, ejaculated human spermatozoa at doses of 25, 50, and 250 mM were investigated in vitro at intervals of 5, 10, and 20 min. Sodium fluoride (NaF) did not affect the extracellular pH of sperm, except that a slight acidification was caused by the 250 mM dose only. The treatment caused a significant enhancement in acid phosphatase (ACPase) and hyaluronidase activities after 5 and 10 min. However, the decrease in the lysosomal enzyme activity after 20
min treatment could have been due to the gradual increase in fluoride accumulation by spermatozoa leading to membrane damage. Silver nitrate staining of sperm revealed elongated heads, flagellation, and loss of the acrosome together with coiling of the tail. Sperm glutathione levels also showed a time-dependent decrease with complete depletion after 20 min indicating rapid glutathione oxidation in detoxification of the NaF. The altered lysosomal enzyme activity and glutathione levels together with morphologic anomalies resulted in a significant decline in sperm motility with an effective dose of 250 mM.

Key words: Fluoride; Human; In vitro; Spermatozoa; Toxicity.
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ULTRASTRUCTURAL STUDIES OF SPERMIOGENESIS IN RABBIT EXPOSED TO CHRONIC FLUORIDE TOXICITY

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Objective: To address the role of fluoride in causing defects to spermatids and epididymal spermatozoa.

Methods: Male rabbits were treated with 10 mg NaF/kg body weight daily for 18 months and maintained under identical laboratory conditions along with the control rabbits not given NaF. Testis and epididymis (caput) were investigated for ultrastructural details of spermatids and spermatozoa.

Results: A wide variety of structural defects were observed in the flagellum, the acrosome, and the nucleus of the spermatids and epididymal spermatozoa of fluoride-treated rabbits. Abnormalities included absence of outer microtubules, complete absence of axonemes, structural and numeric aberrations of outer dense fibers, breakdown of the fibrous sheath, and structural defects in the mitochondria of the middle piece of the flagellum. Detachment and peeling off of the acrosome from the flat surfaces of the nucleus were also observed.

Conclusion: The abnormalities observed render the sperm nonfunctional and ineffective, and thus there is a possible role of fluoride in causing infertility.

Key words: Fluoride; Rabbit; Spermio genesis; Toxicity.
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PREVALENCE OF DEVELOPMENTAL DEFECTS OF ENAMEL IN AREAS WITH DIFFERING WATER FLUORIDE LEVELS AND SOCIOECONOMIC GROUPS IN SRI LANKA AND ENGLAND

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Abstract from International Dental Journal 44 (2) 165-173 1994

Defects of dental enamel were recorded in 607 12-year-old children in Sri Lanka and north-east England in 1990/91. In each country, children were included from areas which received drinking water containing 0.1, 0.5 or 1.0 ppm F. In some of these areas, children from both low and high socio-economic groups were examined. The index of Developmental Defects of Enamel (DDE) was recorded clinically for the undried buccal surfaces of 10 permanent teeth (maxillary incisors, canines and first premolars, and mandibular first molars). The results revealed a higher prevalence of enamel defects and more teeth affected per person in children in the high socio-economic group than in the low socio-economic group in the 1.0 ppm F area in England: in the 1.0 ppm F area than in the 0.1 ppm F area in Sri Lanka (in the low socio-economic groups), and in the 1.0 ppm F area than in the 0.1 ppm F area in England (in the high socio-economic groups but not in the low socio-economic groups): in general in Sri Lanka than in England. The occurrence of diffuse opacities increased greatly with increasing water fluoride level. A high prevalence of hypoplastic lesions was recorded in Sri Lanka.

Key words: Enamel defects; Fluoride; Socio-economic.
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YOUNG CHILDREN AND FLUORIDE TOOTHPASTE

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Abstract from British Dental Journal 177 (1) 17-20 1994

Studies have shown a higher prevalence of enamel mottling in children who live in fluoridated areas than in those from low fluoride areas. It is possible that the additive effect of fluoride ingestion from water and toothpaste may be responsible since it is known that young children may swallow up to half of the toothpaste on the brush. Parents must supervise toothbrushing for young children, low fluoride paste should be used, and the brush merely smeared with paste. The commonly recommended pea-sized quantity may be too much.

Key words: Fluoride, Fluorosis, Toothpaste.
Reprints: W P Rock, Orthodontic Unit, School of Dentistry, University of Birmingham, St Chad’s Queensway, Birmingham B4 6NN, England.
DISTRIBUTION OF FLUORIDE IN THE DENTAL TISSUES AND THEIR SUPPORTING MANDIBULAR BONE FROM THE SAME INDIVIDUAL

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Nagoya, Japan and Leeds, England

Abstract from Archives of Oral Biology 39 (6) 535-537 1994

Dental and skeletal tissues have their own distinct fluoride distribution profiles. It was thought useful to compare these within individuals as normally comparisons are made between different groups of individuals. The average fluoride concentration decreased in the following order; cementum, alveolar bone, cancellous bone, mandible, dentine and enamel.

Key words: Dental tissues; Fluoride; Human; Mandibular bone.
Reprints: K Ishiguro, Department of Preventive Dentistry and Dental Public Health, School of Dentistry, Aichi-Gakuin University, 1-100 Kusumoto-cho, Chikusa-ku, Nagoya 464, Japan.

RELATIONSHIP BETWEEN CARIES, WATER FLUORIDE LEVEL AND SOCIOECONOMIC CLASS IN 15-YEAR-OLD INDIAN SCHOOL CHILDREN

M Rahmatulla and A H Wyne
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Abstract from Indian Journal of Dental Research 4 (1) 17-20 1993

The purpose of this study was to determine the relation between caries experience, water fluoride level and socioeconomic class among the 15-year-old school children of Tamilnadu. The study children were stratified on the basis of water fluoride level and socioeconomic (SE) class. The children were divided into low, medium and high SE classes. There was a highly significant (P < .001) difference in the carious experience of 15-year-old children from low fluoride (LF) areas in relation to the SE class, the low SE class having the highest caries experience. There was almost no difference between the caries experience of low SE class 15-year-old children from the LF area and high fluoride (HF) area (Z < 1.96 and P > 0.05). The difference between caries experience of 15-year-old children from LF and HF areas was not statistically significant (Z < 1.96 and P > 0.05). The present study has indicated towards the need of provision of more vigorous preventive efforts in lower SE class children in both the urban and rural population.

Key words: Children; Dental caries; India; Socioeconomic class; Water fluoride level.
Reprints: M Rahmatulla, College of Dentistry, King Saud University, Riyadh, Saudi Arabia.
FACTORS ASSOCIATED WITH THE USE OF FLUORIDE SUPPLEMENTS AND FLUORIDE DENTIFRICE BY INFANTS AND TODDLERS

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Abstract from Journal of Public Health Dentistry 54 (1) 47-54 1994

Dental fluorosis may be associated with the inappropriate use of fluoride dentifrices and/or dietary fluoride supplements by young children, especially for those who consume optimally fluoridated water. Studies to date have used retrospective designs that rely on anamnestic responses of adults to determine fluoride exposures in their children. The 1986 National Health Interview Survey (NHIS) collected information on current use of fluoride-containing dental products (dentifrices, drops, tablets, and mouthrinses) by all household members during home interviews. This report contains information obtained from adults for 1,996 children younger than two years of age. Nearly half of the children used fluoride dentifrices or dietary fluoride supplements. Eleven percent of the children younger than one year of age and nearly 60 percent of children between one and two years of age reportedly used a fluoride toothpaste. Dietary fluoride supplements were used about equally in these age groups (about 16%). The use of a fluoride dentifrice was similar across racial-ethnic groups, but the use of dietary fluoride supplements was less among blacks and Hispanics. A significantly higher proportion of children whose respondent knew the purpose of water fluoridation used some type of fluoride product. Because young children tend to swallow dentifrices, the findings of this study suggest the need for educational programs targeted to parents and health care providers regarding the appropriate use of fluorides and the risk of fluorosis when they are used inappropriately.

Key words: Dentifrice; Fluoride tablets; Fluorosis; Infants; Toddlers; Toothpaste use.
Reprints: A M Horowitz, Epidemiology and Oral Disease Prevention Program, National Institute of Dental Research, National Institutes of Health, Room 536, Westwood Building, 5333 Westbard Avenue, Bethesda, MD 20892 USA.

FACTORS AFFECTING CARIES EXPERIENCE IN FRENCH ADOLESCENTS

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Clermont-Ferrand, France

Abstract from Community Dentistry and Oral Epidemiology 22 (1) 30-35 1994

Three hundred French 14-15-yr-old adolescents were randomly selected. They were examined clinically and caries experience was determined by using the DMFS index. The aim of this investigation was to evaluate children's habits using a self-administered questionnaire, to clarify the actual influence of well-known factors such as fluoride exposure, diet, oral hygiene and socioeconomic factors on caries experience and to stress those factors of primary importance. A multiple regression analysis revealed the variables which significantly contributed to explain DMFS scores in a final model. Age, sex, frequency of sweet consumption, use of standard or high fluoride toothpastes, bleeding during toothbrushing, living in St Yorre (F⁻ = 0.45 mg/L). At a time when caries experience is decreasing, it seems that fluoride
supply, snacking and oral hygiene are still independent and significant determinants of caries experience in French adolescents.

Key words: Adolescents; Dental caries; Fluoride; France; Oral hygiene; Snacking.
Reprints: S Tubert-Jeannin, Faculté de Chirurgie Dentaire, 11 Bd Charles de Gaulle, 6300 Clermont-Ferrand, France.

SECOLAR TRENDS OF CARIES PREVALENCE IN 6- AND 12-YEAR OLD DUTCH CHILDREN
G J Truin, K G Konig, E M Bronkhorst and J Mulder
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Abstract from Caries Research 28 (3) 176-180 1994

Since a first survey in 1969, juvenile caries prevalence in the second largest city of the Netherlands has attained a European minimum of DMFT = 0.8 in 11.9-year-old children. However, the curves of improvement have been flattening out since the mid-eighties. Incidental variations between 1984 and 1993, especially of caries prevalence in the deciduous teeth of 5- and 7-year-old children, do not indicate a turn to the secular downward trend. The stability of juvenile oral health does not seem to be due to changes in dietary habits, nor to public health measures, but is mainly due to good oral health and use of fluoride dentifrices by the children.

Key words: Caries; Children; Hague; Prevalence.
Reprints: G J Truin, Department of Cariology and Endodontology, School of Dentistry, University of Nijmegen, PO Box 9101, NL-6500 HB Nijmegen, The Netherlands.

PREDICTION OF CARIES INCIDENCE IN SCHOOLCHILDREN LIVING IN A HIGH AND A LOW FLUORIDE AREA
A. Mattiasson-Robertson and S Twetman
Gothenburg, Sweden
Abstract from Community Dentistry and Oral Epidemiology 21 (6) 365-369 1993

A salivary mutans streptococci test and past caries experience were used as predictors for caries increment in a 3-yr study comprising 655 12-yr-old schoolchildren from two areas with contrasting levels of fluoride in the drinking water. The mean caries (DMFS) increment was similar in both groups during the study period, but a significantly (P < 0.05) higher incidence of approximal enamel lesions was registered in children from the high fluoride area. In both groups, a statistically significant (P < 0.05-0.001) positive relationship between salivary mutans streptococci score and/or past caries experience at baseline on one hand and caries increment during the study period on the other was established. The past caries experience was the most powerful predictor of caries risk in both the low fluoride and the high fluoride area. The sum of the sensitivity and specificity was somewhat higher in the low fluoride area (138%) compared to the high fluoride area (123%). The salivary bacterial enumeration used alone or in combination with past caries experience as well as past approximal caries experience were less useful as predictors in both groups. The present findings indicate that the natural fluoride exposure has a limited influence on caries risk assessment and the caries predictive ability of the salivary bacterial test and past caries in populations with a low level of disease.

Key words: Caries prediction; Dental caries; Fluoridation; Mutans streptococci.
Reprints: S Twetman, Department of Pedodontics, Faculty of Odontology, University of Gothenburg, Länsjukhuset, S-301 85 Halmstad, Sweden.
RECENT ADVANCES IN STANNOUS FLUORIDE TECHNOLOGY: ANTIBACTERIAL EFFICACY AND MECHANISM OF ACTION TOWARDS HYPERSENSITIVITY

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Abstract from International Dental Journal 44 (1 Suppl 1) 83-98 1994

Stannous fluoride (SnF₂) is highly susceptible to oxidation and hydrolysis but both anhydrous and aqueous preparations can be well established by proper formulation. When stability in aqueous preparations is achieved by the use of certain strong complexing agents, reduced antibacterial activity is observed which may be attributed to reduced bioavailability of the stannous ion. In contrast, an anhydrous SnF₂ preparation maintains stannous ion in a stable but uncomplexed form. This preparation displays antibacterial activity in saliva and delivers stannous ion which is absorbed onto surfaces making them less susceptible to plaque formation for an extended period of time (hours). When this anhydrous preparation is brushed onto dentine in vitro or in situ, one observes a nearly complete coverage of the dentine surface and occlusion of tubules by a tin-rich surface deposit. This finding indicates that the observed clinical efficacy of this preparation at relieving hypersensitivity is due to occlusion of tubules by a mixture of low solubility complexes of tin. A water-based SnF₂ preparation containing strongly complexed stannous ions does not form a surface coating on dentine in vitro suggesting that this preparation may not be optimal for treating hypersensitivity. Overall, the findings indicate that the stannous ions in a SnF₂ preparation must be maintained in a stable, bioavailable form for optimal efficacy against plaque and hypersensitivity to be obtained. The results suggest that these properties are provided by stable anhydrous preparations but are difficult to achieve simultaneously in aqueous preparations. When properly formulated, stannous fluoride preparations can provide multiple oral therapeutic benefits.

Key words: Antibacterial efficacy; Hypersensitivity; Stannous fluoride.
Reprints: S Miller, Colgate-Palmolive Technology Center, Piscataway, NJ 08854 USA.

RISK FACTORS FOR ENAMEL FLUOROSIS IN A FLUORIDATED POPULATION

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Abstract from American Journal of Epidemiology 140 (5) 461-471 1994

The purpose of this case-control investigation was to investigate the possible association between mild-to-moderate enamel fluorosis and exposure during early childhood to infant formula, fluoride toothpaste, and/or fluoride supplements. Analysis was performed on 401 residents of fluoridated communities in Connecticut, who were 12-16 years old and born prior to 1980. The case and control subjects for this study were selected on the basis of a clinical examination given in 1991. Subject
fluorosis status was determined using the Fluorosis Risk Index. Risk factor exposure was ascertained via a mailed questionnaire with a response rate of 89% and a questionnaire reliability of 87%. Logistic regression analyses, which adjusted for confounding variables, revealed that mild-to-modate enamel fluorosis on early forming (Fluorosis Risk Index (FRI) classification I) enamel surfaces was strongly associated with both milk-based (odds ratio (OR) = 3.34, 95% confidence interval (CI) 1.38-8.07) and soy-based (OR = 7.16, 95% CI 1.35-37.89) infant formula use, as well as with frequent brushing (OR = 2.80, 95% CI 1.15-6.81). A very strong association was observed with inappropriate fluoride supplement use (OR = 23.74, 95% CI 3.43-164.30). Respectively similar associations were observed between mild-to-modate enamel fluorosis on later forming (FRI classification II) enamel surfaces and frequent brushing and fluoride supplement use, but not with infant formula use.

Key words: Dental enamel; Fluoridation; Fluorosis; Mottled enamel; Risk factors.

Reprints: D G Pendrys, Department of Behavioral Sciences and Community Health MC:3910, School of Dental Medicine, University of Connecticut Health Center, Farmington, CT 06030 USA.

PREVALENCE OF FLUOROSIS AND OTHER ENAMEL DEFECTS RELATED TO CARIES AMONG ADULTS IN COMMUNITIES WITH OPTIMAL AND LOW WATER FLUORIDE CONCENTRATIONS

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Huddinge, Sweden

Abstract from Community Dental Health 11 (2) 75-78 1994

The aim of this Swedish study, performed in 1982, was to determine the prevalence of fluorotic and nonfluorotic enamel defects among adults in areas with optimal and low fluoride concentrations in water. The fluorosis prevalence was also related to caries prevalence in these areas. The study was based on clinical examinations of subjects born between 1939-1951 who had been drinking water with a fluoride content representative of their area of residence all their lives. This water was the only appreciable source of fluoride during tooth formation. Two hundred and sixty individuals living in the optimal fluoride area were included in the study and 236 individuals from the low fluoride area. The results showed first, a low prevalence of mild dental fluorosis in the area with optimal fluoride content in its drinking water; secondly, a low prevalence of non-fluorotic enamel defects, which was, however, higher in the low fluoride area than in the optimal fluoride area; thirdly, that caries prevalence was lower among those with fluorotic enamel defects in the optimal fluoride area; and lastly, caries prevalence was not influenced by non-fluorotic enamel defects.

Key words: Dental enamel defects; Fluoride; Fluorosis; Water.
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NON-DENTAL TISSUE EFFECTS OF FLUORIDE
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Abstract from Advances in Dental Research 8 (1) 32-38 1994

The anti-caries effects of water fluoridation are well-established. The non-dental tissue effects of fluoride in drinking water, either naturally occurring or as an additive, have been too poorly studied to permit definitive conclusions to be drawn. Claims have been made that fluoride results in an increased occurrence of malignancies, particularly osteogenic sarcoma. Experimental rat data have not resolved this issue, and epidemiologic studies are equally unclear. Initial claims that fluoride offers protection against atherosclerosis remain viable, but here too, much more directed research is needed. Early studies suggested that a water fluoride content greater than 1 ppm resulted in a lower prevalence of osteoporotic fractures. Recent epidemiologic data seriously question this conclusion and raise the possibility that even this relatively low level may increase the prevalence of osteoporotic hip fractures. Other elements, including calcium and magnesium, also vary in amount as water fluoride content varies, and it has proved difficult to distinguish the independent effects of the various nutrients in water from each other. Therapeutic use of fluoride has been largely restricted to studies of its effect on the osteoporotic vertebral fracture rate. After more than 30 years of detailed study, this important issue remains unresolved. This review provides an overview of these issues, focusing on the uncertainties alluded to, and attempting to develop strategies for future research.

Key words: Fluoride; Malignancies; Nondental tissue effects; Osteogenic sarcoma; Osteoporotic fractures; Vertebral fractures; Water fluoridation.
Reprints: M Kleerkoper, Wayne State University School of Medicine, 4201 St Antoine, UHC-4H, Detroit MI 48201, USA.

[The correspondent who sent us the above abstract commented: "The first sentence is untrue. Comprehensive studies now suggest the opposite. Recent claims of effectiveness rest on small sample studies from selected communities, and the early studies are admitted to be defective. Assertions that anti-caries effects of fluoridation are 'well-established' seem now to accompany admissions, compelled by recent evidence, of the procedure's uncertain safety. The only credible anti-caries effects of fluoride are from its topical, not systemic, uses, at high concentrations." Comprehensive studies which belie the assertion have been reported in Fluoride 27 (4) 238 (2) 59-66 (1) 45-47 1994, 26 (4) 263-266 1993, 23 (2) 55-67 1990, 21 (3) 141-142 (1) 40-41 1989, 20 (2) 51-53 1987. Editor]