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CONTENTS

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MANUSCRIPTS for publication should be submitted in English, double-spaced with generous margins. References should be arranged according to the order in which they are cited in the text, and written as follows: Author, title, journal, volume, pages and year. Each paper must contain a summary of not more than 12 lines.

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EDITORIAL

FOOD-INDUCED SKELETAL FLUOROSIS

Skeletal fluorosis is usually attributed to fluoride in water and to industrial exposure to the halogen. Indeed, many of the early statistical studies on the health effects of fluoride deal solely with waterborne fluoride. For instance, the health survey of Bartlett, Texas (1) with 8 ppm of fluoride in the water supply as compared with low fluoride (0.4 ppm) Cameron - one of the key studies purporting the safety of water fluoridation - rests on the assumption that waterborne fluoride is the major source of fluoride intake. No data were presented on fluoride consumption from food, from inhalation of air or from other sources in the two communities.* Similar epidemiological surveys which disregard fluoride intake from sources other than water have been utilized in establishing safety standards both in the U.S.A. and abroad. Hodge, for instance, (2) stated that "crippling fluorosis develops in individuals drinking water containing elevated amounts of fluoride, for example 10 or more ppm". Referring to the Bartlett-Cameron study he said; "About 10% of the lifetime residents of a U.S. community where the drinking water contained 8 ppm fluoride, exhibited detectable osteosclerosis". These views expressed by Hodge are shared by many others.

In recent years, evidence has accumulated in the literature that substantial amounts of fluoride reach the system from sources other than drinking water. Thus they contribute materially to our daily fluoride intake. Airborne fluorides (3, 4) and longterm hemodialysis (5) have been responsible for the development of skeletal fluorosis.

A case in point is the occurrence of this disease in a man of Hampshire, England who had always resided in a low-fluoride area (6). It was assumed - but not proven - that fluoride in tea may have accounted for his illness.

More tangible evidence of an unsuspected source of fluoride intake resulting in skeletal fluorosis was presented by Klemmer and Hadler.They described the case of a 27-year old nurse who had been habitually sniffing methoxyflurane, a fluoride-containing anesthetic, for 9 years (7).

Whereas such isolated instances of skeletal fluorosis due to non-waterborne fluoride may not be sufficient to question water as the main source of fluoride intake, the recent artice by Huo Daijei on page 51 and an accompanying abstract on page 91 by Wei Zan-dao et al. reveal that under certain conditions foodborne fluoride causes widespread skeletal fluorosis in a population. These authors described an endemic area of the disease in the Chinese province of Guizhou in which the level of fluoride in water was less than 0.2 ppm. They demonstrated that the average daily intake of fluoride in food among the population was as high as 8.7 mg. The excess fluoride content of food was attributed by the

* Only 11 (14.5%) of the subjects studied in Bartlett had lived there during the period of tooth and bone development.

authors to fluoride-laden heavy soil in the area. This is the first carefully documented communication of advanced chronic skeletal fluorosis primarily due to food.

In view of this experience in China one wonders about the significance of fluoride levels of food grown in other countries in the vicinity of fluorspar mines or near fluoride-emitting factories and in areas with high fluoride levels in drinking water. Had such data been presented in the Bartlett-Cameron survey it would have been of considerable interest in connection with the Guizhou, China report.

The presence of fluoride in pharmaceutical products should be given consideration as another important source of fluoride intake. In an article by Bregeon, C., et al. abstracted on page 45 of the January 1981 issue of FLUORIDE, one of the first cases of skeletal fluorosis due to habitual use of a fluoride-containing drug called Niflumique acid is recorded. The patient, an arthritic, had been taking this drug continually for 11 years. It is true the literature on such instances is sparse. However, in view of the large number of fluoride-containing drugs, some of which are taken habitually for prolonged periods of time and because physicians are often not even aware that the drug contains fluoride or of the symptoms which can be induced by the halogen, this problem warrants the attention of the medical and pharmaceutical professions. Waterborne fluoride, therefore, is only one of the sources of fluoride intake which leads to skeletal fluorosis.

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X-RAY ANALYSIS OF 34 CASES OF FOODBORNE SKELETAL FLUOROSIS

by

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SUMMARY: Thirty-four cases of foodborne endemic skeletal fluorosis are reported in an area where the fluoride content in drinking water is very low, but that of food is high. The radiological changes include osteosclerosis, ossification of tendons and ligaments, bony exostoses. These changes are essentially the same as those of waterborne skeletal fluorosis.

Introduction

In 1946, Lyth (1) reported four cases of skeletal fluorosis in the Guizhou Province in southwestern China, (formerly Kweichow). Endemicity of this disease has been reported in many areas of China. In the northern provinces, the chief source of fluoride intake was believed to be the high fluoride content in drinking water.

In 1976, I noted many patients with mottled enamel in a county of Guizhou. On x-ray examination, they showed marked osteosclerosis with ossification of tendons and ligaments, changes characteristic of fluorosis. The analysis of 75 samples of drinking water from wells, collected by my associate, yielded fluoride values less than 0.5 ppm. Because of this low fluoride level in water the question arose whether or not there is another major source of fluoride intake in this area.

Subsequently, Guiyang Medical College and others (2) investigated the cause. Again the water was analyzed for fluoride as well as samples of air, soil, rocks and food. The food samples were ashed and subsequently assayed by the fluoride electrode method. The results are presented in Table 1.

Table 1

Fluoride Contents

Air	0.07 mg/m^3	Average of 10 samples
Water	0.15-0.18 ppm	38 samples
Rocks	303.3-468.5 mg/kg	
Soil	213.7-999.1 mg/kg	

In the area under study, the residents are chiefly vegetarians. The average fluoride content of seven staple food items_ rice, corn, cabbages, soya beans, potatoes and wheat_ ranged between 8.3 and 11.7 mg/kg. Tea showed the highest fluoride content namely between 35.1 and

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59.2 mg/kg, whereas potatoes were lowest in fluoride (0.7-0.8 mg/kg). We concluded that fluoride intake from food is the principal cause of fluorosis in that area.

More than 200 residents were examined by x-ray. On 34 patients,we obtained reliable data with the following results:

General Findings: Of the 34 cases, 26 were males and 8 females. All were over 40 years old. The oldest a peasant, was 68-years of age. Thirty-two subjects had different degrees of dental fluorosis; one was edentulous; in another,the teeth were not examined.

The fluoride content of the urine of 32 cases averaged 6.9 ppm compared with an average of 0.8 ppm in the normal nonendemic Guiyang residents.

The chief symptoms were backache, numbness in extremities, and pain in joints. Physical examination revealed limitation in movements of the vertebral column, hip, knees, shoulders and elbow joints. The advanced

Fig. 1

(Male, age 50)

Increased bone density; partial obliteration of medulla.

Fig. 2

(Male, age 68)

Osteosclerosis of Pelvis and Vertebrae

cases exhibited scoliosis, kyphosis, malformation in extremities, and rigidity of the vertebral column and of joints.

X-ray Analysis: The x-ray examination included head, cervical spine, thoracic spine, lumbar spine, chest, pelvis, upper arms, thighs, legs, hands and feet with the following findings:

1. Density change: There was increased density of the bony structure with thickening of the trabeculation which appeared to coalesce, thus completely disappear. The medullary cavity gradually narrowed and finally became obliterated(Fig.1). The cortical layer was thickened. In advanced cases,the whole bone exhibited a structureless pattern that resembled marble bone. These changes were most prominent in the spine and the pelvis. The peripheral bones were involved to a lesser extent. The cranium was only slightly affected with some degree of thickening.

2. Bony Prominences: Multiple exostoses were seen on the surface of bones. The contour of the bones was uneven and irregular. The exostoses appeared to be due to ossification of tendons, ligaments and periosteal hyperostosis. In the pelvis, bony spurs were frequent around the brim of the obturator foramen. In most cases the sacrospinous, sacrotuberous, and iliolumbar ligaments were ossified (Fig. 2).

In the spine extensive osteophyte formation was noted between vertebrae. In advanced cases, there was complete bridging between vertebral bodies which resulted in limitation of movements.

In the forearms, ossification of the interosseous membrane was common. In the early stage exostoses occurred on the medial surface of the mid-shaft of the radius. As the disease progressed, the exostoses became larger and larger, until at last the radius and ulna were completely fused.

3. Joint Changes: Around the joints marginal osteophytes developed, with calcification of the periarticular ligaments. The articular spaces were usually narrowed. Occasionally free bodies were found in the joint spaces. Most prominently affected were the hip, elbow, and knee joints. All changes were multiarticular, and tended to be symmetrical, quite similar to those seen in hypertrophic osteoarthritis.

4. Other Changes: In one case, generalized calcification of peripheral arteries occurred. Chiefly anterior tibial, posterior tibial, and iliac arteries were involved. On roentgenograms, the calcified arteries take the form of dense parallel lines; they were difficult to differentiate from those caused by atherosclerosis (Fig. 3).

Discussion

The illness of the patients reported here was diagnosed as fluorosis because of:

1. the elevated fluoride content in urine

2. the high fluoride content of food
3. the characteristic x-ray and dental changes

The various sources of fluoride reported in the literature as the cause of skeletal fluorosis are: The high fluoride content in water, fluoride added to wine (3), fluoride-containing compounds used in industry and ingestion of hydrofluoric acid (4). Dental fluorosis caused by fluoride-containing food has been reported in VietNam (5) and Thailand (6). However, we found no reports of endemic skeletal fluorosis demonstrable by x-ray due to fluoride in food. According to our observations, the x-ray changes in foodborne skeletal fluorosis are identical with those of skeletal fluorosis due to other sources.

Fig. 3

(Male, age 68)

Calcification of Femoral Arteries

In the past, high fluoride levels in drinking water have been considered the chief cause of endemic fluorosis. Some authors have tried to establish a "safe threshold value" of fluoride in water which would not lead to endemic fluorosis. According to Stevenson et al. (7), osteosclerosis is not apparent radiologically when the fluoride concentration in drinking water is less than 4 ppm. However Azar et al. (8) reported cases of skeletal fluorosis along the Persian Gulf where the concentration of fluoride in water is less than 4 ppm.

In some countries, 1 ppm fluoride in drinking water is regarded as beneficial in reducing the incidence of dental caries. Where the level of fluoride in water is less than a specified value, fluoride is added artificially to drinking water. According to our data, endemic skeletal fluorosis can prevail in an area where the fluoride level in drinking water is less than 1 ppm. In this endemic area, the chief cause of fluorosis is the high fluoride content of food.

Some authors maintain that most foods are low in fluoride even if grown in high fluoride soil. They believe fluoride in soil is converted to insoluble salt and thus us unavailable to vegetation (9). In the Guizhou area, however, the soil is acidic. The fluoride in acidic soil is more soluble than in other soils and is not converted into insoluble calcium fluoride. This may explain why the fluoride moves from soil into plants.

In an attempt to determine the reason for the low fluoride in water in contrast to the high fluoride content of soil, Guizhou geologists described the soil as adhesive. One may speculate that fluoride in the adhesive soil is firmly attached to soil particles and thus cannot leach into creeks and wells.

Our observations clearly indicate that skeletal fluorosis can occur in areas where the concentration of fluoride in water is negligible. The fluoride content of food should be carefully analyzed and its impact must not be disregarded.

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FLUORIDE BRIEFS

The annual report of the New Zealand Committee on Adverse Drug Reactions includes a fatality in an "elderly" woman with impaired renal function following "high doses of NaF therapy (44 mg/day)" for osteoporosis. She developed dehydration and renal failure with initiation of this treatment.

McQueen, E.G.: New Zealand Committee on Adverse Drug Reactions: Twelfth Annual Report 1977. New Zealand Med. J. 86:248-250, 1977.

FLUORIDE LEVELS IN BONES AND TEETH OF MICE

by

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SUMMARY: Fluoride concentration in long bones and teeth from four successive generations of albino mice on a low-fluoride diet (0.1 - 0.3 ppm F) was determined. The concentration of fluoride in bones and teeth, except incisors, increased significantly with the age of the animals. A trend of reduction in the concentration of bone fluoride with successive generations was observed.

Introduction

A feasibility study was conducted to develop a standard experimental diet in which the concentration of fluoride could be controlled at a very low level (1). The diet was prepared with alga (Chlorella pyrenoidosa) and yeast (Saccharomyces cerevisiae) biomass, sucrose, corn oil, cellulose and a salt mix (1,2). The alga and yeast biomass was produced under standardized culture conditions and provided the dietary protein. The diet was developed through trial feeding experiments (1) with rats and mice. Two generations of rats and four generations of mice were bred on the diet.

The concentration of fluoride in the long bones and teeth of the four generations of mice is reported in this paper.

Material and Methods

Long bones and teeth from two groups of albino mice were used in this study. One group of the mice was fed exclusively with the low-fluoride experimental diet and the other group received a commercial laboratory diet (FFG(M), E. Dixon and Sons Limited Ware, Hertfordshire, U.K.) unchanged. The bones (femur, humerus, tibia-fibula, radius and ulna) and teeth were dissected under a binocular dissecting microscope to remove the attached soft tissues. The material was pooled separately for the experimental and control mice, according to the age of the mice, into the following categories:

1. femur and humerus bones
2. tibia-fibula, radius and ulna bones
3. incisor teeth
4. molar teeth

The material from the experimental mice were further pooled according to their filial generation. The pooled samples were defatted in a 3:1 me-

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thanol:diethyl ether mixture and dried.

Fluoride was separated from the dried, defatted bone and tooth samples by micro-diffusion (3) and determined with the fluoride electrode.

Statistical analysis of variance and covariance using ANOVA and REGRESSION programs (4) was applied to the data from the fluoride determinations.

Results

The experimental low-fluoride diet contained 0.1 to 0.3 ppm fluoride (0.18 ± 0.07, mean ± S.D) and the commercial diet contained 11 - 17 ppm fluoride on a dry weight basis. Growth, reproduction and general health were very similar in both groups of mice.

The concentration of fluoride in the pooled samples of the different categories of bones and teeth is summarized in Table 1. It can be seen

Table 1

F^- Concentration in Pooled Samples of Dried Defatted Bones and Teeth

W	F	n	Femur and Humerus		Tibia, Fibula Radius and Ulna		Incisor Teeth		Molar Teeth	
EXPERIMENTAL										
3	F_2	4	8.0^d	(0.5)	6.6^d	(0.4)	5.4^c	(0.4)	7.8^b	(0.4)
4	F_2	3	12.4^c	(3.6)	10.5^c	(1.5)	14.2^c	(2.9)	7.7^c	(1.0)
5	F_3	5	16.0^d	(1.7)	13.7^d	(1.0)	8.7^c	(0.9)	7.1^c	(1.6)
6	F_1	6	33.0^d	(2.3)	31.0^d	(2.1)	14.5^c	(0.9)	17.6^c	(2.6)
6	F_3	8	17.1^d	(1.5)	14.3^d	(0.8)	11.2^c	(1.8)	12.1^c	(1.0)
9	F_2	4	39.2^d	(2.0)	35.0^c	(0.5)	19.4^b	(0.9)	19.4^b	(0.8)
15	F_2	4	49.4^d	(2.1)	49.0^d	(2.3)	20.7^c	(1.8)	26.1^b	(3.9)
17	F_1	4	68.2^c	(11.8)	68.1^d	(17.6)	30.1^c	(2.2)	50.3^b	(2.3)
21	F_2	4	70.3^d	(10.7)	61.0^d	(7.2)	24.2^c	(1.0)	58.0^b	(3.0)
26	F_1	3	101.5^d	(4.5)	86.7^c	(7.3)	27.6^c	(3.0)	68.5^b	(1.5)
20	F_4	5	42.6^e	(1.4)	31.2^d	(1.4)	17.3^c	(1.2)	25.0^b	(1.0)
52	F_3	3	64.5^d	(3.5)	65.5^d	(3.6)	17.7^d	(1.7)	53.0^b	(4.0)
104	F_2	2	104.0^c	(4.0)	103.0^c	(2.0)	16.4^b	(0.7)	111.5^b	(2.5)
CONTROLS										
4		8	131^e	(22.0)	110^d	(13.0)	106^c	(8.0)	111^c	(15.0)
6		9	378^d	(72.0)	290^d	(23.0)	174^c	(9.0)	180^c	(28.0)
15		6	730^e	(70.0)	669^d	(43.0)	233^c	(12.0)	379^c	(27.0)
26		5	945^d	(78.0)	767^d	(70.0)	332^c	(16.0)	463^c	(19.0)
36		3	888^d	(143.0)	762^d	(134.0)	351^c	(25.0)	-	

W = age in weeks; F = filial generation; n = number of mouse carcasses
a = 1; b = 2; c = 3; d = 4; e = 5 analyses
Mean values in ppm with mean deviation in parenthesis

from this table that the fluoride concentration in the bones and molar teeth of both the experimental and control mice and in the incisor teeth of the controls increased with age. This increase in the concentration of fluoride with age in the tibia-fibula, radius and ulna bones of experimental mice is compared with that in similar bones from the control mice in Figure 1. The increase in the concentration of fluoride with age in the molar teeth of the experimental mice is compared with that in the molar teeth of the controls in Figure 2.

Figure 1

Increase in Bone F^- with Age

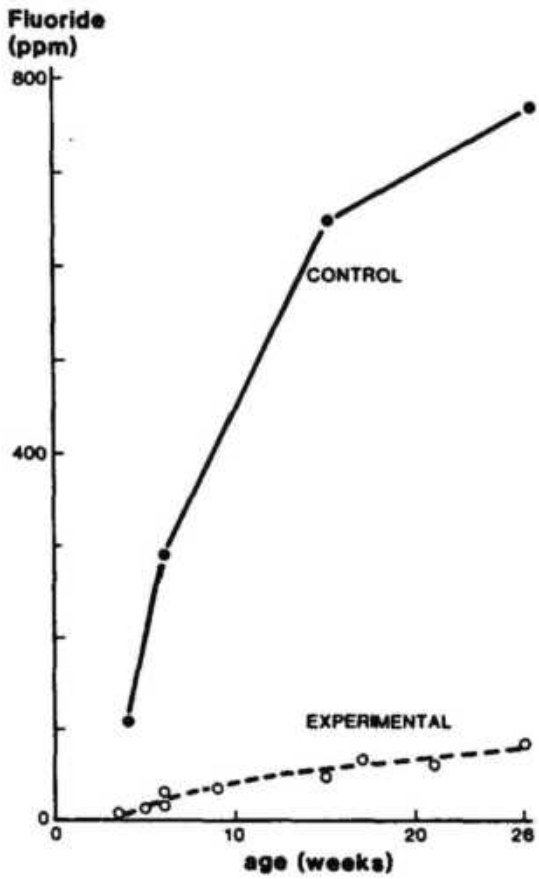
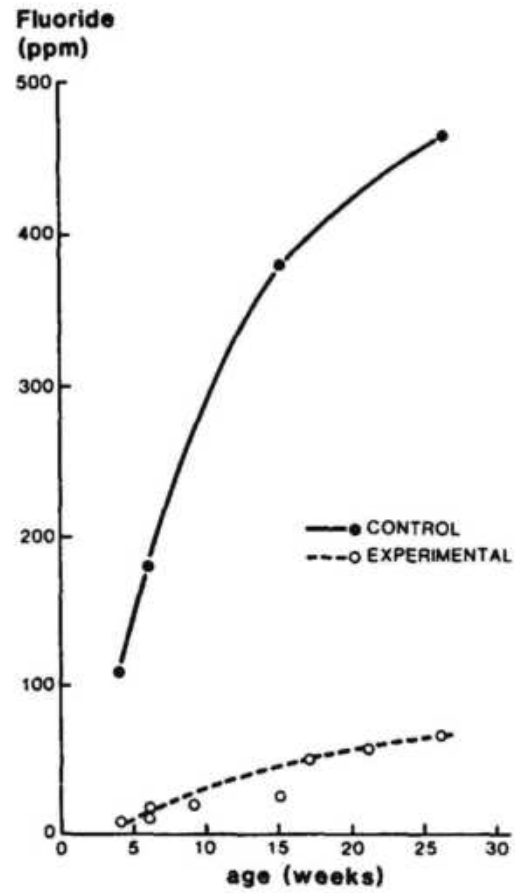


Figure 2

F^- Increase in Molar Teeth with Age



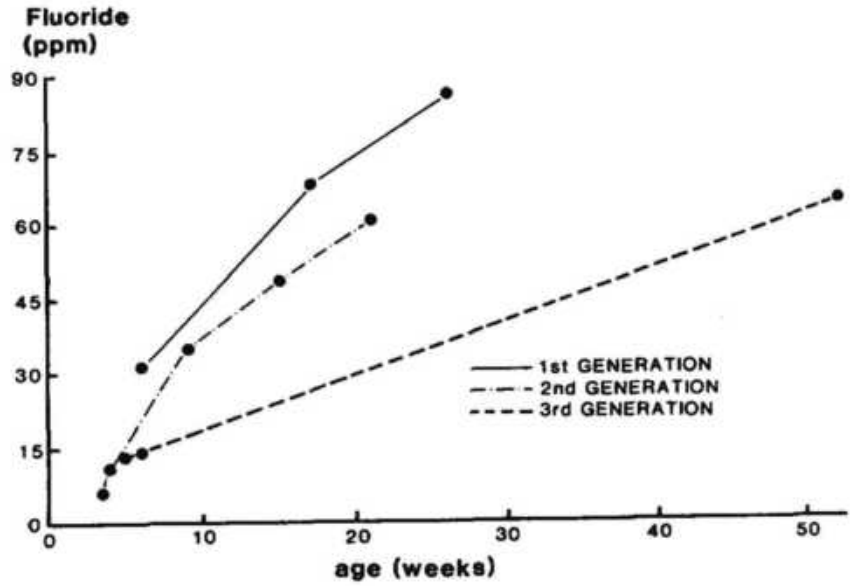
The increase in the concentration of fluoride with age was highly significant ($p < 0.05$) in the two categories of long bones and molar teeth from both the experimental and control groups of mice. The increase in

fluoride concentration with age in the bones of the control mice was more than 20 times that in the corresponding bones from the experimental mice. Similarly the increase in fluoride concentration with age in the molar teeth of the controls was more than 15 times that in the molars of the experimental mice. The increase in fluoride concentration with age was also highly significant ($p < 0.005$) in the incisor teeth of the control mice but not significant ($p > 0.2$) in the incisors from the experimental mice. The fluoride concentration in the incisor teeth of the experimental mice reflected the low level of fluoride intake by these animals.

There was a marked trend of reduction in the concentration of fluoride in bones with successive generations of experimental mice. This trend is illustrated for the tibia-fibula, radius and ulna bones in Figure 3.

Figure 3

Bone F^- in Three Generations Related to Age



Discussion

The present study has shown that there was an increase in the concentration of fluoride with age, in the bones and teeth of the mice at both levels of intake. These observations agree with previous reports on the retention of fluoride in the bones of the mouse (5-7) and the rat (8-16). However, not a great deal is known about the retention characteristics of fluoride by these animals on low controlled levels of intake. In

the present study, for instance, there was no significant increase in the concentration of fluoride in the incisor teeth of the mice on the low fluoride intake compared with the highly significant increase in the controls. This lack of a tendency for the incisor teeth of the experimental mice to show increased levels of fluoride with age was most likely due to a constant low level of fluoride ions available to these continuously erupting teeth. On the other hand, the molar teeth probably acquired small amounts of fluoride by ionic exchange throughout the lifetime of the animal. The molars also acquired small increments of cementum and secondary dentine throughout the lifetime of the mouse and, therefore, further increased their fluoride content.

These observations have indicated a need for further studies on the retention characteristics of fluoride at carefully controlled low levels of intake. Such studies would also explain the accumulation of fluoride in the molar teeth even at the low level of intake at which the incisor fluoride remained constant.

The trend of reduction in bone fluoride level with generation (Figure 3) was probably due to the limited fluoride available for placental transfer from generation to generation in the low fluoride mice. Also, in the present study the fluoride concentration in the bones and teeth of the young experimental mice was very low without any noticeable effect on mineralization. Since the experimental diet used in this study can be prepared to contain less than 0.05 ppm fluoride (1) it could be used in multigeneration breeding experiments to evaluate the transfer of fluoride across the placenta to the developing fetus. If fluorine is essential for the normal mineralization of bones and teeth, the developing fetus would require a certain minimum level of fluoride for such development. The guinea pig can be used as the experimental animal for such studies since the young are born with fully developed teeth. If a physiological process is involved in the transfer of fluoride across the placenta, there is no reason why it should not operate when the maternal fluoride store and level of intake was very low.

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EFFECT OF FLUORIDE AFTER DISCONTINUATION OF OCCUPATIONAL EXPOSURE

by

E. Czerwinski, W. Pospulka,
G. Nowacki and A. Skolarczyk
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SUMMARY: Sixty subjects who had discontinued their work in an aluminum plant for 1 - 7 years were examined. Earlier they had been exposed to fluoride for an average 16.9 years. Orthopedic, radiological and biochemical examinations were made. The fluoride,

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calcium and phosphorus levels in the 24 hour urine, the serum calcium, phosphorus and acid and alkaline phosphatase levels, hemoglobin, erythrocyte count, color index, serum protein, and the electrophoretic fractions were determined. The urine fluoride level was markedly increased and the other analytical test results were within normal limits.

The findings in a group of subjects who had discontinued working in the aluminum plant one year previously were compared with those who had ceased working there for 2 - 7 years (average 3.4 years). In the group without exposure for a longer period, the urinary fluoride level was 25.4% lower, and clinical changes in the locomotor system were less pronounced. No differences in the occurrence of osteosclerosis were observed.

Introduction

Occupational exposure to fluoride occurs during the production of aluminum, glass, iron, phosphate fertilizers, cryolite, etc. (1, 2, 3, 4, 5). Fluoride is readily absorbed both in the alimentary canal and the respiratory tracts. In subjects not previously exposed 20% of the dose received is excreted in the urine after 3 hours and 50% after 24 hours (6, 7, 8, 9). About 90% of the dose retained within the organism is deposited in the bones because fluoride has a specific affinity for the hydroxyapatite in skeletal tissue (10, 11, 12). It exchanges the hydroxyl and carbonate ions of the hydration shell and is then diffused more deeply into the hydroxyapatite crystal (13, 14). As the bone becomes saturated with fluoride, it is deposited in the organism and is excreted in the urine. Eventually the amount of fluoride excreted equals the amount consumed (6, 8, 15).

The skeletal changes are the result of the formation of fluoroapatite and the action of fluoride on the bone cells, and on the enzymes and hormones regulating bone metabolism. Studies on endemic, industrial and experimental fluorosis, as well as the results of fluoride treatment of osteoporosis have shown that osteogenesis and ossification processes are stimulated. They lead to visible radiographic changes of the bone (16,17,18,19). These disturbances are also revealed in analytical tests, especially those of the urine, the serum calcium and phosphorus levels as well as the serum acid and alkaline phosphatase levels (4, 20, 21, 22, 23).

The changes occurring in the organism under the influence of chronic intoxication with fluoride compounds have been well documented, but very little work has been done on observations after termination of exposure, particularly occupational exposure. We have therefore attempted to evaluate the changes due to fluoride in subjects who for any length of time have ceased working in an aluminum plant where exposure to fluoride was considerable. We have evaluated both the result of the analytical tests and the clinical and radiological changes in bones and joints.

Material and Method

Sixty former employees of an aluminum plant, who had discontinued their work in the factory at least 4 months previously or for as long as 7 years, were examined. Morbid changes, especially in the respiratory tract were the reason for their work stoppage. The mean urinary fluoride concentration during their employment in the aluminum plant was 2.4 ppm. In order to evaluate these changes during a prolonged period without exposure, we compared a group of 19 subjects (Group 1) who had discontinued working less than one year earlier(4 - 12 months with an average 9 months) with a group of 41 who had discontinued their work at the plant 2 to 7 years earlier (average 3.4 years) (Group 2). The period of work in the plant was more or less similar in both groups; namely 14 - 24 years with an average of 16.4 in Group 2. In both groups, most of those examined had been working in the electrolysis department. The ages of those examined were similar in both groups, namely 37 - 61 years with an average of 48.5 years in Group 1 and 39-69 years with an average of 50.9 years in Group 2.

Orthopedic and radiological examinations of the locomotor system were made in all cases; in 45 it was possible to carry out full analytical tests, namely serum calcium, phosphorus, alkaline and acid phosphatase levels as well as hemoglobin, erythrocyte count, color index, and serum protein level, together with serum electrophoresis. Calcium, phosphorus and fluoride levels of the 24-hour urine, collected in plastic containers were also determined. The colorimetric method was employed for the urinary fluoride assays (24).

Results

The occurrence of pain and restriction of movements in the spine and limb articulations in both groups is illustrated in Fig. 1. These changes are less frequent in the group with a longer period of freedom from expo-

Figure 1

Frequency of Pain and Limited Motion in Both Groups

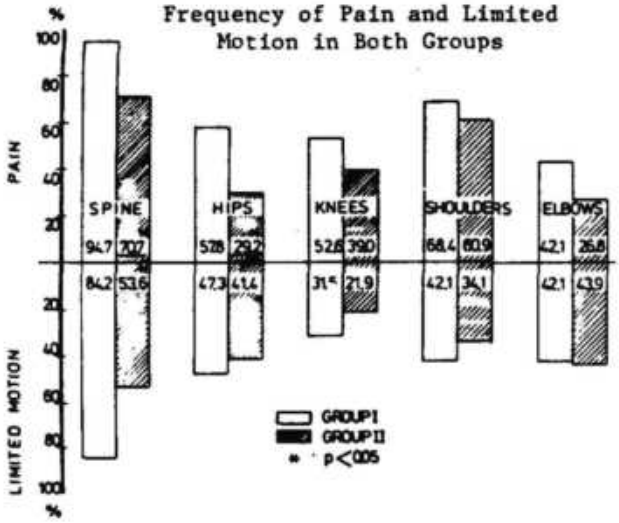
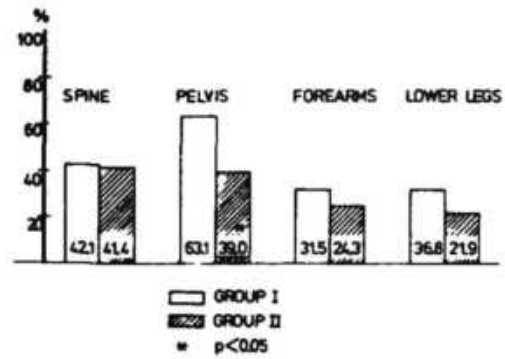


Figure 2

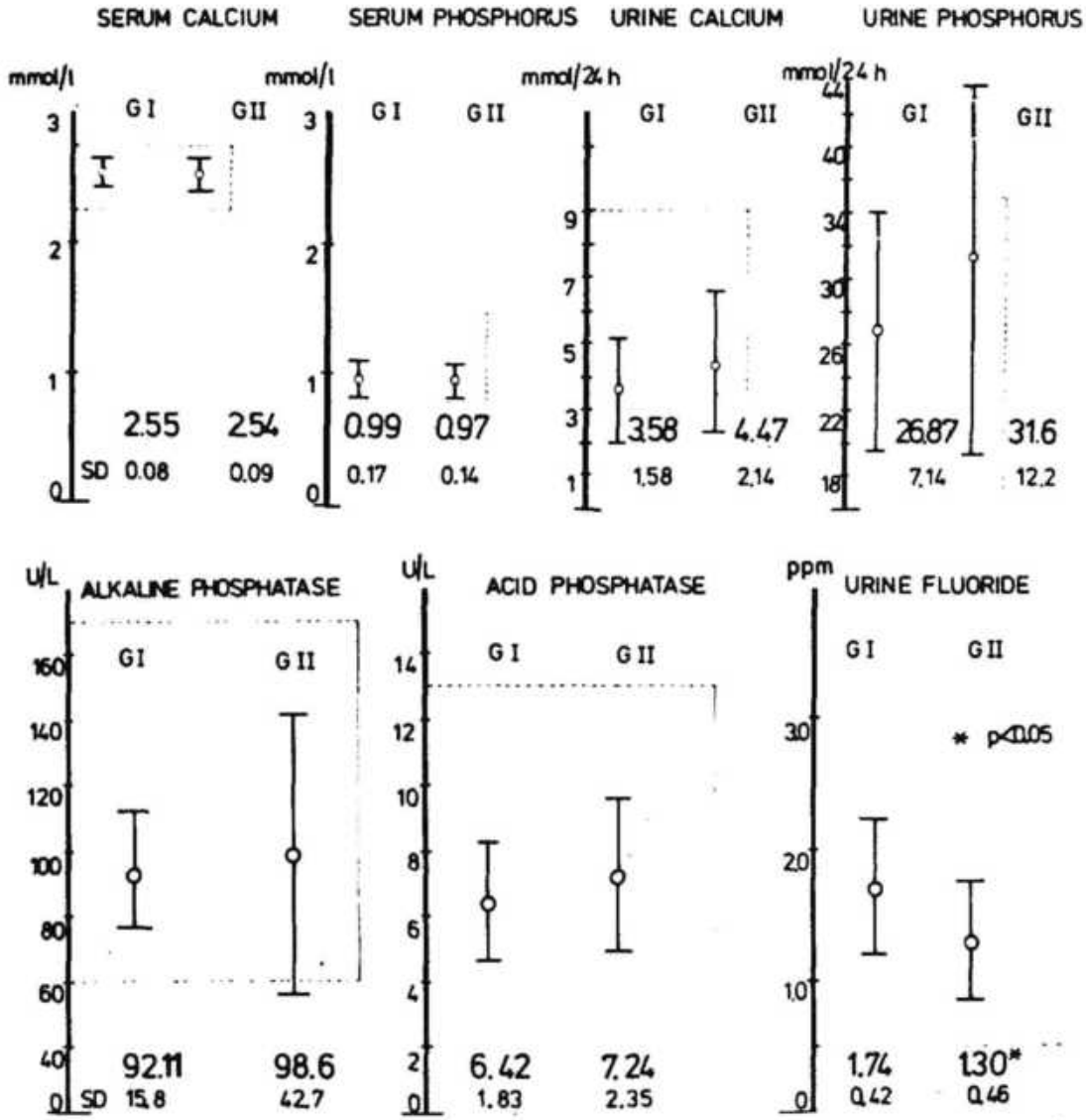
Frequency of Osteosclerosis in Both Groups



sure. Pains and limited mobility in the spine and hip joints were most significant. The frequency of spinal sclerosis is the same in both groups whereas sclerosis of the pelvis (significant) and of the forearms and lower legs (insignificant) is seen less often in Group 2 (Fig. 2).

The serum calcium and phosphorus levels varied within normal limits. Urine calcium was decreased insignificantly (Fig. 3). No abnormal values were noted in the serum acid and alkaline phosphatase activity, in the serum proteins, in the individual electrophoresis fractions, erythrocyte count, and color index (Fig. 4).

Figures 3 and 4



In contrast, the fluoride level was markedly elevated in both groups (1.74 ± 0.42 ppm for Group 1 and 1.30 ± 0.46 ppm for Group 2). The difference in the fluoride levels between the two groups is statistically significant; in Group 2, 25.4% less fluoride was excreted.

Discussion

In both groups the period of exposure to fluoride, the kind of previous work, and the age were similar. The length of the period which had elapsed since exposure differed, namely less than one year in Group 1 and 2 - 7 years, with an average of 3.4 years in Group 2. The urinary fluoride was markedly elevated in both groups, but had decreased significantly in the group in whom the period of nonexposure was longer. In view of the fact that some of those examined were residing in the vicinity of the aluminum plant, we made a careful search for a possible relationship between the urinary fluoride level and the place of residence, but none was found. No appropriate control group residing in the vicinity of the aluminum plant was available, but studies by Balazova (25) and Demole et al. (26) have shown a minimal rise in fluoride level in those residing near a factory. Therefore, the fact that our subjects were living near the aluminum plant could not be of major importance with respect to the amount of fluoride excreted in the urine, and even less concerning the decrease in this level in subjects after a more prolonged period of nonexposure to fluoride.

Roholm (4) reports that elevated urinary fluoride is maintained for many years after cessation of exposure. In Largent's studies (27), the level markedly exceeded the supply for 1.8 years and returned to a state of equilibrium only after 3.8 - 4.3 years. In Group 2 with an average discontinuance of exposure for 3.4 years, the fluoride level is 25.4% lower than that of Group 1 with one year's nonexposure, but it is still about 60% higher than the normal range in Poland namely 0.5 ppm (28). Several more years therefore must elapse before the urinary fluoride in this group returns to normal. This is all the more probable since it follows from the equilibrium studies of Largent (15) that about 8 years are required for the excretion of half the amount absorbed in the skeleton. McCann et al. (13) explains the slow excretion of fluoride on the basis of the difficulty in freeing its ions from the interior of the fluoroapatite crystal, since the exchange of fluoride from the surface of crystal takes place easily. According to Hodge (29), on the other hand, the steady excretion in the later phases may result from osteoblastic and osteoclastic processes in fluorotic bone. It is also possible that secondary resorption of the fluoride already liberated in the immediate vicinity of the bone may play a part (30).

Serum calcium and phosphorus and serum acid and alkaline phosphatase in our cases did not deviate from the norm. Similar observations in industrial fluorosis are reported by Kaltreider et al. (31), Hac et al. (32) Hoogstratten et al. (33), Vischer et al. (34), and Franke et al. (2), except that Franke sometimes observed a rise in the alkaline phosphatase activity. Marked deviations in the analysis mentioned have been reported in endemic fluorosis (20, 22, 23) and also during fluoride treatment of

osteoporosis (18). Reutter et al. (18) observed in addition a decrease in the urinary calcium during fluoride administration. In our material the serum protein and the distribution of its electrophoretic fractions were normal. In contrast, Fradà et al. (20) reports a decrease in the γ-globulin level in 80% of patients with endemic fluorosis. Like Franke et al. (2) and Agate et al. (35), we did not observe an increase in the incidence of anemia. Secondary anemia in industrial and endemic fluorosis has been described by Roholm (4) and by Fradà et al. (20).

Comparison of the painful symptoms and restricted mobility in the two groups indicates that the clinical condition of the locomotor system improves after a prolonged period of discontinuance of occupational exposure. We selected the frequency of occurrence of osteosclerosis - the most characteristic feature of osteofluorosis (21, 36) - for comparison of the radiological changes. Roholm(4) and Franke et al. (2) reported regression of sclerosis after cessation of exposure. In our studies, sclerosis of the spine is the same in both groups, whereas in other parts of the skeleton sclerosis was less common than in Group 2. This divergence indicates that visual evaluation of sclerosis is not precise as was also suggested by Hodge et al. (3). Because we had no densimetric measurements at our disposal, we could not establish objectively the differences between the two groups with regard to osteosclerosis.

Conclusions

After discontinuation of occupational exposure for several years, urinary fluoride was still elevated although it decreased with the passage of time. In the group in which exposure had been discontinued for more than 2.4 years, urinary fluoride was 25.4% lower than in the group with a shorter period of nonexposure. No abnormalities were found in the serum calcium and phosphorus levels, in the serum acid and alkaline phosphatase activity, the hemoglobin level, the erythrocyte count, or the serum protein level and the distribution of its electrophoretic fractions. The clinical condition of the locomotor system improved in subjects after prolonged nonexposure, but no regression of sclerosis was observed.

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Corrections

In the article "Uptake of Fluoride by Magnesium Trisilicate" by Rao et al. (13:77, 1980):
Concentrations of F^- are in µg on p. 77 line 7 and in columns 1, 2, 4 and 5 of Table 5.
In Table 4, concentration of ions are in ppm. Table 5 last column: B'/A' instead of B/A.

"Chemical Profile of Plasma in Fluoride Toxicity II Total Protein-Bound Hexose and Seromucoid Fraction of Rabbit Plasma" 13:151-158, 1980 by A.K. Susheela and Y.D. Sharma:
p. 153 line 4 and p. 154 line 12: 10 mg NaF/kg
p. 154 line 21 and p. 155 line 1: 50 mg NaF/kg
p. 156 lines 16 and 18 from bottom: α globulins instead of γ globulins

HYDRO-GEOCHEMICAL ASPECTS OF ENDEMIC SKELETAL FLUOROSIS IN INDIA - AN EPIDEMIOLOGIC STUDY

by

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SUMMARY: The most common fluorine-bearing minerals which constitute the natural source for fluoride in drinking water are fluorite, apatite, rock phosphate and topaz. The epidemiologic prevalence of endemic fluorosis is directly related to the distribution of fluoride-bearing minerals in the various endemic areas.

Introduction

Endemic fluorosis is widespread through India affecting mainly the states of Andhra Pradesh, Punjab, Rajasthan, Gujrat, Tamil Nadu, Karnataka and Uttar Pradesh. Low calcium, magnesium hardness (soft water) and high alkalinity of the drinking water contribute to the toxic effects of fluoride on bones and teeth. Since the origin of endemic fluorosis is hydro-geochemical, its effective control and prevention can only be achieved through providing low fluoride drinking water from alternate sources. Fluorine rarely occurs in its free state in nature but combines chemically to form fluoride. The principal sources of fluoride intake in man are water, edible vegetation, marine animals and industrial dust.

In contrast to the hydro-geochemical aspects of endemic skeletal fluorosis, its clinical, biochemical, metabolic, radiological and histopathological manifestations have received considerable attention (1-7). In the present communication, therefore, we have studied only the hydro-geochemical phase of endemic fluorosis.

Material and Methods

From 1968 to 1979 we carried out clinical and radiological field surveys and analyses of drinking water for fluoride and its chemical composition. Water samples were collected from different areas throughout the country and analyzed in duplicate for their chemical constituents. Fluoride assays were made by the use of the specific ion electrode; alkalinity, hardness and chloride by standard procedures (1-5); calcium and magnesium by Atomic Absorption Spectrophotometer; and sodium by Flame Photometer. The temperature at the time of the analysis ranged from 28 to 38°C. In order to relate the fluoride concentrations to the chemical constituents of the water a minimum of 50 samples was analyzed for each range of fluoride content. Data on important

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fluorine-bearing minerals in India were obtained from the Geological Survey of India (8).

Results

Table 1 reveals the most important fluoride-bearing minerals as obtained by the Geological Survey of India. The minerals with high fluorine content were fluorite (48.33%), cryolite (53.21%), and topaz (16.80%). Figure 1 shows that fluorites were widely distributed in the states of Rajasthan (region 19), Madhya Pradesh (region 13) and Gujrat (region 7).

Table 1

F^- Bearing Minerals in India

Name	Formula	% F^- Content Analytical Values
A. Fluorides:		
1. Fluorite	CaF_2	48.18-48.61
2. Fluocerite	$(Ce\ La\ Dy)F_3$	19.49-29.44
3. Cryolite	Na_3AlF_6	53.55-54.88
B. Phosphates:		
4. Fluor-Apatite	$Ca_5(PO_4)3^F$	2.57-5.60
5. Wagnerite	$Mg_2(PO_4)F$	5.06-11.48
6. Triplite	$(Mn, Fe, Mg, Ca)_2\ FPO_4$	6.02-9.09
C. Silicates:		
7. Topaz	$(Al\ [F.OH]_2)\ SiO_4$	13.23-20.37
	Sheet silicates with $(OH,F)_4$	
D. Mica Group:		
8. Phlogopite	Magnesium Mica	0.56-9.20
9. Lepidolite	Lithium Mica	4.93-8.08

The chemical analysis of the drinking water is presented in Table 2. With increasing content of fluoride in water, there was an increase in pH, in alkalinity and in the ratio of alkalinity/hardness but a decrease in hardness and in the hardness/fluoride ratio; concentrations of calcium and magnesium decreased and levels of sodium and chloride were higher. These results confirm our previous findings (1): As the fluoride level in water becomes higher, the water becomes more alkaline and softer.

Figure 1

F^- Bearing Minerals

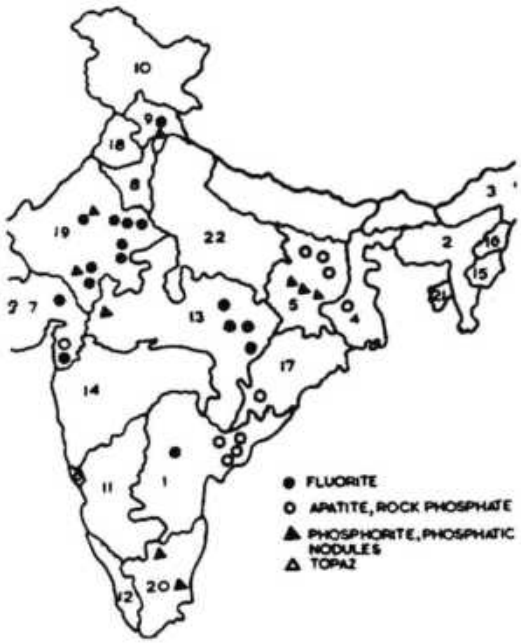
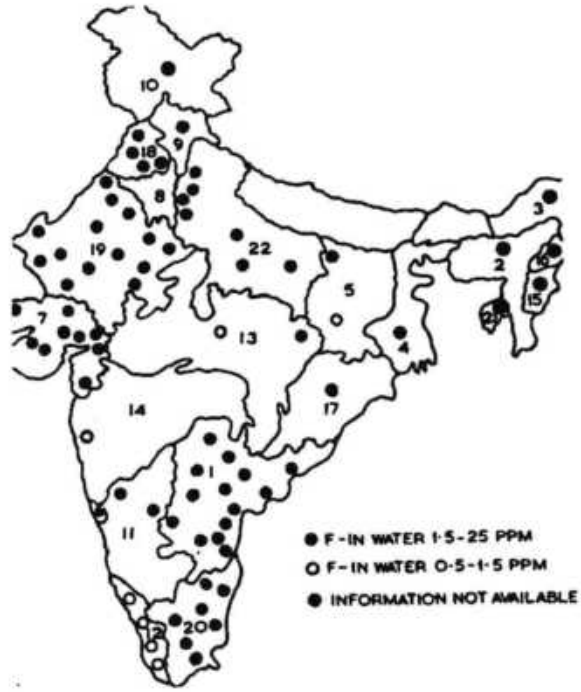


Figure 2

Fluorosis in India



1. Andhra Pradesh 2. Assam 3. Arunachal Pradesh 4. Bengal 5. Bihar 6. Goa 7. Gujart 8. Haryana 9. Himachal Pradesh 10. Jammu & Kashmir 11. Karnataka 12. Kerala 13. Madhya Pradesh 14. Maharashtra 15. Manipur 16. Nagaland 17. Orissa 18. Punjab 19. Rajasthan 20. Tamil Nadu 21. Tripura 22. Uttar Pradesh

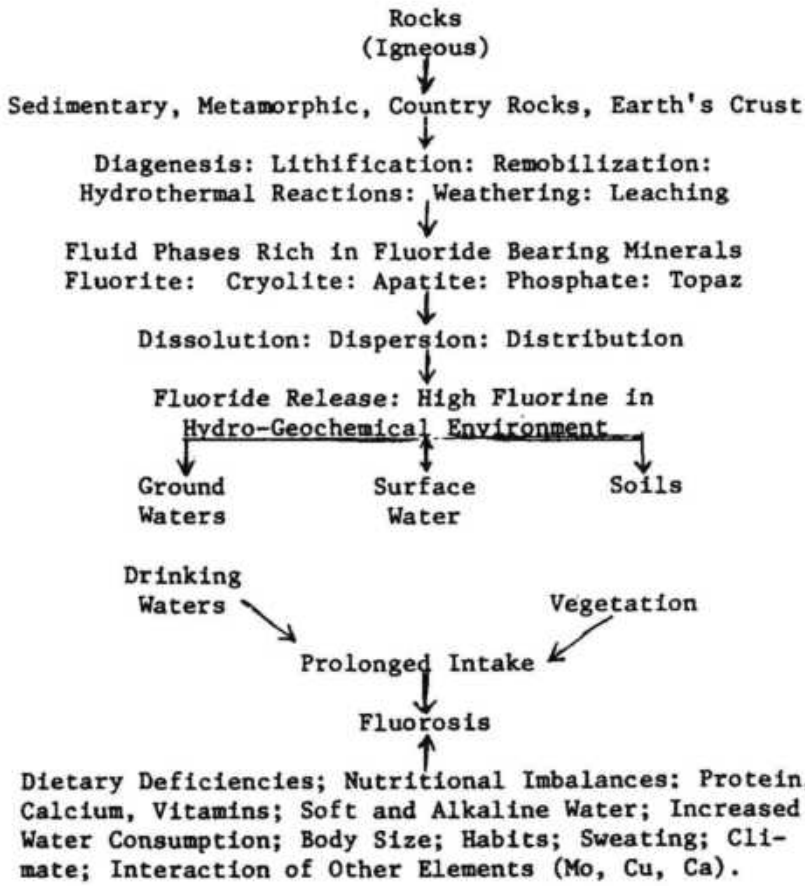
According to a previous epidemiological survey, endemic fluorosis is a great national health problem which is widespread throughout the country (Fig. 2). The most seriously affected states are Andhra Pradesh (region 1), Punjab (region 18), Rajasthan (region 19), Gujrat (region 7), Tamil Nadu (region 20) and Uttar Pradesh (region 22). The severity (clinical and radiological) of skeletal fluorosis in these areas correlated with the level of fluoride in drinking water used by the residents (to be reported separately). It ranged in most of these areas from 1.5 to 25 ppm.

The disease appears to be largely of hydro-geochemical origin as illustrated in Fig. 3. Our epidemiological observations on the nutri-

tional status of the population affected with fluorosis, to be reported separately, indicates that dietary deficiencies and nutritional imbalances, particularly the low intakes of protein, calcium and vitamin D, enhance the severity of fluoride toxicity and its effects on bone metabolism (Fig. 3).

Figure 3

Hydro-Geochemical Basis of Endemic Fluorosis in India



Discussion

The world's fluoride stores in the ground are estimated to be 85 million tons of which nearly 12 million tons are located in India. Nearly one million people in India are believed to be afflicted with fluorosis and about an equal number is exposed to the risk of developing this disease. Endemic fluorosis in India is of hydro-geochemical origin. In-

vestigations have shown that fluoride-bearing minerals are widely distributed. As shown in Fig. 2 there is a close correlation between the distribution of fluoride-bearing minerals and prevalence of endemic fluorosis in these areas.

Chronic fluoride toxicity depends upon the actual amount of fluoride ingested per day and the duration of exposure to high fluoride intake through drinking water since the amount of fluoride taken through food appears to be relatively small. The daily intake of fluoride depends upon (a) concentration of fluoride in drinking water, (b) total amount of water ingested per day. The amount of water ingested is itself dependent upon a number of variables, such as body size, food habits, environmental temperature and extent of physical activity. Hot climate and sweating promote increased consumption of water. During the hot summer season agricultural laborers may drink up to 8 liters of water a day. In addition, Indian diets contain large amounts of water and practically all staples are cooked in water.

Table 2

F^- Content and Relationship with
Chemical Constituents of Natural Drinking Water

Range of F (ppm)	pH	Alkalinity (mg/l) (As $CaCO_3$)	Hardness (mg/l) (As $CaCO_3$)	$\frac{\text{Alkalinity}}{\text{Hardness}}$	$\frac{\text{Hardness}}{\text{Fluoride}}$	Ca (mg/l)	Mg (mg/l)	Cl (mg/l)	Na (mEq/l)
0.0	6.5	20.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
0.1-1	7.1	193.6	242.0	0.84	242.0	70.2	19.8	24.5	1.2
1-5	8.3	402.0	192.0	2.16	56.8	75.3	20.2	75.5	1.5
5-10	8.5	450.0	80.0	5.60	9.4	16.0	20.0	90.3	15.0
10-25	8.5	530.0	28.0	18.90	1.1	8.0	11.0	31.0	15.0

Temperature at Analysis 28-36°; 50 samples in each range

Most urban areas in India are provided with protected drinking water with a fluoride content below 1.0 ppm. In the villages, however, where water is naturally high in fluoride, endemic fluorosis is most prevalent.

According to our investigations, low calcium and magnesium hardness and high alkalinity are characteristic in the majority of the drinking

water samples high naturally in fluoride. With increasing concentrations of fluoride in natural drinking water, calcium and magnesium hardness decreases and the alkalinity increases (Table 2). According to epidemiological surveys on endemic skeletal fluorosis, the toxic effects of fluoride on bones and teeth are more pronounced and severe in individuals who are drinking water of higher alkalinity and lower calcium and magnesium hardness (soft water). Calcium and magnesium hardness in water appear to inhibit fluoride toxicity.

Acknowledgements

The authors are grateful to the Geological Survey of India for their kind help in collecting the data on the distribution of fluoride-bearing minerals in India.

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BIOLOGICAL MONITORING FOR OCCUPATIONAL FLUORIDE ABSORPTION

by

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SUMMARY: Urinary fluoride concentrations, measured to monitor occupational fluoride absorption, were corrected on the bases of specific gravity (SG), creatinine concentration and osmolarity. Uncorrected and corrected concentrations immediately, four and fourteen hours after the end of a final shift and immediately before a first shift were compared with pre and post-shift serum fluoride concentrations. Creatinine and osmolarity correction produced better correlation with serum fluorides than SG correction but all were dependent on a few high values. The ratio between SG corrected urinary fluoride concentrations and serum fluoride correlated significantly with SG over the range of encountered values and there was no evidence to support rejection of urinary fluoride estimates where SG is below 1.010. An empirical SG correction formula was evolved that was as good as creatinine and osmolarity correctors.

Introduction

Exposure to fluoride ion (F^-) in workplace air occurs in a variety of industrial situations and may be assessed by atmospheric and biological monitoring. Standards (1) for evaluation of such measurements have been published by the National Institute of Occupational Safety and Health (NIOSH) in the U.S.A. and include the analysis of urine samples for fluoride content with correction of the results for urinary dilution to a specific gravity of 1.024. The correction factor becomes large as the specific gravity approaches unity and the NIOSH standard recommends discarding samples where the specific gravity is less than 1.010.

There is no British Standard for the biological monitoring of workers exposed to fluorides, and the practice at this factory has been based on the NIOSH Standards for biological monitoring of process operators involved in the production of sodium monofluorophosphate (SMFP). Atmospheric levels are usually 0.5 ppm HF and have never exceeded 1 ppm on random grab sampling. It is also the practice to offer a post-work urine fluoride estimation to any maintenance personnel who, during a single period of work on the plant, believe they may have been exposed to fluoride ion. In the latter case, it is not possible to obtain a further sample for analysis if the urine specific gravity is found to be less than 1.010 since there is no regular pattern of exposure. In some cases fluid consumption during work is so great and the urine so diluted that its speci-

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fic gravity is usually less than 1.010. Moreover, it is often the case that the volume of the urine sample that can be produced is insufficient to permit measurement of the specific gravity by a hydrometer(urinometer) and recourse must be had to comparison of the weight of the pipetted aliquot of urine with the weight of the same volume of distilled water at the same temperature. This technique requires an accurate balance which, if it is purpose dedicated, is expensive. Accordingly, other indices of urine dilution, such as osmolarity or creatinine concentration, may stand comparison on cost grounds with specific gravity if they can be shown to be equally useful as correctors for urinary dilution, and would be preferable if they could be shown to be better correctors. It also seemed worthwhile to examine the choice of 1.010 as the density limit below which urinary fluorides would be unreliable, since this limit might be unnecessarily rigorous.

Thus, this study was designed to examine the relationships between fluoride concentrations, both pre and post-shift, in serum and in urine, with the concentrations in urine being corrected for urinary dilution on the bases of specific gravity, creatinine concentration and osmolarity.

In addition, there was an examination of the timing of urinary fluoride estimations to estimate recent absorption and accumulated load by comparing the correlations between immediate and 4-hour post-shift urinary fluorides and post-shift serum fluorides and also between pre-shift serum fluoride and 14-hour and 96-hour post-shift urinary fluorides. Healthy male process workers producing sodium monofluorophosphate by a process involving slight exposure to HF were asked to supply a sample of their individual domestic piped water supply and the works' water supply was also sampled. In every case the fluoride concentration was less than 8 μM (0.15 ppm). The purpose and procedure of the study was explained carefully to the men and their representatives and their consent was obtained without exception. In nine out of ten cases there was a complete compliance with the protocol, the tenth forgetting one urine sample (see asterisks, Table 1). The shift-pattern of the men is a sixteen day rota comprising 4 twelve hour day shifts, 4 rest days, 4 twelve hour night shifts and finally 4 rest days.

Samples and Analytical Methods

Urine and blood samples, U1 and S1, were taken at about 6:00 P.M., after the subjects had showered and changed at the end of the fourth day shift. Urine samples, U2 and U3 were provided 4 hours and 14 hours later respectively and urine and blood samples, U4 and S4 were taken at about 6:00 P.M. prior to changing before commencing the first night shift. Usually, this was 96 hours after the first samples, but in one case an additional shift was worked so that these samples were taken 72 hours after the initial samples. Subjects emptied their bladders some 30 minutes before collecting the urine samples. Urine samples (referred to generally as Uj, where j = 1, 2, 3 or 4) were refrigerated immediately and frozen as soon as possible thereafter. Blood was allowed to clot overnight at room temperature. The serum was separated by centrifuga-

tion and frozen for subsequent batch analysis.

Urine (uj) and serum (Sj) fluoride concentrations were measured with an ion-specific electrode (ORION 9609) used in conjunction with a pH meter (EIL 7050) after dilution with an equal volume of Total Ionic Strength Buffer (ORION 940909). Preliminary experiments had shown that this technique was superior to other methods dependant on colorimetric determination of Lanthanum nitrate - alizarin fluorine blue complex applied to a solution of chloride - free serum ash or to serum dialysate. The accuracy of measurements of fluoride concentration in low-fluoride serum spiked with various known amounts of fluoride was of the order of 10%.

The specific gravity (SG) of each urine sample (Uj) was calculated as the ratio of the measured weight of 10 ml of distilled water delivered by the same pipette, all at room temperature. The value was expressed as GJ = 1000 (SG-1) and is referred to as the "density index". Urine creatinine concentration (Cj) of each urine sample was measured by standard clinical autoanlyzer methods in the Wolfson Research Laboratories, Birmingham. Urine osmolarities (Mj) were measured on freshly-thawed urine by the freezing point depression method, using a Knauer cryoscopic osmometer.

Calculation of Results

Correction of measured urine fluoride concentration (uj) for urinary dilution were made as follows:

Density corrected fluoride, ufg = uj 24/Gj
(Where SG was measured as 1.000 (Gj=0), it was given the value 1.001 (Gj=1)
Creatinine corrected fluoride, ujc = uj/Cj
Osmolarity corrected fluoride, ujm = um/Mj

Regression lines and correlation coefficients were calculated by standard statistical methods with the aid of a pre-programmed electronic calculator.

Results

The raw data is presented in Table 1. In five urine samples (12.5%), the specific gravity was less than 1.010 and in one, 1.000. One individual had a density-corrected post-shift urinary fluoride greater than the NIOSH standard 4 ppm = 210 µM. In most cases the post-shift serum fluoride exceeded 3 µM. In the individual already referred to and in one other a pre-shift serum fluoride was greater than 3 µM.

1. Relationship between density index, creatinine concentration and osmolarity of urine samples.

Figs. 1a, 1b and 1c illustrate the relationship between Gj, Cj, Mj and Cj and Mj and Cj. The correlation between Cj and Mj is better than that between either and Gj.

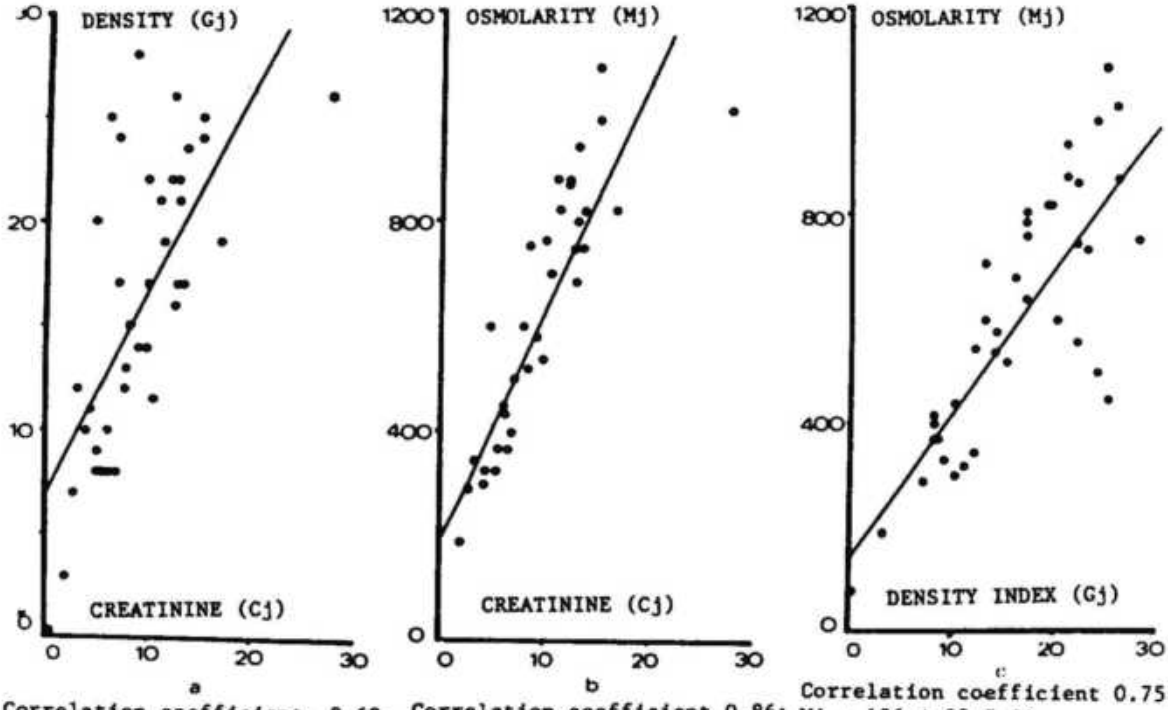
Table 1

Subject Age	Sample No. j	Serum F^- M SJ	Urine F^- M uj	Density Index Sg-1 x 10^3 GJ	Creatinine mM CJ	Osmolarity mOsm/l Mj	Corrected Urinary Fluorides ujg	ujc	ujm
BW	1	4.2	157	25	6.0	452	151	26.1	346
	2		178	24	7.0	504	178	25.4	353
31	3		121	23	13.5	744	126	9.0	163
	4	2.1	71	13	10.5	708	130	6.7	100
OP	1	8.4	150	7	2.9	291	516	51.9	518
	2		67	3	2.2	192	539	30.6	351
49	3		149	14	9.8	538	256	15.3	278
	4	4.2	89	8	5.1	416	268	17.5	115
HE	1	2.6	83	12	7.8	546	166	10.7	152
	2		92	17	13.4	821	129	6.8	112
49	3		48	17	12.9	792	68	3.1	61
	4	2.1	89	17	10.0	765	126	8.9	117
WX	1	2.6	94	20	4.8	600	112	19.5	156
	2		52	9	5.2	328	138	9.9	157
52	3		45	10	4.2	300	109	10.8	151
	4	2.1	66	22	12.1	872	72	5.5	76
TD	1	2.6	67	11	4.6	328	147	14.7	205
	2		*	*	*	*	*	*	*
29	3		41	10	6.2	436	99	6.6	94
	4	2.6	80	19	11.4	824	101	7.0	97
AB	1	6.3	180	28	8.4	756	154	21.4	238
	2		114	12	3.3	344	227	34.5	327
53	3		124	15	8.3	520	199	15.0	236
	4	3.2	80	14	9.2	580	137	8.7	136
UV	1	3.2	43	25	15.0	1096	42	2.9	39
	2		124	26	12.3	880	114	10.1	141
42	3		63	24	14.9	992	63	4.2	64
	4	2.6	132	21	12.9	944	149	10.2	139
WM	1	3.7	93	16	12.8	684	139	7.2	135
	2		117	22	12.7	748	128	9.2	156
31	3		80	8	6.4	368	240	12.5	217
	4	2.1	76	13	7.9	600	140	9.6	126
QR	1	3.7	197	26	27.6	1022	182	6.6	177
	2		48	8	6.9	400	145	7.0	121
42	3		40	8	5.6	372	120	7.1	107
	4	2.1	94	19	16.8	824	118	5.6	114
EF	1	3.2	147	21	11.0	880	168	13.4	167
	2		95	22	9.7	560	103	9.8	169
47	3		47	17	7.2	640	67	6.6	74
	4	2.1	9	**	0.7	80	215	12.8	112

* Missing sample; ** (SG-1.000) x 10^3 taken as 1 for this correction.

Figure 1

The Relationships Between Density Index, Gj, Creatinine Concentration Cj, and Osmolarity Mj (39 Urine Samples)



a Correlation coefficient, 0.68; Gj = 7.3 + 95 Cj

b Correlation coefficient 0.86; Mj = 212 + 43 Cj

c Correlation coefficient 0.75; Mj = 136 + 28.5 Cj

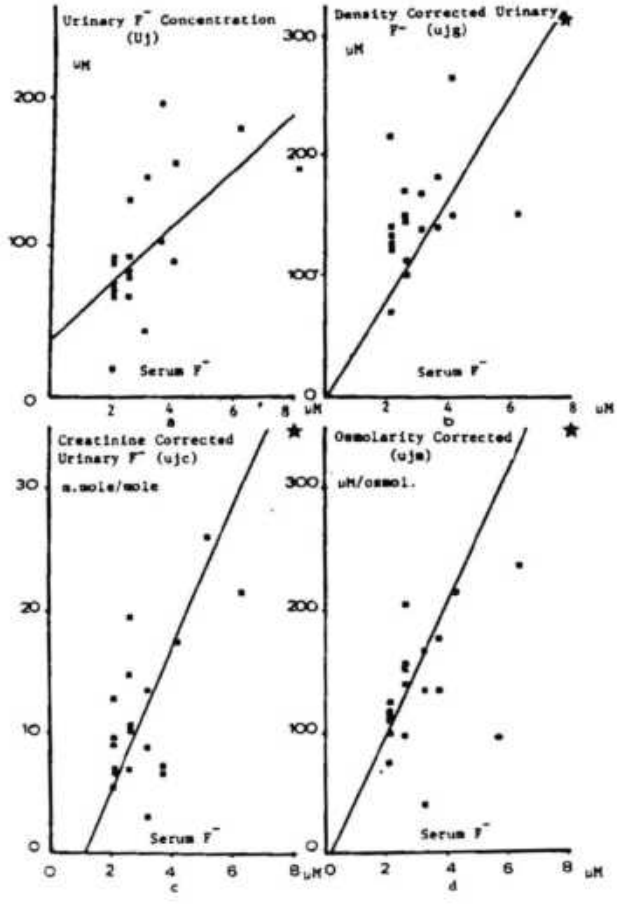
2. Relationship between urinary fluoride concentration, variously corrected, and serum fluoride concentrations.

Figs. 2a - d illustrate the relationship between uj, ujg, ujc, ujm respectively with Sj.

Correlations between uj and Sj and between ujm and Sj are better than between ujg and Sj. The correlation between uj and Sj is considerably worse than the other three. However, all correlations are dependent on the presence of four values of Sj greater than 4 µm (0.075 ppm). If these pairs of values are omitted in each case, correlation coefficients for ujg, ujc and ujm with Sj are + 0.1., - 0.1 and + 0.28 respectively. These are all statistically insignificant.

Figure 2

Relationships Between Urinary F^- Concentrations (Corrected and Uncorrected) with Serum F^-

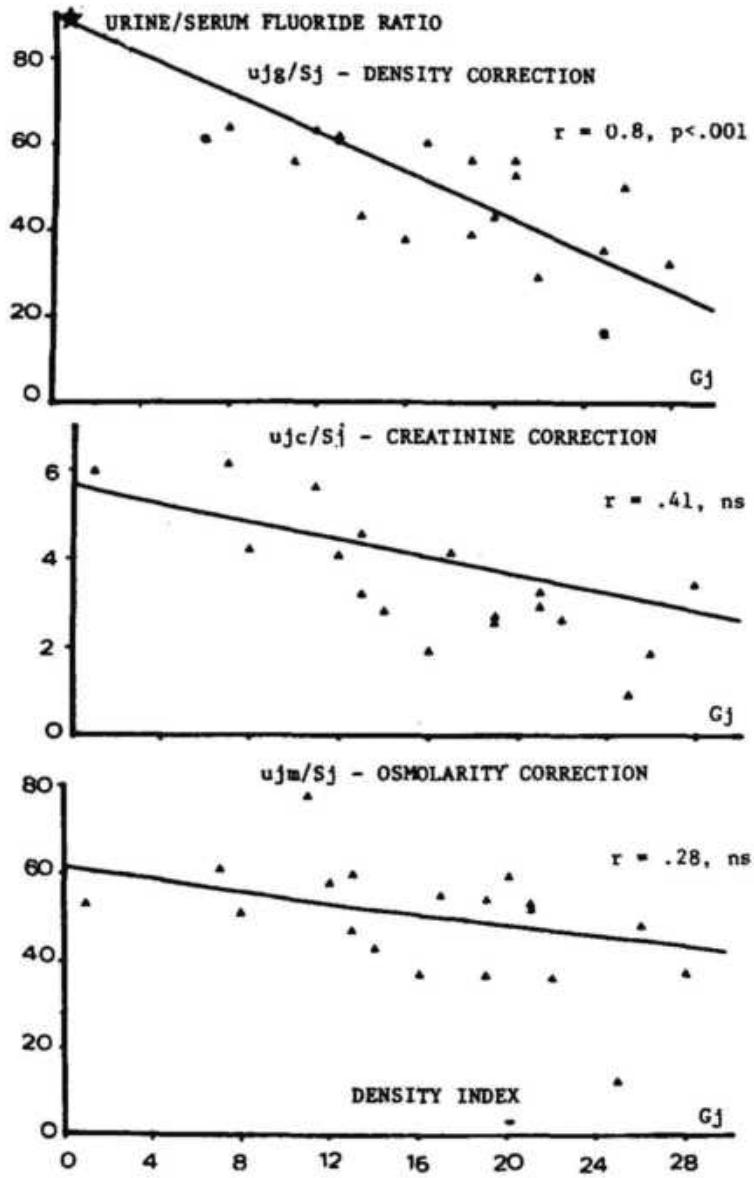


3. The variation with density index in the relationship between corrected urinary fluoride and serum fluoride concentrations.

Figs. 3a, 3b and 3c illustrate how the ratios of corrected urine fluoride to serum fluoride vary with urine specific gravity. The ratio for density-corrected fluoride (ujg/Sj) varies by 5.9% of its value at

Figure 3

Relationship Between Urinary F^- and Serum F^-



Gj = 24 per unit density index. The corresponding variations in the ratio for creatinine correction (ujc/Sj) and osmolarity correction (ujm/Sj) are 3.1 and 1.4% respectively. In the case (Fig. 3a) of density-corrected urines, the correlation coefficient (0.80) for a linear regression was better than that (0.64) for a power law relationship and there

was in general, no suggestion of a progressively increasing effect of SG on the urine/serum ratio as specific gravities decreased below 1.010.

4. The timing of urine samples for indication of basal and post-shift serum fluorides.

Table 2 sets out the correlation coefficients between corrected urine fluorides and serum fluorides. Four hour post-shift urine samples appear slightly better than immediate post-shift urines as predictors of serum fluorides. Fourteen hour post-shift urines also correlate reasonably with post-shift serum values and weakly with pre-shift serum values. Ninety-six hour post-shift urines reflect post-shift serum levels and pre-shift levels to a similar degree.

Table 2

Correlation Coefficients Between Corrected Urinary F^- 0, 4, 14 and 96 hrs. Post-Shift and Post- and Pre-Shift Serum Concentrations

	Hours Post-Shift	S1 Post-Shift	S4 Pre-Shift
U1g	0	0.8	
U2g	4	0.92	
U3g	14	0.77	0.60
U4g	96	0.69	0.64
U1C	0	0.81	
U2C	4	0.85	
U3C	14	0.77	0.60
U4C	96	0.65	0.70
U1M	0	0.80	
U2M	4	0.80	
U3M	14	0.80	0.65
U4M	96	0.85	0.86

Discussion

Current concepts regard fluoride in the body as distributed in a two compartment system consisting of a skeletal compartment with a low turnover interfacing with body fluids (exemplified by blood) by a high impedance interface. The body fluid compartment exchanges readily and unidirectionally with alveolar and the intestinal contents as sources of fluoride and tubular urine as the excretion medium. According to such a model, both blood and urinary fluorides in the absence of recent industrial fluoride exposure will reflect any gradient there may be between the skeletal load and the environmental fluoride concentrations in drinking water and food. Substantial recent exposure will markedly affect blood and urine levels during and immediately after exposure but,

unless sustained for long periods, will not have a great effect on skeletal fluoride content. Accordingly, post-shift concentrations are regarded as reflecting exposure in previous shifts and pre-shift concentrations(after several rest days) are regarded as an index of cumulated past exposure.

Whereas there is an extensive literature on urinary fluorides as an index of occupational exposure, which has recently been reviewed by Smith and Hodge (2), there is little information regarding blood, plasma or serum fluorides. Fluoride levels in blood, saliva and urine were studied by Domzalska et al. (3) and blood levels correlated very closely with the duration of occupational exposure. Krechniak (4) reported blood levels and urine levels in machine welders, hand welders and controls. Relative differences in urine fluoride concentrations between machine welders and controls were more pronounced than differences in blood fluoride.

The renal clearance of fluoride is much higher than that of chloride but less than that of creatinine, indicating net tubular resorption (5). The degree of tubular resorption depends on the renal tubular transit time and hence fluoride clearance increases with urinary flow rates. If the clearance is C_f at urinary flow rate V and plasma fluoride is equal to serum fluoride (Sj).

$$Uj \times V = C_f \times S_j$$

To a first approximation $V \propto 1/C_j$ and $\propto 1/Mj$ and thus Uj x V might be replaced by U_j/C_j or U_j/Mj, i.e. by ujc or ujm.

$$ujc \propto C_f Sj \quad \text{ie} \quad ujc/Sj = C_f$$
or
$$ujm \propto C_f Sj \quad \text{ie} \quad ujm/Sj = C_f$$

If C_f were not dependent on V, corrected urinary fluoride would be directly related to serum fluorides. As it is, the relationship is dependent on urine flow rate and hence the SG as is shown in Fig. 3. The fact that the slope of the relationship with SG of the ratio of corrected urinary fluoride and serum fluoride is less for osmolarity correction that creatinine correction reflects the fact that osmolar clearance, as well as fluoride clearance, is flow dependent whereas creatinine clearance is not.

Whatever the clinical value of serum fluoride concentration in biological monitoring, it is a useful standard for the comparison of different methods of correcting urinary fluorides.

The one individual with elevated urinary fluoride concentration was a man who, despite continuing low levels of exposure, was excreting fluoride absorbed previously in different circumstances. His urinary fluorides had been falling and continued to fall steadily over a period of months. There had been a full examination of his current work practices and exposure. His urinary fluoride levels had never been consistently high enough to require skeletal x-rays. Other ele-

vated serum fluoride concentrations contributed to, but did not determine, the individual clinical assessments which were based on the results of regular urinalysis, knowledge of plant atmospheres and periodic medical examinations. In most cases, they simply reflected recent exposure in the preceding shift.

It is to be expected that there would be good correlations between the density index, osmolarity and creatinine concentrations and the correlations obtained agree well with those determined for the data of Araki (6) which were made available to us. For his data, Mj was measured as osmolarity and Gj = 6.3 + 1.5Cj, Mj = 76 + 68Cj, Mj = 23 + 33Gj. These lines are quite close to those shown in Fig. 1. Because of the correlations between the correctors (Fig. 1), the "density index", creatinine and osmolarity corrections produce broadly similar improvements in the usefulness of urinary fluorides in the estimation of serum fluoride.

Since osmolarity and specific gravity both reflect total solute concentration in a non-specific manner, it is rather surprising that osmolarity appears so much more similar to creatinine than to density index in its usefulness (Fig. 2). Though the correlation coefficients of the linear regressions of the corrected urinary fluoride concentrates on the serum fluorides are statistically significant, the relationships are in fact not as good as they would seem, since the correlation is entirely a result of the association of particularly high serum fluorides with high urinary fluorides. With serum fluorides below about 4 μM (0.075ppm), there is no correlation whatever. Accordingly, urinary fluorides cannot be used to follow changes in serum fluorides within the acceptable range of urinary fluorides in industrially exposed people, although all correctors are effective in indicating excessive exposure.

While the lack of such associations might simply be a result of the small numbers in this study, the lack of correlation at low values is so profound that any correlation identified in larger numbers is likely to be insufficiently direct for conclusions to be drawn in the case of a particular exposed individual and it is this situation which confronts the occupational physician. It may therefore be concluded that creatinine concentration and osmolarity are as good as specific gravity as correctors of urinary fluoride concentrations but confer no compelling advantages in the clinical situation.

Figure 3 shows that the ratio of corrected urinary fluoride to serum fluoride is a significant function of density index in the case of density-corrected urinary fluoride concentrations. The equation of the regression line of ujg/Sj on Gj could be used to calculate a different method of correcting urinary fluorides for urinary dilution on the basis of specific gravity. Such a new correction, ujg is given by:

$$ujg = Uj \times 24 \,/\, Gj \times (87 - 2.13\ Gj)$$

Whereas the correlation between ujg and Sj is 0.79, that of ujg and Sj is 0.83, which is very close to the correlations between ujc and Sj

and ujm and Sj. ujg is not dependent on Gj (r = 0.06) and more simple approximations to ujg could be achieved using the binomial expansion, e. g.

$$ujg = Uj \times 0.28\ (0.024 + 1/Gj)$$
$$\text{Where } Gj = 1000 \times (S.G. - 1)$$

Whatever the value of density correction on the traditional basis or some basis as that suggested above, it is clear that there is no particular specific gravity below which the nature of the relationship between density-corrected urinary fluoride concentration and serum concentration deteriorates. While it is necessary to be guarded about specific gravities close to 1, there is no sound cause to reject corrected values of urinary fluoride where the specific gravity exceeds 1.005 on the basis of poor reflection of serum values.

Table II indicates that the timing of post-shift urine samples is not critical and that a urine sample several hours post-shift is as useful as one taken at the end shift. In five out of nine subjects for which data are complete U2g was greater than Ulg. This time course of excretion corresponds to that reported by Collings, Fleming and May (7, 8).

With the limitations of the small numbers in this study we may conclude that the relationship between corrected urinary fluorides and plasma fluoride is weak at low fluoride concentrations, but that osmolarity-correction is marginally better than creatinine correction which is in turn better than traditional density correction and that all methods of correction efficiently indicate excessive occupational exposure. There is no reason to regard density corrected fluorides as valuable where SG is greater than 1.010 and valueless otherwise. There is a theoretical basis for a more complex correction of urinary fluoride on the basis of specific gravity, but there is no evidence to suggest that it offers significant improvements in practice.

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PREVALENCE OF FLUOROSIS IN A RURAL COMMUNITY NEAR VARANASI

by

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SUMMARY: A study, in a rural area near Varanasi, showed an incidence of 28.21% of dental fluorosis in the general population. The prevalence rate was highest in the age group 13-18 and was higher in males than in females, with a rising trend associated with an increase in fluoride content of the water. At a concentration of <0.5 ppm fluoride in water, the incidence of dental fluorosis was 16.98%.

Introduction

Fluoride is widely distributed in nature. The soils of the different areas of the world vary greatly in their fluoride content. All drinking water contains some fluoride naturally, ranging from 0.1 ppm to more than 20 ppm. Fluorosis due to fluoride in drinking water occurs in different parts of the world. In India, the pioneering investigations were made by Shortt and collaborators (1) in 1957 in Andra Pradesh. Singh et al. (2) in 1962 reported a belt, in which the fluoride

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content of drinking water was high, that covered at least one fourth of Punjab exposing roughly five million people to the toxic potentialities of fluoride. In Andhra Pradesh and Tamil Nadu (3), an even larger population was exposed to high fluoride consumption. Prevalence of genu valgum, a disease usually found in endemic fluorosis areas, has also been reported from Andhra Pradesh (4).

To date, no survey is available from the Varanasi area. Reports received from the dental and radiology department of S.S. Hospital, Varanasi, and also from subcenters of rural training centers of the department of Preventive Social Medicine indicated that fluorosis was encountered in the out-patient department and field settings. We therefore studied the Varanasi situation to determine:

1. The magnitude of the problem of fluorosis in the community.
2. The fluoride content of water used for drinking by the community.

Material and Methods

The preliminary study covered the population and drinking water sources of Rustampur village near the Rural Health Centre, Chiraigaon, about 18 km from the city of Varanasi. The reason for selecting this area was its approachability as well as good relations between the villagers and the Rural Health Centre for cooperation in the study. At first a survey of village wells was carried out. After giving each drinking waterwell a number, the aggregate of consumers from each of the wells was recorded. For fluoride estimation, a random sample comprised of one third of the wells from each hamlet was taken for analysis. A house to house survey of the population was carried out according to a predesigned plan. The teeth of the population under study were examined according to criteria laid down by WHO (5).

Radiological Investigation: Due to limitation of x-ray facilities, radiological examination was confined to those persons in whom signs and symptoms of skeletal fluorosis were associated with dental fluorosis.

Laboratory Procedure: The water samples containing fluoride were distilled with perchloric acid at 135-137°C following the microdistillation method of Singer and Armstrong (6). The distillate was estimated colorimetrically for its fluoride content by Zirconium-Erychrome-cyanine color lake.

Results and Discussion

The association between fluoride concentration of drinking water and dental fluorosis is shown in Table 1. The highest prevalance of 46.15% was found at concentrations of 2 ppm, followed by 35.82% at 1 to 1.2 ppm, 27.44% at 0.6 to 0.9 ppm and 16.98% at 0.5 ppm and below. The lowest level of fluoride in drinking water associated with dental fluorosis was 0.4 ppm. The differences in the prevalance of fluorosis and the level of fluoride in water were statistically significant ($p < 0.05$).

Table 1

Prevalence of Dental Fluorosis Related to F^- Concentration in Drinking Water

F^- in Water (ppm)	Population surveyed	Questionable	Fluorosis				
			Very mild	Mild	Moderate	Severe	Total	%
Up to 0.5	53	7	2	0	0	0	9	16.98
0.6 - 0.9	406	66	27	9	7	0	109	27.44
1.0 - 1.2	237	46	19	10	11	0	86	35.82
2.0	26	6	1	0	5	0	12	46.15

Venkateswarlu, Rao and Rao (as quoted by Siddiqui (3)) found that 0.9 to 1 ppm fluoride in Indian drinking water was associated with mottled enamel. In the present study, dental fluorosis was found at the low fluoride level of 0.4 ppm in drinking water.

Most dental fluorosis (60.27%), was observed in the age group 13-18 years, followed by 45.98% in the 7-12 year old group and 45.25% in those 19-24 years old. Thereafter there was a gradual decline. The lowest prevalence of dental fluorosis was noted in the group 1-6 years of age. The difference in the age groups was found to be statistically significant (Table 2).

Table 2

Agewise Prevalence of Dental Fluorosis Among Population Surveyed

Age Years	Total population examined (6 mos omitted)	Questionable	Fluorosis					
			Very mild	Mild	Moderate	Severe	Total	%
1 - 6	236	18	2	1	1	0	22	9.36
7 - 12	224	62	22	5	14	0	103	45.98
13 - 18	73	19	13	4	8	0	44	60.27
19 - 24	71	17	8	5	0	0	30	45.25
25 - 30	109	22	3	7	4	0	36	33.02
Above 31	276	27	9	5	3	0	44	15.94
TOTAL	989	165	57	27	30	0	279	28.21

Our observations are in accordance with the findings of earlier workers (1, 2). However, Daver (7) reported that prevalence of fluorosis was greatest among children between 6-14 years of age in contrast to 13-18 years in the current study.

Sex distribution of dental fluorosis is shown in Table 3. Among males 37.07% were affected, and among females, 19.56%. The difference was statistically significant ($p < 0.0001$). This observation also requires further investigation.

In two persons, x-rays of forearms for interosseous membrane calcification were negative. Additional studies on skeletal fluorosis will

Table 3

Sex Prevalence of Dental Fluorosis

Sex	Total population examined (11 mos omitted)	Fluorosis						
		Questionable	Very mild	Mild	Moderate	Severe	Total	%
Male	584	124	38	19	18	0	199	34.07
Female	405	41	19	8	12	0	80	19.59
TOTAL	989	165	57	27	30	0	279	28.21

be carried out. Jolly et al. (8) found an incidence rate of 2.4% for skeletal fluorosis, with the fluoride concentration of drinking water varying from 0.9 to 2.5 ppm.

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Abstract

EFFECT OF SODIUM FLUORIDE ON COLLAGEN

by

M. Drozdz, E. Kucharz, and E. Grucka-Mamczar
Sosnowiec, Poland

(Abstracted from Acta Biol. Med. Germ. 39:287-293, 1980).

Rats were given 10 ppm sodium fluoride in water for 7 weeks prior to and during pregnancy, as well as after delivery. Their offspring was treated in the same manner up to 6 months after birth. Sodium fluoride increased hydroxyproline and hydroxylysine concentrations and urinary excretion of the catabolites. Soluble and insoluble collagen decreased in skin and lungs.

The increase in serum and urinary collagen catabolites was directly related to the rats' age, the maximum values occurring in animals 6 months of age.

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ENDEMIC FOODBORNE FLUOROSIS IN GUIZHOU, CHINA

by

Wei Zan-dao, Zhou Lin-ye, Bao Ri-chuan
et al.
Guizhou, China

(Abstracted from Chinese Preventive Med. J. 13:148-151, 1979)

During 1976, the authors discovered a focus of skeletal fluorosis in the Bijie county in the western part of Guizhou province where the fluoride level in the water averaged 0.18 ppm. The area is not unusually dry nor is there excessive moisture in the air. The high fluoride content of food was established as the source of the disease.

The authors carried out an investigation of the population and the environment which included the intake of fluoride by adults from drinking water, food and air.

Altogether 1637 persons were examined, 211 of whom had x-rays, 99 had blood tests and, in 184, urine was analyzed for fluoride. The following observations were made:

Studies on the Population: The rate of dental fluorosis was 98.2%. Only in 1.8% of the population were teeth normal. On the basis of a classification involving 3 degrees according to severity, most mottling (96.7%) fell into "degree 2" and higher.

The history revealed joint pains in 52.1% of the cases. Of joint pains in four extremities and back, 17.8% were at one site, 18.4% at two sites and 15.9% at three sites. In 34.9% of the cases, the joints were limited in movement. More than 1/2 of the 16-45 year olds complained of dizziness, approximately 1/3 of headaches and 1/5 of paresthesias. There was evidence of heart disease in 14.3%, kidney involvement in 13.4%, liver disease in 3.9% and of lung disease in 2.9%. Among the female subjects above 16 years of age, there was a significant difference ($P<0.05$) in the body height compared with controls. No change in body weight was noted.

Urinary fluoride in 134 cases showed a mean value of 6.4 ppm with a range of 1.6 - 20.4 ppm. In 57 cases, the serum calcium was 7.69 ± 1.10 mg%, the inorganic base 3.46 ± 0.69 mg% and the alkaline phosphatase 10.7 ± 5.07 (King unit).

Ninety-two of the 211 cases 20 years of age and older on whom x-rays of bones were taken showed changes of skeletal fluorosis as reported by Dr. Huo Daijei on page 51.

Environmental Study: The environmental study included fluoride assays in air, drinking water, food, soil and rock. The air indoors of 12 households contained 0.07 mg/l which indicates that a patient inhaled about 0.5 mg of fluoride per day.

Abstract

In March 1976,75 samples of water were collected from endemic areas during the dry season and assayed by several methods including the fluoride electrode. They revealed an average level of 0.5 mg/l of fluoride. Forty-six water samples were collected in June 1976 during the rainy season from two areas under investigation and from control areas (Table 1). All concentrations of fluoride were below the international standard level. Sixty-two samples of food analyzed for their fluoride content revealed levels given in Table 2.

Table 1

Average Levels of F^- and Other Minerals in Drinking Water

F^- mg/l	pH	Hardness (degree)	Ca mg/l	Mg mg/l	Chl mg/l	F^- Hardness	F:Ca	Mg:Ca
0.18	7.2	14.5	50.1	32.6	7.6	1:80.7	1:278.3	1:1.5

Table 2

Fluoride in Food (mg/kg)

Rice	Wheat	Maize	Soybean	Potato	Cabbage	Tea
3.3	4.6	5.2	4.3	0.7	4.4	59.2

It was estimated that the average fluoride intake through food of regions under investigation was 7.6 mg/day.

Soil: The analysis of fifteen soil samples and 41 samples of rock revealed that the dolomite of the medium and upper Cambrian periods is the source of fluoride in the region. This geological structure is widely distributed in the western part of Guizhou. The average fluoride level in rock was 468.5 ppm and that in soil, 999.1 ppm.

The authors estimated the total daily fluoride intake for food, air and water at 8.6 mg; that from food alone, the major source, 7.6 mg.

In the discussion, the authors are critical of the general trend which considers the level of fluoride in water exclusively as the determinant for prophylaxis of tooth decay. They point out that dental fluorosis has been shown to prevail in VietNam and Thailand where water is low in fluoride but food contains high levels of fluoride. This is the first report documenting the occurrence of endemic skeletal fluorosis from fluoride-containing food.

With respect to the manner in which fluoride enters edible vegetation, a preliminary survey revealed that springs and wells are shallow - about 1 meter deep. Due to the high content of clay and sub-clay, filtration of fluoride into the lower strata of the soil is inhibited.

The authors believe that the current standard of 1 ppm in drinking water requires reassessment because other sources of fluoride are not being taken into consideration. They report that in Kuangzhou, where fluoride was added to water which already contained 0.2 - 0.3 mg F/1 - to bring it up to the standard of 0.8 mg/1 - in 10 years the incidence of dental fluorosis had risen as high as 40%. They recommend a re-evaluation of the standards for fluoride in water.

The authors advise against the use of fluoride toothpaste in endemic regions and warn about the danger of excessive tea drinking. There is need for further studies on the effect of fluoride on muscles, kidneys and heart, in addition to those concerned with the skeleton.

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FLUORIDE TISSUE DISTRIBUTION INTRACELLULAR FLUORIDE CONCENTRATIONS

by

W.D. Armstrong and L. Singer
Minneapolis, Minnesota

(Abstracted from Proc. Soc. for Exp. Biol. and Med. (164:500-506, 1980)

In groups of 6 - 15 rats sacrificed 80 - 240 minutes after intraperitoneal injections containing radiofluoride (^{18}F) and radiochloride (^{36}Cl) their distribution in muscle, liver and tendon was studied. The ratio of fluoride in liver tissue water (tw) and in plasma water (pw) was constant over 120-220 minutes and in the muscle during 80 - 120 minute. The $^{18}F_{tw}/^{18}F_{pw}$ ratios for muscle were lower than those of liver. The ratios of fluoride distribution for both liver and muscle declined significantly at the longest time periods probably as a result of reductions of intracellular pH and/or increases of extracellular pH.

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FLUOROSIS: STUDIES ON SURAL NERVE BIOPSIES

by

S. Harinarayana Rao, D. Krishnamurthy, B. Sesikeran
and D. Raja Reddy
Hyderabad, India

(Abstracted from a Paper Presented at the 29th Annual Conference of the Neurological Society of India in Bangalore, December, 1979).

A survey of the literature on osteofluorosis reveals little information on the morphological changes of the peripheral nervous system in this disease.

Biopsies of the sural nerve at the ankle level removed from 13 patients with osteofluorosis were studied by conventional methods. In 10 out of the 13 cases, the mean fiber densities (number of fibers/mm^2) of the myelinated fibers were reduced, indicative of nerve fiber loss. In about half of the cases there was a decrease in the number of the fibers of small size (<7μm). A very poor correlation between the internodal lengths and internodal diameters, found in 7 of these patients, suggested a process of demyelination and remyelination. The presence of other features such as irregularities and wrinkling of myelin and considerable variation in the diameters within the internodes are suggestive of axonal damage as well.

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FLUOROSIS: STUDIES ON MUSCLE BIOPSIES

by

D. Krishnamurthy, D. Raja Reddy and M.V.R.R. Reddy
Hyderabad, India

(Abstracted from a Paper Presented at the 27th Annual Conference of the Neurological Society of India, in Poona, December 1977).

Twenty-two patients with skeletal fluorosis (19 males and 3 females ranging in age from 25 to 65) were subjected to muscular biopsies. Sixty had variable degrees of restricted spinal movements, four had quadriparesis and two paraparesis.

In sixteen patients electromyograms were made and motor and sensory nerve conduction rates were determined. In ten, CPK levels were obtained. Small angular filures suggestive of denervation were noted and in 11 out

of 22 cases, evidence of reinnervation was found (type fiber of predominance grouping). The remaining patients exhibited no changes suggestive of denervation. Dystrophic changes were uniformly absent and the values of VPK were within normal limits.

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EFFECT OF ALUMINUM HYDROXIDE ON FLUORIDE METABOLISM

by

H. Spencer, L. Kramer, C. Norris and E. Wiatrowski
Hines, Illinois

(Abstracted from Clin. Pharmacol. Ther. 28:525-539, 1980)

Small amounts of aluminum hydroxide (30 ml three times daily containing 1.8 gm elemental aluminum) were given to seven patients in thirteen experiments for 12 to 58 days subsequent to a control period of 24 to 30 days.

The diet contained 200 mg calcium per day in nine of the thirteen studies. In one experiment the calcium intake was 1400 mg/day, and in three it was 2000 mg/day. The phosphorus intake was 800 mg/day in eight experiments and was increased to 1700 mg/day in five experiments. The daily fluoride intake ranged from 3.5 to 5.0 mg.

Fluoride balances were determined by measuring fluoride in the diet, in drinking water, urine, stool, aluminum hydroxide, sodium fluoride tablets, calcium gluconate tablets and sodium glycerophosphate.

On a calcium intake of 200 mg/day, urinary fluoride excretion was approximately 60% of the average fluoride intake of 4.4 mg/day. Fecal fluoride excretion averaged 0.2 mg/day. In the aluminum hydroxide group there was greater excretion of fluoride in the feces and a decrease in the net absorption of fluoride regardless of the intake of fluoride, calcium, phosphorus or magnesium. On high fluoride intake, aluminum hydroxide reduced fluoride absorption less (30%) than when fluoride intake was low (57.6%). After aluminum hydroxide was discontinued, the urinary and fecal fluoride excretion and fluoride balance returned to baseline values. The authors concluded that small amounts of aluminum hydroxide inhibit intestinal absorption of fluoride in man.

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HUMAN URINARY FLUORIDE EXCRETION AS INFLUENCED BY RENAL FUNCTIONAL IMPAIRMENT

by

H.H. Schifli and U. Binswanger
Zürich, Switzerland

(Abstracted from Nephron, 26:69-72, 1980)

The authors studied creatinine clearance, fluoride clearance, fluoride excretion, fractional excretion of fluoride, sodium and chloride in 23 subjects (10 women and 13 men). Eight had variable degrees of chronic renal insufficiency, 7 were undergoing hemodialysis treatment and 8 served as controls. The dialysate water contained .6 ppm fluoride (60 µg/l). In the hemodialysis patients, the urine was collected on the day before dialysis.

In patients with impaired kidney function and those undergoing regular hemodialysis, mean serum fluoride concentrations were significantly increased. Normal dietary amounts of fluoride were excreted until the creatinine clearance values dropped below 25 ml/min. The serum fluoride concentration increased concomitantly with the decline in urinary fluoride excretion. The ratio of renal fluoride clearance to creatinine clearance indicated that each percent of filtered fluoride is reabsorbed by the tubular system. Extracellular volume expansion exerts an inhibitory effect on tubular reabsorption of fluoride.

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THE EFFECTS OF LONG-TERM FLUORIDE ADMINISTRATION ON IMMATURE MURINE LEUKOCYTES

by

S. R. Greenberg
Chicago, Illinois

(Abstracted from Anat. Rec. 196:232, 1980)

The author presents the results of experiments on two groups of 20 mice each of which received 11 ppm and 22 ppm sodium fluoride in their drinking water. A third group of animals was given distilled water as control. The mice were sacrificed at intervals of 1 to 280 days and sections of decalcified sternum and femur were studied.

After eight weeks increases in both metamyelocytes and prolympho-

cytes and increased chromatin density were observed. An increase in the amount of RNA in the younger cells of both the myeloid and lymphoid series was noted which was uniformly distributed in the cytoplasm. This finding was indicative of protein synthesis. During the course of the experiment the neutrophils increased by about 23% in the 11 ppm group and 35% in the animals receiving 22 ppm fluoride. After the first month the author found degenerating leukocytes (so-called basket cells), which continued to increase during the course of the experiment. There were also abnormalities in the cytoplasmic RNA. Only a slight increase of DNA was noted.

The author concluded that "fluoride in drinking water may induce leukocytic degeneration accompanied by alterations in the RNA content of the affected cells. Changes in the distribution of intracellular RNA resemble those in bronchial epithelial cells undergoing malignant transformation."

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INDUSTRIAL FLUORIDE POLLUTION: CHRONIC FLUORIDE POISONING IN CORNWALL ISLAND CATTLE

by

L. Krook and G.A. Maylin
Ithaca, N.Y.

(Abstracted from Cornell Vet. 69, 3, Suppl. 8, 1978)

Chronic fluorine poisoning in cattle due to emission from an aluminum plant caused stunted growth and severe dental fluorosis which interfered with drinking and mastication. Cows died or had to be slaughtered during, or after, the third pregnancy. Fluoride levels in bones increased with age and in relation to the proximity of the plant. Cancellous bone retained more fluoride than cortical bone. Fluoride levels exceeding 10 g/kg (10,000 ppm) were found in the cancellous bone of a 5-year old cow. In a 7-month fetus, bone levels exceeded 500 mg/kg. Target cells to fluoride in teeth were ameloblasts, dental pulp cells and odontoblasts and in bone, the resorbing osteocytes and osteoblasts. Of cattle with deciduous teeth, only about one third had no dental fluorosis. With the eruption of permanent teeth, fluorosis increased. Eruption of permanent incisor teeth was delayed up to 3.5 years.

The tolerance levels for forage (40 mg/kg) were not exceeded in local hay during 1977. However, these tolerance levels which were set with reference to calves from normal cows cannot be applied to cattle exposed to fluoride as fetuses and continually throughout life.

M.N. Egyed

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