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The Fifteenth Conference of the International Society for Fluoride Research will be held on the Utah State University Campus, July 30—August 2, 1986. Our host will be Professor G.W. Miller, Department of Biology, UMC 45, Utah State University, Logan, Utah 84322.

Editorial

PLENARY LECTURES OF 13TH ISFR CONFERENCE

Under the appropriate title "Fluoride Toxicity," the nine plenary lectures as well as highlights and discussion of the 13th Conference of the International Society for Fluoride Research, which convened November 13-17, 1983, in New Delhi, India, have recently become available in a handsomely bound volume edited by Dr. A.K. Susheela, Associate Professor of Histocytochemistry, All India Institute of Medical Sciences, New Delhi. Delegates from 13 countries attended the conference, which included, for the first time, one from the People's Republic of China, Dr. Li Yumin, and two from Kenya, Mr. J.N. Gitonga and Dr. K.R. Nair. Participants from 10 countries in addition to India presented papers.

The plenary lectures, which dealt with numerous aspects of fluoride toxicity, were delivered by distinguished scientists representing research, with their coworkers, in many disciplines: Dr. Philippe Grandjean of Denmark discussed the "Long-Term Significance of Industrial Fluoride Exposure - A Study of Danish Cryolite Workers;" Prof. F.H. Tsunoda of Morioka, Japan, "Studies on the Effects of Environmental Fluoride on Goats;" Prof. A.W. Davison, Newcastle on Tyne, U.K., "The Dynamics of Fluoride Accumulation by Vegetation;" Mr. K.R. Bulusu of Nagpur, India, "Fluoride Removal from Potable Waters by Various Methods: Operating and Capital Cost Estimation."

The following scientists completed the line-up: Prof. Gene W. Miller of Utah, U.S.A., "The Effect of Fluoride on Membrane Properties and Oxidative Phosphorylation in Plant Mitochondria;" Dr. Graham Embery, Liverpool, U.K., "The Metabolism of Proteoglycans and Glycosaminoglycans in Dental Fluorosis;" Prof. C.A. Baud of Geneva, Switzerland, "Biophysical and Morphometric Study of Bone Tissue in Endemic Fluorosis;" T.N. Khoshoo of New Delhi, India, "Integrated Approach to Fluoride Pollution;" and Dr. A.K. Susheela, also of New Delhi, India, "Fluoride Toxicity -- A Molecular Approach."

In her preface to the book, Dr. Susheela, the organizing secretary, pointed out that India, "a third world country," is third largest in industrial development, that endemic fluorosis was first reported from India in 1937, and that much of the early fluoride epidemiology was carried out in India. Radiological changes in cryolite workers led to Roholm's classical work published in 1937. In 1960, Dr. Amarjit Singh, assisted by Prof. S.S. Jolly described skeletal fluorosis in the Punjab.

Parenthetically, these events recall the late Dr. G.L. Waldbott's delight when, at a pre-ISFR Conference held in Bern, Switzerland, organized by Prof. A. Gordonoff in collaboration with Dr. Waldbott, October 15-17, 1962, the late revered Professor Amarjit Singh, Head of Department of Medicine, University of Patiala, his country's foremost expert on fluorosis, arrived. At this early conference papers were given by such outstanding scientists as Prof. N.P. Buu-Hoi of the National Research Center in Paris -- who had received his country's highest award in 1962, the Cross of the Legion of Honor, for outstanding research; two German scientists, Profs. W. Wohlbier and W. Oelschlager of Stuttgard-Hohenheim; Profs. E. Hupka and G. Rosenberger of the Hannover Veterinary School, Dr.

F. Spierings, Instituut voor Plantenziekten Kundig Onderzoek, Wangeningen, Holland; Dr. L. Gisiger of the Swiss Government Agricultural Station at Liebefeld; Prof. K. Garber, Staats Institut für Angewandte Botanik, Hamburg, Germany; Prof. E. Uehlinger, Head of the Department of Pathology, University of Zürich; and Dr. Ch. Leimgruber of Bern, dental research scientist. The Proceedings of the Bern Conference were published by Schwabe and Co., Basel/Stuttgart, 1964, entitled "The Toxicology of Fluorine."

The following are some of the highlights of the New Delhi Conference. Airborne fluoride from aluminum or phosphate plants, brick kilns or potteries settles on vegetation which itself may be poisoned or it may adversely affect goats, cattle or buffalo which feed on the vegetation. How fluoride affects vegetation was reviewed by Davison. He showed the correlation in tea plants between aluminum and fluoride, and explained that *Eurya japonica* contains about 1,000 ppm fluoride. Dr. H.C.Sharma, Nagpur, India, suggested that fluoride, by removing magnesium from chlorophyll, interfered with photosynthesis and Miller, U.S.A., showed that glucose-6--phosphate dehydrogenase is greatly increased by fluoride.

According to Prof. Amrit Tewari, of Chandigarh, India, at 1.1 ppm F^- in water, 74 per cent of permanent teeth become mottled; at 2.0 ppm, 95.5 per cent; incisors and molars are the teeth most adversely affected by fluoride. Above 1.1 ppm, according to Tewari, the percentage of children with caries increased; moreover, pitting caused by fluoride might allow plaque to accumulate and, eventually, the increased bacteria cause caries.

In this connection Professor Hugh Sinclair, in "Highlights of the 13th ISFR Conference," designated the Lord Mayor of Copenhagen the most distinguished patient mentioned at the conference. Without giving details Sinclair indicated that he had been featured in Roholm's book for mottling at age 13, and that now he is edentulous.

Dr. Susheela, who has been associated with the All-India Institute of Medical Sciences for 21 years and has been involved with fluoride research during the last 13 years, described in detail her studies on the morphological and biochemical differences between cortical and cancellous bone, the latter of which has three times as much glycosaminoglycans as the former. When fluoride is administered to rabbits, the concentration of fluoride in cancellous increases twice as much as in cortical bone.

Fluoride causes the appearance of Dermatan sulphate in tendon, cartilage and skin as well as in cancellous but not in cortical bone. It is not found in normal bone or teeth. In trabecular bone, Ruthenium Red used to stain glycosaminoglycans produces red patches that look like the chondrocytes of cartilage. Dermatan sulphate is present in regions which fail to calcify.

In rabbit serum, when the fluoride concentration rose 6½ times, sialic acid decreased about ¼ and hydroxylysine one half; glycosaminoglycans, however, doubled. In man, results are similar. Therefore, the ratio of sialic acid to glycosaminoglycans falls by about one third in rabbits; in human fluorosis, from average normal of 6.47 to 2.73 (about 30 to 50

per cent). Dr. Susheela believes that this ratio could constitute an important method of diagnosing fluoride poisoning.

The publication "Fluoride Toxicity" was dedicated to the memory of George L. Waldbott, M.D. pioneer in research on allergy, internationally recognized specialist and eminent scientist, founder of The Society, who served as Secretary and Editor of its official journal, *Fluoride*, for fifteen years until his death in July, 1982. His original clinical research findings on fluoride and preskeletal fluorosis -- classics in the field of fluoride, recorded in more than 80 publications -- will undoubtedly guide present and future generations.

The book "Fluoride Toxicity," which contains 128 pages, is available through Dr. A.K. Susheela, Dept. of Anatomy, All India Institute of Medical Sciences, New Delhi-110 029, India. To obtain a copy of it, send a bank draft of $20 U.S., or 12 pounds sterling, made out to: Organizing Secretary, 13th ISFR Conference Account, State Bank of India, Ansari Nagar Branch, New Delhi-110 029, India.

The Proceedings of the 1983 International Symposium entitled "Fluorides, Effects on Vegetation, Animals and Humans" contains articles by over 39 researchers. An excellent source of information for workers in the field, it can be purchased through Dr. J.L. Shupe, Veterinary Science, Utah State University, Logan, Utah 84322 for $27.50.

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EVALUATION OF ENVIRONMENTAL CONTAMINATION BY A MINERAL FERTILIZER FACTORY ON THE BASIS OF THE CONTENT OF FLUORIDE IN VEGETABLES

by

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Szczecin, Poland

SUMMARY: To evaluate environmental contamination by industrial emissions, vegetables were analyzed for fluoride. Moreover, the fluoride level in vegetables was related to meteorological and topographical conditions.

KEY WORDS: Environment; Fluoride; Food

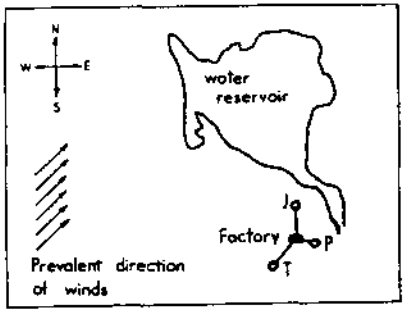
Introduction

The content of fluoride compounds in plants was intended to provide the basis for estimating the level of environmental contamination by industrial emissions. The fluoride level in common vegetables is important for calculating the fluoride balance in humans and animals that consume food-stuffs of vegetable origin.

The investigations, commenced in 1978, analyzing the fluoride content in vegetables grown in areas exposed to industrial emission (1), were continued during 4 successive years, up to 1982. The results of analyses are herewith presented.

Figure 1

Prevalent Direction of Wind



Material and Methods

During the years 1978-82, the F content in vegetables from three localities (P, J, T) 1-3 km distant from a plant producing phosphoric fertilizers, as well as that in vegetables from control areas 100 km distant from the the plant, was determined. Northwesterly winds prevail in the localities where the vegetables used for investigation were grown (Fig. 1). Locality P is nearest to the plant, J is farther away and T is farthest.

Initial preparation of vegetables designed for fluoride determination have been described earlier (1). Establishment of fluoride in distillate was performed - as far as was permitted - by reagents we possessed, according to the following methods: colorimetric (2, 3, 4), titrimetric (5) and potentiometric, using a fluoride ion measuring instrument from the "Radelkis" (6). Prior to analysis for fluoride, the material had been dried to a solid mass.

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Table 1a

F^- (ppm) in Underground Vegetables (Dry Weight)

Place	Year	Carrot	Parsley Root	Potatoes	Beets
P	1978	5.46	5.09	-	-
	1979	6.56	6.57	-	-
	1980	4.68	4.29	6.69	-
	1981	9.40	7.84	3.07	3.78
	1982	3.00	3.52	3.49	7.26
J	1978	1.98	5.30	-	-
	1979	3.13	4.67	-	-
	1980	3.71	4.92	7.62	-
	1981	5.34	7.45	6.10	2.94
	1982	5.99	9.19	4.01	5.73
T	1978	0.92	2.82	-	-
	1979	2.27	4.47	-	-
	1980	2.15	3.46	6.10	-
	1981	2.61	7.18	3.04	1.27
	1982	2.84	5.43	4.55	3.10
Control	1978	2.16	2.06	-	-
	1979	2.39	2.37	-	-
	1980	2.23	2.80	5.13	-
	1981	4.86	3.97	3.99	4.22
	1982	4.34	3.26	5.21	4.17

Table 1b

F^- (ppm) in Aboveground Vegetables (Dry Weight)

Place	Year	Parsley	Cabbage	Beet Leaves
P	1978	14.94	-	-
	1979	19.00	-	-
	1980	13.18	9.97	-
	1981	20.80	6.74	8.88
	1982	32.96	9.72	17.83
J	1978	12.84	-	-
	1979	17.96	-	-
	1980	10.85	9.42	-
	1981	14.70	11.13	13.59
	1982	32.66	10.37	15.05
T	1978	10.37	-	-
	1979	8.82	-	-
	1980	9.10	9.15	-
	1981	11.36	9.09	11.21
	1982	22.81	7.37	12.89
Control	1978	10.28	-	-
	1979	9.94	-	-
	1980	7.01	4.04	-
	1981	9.52	6.08	6.71
	1982	9.82	6.01	8.26

Results

The results obtained by means of the above methods were compared and reported in another publication (7); and relations established between them are presented in Tables 1 and 2, and in Figures 2 and 3.

Table 1 records the F content in vegetables throughout the entire period of investigation in localities directly exposed to industrial emission and in the control area. The division into groups according to F content in vegetables from air polluted and control areas is shown in Table 2. Figure 2 illustrates the relation between the fluoride content in parsley leaves from locality "P" and the amount of rainfall. According to Fig. 3 the mean quantity of fluoride in individual vegetables is related to the increasing distance of cultivated plots from the source of contamination.

Figure 2

Relation between F Content in Parsley Leaves and Rainfall

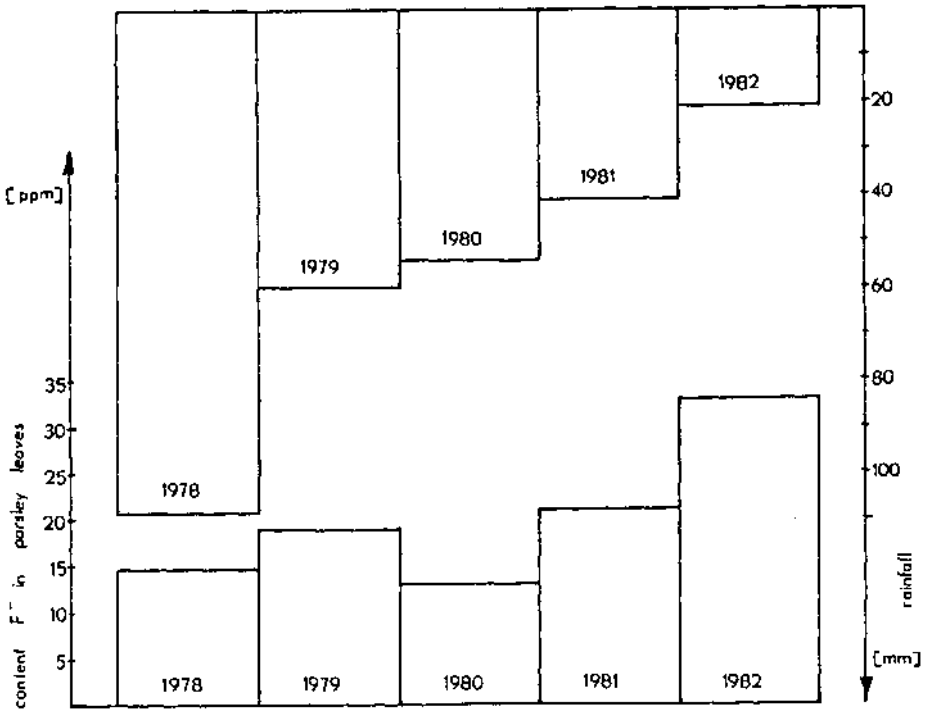
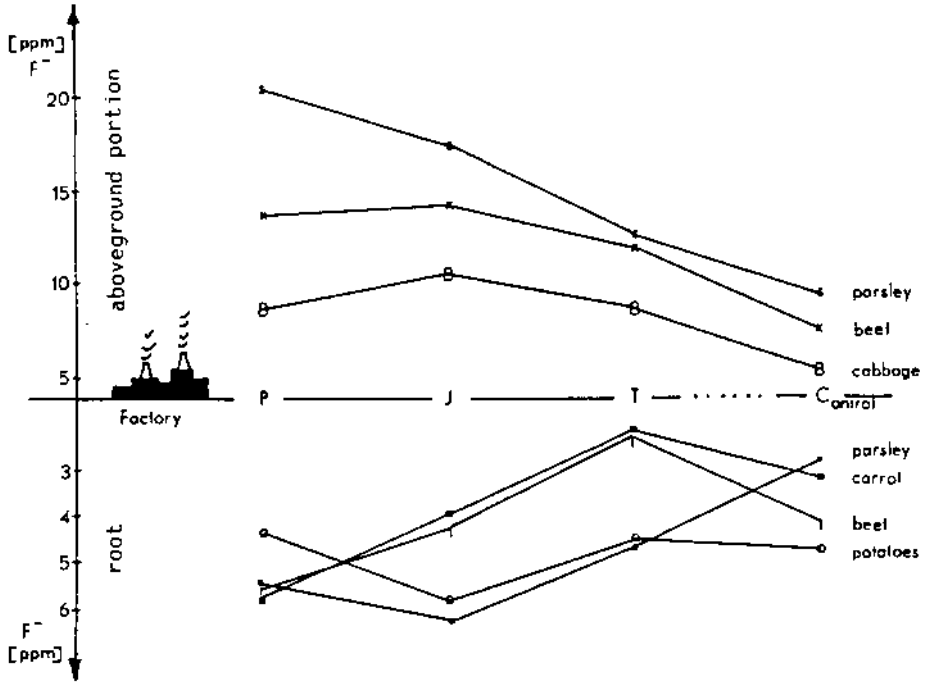


Figure 3

F in Vegetables Related to Distance from Industrial Emission Source.



Discussion

According to data in Table 1, in the majority of areas the fluoride content in vegetables grown in localities exposed to industrial emission is higher than in vegetables from the control area. The fluoride level in aboveground parts of vegetables is markedly higher than in the roots.

During the years 1981-82, the F content in all aboveground parts of vegetables, i.e. F in parsley tops, cabbage, beet leaves originating from localities exposed to industrial emission, was higher than in control areas. It should be added that in the years 1981-82, rainfall was meager in those areas.

In root vegetables from locality "T", southwest of the Establishment, the fluoride content in certain cases was lower or approached the level of fluoride in root vegetables from the control area, as explained later on the basis of atmospheric conditions. The higher F content in aboveground parts of vegetables compared to that in roots suggests that fluoride compounds in the air directly influence the fluoride level in plants.

Table 2

Fluoride (ppm) in Studied Vegetables
From Endangered and Control Areas

Place	Year	Content of F^- (ppm) <5	5 - 10	10-15	15-20	>20
P	1978	-	c, pr	pl	-	-
	1979	-	c, pr	-	pl	-
	1980	c, pr	cb, p	pl	-	-
	1981	p, b	c, pr, cb, bl	-	-	pl
	1982	c, pr, p	cb, b	-	bl	pl
J	1978	c	pr	pl	-	-
	1979	c, pr	-	-	pl	-
	1980	c, pr	cb, p	pl	-	-
	1981	b	c, pr, p	pl, cb, bl	-	-
	1982	p	c, pr, b	cb	bl	pl
T	1978	c, pr	-	pl	-	-
	1979	c, pr	pl	-	-	-
	1980	c, pr	pl, cb, p	-	-	-
	1981	c, p, b	pr, cb	pl, bl	-	-
	1982	c, p, b	pr, cb	bl	-	pl
Control	1978	c, pr	-	pl	-	-
	1979	c, pr	pl	-	-	-
	1980	c, pr, cb	pl, p	-	-	-
	1981	c, pr, p, b	pl, cb, pl	-	-	-
	1982	c, pr, b	pl, cb, p, pl	-	-	-

c - carrot, pr - parsley root, bl - beet leaves, pl - parsley leaves, p - potatoes, b - beet root, cb - cabbage

Rarely had the permissible atmospheric fluoride concentrations been exceeded in the studied areas (8).* Thus it may be presumed that the increased content of fluoride in plants, in relation to the control area, depends not only on the amount of industrial emission, but also on the length of time the plants are exposed to variable, although infrequently surpassed permissible atmospheric F concentration (in Poland the permissible average concentration of fluorine compounds for 24-hours is 0.01 mg F/m^3).

In vegetables which were studied the fluoride level differed from year to year. One cause of this variability may be a varying amount of industrial emission; another, the influence of meteorological conditions, particularly rainfall. For example, the level of fluoride in leaves of parsley grown in locality "P" was influenced by rainfall. During the course of the entire study period the quantity of rainfall was decreasing, whereas the fluoride content in parsley tops, with one exception (the year 1980), was increasing (Fig. 2).

*In Poland the permissible fluorine concentration in air refers to fluoride compounds soluble in water.

These results suggest that rainfall constitutes a natural protection against excessive accumulation of fluoride in plants, a finding consistent with the view expressed by Waldbott (9) that absorption of F^- from the air by plants occurs during dry periods, and is lowest after rainfall.

Wind direction also influences the fluoride content in vegetables. Southwestern winds prevail in the studied region as reflected in the fluoride content in leaves of vegetables grown in localities "J" and "P". However, in vegetables from locality "T", which is not in the main line of wind direction, the least amount of fluoride in parsley tops, beet leaves and cabbage was found.

The mean content of fluoride in investigated vegetables distinctly points to the relation between F level in aboveground parts and increasing distance from the source of environmental contamination (Fig. 3).

On the basis of data obtained and compared with data from other countries, the extent of environmental fluoride contamination, emitted by a large phosphoric fertilizer factory is debatable. During the 5 year long investigation, the content of fluoride in vegetables exceeded that in the control area about threefold in 9 cases, and about twofold in 30. From Table 2, the fluoride content in vegetables originating from the control area lies between 0-10 ppm with the exception of parsley tops in 1978. In vegetables grown in areas exposed to industrial emission, the most vulnerable are the aboveground parts, i.e. parsley, cabbage and beet leaves. The underground parts of vegetables are less contaminated or are not affected at all, as shown expecially in locality "T".

According to the analyses which have been presented, the extent of environmental contamination by industrial emission is not great.* Various kinds of technology applied by the Establishment in the production of mineral fertilizers, and also concurrent production of other chemical alkaline compounds may be responsible. Moreover, we are not familiar with the effect of a big, natural water reservoir, northeast of the Establishment, and its influence on varying environmental conditions during the various seasons of the year.

Nevertheless, regarding the aspect of human health the most unfavorable variant should be taken into consideration. In other words, small scale contamination of vegetables, as food-stuff, is present; it may become more serious with further activity of the Establishment. Therefore, a continuous control of the fluoride level in the air, water, soil and food of plant origin is indispensable.

*Environmental pollution, undergoing rapid and unfavorable changes, seems to cause an increase in the quantity that is looked upon as the "normal" level of fluoride in plants. According to The European Environmental Commission Report "Acid Rain", Poland in 1983 was classified first in Europe with regard to air pollution. Therefore, the content of fluoride in plants coming from our regions may be higher than is the case in other countries.

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FLUORIDE CONTENT OF EFFLUENT AND BYPRODUCTS OF AN ALUMINUM INDUSTRY IN INDIA

by

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Raipur, India

SUMMARY: The extent of effluent discharges from alumina and smelter plants, and that of solid waste discharges such as red mud, vanadium sludge and cryolite mud have been evaluated. Fluoride concentration in a number of samples, collected over a prolonged period, have been determined using a Fluoride Ion-Selective Electrode Measuring System and the fluoride dispersal capacity of each channel has been assessed.

KEY WORDS: Alumina plant; Cryolite mud; Effluents; Fluoride; Red mud; Vanadium sludge

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Introduction

The present studies have been carried out at Korba (State of Madhya Pradesh, India) where an aluminum plant of a public sector undertaking is located. The plant has an annual capacity of producing 200,000 tons of alumina and 100,000 tons of aluminum. The main raw materials consumed per annum, in tons, are: bauxite-550,000; caustic soda-2,000; fuel coal--4,000; lime-26,000; starch-200; coal-160,000; cryolite-2,000; aluminum fluoride-2,600; sodium fluoride-600; petroleum coke-4,500; and soda ash--500. The fluoride in an aluminum plant originates from the huge use of fluoride-loaded raw materials such as (cryolite 3 $NaF.AlF_3$), aluminum fluoride (AlF_3) and sodium fluoride (NaF). Fluoride contamination of bauxite, the chief raw material, also contributes toward dispersal of fluoride into the environment.

As shown in Figure 1, the routes of dispersal of fluoride from alumina plant wastes are mainly through the following channels: (1) Factory waste water, which includes effluent from alumina and smelter plants (2) Red mud (3) Vanadium sludge, and (4) Cryolite mud. Quantities of wastes produced per ton of aluminum are (1) Factory waste water: from alumina plant-30 kiloliters; from smelter plant-70 kiloliters (2) Red mud-0.13 ton (3) Vanadium sludge-0.002 ton (4) Cryolite mud-0.02 ton.

Material and Methods

Sample Collection: a) Effluents - Four samples, each measuring 2.5 liters, were collected from the outflow stream of the alumina plant, using the prescribed procedure (1) allowing 30 days between consecutive collections. Another set of 4 samples was similarly collected from the outflow stream of the smelter plant. b) Red mud - Two samples, each weighing 1 kg, were scooped out from each of the two red mud ponds, after a 30 day interval, following the procedure prescribed for sampling local problem spots (2). c) Vanadium sludge - Four samples, each weighing about 500 g, were collected from the sludge yard of the alumina plant, each after a 30 day interval, following the prescribed sampling procedure (2) for red mud. d) Cryolite mud - Four samples, each weighing 1 kg, were collected from the cryolite mud pond after a lapse of 30 days, also following the prescribed sampling procedure (2).

Table 1*

Fluoride Content of Effluents and Byproducts of Factory

Description of Samples	Sample 1	Sample 2	Sample 3	Sample 4	Mean
1. Alumina Plant Effluent:	0.88	0.90	0.92	0.95	0.91
2. Smelter Plant (ppm) Effluent:	3.20	3.50	3.10	3.70	3.33
3. Red mud (ppm)	180	140	140	140	150
4. Vanadium sludge (%)	12.0	17.0	14.0	9.2	13.05
5. Cryolite mud (%)	5.3	5.8	5.6	5.5	5.55

* The fluoride values in Table 1 may differ from aluminum plants in other parts of the world due to differences in quality of raw materials, manufacturing procedures, wastes utilization, their treatment and disposal.

Sample Preparation: The effluent samples were filtered using Whatman filter #40, and the filtrates were used for fluoride measurements. Samples of red mud, vanadium sludge and cryolite mud, were first air dried, after which they were dried in an oven at 100°C for 3 hours. An accurately weighed quantity (0.1 to 1.0 g, depending on the fluoride content) of mud samples was mixed with anhydrous sodium carbonate (5 g) and zinc oxide (1 g) in a platinum crucible (20 ml), covered with lid and heated in a muffle furnace at 900°C for 30 minutes (3,4). After cooling, the crucible and contents were maintained at a high temperature with deionized water in a beaker for 3 hours. The crucible and the lid were washed and removed. The content was filtered (Whatman #40) at room temperature into a volumetric flask (250 ml), and repeatedly washed with 0.1% NA_2CO_3 solution. The filtrate was treated with 5 ml HCl(6N), the flask was shaken to expel all CO_2, after which the solution was brought up to the mark with deionized water. A blank solution containing all the above-mentioned reagents in the ratios described, and without any fluoride bearing substance was also prepared.

Apparatus: A fluoride Ion-Selective Electrode Measuring System (Orion Model 409) was used.

Procedure: Ten-ml aliquots of the two standard fluoride solutions of 2 ppm and 4 ppm, and the same aliquots of sample solutions of effluents, red mud, vanadium sludge and the blank solution were separately pipetted into 100 ml polyethylene beakers and each was mixed with 10 ml sodium citrate-potassium nitrate (0.2m) TISAB solution. The ion-selective fluoride electrode (Orion Model 409) was calibrated (5) using 2 ppm F and 4 ppm F solution. The electrodes were then placed in the sample solution with the knob in the measuring position of 0.1 - 10 ppm, and the fluoride concentration in ppm (lower scale of reading) was recorded. If pointer showed over-range, the sample solution was diluted with the blank, and the concentrations were measured following the same procedure. A duration of 10 minutes was allowed in each case for the ion-electrode to remain in contact with the fluoride ions to ensure a steady equilibrium. The fluoride concentrations in the twelve mud/sludge samples and in the eight samples of effluent were determined by this method (Table 1).

Results

The fluoride contamination of the effluents discharged from the alumina and the smelter plants varied only marginally during the four-month period of the study. The mean fluoride contamination of the alumina plant effluent, slightly lower than 1 ppm, represents mainly the sweep of soluble fluoride from bauxite ore which, in this case, contains around 240 ppm fluoride. The fluoride contamination of the smelter plant effluent (mean value 3.33 ppm) is about 3 times that of effluent from the alumina plant (mean value 0.91 ppm). The additional factor involved in the fluoride contribution here is cryolite ($AlF_3.3NaF$) which is used in aluminum smelting.

The mean fluoride contamination of red mud (150 ppm) represents mainly the insoluble portion of fluoride impurities from bauxite ore, about 13% of which is contained in vanadium sludge. The latter is heavily load-

ed with fluoride. During the four month study period its fluoride content varied from 9.3% to 17.0%. This sludge is a product of evaporation of the spent liquor after separation of the alumina; progressive increase in the concentration of soluble fluoride is the result.

The mean fluoride content in cryolite mud (5.55%) is quite significant. This mud represents the waste matter rejected by the aluminum smelter where cryolite, the fluoride-bearing mineral, is used as a flux.

Discussion

Regarding the hazard aspect, the fluoride content in the alumina plant effluent which is below 1 ppm, is within the limit, prescribed in India for industrial waste water discharges (6). On the other hand, the fluoride level of the smelter plant effluent which narrowly exceeds the permissible limit of 2 ppm requires lowering. Red mud waste, which contains about 150 ppm insoluble fluoride should not arouse serious concern as long as the fluoride is confined to red mud pond boundaries. Should adjoining areas be used for vegetation or agriculture, possible migration of fluoride to soils through seepage would necessitate investigation.

Vanadium sludge, the chief fluoride dispersing channel, about 2 kg of which is formed per ton of aluminum produced, is continuously removed from the alumina plant site to distant areas where it is used for manufacture of ferrovanadium alloy. Thus, the fluoride of this sludge is migratory in nature, and the zone of fluoride hazard shifts from the alumina plant-site to that of the ferrovanadium plant.

Cryolite mud, which is discharged at the rate of about 20 kg per ton of aluminum produced, is progressively deposited in the form of mud. Due to its fluoride content (mean 5.55%) it is the most potential channel for dispersal of fluoride.

Acknowledgement

The authors are grateful to the management of Bharat Aluminum Company, Korba, India, the Director of Geology & Mining, Govt. of M.P. and the Principal of Govt. College of Eng. and Tech. Raipur, India for providing necessary facilities.

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WIND-BLOWN DUST FROM SALTY AREAS, A SOURCE OF FLUORIDE IN PLANTS

by

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SUMMARY: As a source of F^- in plants, in addition to that absorbed by roots, wind-blown dust carrying fluoride salts was studied. The salts and F^- originated by capillary rise from groundwaters. The F^- content in salt efflorescences ranges from 31 to 284 mg/kg and the F^- in plants growing in different soils ranged from 10 to 30 mg/kg. The F^- retained externally in leaves and stems ranged from 1 to 30 mg/kg. In one case more F^- was retained outside the plants than in tissues. The rain F^- content was similar to that found in other areas of the world. In addition to the natural F^- content of soils and consequent root absorption, airborne fluoride-containing dust increases F^- concentration in plants.

KEY WORDS: Airborne dust; Fluoride in plants; Saline soils; Soil fluoride.

Introduction

In the northwest of Buenos Aires province of Argentina, mollisols in association with entisols and alfisols are the predominant soils. Saline phases, originating from capillary rise from salty and shallow groundwater, are spread in the lower landscape position (1). These groundwaters, rich in F^-, produce F^- enrichment in salt-affected soils (2, 3). In some places, where the salt concentration is very high at the surface, the soils are covered by efflorescences. Moreover, small salty ponds, usually dry in summer, form salt fields. Plants may be high in fluoride independently of the soil F^- content (3). Plant F^- concentrations were high in comparison with other published data; some high enough to be harmful to plants and even to animals (4 - 7). Because of these high values, a search was initiated to discover the sources of plant F^- enrichment apart from root uptake.

In dry and windy weather, dust suspensions common in the air include crystals from salt pans and salty soil surfaces. The soluble part of dust particles in the atmosphers, which includes F^-, dissolves in rainwater or dew on vegetation. Such dust, after entering plants, could be an additional F^- source for vegetation and crops. Airborne dust, far distant from its place of origin, can therefore increase F^- concentration in plants where soils are low in F^-. Airborne dusts have been studied as a source of salts in soils (8) or from a pedogenetical point of view (9). In addition, this result could be considered a natural plant F^- enrichment process parallel to that in industrially contaminated areas (6, 10).

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This present work was carried out to study such an hypothesis.

Materials and Methods

Salt efflorescences: Ten samples replicated 10 times were taken in the spring of 1983 from different salt fields in C. Tejedor county, located in the northwest of Buenos Aires province. Samples 1, 2 and 3 were taken in the morning, noon and afternoon to study the influence of dew deposition on its chemical composition, the remaining samples in the afternoon.

Plant samples: Ten samples replicated ten times, of plant material taken from C. Tejedor county cover four different situations in relation to salinity.

Rainwater samples were obtained from a meteorological facility near Husares town, the only source available in C. Tejedor county, far from human settlements, a few km distant from salt fields. At the same time, to compare the F^- content, rainwater was sampled in the humid part of the Pampean prairie with no salt pan areas. All rain samples were collected in acid washed plastic bottles throughout the spring of 1983. The meteorological facility was A. Korn town, south of Buenos Aires city, 350 km west from Husares town.

Analysis: The chemical composition of the salt efflorescence was analyzed as follows: Ca, Mg, Na and K by atomic adsorption spectrophotometry; Cl^- volumetrically with $AgNO_3$; $CO_3^=$ and HCO_3^-, volumetrically with H_2SO_4; $SO_4^=$, gravimetrically; No_3^-, colorimetrically. Water soluble F^- was also determined.

Distinction was made between water dissolved "external F^-" (11) namely that in crystals and dust which had settled on leaves, stems, and other plant surfaces and "internal F^-" in plants namely that from digestion and distillation of previous leached material (12) which is bound in organic structures in plant tissues. In all cases F^- was determined by titrimetry, using thorium nitrate (12). Previous to analysis, rainwater samples were concentrated.

Table 1

F^- Content in Efflorescences (mg/kg)

Sample	F^-
1	259.2
2	204.1
3	195.8
4	284.4
5	212.3
6	177.0
7	105.1
8	91.1
9	162.0
10	31.6

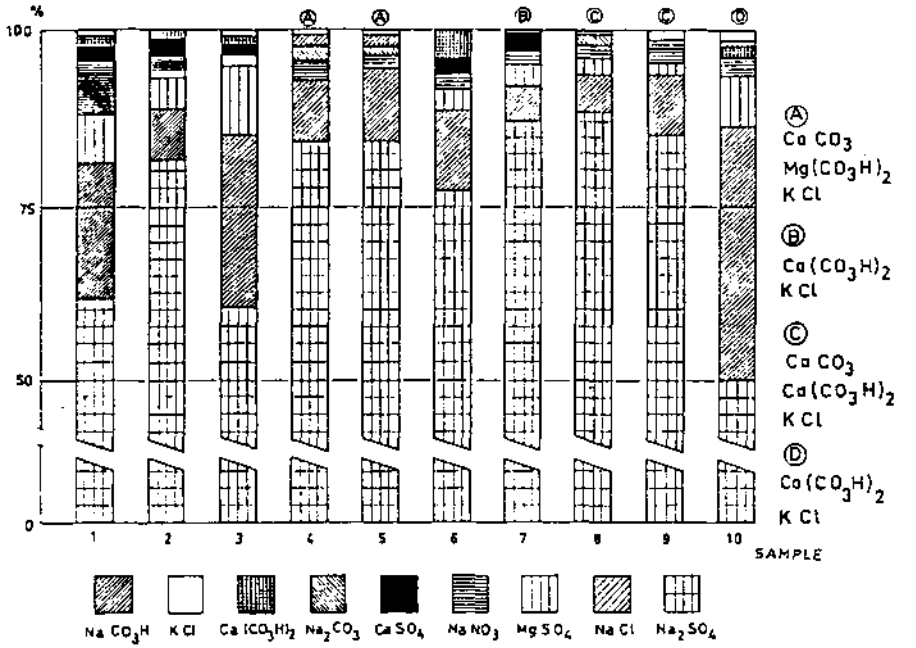
Table 2

F^- Content in Plants (mg/kg)

Place of Sample	Species	Internal F^-	External F^-
Non salt-affected soils area	Sorghum sudanensis	17.0	1.7
	Vicia sativa	10.0	1.3
	Eragrostis curvula	15.0	1.4
Near salt-affected soils area	Trifolium repens	25.4	8.4
	Bromus unioloides	23.8	6.9
Saline soils	Agropyron elongatum	24.9	7.0
	Eucalyptus sp.	30.3	2.7
Salty fields	Glyceria multiflora	24.1	30.1
	Distichlis spicata	16.5	8.3
	Salicornia ambigua	26.3	4.1

Figure 1

Chemical Composition of Efflorescences



Results and Discussion

The chemical composition of the efflorescences, considering the most probable chemical species in the crystals, is shown in Fig. 1. The most important salt was Na_2SO_4 more than 80% of which was contained in six samples, 3 contained 60 to 80% and the tenth almost 50%. NaCl was the second most important one. From 80 to 95% of the chemical species are NaCl and Na_2SO_4. The remaining consist of a mixture of 9 other salts. The chemical composition was similar to those found in efflorescences in salt-pans of other parts of the world (13 - 15); some differences were found in salt composition during the day. The range in F^- concentration (Table 1) was almost 10 times between extremes. It is not known whether some F^- content scale in efflorescences exists; in some samples, the F^- content may be high but no relationship was found between F^- and other chemical species concentrations.

F^- in plant tissues (internal) and F^- on the outside of plants (external) (Table 2) showed a parallel pattern. Values in the three samples from plants growing in areas with no salty soils were least statistically significant. All others, with the following exceptions, were significantly high with no differnces between them: a) A sample from salty fields,

the internal F^- content of which was equal to that in samples from non-salty soils due possibly to differences in plant species (16), in enviromental characteristics (11, 16) or in soil F^- content according to salinity and alkalinity (3). External F^-, high in one plant growing in salty fields, was not only significantly different from the others but was higher than the internal F^-.

The high values of "external" (dust-borne) F^- on plants growing near or in salty areas show that particulate F^- is intercepted by vegetation and deposited on its leaves. The magnitude of foliar F^- absorption depends on climatic events (for instance, rainfall intensity), plant characteristics (e.g. leaf shape) but foliar absorption could be the reason for high F^- values in plant tissues. Rainfall F^- concentration, the same in both sites, averaged 0.3 mg/l, somewhat higher than in other places (17). Salts may travel long distances before being deposited on surfaces through rainwater (15, 18).

Conclusion

The F^- concentration in salt efflorescences and the proportion of internal and external F^- on plants support the initial hypothesis that wind-borne transportation of soil salt crystals and deposition of F^- compounds on vegetation, may explain F^- enrichment in the studied region. However, these data show that F^- transport is mainly local, and that rainfall plays an insignificant role in relation to solid deposition.

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LIGHT MICROSCOPIC AND SCANNING ELECTRON MICROSCOPIC OBSERVATIONS ON HUMAN FETAL BONES FROM AN ENDEMIC FLUOROSIS AREA

by

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SUMMARY: In an endemic fluorosis area of Guizhou, China, five human fetuses were delivered during the eighth month of intrauterine life by means of artificial abortion. Bone samples of humerus and femur were studied under light and scanning electron microscope. New bone formation was more active in fetuses from the endemic area than in those from a non-endemic area. In the former, calcification was inadequate and development of epiphyseal chondrocytes was abnormal. The higher level of fluoride ion in bone samples from the endemic area was ascribed to fluoride ion deposited in fetal bones via placental circulation.

KEY WORDS: Histological changes; Skeletal fluorosis in human fetuses; Transfer of fluoride via placenta.

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Introduction

Numerous reports in the literature indicate that fluoride ion is transferred from maternal blood via the placenta into the fetus. In recent years, many authors have signified that skeletal fluorosis might begin during the fetal period (1, 2). Various fluoride-induced effects on fetal organs, which have been reported (3), indicate that the placenta can be penetrated by the fluoride ion. The authors studied the fluoride-induced changes in fetal bones.

Material and Methods

Five human fetuses, two males and three females, in an endemic fluorosis area in Guizhou, China, were delivered during their eighth month of gestation by means of artificial abortion. No congenital malformations were revealed on gross examination of the fetuses. Their mothers, the five puerperae, aged 28, 36, 38, 40 and 46 respectively, who had been residing in the endemic area since birth, had mottled enamel, or dental fluorosis. The fetal humeri and femora were excised for further study. For comparison, bone samples of five male fetuses from a non-endemic area, delivered during their eighth month of gestation, were also studied.

Chemical Study: The bone samples, excised from the right fetal femora, were ashed and assayed for fluoride content by the specific fluoride method. To avoid bias, the origin of the samples was unknown to the laboratory technician. The results are shown in Table 1. Statistically, the fluoride levels in the right fetal femora in the endemic area were significantly higher than in controls from the non-endemic area ($0.02 < P < 0.05$).

Table 1

F^- (ppm) in Right Fetal Femora (Dry Weight)

Area	Cases	Mean	Standard Deviation	Standard Error
Endemic	5	17.02	5.25	2.35
Nonendemic	5	9.46	3.49	1.56

Light Microscopic Observations: After fixing in 10% formaldehyde, the samples were decalcified in 5% nitric acid, embedded in paraffin, sliced into 7 micrometer thickness and stained with hematoxylin and eosin or with Mallory's trichrome.

The samples from the non-endemic area showed a smooth cortical surface encircled with periosteum. Subperiosteal osteoblasts were abundant, especially in the shaft area. Cells in various zones of epiphyseal cartilage (zone of germinal cells, zone of proliferation, zone of maturation, zone of provisional calcification) appeared normal. Chondrocytes in zones of proliferation and maturation, regularly lined in parallel rows (Fig. 1), enlarged gradually toward the zone of provisional calcification. Just beneath the zone of provisional calcification, most trabec-

ulae were arranged parallel to the longitudinal axis of the bone, a few were arranged transversely. Between trabeculae, hemopoietic tissue was distributed evenly. On the surface of the trabeculae, numerous osteoblasts and osteoclasts were noted.

In samples from the endemic area, chondrocytes in the epiphyseal cartilage were arranged irregularly. In some slices, chondrocytes were arranged in clusters instead of parallel rows (Fig. 2). Beneath the zone of provisional calcification, many trabeculae were poorly calcified. In their matrix, much chondroitin sulfate stained in blue color was noted (Fig. 3). Between the trabeculae, hemopoietic tissue was distributed unevenly. In the cortex, many Haversian canals were filled with osteoblasts and fibrous tissue (Fig. 4), a change more prominent in the humerus than in the femur. In two cases, subperiosteal new bone formation resulted in a layer of woven bone on the surface of diaphysis or metaphysis (Fig. 5).

Scanning Electron Microscopic Observations: After fixing in 10% formaldehyde, the samples were immersed in 5% sodium hypochlorite for four hours to eliminate organic components. Subsequently they were rinsed in distilled water, dehydrated in acetone of increasing concentrations, coated with gold, and studied with an ASM-SX scanning electron microscope which operated at 25 kilovolts with 80 seconds time of photography.

The longitudinal section of the fetal epiphysis from the endemic area was characterized by irregularly patched chondrocyte lacunae (Fig. 6). On the surface of metaphyseal trabeculae, samples of the non-endemic control showed well-mineralized smooth surface; their trabeculae retained regular, cylindrical shape (Fig. 7). In contrast, the surface of the metaphyseal trabeculae from the endemic area showed patchy smooth areas intermingled with uneven, rough areas which suggested the presence of chondroitin sulfate and inadequate calcification (Fig. 8, 9). In the endemic area samples, the diaphyseal endosteal surface was rough, uneven and granular, indicative of inadequate calcification; prominent resorption depressions of Howship's lacunae were noted, which were sharply demarcated and subdivided by ridges into compartments (Fig. 10). In contrast, the diaphyseal endosteal surface of the non-endemic control was not as rough. The periosteal surface from fetal controls was dominated by a wave-like plane in which multiple osteocyte lacunae were scattered (Fig. 11). The wave-like character was attributed to the underlying pattern of orderly arranged, fully calcified collagen fiber bundles, and the osteocyte lacunae found there were of relatively uniform size and depth (Fig. 12). Areas of woven bone, characterized by an increased number of osteocyte lacunae of uneven size and depth, were noted on the periosteal surface in samples from the endemic area but not in samples from the non-endemic area (Fig. 13).

Discussion

Many fetuses from the endemic area differed from non-endemic area fetuses both under light microscope and scanning electron microscope. In

LIGHT MISROSCOPIC OBSERVATIONS

Figure 1

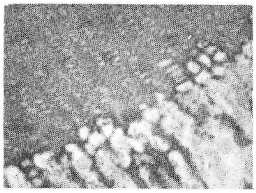


Figure 2

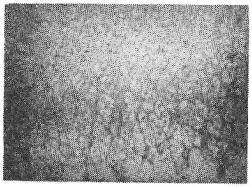


Figure 3

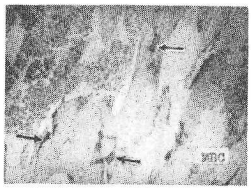


Figure 4

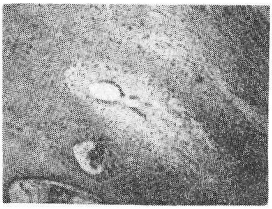
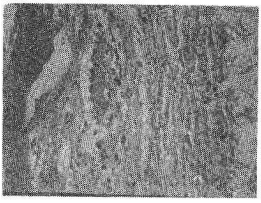


Figure 5



SCANNING ELECTRON MICROSCOPIC OBSERVATIONS

Figure 6

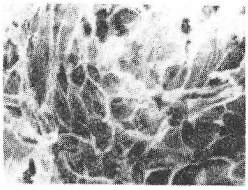


Figure 7

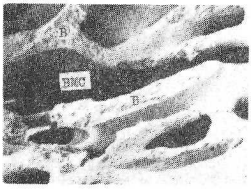


Figure 8

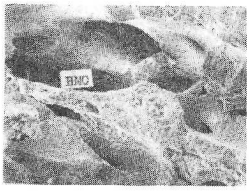


Figure 9

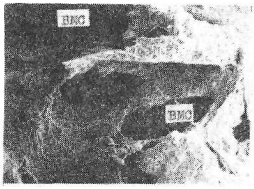


Figure 10

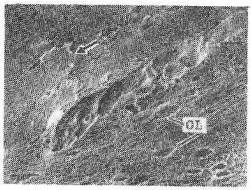


Figure 11

Figure 12

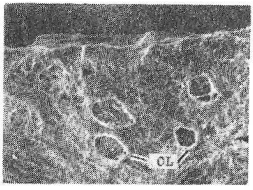


Figure 13

fetuses from the endemic area,active new bone formation resulted in newly-formed, poorly calcified woven bone sub-periosteally. Newly formed bone tissue, also found in Haversian canals and on the endosteal surface of trabeculae, was not as prominent as that on the cortical surface. According to scanning electron microscopy, calcification in some areas of the endosteal surface was inadequate. Abnormalities of chondrocytes in epiphyseal cartilage were also noted. In view of the higher fluoride levels in bones from the endemic area, it is reasonable to ascribe the morphological changes to deposition of fluoride ion in fetal bones.

Conclusion

In the endemic area in Guizhou, China, skeletal fluorosis begins during the fetal period. Whereas it does not present clinical or radiological changes, it does cause a series of histological changes.

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IMPROVED METHODS FOR DETERMINATION OF FLUORIDE IN BIOLOGICAL MATERIALS

by

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SUMMARY: A modified method is reported for fluoride determination in soft tissues without ashing. Measurements were also made on the fluoride content in urine of persons with and without fluoride exposure as well as in patients with renal disease by means of a flow injection analysis system.

KEY WORDS: F^- analysis; Soft tissue F^-; Urinary fluoride.

Introduction

The literature on fluoride content in cartilage and aortic tissue in adults and newborns is sparse. The few reports which have been published fail to describe the chemical analysis employed. Therefore, the fluoride content of cartilage tissue from various localities as well as aortic

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tissue in adults and newborns was determined with a fluoride ion-selective electrode (ISE). Furthermore because, in our country, many workers are exposed to fluoride in industry, including glass making factories, the excretion level of fluoride must be determined on a large number of workers. Hence a simple, fast method to determine fluoride exposure was developed. Moreover, because in our country, the fluoride content of bone, cartilage, and aortic tissue from newborns has not been recorded, 12 such analyses were made.

Material and Methods

Cartilage and aortic tissues were first ashed; the fluoride content in ash was determined as in bone ash. Since the method employed for fluoride determination in aorta and cartilage presented a number of problems, among which are the low content of inorganic material, differing water content in soft tissues, and the handling of low amounts of ash, we adapted a known method (1) for separation of fluoride from soft tissues which made it possible to analyze the fluoride from soft tissues without ashing. Fresh tissue was dissolved in sulfuric acid in a closed glass apparatus which consists of 100 ml flask with Claisen head-piece, 50 ml droping funnel, condenser and two gas bubblers, 50 ml with fritted glass filter. Silicone rubber tube connected the condenser with the bubbler; 50 ml water, 2 drops of hexamethyldisiloxane and the sample (1-2 g of cartilage or aortic tissue) are added to the flask. Eash bubbler is filled with 25 ml 0.1 N NaOH. By means of the dropping funnel, 40 ml of sulfuric acid is cautiously added to the sample. The following reactions take place:

$$(CH_3)_3\text{-Si-O-Si-}(CH_3)_3 + H_2O \xrightarrow{H^+} 2\ (CH_3)_3\text{-Si-OH} \qquad 1$$

$$(CH_3)_3\text{-Si-OH} + F^- + H^+ \longrightarrow (CH_3)_3\text{-Si-F} + H_2O \qquad 2$$

$$(CH_3)_3\text{-Si-F} + OH^- \longrightarrow (CH_3)_3\text{-Si-OH} + F^- \qquad 3$$

From hexamethyldisiloxane in acidic solution, threemethylsilanol, which results, in turn reacts with fluoride in acidic solution forming threemethylfluorsilane 2. The threemethylfluorsilane, b.p. 16.4°C comes to the bubbler by means of a nitrogen carrier gas stream (50 ml/min). In the bubbler in alkaline solution, reaction 3 takes place. In order to remove the threemethylsilanol, the absorption solution from the bubbler must be extracted with about 20 ml of toluene before measurement in acidic solution can be carried out, a necessary operation to avoid the start of reaction 2.

Measurement was carried out in about 0.45 N perchloric acid solution by means of a LaF_3-fluoride sensitive electrode and a pH-glass electrode as a reference. To 50 ml solution extracted with toluene, 2 ml perchloric acid concentration are added. During measurement the solution is stirred with a plastic-coated stirring bar. More detailed information regarding measurement of fluoride in acidic solution has been published elsewhere (2).

For fluoride determination in urine, a flow-injection system was con-

structed (Fig. 1), the main constituents of which were two fluoride ISE, a pH-amplifier, a strip-chart recorder and the injection port for sample injection. The carrier solution was 0.5 M perchloric acid with 0.001% Triton X 100 to reduce surface tension. With this arrangement, the fluoride content of about 60 samples per hour could be analyzed manually. Automatically, however, up to 200 samples per hour (Fig. 2) could be analyzed.

Table 1

F^- Content of Adult Cartilage (ppm ashed)

cartilage localization	n	mean	♂	♀
knee joint	14	663.9	660.5	672.5
3rd rib	16	433.1	465.8	335.0
7th rib	15	503.0	505.9	495.0

Table 2

F^- Content of Adult Bone (ppm ashed)

bone localization	n	mean n = 61	male n = 36	female n = 25
femur trochanter	61	931.9	970.0	747.6
iliac crest	61	805.8	856.3	703.6
3rd lumbar vertebra	61	958.0	970.5	927.3

Tables 3 and 4 show the fluoride content of soft tissues found using the non-ashing method calculated at fresh weight. For urinary fluoride investigations, screened groups were divided under the following categories (Fig. 3): 1) Persons, without atmospheric fluoride exposure, who were drinking water containing 1 ppm F^- (co-workers from our institute), 2) Urological patients drinking 1 ppm fluoridated water (exposure to F^- in air unknown, but possible), 3) Dialysis patients from our district hospital drinking 1 ppm fluoridated water, 4) Persons exposed to atmospheric fluoride in glass factories whose drinking water contained 0.1 - 0.2 ppm F^-, 5) Persons exposed to atmospheric fluoride in aluminum plants whose drinking water contained 0.1 - 0.2 ppm F^-, 6) Persons exposed to atmospheric fluoride in a factory producing fluoride compounds.

To determine the daily rise in urinary fluoride, urine of Group 6 was analyzed before and after work. Because creatinine content is one of the main parameters indicating kidney disfunction, we desired to learn whether fluoride and creatinine were related. For our regression line, a correlation coefficient r = 0.54 was found, which implies a possible correlation between these two parameters. An extremely low urinary fluoride level might indicate kidney disfunction.

Analysis of fluoride in cartilage tissue of the knee joint, 3rd and 5th rib from deceased adults, average age 65.5 years, (Table 1), revealed the following averages: in cartilage of knee joint, 663.9 ppm F^-; of 3rd rib, 433.1 ppm; of 7th rib, 503.0 ppm F^- related to ashed samples. No statistically significant differences were observed between sexes.

Table 2 shows the results of fluoride analysis of bone tissue from deceased persons, average age 63.7 years, carried out by the same method of chemical analysis. In bone samples from the trochanter femora, the iliac crest, and the 3rd lumbar vertebra, mean fluoride ranged from 958.0 ppm F^- in the lumbar vertebra to 805.8 ppm F^- in the iliac crest. Mean values of bone tissue in female subjects were always lower than in males.

Mean F^- value (Table 3) for cartilage of the knee joint was 14.4 ppm (fresh weight); of the 3rd rib: 27.7 ppm and of the 7th rib: 21.9 ppm F^-. In aortic tissues F^- averaged 4.1 ppm. Whereas arteriosclerotic altera-

Table 3

F^- Content of Adult Cartilage and Aorta (ppm fresh weight)

tissue localization	n	mean	♂	♀
knee joint	29	14.4	16.9	11.5
3rd rib	29	27.7	31.0	25.7
7th rib	29	21.9	24.5	17.5
aorta	16	4.1	3.2	4.6

Table 4

F^- Content of Infant Bone, Cartilage, Aorta (ppm ashed bone/fresh weight cartilage, aorta)

tissue localization	n	mean	♂ n = 6	♀ n = 6
femur trochanter	12	227.2	273.1	187.8
iliac crest	12	187.0	177.8	198.6
3rd lumbar vertebra	12	132.8	120.3	145.3
knee joint	12	2.0	1.6	2.3
3rd rib	12	7.7	5.6	9.0
7th rib	12	5.3	5.8	4.8
aorta	12	4.9	5.8	4.0

tions were seen in the aortic wall of the 16 deceased persons, arteriosclerotic calcifications were not found. In newborns, the mean fluoride content ranged from 227.2 ppm in trochanter femora, to 132.8 ppm in the 3rd lumbar vertebra (Table 4). In cartilage and aortic fresh tissues, mean levels were less than 10 ppm F^-. The fluoride content of bone, cartilage and aortic tissues of newborns is surprisingly high compared with adult bone tissue.

Conclusion

Our first results with the flow injection analysis (FIA) for fluoride determination in urine have been presented here. By our adapted method, the aorta and cartilage fluoride content can now be determined quickly and easily. Additional details on fluoride determination by means of flow-injection-analysis will appear in the near future in an analytical chemistry journal (3).

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FLUORIDE IN BLOOD AND URINE IN HUMANS ADMINISTERED FLUORIDE AND EXPOSED TO FLUORIDE-POLLUTED AIR

by

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SUMMARY: Distribution of fluoride in human blood and urine was determined spectrophotometrically by using color complex of zircronium-eriochromcyanine lake. In healthy controls, the total mean fluoride concentration in blood serum was 11.2 µmol; the daily urinary fluoride, 1.83 mg. According to the present method, the fluoride concentration connected with serum protein was 10.15 µmol/l; nonprotein fluoride, 1.05 µmol/l. Fluoride increased in blood serum and in urine of workers professionally exposed to it, 16.69 µmol/l and 3.574 mg respectively. The mean fluoride concentration in erythrocytes of controls is about 6 times higher (59.97 µmol/l) than that in blood serum (11.2 µmol/l).

KEY WORDS: Fluoride in human blood, urine, erythrocytes; in normal and exposed humans.

Introduction

Elementary fluorine demonstrates the greatest reactivity among elements (1). In the atmosphere, fluorine is generally in the form of hydrogen fluoride or fluosilicate which originates in the process of superphosphate production and aluminum metallurgy. Fluoride as well as hydrogen fluoride have suffocative properties; they burn mucous membranes of mouth, lungs, eyes and nose.

Sodium fluoride poisoning in man causes bloody vomiting, severe stomach ache, convulsions, shock, heart insufficiency and anuria (2-4). During the production of superphosphate from apatites in Poland, 5000 tons of fluoride are emitted into the atmosphere annually (5). Exposure of humans, animals and plants to elevated fluoride doses increases daily, especially in large industrial centers (6). Fluoride in the human organism causes non-specific enzymatic changes, stimulating phosphohexoseismoerase and alkaline phosphatase activity (1, 7-8). The increased fluoride dose adversely affects the thyroid gland and contributes to reduction of iodine (9). Increased fluoride in an organism may disturb the carbohydrate metabolism because of glycolytic enzyme inhibition (1). Divergent results of fluorine content labelings in the healthy organism and primarily in blood serum interfere with proper evaluation of the degree of exposure to fluoride and its compounds.

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A detailed knowledge of fluoride pharmacokinetics is necessary to adequately understand its pharmacologic and toxicologic effect (10). For this reason, experiments considering the pool of fluoride in blood and the dynamics of its changes as a burden to the organism seems appropriate.

Material and Methods

Blood and urine: In order to determine fluoride in particular human blood elements, it was introduced into 2 test tubes - one heparinless tube and the other heparinized. After about 2 hours, the blood was centrifuged to separate serum or plasma from blood corpuscles. The resultant serum was designated nonprotein fluoride, total fluoride and fluoride connected with albumins, globulins and gamma-gobulin. Blood serum bearing hemolysis traces was eliminated. For determining their fluoride content, erythrocytes were not washed. Capillary blood was taken from finger tips with calibrated 0.2 ml micropipette. For determining daily 24-hr. urinary fluoride, urine was collected in plastic containers and kept in a cool place during collection. All urine was mixed and its volume measured; about 10 ml of urine was kept for examination in corked test tubes.

Method for Fluoride Determination

Fluoride obtained from blood serum and urine through distillation was determined spectrophotometrically by using color complex of zirconium and eriochromcyanine R (Zr -ER). Color complex was formed as the result of the combination of multivalent zirconium cation and organic indicator - eriochromcyanine R has red coloring which, under the influence of fluoride ion, changes into orange and yellow (11). The concentration of fluoride connected with serum proteins and ionized fluoride was also determined. Total protein was received in the course of the proteining of blood serum. 2 ml of 2M perchloric acid were introduced into a centrifuge tube after which 1 ml serum was added and the contents of the test tube thoroughly mixed with a glass rod. Left to stand for 5 minutes, it was centrifuged for 10 minutes at 5000 rpm.

Supernatant liquid was collected with a Pasteur pipette to the distillation bulb and ionized fluoride concentration was determined. The remaining protein sediment was used for determining fluoride connected with this protein.

Experiments were carried out on 35 healthy adults aged 20-30, 30-40, and 40-50. Because the subgroups did not differ significantly, total mean fluoride concentration in serum 11.2 ±0.82 µmol/l was accepted.

Results

Mean daily urinary fluoride in controls was 1.83 mg/24 h ±0.48. This excretion, although low in comparison to other elements contained in urine, proves that man today is consuming excess fluoride from a normal diet (Table I).

On the basis of these determinations, Table 2 shows the results of fluoride concentration in blood serum as well as daily urinary excretion

in workers employed for a prolonged period at a phosphate fertilizer factory in Wrocław (Table 2).

Table 1

Mean Total F in Blood Serum in Healthy Adults (μmol/l) and Daily Urinary Excretion (mg/24 hr)

Mean Total F and Standard Deviation (SD) in Blood Serum μmol/l in 35 cases		Mean Daily Urinary Fluoride (mg/day) and Standard Deviation (SD) in 28 cases	
M	SD	M	SD
11.2	±0.82	1.83	±0.48

Table 2

Total F in Blood Serum and Daily Urinary Excretion in 13 Workers

Mean Total F^- μmol/l in Blood Serum		Mean Daily Urinary F^- Excretion mg/day	
M	SD	M	SD
16.28	±4.1	3.574	±2.16

Table 3

Mean Concentration of Protein and Non-Protein F in Blood Serum of 26 Subjects

Cases	Mean Values in μmol/l			
	F^- Protein		F^- Non-protein	
	M	SD	M	SD
26	10.15	±0.82	1.05	±0.03

Mean urinary fluoride, 3.57 mg/day in this group, is higher than that in individuals not exposed to fluorine compounds (1.83 ±0.48 mg/day). Fluoride concentration in blood serum of workers professionally exposed to it, namely 16.28 μmol/l, was also significantly higher than in those not professionally exposed, 11.2 μmol/l ($t = 7.78$).

The next step was to determine the different fluoride forms which may contribute to the total content of this element in blood serum. The concentration of serum protein and nonprotein fluoride was determined according to the method explained in the introduction. Twenty-six people (both sexes) participated in these experiments (Table 3).

Mean nonprotein fluoride in 26 examined cases amounted to 1.05 μmol/l with ±0.03 deviation. All results fall into the concentration range between 1.0 and 1.1 μmol/l. Many scientists assume that the fluoride concentration (1.05 μmol/l), determined by means of the fluoride electrode, is the total fluoride concentration in blood serum. However, it is difficult to establish the level of fluoride in human blood without knowing its concentration in erythrocytes (Table 4).

Table 4

Mean F^- Level in Blood Serum and Erythrocytes in 8 Control Adults (μmol/l)

Number of cases	F in Blood Serum	F in Erythrocytes
8	10.1	59.97

Table 5

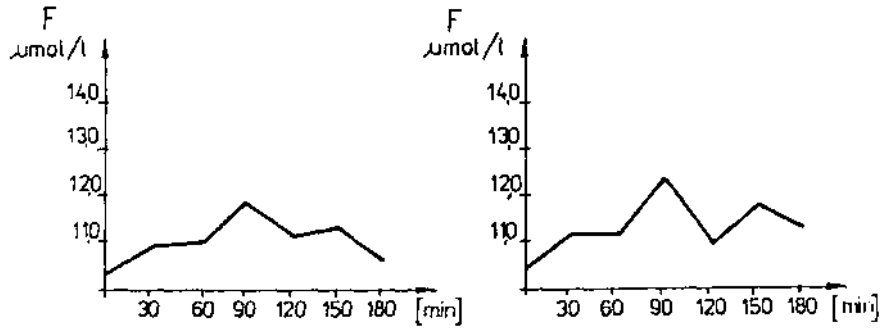
Increase of F^- in Human Blood Serum 1½ hrs after Administering 5 mg F^-

Cases	Mean F^- Concentration in Blood Serum μmol/l		Increase
	Before	After	
21	9.03	10.46	1.43

In experiments carried out on patients taking a cure in the watering place, Cieplice Zdroj, ½ liter of mineral water containing 10 mg/l fluoride (Marysienka), or 5 mg of fluoride was introduced into the organism. A number of experiments have established that maximum increase of fluoride concentration in serum occurs ninety minutes after an oral dose of fluoride (Fig. 1).

Figure 1

Increase of F in human blood serum (μmol/l) after the oral administration of 5 mg F.



At this time, i.e. one and one-half hours after administering fluoride, the concentration of this element in blood serum and urine was determined in the group of 21 people; the fluoride concentration in blood serum had increased; the lower its initial concentration, the greater the increase (Table 5).

This 18% increase in fluoride concentration in serum was accompanied by a relatively small increase in urinary fluoride. Prior to administration, mean fluoride excretion was 2.53 mg/24 hr; afterwards it was 2.75 mg/24 hr.

Regarding analysis of urinary fluoride in individual cases, in general, a high increase in fluoride concentration in blood serum was associated with minimum uninary excretion; in three cases, urinary fluoride decreased. In a group of 8 people, fluoride concentration in blood serum increased 3.15 umol/l (Table 6).

Table 6

The Increase of F^- in Blood Serum and Erythrocytes, 90 Min. after 5 mg F^- Administered Orally

Number of cases	Mean F^- Concentration (umol/l) Blood Serum before	Blood Serum after	Erythrocyte before	Erythrocyte after
8	10.13	13.28	60.09	120.79

On the basis of results, we conclude that fluoride is bound in blood by means of erythrocytes where the fluoride concentration is doubled.

Discussion

For evaluation of the changes which take place under the influence of administration of fluoride and exposure to it in industry, the results must be compared to the fluoride concentration in blood serum and daily urine of a control group of healthy adults.

The fluoride level 11.2 μmol/l, in blood serum, has not been established as far as investigations of its contents in biological liquids in the human organism are concerned. A Polish scientist (3) on the basis of Anglo-Saxon literature, presents the approximate value of fluoride concentration in blood as 18-76 μmol/l. On the other hand, Nielsen et al. (12) gave 10 ±3 μmol/l concentration of serum fluoride. Fry and Taves (13), analyzing serum fluoride by using the fluoride electrode, present a very low value of ionized form, namely 1 μmol/l. In fluoride balance studies, 1 mg F was retained per day when fluoride intake averaged 4.3 mg/day (14).

Production technology for superphosphate from phosphorites and apatites still exposes humans and their surroundings to fluoride compounds. In 77% of examined healthy workers from a superphosphate factory, the fluoride concentration in blood serum was higher than 11.2 ±0.82 μmol/l (the level anticipated in healthy humans). In spite of high variation (s = 2.15) of urinary fluoride, the essential difference of daily urinary excretion of this element in these workers was confirmed at 3.574 mg/24 hr. compared to 1.83 ±0.48 mg/24 hr. in the control group. In 397 healthy persons, normal urinary fluoride ranged between 0.61 - 2.00 mgF/l (15).

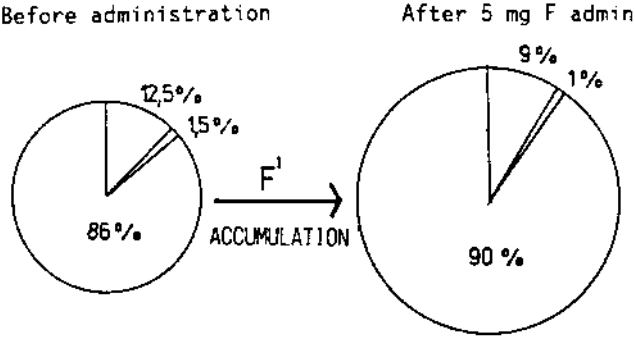
The determined fluoride content in controls of 11.2 μmol/l is connected with blood serum proteins and free form of fluoride, called by some scientists ionized or non-protein (12, 16). The sum of concentrations of these two forms of fluoride in blood serum in healthy adults does not differ from the normal value (11.2 μmol/l) and indicates that about 90% of this element is connected with proteins. Binding must be relatively strong because the precipitation of proteins with a strong perchloric acid of the final concentration (0.32 μmol/l) causes their sedementation with co-valently bonded fluoride.

In the world literature, devoted to chemistry and biochemistry of the erythrocyte, the fluoride ion has not received much attention. As a result of using the zirconium-eriochromcyanine method with distillational fluoride effusion from blood corpuscles a higher concentration of this element has been found in ercthrocytes than in blood serum. From the point of view of physiology, especially toxicology, the loading of the organism with fluoride and the observation of the dynamics of concentration changes of this element in blood serum in bound and unbound protein form and its concentration in erythrocytes is of interest.

The experiments, presented in Tables 4 and 5, confirm the increase of fluoride concentration in blood serum after oral administration. They especially draw attention to erythrocytes in the blood stream in which large amounts of fluoride are bound. Fluoride in erythrocytes and that bound with blood serum proteins constitute a so-called primary depot of this element out of which the active ionized form of fluoride can be created. The pool of fluoride in human blood may be presented in physiological terms as a circle area in which about 86% of fluoride is connected with erthrocytes, 12.5% with blood serum proteins; only 1.5% remains in the dissociated form (Fig. 2). Furthermore, we know that when the human organism is loaded with fluoride, binding by erythrocytes increases up to about 90%; only 10% of fluoride remains bound with proteins and dissociated.

Figure 2

F^- in human blood (circle area) before and 90 minutes after administration of 5 mg F^-.



Before - F distributed as follows: 86% connected with erthrocytes, 12.5% with blood serum proteins, 1.5% in dissociated form. After - pool of F^- distributed as follows: 90%, 9%, 1% respectively.

Conclusion

In light of the current investigation we suggest that, similar to the toxicology of heavy metals particularly lead, the fluoride concentration in full blood should be investigated to make it possible to evaluate the entire pool of fluoride bound with blood proteins and erythrocytes.

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CORRECTION

The following names were inadvertently omitted from the Author Index in the October, 1985 issue.

McNamara, T.F. 175
Mehta, N.R. 80-86
Melde, S. 135-140
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A replacement/substitute page is included with this issue for placement in the permanent record.

SEX DIFFERENCES IN HALOTHANE METABOLISM AND HEPATOTOXICITY IN A RAT MODEL

by

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Mark A. Jenner, and Michael J. Cousins
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(Abstracted from Anesth. Analg., 64:563-9, 1985)

This study was designed to investigate sex differences in halothane metabolism and heptotoxicity in the hypoxic rat model. Phenobarbital--induced male and female rats were anesthetized with 1% halothane in 14% oxygen for two hours. Female rats were found to metabolize halothane by the oxidative pathway to a similar extent as males, but the extent of metabolism by the reductive pathway was less in females. All male rats exposed under these conditions developed confluent centrilobular hepatic necrosis. Females were less susceptible than males to the hepatotoxic effect of halothane, with responses ranging from no hepatic injury to confluent centrilobular necrosis limited to within a few cells of the central veins. This lesser susceptibility was not however, solely due to the lesser extent of reductive metabolism in females, as lowering the inspired oxygen concentration to 12% increased the extent of reductive metabolism but did not increase the severity of the hepatic injury.

KEY WORDS: Anesthetics; Biotransformation (drug), halothane; halothane, toxicity; halothane, volatile; liver

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ENAMEL FLUORIDE IN NURSING RATS WITH MOTHERS DRINKING WATER WITH HIGH FLUORIDE CONCENTRATIONS

by

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(J. Dental Research, 64:877-880, 1985)

The purpose of this study was to determine the F levels in plasma and molar enamel from rat pups whose mothers had received various levels of F during pregnancy and/or lactation. Rats were started on water containing 0 (Group I), 50 (Group II), or 100 (Group III) ppm F at the beginning of

pregnancy or on the day of delivery, and plasma F levels, milk F levels, and pup molar enamel F levels were determined.

The mean maternal plasma F concentrations were 0.02 ±0.005 ppm in Group I, 0.10 ±0.031 ppm in Group II, and 0.21 ±0.057 ppm in Group III. The milk F values were about twice as high as the respective plasma concentrations. The plasma F concentration in control pups was 0.003 ±0.0002 ppm, and there was a rise to 0.006 ±0.0002 ppm in Group III. Enamel F concentrations were 0.62 ±0.13 ppm, 4.72 ±0.79 ppm and 8.80 ±1.74 ppm, respectively. The plasma and enamel F values obtained from pups were not significantly different between the pre-natal/post-natal, and the post-natal-only groups. It was concluded that (1) fluoride levels in the plasma and enamel of control rat pups were much lower than those found in adult rats, (2) such values could be increased only slightly when high doses of F were given to the mother, and (3) unlike values reported for other species, rat milk fluoride concentrations were higher than the respective plasma values.

KEY WORDS: Enamel, rat; milk, rat; plasma, rat.

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URINARY FLUORIDE EXCRETION IN FLUORIDE EXPOSED WORKERS WITH DIMINISHED RENAL FUNCTION

by

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(Abstracted from Industrial Health [Japan] 22:33-40, 1984)

Renal clearance of fluoride (C_F), the amount of fluoride filtered by the glomeruli per minute (F_F), and tubular reabsorption of fluoride (TrF), which were calculated from the serum concentration, as well as the quantity concurrently excreted in the urine, and the glomerular filtration rate (GFR), were investigated in patients with chronic renal failure (CRF) and healthy controls after oral administration of 4 mg NaF, with water loading.

Twenty-four hour fluoride excretion in patients with CRF was significantly lower ($p < 0.001$) than in controls. C_F, F_F, and TrF were also lower. C_F and creatinine clearance (Ccr) were well correlated ($\Delta = +0.87$); C_F averaged 48% of Ccr.

In patients with CRF and in HF workers, serum concentrations of fluoride were markedly higher ($p < 0.001$) than in controls. In HF workers, urinary concentration of fluoride was also higher ($p < 0.001$). Urinary fluoride content remained normal in spite of markedly higher serum fluoride concentrations in CRF patients than in controls.

After oral administration of sodium fluoride with water loading - in both groups fluoride intake before and during the experiments was very low - 24-hour urinary fluoride excretion in 5 patients with CRF and in 5 healthy controls was 1326 ± 693 compared to 1789 ± 476.

In patients with CRF, only 6.2% of ingested fluoride was excreted in the 24-hour urine which was markedly lower than in control subjects (48.8%). In the same patients, those with CRF and controls, 2 hours after fluoride administration with water loading, mean serum concentrations of fluoride were similar. On the other hand, urinary concentrations of fluoride at that time, urinary flow per minute, Ccr, C_F, F_F, and TrF in patients were markedly lower than in controls.

Once renal function is severely impaired, excretion of fluoride in the urine decreases and serum fluoride concentration increases.

These findings indicate increased retention of fluoride in the body of patients with CRF, especially in those exposed to fluoride in the work place. In the case of HF workers with diminished renal function, measurement of urinary fluoride concentration may not be adequate. Frequent monitoring of serum fluoride also appears to be necessary as an indicator of excess fluoride intake.

In patients with kidney hypofunction, F^- levels in serum appears to be a more reliable indicator of exposure than urinary F^- levels.

KEY WORDS: Fluoride metabolism; Hydrofluoric acid workers; Index of fluoride exposure; Patients with chronic renal failure; Renal fluoride clearance

Reprints: Department of Environmental Health, Fukui Medical School, Matsuoka-cho, Fukui 910-11, Japan.

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RENAL CLEARANCE OF FLUORIDE IN CHILDREN AND ADOLESCENTS

by

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(Abstracted from Pediatrics 75:575-9, 1985)

To study renal fluoride clearance in children and adolescents, renal function was tested in thirty-eight children (29 girls and 9 boys) in whom renal involvement associated with a systemic disorder such as diabetes was suspected.

A close linear relationship was observed between renal fluoride clearance and glomerular filtration rate, urinary flow, and free water clearance.

Mean renal fluoride clearance was 31.4 $\pm$ (SD) 8.8 mL/min in the group of patients with low glomerular filtration rates (GFRs) and 45.0 $\pm$ 9.8 in the group with normal GFRs. The difference between renal fluoride clearance in these groups was statistically significant ($P < .01$). The plasma fluoride concentration was somewhat higher in the group of patients with low GFRs, namely 1.4 $\pm$ 0.2 μM compared with those with normal GFRs 1.2 $\pm$ 0.2 μM. About 60% of the filtered fluoride was reabsorbed. Children with suspected renal disease but whose GFR values were within the range for healthy children served as controls.

This study shows that children have a lower rate of renal fluoride clearance than adults. It also shows that, with only a moderate decrease in glomerular filtration, renal fluoride clearance was reduced, and retention of fluoride increased compared with children whose kidney function is normal.

KEY WORDS: Children and adolescents; Renal F^- clearance

Reprints: (C.J.S.) Department of Cariology, School of Dentistry, Karolinska Institutet, Box 4064, S-141 04 Huddinge, Sweden.

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EFFECTS OF CORTISOL AND FLUORIDE ON ION-TRANSPORTING ATPase ACTIVITIES IN CULTURED OSTEOBLASTLIKE CELLS

by

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(Abstracted from In Vitro 20:847-855, 1984)

Na^+, K^+-ATPase, HCO_3^--ATPase, Ca^{2+}, Mg^{2+},-ATPase, Ca^{2+}-ATPase, and alkaline phosphatase activities were measured in cultures of osteoblastlike cells treated with fluoride and cortisol separately and in combinations. Low concentrations of cortisol increased HCO_3^--ATPase [10^{-11} to 10^{-18} M cortisol] and alkaline phosphatase [10^{-11} to 10^{-9} M cortisol] activities, but higher cortisol concentrations reduced these activities. Na^+, K^+-ATPase, Ca^{2+}, Mg^{2+}-ATPase, and Ca^{2+}-ATPase activities tended only to be reduced by cortisol.

Fluoride [10^{-6} and 5 X 10^{-6} M] increased HCO_3^--ATPase and alkaline phosphatase activities, but these activities were similar to controls in the presence of 10^{-5} M fluoride. Ca^{2+}, Mg^{2+}-ATPase activity was decreased and Na^+, K^+

-ATPase activity was increased as the concentration of fluoride increased [10^{-6} to 10^{-5} M]. Preliminary experiments with fluoride indicated that lower concentrations [10^{-7} M] were without effect.

Cortisol concentrations of 10^{-9} and 10^{-8} M were chosen for studies with combinations of cortisol and fluoride because the effects of these concentrations on alkaline phosphatase activity were opposite, i.e. 10^{-9} M increased whereas 10^{-8} M decreased activity. Fluoride concentration of 10^{-6}, 5 X 10^{-6}, and 10^{-5} M were chosen because a peak of alkaline phosphatase activity occurred at 5 X 10^{-6} M fluoride. Higher [10^{-4} M] and lower [10^{-7} M] fluoride concentrations were without effect.

The effects of combinations of cortisol and fluoride depend on the enzyme activity measured. Fluoride [10^{-6} M] combined with cortisol [10^{-9} M] produced a peak of Na^+, K^+-ATPase activity. The increased activity obtained with all concentrations of fluoride alone was preserved when fluoride was combined with 10^{-8} M cortisol, although the activity tended to be reduced at 5 X 10^{-6} and 10^{-5} M fluoride. HCO_3^--ATPase activity was increased by fluoride combined with 10^{-8} M cortisol and decreased by fluoride combined with 10^{-9} M cortisol compared to the activities obtained with fluoride alone. The decrease in Ca^{2+}, Mg^{2+}-ATPase activity caused by fluoride alone was prevented by 10^{-9} and enhanced by 10^{-8} M cortisol, although all treatments produced the same activity at 10^{-5} M fluoride. Ca^{2+}-ATPase activity tended to be increased by combinations of fluoride and cortisol, but significantly so only at 10^{-5} M fluoride in combinations with 10^{-8} and 10^{-9} M cortisol. Alkaline phosphatase activity was increased by fluoride combined with 10^{-9} M cortisol and decreased by fluoride combined with 10^{-8} M cortisol compared to the activities obtained with fluoride alone.

These results suggest that the abilities of bone cells to regulate ion transport [as reflected in their ion-transporting ATPase activities] are modulated by lucocorticoids and fluoride. Inasmuch as these cells may regulate the ionic composition and concentrations of the bone extracellular fluid [ECF] in vivo, the modulation of their activities by cortisol and fluoride may result in altered bone ECF composition.

KEY WORDS: ATPase; Cortisol; Culture; Fluoride; Osteoblast.

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EXTENDED TREATMENT OF PRIMARY OSTEOPOROSIS BY SODIUM FLUORIDE COMBINED WITH 25 HYDROXYCHOLECALCIFEROL

by

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(Abstracted from Clinical Rheumatology, 3:145-153, 1984)

Nineteen patients suffering from primary osteoporosis, all having at least one vertebral collapse, initially received 50 mg of sodium fluoride (NaF) alone per day for 6-18 months. Subsequently, in 12 of these patients, fluoride was associated with 25-50 µg of 25-OH cholecalciferol (calcifediol) per day for 6-18 months; 9 were treated for 31-58 months.

As controls, 9 patients were given a placebo for 6-18 months. In each group there was a significant increase in trabecular bone volume, osteoid volume, osteoid surfaces and a significant decrease in mineralization fronts. On the other hand, changes in osteoblastic and osteoclastic surfaces, number of osteoclasts/mm2, were not significant in any group. No change was observed in the placebo group.

These data suggest that the increase in trabecular volume of fluorided bone is mainly due to the increase in osteoid which itself is due to a bone mineralization defect despite the administration of calcifediol.

Treatment by NaF caused gastralgia in six cases which disappeared after some days when the NaF had been carefully mixed with food. Arthralgia, observed in two cases, was accompanied by articular swelling in one case, without abnormality on x-rays. A bone fissure of the left femoral neck was observed in one case treated for 36 months.

It is possible that fluoride had little effect on the structure of cortical bone (of which the hand bones are chiefly comprised); that it exerted its activity mainly upon spongy bone.

The important and constant decrease in mineralization fronts observed with fluoride alone, shows a defect in bone mineralization which calcifediol is unable to improve. There is probably another reason why Ca has not changed significantly.

Fluoride may induce changes in the physicochemical properties of bone apatite crystals, the crystal of fluoroapatite itself being fixed more slowly on bone matrix. Nor can the possibility be excluded that osteoblasts, stimulated by fluoride, build up a matrix incapable of normal mineralization, suggested by the aspect of fluorescence of the mineralization fronts, often irregular and less bright, and by the abundance of woven bone in some biopsies.

In osteoporotics treated with fluoride, several cases of bone fissures situated near the cortex have recently been reported. The mechanism

of these fissures is mysterious. Some of them may be due to the defect in mineralization of the fluorided bone and to the persistent weakness of the cortex of the long bones in osteoporotics.

Whereas sodium fluoride administered in an extended manner to osteoporotics stimulates osteoformation of spongy bone, the quality of newly-formed bone and its degree of mineralization, especially its structure, is still open to question.

KEY WORDS: Bone mineral content; Fluoride; Histomorphometry; Osteoporosis; Vitamin D.

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RISK OF MYOCARDIAL INFARCTION IN FINNISH MEN IN RELATION TO FLUORIDE, MAGNESIUM AND CALCIUM CONCENTRATION IN DRINKING WATER

by

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(Abstracted from Acta Med Scand 213:171-6, 1983)

To study the influence of drinking water composition on the risk of myocardial infarction, the following study was conducted: The cases (C), men 30-64 years of age, had been discharged with a first acute myocardial infarction (AMI) from Kotka Central Hospital. The hospital controls (HC), matched for age and type of community, were selected for each case among surgical patients. Population controls (PC), matched for age and municipality, were drawn for each case from the population register. Subjects submitted a sample of their drinking water and a filled-in questionnaire. After exclusions, a series of 50 C-HC and 50 C-PC pairs was finally constructed. The point estimate of relative risk (RR) for the association between low F (<0.1 ppm) and increased risk of AMI was 3.0 in the C-HC series. In the C-PC comparison RR was 4.4. RR for low Mg (<1.2 ppm) was 2.0 in the C-HC comparison and 4.7 in the C-PC comparison. The results are consistent with the hypothesis that both a low F and a low Mg intake are conducive to atherosclerosis leading to AMI.

KEY WORDS: Atherosclerosis; Calcium; Drinking water; Fluoride; Magnesium; Myocardial infarction

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Authors' Abstract

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PREVALENCE OF DENTAL CARIES IN HIGH AND LOW FLUORIDE AREAS OF SALEM DISTRICT, TAMILNADU, IN SOUTH INDIA

by

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(Abstracted from the J. Indian Dent. Assoc.,55:451-484, 1983)

This study is a preliminary attempt to assess the magnitude of dental caries in a population consuming high and low fluoride levels in water. Salem district of Tamilnadu, South India, was selected for the study because of its prevalence of endemic fluorosis.

A total of 209 persons of either sex, between 12-75 years of age, were surveyed in four villages of Salem district where fluoride concentration in well water, used for drinking, ranged from 0.3 to 6 ppm. In Sengatoor and Nirmalakottai, the high fluoride communities, water contained 6 ppm and 3.2 ppm, respectively; in the low fluoride communities, Reddiampettair and Sengapuram, 0.5 ppm and 0.3 ppm respectively.

Permanent erupted teeth were examined with a mirror and probe in natural daylight. Palpable softening of enamel and dentine was counted as caries. Early enamel lesions in pits and fissures where softness could not be elicited by probe, were not included for the study. Radiographs were not taken.

The average community DMF rate was 0.91 where F^- in water is 6 ppm; the DMF was 2.18 where water content is 0.5 ppm F^-. Similarly, the dental caries frequency was low in high fluoride group compared to the low fluoride counterparts who displayed more than twice the frequency.

On the other hand, females consistently showed relatively high dental caries frequency despite the high fluoride level in water. In Sengatoor (6 ppm F^-), DMF in females was 1.67, not too different from that in Reddaimpettai namely 1.73 DMF, where water contains 0.5 ppm. Moreover, caries frequency in Nirmalakottai (3.2 ppm) and Sengapurum (0.3 ppm) was practically the same namely, 39.6 for the former and 39.8% for the latter.

KEY WORDS: Dental caries prevalence; High and low fluoride areas; Salem District; South Africa.

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EXPERIMENTAL OSTEOFLUOROSIS IN THE DOMESTIC PIG: A HISTOMORPHOMETRIC STUDY OF VERTEBRAL TRABECULAR BONE

by

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(Abstracted from J. Dent. Res. 63:885-889, 1984)

The present study was carried out to determine the effects of fluoride on structure and remodeling of trabecular bone in the domestic pig and to asses morphologic changes by quantitative histology using fluorochromes as tissue markers. Eight animals that received a supplement of 2 mg F^-/kg b.w. per day from eight months of age for the following 6 mos. were compared with controls. Plasma fluoride in pigs receiving fluoride increased from 0.7 ± 0.1 µM/l (0.013 ppm) to 12.7 ± 2.0 µM/l (0.24 ppm). Fluoride exposure was estimated by plasma fluoride concentrations, a more reliable parameter for fluoride exposure than oral doses which have varying bio-availability depending,for example,on calcium content of the diet. The domestic pig was chosen as the experimental animal because it has a blood compartment large enough to allow for frequent blood sampling.

At slaughter, the fluoride level in dry fat-free bone of fluorotic animals was 149.3 ± 10.5 mM/kg (2837 ppm), 9.5 ± 0.9 mM/kg (181 ppm) for controls.

Morphologic changes were assessed in undecalcified specimens of the fourth lumbar vertebra by quantitative histology using fluorochromes as intra-vital tissue time markers. The volume of trabecular bone tissue (bone + marrow) was unchanged in fluorotic animals; bone density, however, had increased by 17%. Surface densities of cancellous bone remained almost unchanged whereas trabecular thickness increased in fluorosis. Fluoride enhanced remodeling of trabecular surfaces. The fraction of surface occupied by resorption lacunae had increased 40%. Increases of approximately 30% were found for fractional osteoid-covered surface (Ss [osteoid, total]) and fractional calcein-labeled surface (Ss [label total]) ($p < 0.05$).

The experiment confirmed previous studies demonstrating an increased volume density of trabecular bone in fluorosis. The surface density of the tissue was unchanged, whereas the thickness of trabeculae appeared to be increased in fluorotic pigs. Fluoride might, however, reduce the depth of resorption at remodeling sites. To date,no reliable methods for estimating the resorption depth exist.

Fluorosis is not a condition that effects enamel exclusively. Other hard tissues, such as dentine and bone, which derive from the mesenchyme, may likewise be changed. Fluoride may interfere with some basic metabolic mechanism in mineralizing tissues, regardless of the origin of the tissue. According to this hypothesis, the varying manifestations of fluo-

rosis are due to differences in mode of mineralization and turnover of tissues. Fluoride affects remodeling and increases the mass of trabecular human bone. Information concerning the remodeling process in fluorotic bone is, however, incomplete.

The authors conclude that their findings cannot be explained by fluoride-induced changes in a single cell, namely the osteoblast, and that fluoride appears to affect all cells involved in remodeling by direct or indirect mechanisms. Additionally, no change in the total volume of trabecular bone tissue [V (tissue)] was found ($p > 0.10$), but the volume density of bone trabeculae [Vv (bone)], which had increased 17% in fluorotic pigs ($p < 0.05$), led to an increase in absolute volume of bone trabeculae [V (bone)] ($0.05 < p < 0.10$).

The increased volume appeared to be due to an increased trabecular thickness in fluorosis ($0.05 < p < 0.10$). Fractional resorptive surface [Ss (resorption lacunae, total)] was more than 40% larger in the fluorotic group ($p < 0.05$). The bone was not in a steady state with respect to fluoride exposure, which might partly explain why the area of resorptive surface apparently increased slightly more than the formative surface. At remodeling sites, resorption precedes formation and any change in the extent of remodeling surfaces initially affects resorption only. The pathogenesis of the fluorotic lesion, however, is still unknown.

KEY WORDS: Osteofluorosis; Pig, histomorphometric study; Vertebral bone F^- effect on.

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EFFECTS OF SODIUM FLUORIDE ON BLASTOGENESIS IN MICE LYMPHOCYTES, WITH SPECIAL REFERENCE TO THE UPTAKE OF [^{3}H]THYMIDINE, [^{3}H]URIDINE, OR [^{3}H]LEUCINE

by

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(Abstracted from Shika Gakuho, 84:220-251, 1984)
(in Japanese)

The toxicity of NaF used in dentifrices to reduce dental caries was demonstrated by showing the inhibitory activities of NaF on the uptake of tritiated thymidine, uridine, and leucine by lymphocytes in vitro. Similar inhibitory activities occurred in the spleen of mice which received NaF orally.

KEY WORDS: Fluoride effect on blastogenesis; Mice lymphocytes

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UTERINE ADENYLATE CYCLASE ACTIVITY DURING THE ESTRUS CYCLE AND EARLY PROGESTATION IN THE RAT: RESPONSES TO FLUORIDE ACTIVATION AND DECIDUAL INDUCTION

by

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(Abstracted from Biology of Reproduction 31:742-751, 1984)

Uterine adenylate cyclase (AC) activity of the rat was measured by radiochemical analysis during the estrus cycle and early pseudopregnancy. During the estrus cycle, AC activity increased from 4.6 to 16.9 pmol cAMP formed/min·mg protein between metestrus and proestrus. Although AC activated 2- to 3- fold at all cycle stages by 10 mM NaF, the resulting pattern of activity was similar to that measured in the absence of fluoride. The results demonstrated that the pattern of AC activity during the cycle was similar to that of other estrogen-sensitive uterine enzymes and that the ovarian hormones probably altered enzyme biosynthesis and turnover to a greater extent than activation and kinetic properties.

Following the induction of pseudopregnancy by cervical stimulation, enzymic activity increased from 3.5 to 9.4 pmol between Days 1-4 (Day 1 = leukocytic vaginal smear) and declined thereafter. AC activity was increased 2- to 5- fold by NaF on all days. AC activity was similarly increased by a mechanical trauma to the uterus, but only when the trauma was applied on Day 4. Following trauma to the uterus, AC activity was not increased further by NaF.

The similarities between the physicochemical characteristics on AC during the estrus cycle and early progestation suggested that the enzyme during all endocrine states had virtually identical properties. However, the transient sensitivity to activation after trauma on Day 4 was unique to progestational uteri. Because the properties of enzyme were not altered by the endocrine state of the tissue the transient sensitivity to activation by trauma was suggested to be a result of hormone-induced alterations in the membrane in which AC is sequestered.

KEY WORDS: Adenylate cyclase; Estrus cycle; Fluoride activation of adenylate cyclase.

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Authors' Abstract

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DENTAL STUDY UPSETS THE ACCEPTED WISDOM

by

J. Raloff
Editor, Science News, Washington, D.C.

(Abstracted from Science News, Vol. 125, Jan. 7, 1984)

Ten years ago, it was assumed that dental caries could be all but eliminated in school-age children by means of a combination of treatments aimed at caries prevention - namely sealants and fluorides. However, the results of the largest ever controlled field test of preventive dental procedures in the USA suggest that this assumption was erroneous on both counts.

Initiated in 1977, the study was conducted under the auspices of the National Preventive Dentistry Demonstration Program - the Chicago-based American Fund for Dental Health, a nonprofit group that raises funds for dental research, education and health-care delivery. A total of almost 30,000 children aged 5 to 14 were examined over a four-year period in 10 communities. In half of the communities, fluoride was being added to drinking water. The program focused on four caries prevention techniques: sealants, professional teeth cleaning with a fluoride paste followed by fluoride gel treatment every six months, weekly rinses with fluoride mouthwashes and, in nonfluoridated communities, a daily fluoride tablet, accompanied by classroom instructions on dental health, plaque control through brushing, flossing and use of fluoride toothpastes.

The program's goal was to determine which, if any, combination of these preventive measures would eliminate childhood dental decay and at what cost.

In 1981, the National Institute of Dental Research confirmed with its own data that children 5 to 17 years of age now experience one-third fewer cavities than previously recorded in national surveys. Overall, 60% of the cavities occurred in 20% of the children; those affected were among those in the caries prevention program.

The mouth rinse tablet program achieved, not 20-50% as anticipated but,only 21.4% reduction in the four-year period - even this rate occurred in only one of the groups. On the average, less than one tooth surface was spared from decay (28 permanent teeth contain 128 surfaces). Those receiving the full battery of anticaries techniques - sealants, topical application of fluoride paste, gel, mouthrinses and tablets, in nonfluoridated communities, plus education, saved approximately two surfaces during the four-year test.

Untreated younger children from fluoridated communities had one fewer decayed surface over the four-year period than those in nonfluoridated communities.

Providing routine, standardized, individually applied, preventive dentistry procedures to all children can no longer be justified. Under a new research initiative, the American Fund for Dental Health has begun work on developing a model target measure on the high risk sections of the population, namely the 20% currently who are afflicted with 60% of the cavities.

KEY WORDS: Caries prophylaxis; Fluoride treatment; Preventive dentistry program.

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MECHANISM OF THE MUTAGENIC ACTION OF FLUORINE

by

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Sverdlovsk, USSR

(Abstracted from Tsitol Genet, 16:40-2, 1982)
(in Russian)

Doses of 1000 and 1500 µg NaF increased mutation frequency in Salmonella Typhimurium TA 1535 and TA 98 7-12 fold and 9-17 fold compared to the control. The survivability of the microorganisms was also sharply reduced. The mutagenic effect of F is probably via inhibition of DNA repair processes.

KEY WORDS: Ames Test, Mutagenis by fluoride; Salmonella; Typhimurium

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NEW EVIDENCE ON FLUORIDATION

by

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(Abstracted from Social Science & Medicine 19:1239-1246, 1984)

During 1980 the author made a world study tour for the New Zealand Department of Health in order to investigate and report upon the current state

of water fluoridation practice and research in other countries. "By far the most significant observation, during my tour," Dr. Colquhoun states "was the growing evidence that there has been a dramatic drop in dental decay prevalence in most of the developed countries of the world, and that this reduced prevalence has occurred also in areas where water fluoridation is not practised." Earlier differences between child dental decay rates in fluoridated and nonfluoridated areas in New Zealand have now disappeared in most places, including our most populous region, Auckland. The difference claimed nationally - around 15% for DMF (mainly fillings) but not percent caries-free, between dissimilar populations - could be related to other variables. It is actually smaller than differences previously recorded for such variables as operator judgement on number of fillings required, soil composition (differences up to 57%), and social class (differences up to 98%). Also, the percentage of children caries-free (long accepted as a measure of the effectiveness of fluoridation) is more often greater in nonfluoridated than in fluoridated areas.

Rather than preventing decay by systemically increasing the fluoride content of sound enamel, fluoride could mainly act topically by arresting decay in its very early stages. The systemic dental effect of fluoride - increase of fluoride in sound enamel - is not as great an advantage as was previously thought.

Some evidence suggests an increased hazard brought about partly because of increased intake of fluoride. Two recognized deleterious effects of fluoride in drinking water are dental fluorosis and skeletal fluorosis. Even at the low 1 ppm fluoride concentration it is still possible for some individuals in the population to show more advanced (and possibly unsightly) enamel mottling. A rise in incidence of dental fluorosis in children has brought about reduction in recognized doses of fluoride tablets. Increased fluoride in the food chain, fluoride-rich baby foods and swallowing of fluoride toothpastes are other possible causes. Water fluoridation, by contributing to the total intake of fluoride, obviously influences such effects. A recent study concludes that there is no threshold level, as formerly believed, for fluoride toxicity.

Far more serious is skeletal fluorosis, which has been studied most extensively in India, where the disease is endemic. The symptomatic (painful, crippling or deforming) form of the disease occurs mostly in adults, after long exposure to high levels of fluoride. Skeletal fluorosis has also been reported in children. However, since the earlier asymptomatic form (abnormal bone growth, sometimes only with vague pains) can be detected solely by X-ray, it is not always discovered. It can be misdiagnosed as osteo or rheumatoid arthritis, and in India has been associated with less than 1 ppm water fluoride levels.

Subtle deleterious effects from even earlier subclinical stages of skeletal fluorosis can only be resolved by further research. Lack of obvious harm is only partly reassuring. It is known that some kinds of subtle effects could not be detected without the most meticulous epidemiological investigations.

In addition to its direct influence on human health, minute fluctuations in the level of airborne and water fluoride can affect vegetation and aquatic

life, according to a report by the National Research Council of Canada on enviromental fluoride. The Danish Enviromental Protection Agency and the Swedish Fluoride Commission have rejected fluoridation because of the combined long-term environmental effects of fluoride.

In view of a reduced benefit from fluoridation, following the widespread reduced prevalence of dental decay, use of topical fluoride, though not without its own risks, appears to be an effective alternative.

KEY WORDS: Fluoridation, reduced benefits; Fluorosis increase; F^- toxic effect; Reduced dental decay; Topical fluoride use.

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FLUORIDE IN MIXED HUMAN SALIVA AFTER DIFFERENT TOPICAL FLUORIDE TREATMENTS AND POSSIBLE RELATION TO CARIES INHIBITION

by

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(Abstracted from Community Dent. Oral Epidemiol. 10:124-129, 1982)

In the present study the authors have attempted to relate measurements of fluoride concentrations in mixed saliva following various forms of topical treatments with available findings from corresponding clinical trials. It is estimated that a caries reduction of about 30% might be obtained from any of these treatments.

No simple relationship between fluoride levels in saliva and caries reduction was observed. The potential of remineralizing solutions like saliva is markedly increased by the presence of fluoride ions in concentrations as low as about 1 ppm or even lower. The higher caries reductions obtained with supervised toothbrushing as compared with unsupervised brushing may in part be related to the controlled removal of plaque, which may facilitate the action of fluoride.

In conclusion, caries inhibition obtained from any of these treatments can be ascribed to the capacity of fluoride in the local environment to reduce caries progression at clinical and subclinical levels.

KEY WORDS: Caries inhibition; Salivary fluoride; Topical fluorides.

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FLUORIDE IN HUMAN MILK

by

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(Abstracted from Acta Paediatr Scan., 72:699-701, 1983)

The aim of this study was to determine the F^- content in human milk associated with different levels of F^- intake using a silicon-facilitated micro-diffusion technique, capable of good accuracy and precision. The mean F^- concentration of colostrum was 0.28 ± 0.02 umol/l. The difference between the samples from the two fluoride areas was not statistically significant.

In breastmilk collected from 10 mothers at different times during a 24-hour period, no diurnal differences in F^- content were observed. In a subgroup, there were no differences in F^- concentration between the first, the mid and the last portion of the milk.

Ekstrand et al. observed that administration of 1.5 mg F to the mother, does not influence the F concentration of her breastmilk. On the other hand, Elsala et al. found higher F levels in human milk from a 1.7 ppm F area than in a control (0.2 ppm) area. Thus, chronic exposure to high fluoride levels induces a slight increase.

In an infant of the same age, receiving water-diluted baby formula, F^- intake will be much higher because of the F^- content of the water. In the 0.2 ppm area, the daily intake will be about 160 µg whereas in the 1.0 ppm area it will be about 800 µg, about 30 and 160 fold the intake of the breast fed infant in the respective areas.

In conclusion during early infancy, when breastmilk is the predominant source of food, the infant will have a very low F^- intake, ranging between 5 to 10 µg per day.

KEY WORDS: Breastmilk; Fluoride intake; Human milk; Infants.

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ABSTRACTS FROM FOLIA MEDICA CRACOVIENSIA

Dr. Zdzisław Mach, Editor
Krakow, Poland

The following are abstracts of papers which were published in an issue of Folia Medica Cracoviensia, devoted entirely to fluoride (Kraknow, Poland, Vol 23, Nos. 3-4), 1981.

K. Lejman, K. Szwarc, and Z.F. Szydlowski of Krakow reported skin lesions in workers of the electrolysis department of the Skawina Aluminum plant. The effects occurred in 10% of workers employed between 13 and 20 years and exposed to fluorine compounds. Maculo-vascular lesions of the skin - not surpassing 1 cm in diameter - were localized preponderantly on the trunk. Their histopathological structure indicated damage to elastic fibers and collagenous bundles and of the walls of the blood vessels in the upper layers of the skin as well as destruction of lanuga haris and atrophy of their follicles (page 360).

Regarding the effect of fluoride on the locomotor system, E. Czerwinski, A. Skolarczyk, and J. Dutka, also of Krakow, who examined clinically 200 aluminum plant workers in Sakwina and KiZPS "Siarkopol", with prolonged fluoride exposure, observed that pain in the lumbar spine and joints occurred frequently. Among radiological changes, the most frequent were marginal osteophytes of the vertebral bodies, ossification of muscle attachments, ligaments and interosseous membranes. In all cases, urinary fluoride was elevated (p. 367).

In recent years, in Krakow and neighboring Skawina, where fluorides are released from chemical factories, K. Dluzniewska, Z. Krzyzewski, and B. Wojtowicz found that the mean concentration of atmospheric fluoride for a 24-hour period exceeded, in about 25% of the samples, the MAC values of 9.01 mg F/m^3 for this period. The mean yearly values of fluoride were 2 to 4 times the MAC for a one-year period. In circa 30% samples of infant formulas (human milk included) and in meals of small children, fluoride intake exceeded the maximal safe amount of this micro-element. It was associated with a rise in fluoride concentration in about 30% of the morning urine samples of young children examined in Krakow and Skawina (p. 340).

With respect to the toxic effect of fluoride compounds on the respiratory system E. Nikodemowicz observed, among fluoride compounds, that hydrogen (HF) is the most irritant to the mucous membrane of the bronchial tree. In gaseous form, it penetrates the bronchial tree as far as the alveolar epithelium. Consequently, destruction occurs followed by pulmonary emphysema and respiratory insufficiency with instability. Symptoms of alveolar transudation predominate with multiple moist rhonchi.* This special form of bronchitis which develops after inhalation of fluoride compounds as well as the role of smoking in respiratory insufficiency warrants further study (p. 345).

According to M. Sterecki, who discussed professional diseases assoc-

* Rattling or whistling sound in respiration.

ciated with fluoride, the number of cases of illness among white collar workers at an aluminum plant was 210 times higher than the mean morbidity in other Kracow district plants. Among professionals, in the Kracow district, morbidity values were 40% higher than those in the entire country. The number of sick leaves caused by respiratory and cardiovascular diseases in the same aluminum plant is higher by 250% and 280% respectively, than mean values for the entire country; in the Kracow district they were about 40% higher than those for the entire country. The number of cases of musculoskeletal diseases in the above-mentioned aluminum plant workers and in the whole Kracow district when compared with the total mean value for the country are higher by 340% and 30% respectively. The causes of such an epidemiological situation are very complex but the action of fluoride as an aggressive agent for humans working in the above-mentioned aluminum plant as well as for those living in the Kracow district should not be disregarded (p. 383).

To determine the environmental influence of fluoride in aluminum factory workers, H. Mlynarska of Krakow, Poland, performed 661 resting electrocardiograms which were compared with 477 of white-collar workers. Right ventricular hypertrophy as well as other abnormalities were detected. An extreme pattern of advanced right ventricular hypertrophy in all age groups of aluminum factory workers and increased resistances in pulmonary circulation was manifest (p. 414).

Whereas the maximum concentration of F^- in air in Poland is 0.01 mg F/m^3, that inside some factories at the place of work is >0.5 mg/m^3. Total absorption during 8 hrs. at work is > 2 mg. In aluminum plants it is many times higher. Allergic responses to F^- in water at the Polish norm, are frequent. In 7-12 year old children, who obtained 0.5 mg F/day up to age 3, the number of teeth had decreased and fluorosis of teeth was common. In the last 12 years from 1968 to 1980, 1.4% of the aluminum plant workers in Skawina were forced to retire early due to poor health and illness, 63% of them due to respiratory problems in the bronchial tree. Because 3/4 of the workers were also heavy smokers, additional studies are needed to prove that F^- is the principal cause of their problem (p. 343).

Without necessary air pollution control, the aluminum plant in Skawina emits 22,000 ton/year directly into the air. In 1980, 23,367 tons of fluoride were emitted into the atmosphere, 48.24 kg F/g of aluminum, 40 times more than the limit. The world norm is 1.0-1.5 kg F/t. The soil, 3-4 km from the plant, contained 400-3200 ppm; that in Kracow 150 ppm; the average in the country is 80 ppm (page 376). The risk of illness for people working within 5 km of the aluminum plant is 600 times higher than the average for the entire country (page 378). Absence from work at the aluminum plant was 32 days per worker, 20 days for those in Kracow and 16.5 per worker for Poland as a whole (page 380). In highly populated industrial Japan, intake of fluoride per day is higher than 11 mg. Longterm exposure leads to respiratory problems, bone fluorosis, interaction of F^- complex on many enzymatic systems. HF dissolves SiO_2 leading to destruction of buildings, etc. (page 325).

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