FLUORIDE
Quarterly Reports
Issued by
THE INTERNATIONAL SOCIETY FOR FLUORIDE RESEARCH

CONTENTS

EDITORIAL
The Diagnosis of Fluorosis ........................................... 1-3

ORIGINAL ARTICLES
Maternal Ionic Plasma Fluoride Concentrations During and After Delivery — by H. Hanhijarvi, Minneapolis, Minnesota ........................................... 4-9

Fluoride Concentration in the Cortex and in Full Thickness Samples of the Iliac Crest — by E. Czerwinski, A. Skolarczyk, A. Klewska, J. Kajfosz and S. Szymczyk, Cracow, Poland ................................... 10-13


Fluoride Absorption by the Root and Foliar Tissues of the Horse-Bean (Calcicole) and Lupin (Calcifuge) — by J.P. Garrec and L. Letourneur, Grenoble, France ........... 30-38

Effect of Fluoride on Hemoglobin and Hematocrit — by B. Uslu, Eskisehir, Turkey ........................................... 38-41

ABSTRACTS
Radiofluoride Distribution in Rat Lung, Colon and Heart — by G.M. Whitford, R.S. Callan and D.E. Pearson, Augusta, Georgia ........................................... 42

Fluoride Inhibition of DNA Synthesis in Isolated Nuclei from Cultured Cells — by R.I. Holland, Oslo, Norway

Hydrofluoric Acid — A Chronic Poisoning Effect — by D.A. White, Edinburgh, Scotland

Incidence of Atmospheric Fluoride upon the State of Health of a Population in the Hydrogeochemical Province of Bučak — by A.S. Kas'jenenko, UdSSR, Ukraine

Fluoride Osteosclerosis after 11 Years of Uninterrupted Treatment with Niflumique Acid — by C. Bregeon, M. Bernat, J.R. Renier, A. Reble, and M. Basile, Angers, France

Some Observations on Atmospheric Fluoride Concentration in Stoke-on-Trent — by A.J. Bennett and R.S. Barratt, Stoke-on-Trent and Birmingham, England

FLUORIDE BRIEFS

BOOK REVIEW

Critical Survey of Stability Constants and Related Thermodynamic Data of Fluoride Complexes in Aqueous Solution — by A.M. Bond and G.T. Hefter

The Eleventh Conference of the International Society for Fluoride Research will take place in Dresden, G.D.R. at the Kulturpalast April 8 - 10, 1981. The program, one of the most comprehensive of all previous meetings, will be divided under the following headings: I. Human Endemic and Industrial Fluorosis, II. Animal Fluorosis and Experimental Fluorosis, III. Fluoride Therapy, IV. Fluorides and the Environment.

For details regarding the program and accommodations kindly contact Dr. Sc. Med. J. Franke, Orthopaedic Clinic Martin Luther University, Johann-Andreas-Segnar-Strasse 12, 402 Halle (Saale) G.D.R.

Those planning to attend the conference from the U.S.A. must apply in advance for a visa from the G.D.R. embassy at 1717 Massachusetts Ave., N.W. Washington, D.C. 20036.

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

FLUORIDE is listed in Current Contents Agricultural Food and Veterinary Sciences
EDITORIAL

THE DIAGNOSIS OF FLUOROSIS

Advanced fluorosis can be readily diagnosed by the osteosclerotic changes evident upon radiography. Even prior to the development of visible bone changes, new sophisticated methods such as morphometric measurements and photon absorptiometry permit the recognition of the early stage of the disease. Similarly the appearance of dental fluorosis, especially when it involves most of the denture, is so characteristic that a prompt diagnosis can be made by merely inspecting the mouth.

Another diagnostic sign early in the disease, especially in children and women is Chizzola Maculae, the round pinkish-brown skin lesions which clear spontaneously within a week and are occasionally accompanied by muscle pains, gastric upsets and headaches. These lesions are often overlooked by clinicians because of their close resemblance to traumatic bruises. Since they are painless, they can escape the patient's attention so that he fails to report them to his physician.

On the other hand, the initial nonskeletal phase of chronic fluoride intoxication is difficult to diagnose. Like in many other kinds of chronic intoxication, objective criteria are lacking early in the disease. The diagnosis is further hampered because the wide spectrum of symptoms mimics many other diseases. The combination of gastrointestinal and musculoskeletal manifestations, especially the involvement of joints, furnishes a clue for the diagnosis, particularly when accompanied by respiratory symptoms if atmospheric fluoride is involved. Excessive thirst, muscular fibrillation, chest pain and the presence of scotomas often suggest the possibility of chronic fluoride poisoning. Nevertheless, strict avoidance of fluoride and careful observation of the patient when he resumes fluoride intake either knowingly or on a double blind basis remain the mainstay of the diagnosis prior to development of bone changes. In practice, however, patients are not always willing to submit to such procedures once they have regained their health.

Clinicians have therefore been searching for laboratory methods to pinpoint the disease. The three parameters which at the moment are being considered of value are fluoride assays of urine, plasma and bones. Bone fluoride is obtained by biopsy of the iliac crest. The results of fluoride assays, however, are difficult to interpret. Whereas in large-scale statistics they clearly reflect the degree of fluoride intake of a population, there are wide variations among individuals which interfere with the reliability of these parameters as a diagnostic criterion. They certainly do not constitute proof of damage to any specific organ.

In this issue (p10) Czerwinski has shown how the bone fluoride content varies according to the site from which the bone specimen is obtained. Spongy bone contains more fluoride than cortical bone. Age is another variable which influences bone fluoride levels (1). Obviously the fluoride content of bone cannot be considered an indicator of fluoride damage to muscle tissue or to the gastric mucosa. Furthermore, there is disagreement as to what level of fluoride in bone should be considered normal. Whereas formerly (2) 300 ppm was considered the normal limit, we now know
that tea drinking persons residing in nonfluoridated London may show levels as high as 2000 ppm. Whether or not such values affect the health of the respective individuals is not known. On the other hand, in advanced skeletal fluorosis, Singh et al. (3) reported levels as low as 600 ppm which some consider to be near, or within, the "normal" range.

Determination of plasma fluoride has been of great interest to scientists. With respect to the degree of damage to the human body, however, it is of questionable value. Here too, there is no final agreement as to what constitutes the "normal" fluoride level of plasma and whether or not this level is being regulated by homeostasis. Even if plasma fluoride should be persistently high as it is in residents of high fluoride areas in India, there is not always a positive correlation with the degree of sickness or health of the individuals.

Similarly, urinary fluoride excretion provides no definite answer with regard to fluoride intoxication. In large scale statistics some correlation between fluoride intake and urinary fluoride has been reported. However, high fluoride values as, for instance, 10 mg or more in urine are not necessarily associated with illness, whereas low urinary fluoride levels have been found in patients with nonskeletal (4) and even with skeletal symptoms (5). Children rarely excrete large amounts of fluoride in the urine during the growth of their skeleton whereas persons, in whom fluoride intake is temporarily discontinued, show urinary excretion in excess of intake.

In this issue Elsair et al. (p 21) have reported that fluoride in nails correlates with that of bones. They suggested that this might be a useful parameter, equally as valuable as a bone biopsy, but involving much less discomfort to the patient. This interesting observation requires further studies.

Other quests for diagnostic criteria for preskeletal fluoride intoxication have not been fruitful, undoubtedly because of the variable nature of the low-grade symptomatology. Serum and urinary calcium, phosphorus, alkaline phosphatase, succinic dehydrogenase and other enzymes as well as hematological studies have been carried out by various investigators of fluorosis but results have not been consistent enough to permit the use of these parameters as precise criteria for the diagnosis. Ferguson in a recent article abstracted on pages 42-3, showed inconsistent values of plasma alkaline phosphatase in a group of thirteen subjects residing in a nonfluoridated area. Such inconsistency is not unexpected because alkaline phosphatase activity is dependent on numerous pathological processes other than fluoride intake. Similarly, calcium and phosphorus levels of the blood have been found to be altered by fluoride intake (6) but the results are too inconsistent to serve as a diagnostic criteria. There is also considerable doubt as to whether hematological findings are helpful in diagnosing fluorosis as shown in the article by Burhan Uslu on pages 38-41.

To the clinician confronted with the diagnosis of the early stage of chronic fluoride poisoning, therefore, a careful history and thorough observation of the patient remains his most effective diagnostic tool.

Volume 14 Number 1
January 1981
Editorial

Bibliography


*******

FLUORIDE BRIEFS

Through analysis of market basket collections, the total fluoride intake for young male adults was estimated to vary from 0.912 mg per day in unfluoridated Kansas City, Missouri to 1.720 mg/day in fluoridated Atlanta, Georgia in 1975. The 1977 collection from San Francisco, California revealed a higher fluoride intake (1.636 mg/day) than in 1975 (1.213 mg/day).


*******
MATERNAL IONIC PLASMA FLUORIDE CONCENTRATIONS
DURING PREGNANCY AND AFTER DELIVERY

by

Hannu Hanhijarvi
Minneapolis, Minnesota

SUMMARY: Strong evidence that fluoride accumulates in fetal bone is probably reflected in the maternal fluoride balance. The present study further supports the earlier findings that maternal ionic plasma (IPP) concentrations significantly decrease during pregnancy compared to concentrations in nonpregnant controls of the same age. After delivery the mean IPP concentrations start to return to usual levels despite the onset of the excretion of milk. Normalization takes place in about two weeks. The reason for the inverse correlation between maternal IPP-concentration and the birth weight of the child remains unsolved.

Introduction

In recent years it has become clear that fluoride penetrates the placenta. This has been demonstrated in animals (1-3) and in man (4,5). It is characteristic for fluoride to accumulate in human calcified tissues especially in bones and teeth. The same phenomenon takes place in the fetus during pregnancy (6). According to Gedalia et al., fluoride accumulation in the fetus may account for the decrease of maternal urinary fluoride concentrations during pregnancy which is inversely correlated with the increase in fetal bone fluoride (7). Plasma fluoride concentrations as well tend to decrease during pregnancy (7-9).

In mothers residing in a low-fluoride community (0.1 - 0.2 ppm fluoride in the drinking water), Hanhijarvi et al. found a significant inverse correlation between human ionic plasma fluoride (= IPP) and the duration of pregnancy (8). There was also evidence that after delivery the level of IPP again started to increase towards the control level. Similar observations have been made in pregnant women residing in a community with artificially fluoridated drinking water (9). In this study, however, the selection of patients was inadequate because many women, who had recently delivered a child were not studied more closely but were all incorrectly included in the group called "in labor". Furthermore, interruptions in the artificial fluoridation of the tap-water had occurred. Moreover new data have also become available.

Therefore our aim in this study is to revise and make more precise the earlier findings of IPP in pregnant women residing in a community with 1.0-1.2 ppm fluoride in the tapwater. Does the decrease of IPP concentration during pregnancy still remain significant as compared to non-pregnant controls?

From the Institute of Dentistry and Department of Clinical Chemistry, University of Kuopio, Kuopio, Finland.
A second question to be explored is how do IPF concentrations behave after delivery in a fluoridated area? According to Bercovici et al., the urinary fluoride concentrations returned to the usual level within 4 months, when the patient consumed 0.55 ppm fluoride in the drinking water (10). Our earlier findings indicate a more prompt return of the maternal plasma fluoride in a low-fluoride (0.1 - 0.2 ppm) area (8). This portion of the earlier investigation, however, was based on a few samples only.

The third part of this study was to determine whether or not the weight of the infant correlates with the IPF-concentration of the mother.

Material and Methods

The study was carried out on pregnant women and mothers who had recently delivered in the Central Hospital of Kuopio. All patients had been residing inside the City of Kuopio, where the drinking water contains 1.0 to 1.2 ppm of fluoride. Among the 67,000 inhabitants of Kuopio, the home tap water of approximately 9,000 was not fluoridated. Thus some patients may have been included who obtained fluoridated water only in the hospital. IPF-concentrations, serum creatinine levels, age and week of pregnancy or day after delivery were determined.

The plasma samples were drawn early in the morning while fasting, following the night's rest in the hospital. The method for the determination of IPF was electrometric with a slight modification described elsewhere (11, 12) of that published by Fry and Taves in 1970 (13). Serum creatinine was analyzed by an autoanalyzer used routinely in the hospital (Technicon autoanalyzer II apparatus). The limit of normal serum creatinine concentration was 115 umol/l in this hospital.

Plasma samples of females of the same age and from the same community were used as controls. The final material consisted of 233 hospitalised women, 68 of whom were included in the group of pregnant women, 86 had delivered a child recently and 79 were included in the control group of the same mean age.

Results

Table 1 and Figure 1 present our principal data. Figure 1 reveals an inverse correlation between the IPF-concentration and the week of pregnancy; all pregnant women are included. The result of regression analysis is: intercept 0.99 umol/l, regression coefficient -0.0036, r = 0.20, n = 68. The regression coefficient does not differ from zero significantly (p = 0.1).

When the pregnant women are grouped according to the trimester of pregnancy (Table 1), the mean IPF concentration of the women of the last trimester is significantly lower than in the control group (p < 0.01). The group of the third trimester of pregnancy could be divided into some subgroups, too, e.g. the IPF concentration of 9 women during the third trimester who had hypertension or toxemia, which was known to be medicated
Table 1

Mean Ionic Plasma Fluoride

<table>
<thead>
<tr>
<th>Trimester of Pregnancy</th>
<th>Weeks</th>
<th>Plasma $F^-$ (μmol/l ± S.D.)</th>
<th>Age (mean)</th>
<th>Serum creatinine (μmol/l ± S.D.)</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>First</td>
<td>10</td>
<td>$0.97 ± 0.22$</td>
<td>31</td>
<td>$63 ± 15$</td>
<td>12</td>
</tr>
<tr>
<td>Second</td>
<td>19</td>
<td>$0.90 ± 0.25$</td>
<td>27</td>
<td>$62 ± 14$</td>
<td>11</td>
</tr>
<tr>
<td>Third</td>
<td>36</td>
<td>$0.86 ± 0.18**$</td>
<td>26</td>
<td>$62 ± 9.4$</td>
<td>45</td>
</tr>
<tr>
<td>Days after Delivery</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>0</td>
<td>$0.92 ± 0.14$</td>
<td>32</td>
<td>$62 ± 9.3$</td>
<td>3</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>$0.99 ± 0.32$</td>
<td>20</td>
<td>$64 ± 2.6$</td>
<td>4</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>$0.95 ± 0.29$</td>
<td>26</td>
<td>$62 ± 6.8$</td>
<td>10</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>$0.84 ± 0.17**$</td>
<td>26</td>
<td>$63 ± 6.6$</td>
<td>14</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>$0.86 ± 0.20*$</td>
<td>26</td>
<td>$60 ± 6.7$</td>
<td>20</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>$0.84 ± 0.25$</td>
<td>27</td>
<td>$66 ± 13$</td>
<td>14</td>
</tr>
<tr>
<td>6</td>
<td>6</td>
<td>$0.90 ± 0.27$</td>
<td>27</td>
<td>$60 ± 8.9$</td>
<td>24</td>
</tr>
<tr>
<td>7 or more</td>
<td>10</td>
<td>$0.97 ± 0.33$</td>
<td>28</td>
<td>$64 ± 8.4$</td>
<td>14</td>
</tr>
<tr>
<td>Nonpregnant control group</td>
<td>-</td>
<td>$1.0 ± 0.30$</td>
<td>27</td>
<td>$75 ± 14$</td>
<td>79</td>
</tr>
</tbody>
</table>

** = p<0.01, * = p<0.05, o = p<0.1

Figure 1

Maternal IPF Concentration and Week of Pregnancy

The mean IPF levels each day after delivery (+ S.E.) and number of patients.

Volume 14 Number 1
January 1981
Plasma F⁻ in Pregnancy

with diuretics was 0.89 ± 0.20 μmol/l (± S.D.). This mean value is similar to the mean value of the whole group in the third trimester (Table 1). Only 5 pregnant patients whose edema was recorded and who were not using diuretics had slightly elevated IPF-concentrations (1.0 ± 0.21 μmol/l) when compared with other women (Table 1) of the same trimester. When these five patients are excluded, the regression analysis between the IPF concentration and the week of pregnancy slightly changes (intercept 1.0 μmol/l slope = -0.0046, r = 0.27, n = 63, p < 0.05).

At one and two days after delivery, the maternal IPF-concentration is slightly elevated (Table 1 and Figure ). Three days after delivery, coincident with the start of milk excretion, the mean maternal IPF-concentrations are again significantly lower than in the nonpregnant controls (p < 0.01), after which the mean IPF levels begin to increase steadily. They reach the control level about ten days after delivery. The regression analysis between the IPF-concentrations and the day after delivery was also performed including all plasma samples, which were drawn on the third day or later following delivery. The intercept was 0.78 μmol/l, the regression coefficient 0.019, r = 0.21, and n = 86. The correlation coefficient differs almost significantly from zero (p < 0.05).

The regression analysis between the birth weight of the child and the IPF-concentration is given in Figure 2. The correlation coefficient differs almost significantly from zero (p < 0.05). The regression coefficient = 0.15, intercept 0.28 μmol/l, r = 0.51 and n = 19.

Figure 2

Maternal IPF and Birth Weight of Infant

Regression coefficient = 0.15, intercept - 0.28 μmol/l, r = 0.51, n = 19

FLUORIDE
Discussion

As shown previously the present findings demonstrate a significant decrease of maternal IPF during the last trimester of pregnancy. It is probable that this is due to the absorption of fluorides into fetal calcifying tissues. Increased renal excretion of fluoride does not account for the decrease in IPF because the amounts of fluoride excreted daily are lower during pregnancy than in the nonpregnant controls (14). One possibility might be an increased uptake of fluoride in the maternal bone. This however is unlikely because during the last trimester the fetus needs so much calcium that the maternal plasma parathormone levels are higher than usual (15). Furthermore, according to the earlier findings of Ericsson, increasing IPF levels should be expected with elevation of bone fluoride (16).

The significance of edema on IPF levels during late pregnancy remained poorly quantitated. As stated above, five women had edema but did not use diuretics. During late pregnancy edema is very common. The series may contain more such cases, because we lacked clear criteria for differentiation of "normal" and "abnormal" edema. We know that in the five women, the edema was untreated. It is probable, however, that edema, regardless of the cause, may account for slight elevation of IPF concentrations (17). If the edema is controlled by diuretics, the IPF levels also react favorably as our results indicate. The difference between the IPF-concentrations of edematous and nonedematous pregnancies disappears.

After the birth of the child the material IPF levels start to increase and serum calcium levels return to normal levels. It is probable that maternal bone starts to accumulate calcium and fluoride(15). However, according to the present results the excretion of milk slightly slows down the accumulation of fluoride, because the material IPF levels are slightly higher before the onset of milk excretion than after it. Despite a slight loss of fluoride into the milk, the maternal IPF-concentrations return to the control level after two weeks.

The explanation for the positive correlation between the IPF-concentration and fetal body weight remains unsolved. An inverse correlation would have been expected. This finding should not be overemphasized, because the samples were drawn between 35 and 41 weeks of pregnancy and the weight of the infant was obtained at birth. However, it is possible that women with a large fetus drink more water or their parathormone activity is stronger during pregnancy than that of the women who give birth to a smaller child.

Bibliography


**********
FLUORIDE CONCENTRATION IN THE CORTEX AND IN FULL THICKNESS SAMPLES OF THE ILIAC CREST

by

E. Czerninski, A. Skolarczyk, A. Klewska
J. Kajfisz and S. Szymczyk
Cracow, Poland

SUMMARY: The fluoride content was evaluated in iliac crest samples taken from cadavers without previous history of fluoride exposure. Fluoride concentration in the cortex before and after ashing was determined by the Coulomb excitation method using a C-48 cyclotron. Fluoride was then estimated in the same samples by the microdiffusion method. Fluoride assays in full thickness iliac crest samples were also made.

Varying fluoride concentrations in adjacent areas were noted as well as in the cortex and in full thickness samples. The significance of the differences is discussed.

Introduction

The fluoride content of the skeleton is considered to be directly related to exposure to chronic poisoning. It is the most important criterion in the diagnosis of industrial fluorosis. A bone sample is usually obtained by needle biopsy of the iliac crest 2 cm below and posterior to the spina iliaca anterior superior. A cylinder of bone is taken through the full thickness of the ilium, namely the outer compact bone, the cancellous bone, and the inner compact bone (1-4).

In practice it is possible to make only an approximate determination of the site of the percutaneous bone biopsy. Often tissue of the inner cortex cannot be obtained. Individual differences in the structure of the ilium should be taken into consideration, as well as morphological changes in those exposed to the action of fluoride.

The present paper reports an attempt to determine whether or not the macroscopic structure of the sample as well as the site on the iliac crest from which it is taken may influence the determination of the fluoride content of the skeleton in man.

Material and Method

Bone samples were obtained from cadavers of persons aged 42 to 50 years (average 45.9), who had not previously been exposed to fluorides. A section 4 x 4 cm in size was taken from the ilium adjacent to the
spina iliaca anterior superior. Preparations of the full thickness of the ilium as well as of the cortex alone were made of each sample. The samples of the cortex were obtained by mechanical abrasion of the cancellous layer. In four cases two preparations of the cortex were made from two adjacent areas of the ilium. In preparation of the cortex, the fluoride content was determined by the Coulomb excitation method for further treatment. The cortical preparations as well as the full thickness samples were ashed and the fluoride content determined by the microdiffusion method.

**Figure 1**

Fluoride Content in the Cortex and in the Full Thickness Bone Samples Estimated by Microdiffusion

<table>
<thead>
<tr>
<th>F (ppm)</th>
<th>800</th>
<th>600</th>
<th>400</th>
<th>200</th>
</tr>
</thead>
<tbody>
<tr>
<td>cortex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>full thickness</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>347</td>
<td>550</td>
<td>445</td>
<td>580</td>
<td>440</td>
</tr>
<tr>
<td>430</td>
<td>553</td>
<td>586</td>
<td>635</td>
<td>710</td>
</tr>
<tr>
<td></td>
<td></td>
<td>310</td>
<td>500</td>
<td>559</td>
</tr>
</tbody>
</table>

**Results**

The fluoride content, determined by the microdiffusion method (5), in the cortex and in full thickness samples from the iliac crest is illustrated in Fig. 1. The fluoride content varied in the cortex from 148 to 728 ppm with an average of 429 ppm, and in the full thickness samples from 310 to 710 ppm (average 524 ppm). The relation of the fluoride content of the full thickness samples to that of the cortex was 1.23 ± 0.03. In the cases VII to X the fluoride content in two adjacent areas of the cortex was determined. The mean difference in the levels in the two samples was 71.2 ppm, i.e. 16% of the contents determined. In the same cortex samples, the fluoride content was also determined by the
Coulomb excitation method. Differences of 30% were obtained. The detailed results of measurement by this method together with a description will be the subject of a separate paper.

Discussion

The fluoride content found in full thickness samples from the iliac crest in nonexposed subjects is in agreement with Shelman's report on the same age group (6).

Our investigations show that the fluoride level in full thickness samples is higher than that in the cortex alone. It is known that the distribution of fluoride in various parts of the skeleton is unequal, but the data refer rather to individuals charged with an excessive supply of fluoride (7,8,9,10). Both Gardner (11) and Weidmann (12) found a higher fluoride content in the cancellous metaphysis than in the cortical diaphysis. Wallace-Durbin (8), using $^{31}P$, observed a sequential decrease in the fluoride concentrations in the mandibles, the epiphyses and the metaphyses. In studies on cadavers, Weatherell (9, 13) observed a similar decrease in the fluoride concentration in the direction: rib - cancellum, rib - compacta, metaphysis - cancellum, diaphysis - compacta. The ratio of the fluoride content in the cancellous and cortical bone of the rib is estimated as 1.5 - 3.5, as is the cancellous and cortical bone of the metaphysis (9,13,14). This ratio is probably the same for the cortex of the cancellous bone of the ilium, but we have not found any relevant data in the available literature. The relation of 1.23 which we found between the fluoride content in full thickness samples and the cortex itself are in approximate agreement with the factors just given.

A markedly larger deposit of fluoride in the cancellous bone was noted by Perkinson (15) in histological autoradiograms when using $^{31}P$. The larger deposit of fluoride in the cancellous bone results from the better blood supply in cancellous than in cortical bone. Similar differences have been observed in fluoride deposits in the long and flat bones (16).

The differences in fluoride content which we have found in two adjacent areas of the cortex confirm the observation of the unequal distribution of fluoride in the bony tissue. These differences appeared particularly marked when measurements were made by the Coulomb excitation method, which determines the fluoride content solely in the superficial layer of a specimen a few microns in thickness and 0.5 cm in area. The fluoride content in two adjacent areas varied much less after the samples were ashed. Hence the local structure of the cortex, which is more homogeneous after ashing, may have a decided influence on the results of measurement.

Conclusions

The fluoride content in full thickness samples from the iliac crest in subjects not exposed to fluoride contamination, is more than 1.23 times as high as that in the cortex. Adjacent areas of the cortex may
differ by 16% in fluoride content. Both the macroscopic structure of the sample and the site from which it is taken may affect the fluoride content in the skeleton. For the relation between the fluoride content in the cortical and cancellous bone of the iliac crest in subjects exposed to fluoride contamination further studies are warranted.

Bibliography


*******
EFFECT OF LONGTERM FLUORIDATION OF DRINKING WATER ON MINERAL CONTENT OF THE SKELETAL SYSTEM

by

K.J. Franke, H.G.C. Runge, and F.P.B. Fengler
Halle (Saale), G.D.R.

SUMMARY: By means of photon absorptiometry the mineral content of bone (radius) of 1160 residents of Karl-Marx-Stadt (fluoridated since 1959) was compared with that of 4150 inhabitants of nonfluoridated Halle.

Only in the age group 16–20, among those who had been drinking fluoridated water since birth, was an increase in bone mass encountered following longterm fluoridation of drinking water. In the other age groups, a tendency to lower values was observed in the fluoridated city.

Introduction

That chronic fluoride intoxication leads to skeletal fluorosis was established by the work of Møller and Gudjonsson (1) and Roholm (2, 3). This bone disease is characterized by hyperossification and hypermineralization (4–6). Chronic fluoride intoxication is attributable to inhalation of airborne fluoride and to ingestion of fluoride-containing dust and food. In such industries as aluminum smelting, in production of cryolite, of hydrofluoric acid, of magnesium, of fertilizers, and in brickworks from 15 to 20 years are required for severe fluorosis to develop.

In endemic fluorosis, caused by a 10–30 years' intake of drinking water naturally containing fluoride (0.7–46 ppm) mainly in India, osteosclerosis is the major feature (7–9). In industrialized countries such as the German Democratic Republic (G.D.R.) in which osteoporosis is the most frequent metabolic bone disease affecting approximately 350,000 or 2% of the population (10), investigators have reported success with fluoride treatment.* Osteoporosis is reported to occur less frequently in natural fluoride areas namely, Texas (formerly 8 ppm) (13, 14), North Dakota 4–5.8 ppm (15), Sweden 4–6.8 ppm (16, 17), and India 8–10.5 ppm (18) than in areas where water contains little or no fluoride.

The aim of this study is to determine whether or not fluoridation of drinking water (1 ppm) over a period of 19 years increases bone mass in normal persons and may thus be of prophylactic value in osteoporosis.

Material and Methods

Normal subjects were examined from two cities of the G.D.R., Halle including Halle-Neustadt with 326,000 inhabitants, and Karl-Marx-Stadt with 307,000. In Karl-Marx-Stadt, drinking water has been fluoridated (1 ppm)

* Editor’s Note: Others have been recommending caution because of adverse side effects (11, 12).
From the Orthopedic Clinic of Martin-Luther-University, Halle (Saale) G.D.R.
The fluoride content of the air ranges between 5 and 6 μg/m³. In Halle and Halle-Neustadt fluoride in drinking water ranges between 0.1 and 0.2 ppm and the air contains an average of 5 μg/m³. Bone mineral contents were studied in Karl-Marx-Stadt, 509 men and 651 women (1,160 subjects) on the occasion of routine chest x-ray examinations. Only those persons who had been residing in Karl-Marx-Stadt since the initiation of drinking water fluoridation in 1959 were included in the survey.

Figure 1
Bone Mineral Analyzer

In Halle, 2,158 males and 1,996 females (4,154 subjects), patients of the Orthopaedic Clinic and residents of a home for the aged were included in this study. In all persons a thorough history was taken. Subjects suffering from diseases that can influence bone metabolism were excluded, such as gastrointestinal and hormonal disturbances, liver and kidney diseases, diabetes, intake of steroids and confinement to bed for a prolonged period.

The bone mineral content was determined by photon absorptiometry according to Cameron and Sorenson (19) at the level of the radius, one-third of its length from the styloid process. The transportable Norland-Cameron Bone Mineral Analyzer (USA) comprised of a measuring device and a computer was used. The measuring device consists of a monochromatic radionuclide source, iodine 125, and a well collimated scintillation detector in the form of a sodium iodide crystal (Fig. 1). With the help of a wa-
ter-filled rubber cuff applied around the arm, the irregularities of soft
tissue were compensated. The scanner, which approaches the bone with con-
stant speed, first measures the soft parts' absorption and the area across
the bone. Absorption of the radiated protons is dependent on the bone
mineral content. The impulse rate in the detector is diminished appropri-
ately. The scintillations are transformed into electric impulses.

Resulting from integral of the absorption curve, the computer module
gives a digital read-out of the bone mineral content in g/cm and of the
width of the bone in cm. In order to make a comparison independent of the
variable bone width and thus of the skeletal size, in accordance with in-
ternational custom, the quotient (index) of measured mineral content and
bone width (Mc/BW in g/cm²) is presented. Four measurements are carried
out at the "off-handedness" radius, i.e. the left radius for a right-hand-
ed person after which the average value is calculated. The reproduc-
ability and accuracy of repeated measurements are very reliable. They are
at the 2% level for bone mineral content and bone width (20). For the age
groups 16-20 years, 21-30 etc. up to 81-90 years for men and women from
Halle and Karl-Marx-Stadt, the mean values and standard deviations were
calculated for bone mineral content, bone width, and quotient (index) =

\[
\frac{\text{mineral content}}{\text{bone width}}
\]

The mean values of the single age groups from Halle and Karl-Marx-
Stadt were compared by means of the Student's paired t-test (variant ac-
cording to Welch) concerning their significant differences.

**Results**

The results are shown in Figures 2 and 3 and Table 1:

1. Men and women aged 16-20 from Karl-Marx-Stadt show a significantly
   higher index \(\frac{\text{mineral content}}{\text{bone width}}\) than those in Halle.
2. In the female groups, there were no further significant differences in the index. In Karl-Marx-Stadt, however, the simple mineral
   content declines at ages 31-40, 41-50 and 71-80, but decreased bone width compensates for this phenomenon in the index.
3. The male residents of Karl-Marx-Stadt 31-40 and 41-50 years old
   show a significant decrease in mineral content (index and partly mineral content). Bones of the 61-70 year old also showed a de-
   crease in mineral content.

**Discussion**

The expected positive effect of 19 years of fluoridation of drinking
water on bone mass and on mineral content of the peripheral skeleton (ra-
dium) respectively was not confirmed, except in the age groups 16-20 years.
In Karl-Marx-Stadt, a tendency to lower mineral values than in nonfluori-
dated Halle was observed, especially in men. One could therefore conclude
that fluoridation of drinking water has a positive effect on the skeleton only if the persons have been consuming fluoridated water since birth, in
Figure 2
Bone Mineral Index of Males in Karl-Marx-Stadt and Halle

\[ \text{index} = \frac{\text{BMC}}{\text{BW}} \]

Figure 3
Bone Mineral Index of Females in Karl-Marx-Stadt and Halle

\[ \text{index} = \frac{\text{BMC}}{\text{BW}} \]

FLUORIDE
<table>
<thead>
<tr>
<th>Men in Halte &amp; Karl Marx-St.</th>
<th>Women in Halte &amp; Karl Marx-St.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bone Width (cm)</strong></td>
<td><strong>Bone Width (cm)</strong></td>
</tr>
<tr>
<td><strong>Metal Content (g/cm³)</strong></td>
<td><strong>Metal Content (g/cm³)</strong></td>
</tr>
<tr>
<td><strong>Bone Width (cm)</strong></td>
<td><strong>Bone Width (cm)</strong></td>
</tr>
<tr>
<td><strong>Metal Content (g/cm³)</strong></td>
<td><strong>Metal Content (g/cm³)</strong></td>
</tr>
</tbody>
</table>

Table 1

Measurements of Bone Metal Content in Halte and Karl Marx-Stadt.
view of the fact that the age groups 16-20 years from Karl-Marx-Stadt were the only ones who showed a significantly increased index.

For the decreased values at higher ages, especially among men 31-50 years of age in Karl-Marx-Stadt, we have no explanation. Nutritional habits and occupation (brain or heavy work) may influence the bone mineral content. In the framework of such an extensive experiment no precise conclusion for these problems was possible.

In the literature likewise the results obtained to date have not been unequivocal.

Whereas Iskrant (21) observed a significant decrease in the number of fatal accidents from falls in old people in areas where water contains fluoride naturally, no such effect was encountered from artificial fluoridation of drinking water. After 20 years of fluoridation of drinking water, Korns (22) too, found no differences in the frequency of osteoporosis and fractures in comparison with those in a nonfluoridated town. Alffram et al. (17) observed no change in the rate of fractures of the neck of the femur at 0.8 to 1.2 ppm in drinking water compared to lower levels of fluoride in water. Even at 2-3 ppm fluoride in drinking water naturally, Nordin (23) found no differences at autopsy in bone volume of the iliac crest in comparison with that in persons without fluoride in drinking water. No change in the lumbar spine other than a decrease in osteoporosis of the cervical spine and of the hands was found by Ansell and Lawrence (24) after five years of fluoridation.

Our investigation can be compared with those of Sluys Veer et al. (25) who determined the mineral content of the radius in residents of two Dutch towns by 125J-photon absorptiometry, the same method that we used: Tiel (21,900 inhabitants) had been artificially fluoridated at 1 ppm since 1953 and in Culemborg (15,600) drinking water contained 0.01 ppm fluoride. They compared five hundred subjects from Culemborg (nonfluoridated) with 518 from Tiel (fluoridated) between 25 and 74 years. The mineral content in all age groups in the fluoridated town had increased. The differences, however, were only significant when all men and women were considered together. Using the same examination method, Donath et al. (26), failed to find any differences between 400 residents of a Swiss village, where natural fluoride content in the drinking water was 10 ppm compared with 3000 residents of low fluoride Geneva.

Obviously the fluoride content of 1 ppm in drinking water, considered optimal for caries prophylaxis, is not sufficient to exert a positive influence on bone metabolism. According to our results an increase in bone mass occurred only in persons who had been drinking fluoridated water since birth. For proof of this thesis, however, another 10-20 years will be required.

**Acknowledgement**

We are grateful to Dr. E. Auermann, Karl-Marx-Stadt for his helpful assistance and to Preventive Stomatologie of G.D.R. for support.
Bibliography

BORON AS ANTIODE TO FLUORIDE: EFFECT ON BONES AND CLAWS IN SUBACUTE INTOXICATION OF RABBITS

by

J. Elsair, R. Merad, R. Denine, M. Azzouz, K. Khelfat, M. Hamrour, B. Alamir, S. Benali and M. Reggabi
Algiers, Algeria

SUMMARY: Rabbits were "subacutely" intoxicated by administration of 30 mg/kg/day of fluoride for 3 months followed by 15 mg/kg/day for a subsequent 3 months (F). Boron was given alone (B) as preventive and simultaneously with fluoride prophylactically (F + Bp), as well as therapeutically namely midway during the experimental period (F + Bpc) while fluoride was being administered and after it was discontinued (Bc compared with fluoride interruption F↓), at a constant F/B ratio. All groups were compared to normal controls.

From the Laboratories of Physiology, Toxicology and Galenic Pharmacy, Medical Institute, Algiers, Algeria.
Boron, administered during fluoride intoxication or after its interruption, reduces fluoremia and increases urinary fluoride excretion. Skeletal fluoride levels are directly related to those of claws. They bear no relationship to fluoride in hair. The high fluoride content in bone in lot F decreases with addition of boron. It is still high in lot F but returns to normal in lot Bc. Calcium content of bones remains normal in all lots. Posterior pad radiography shows a cortical thickness in lot F which is less pronounced in lots F + Bpc and F, and returns to normal in lot Bc.

Introduction

Boron has been considered an antidote in fluoride intoxication (1, 2). When administered to rabbits preventively at the beginning of subacute fluoride intoxication, boron counters the adverse effects of fluoride upon hemostasis (3) and respiration (4). During balance studies with large short-term doses of fluoride, boron administered as a preventive, does not alter the fluoride balance but counteracts the decline of the phosphorus and calcium balance (5, 6), due to formation of a F + B complex which is less damaging than fluoride. When boron was given under the same conditions therapeutically after interruption of fluoride administration, excretion of fluoride increased and residual phosphorus and calcium disturbances were corrected (6, 7).

In the current study, we determined the effect of boron, administered alone as a preventive starting at the beginning of subacute fluoride intoxication, as "preventive-curative" during the course of fluoride intoxication and as a therapeutic measure after interruption of fluoride. The following parameters were investigated during the various plans of administration: fluoremia, fluoruria, fluoride and calcium content of bones, of claws and of hair as well as skeletal radiography.

Materials and Methods

Subacute fluoride intoxication was induced in rabbits by addition of 30 mg F/kg/day to their drinking water for 3 months, followed by 15 mg/kg/day for 3 subsequent months (F). Boron was administered alone (B) in doses of 11.55 mg/kg/day for 3 months followed by 5.78 mg/kg/day for the following 3 months. In other groups, boron was given simultaneously with fluoride for the entire period prophylactically (F + Bp); it was started midway during the period of intoxication (F + Bp), or curatively (Bc) after fluoride was discontinued, compared with lot F in which fluoride had been given without boron for 3 months. Data on all these groups were compared with those of normal controls (Fig. 1).

Fluoremia after mineralization (8) and urinary fluoride were measured by the specific electrode method (9, 10), and related to 24-hr. excretion of creatinine. Bone, claws and hair fluoride content was deter-
minded after breaking, drying, delipidation and mineralization. Posterior
pad radiography was performed in all lots on the same day at the same
distance and with the same intensity.

**Figure 1**
Outline of the Experiments

<table>
<thead>
<tr>
<th>11.55 mg B/kg/day</th>
<th>15 mg B/kg/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 months</td>
<td>3 months</td>
</tr>
</tbody>
</table>

**F + B Prophylactically**

<table>
<thead>
<tr>
<th>30 mg F/kg/day</th>
<th>15 mg F/kg/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 months</td>
<td>3 months</td>
</tr>
</tbody>
</table>

**F Discontinued**

**Boron curative**

**Results**

In lot F, the group receiving fluoride alone, fluoremia (Fig. 2) was very high. In lots of F + Bp and F + Bpc, the elevation of the fluoride content in blood was less than in lot F (p 0.05 or p 0.10). After interruption of fluoride intake in lot F and Bc, fluoremia returned to normal. Fluoruria (Fig. 2) was very high in lot F (p 0.001) and further
increased in lot F + Bpc as compared to lot F (p 0.10). After interruption of fluoride, the urinary excretion of fluoride remained high (p 0.01), but was more pronounced in lot Bc than in Lot F (p 0.10). When boron was administered midway during the period of intoxication (F + Bpc) or after interruption of fluoride (Bc), the blood level of fluoride decreased and urinary excretion of fluoride increased.

**Figure 2**

F⁻ Levels in Blood and Urine

The fluoride content of bones (Fig. 3) remained at normal levels in lot B. It was very high in lot F (p 0.01), and seemed to decrease when boron was added (F + Bpc) (p 0.05). After interruption of fluoride, the fluoride content of bones was still high in lot F (p 0.05), but when boron was administered therapeutically (Bc), bone fluoride remained normal. The calcium content of bones (Fig. 3) was within the normal range in all groups without retention or loss with the doses used in this study.

Whereas the fluoride content of hair did not vary, fluoride levels of the claws paralleled those of bones (Fig. 4). There was a marked increase of fluoride in claws in all lots, compared to normal (p 0.001),
but a partial reduction when boron was administered midway during the period of intoxication (difference F + Bpc and F: p 0.10), or after interruption (difference Bc and F: p 0.10).

**Figure 3**
Fluoride and Calcium in Bones

**Figure 4**
Fluoride in Claws and Hair

---

**FLUORIDE**
Posterior pad radiography (Fig. 5) was normal in lot B. Thickness of the cortex was less pronounced in lots F + Bpc than in lot F. When boron was administered after interruption of intoxication (Bc), the x-ray findings returned to normal.

Figure 5
X-ray Appearance of Leg

Discussion
In our experiment, the antagonistic effect of boron to fluoride is
<table>
<thead>
<tr>
<th>F&lt;sup&gt;-&lt;/sup&gt; Levels (ppm)</th>
<th>0</th>
<th>10</th>
<th>25</th>
<th>0</th>
<th>10</th>
<th>25</th>
<th>0</th>
<th>10</th>
<th>25</th>
<th>0</th>
<th>10</th>
<th>25</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Alk. phosphatase</td>
<td>Acid phosph.</td>
<td>ATPase</td>
<td>LDH</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>KIDNEY</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outer cortex</td>
<td>++++</td>
<td>+++</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>Proximal tubules</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distal tubules</td>
<td>++++</td>
<td>+++</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>Glomeruli</td>
<td>±</td>
<td>±</td>
<td>±</td>
<td>+</td>
<td>+</td>
<td>±</td>
<td>+</td>
<td>+</td>
<td>±</td>
<td>±</td>
<td>±</td>
<td>±</td>
</tr>
<tr>
<td>Inner cortex</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>±</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Outer medulla</td>
<td>±</td>
<td>±</td>
<td>±</td>
<td>±</td>
<td>±</td>
<td>±</td>
<td>±</td>
<td>±</td>
<td>±</td>
<td>±</td>
<td>±</td>
<td>±</td>
</tr>
<tr>
<td>Inner medulla</td>
<td>±</td>
<td>±</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>±</td>
<td>±</td>
<td>±</td>
<td>±</td>
</tr>
<tr>
<td>LIVER</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parenchymatous cells</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
</tr>
</tbody>
</table>

Activity: ++++ very strong; +++ strong; ++ moderate; + low; ± negligible; - none
noticeable mainly when boron is administered midway during the period of fluoride intoxication or following interruption of fluoride administration. This confirms the hypothesis of Baer et al. (1) that a B + F complex is formed which follows the same metabolic kinetics as fluoride but is less toxic. Boron as preventive (F + Bp), reduced fluorexia compared to lot F (p 0.05) but failed to increase urinary fluoride excretion; nor did boron decrease the fluoride content of bones and claws (Fig. 3 and 4). However, when administered during intoxication (F + Bpc) or after interruption of fluoride administration (Bc) it apparently reduced the body burden of fluoride by substituting an F + B complex for fluoride. In lots F + Bpc and Bc, fluoruria was more pronounced than in lots F and F (interruption: F ) (Fig. 2). In lot Bc, boron had a distinct effect upon the skeletal radiography (Fig. 5). Therapeutically, therefore, boron seems to be more effective than prophylactically. It could be used as an antidote after discontinuance of fluoride intake to assure more efficient excretion of fluoride from the body and prompter detoxification.

Our studies also indicate that the claws (but not the hair) represent an interesting parameter of body fluoride which is more precise but less injurious than skeletal radiography (11) or bone biopsies (12). Five milligrams of nails in man could be an indicator of fluoroosis if our observations in rabbits can be extrapolated to those of man. Herman et al. (13) showed that in human fluorosis nails, hair and skin contain less fluoride than bone, teeth and aorta, levels which are similar to those of kidney and urinary tract, but higher than in all other soft tissues.

The fluoride content of bones is elevated in our experiment in the F lot which is in accordance with the findings of several authors on fluoroosis (11, 14, 15, 16). Some are treating osteoporosis with fluoride (17, 18), whereas others have reported adverse effects with this treatment (19). Large doses of fluoride may induce demineralization of bones due to hyperparathyroidism (20, 21) related to intestinal malabsorption of calcium (5, 6, 7, 22). Fluoridated bone is a mixture of osteosclerosis and demineralization induced by hyperparathyroidism. The total bone mineral content increases in fluorosis (14, 16, 23) and the calcium balance improves (24). With large doses in rabbits, we observed an interference in the calcium balance due to a reduction in the calcium digestive utilization coefficient (5, 6, 7). In the current experiment, with or without fluoride and boron, the calcium content of bone does not vary (Fig. 3). This observation provides evidence neither for nor against fluoride treatment of osteoporosis in doses used in our experiment.

Finally claws or nails (but not hair) represent an interesting parameter of the body's fluoride burden similar to radiography and biopsy of bones. Boron acts as an antidote to fluoride. Administered initially, boron simultaneously with fluoride had no effect upon the fluoride body burden, but when added during intoxication or after interruption of fluoride a decline in the fluoride content of bone and claws was observed.
Bibliography


**********
FLUORIDE ABSORPTION BY THE ROOT AND FOLIAR TISSUES OF THE HORSE-BEAN (CALCICOLE) AND LUPIN (CALCIFUGE)

Preliminary Studies

by

J. P. Garrec and L. Letourneur
Grenoble, France

SUMMARY: In the root and foliar tissues of calcicole (horse-bean) and calcifuge (lupin) plants, absorption of fluoride, at least in weak concentrations, does not appear to be related to the metabolism of these plants.

Nevertheless the comparison of these two tissues highlights clearly the differences in absorption of fluoride in the two species. Absorption appears to be slower and of longer duration in calcifuge plants whereas between the two tissues, absorption is essentially quantitative, the foliar tissues always showing higher levels of fluoride than the roots. On the other hand, fluoride is only weakly attached to the tissues since most of it can be easily exsorbed into the water.

Our data disclose a great similarity in the absorption mechanism of fluoride and calcium ions in calcicole and calcifuge plants.

Introduction

Previous studies of different physiological processes have shown a strong link between calcium and the transport of fluoride in plants subjected to fluoride pollution. Numerous authors have shown experimentally that the calcium concentration of the culture influences, in most instances, the penetration and accumulation of fluoride in roots and leaves (1-7) as well as in different tissues (8, 9).

It must also be pointed out that natural variations of calcium in plants bring about differences in the accumulation of fluoride. Indeed, the resistance of leaves to the necrotizing effects of fluoride varies during their development (10 - 12). We have been able to relate these variations to the changes in the amount of calcium in the leaves during their aging (13, 14). In polluted trees, fluoride and endogenous calcium concentrations in different parts of the tree (15 - 17) are closely related.

To follow up these various studies, we investigated whether or not the calcicole-calcifuge character of certain plants, which naturally involves important differences on the level of calcium absorption (18),
also induces fundamental differences in the absorption mechanism of fluoride.

Material and Method

I. Vegetable Material: Source and Preparation: Two leguminous fodder-plants were used for the study: the yellow lupin (*Lupinus luteus* L.) a calcifuge species and the calcicole horse-bean (*Vicia faba* var.minor).

Of the two plants, two types of tissues, namely foliar and root tissues were investigated simultaneously. The leaves are the preferential absorption sites for fluoride at the time of atmospheric pollution, whereas the calcicole-calcifuge selectivity takes place at root-level.

a) Preparation of the Excised Roots: After germination in distilled water, the seeds were planted in constantly aired trays; the environment of the culture contained a very dilute inorganic solution with the following composition:

\[
0.1 \text{ mM/l of } \text{Ca(NO}_3\text{)}_2, 0.1 \text{ mM/l of } \text{MgSO}_4 \text{ and } 0.1 \text{ mM/l of } \text{KH}_2\text{PO}_4
\]

Twenty-four hours before the experiment, this solution was replaced by distilled water at which time the roots had weak inorganic reserves. At the time of the experiments, namely eight or nine days after replanting, the roots were excised at collar-level, washed in distilled water, dried between two sheets of filter paper, and immersed in the fluoride solutions. Each sample consisted in about five roots.

b) Preparation of the Foliar Discs: The plants had been cultivated in the constantly aired KNOP environment. For the experiment, i.e. fifteen to twenty days after replanting, discs of 4 mm diameter were cut out trenchant-style from the adult leaves. The cuts were made between the principal veins. These discs were rinsed in distilled water, dried between two sheets of filter paper, and soaked in the fluoride solutions. Each sample was made up of about one hundred foliar discs.

II. Experimental Techniques: For the fluoride solutions we used NaF and each one had a volume of one liter so that the concentration of the surroundings did not vary during the course of the experiment. The temperature of the solutions was maintained at 26°C and the pH adjusted to 6. For the excised roots, the solutions were constantly aired during absorption. At the end of the experiment, the plant material was quickly taken out of the solution, rinsed in distilled water and dried between two sheets of filter paper.

III. Analytical Techniques: The plant material was dried in a drying cupboard at 70°C for three days after which it was finely ground. The fluoride concentration was obtained by using about 80 mg of the homogeneous powder. For fluoride analysis, the method of Levaggi et al.(19) was used. By this method the mineralization of the samples in a Schöniger oxygen flask is followed by a measurement of the fluoride which has been obtained and taken from an absorbing solution by means of a specific electrode. The results are given in µg of fluoride per gram of dry material (ppm).
Figure 1: Fluorine Absorption as a Function of Time

Figure 2: Fluorine Absorption as a Function of Concentration
Results

I. Fluoride Absorption as a Function of Time

a) Experimental Conditions: The fluoride concentration of the absorption solution was fixed at 50 meq/l, i.e. 950 μg F/g, a strength similar to that of solutions used by other authors (20, 21). The absorption period was 30 min., 1 hr., 2 hrs., 3 hrs., and 8 hrs. For each experiment we determined the initial fluoride strength of the tissues.

b) Interpretation of the Curves (Fig. 1): The curves obtained suggest that in the two species and for the two tissues used, fluoride absorption is a passive phenomenon. As a matter of fact, these curves do not take the form of a linear phase of a constant gradient indicating an active phenomenon according to the usual interpretation, but represent a horizontal straight line corresponding to a constant rate of absorption.

The initial fluoride strengths show little variation (Lupin: roots = 23 ppm, leaves = 108 ppm - horse-bean: roots = 33 ppm, leaves = 250 ppm). The amounts of fluoride after absorption are greater in the lupin (calcifuge) than in the horse-bean (calcicole), and greater in the leaves than in the roots. The lupin contain 8200 ppm of fluoride in its roots and 15,000 ppm in its leaves compared to 7200 ppm and 11,700 ppm in the roots and leaves respectively of the horse-bean.

Above all we noted that the form of the curves for the two species differ distinctly. For the lupin, the absorption time is longer, namely 5 hrs. for the root tissues and 8 hrs. for the foliar tissues whereas the respective absorption times in the root and foliar tissues of the horse-bean are 3 hrs. and 4 hrs. Furthermore, initially the phenomenon is slower in the lupin, since during the first hour 2,000 ppm and 2,300 ppm of fluoride is absorbed respectively in its roots and leaves compared with 3,000 ppm and 4,700 ppm in the roots and leaves respectively of the horse-bean during the same period.

II. Fluoride Absorption as a Function of the Environment Concentration

a) Experimental Conditions: The concentration range studied was 1 to 100 meq F/l (20, 21). The absorption time was fixed at 5 hrs. to allow sufficient time, in the majority of cases, for the curves to reach a plateau.

b) Interpretation of the Curves (Fig. 2): It seems that the absorption increases as a function of concentration, slowly in a first step (between 0 and 10 meq F/l), then more rapidly from 10 meq F/l. The absorption increase of concentration seems to be identical in the two species up to about 50 meq F/l. Above this point it becomes much more significant in the lupin (calcifuge) than in the horse-bean (calcicole). The curves have the same form for the foliar tissues as for the root tissues, but in this experiment root tissues appear to accumulate more fluoride.

From these curves it appears that, above all, we must distinguish
between the weak (0 to 10 meq/l) and the strong (10 to 100 meq/l) fluoride concentrations. Effectively, for the weak concentrations the curves quickly show a horizontal asymptote from 1 meq F/l onwards; in this region the absorption seems to be slightly more significant in the horse-bean.

For the strong concentrations, on the other hand, the absorption increases with concentration and it is very marked in the lupin (calcifuge). The curves have a very different form and the mass absorbed does not tend towards an asymptotic value.

**Figure 3**

Fluoride Exsorption as a Function of Time

Legend:

- Lupin (△)
- Horse-bean (●)

**Foliar Tissues**

**Root Tissues**
III. Fluoride Exsorption as a Function of Time

a) Experimental Conditions: The excised roots or foliar discs were left for 24 hrs. to absorb in a fluoride solution of 10 meq/l. At the end of this time the plant material was quickly rinsed in distilled water and then transferred into a large volume of distilled water for exsorption during periods of 30 min., 1 hr., 2 hrs., 3 hrs. and 8 hrs.

b) Interpretation of the Curves (Fig. 3): These fluoride exsorption studies allow us to evaluate the extent of the fixation of the fluoride absorbed during these experiments. For the root tissues, the exsorption was initially faster in the horse-bean than in the lupin, and the quantity of fluoride lost by these tissues was greater in the horse-bean than in the lupin.

For the foliar tissues the exsorption phenomenon is explained by the same type of curve as for the root tissues, but the lupin appears to have lost more fluoride than the horse-bean. At the end of the experiment the fluoride strength is practically the same in both specimens, being slightly more in the calcifuge (lupin) regardless of the kind of tissue.

Interestingly, the quantities of fluoride eliminated by the different tissues of lupin and horse-bean practically correspond to the quantities absorbed. Ultimately we found 100 ppm fluoride in the leaves and 40 ppm in the roots which are of the order of the fluoride test strengths. So it seems that little of the absorbed fluoride is strongly fixed inside the various tissues.

Discussion

The results of the experiments on fluoride absorption as a function of time in the foliar discs and excised lupin and horse-bean roots indicate that we are dealing with a passive phenomenon independent of metabolism. These results agree with the findings of Venkateswarlu (21) who used barley roots.

The experiments on absorption as a function of fluoride concentration show that the absorption mechanism is concentration dependent. In fact at weak concentrations (<10 meq F/l) fluoride absorption as a function of the strength of the surroundings seems to be explained by a hyperbolic curve according to Epstein (22). Beyond this, the shape of the curve differs and the mass absorbed does not tend to an asymptotic value. Moreover at strong concentrations fluoride accumulates significantly. This accumulation is much more marked in the calcifuge specimen. If in the weak concentration regions the process is one of passive absorption we can hypothesize an active transportation mechanism.

Finally, the experiments on exsorption as a function of time have shown that practically all fluoride absorbed could be desorbed by water. This would seem to indicate that very little of the absorbed fluoride is strongly fixed inside the tissues.
Generally speaking, the independence of the metabolism and the short time required for the absorption and elimination processes which quickly tend toward limited values, suggests that fluoride fixes itself on a limited number of sites essentially located at the cell-medium interfaces. This fixation of fluoride on these sites is very weak and is easily displaced.

**Comparison Between the Calcicole and Calcifuge Species**

From our results it appears that respecting fluoride absorption with time, as well as absorption as a function of fluoride concentration, the comparison between the two species demonstrates clearly differences in reaction providing distinguishing criteria between calcicole and calcifuge plants. These differences are of limited importance on a quantitative level: the initial fluoride reserves are equivalent and the masses of fluoride absorbed by the two species are more often of the same order. A surplus accumulation in the lupin results only in connection with high levels of fluoride (100 meq/l).

On the qualitative level, on the other hand, differences are marked. In fact the absorption curves differ for the two species; the phenomenon appears to be slower and of longer duration in the calcifuge plants.

**Comparison Between Foliar and Root Tissues**

On the qualitative level, the absorption phenomena in the two tissues are similar, the forms of the curves being identical. On the other hand, on the quantitative level, the foliar tissues always show higher fluoride levels except for the roots when the concentrations are high.

**Comparison with Calcium Absorption**

By comparison with identical studies carried out on the roots of calcicole and calcifuge plants (18), there were close similarities on the level of the absorption mechanism of calcium and fluoride ions. Indeed these curves show exactly the same form. The effect of the calcicole and calcifuge absorption characteristics can be explained in the same way. In particular the absorption characteristics at strong concentrations which very clearly distinguish calcium from all other cations are the same as those for fluoride. Furthermore, the differences in fluoride absorption for the calcicole and calcifuge species are not very pronounced on the quantitative level but are particularly prominent on the qualitative level. Only the fixation mechanisms of the two ions seem to be different. Indeed whereas Salzac (18) has shown that very little of the calcium absorbed by the excised roots can be exsorbed, our experiments demonstrate that practically all absorbed fluoride can be quickly desorbed.

The reason for this similarity between this cation and anion absorption mechanisms is difficult to explain. It requires investigation at the level of the strong chemical affinity which exists between these two elements.
Bibliography


**********

EFFECT OF FLUORIDE ON HEMOGLOBIN AND HEMATOCRIT

by

Burhan Uslu

Eskisehir, Turkey

SUMMARY: Hemoglobin and hematocrit values in human subjects residing in an endemic fluorotic area were within the normal range. Rats that received 30 to 100 ppm NaF in drinking water up to 45 days showed no significant change in hemoglobin and hematocrit levels.

Introduction

The effect of fluoride on hemoglobin and hematocrit levels in laboratory animals has received considerable attention in the literature (1). Ginn and Volker (2), observed a reduction of hemoglobin values in rats which received 50 ppm of fluoride as NaF in water daily for 150 days. Valjavec (3) noted only a slight reduction in hemoglobin levels in nine rabbits, which received daily intravenous injections of 10 to 30 mg/kg NaF up to 159 days. However, Greenwood et al. (4) found no changes in the hemoglobin and blood coagulation time after young dogs received intravenous injections. In humans, Roholm (5) noted a slight reduction in the number of erythrocytes but hemoglobin levels were unaffected. Balazova et al. (6) observed in children living in close proximity to an aluminum factory since birth that hemoglobin values were low-

From the Orthopaedic Department, Anadolu Univ., Medical Faculty, Eskisehir, Turkey.
er, erythrocyte values higher than in the control area. In children in fluoridated Newburgh, N.Y., the incidence of cortical bone defects was significantly greater than in the nonfluoridated control city of Kingston, N.Y. but the hemoglobin values did not differ significantly (7).

**Material and Method**

This investigation was made on sixty rats and 241 humans. The experimental animals were divided into four groups namely, fifteen control rats which received tap water (0.1-0.6) (Group 1); fifteen received 30 ppm NaF in their drinking water for 15 days (Group 2); fifteen were given 50 ppm for 30 days (Group 3) and fifteen received 100 ppm for 45 days (Group 4).

The group of humans was composed of 62 males, 51 females and 128 children. All of them had been residing in the endemic fluorotic area of Eskisehir throughout their lives, where drinking water contained 3.8-4.9 ppm fluoride. They were examined for evidence of skeletal fluorosis by means of x-rays. The diagnosis of dental fluorosis was established by a dental surgeon.

Hemoglobin and hematocrit levels were determined in 119 male and 122 females afflicted with fluorosis; their ages ranged between 2 and 70 years. Sixty-eight of the 119 males were below age 16. Of the 122 females, 60 were below age 16. The results were compared with those of nonfluorotic patients admitted to the hospital for other complaints.

**Results**

In the fifteen rats of Group 1 with 0.1-0.6 ppm fluoride in drinking water, the hemoglobin levels ranged between 10.5-12.6 gm % and hematocrit values were between 39-50 (Table 1). In Groups 2, 3 and 4 the hemoglobin

**Table 1**

Hemoglobin and Hematocrit Values in Rats

<table>
<thead>
<tr>
<th>Group I</th>
<th>Hemoglobin gm %</th>
<th>Mean</th>
<th>Hematocrit %</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>10.5-12.6</td>
<td>11.38</td>
<td>39-50</td>
<td>45.8</td>
</tr>
<tr>
<td>Group II</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30 ppm NaF</td>
<td>10.2-12.4</td>
<td>11.16</td>
<td>37-55</td>
<td>45.7</td>
</tr>
<tr>
<td>15 days</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group III</td>
<td>10.4-11.8</td>
<td>11.21</td>
<td>39-50</td>
<td>44.1</td>
</tr>
<tr>
<td>50 ppm NaF</td>
<td>10.4-11.8</td>
<td>11.21</td>
<td>39-50</td>
<td>44.1</td>
</tr>
<tr>
<td>30 days</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group IV</td>
<td>9.8-11.8</td>
<td>11.08</td>
<td>39-48</td>
<td>43.2</td>
</tr>
<tr>
<td>100 ppm NaF</td>
<td>9.8-11.8</td>
<td>11.08</td>
<td>39-48</td>
<td>43.2</td>
</tr>
<tr>
<td>45 days</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
and hematocrit values revealed no significant differences between the control and the fluorotic animals at the termination of the experiments. 

Table 2 presents the hemoglobin and hematocrit levels of the residents of the endemic fluorotic area. No significant differences were observed between the fluorotic and nonfluorotic subjects

<table>
<thead>
<tr>
<th></th>
<th>Hemoglobin gm %</th>
<th>Mean</th>
<th>Hematocrit %</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>11.40-14.15</td>
<td>13.18</td>
<td>35-47</td>
<td>42</td>
</tr>
<tr>
<td>Women</td>
<td>10.50-13.20</td>
<td>11.92</td>
<td>32-45</td>
<td>41</td>
</tr>
<tr>
<td>Boys</td>
<td>9.12-12.56</td>
<td>11.26</td>
<td>33-42</td>
<td>38</td>
</tr>
<tr>
<td>Girls</td>
<td>10.10-13.08</td>
<td>12.07</td>
<td>33-40</td>
<td>38</td>
</tr>
</tbody>
</table>

**Discussion**

In evaluating these data it appears that when anemia occurs in fluorosis, it should be considered a secondary manifestation due either to nutritional imbalance or to partial obliteration of the medullary space because of its reduction due to osteosclerosis. In the series of 55 cases by Singh et al. (8) in which the fluoride concentration of water ranged mainly between 1 and 2 ppm, hemoglobin levels from 8 to 15.5 gr/100 ml were found. Our results compare favorably with those of Agate et al. (1), who noted normal blood counts and hemoglobin levels in industrial fluorosis. Their finding was also supported by our animal experiments in which no difference was noted between the control and the fluorotic rats.

**Bibliography**


Volume 14 Number 1
January 1981

**********

FLUORIDE BRIEFS

The authors found, in the combined backs and necks of broiler chicks, about 20 times as much fluoride as in bone-free meat. The range of fluoride in various parts of a broiler carcass was 0.9 to 45 ppm (wet weight).

Among the commercial phosphate supplements administered to chicks, the fluoride content of "soft phosphate" was 17,100 ppm, of defluorinated rock phosphate 1820 ppm, and of fish meal 188 ppm.


**********

The authors reported in isolated rat hepatocytes significant inhibition by sodium fluoride and monofluoride enzymes of three glycolytic enzymes namely, enolase, phosphoglucomutase and pyruvate kinase. This inhibition appears to take place inside the cells and may be due to cAMP dependent phosphorylation of the enzyme.


**********

FLUORIDE
RADIOFLUORIDE DISTRIBUTION IN RAT LUNG, COLON AND HEART

by

G.M. Whitford, R.S. Callan and D.E. Pearson
Augusta, Georgia

(Abstracted from J. Dent. Res. 59:1171, 1980)

In most soft tissues, fluoride enters the intracellular spaces as indicated by the tissue water-to-plasma fluoride concentration ratio which ranges between 0.4 to 1.0.

The authors injected intravenously 8 female Wistar rats with $^{18}_F$, 9.1 μCi/rat. They sacrificed four rats after 30 minutes and the other four after 60 minutes and collected blood from the neck wound, heart, colon, and lungs. They removed the colon, heart, and lungs. Fecal pellets were removed from the colon and special care was taken to dissect the lung from the major bronchi and trachea because cartilage tends to attract fluoride. Samples were weighed and counted for $^{18}_F$ in a well-type scintillation counter.

The tissue water-to-plasma concentrations were lowest for the heart and colon and highest in the lung and trachea tissue. There was no evidence of $^{18}_F$ binding by colon or by peripheral lung tissue. The authors stated in conclusion that earlier reports of the $^{18}_F$
Abstract

Thirteen subjects residing in a nonfluoridated area (0.1 ppm in drinking water) on a normal and roughly comparable diet, were divided into experimental groups. Both groups received daily for 6 weeks, two placebo tablets without fluoride. Subsequently, the first group of 6 subjects were given two tablets daily for 7 weeks, one of which was a placebo, the other one contained 1 mg fluoride. The second group of 7 subjects continued on the placebo tablets for another 8 weeks after which they received two 1 mg fluoride tablets daily for 7 weeks.

The plasma alkaline phosphatase showed wide variations within normal limits among the subjects receiving two placebo tablets. The values in those receiving fluoride tablets did not differ significantly from the control values. However, in the subjects receiving 1 mg fluoride daily, the mean reduction in plasma alkaline phosphatase activity was 11% and in subjects receiving 2 mg fluoride daily the reduction was 13% during the first five weeks following the change from placebo tablets. After 5 weeks the mean in the subjects on fluoride tablets was close to that of the controls.

Subjects who received (2 mg F⁻) daily after a period on one tablet (1 mg F⁻) showed a decrease in alkaline phosphatase below the control levels. In both groups (1 and 2 mg F⁻), the plasma alkaline phosphatase was below normal during the first week of administration.

**********

FLUORIDE INHIBITION OF DNA SYNTHESIS IN ISOLATED NUCLEI FROM CULTURED CELLS

by

R.I. Holland
Oslo, Norway

(Abstracted from Acta Pharmacol. and Toxicol. 45:302-305, 1979)

Fluoride inhibits protein and DNA synthesis in LS cells. The author elucidated the mechanism for this effect by isolating DNA synthesizing nuclei from LS cells and from LS cells resistant to 6 mM (114 ppm) fluoride. Fluoride concentrations of 1.5 mM (28.5 ppm) had no effect, but 3 and 6 mM inhibited DNA synthesis in both groups of cells, the sensitive and the resistant cells. In intact cells - as distinguished from their nuclei - fluoride affects exclusively the DNA synthesis in sensitive cells. Their intracellular fluoride concentration is only 30 to 40% of that of the extracellular concentration. Inhibition of DNA synthesis by fluoride is secondary to fluoride inhibition of protein synthesis.

**********
Abstract

HYDROFLUORIC ACID – A CHRONIC POISONING EFFECT

by

D.A. White
Edinburgh, Scotland


The author points to the hazard of longtime occupational exposure to hydrofluoric acid. In three men engaged full time in the department of a plant where glass is dissolved from the surface of metallic platinum by means of concentrated hydrofluoric acid (80%), mean fluoride levels in the urine were as high as 12.02 ppm. This value exceeds the levels known to cause osteosclerosis. However, neither data on the patients' health nor x-ray changes were recorded. One of the employees had essential hypertension.

In the breathing zones in one room where the acid was used, the atmospheric hydrofluoric acid was well within the threshold limit of 2 mg/m³. However higher levels (5.1 mg/m³) were detected in the other room. Following installation of local exhaust ventilation over the positions involved, the mean atmospheric fluoride levels were 0.7 mg/m³ and the mean urinary fluoride declined to 1.41 ppm.

The author emphasizes that standards of occupational health designed to protect the worker from acute effects of HF, do not protect the worker from chronic exposure at lower levels. He recommends routine monitoring of urinary fluoride in employees working with hydrofluoric acid.

**********

Vlijanie ftora okruzajuscej sredy na zhorov'ye usloviyah bukatskoj gidrogeochemiceskoj provinicii

INCIDENCE OF ATMOSPHERIC FLUORIDE UPON THE STATE OF HEALTH OF A POPULATION IN THE HYDROGEOCHEMICAL PROVINCE OF BUCAK

by

A.S. Kas'jenenko

(Abstracted from Vrach Delo 12:105-111, 1978)

The author carried out studies in six different areas of the province of UdSSR in Bukack of the Ukraine, the part of the USSR where water contains the highest levels of fluoride naturally in water.
Abstract

In each of the six communities 100-200 children were examined. In an area with 1.2 ppm fluoride in water, dental fluorosis exhibiting small white spots on the teeth (Stage 1 according to Gabovic) was observed in 13.4%. Above 1.6 ppm, the incidence of dental fluorosis showed an increase to 52%. When these percentages were compared with those reported by Gabovic 30 years ago in the same area, there was a distinct decline in the incidence of fluorosis at the same fluoride concentrations in water. The author attributes this improvement to social hygienic conditions which have enhanced the tolerance to fluoride.

The electrical resistance of the teeth was measured in order to determine fluoride-induced changes of the structure and the chemical composition of the teeth. With addition of fluoride to drinking water, the electrical resistance, which normally amounts to 150-200 kΩ declined to 40 kΩ in cases with fourth grade fluorosis.

The caries incidence among children below 16 years, in areas with 1.2 - 4.2 ppm fluoride in drinking water showed a 50-70% reduction compared to that of the control area with water fluoride levels of 0.1-0.35 ppm.

Two thousand female workers aged 50 to 60 were studied in two cities, one with 1.5-1.6 ppm and the other with 0.1-0.35 ppm fluoride in water. There appeared to be less caries and less extracted teeth in the fluoride group drinking the water with a higher fluoride level.

The fluoride concentration above 1.5 was associated with a delay in eruption of teeth at ages 8-10. In children 13 years of age, however, there was no difference in delay compared with normal. At age 13, with 8.2 to 10.3 ppm in water, more teeth were erupted than in the control area.

The effect on bones was studied in six localities with varying fluoride levels in the drinking water. Six hundred x-ray films were taken of the hands of 9-year old children and 600 of the cervical spine of 50-year olds. In addition, chemical and histological studies were carried out.

At 1.0-2.5 ppm the density of the bones had increased compared with the controls. At 4.0-4.2 ppm the density appeared to be reduced and at 8.2-10.3 ppm there was a distinct decrease in density to the extent that osteoporosis occurred. In the last-mentioned group, a delay in ossification was observed. Among the 50-year old subjects, "old-age" changes of the cervical spine appeared to be more frequent and more pronounced than in controls. Histologically, no clear-cut changes were found in bones of individuals who had expired as a result of accidents. The citrate content of their bones decreased when the drinking water contained 2 ppm fluoride. At 2-2.5 ppm and above in drinking water, children showed an increase in the threshold for sensitivity of the eye to red color. At the highest concentration of 8.2-10.3 ppm the degree of this deficiency was similar to that among workers in fluoride industries.

J. Franke

**********

FLUORIDE
Abstract

**Osteose fluorée après 11 ans de traitement interrompu par l'acide niflumique**

**FLUORIDE OSTEOSCLEROSIS AFTER 11 YEARS OF UNINTERRUPTED TREATMENT WITH NIFLUMIQUE ACID**

by

Bregeon, C., Bernat, M., Renier, J.C.
Rebel, A., and Basile, M.
Angers, France

(Abstracted from La Nouvelle Presse Medicale, 9:1446-1447, 1980)

The first report of fluoride osteosclerosis due to a drug was presented in 1978 by Prost et al. The current report describes the case of a 57-year old male afflicted with rheumatoid arthritis which had been developing gradually since 1945. Mainly involved were the hips and the left carpal-phalangeal joints. His condition was treated at first with prednisone which had to be discontinued because of the presence of anemia. It was followed by a fluoride-containing drug Noflumique acid. At first, 2000 mg/day was administered for 15 days; he then received 1500 mg/day until January 1969 when the patient was subjected to arthroplasty at the right hip.

Subsequently the patient was taking 6 capsules (1500 mg/day) of the above-mentioned acid together with Indomethacine and Aspirin continuously up to May 1978. The total dose of fluoride consumed by this patient at 0.3 g/day during 4120 days was estimated to be 1240 grams.

The first signs of osteosclerosis appeared in 1974. By May 1978, extensive lesions had appeared in the pelvis, spine and ribs, whereas the skull and other bones remained within normal limits.

Biochemical studies in April - May 1978 and in June 1979, thirteen months after discontinuance of treatment, revealed a slight decrease in the serum, calcium and alkaline phosphatase. Urinary calcium had decreased to 62 mg/day, urinary phosphorus was 685, plasma ionized fluoride 0.2 mg/liter and 24-hour urinary fluoride 5.6 mg. By June 1979 the urinary calcium had increased to 114 mg/day, urinary phosphorus to 820mg/day and hydroxyprolinuria to 43 mg/day. Both urinary and plasma fluoride were slightly lower than in 1978.

Histomorphometric bone studies in 1979 showed that the volume of trabecular bone was 40.6% compared to 17.4±5.6% (normal); resorption surface was 10.4% (normal 3.6±1.1%), periosteocytic lacunae 58 µ2 (normal 50.7±5.5 µ2). The structure of bone tissue and of the osteoid was of lamellar type, the rate of mineralization had decreased and the number of active osteoclasts had increased.

The authors pointed out that the fluoride doses during 11 years were as high as the ones reported previously by Prost et al. They also emphasized that thirteen months after discontinuance of fluoride intake, the urinary fluoride level remained considerably elevated.

************
SOME OBSERVATIONS ON ATMOSPHERIC FLUORIDE CONCENTRATION IN STOKE-ON-TRENT

by

Bennett, A.J., and Barratt, R.S.
Stoke-on-Trent and Birmingham
England


The authors carried out an atmospheric fluoride survey in the industrial city of Stoke-on-Trent, the seat of pottery and brickworks. To collect particulates they used membrane filters; for gaseous fluorides, alkali-impregnated cellulose pads were placed after the membrane filter. Air samples daily during a two-week period in 1978 at two sites, were averaged. At the non-industrial site, with one exception, the total fluoride concentrations were below the limit of detection by the method used, namely 0.1 μgF/m³. In the industrial site, the highest concentration was 7.11 μgF/m³ air. The calculated weekly mean concentration of total atmospheric fluoride was 2.81 μg/m³ during the first week. During the second week however, which coincided with the annual holiday period, it was only 0.48 μg/m³. Although a strong correlation was observed between the sulphur dioxide concentrations and those of fluoride, none existed between airborne fluoride and smoke concentrations.

The authors attributed the relatively low amount of particulates to the possibility that particulates were lower during the sampling periods or they may have been deposited before they reached the sampling sites. Smoke concentrations were low during the survey period in the industrial area. The lack of relationship between smoke and fluoride indicates that combustion of domestic coal is not the source of fluoride or of SO₂. Possible sources include industrial processes in which both pollutants are emitted such as firing and clay material using sulphur-bearing fuels.

The authors tabulated data from similar surveys, both in England and in other countries. In the yard of a Japanese aluminum refinery, the concentration of total fluoride in air ranged up to 92.4 μg/m³. In the U.S.S.R. near a superphosphate plant, the levels rose as high as 98 to 485 μg/m³.

Although the values reported by Bennett et al. are relatively low, the authors suggest that persons residing in areas where atmospheric fluoride levels are elevated, where both locally grown vegetables as well as considerable tea are being consumed and, in addition, the water is fluoridated, the daily fluoride intake may possibly be above 5 to 8 mg, the level of intake at which osteosclerotic changes occur.

**********

This volume is one of the latest in the series of critical compilations being prepared by the Commission on Equilibrium Data of the Analytical Chemistry Division of the International Union of Pure and Applied Chemistry. Because of the importance of fluoride complexes in many chemical and biological systems, virtually every scientist engaged in fluoride research will find it of great practical value.

In the introductory section the authors summarize and compare how fluoride-metal ion stability constants are measured and what are some of the frequently overlooked difficulties and complications in their determination. They also comment on the measurement and reporting of enthalpies of fluoride complexation. Finally, they explain how the extensive data collected here have been evaluated and arranged.

In the main table, stability (formation) constants of fluoride complexes are assembled with over 70 metal ions and hydrogen ion at various ionic strengths. The second table lists enthalpy and entropy data for the more important complexes. Finally, the third table presents what the authors regard as the "best" values for the stability constants given in the main table. More than 250 references, arranged by year and alphabetically by first author, are cited.

For those who need a handy compilation of data on fluoride complexes in aqueous solution, this volume is warmly recommended, although it is quite expensive for only 71 pages of typescript printing.

A.W.B.