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FLUORIDE
Quarterly Reports
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THE INTERNATIONAL SOCIETY FOR FLUORIDE RESEARCH

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The International Society for Fluoride Research will hold its Tenth Conference in Oxford, England, September 16-18, 1979. Further details will appear in subsequent issues. The Program Committee is soliciting abstracts (up to 300 words) of papers to be presented at the conference dealing with any phase of fluoride research. Kindly send abstracts to the Society’s office, P.O.Box 692, Warren, Michigan 48090.

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

FLUORIDE is listed in
Current Contents Agricultural
Food and Veterinary Sciences

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EDITORIAL REVIEW

ENVIRONMENTAL FLUORIDE

Since 1971 the National Research Council of Canada, through its Associate Committee on Environmental Quality, has been issuing an impressive series of valuable reports on important environmental topics. What is particularly striking about these reports, especially the present one (1), is that their conclusions do not always concur with those of the U.S. National Academy of Sciences-National Research Council (2). The latter organization has addressed itself repeatedly during the last three decades to various aspects of environmental fluoride, but, unlike the present document, it has consistently failed to recognize the evidence for toxic effects to man produced by fluoride exposures commonly encountered in today's environment.

In this report, which is an updated and greatly expanded version of their earlier, 1971 report, Rose and Marier ably identify and examine the major sources, nature, magnitude, interactions, and effects of contemporary fluoride emissions and intrusions into air, water, soil, and food. They show, for example, how failure to consider the erratic character of air-flow patterns and the fluoride-shielding effects of vegetation has led to serious underestimates of the actual exposure of wildlife, crops, forage, livestock, and even human populations to airborne fluoride. Under many circumstances, they point out, present permissible fluoride levels in forage (30-40 ppm) are much too high.

Yields of citrus fruits are adversely affected by long-term exposure of orchards even to fluoride levels of less than 0.1 μg/m³ in air. A further effect is increased susceptibility to damage from disease, insects, and other air pollutants. Recent findings regarding the mutagenic activity of fluoride are also reviewed, along with evidence of a possible association between cancer and fluoride, particularly between lung cancer and industrial emissions.

In considering the health effects of waterborne fluoride, the authors give close attention to the role of nutritional factors and water hardness in moderating fluoride toxicity. Likewise, they point to the enhanced requirements of calcium, magnesium, vitamin C, and manganese with increased fluoride intake. Summarizing this section, they conclude: "There is no doubt that inadequate nutrition increases the severity of fluoride toxicosis."

Also emphasized is the growing evidence of adverse changes in the biochemistry of the blood, kidneys, liver, spleen, brain, nerves, and other organs of the body, besides the bones and teeth, caused by continuous ingestion of even comparatively small amounts of extra fluoride. When blood plasma concentrations of ionic fluoride exceed 2-3 μM (normal 0.5-1.0 μM), particularly in the elderly, bone fragility and
spontaneous fractures become more frequent. Trends suggesting a contributory role of fluoride in nephrogenic diabetes are discussed, and careful monitoring of blood plasma fluoride is recommended among persons at risk to detect latent or potential injury. This procedure is especially important for individuals with impaired kidney function or exposure to excess fluoride as, for example, from fluorinated anesthetics.

The authors also show that commercial food processing with fluoridated water has significantly increased the average dietary intake of fluoride in Canada and the United States. Using the most current available data, they estimate that the average adult intake of fluoride from such food and beverages, including 1 ppm fluoridated drinking water, is now between 3.5 and 5.5 mg/day—about double previous estimates. Not included in these figures is the additional intake from air, cigarettes, dentifrices, mouth washes, and pharmaceuticals. An important but little-known fact in this connection is that mechanically deboned meat, now a very common commodity, contains about ten times more fluoride than meat deboned by hand.

Unfortunately, the report gives only scant attention to clinical findings of reversible ill effects from fluoride, especially in drinking water, and therefore is disappointing in its "attempt to assemble and review reports relating to fluoride-induced illness in humans" (p. 75). It does, however, single out key subgroups in the population that are in greatest danger from fluoride intoxication, even at exposure levels currently regarded by health authorities as perfectly safe. These categories include:

(1) Individuals in poor health or with sub-optimal nutrition, especially with respect to calcium and magnesium.
(2) Persons residing near or working in fluoride-polluting industries.
(3) People living in regions where goiter is endemic.
(4) Persons with kidney impairment and related disorders.
(5) Individuals who drink excessive amounts of fluoridated water.

Clearly, the authors recognize that there are serious fluoride hazards to millions of people. Such a frank acknowledgment in a high-level government document such as this stands in sharp contrast to the attitude of the U.S. National Academy of Sciences—National Research Council. That body, in the fluoride chapter of its recent report Drinking Water and Health (1977), recommended that more research be undertaken but largely discounted or ignored the extensive published evidence of harm by fluoride to such persons (2).

Too many scientists are still not acquainted with the nature and magnitude of fluoride pollution. For this reason, the importance of the present report cannot be overestimated.

A.W.B.

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EDITORIAL

THE DIAGNOSIS OF INCIPIENT FLUOROSIS

The report by Klemmer and Hadler abstracted in this issue of FLUORIDE, page 49, of a 27-year-old nurse who had been illicitly inhaling the fluorinated anesthetic methoxyflurane (Penthrane) for about 9 years is remarkable for two reasons:

The case re-emphasizes the well-known fact that certain organofluorides can produce a clinical picture characteristic of fluoride poisoning rather than of poisoning by the nonfluoride moiety. In the body the fluoride ion dissociates from the compound's molecule. Whereas in some organic fluoride compounds, which are biologically inert, the fluorine atom is tightly linked to carbon, in others it becomes readily dissociated.

The second important feature of the case is the fact that this patient's skeletal changes were preceded for 4 years by a variety of symptoms which had baffled the attending physicians; they had been unable to make a diagnosis. These symptoms were vague pain, "exceedingly painful bone", headache, polydipsia, polyuria, and epigastric distress. In addition, she had marked hypertension (blood pressure 220/130) which gradually subsided as she improved. The presence of a gastric ulcer is notable in view of recent reports by Czerwinski (1) and by Franke (2) which link fluoride with gastric ulcer. The patient also exhibited "multiple, fixed, exquisitely painful nodules on her extremities" probably a chemically induced lymphadenitis. She also had severe mental depression, another symptom often encountered in preskeletal fluorosis, which required extended hospitalization on the psychiatry service.

The classical symptoms of the nonskeletal phase of fluorosis
occurring in conjunction with skeletal changes were first delineated by Roholm (3) in 1937. Since 1955 Waldcott (4) has been encountering the same symptoms prior to the onset of bone changes. Other investigators have subsequently confirmed the nonskeletal phase of fluorosis (5).

Unfortunately medical texts on chronic fluoride intoxication usually refer to the dental and skeletal changes exclusively without considering the nonskeletal effects. Consequently this case remained undiagnosed until the authors became aware of the nurse's clandestine use of methoxyflurane which led them to suspect fluoride involvement.

G.L.W.

Bibliography

HUMAN RENAL FLUORIDE EXCRETION: ALTERATIONS OBSERVED IN CHRONIC RENAL FAILURE (A PRELIMINARY REPORT)

by

H. Schiffi, U. Flueeler and U. Binswanger
Zürich, Switzerland

SUMMARY: The mechanism of renal fluoride excretion by the human kidney is glomerular filtration and tubular reabsorption. Higher fluoride clearances than those for creatinine were never observed indicating that tubular secretion of fluoride can be excluded. Patients suffering from renal diseases tend to continue to excrete normal dietary loads of fluoride quite well until renal excretory function is reduced to 1/4 of normal. In chronic renal failure, elevation of plasma fluoride is delayed and less than might be expected from impairment of glomerular filtration rate, because tubular reabsorption diminishes. End stage renal disease is characterized by elevated plasma fluoride concentrations and excessive deposition in the bone.

Introduction

The basic homeostatic mechanisms whereby the body disposes of absorbed fluoride and regulates the plasma fluoride concentration within a narrow range are deposition of fluoride in calcified tissue and excretion through the kidneys into the urine (1,2). In chronic renal failure, the ability to remove fluoride from the blood stream is impaired (3) and elevated serum levels associated with a tendency for increased storage in bone were observed even in an area where the fluoride content of drinking water was low (4). Much of the basic research into the renal physiology of fluoride is provided by animal experiments (5-9) whereas observations in humans are few (10-13). Investigations in humans of the tubular mechanism which may be involved in fluoride excretion are contradictory (14).

The present study was undertaken to define some features of the renal handling of fluoride in normal volunteers and in patients with variable degrees of chronic renal failure.

Methods

A total of 17 subjects, 9 women and 8 men, aged 22-66 years, from the Section of Nephrology, Department of Internal Medicine, University of Zürich, Switzerland.

were studied. Group I was composed of 6 healthy volunteers with no previously recognized disease; group II consisted of 5 patients with variable degrees of impaired renal function and 6 patients on hemodialysis made up group III. The drinking water which was also used for dialysate preparation contained 0.06 ppm fluoride.

Blood samples, obtained by venupuncture, were taken for biochemical analysis. 24-hour urine collections were made for estimations of electrolytes, fluoride and creatinine. From these data excretion rates and clearances were calculated.

Plasma and urine inorganic fluoride levels were measured by a fluoride ion-sensitive electrode (Orion, Model 96-09) using the combination of the single-known addition method and the electrode slope-by-dilution method as described by Fuchs et al. (15). The complete electrode measuring device consisted of 6 fluoride electrodes, which were connected to an Orion electrode switch (Model 605). Each electrode potential was measured by an Orion Digital mV meter (Model 701).

Analyses of creatinine and chloride were performed by clinical routine methods adapted to autoanalyzers.

Results and Discussion

1. Urinary Excretion of Fluoride: In accord with the study of Parsons (3) total urinary fluoride excretion decreases, as chronic renal failure progresses (Table 1). In patients suffering from advanced

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Renal Function, Fluoride Excretion and Serum Fluoride Concentration (mean ± SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group I</td>
</tr>
<tr>
<td>Number of studies</td>
<td>norm. ren. func.</td>
</tr>
<tr>
<td>Cr.-clearance m/l/min.</td>
<td>107,0 ± 16,5</td>
</tr>
<tr>
<td>F⁻ - clearance m/l/min.</td>
<td>26,5 ± 3,5</td>
</tr>
<tr>
<td>F⁻ - c1./Cr.-c1.</td>
<td>0,25 ± 0,03</td>
</tr>
<tr>
<td>Urinary excretion F⁻ ug/24 hr</td>
<td>401,3 ± 81,5</td>
</tr>
<tr>
<td>Serum conc. F⁻ ug/l</td>
<td>10,43 ± 1,34</td>
</tr>
<tr>
<td>Urinary flow (V) m/l/min.</td>
<td>0,96 ± 0,14</td>
</tr>
</tbody>
</table>

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renal failure, the reduction of creatinine clearance to 1/4 of normal is accompanied by a similar drop in the fluoride clearance. Since fractional fluoride excretion \( \frac{C_{F}}{C_{Cr}} \) does not significantly change, the reduced glomerular filtration rate may fully explain the impaired fluoride excretion observed in this group. With further deterioration of renal functional mass, however, the excretion pattern of fluoride is changed in that the normal ratio of fluoride to creatinine clearance increases. This indicates that the tubular reabsorption of fluoride decreases, thereby counteracting the impairment of fluoride excretion due to low glomerular filtration rate.

2. Plasma Concentration of Fluoride in Chronic Renal Disease:
As a result of the decrease in urinary fluoride excretion, high fluoride concentration of the plasma can be observed. There is a striking relationship between plasma creatinine and plasma fluoride (Fig. 1). As can be seen in Figure 2 an increase of the plasma fluoride concentration
can be expected at a filtration rate of about 25 ml/min. With further deterioration of the kidney function plasma fluoride concentration levels are increasing at an exponential rate.

Bibliography


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THE RELATIONSHIP OF FLUORIDE TO VISIBLE GROWTH/HEALTH CHARACTERISTICS OF PINUS MONTICOLA, PINUS CONTORTA, AND PSEUDOTSUGA MENZIESII

by

C.E. Carlson, C.C. Gordon and C.J. Gilligan
Missoula, Montana

SUMMARY: An intensive field study during the summer of 1977 near an aluminum plant in northwestern Montana, U.S.A., was initiated to determine the relationship of foliar-accumulated fluoride to various growth/health characteristics of three commercially-important conifer species. Regression techniques were used to analyze the data obtained from nearly 110,000 needles. Increasing foliar concentrations of fluoride in Pseudotsuga menziesii were associated with decreased needle retention and length, and with increased tip necrosis. Both mottle and tip necrosis of Pinus contorta increased in direct relation to the concentration of fluoride, whereas needle retention decreased. Tip necrosis and mottle of Pinus monticola also increased with foliar fluoride. No threshold foliar fluoride concentration was observed; adverse effects were visible on needles when their fluoride concentration reached 8-10 ppm, on a dry weight basis. Control concentrations were 3-5 ppm. It is concluded that no emission or ambient fluoride standard allowing detectable amounts of atmospheric fluoride will truly protect coniferous vegetation.

Introduction

Visible fluoride-induced injury on plant leaves has been discussed (1-5). Fluoride, primarily in the gaseous form, enters leaves through the stomata, is dissolved in the aqueous medium of the mesophyll cells, and enters the transpirational stream. Much of the fluoride is transported to the tips of conifer and monocot leaves and to the margins of dicot leaves (6-8). Depending on the tissue, fluoride concentrations and numerous environmental variables, necrosis of conifer and monocot leaf tips and death of dicot leaf margins occurs. Usually a dark reddish-brown zone line occurs between necrotic and healthy tissue. It has been stated that no correlation has ever been shown between foliar fluoride uptake and leaf necrosis (4), but other data tend

From the U.S. Dept. of Agriculture, Forest Service, Missoula, Montana,
to refute that assumption. Under controlled conditions Adams et al. (9) showed that exposure factor (the sum of products of exposure duration and ambient fluoride concentration) was significantly correlated ($P < .05$) to foliar fluoride content in the genus Pinus. During daylight fumigations, Pseudotsuga menziesii accumulated 238 ppm fluoride after 159 hours of fumigation at 1.5 ppb (parts per billion) HF. Pinus ponderosa, Pinus monticola, and Pinus contorta accumulated 83 ppm, 70 ppm, and 39 ppm after 367, 135, 217 hours of fumigation with 1.15 ppb HF, respectively.

In a field study near an aluminum plant in eastern Washington, the amount of foliar necrosis on Pinus ponderosa and Gladiolus was markedly correlated with atmospheric fluoride concentrations ($r = 0.99$ for P. ponderosa)(10). Foliar injury occurred at 0.5 ppb hydrogen fluoride in the atmosphere. It follows that if foliar fluoride concentration and fluoride-induced foliar injury are dependent on the fluoride content of the atmosphere, then foliar injury must be directly related to foliar fluoride concentrations.

The purpose of this study was to assess the statistical relationships between foliar-accumulated fluoride and various foliar growth/health characteristics on three temperate conifer tree species: Pinus contorta, Pinus monticola, and Pseudotsuga menziesii.

**Methods**

The study was done under field conditions near an aluminum plant in northwestern Montana. Previous field studies in the same area documented environmental damage (11,12), a related insect epidemic (13), and growth impact on Pinus contorta (14) but no work has been done to relate visible foliar degradation to foliar fluoride accumulation.

Twenty-eight conifer stands were randomly selected, eight of which were within the area previously described as severely polluted (11), ten were within the moderately polluted area and ten were selected as controls. Depending on stand area, 5-40 plots were established in each stand, and foliage was collected from 3-5 dominant or codominant conifer trees at each plot.

About 1.5-2 kg of foliage from midcrown facing the aluminum plant was placed in a plastic bag, labeled, transferred to the laboratory and placed in cold storage. Each sample consisted of needles originating in 1975, 1976, and 1977.

Conifer foliage samples were always kept separate by stand, point, and tree number. First, the internodes possessing needles were clipped and segregated by year of origin—1977, 1976, and 1975 and for each sample the following characteristics were measured or counted by age class:

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Needle Retention: Five internodes were randomly selected and the needles present were counted. Missing needles were estimated by counting basal needle scars. Percent needle retention was derived as:

\[
\text{Percent Needle Retention} = \frac{\text{Needles Present}}{\text{Needles Present} + \text{Basal Scars}} \times 100
\]

Needles were then stripped from the internodes but kept separate by year of origin. The following observations were made:

Needle Length: Twenty-five needles were randomly selected; the length of each was measured to the nearest mm and recorded.

Needle Pathology (abnormalities): One-hundred needles were randomly selected and observed for tip burn, basal necrosis, insect, and mottling type injury. Tip burn is basipetal necrosis from the needle tip, basal necrosis is a lesion within the fascicle sheath at the needle base, insect damage includes chewing or sucking types of activity, and mottling is a random chlorotic pattern on the needle (15). Percentage of needles injured by the various pathologies was calculated and recorded. Symptomless needles were labeled "healthy."

Fluoride Analyses: Collected foliage was dried for 48 hours in a forced-draft oven at 45°C, ground to pass a 20-mesh screen, and analyzed for total fluoride by the specific ion method (12). Results were calculated as ppm fluoride on a dry weight basis.

Data were subjected to stepwise multiple linear regression analysis to test for statistically important relationships. Meristic variables (percentages) were transformed by the arcsin for percentages (16) in an attempt to normalize the data. Acceptable sampling error was set at .20 at a probability of $P \leq .05$.

Results

Table 1 shows the sample size used for this study. The sampling error criterion was met for all variables except for basal necrosis. Stepwise multiple regression selects from the total array of vari-

Table 1
Data Base for Foliar Symptom and Impact Analyses

<table>
<thead>
<tr>
<th>Stratum</th>
<th>Severe</th>
<th>Moderate</th>
<th>Control</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of stands</td>
<td>8</td>
<td>10</td>
<td>10</td>
<td>28</td>
</tr>
<tr>
<td>No. of plots</td>
<td>137</td>
<td>104</td>
<td>90</td>
<td>331</td>
</tr>
<tr>
<td>No. of needles measured, length</td>
<td>11,700</td>
<td>8,325</td>
<td>7,125</td>
<td>27,150</td>
</tr>
<tr>
<td>No. of needles for pathology</td>
<td>46,800</td>
<td>33,300</td>
<td>28,500</td>
<td>108,600</td>
</tr>
<tr>
<td>No. internodes interpreted, retention</td>
<td>2,340</td>
<td>1,665</td>
<td>1,425</td>
<td>5,430</td>
</tr>
<tr>
<td>No. F⁻ on trees</td>
<td>468</td>
<td>333</td>
<td>285</td>
<td>1,086</td>
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</tbody>
</table>
ables only those that are related in a statistically significant fashion at a given probability. Any variable with $F = 4.00$ or greater was selected, the remainder were not used.

The statistical model employed was $Y = a + b_1x_1 + b_2x_2 + \ldots + b_ix_i + e$

where $x_1, x_2, \ldots, x_i$ represent fluoride concentration, percent mottled needles, etc., and $Y$ = any one of the various foliar characteristics, used one at a time. Thus, separate regressions were made using each of the foliar characteristics as the dependent variable while the rest were assigned independent status, except that fluoride was always considered independent. Means (not transformed) for each variable by species and strata are shown in Table 2 and a summary of the statistically significant relationships of foliar fluoride concentrations to the foliar characteristics is given in Table 3.

The regression summary presented in Table 3 supports the hypothesis that foliar fluoride concentration exerts a significant effect on several of the measured foliar characteristics of all species sampled. The sign of the regression and of partial correlations indicates whether the relationship is direct (positive) or indirect (negative). In *Pseudotsuga menziesii*, increased fluoride was associated significantly with decreased needle length, increased tip burn, increased insect injury, increased mottle, and lowered needle retention. Elevated foliar fluoride in *Pinus contorta* was related to decreased needle length and needle retention, increased tip burn and mottle; in *Pinus monticola* elevated fluoride was associated with increased tip burn, insect injury, and mottle.

True sample means of percent tip burn on *Pinus contorta*, percent mottle on *Pinus monticola*, and percent healthy on *Pinus monticola* for three needle ages in relation to mean fluoride concentration are shown graphically in Figures 1-3, data is from Table 2. As foliar age and fluoride concentration increased, percent healthy needles decreased in all species; the relationship with fluoride is weakest in the youngest foliage. Percent mottle and tip burn increased substantially in older foliage and as fluoride concentrations rose. The tip burn-fluoride relationship is weakest in *Pseudotsuga menziesii* but quite strong in *Pinus monticola* and *Pinus contorta*. The direct association of percent mottle with foliar fluoride was consistently strong within all three of the above species. Average fluoride in control foliage was less than 4 ppm.

**Discussion**

Statistical analyses do not provide proof of a causal relationship; however, they do enable one to make probability statements about events in time and space, such as the association of fluoride with conifer foliage abnormalities, reduced radial and height growth, and other characteristics; they can also be used to support or refute hypotheses.
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<td>1.96</td>
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<td>19.77</td>
<td>84.94</td>
<td>76.50</td>
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<td></td>
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<td>94.90</td>
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<td>22.19</td>
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1/ Percentages are original data, not transformed.
Table 1: Statistically Significant Relationships of Foliar Fluoride Concentrations to Various Foliar Characteristics within Species

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<th>Species</th>
<th>Dependent Variable</th>
<th>Intercept</th>
<th>Independent Variables</th>
<th>Coefficient</th>
<th>Std. Error of Coefficient</th>
<th>Std. Reg. Coefficient</th>
<th>For Coefficient</th>
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\( I^2 / F < .05 \)
Figure 1 Relation of Percent Tipburn to Fluoride Concentration for Three Needle Ages of Pinus contorta

Figure 2 Relation of Percent Mottle to Fluoride for Three Needle Ages of Pinus monticola

Figure 3 Relation of Percent Healthy to Fluoride for Three Needle Ages of Pinus monticola

- ■ 2-3 month-old needles
- ⭐ 14-15 month-old needles
- ● 26-27 month-old needles

FLUORIDE
of biological events. The literature concerning toxic effects of fluoride on plants has established that gaseous fluorides are indeed highly toxic to conifers and other vegetation at very low ambient concentrations. More than 60 percent of the time, fluoride at .20-.25 ppb caused injury to conifers (17) and tissue concentrations of 6-10 ppm caused adverse effects in fruit trees (18). Other studies (9,10), clearly established a causal relationship between fluoride and decline of Pinus ponderosa.

We have not measured airborne fluoride; tissue analyses of fluoride were used as the index of fluoride pollution. Elevated foliar fluoride was associated with increased incidence of foliar abnormalities such as tip necrosis, mottle, decreased needle retention and length, as observed and measured on several coniferous species. Therefore, based on this data and supportive literature, it is concluded that fluoride from the aluminum plant caused these adverse foliar effects.

Foliar injury generally appeared at foliar concentrations less than 10 ppm, fluoride-related tip burn on Pinus monticola—a very sensitive species—at 5-8 ppm, tip burn on Pinus contorta at about 15 ppm F. Mottling, or chlorosis of foliage, was evident at less than 6-8 ppm F in Pinus monticola and Pseudotsuga menziesii and at 12-15 ppm in Pinus contorta. Thus, based on visible foliar characteristics, the data indicate that Pinus monticola is more sensitive to fluoride than Pinus contorta and Pseudotsuga menziesii. Figure 3 shows the relationship of "percent healthy" foliage to fluoride for Pinus monticola. "Percent healthy" equals 100 minus the combined influence of all other pathologies. The graph clearly shows that "percent healthy" begins to decrease at less than 10 ppm fluoride for all ages of foliage. There does not appear to be a threshold effect; adverse effects begin at slightly over baseline concentrations, agreeing with other data (17,18). It is concluded that no emission or ambient fluoride standard allowing detectable amounts of atmospheric fluoride will truly protect coniferous vegetation.

Bibliography


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FLUORIDE
BONE MINERAL ANALYSIS IN PERSONS WITH LONG-TIME FLUORIDE EXPOSURE

by

Halle, Bitterfeld, Heidenau, G.D.R. and Martin, C.S.S.R.

SUMMARY: The bone mineral content and the width of the left radius of persons with long-term fluoride exposure were determined by means of the bone mineral analyzer. Observations were made on 245 aluminum smelter workers exposed to high atmospheric fluoride and compared to 292 workers in another aluminum factory with lower fluoride exposure. A third group consisted of 485 persons, whose drinking water has an average fluoride content of 2.5 ppm. All measured values were compared to normal values. We found an increase of bone mineral content and especially of the bone width which was dependent on the fluoride exposure (level and time). Photon-absorptiometry permits an early recognition of fluoride-dependent changes in bones and is suitable for follow-up studies on persons with long-term exposure to fluoride.

Since Roholm published his classical monograph about fluoride intoxication in 1937 (1) many research groups have been working on the effect of fluoride on the living organism. Meanwhile the fluoride literature has risen to the extraordinary number of some 20,000 publications. In addition to many reports on animal experiments, data about industrial fluorosis have become more and more numerous (2-17).

New methods of examination and experiments of quantification of histological and roentgenological changes in skeletal fluorosis have been reported. Now we are able to diagnose osteosclerosis even in its initial stage by the aid of X-rays. However, serial examinations of large population groups are still not possible with such new equipment as computertomography and roentgenological substance analysis which employs two different qualities of rays (18-19).

Another means of estimating bone density and mineral content, which would permit examination of large groups of persons, is the bone mineral analyzer, which works on the principle of photon-absorptiometry (22).

We obtained such an American apparatus (model 178/NORLAND - In-

From Halle, Bitterfeld, Heidenau, G.D.R. and Martin, C.S.S.R.
It consists of a measuring and a computer part and can easily be transported by car which makes it suitable for examinations in factories at the place of work or for examination of population groups concerning their mineral content in different regions.

The measuring part of the bone mineral analyzer consists of a detector of scintillation and of a monochromatic radiation source, which emits radiation focussed by a collimator. We use iodine as radiation source, which has to be exchanged every 3rd month.

Methods

As to the site of bone to be measured we selected the transition from the middle to the distal third of the forearm at the radius, because the range of variation in male and female humans is lowest when measuring the radius (21) and because the radius of peripheral bones reflects reliably the mineral content at spine and pelvis.

By means of a gum-water-cushion the irregularity of soft parts is compensated. The scanner approaches the bone with constant speed, first measuring the absorption of soft parts and subsequently the absorption of bone.

The rays of the radiated photons are absorbed according to their mineral content. Their scintillations are transformed into electric impulses. From the integral of the absorption curve the mineral content of bone in gram per centimeter is fed by the computer part. In addition, the bone width is measured. In order to compare the individual results, considering the variable bone width, it is customary to give the ratio of the measured mineral content and the bone diameter (in gram per square centimeter).

Four measurements are carried out at the left radius, from which the average value is recorded. The reproducibility of measurements is very good, the average range of errors for the mineral content of bone and the bone width amounts to 2% (22). The examination of a patient including the documentation requires approximately 5 minutes. The above-described method seems to be very suitable for examinations of persons with long fluoride exposure.

We were especially interested in the mineral content of bone and the bone width of persons who showed no distinct signs of bone fluorosis by other examinations (roentgenological, biochemical, and clinical findings). This is an exact method for in vivo examinations and reveals changes before the signs of chronic fluoride intoxication occur.

Method of Examination

The upper portion of Table 1 represents results based on an
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<th>Group</th>
<th>Age-Class</th>
<th>Number of Cases</th>
<th>Exposed (years)</th>
<th>Mineral Content Mean</th>
<th>S.D.</th>
<th>Bone Width Mean</th>
<th>S.D.</th>
<th>Quotient Mean</th>
<th>S.D.</th>
</tr>
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<td>1. (Al-smelter with 3.2 mgF⁻/m³ in air)</td>
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<td>17</td>
<td>25.9</td>
<td>1.30</td>
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S.D. = Standard Deviation
examination of 245 male aluminum smelter workers from a chemical factory near the town of Halle. At their place of work the average fluoride concentration in the air was 3.2 mgF\(^-\)/m\(^3\).

The second group examined were 292 workers of an aluminum factory in Czechoslovakia. The fluoride content in the air of their halls averaged less than 2.75 mgF\(^-\)/m\(^3\) during the past few years. No one in either group had clinical evidence of bone fluorosis on routine prophylactic examinations (clinical and roentgenological). All those suspected of fluorosis had already changed their job and were no longer exposed to fluoride.

The third group included 195 male and 290 female persons, aged 15 to 89, residing near a hydrofluoric acid factory (23) whose drinking water has an average fluoride content of 2.5 ppm. These subjects had only worked in the hydrofluoric acid factory for a short time or not at all. The average periods of exposure were 10 to 25 years except in the youngest age group.

These three groups were compared with 1,050 "normal" persons (male and female) of different ages. The single age decade groups in our three fluoride-exposed groups were compared with the age decade groups of normal people and the significance was calculated by means of the t-test (Table 2).

<table>
<thead>
<tr>
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<td>Comparisons of the 4 Groups with Long-Term Fluoride Exposure With Normal Persons at 5% Significance Level</td>
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<table>
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<tr>
<th>Group</th>
<th>Type</th>
<th>70-89</th>
<th>60-69</th>
<th>50-59</th>
<th>40-49</th>
<th>30-39</th>
<th>10-29</th>
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</thead>
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<tr>
<td>1. Al-smelter with 3.2 mgF(^-)/m(^3)</td>
<td>Min. cont.</td>
<td>s</td>
<td>s</td>
<td>s</td>
<td>s</td>
<td>s</td>
<td>s</td>
</tr>
<tr>
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<td>Bone w.</td>
<td>ns</td>
<td>s</td>
<td>s</td>
<td>s</td>
<td>s</td>
<td>s</td>
</tr>
<tr>
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<td>Quotient</td>
<td>s</td>
<td>s</td>
<td>s</td>
<td>ns</td>
<td>s</td>
<td>s</td>
</tr>
<tr>
<td>2. Al-smelter with &lt; 2.75 mgF(^-)/m(^3)</td>
<td>Min. cont.</td>
<td>s</td>
<td>s</td>
<td>s</td>
<td>s</td>
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<td>s</td>
</tr>
<tr>
<td></td>
<td>Bone w.</td>
<td>s</td>
<td>s</td>
<td>s</td>
<td>s</td>
<td>s</td>
<td>s</td>
</tr>
<tr>
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<td>Quotient</td>
<td>ns</td>
<td>s</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
</tr>
<tr>
<td>3. Males with 2.5 ppm F(^-) in drinking water</td>
<td>Min. cont.</td>
<td>ns</td>
<td>ns</td>
<td>s</td>
<td>ns</td>
<td>s</td>
<td>ns</td>
</tr>
<tr>
<td></td>
<td>Bone w.</td>
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<td>ns</td>
<td>ns</td>
<td>ns</td>
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<td>ns</td>
<td>ns</td>
<td>ns</td>
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<tr>
<td>4. Females with 2.5 ppm F(^-) in drinking water</td>
<td>Min. cont.</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
<td>s</td>
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<tr>
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<td>Bone w.</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
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<td>ns</td>
<td>ns</td>
<td>ns</td>
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<td>t-test according to WELCH</td>
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</table>

By the computer ROBOTRON 300 regression was made within the single age classes to determine the relation between age and exposure time and single measuring results. Only in the youngest and oldest age groups of those exposed to high fluoride levels did we find a correlation between exposure time and bone mineral.
Results

Figure 1 presents the mineral content of bone in our three fluoride-exposed groups in comparison with normal values of male persons of the same age.

The aluminum smelter workers from the district of Halle showed a distinctly increased mineral content with the highest exposure to fluoride. The maximum mineral content occurred at ages 30 to 49, but persons over 60 showed an approximately 20% higher mineral content than normal subjects. The differences are significant (P = 1%).

In the aluminum smelter workers from Czechoslovakia with a lower fluoride exposure to age-dependence of mineralization could be seen, for unexplained reasons. These values were controlled and found to be correct. In all age decade groups we found a significant difference compared with the controls except for the age-group from 30 to 39 years.

The third curve demonstrates the finding of male persons living near the hyd ofluoric acid factory whose drinking water has an average fluoride content of 2.5 ppm. Here we can see a shifting of the maximum bone mineral content to the right, namely from 40 to 49 years. The difference is remarkable and a significance exists in the age classes 10 to .9 years and 40 to 49 years.

The bone width is demonstrated in Figure 2 which shows that the width of bone increases with advancing years, as is normal. Here again the workers with higher fluoride exposures show the highest values, followed by the two other fluoride groups. This can be explained if we consider that also periosteally the fluorotic bone is slightly thickened (24,25).

Figure 3 demonstrates the quotient of mineral content and bone width. Here the differences are not very distinct. However, the sequence is the same as in the other figures. Consequently, the mineral content is increased to a slightly higher degree than the bone width.

Figures 4 and 5 represent the conditions in females whose fluoride content in drinking water is 2.5 ppm. They too showed a deviation from normal values, but not as high and only partially significant.

Discussion

In 1973 Donath et al. (26) studied, on a healthy population of Switzerland, the influence of the natural calcium and fluoride supply and of calcium supplementation on bone mineral content. They found no significant differences in bone mineral content between a population group of Geneva and the inhabitants of a village in the mountains where the natural fluoride content in drinking water is approximately 10 mg/l.
Nilsson (27) in a 1968 report on the influence of fluoride naturally in water on bone density found a "suggestive" difference between two population groups with different fluoride content in drinking water.

According to Hamamoto et al. (28), Kumar and Harper (29), Siddiqui (30), and Singh (31), fluoride-induced bone changes occur at a 6 to 8 ppm level of fluoride in drinking water.* In our own group with 2.5 ppm fluoride in drinking water we found a higher mineral content in com-

parison with normal people and significant differences, especially in bone mineral content, which seem to be related to the degree of fluoride exposure.

Finally, we want to emphasize that photon-absorptiometry permits an early recognition of fluoride-dependent changes in bone mineral content. This method is suitable for investigations of large population groups, but often fails in individual cases because the range of dispersion is larger (see Table 1).

Within our extensive prophylactic examinations of working people in the chemical industry already reported by Franke (7) we plan further studies of bone mineral content and bone width of fluoride-exposed workers. This possibility of an early diagnosis enables us to shift workers to another type of work before the occurrence of stage I and II bone fluorosis and therefore to avoid severe occupational disease.

Bibliography


Discussion

Dr. Teotia: I must congratulate the speaker on this first study of its kind using the photon absorptiometric method.

Dr. Czerwinski: We need exact methods for diagnosing osteosclerosis and establishing the relationship between diseased and normal bone. Can you compare the effectiveness of your method with that of X-rays?

Dr. Runge: We studied 1000 persons with fluoride-exposure. It would have been difficult to cover so much ground with X-rays or other techniques. In former investigations in aluminum workers we found a significant correlation between sclerosis and fluoride content of bones and a marked increase in bone width which was more pronounced than bone mineral content.

Question: If I understand you correctly you are just scanning mass surface in forearm. If background absorption is a problem, would it be possible to use two different camera sources? Is elimination of background a problem?

Dr. Runge: It is not a problem because the computer calculates these parameters. It does not measure calcium, only general mineral content.

Dr. Wix: What happens to the workers? Do they want to change their jobs? Do they resort to legal measures?

Dr. Runge: With this method prefluorosis is discernible with minor changes in bones which are probably reversible. If we diagnose fluorosis, stage I or more (according to Roholm), the worker must change his job and he receives a pension.

***************

FLUORIDE
FLUORIDE IN SALT AFFECTED SOILS OF
LA PAMPA (REPUBLICA ARGENTINA)

by

R.S. Lavado and N. Reinaudi
Santa Rosa, Argentina

SUMMARY: Data on both the total and the water-soluble fluoride in salt affected soil of La Pampa (Argentina) are presented. The total fluoride ranges between 24 and 1220 ppm and the water-soluble fluoride between 0.53 to 8.33 ppm.

The concentration of water-soluble fluoride correlates with the pH \( r = 0.824 \) and the salinity \( r = 0.521 \) of the soil. We concluded that the water-soluble fluoride is associated with salt concentrations and even more with soil pH, which in the alkaline state affects the fluoride's solubility, reaching high values.

Analysis of three soils which were neither saline nor alkaline showed that values of both total fluoride and water-soluble fluoride were low and within normal limits.

Introduction

In certain areas of arid and semiarid regions of Argentina groundwaters are rich in fluoride. In several towns of the Provinces of La Pampa and San Luis, drinking water must be defluorinated and cases of fluorosis have been found in inhabitants of rural areas (1,2).

Although investigations on water fluoride in Argentina have been carried out for many years (3,4) information about soils and plant fluoride is limited*. We studied salt affected soil because they are influenced by capillary rise of saline groundwaters or irrigation waters. Both could carry large amounts of fluoride to the soil.

Materials and Methods

Soils: Soil samples were selected from different places within

*The following is the only report on this subject known by the authors: Ares, J.O.: Fluoride Cycling Near a Coastal Emission Source. JAPCA, 28: 344-349, 1978.

From the Facultad de Agronomía, Universidad Nacional de La Pampa, Santa Rosa (L.P.), Republica Argentina. The senior author is member of Scientific Investigator Career of Consejo Nacional de Investigaciones Científicas y Técnicas de la Argentina.
the territory of La Pampa Province (Table 1). Samples 1 to 19 are obtained from grazing areas, mainly for cattle but also for sheep. In all cases the soils are covered by natural vegetation. In certain areas they are halophytes. Samples 20 to 23 are from irrigated areas whereas samples 24 to 26 are from cultivated areas.

Analytical Procedure: In each sample three determinations were made of total and water-soluble fluoride by the following methods. The

<table>
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<th>Depth (cm)</th>
<th>E.C.* mmho/cm</th>
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<td>26</td>
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</table>

* Electrical conductance in saturation extracts.
total fluoride was extracted at 165° C by the sulfuric acid method with steam distillation for separation of fluoride from interfering substances. Measurement of fluoride in solution was made with the acid-zirconium method (5,6). The water-soluble fluoride was obtained by extracting the soil solution from 1:1 soil-water suspension, separating the interfering substances and measuring the fluoride with the above-mentioned methods (5,6).

Results and Discussion

Table 2 shows average data of total and water-soluble fluoride. The mean values for total and water-soluble fluoride, respectively, are 388.4 ppm and 5.53 ppm in alkaline soils; 344 ppm and 2.68 ppm in saline soils; and 283 ppm and 0.14 ppm in normal soils. Control samples 24, 25 and 26 from cultivated soils which have not been affected by groundwater nor by irrigation, have values for soil fluoride which are considered normal by several authors (7-9) and are in agreement with environmental characteristics. In the other samples from halomorphic soils the total fluoride concentration fluctuates between 24 to 1220 ppm. These values are within the usual level of fluoride in soil (7-9), although some consider these values somewhat high.

<table>
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<th>Sample</th>
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<th>Water Soluble Fluoride (ppm)</th>
<th>Sample</th>
<th>Total Fluoride (ppm)</th>
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<td>2.10</td>
<td>20</td>
<td>875</td>
<td>2.13</td>
</tr>
<tr>
<td>8</td>
<td>170</td>
<td>1.92</td>
<td>21</td>
<td>40</td>
<td>0.53</td>
</tr>
<tr>
<td>9</td>
<td>96</td>
<td>5.70</td>
<td>22</td>
<td>500</td>
<td>1.73</td>
</tr>
<tr>
<td>10</td>
<td>145</td>
<td>2.50</td>
<td>23</td>
<td>117</td>
<td>2.82</td>
</tr>
<tr>
<td>11</td>
<td>112</td>
<td>5.70</td>
<td>24</td>
<td>266</td>
<td>0.11</td>
</tr>
<tr>
<td>12</td>
<td>90</td>
<td>7.95</td>
<td>25</td>
<td>450</td>
<td>0.11</td>
</tr>
<tr>
<td>13</td>
<td>270</td>
<td>3.66</td>
<td>26</td>
<td>133</td>
<td>0.20</td>
</tr>
</tbody>
</table>

We also observe considerable horizontal and vertical heterogeneity, which is not unexpected considering the different parent material, age, climate, etc. of these soils.

In the salt-affected soils, the water-soluble fluoride varies between 0.53 and 8.33 ppm. Values are well above "normal" in noncontaminated soils (8). The samples from irrigated areas usually have low values.
No relationship was found between total and water-soluble fluoride ($r = 0.071$), as reported by others. On the other hand, a high positive correlation existed between soil pH and water-soluble fluoride for all soils, except for the three normal soils (correlation coefficient $r = 0.763$). If one considers only the alkaline soils, the correlation between pH and water-soluble fluoride rises to $r = 0.824$.

No correlation between salinity (mmho/cm) and water-soluble fluoride was found for all soils ($r = 0.071$), but the correlation between the salinity of saline soils alone and water-soluble fluoride is positive and moderately high ($r = 0.521$).

We estimate that the higher the saline concentration of soil solution, the higher is the concentration of water-soluble fluoride, with some modifications due to the solubility of CaF$_2$, products of solubility, adsorption, etc. The soil reaction in particular influences considerably the concentration of fluoride, which accounts for the change in the correlation coefficients between water-soluble fluoride and salinity in all soils or in saline soils only.

In alkaline soils the pH plays an important part in the solubility of fluoride (10,11), as shown in Figure 1.

![Relation Between pH and Water-Soluble Fluoride](image)

The importance of the pH of the soil in the solubility of fluoride is also shown by the fact that in normal soils water-soluble fluoride is only 0.05% of the total fluoride, whereas in saline soils this percentage rises to 0.78% and in alkaline soils, it is 1.24% of the total fluoride.
Although it is known that a combination of fluoride and salinity exert an accumulative effect on some cultivated plants (12), information is limited about the content and influence of fluoride in the natural grasses of the region and in the animals which graze on it (13). Judging by the results of this study it must be important in certain areas and requires additional investigation.

Alberto Sosa, Juan A. Vaquero, and Abel A. Parodi collaborated in this study.

Bibliography


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Volume 12 Number 1
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THE EFFECT OF FLUORIDE ON THE POLYPHENOLOXIDASE AND PEROXYDASE ACTIVITIES OF TOBACCO LEAVES (NICOTIANA TABACUM L. VAR PB 91)

by

A.M. Lhoste
Grenoble Cedex, France

SUMMARY: Electron microscopy has revealed that chloroplasts are the first organelles damaged by fluoride in plant cells, the main alteration being in the intra-thylacoidal spaces of grana. Moreover, electron microscopy of enzymes indicates that polyphenoloxidase activity takes place in the intra-thylacoidal spaces. The current study is concerned with the effect of fluoride on polyphenoloxidase activity in plants.

Plants of Nicotiana tabacum L. var. PB 91 were fumigated for several weeks with 250 μg HF/m³, and the polyphenoloxidase activity of the leaves was compared with that of control plants. Spectroscopic measurements of the extracts revealed that fluoride increased the polyphenoloxidase activity. Similar results were obtained on peroxidase activity.

Introduction

Our aim was to determine the physiological effects of fluoride on vegetation prior to the appearance of visible necrotic lesions. All our observations were made on parts of the plants which were still green and which had been subjected to the action of fluoride.

As we have previously shown with Zea mays, chloroplast is the leaf organelle most susceptible to fluoride (1,2). Fluoride causes changes mainly at the level of intra-thylacoidal spaces of grana.

We have been able to localize by cytochemical methods (3) the presence of polyphenoloxidasic activity inside these intra-thylacoidal spaces. For a better understanding of the effect of fluoride, it is essential to learn how polyphenoloxidase acts.

Moreover, we have studied the effect of fluoride on peroxidase, since we have localized this enzyme in peroxysomes (3) the functioning

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of which is closely related to that of chloroplasts.

Materials and Methods

The tobacco plants (Nicotiana tabacum, L. var. PB 91), which are more fluoride-resistant than maize, came from cuttings planted in pots provided with a supply of irrigation water. They were used for the experiment after two or three leaves had appeared. At this stage, five plants were housed in a fumigation chamber and five control plants outside the chamber under identical conditions except for the exposure to fluoride.

Two series of cultures were thus produced with fluoride levels of 125 and 250 µg/m³ (or parts per billion) inside the fumigation chamber. Samples were taken after 2 weeks of growth. At this stage the tobacco plants had about 10 leaves. One third and one half respectively of their apical extremities were necrotic.

One control plant and one fluoridated plant were set aside to determine the amount of fluoride accumulated in the leaf tissues (4,5).

Production of Enzymatic Extract

We chose completely green shoots as well as the oldest leaves which did not present necrotic lesions. The material thus obtained was weighed immediately in order to establish the fresh weight. It was then ground in a phosphate buffer as recommended by Stafford and Galston (6).

The resulting ground mass was centrifuged, still at 4° centigrade, at a speed of 12 500 g for 10 minutes. The pellet contained all the cellular debris; the supernatant was used as enzymatic extract.

Spectrophotometric Measurement of Enzymatic Activity

We used an Acta C III Beckman spectrophotometer at a temperature thermostatically controlled at 25°C. The substrate used for the measurements of polyphenoloxidase activity was dihydroxyphenylalanine (DOPA), which produces with the enzyme an orange colored complex, absorbed at 475 nm (7-9). The substrate used for the measurement of peroxycodaslic activity was guaiacol which produces with the enzyme an orange colored complex, absorbed at 740 nm (6).

The enzyme extract was added at zero time. For an element of comparison between the different curves we chose the Optical Density read after one minute and divided by the weight of proteins contained in the extract, i.e. O.D./nm/µg proteins. Protein content of the enzyme extract was measured by the method of Varley (10,11).
Results

The results are summarized in Table 1. This table shows a heavy increase in polyphenoloxidase activity in the fluoridated tobacco plants, particularly very marked in the young shoots, namely 263%, but smaller in mature leaves, namely 126%. We obtained exactly the same result with regard to peroxidase activity, summarized in Table 2. A marked increase (200%) of this activity took place in the young shoots. In older leaves, on the other hand, peroxidase activity was the same in the enzymatic extracts from healthy tobacco as in polluted tobacco.

Table 1

Polyphenoloxidases Activities of Healthy and Fluoride Polluted Tobacco (D.O/mn/μg of Protein)

<table>
<thead>
<tr>
<th>Age of Leaves</th>
<th>Fluoride Content (ppm)</th>
<th>Quantity of Enzyme Extract/2 ml of Substrate</th>
<th>DO/mn/μg of Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy Tobacco</td>
<td>Polluted Tobacco</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bud</td>
<td>68.6*</td>
<td>200 μl</td>
<td>2.3</td>
</tr>
<tr>
<td>Bud</td>
<td>19.2</td>
<td>100 μl</td>
<td>44</td>
</tr>
<tr>
<td>Adult</td>
<td>41.6</td>
<td>100 μl</td>
<td>19</td>
</tr>
<tr>
<td>Bud</td>
<td>5057*</td>
<td>200 μl</td>
<td>8.3</td>
</tr>
<tr>
<td>Bud</td>
<td>561</td>
<td>100 μl</td>
<td>160</td>
</tr>
<tr>
<td>Adult</td>
<td>2410</td>
<td>100 μl</td>
<td>43</td>
</tr>
</tbody>
</table>

*These values correspond to the fluoride content in the entire plant.

Table 2

Peroxydases Activities of Healthy and Fluoride Polluted Tobacco (D.O/mn/μg Protein)

<table>
<thead>
<tr>
<th>Age of Leaves</th>
<th>Fluoride Content (ppm)</th>
<th>Quantity of Enzyme Extract/2 ml of Substrate</th>
<th>DO/mn/μg of Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy Tobacco</td>
<td>Polluted Tobacco</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bud</td>
<td>68.6*</td>
<td>200 μl</td>
<td>47.9</td>
</tr>
<tr>
<td>Bud</td>
<td>19.2</td>
<td>50 μl</td>
<td>54</td>
</tr>
<tr>
<td>Adult</td>
<td>41.6</td>
<td>50 μl</td>
<td>185</td>
</tr>
<tr>
<td>Bud</td>
<td>5057*</td>
<td>200 μl</td>
<td>144</td>
</tr>
<tr>
<td>Bud</td>
<td>561</td>
<td>50 μl</td>
<td>192</td>
</tr>
<tr>
<td>Adult</td>
<td>2410</td>
<td>50 μl</td>
<td>195</td>
</tr>
</tbody>
</table>

*These values correspond to the fluoride content in the entire plant.
Thus we found similar results concerning the effect of fluoride on the two enzymatic processes which we studied: fluoride has an early effect on young leaves in which it causes an increase in polyphenol oxidase and peroxidase activities. As these two enzymes are characteristic phenomena of aging, we conclude that the aging process is accelerated by fluoride.

When the leaves mature, the differences in the activity between healthy and polluted tobacco are less spectacular: we believe that the healthy and the polluted leaves have reached the same stage of aging as far as their polyphenoloxidase and peroxidase activities are concerned.

Discussion

The increase of polyphenol oxidase activity is often the symptom of a metabolic disturbance in relation to growth (12,13), maturation (14,15), and senescence (16). This could also be a consequence of tissular or cellular injuries induced by pathogenic agents like fungi (17-19) and viruses (20,21). On the other hand, Siegenthaler and Vaucher-Bonjour (22), showed that polyphenol oxidase activity is closely linked with aging processes. In consequence, the fluoride inducing an increase of polyphenoloxidase activity could be involved in accelerating the aging process.

We must cite meanwhile a contradictory result obtained by Lee and Miller (8) on soybean leaves, in which the polyphenol oxidase activity is inhibited by fluoride. Yee-Meiller (23) showed an increase of phenol content in spruce needles polluted by fluoride.

Our results concerning peroxidase activity support our theory that fluoride could induce premature aging. Several workers (8,24,25) agree that peroxidase activity is stimulated by fluoride.

In conclusion, it appears that fluoride has an early effect on polyphenoloxidase and peroxidase activities in tobacco leaves. These activities are greatly enhanced by fluoride, chiefly in the shoots and the young leaves, even before external signs of necrosis appear, thus causing an acceleration of the aging process.

Acknowledgement

The author wishes to thank Mrs. A.R. Cooper, MIL, for translation into English.

Bibliography


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**Discussion**

Dr. Oelschlager: Fumigation with 250 µg HF/m³ caused only slight browning but how do you explain that exposure in the natural environment to 2 µg caused vegetation to turn brown?

Dr. Lhoste: In the natural environment, fluoride accumulates over a prolonged period but the duration of fumigation is shorter. Therefore it is not as harmful.

Dr. Miller: Would the shock to the plant by fumigation with relatively large amounts of HF affect the degree of damage?

Dr. Lhoste: This is difficult to say. Incidentally, although we used the same procedure the results differed with shoot and adult plants.

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**DENTAL CARIES AND FLUORIDE TOXICITY**

by

O.P. Bagga, S.P. Mehta, K. Berry, L. Sarada and V. Parkash

New Delhi, India

**SUMMARY:** 491 persons of Dabri village near Delhi, belonging to various age groups, were investigated for fluorosis. The incidence of skeletal fluorosis was quite high in the population (60.89%). The fluoride content of the drinking water in the village ranged between 1.5 to 3.93 ppm with an average of 2.76 ppm.

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Dental fluorosis affected all age groups, adults more than children, males more than females and school children more than young toddlers. Permanent as well as deciduous teeth. Dental mottling was associated with caries in 15.7 percent of the total fluorosis cases and in 14.18 percent of the school children. The severity of fluorosis was influenced by occupation and socio-economic status of the individual. No correlation could be established between skeletal fluorosis and dental fluorosis.

Livestock was as severely affected as humans. The youngest subject with dental mottling was a calf one month old. The major supply of fluoride was milk and water. Milk contained 5 to 20 times normal levels of fluoride.

Endemic fluorosis has been reported from various parts of the world where drinking water contains excessive quantities of fluoride naturally. Shortt et al. (1) considered a period of 30-40 years of residence necessary for the development of skeletal fluorosis, whereas according to Singh and Jolly (2) 10-20 years were sufficient for skeletal fluorosis to develop. Siddiqui (3) suggested that fluorosis can develop in as short a period as 4 years where the climate is hot and the diet is nutritionally poor.

Dental fluorosis has been accepted as a sensitive index of chronic fluoride toxicity and may be its earliest and only visible manifestation in children. Furthermore, a relationship between dental fluorosis and the fluoride content of drinking water has been established but the minimum safe limit is not known. Ericsson (4) stated that "1 ppm fluoride would be appropriate to a water supply in Britain, but would be too great for countries such as India and Japan."

McKay and Black (5) were the pioneers in describing dental mottling but its definite association with fluoride toxicity was reported by Lantz and Smith (6). Since then, a number of reports have appeared from various parts of the world. However, Shortt et al. were the first to report cases from the Indian Nellore district of Madras Presidency. Later, others made similar observations from other States of India and other countries (3,7-12).

Anand et al. (13) reported endemicity of fluorosis around Delhi in a village the drinking water of which contains 0.4 - 2.1 ppm of fluoride. He observed skeletal fluorosis and dental mottling associated with dental decay. As 1 - 1.2 ppm of fluoride in drinking water has been advocated as an anticariogenic measure (14), the present study was
designed to determine the safety of this measure. Dabri village, which is adjacent to Bindapur village, was selected for investigation.

Material and Methods

In Dabri village, total population of 800, the main sources of drinking water are 86 hand pumps, 3 wells and 1 pankhat (impounded water reservoir). Its population is composed of Jats, Brahmins, Harijans and Kumhars, but the main bulk are Jats and Harijans. In both communities, the inhabitants irrespective of sex, work in the fields.

Water samples for fluoride analysis were collected in the early hours of the morning. By means of a questionnaire, information was obtained regarding complaints such as anorexia, vomiting, gastrointestinal disorders, vague aches and pains in the body, easy fatigability, general debility, backache and diminished capacity to work. Each individual was given a thorough medical check-up. Special attention was paid to bones and joints for evidence of exostoses, limitation of movement, stiffness of neck and lumbo-dorsal spine, anemia, goiter and other relevant signs. The teeth were examined by the dentist for evidence of chalky opacities, yellow to brown pigmentation and pitting of enamel, chipping of edges, etc. The population showing dental fluorosis was divided into four categories namely, questionable, mild, moderate and severe.

Animals were surveyed by veterinary surgeons for signs of fluorosis. Milk samples were collected for analysis of their fluoride content. Serum and urine samples were also collected and the results are reported elsewhere.

Water was analyzed by the method of Scott (15). The serum and urine samples were investigated by the fluoride electrode technique as modified by Taves (16). Milk, after deproteinization, was analyzed in the same way as water.

Observations

Three repeat analyses were done on each sample of drinking water obtained from 86 hand pumps, 3 wells and 1 pankhat, the results of which are given in Table 1.

Of the total population of 800, 491 persons were examined. The remaining were not available because they were either working outside the village or were visiting relatives. For purposes of analysis the population was divided into two groups namely (A) General Population and (b) School Children.

(A) General Population: Out of 491 examined, 299 presented evidence of fluorosis. In general, 60.89 percent of the total population suffered from fluorosis. All except 11 had dental mottling. The
Table 1
Fluoride Content in Drinking Water in Dabri Village

<table>
<thead>
<tr>
<th>Fluoride Content</th>
<th>N - W</th>
<th>N - E</th>
<th>CEN</th>
<th>S - W</th>
<th>S - E</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average Fluoride (ppm)</td>
<td>2.638</td>
<td>1.5</td>
<td>1.65</td>
<td>3.93</td>
<td>1.47</td>
</tr>
<tr>
<td>S.D.</td>
<td>+0.528</td>
<td>+0.133</td>
<td>+0.2515</td>
<td>+0.344</td>
<td>+0.113</td>
</tr>
<tr>
<td>S. Error of Mean</td>
<td>0.103</td>
<td>0.368</td>
<td>0.44</td>
<td>0.81</td>
<td>0.246</td>
</tr>
<tr>
<td>Coeff. of Variation</td>
<td>20.015</td>
<td>0.866</td>
<td>0.152</td>
<td>8.72</td>
<td>0.246</td>
</tr>
</tbody>
</table>

N = North zone, S = South zone, E = East zone, W = West zone, CEN = Central

11 cases of skeletal fluorosis were radiologically positive. Fluorosis was more severe in men than in women and worse in adults than in children (Tables 2 and 3, Figs. 1 and 2).

As regards severity, fluorosis did not discriminate between toddlers and children, adolescents and adults, men and women. However,

Table 2
Incidence of Dental Fluorosis in Dabri Village

<table>
<thead>
<tr>
<th>Persons Examined - 491 (Total Population - 800)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults (M - 85)</td>
</tr>
<tr>
<td>(F - 124)</td>
</tr>
<tr>
<td>Children (M - 134)</td>
</tr>
<tr>
<td>(F - 148)</td>
</tr>
<tr>
<td>Total Percent with Fluorosis</td>
</tr>
<tr>
<td>No. of Adults with Fluorosis out of 209</td>
</tr>
<tr>
<td>No. of Children with Fluorosis out of 282</td>
</tr>
</tbody>
</table>

<p>| |</p>
<table>
<thead>
<tr>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>209 (42.56%)</td>
</tr>
<tr>
<td>282 (57.43%)</td>
</tr>
<tr>
<td>60.9%</td>
</tr>
<tr>
<td>146 (69.85%)</td>
</tr>
<tr>
<td>153 (54.25%)</td>
</tr>
</tbody>
</table>

Table 3
Sex Incidence of Dental Fluorosis in Dabri Village

<table>
<thead>
<tr>
<th>Persons Examined - 491</th>
</tr>
</thead>
<tbody>
<tr>
<td>General Population with Dental Fluorosis</td>
</tr>
<tr>
<td>299 (60.89%)</td>
</tr>
<tr>
<td>Male Adults with Dental Fluorosis out of Total of 85</td>
</tr>
<tr>
<td>72 (84.7%)</td>
</tr>
<tr>
<td>Female Adults with Dental Fluorosis out of 124</td>
</tr>
<tr>
<td>74 (59.7%)</td>
</tr>
<tr>
<td>Male Children with Fluorosis out of 134</td>
</tr>
<tr>
<td>79 (58.9%)</td>
</tr>
<tr>
<td>Female Children with Dental Fluorosis out of 148</td>
</tr>
<tr>
<td>74 (50.0%)</td>
</tr>
</tbody>
</table>
the severity varied from mild to moderate in children below 8 years of age and from mild to moderate to severe in the remaining age groups (Table 4).

The incidence of dental fluorosis was highest among 5 to 15 year olds, it remained high up to the age of 40 and thereafter declined. Dental mottling was evident in a child aged 2, caries with dental fluorosis was seen after 5 years of age and reached its maximum between ages 20 and 50; 51.94 percent of the group showed total dental decay with dental mottling.

Analysis of the data relating to occupation and caste revealed that Kumhars (Potters) were the maximum sufferers but, since they constitute only 0.81 percent of the total population, it had no statistical significance. The same was the case with Muslims and Brahmins. Jats and Harijans formed the bulk of dental fluorotic cases and a large number of them were classified moderate to severe.
Table 4
Incidence of Dental Fluorosis in School Children

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Total No.</th>
<th>Normal Children</th>
<th>Normal w/o Caries</th>
<th>Mottling w/o Caries</th>
<th>Mottling w/ Caries</th>
</tr>
</thead>
<tbody>
<tr>
<td>Up to 8 1/2 years</td>
<td>44</td>
<td>12</td>
<td>27.3</td>
<td>28</td>
<td>63.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4</td>
<td>9.09</td>
</tr>
<tr>
<td>Above 8 1/2 years</td>
<td>90</td>
<td>27</td>
<td>30.0</td>
<td>48</td>
<td>53.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>15</td>
<td>16.6</td>
</tr>
</tbody>
</table>

Total incidence of dental fluorosis in school children - 70.89%; Mottling without caries - 56.7%; Mottling with caries - 14.18%

*63.6% of the children below the age of 8 1/2 years had dental fluorosis without caries and 9.09% with caries. Total is 72.69%.

(B) School Children: The school children were subdivided into (1) below 8 years of age and (2) above 8 years of age.

Evidence of fluorosis in the form of mottling varying from mild to severe was fairly high in both groups. It affected 70.89 to 72.69 percent of the children. Dental decay with dental mottling occurred in 14.18 percent of the children (Table 4). The youngest child with evidence of dental fluorosis was two years old. Surprisingly, 15.7 percent of the adult fluorotic cases also had evidence of dental decay (Table 5).

Table 5
Distribution of Dental Fluorosis by Age Group in Dabri Village

<table>
<thead>
<tr>
<th>Age (yrs.)</th>
<th>Persons with Fluorosis</th>
<th>Normal</th>
<th>Total</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>With Caries</td>
<td>Without Caries</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 - 5</td>
<td>0</td>
<td>14 (14.43%)</td>
<td>83</td>
<td>97</td>
</tr>
<tr>
<td>5 - 10</td>
<td>11 (12.35%)</td>
<td>57 (64.00%)</td>
<td>28</td>
<td>96</td>
</tr>
<tr>
<td>10 - 15</td>
<td>9 (10.11%)</td>
<td>59 (66.29%)</td>
<td>21</td>
<td>89</td>
</tr>
<tr>
<td>15 - 20</td>
<td>6 (11.32%)</td>
<td>29 (49.15%)</td>
<td>18</td>
<td>53</td>
</tr>
<tr>
<td>20 - 30</td>
<td>13 (21.66%)</td>
<td>30 (50.0%)</td>
<td>17</td>
<td>60</td>
</tr>
<tr>
<td>30 - 40</td>
<td>16 (34.02%)</td>
<td>15 (35.6%)</td>
<td>10</td>
<td>41</td>
</tr>
<tr>
<td>40 - 50</td>
<td>11 (45.83%)</td>
<td>4 (16.60%)</td>
<td>9</td>
<td>24</td>
</tr>
<tr>
<td>50 - 60</td>
<td>5 (31.25%)</td>
<td>5 (31.25%)</td>
<td>6</td>
<td>16</td>
</tr>
<tr>
<td>60 - 70</td>
<td>2 (50.0%)</td>
<td>2 (50.0%)</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>70 &amp; Above</td>
<td>4 (36.36%)</td>
<td>3 (27.27%)</td>
<td>4</td>
<td>11</td>
</tr>
</tbody>
</table>

Total 77 218 196 491 (15.7%) (44.4%) (39.91%)

Diet Survey: The entire community was strictly vegetarian, their

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staple food being wheat during summer and Bajra, maize and Sag (green leafy vegetables) during winter. Consumption of beans and pulses was low but the ingestion of milk, yogurt, lassi (butter milk) and butter was adequate.

Dental Fluorosis in Animals: Sixty animals (buffaloes, camels, calves, cows, dogs, etc.) were examined by the veterinary surgeons for evidence of dental fluorosis. Twenty-five showed evidence of mottling and browning of the teeth (41.7%). The youngest sufferer was a calf, one month old; the majority were above 5 months of age.

The presence of dental fluorosis in a child of two years and a calf of one month prompted us to analyze the milk which was found to provide a high level of fluoride to children in addition to drinking water. In adults, tea constituted an additional factor.

The custom of boiling milk in earthen vessels throughout the day is well established in these villages. This procedure concentrates the fluoride content 5 to 20 times its normal concentration.

Discussion

It is generally accepted that ingestion of 2 ppm of fluoride in drinking water for a prolonged period produces features of chronic fluoride toxicity as indicated by dental mottling in children during their first eight years of life and by osteosclerosis in about 10 percent of the adult population. Accumulation of fluoride occurs in teeth and bones. Young bones accumulate more than the older ones and cancellous more than compact bone. Weidman and Weatherell (17) demonstrated that the fluoride ions replace the carbonates of the bones and combine with magnesium ions forming magnesium fluoride complex. Weinmann and Sicher (18) reported that fluoride in bones affects the osteoblastic and osteoclastic activity. Seams of uncalcified osteoid tissue appear and disorganization of the lamellar system results in the defective Haversian canal system. However, no correlation has been found between the incidence of dental mottling and skeletal fluorosis. In the present study only 11 cases had radiological evidence of skeletal fluorosis though 123 presented various complaints suggestive of clinical fluorosis. Dental fluorosis was more common and involved 60.89 percent of the total population examined: more adults (69.85%) were affected than children (54.25%), and more men than women. No age group was spared; decidual and permanent teeth were equally affected.

Russell and Elvove (19) showed that fluoride effectively reduces susceptibility to dental caries when incorporated in the structure of teeth during their calcification or after their eruption. Zipkin et al. (20) demonstrated that increasing fluoride concentrations were associated with increased crystallinity of the hydroxyapatite with increase in its size and nearly perfect formation. This change in crystallinity re-
duces the effective surface area and decreases the area for deposition and orientation of carbon dioxide and citrate in particular. Jenkins and Speirs (21) determined the level of fluoride in various strata of the enamel and found that it concentrated more in the outer surface than in the deeper layers. They stated that "probably it is Nature's developmental arrangement of the concentration of fluoride and not a distribution that took place after the teeth had erupted." Recently, Ahrens (22) ingeniously placed 2-3 mm thick enamel sections in the mouth of medical students by means of acrylic appliances and observed that placing of a tablet of sodium fluoride of one milligram caused a temporary increment of 147 ppm of fluoride in the enamel in 30 minutes; however, no stable binding of enamel and fluoride took place. In the present survey, in spite of the high fluoride consumption, 15.7 percent of the total population had dental decay associated with dental mottling and 14.1 percent of the school children suffered in a similar manner.

The animal survey data authenticated the dental fluorosis found in humans but questioned whether or not tea is an important contributory factory. We believe that, in the present series, the dental fluorosis observed in animals and in toddlers and children is due to the high levels of fluoride in water and milk, especially since the concentration in some milk samples was as high as 27 ppm. In adults, the use of such concentrates of milk for the preparation of yogurt, lassi and tea further increases the supply of fluoride.

It has been proven beyond doubt that climatic environment, food habits and occupation influence the manifestations of fluorosis. In the present series the Kumhars, though small in number of the total population, were most severely affected (100%). Muslims were second, the Jats and the Brahmins were third and the Harijans last (Table 6, Fig. 3). The dietary survey facilitated the understanding of the high incidence in Jats and Brahmins, who consume large amounts of milk and milk products. However, the high incidence in Harijans, residing in a poverty stricken community, could not be explained.

Table 6
Distribution of Dental Fluorosis in Dabri Village (by Caste and Profession)

<table>
<thead>
<tr>
<th>Caste</th>
<th>Total Examined</th>
<th>Dental Fluorosis</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jaat</td>
<td>328</td>
<td>206</td>
<td>62.8</td>
</tr>
<tr>
<td>Harijan</td>
<td>107</td>
<td>63</td>
<td>58.7</td>
</tr>
<tr>
<td>Brahmin</td>
<td>28</td>
<td>18</td>
<td>64.3</td>
</tr>
<tr>
<td>Muslims</td>
<td>13</td>
<td>9</td>
<td>69.2</td>
</tr>
<tr>
<td>Barber</td>
<td>11</td>
<td>2</td>
<td>18.1</td>
</tr>
<tr>
<td>Kumhars</td>
<td>4</td>
<td>4</td>
<td>100.0</td>
</tr>
</tbody>
</table>

FLUORIDE
Figure 3
Severity of Fluorosis by Caste Groups

JAAT  HARIJAN  BRAHMIN  MUSLIM  BARBER  KUMHAR

SEVERE  MODERATE  MILD  VERY MILD

Acknowledgements

The authors are grateful to Dr. S. Chawla, Principal and Medical Superintendent, Lady Hardinge Medical College and Sucheta Kripalani Hospital, New Delhi, for encouragement and for providing facilities for this work. The authors owe special thanks to Dr. Singal, the dentist, Dr. Nayar and Dr. Dube, the veterinary surgeons, and to Dr. Ashish, Dr. Anita and Dr. Ravi Gupta for their untiring help in the epidemiologic survey.

Bibliography


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RENAL FLUORIDE EXCRETION AS A USEFUL PARAMETER FOR MONITORING HYDROFLUORIC ACID-EXPOSED PERSONS

by

A. Zober, M. Geldmacher v. Mallinckrodt and K.H. Schaller
Erlangen, D.B.R.


In the manufacture of lead crystal glass "acid polishing" is required to remove the opaqueness of the end product; glass is dipped into a 73% HF solution followed by a 66% H2SO4 solution. The urinary fluoride was determined in 20 workers from three plants involved in this procedure. Urine specimens of 9 nonexposed office workers in the same plants were used as controls. The 20 cases included two ex-workers, one retired for 3 months and the other for 3 years; they had been exposed to HF vapors for 3 and 34 years respectively. In each of the three plants the air was sampled close to the exposed areas during periods ranging up to 60 minutes. Urine was collected in mid-week for pre-shift and post-shift sampling. Spot samples as well as 24-hour samples were taken.

The atmospheric fluoride concentration ranged from 0.58 to 1.24 mg/m3 in factory A, it was 14.40 in factory B and 1.60 in factory C. The level in factory B exceeded the currently valid MAC value for HF.

Results: In the nine unexposed subjects, the urinary excretion averaged 0.5 mgF- /24h, which the authors considered normal in an area where drinking water contained 0.2 mgF- /l. In the exposed persons all urinary fluoride values were above these "normal" values; fluctuations in individuals were attributed to varying exposure conditions and non-reproducible exposure peaks.

In four subjects working directly on the dip, the pre-shift mean value after a 14 day working pause averaged 1.8 ppm and 8.1 ppm after a single day's 8 hour exposure. The mean pre-shift samples of the four persons contained 3.7 ppm F-.

A subject who had been exposed to HF for 34 years was excreting 66 ppm in the urine 3 years after his retirement, one of the highest values ever reported. According to the literature quoted, the tolerable limits for urinary fluoride concentrations range from 2 to 8 ppm per day; the U.S. National Institute for Occupational Safety and Health (NIOSH) in 1975 considered a range from 4 ppm pre-shift to 7 ppm post-shift safe with respect to development of fluorosis.

Daily renal fluoride elimination, related to inhaled fluoride, showed that only 20% was excreted. Assuming an average shift inhala-
tion of 20 m³ of air, excretion of only 20% of fluoride conflicts with other reported (40% to 60%) findings. Even in factory A and C where the atmospheric fluorides were below the MAC values for HF, two workers in each plant eliminated urinary fluoride in excess of the NIOSH limits. As inhalation of fluoride increased, its elimination decreased. During prolonged exposure to high levels, therefore, considerable accumulation of fluoride takes place in the body. No correlation between renal fluoride elimination and long-term exposure was observed. The coefficient of correlation was 0.3568 for all subjects who were studied.

In view of the difference in the physical and chemical state of inhaled fluoride (HF fumes vs. fluoride-containing dust) the authors believe that results from studies in the aluminum industry (dust) should not be compared with those in the glass industry (HF).

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SUBACUTE FLUOROSIS
A CONSEQUENCE OF ABUSE OF AN ORGANOFLUORIDE ANESTHETIC

by

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A 27-year-old nurse experienced headaches, polyuria, polydipsia, and epigastric distress at age 18 and a recurrence of these symptoms at age 22 including marked hypertension (220/130 mm Hg), severe bone pain in the pelvis, upper femurs, anterior tibias, and both hands. She had nodules on her fingers, a slightly elevated alkaline phosphatase; her kidney function was normal.

These manifestations subsided for four years until age 26 when she was referred to the North Carolina Memorial Hospital. On examination she exhibited multiple, fixed, subcutaneous nodules on the extremities. Technetium polyphosphate bone scintiscanning revealed an increased (mineral) uptake throughout the skeleton. Although she had an ectopic right kidney, a split renal function scan showed normal overall renal function.

Six months later she was again hospitalized because of gastric

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ulcer, in conjunction with progressive generalized osteosclerosis. On one occasion she was found somnolent having placed a cotton wadding saturated with a very volatile and sweet-smelling liquid over her nose. She confessed intermittent abuse of methoxyflurane. A distal renal tubular acidosis was treated with bicarbonate and potassium supplementation. Because of a severe mental depression she was transferred to the psychiatric service. One month after her last admitted exposure to methoxyflurane, she still had a very high serum fluoride level (180 μM/litre, 3.4 ppm) although her bone pain had lessened in severity and the hypertension was under control.

Metabolic studies revealed that the patient remained in positive calcium balance by approximately 200 mg/day. The strikingly low urinary excretion of calcium averaged only 12 mg/day. The phosphorus balance was negative during the initial 5 days of the study period but returned to zero during the second half. There was a constant high level of uric acid in the blood (14 mg/dl).

During the study, measurements of the following biochemical agents were made: calcitonin, 25-hydroxycholecalciferol, fasting growth hormone, somatomedin, fasting insulin, and acid phosphatase were normal. The following abnormal parameters were noted: parathyroid hormone, 65 uIeq/ml (normal, < 40); thyroxine, 2.5 μg/ml (normal, 4.5 to 11.5); triiodothyronine resin uptake, 42%; free thyroxine iodide, 1.39 (normal, 1.58 to 5.18); alkaline phosphatase, 26 U (normal, 2 to 6); alkaline phosphatase isoenzyme 90% bone fraction, and serum glutamic oxalacetic transaminase, 75 U (normal, 6 to 60). Urinary excretion of hydroxyproline was 67 mg/24 h, (normal, 25-77).

Bone biopsy revealed the typical findings of osteosclerosis. Bone fluoride content amounted to 801 nmoles/mg ash (or 15,000 ppm fluoride/ash). A high serum inorganic fluoride level was observed long after exposure had ceased; it was attributed to "near skeletal saturation" and to renal insufficiency. The acute episodes of periostitis were believed to have resulted from increments in fluoride concentration and to increased osteoblastic activity coincident with the exposure to the narcotic.

The overt clinical toxicity threshold of the serum fluoride level in human and animal studies is reported to be approximately 50 μM/l (0.95 ppm), and acute toxicity has been associated with serum fluoride levels exceeding 90 μM/l (1.7 ppm). In this patient the serum fluoride was reported to range from 455 to 540 μM/l (8.6 to 10.3 ppm).

The authors noted tubular toxicity, namely a defect in distal tubular secretion of hydrogen ion which resulted in acidemia and probably contributed to the cellular toxicity of fluoride. They attributed the nephrotoxicity to the fluoride ion rather than to oxalate ions both of which are formed during the biotransformation of the anesthetic in
the system. The urine did not show oxalate crystals.

From their experience with this patient the authors conclude that fluorosis is a multi-system disease—not solely confined to bones and teeth—with abnormal findings in liver, thyroid function, gastric mucosa, and hypertension.

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FLUORIDE
BOOK NOTICE

NEW FOCUS ON FLUORIDE

Fluoridation: The Great Dilemma, by George L. Waldbott, M.D., in collaboration with Albert W. Burgstahler, Ph.D. and H. Lewis McKinney, Ph.D. Foreword by Alton Ochsner, M.D. Pp. 423+xxx, 45 illustrations, 35 tables, symptoms of chronic fluoride toxicity, sources for further reading, index, biographical sketches of the authors. Coronado Press, Inc., P.O. Box 3232, Lawrence, Kansas 66044, U.S.A. Hardcover, $14.95; paperbound, $7.50 (plus $1.50 for postage and handling).

In an age of increased awareness of the hidden, often insidious, hazards of many environmental pollutants, it is tragically ironic that fluoride—one of modern industry's most widely dispersed and persistent effluents—is, to quote the opening chapter of this book, "inadequately assessed and poorly understood, although countless articles have appeared in the medical literature clearly demonstrating its deleterious effects on human health."

No doubt one of the main reasons why the toxicity of continual exposure to comparatively low levels of fluoride is not better known is because of the generally favorable image that still surrounds the fluoridation of drinking water. Even though much contradictory evidence exists, dental and public health officials, as well as many scientists, persist in promoting and upholding the procedure because they evidently continue to believe "it is medically safe for all people of all ages."

Herein, then, lies the source of The Great Dilemma. Fluoridation is motivated by the well-intentioned desire for better teeth and less tooth decay, but even that result, as the book clearly shows, is questionable or, at best, marginal. A laudable dental goal has been allowed to outweigh the extensive, well-verified medical evidence, collected in this book, showing that fluoride in drinking water at the recommended concentration of 0.7 to 1.2 parts per million parts of water has produced numerous instances of serious toxic effects (usually incorrectly attributed to other causes) and countless episodes of chronic fluoride illness in its human users. The specific role played by fluoride in this illness has been unequivocally demonstrated by virtue of the ease with which the syndrome is usually reversed simply by the patient's withdrawal from—and reprecipitated by re-exposure to—artificially fluoridated water or fluoride from whatever source.

Though the title might suggest that the book was written primarily for the general reader (who should have no difficulty comprehending it), in fact it is also directed especially to researchers and practitioners in the area of the health sciences. In it they will find a
comprehensive, up-to-date review and discussion of the nature and biological effects of fluoride, including a large number of detailed clinical case reports of reversible illness from artificially fluoridated water, along with much new, previously unpublished, information.

Historians of science and others who are interested in knowing more about the subject will also find in the pages of Fluoridation: The Great Dilemma a rich store of fully documented answers to such important and intriguing questions as: how fluoridation came about, how it was originally (and still is) promoted, how its many endorsements have been obtained, what stake industries and governments have in it, what critics have said about poisoning reports, why adverse findings are generally discounted and ignored, and why so many physicians, dentists, and scientists are appallingly ignorant of its injurious effects.

Besides topics such as these, the book deals at length with the toxic effects of airborne fluoride on man as well as plants and animals. It also presents an extensive account of the action of fluoride on soft-tissue organs and its potential for causing or promoting chromosome damage, birth defects, and cancer. Likewise, it provides a clear exposition of acute as well as chronic fluoride intoxication, together with answers to criticisms of reports of poisoning from artificially fluoridated water. Moreover, it gives a useful survey of the question of fluoride's essentiality in mammalian nutrition, along with the history of the discovery of fluorne and its compounds. It also outlines their uses as well as the distribution of fluoride in air, water, soil, and food—both plant and animal.

The closing chapter broadly summarizes the vexing problems of illness from environmental fluoride, especially as they relate to fluoridation, and offers practical recommendations on how to overcome them. It shows how tooth decay can be and has been prevented by the use of safe and far more effective alternatives. Finally, it delineates important steps that must be taken to solve and ultimately end The Great Dilemma caused by fluoridation.

Throughout the book virtually every specific statement or allegation of fact is documented by references given at the end of each chapter. Complete titles of all literature sources are provided, and an appendix lists a number of general and scientific books for further reading. The 45 illustrations and 35 tables, with their clear and informative captions, assist the reader.

In the closing paragraph of his Foreword, Dr. Alton Oschner generously comments:

"Fluoridation: The Great Dilemma is a detailed, comprehensive survey of the fluoride question... It
is without doubt the most complete and authentic work on the highly emotional subject of fluoride and its use.

A.W.B.

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BOOK REVIEW

FLUORINE IN FOODS

by

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Helsinki, Finland


The authors, in the Department of Food Chemistry and Technology, University of Helsinki, Finland, review the fluoride content of foods of animal and vegetable origin, as well as the effects of fluoridated water and of processing and preparation of food on its fluoride content. They also discuss the different fluoride compounds present in certain foods and the average daily fluoride intake in various countries. In explanation of their findings, they investigated the role of fluoride from rock beds, soil and air as sources of contamination of the environment, especially of food. They recommend that national, local and individual food habits be taken into account when fluoridation of drinking water is contemplated. In food of plant origin, they state that tea and spinach contain the highest amounts of fluoride whereas in food of animal origin marine fish ranks highest.

The authors recommend control of fluoride levels in commercially prepared food, especially in those items destined to be a principal food source, such as baby foods. They point out that teflon-coated cooking vessels may increase the fluoride content of food. Sixteen tables make the review particularly lucid and the 56 well-chosen references ensure a balanced approach to the problem.

M.N.E.

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