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FLUORIDE
Quarterly Reports
Issued by
THE INTERNATIONAL SOCIETY FOR FLUORIDE RESEARCH

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The Seventh Conference of the International Society for Fluoride Research will take place on February 8-10, 1976, in Zandvoort, Holland. Abstracts (up to 300 words) of papers on any phase of fluoride research are now being solicited by the program com-
EDITORIAL

SERENDIPITY AND RESEARCH ON FLUORIDE

Serendipity is defined in the dictionary as "the faculty of happening upon fortunate discoveries when not in search of them". Several important findings relating to the biological effect of fluoride owe their origin to serendipity.

For instance, the late Prof. Amarjit Singh of Patiala, India, who made an invaluable contribution to the clinical evaluation of hydrofluorosis in India, was studying paraplegia, quadriplegia and other neurological conditions when he became aware of the high incidence of these manifestations in certain areas of the Punjab. His attention was thus drawn to possible environmental factors. Further investigation led to the detection of endemic areas of fluorosis in the Punjab in which drinking water showed high concentrations of fluoride (1).

Another case in point is the experience of the late Prof. Tokio Takamori who was studying Kaschin-Beck disease, an unusual endemic bone affliction in Mongolia. During the course of his investigation a similar bone disease in the Aso Vulcano district, unrelated to the one in which he had been originally interested, attracted his attention. The new discovery gave rise to an extensive series of studies on the health effects of fluoride (2, 3).

Dr. J. Franke, an orthopedic surgeon at the University of Halle, D.D.R. was confronted with a case of general osteosclerosis. He had tentatively diagnosed it as Strumpel-Bechtereff disease, an ailment characterized by sclerosis of vertebrae, and was about to publish an account of the coincidence of the two conditions when he read a brief reference in a textbook, to the fact that osteosclerosis can occur in workers in aluminum factories. He was thus prompted to inquire in greater detail into the occupational background of his patient. Before long, he had accumulated a series of similar cases which eventually culminated in one of the most comprehensive and thorough studies on industrial fluorosis (pp. 61-85 in this issue).

Another incidental finding is the high fluoride content of soft tissue organs reported by Herman et al. (4). These authors investigated the fluoride content of kidney stones and its possible effect on human health. They did not find any untoward manifestations due to fluoride in their patients with kidney stones. However, specimens of kidneys, skin, prostate gland, etc. obtained at surgery and analyzed for fluoride contained concentrations up to 290 ppm. Hence a fore, high fluoride levels in tissues other than bones and teeth had received only little attention in the literature.

Excessive amounts of fluoride (up to 2340 ppm) in the aorta were also recorded in another survey by Geever et al., whose primary
interest was in the quantity of fluoride in skeletal tissues in Grand Rapids residents and the microscopic structure of such tissues after prolonged consumption of fluoridated water. Both the high values found by Herman et al., and those by Geever et al., had occurred in non-fluoridated cities, namely New York City prior to fluoridation and another non-fluoridated city in New York state respectively. That such extensive storage in soft tissues is possible where water supplies contain as little as 0.1 ppm fluoride must be considered one of the most important discoveries in the area of fluoride research which undoubtedly demands more attention in the future. A partial answer to this phenomenon is being provided by the Farkas article, pp. 98-105 of this issue, which shows that food contains considerably more fluoride than was formerly anticipated. What other sources of fluoride intake account for such high storage - perhaps inhalation of airborne fluoride - will need to be further investigated.

A recent study, designed to explore the effect of fluoridated water on heart disease abstracted in this issue on page 114 revealed no untoward effects upon comparing mortality rates, serum lipids and serum ions in subjects of two communities: fluoridated Easton, Pennsylvania and non-fluoridated Phillipsburg, New Jersey. However, this investigation yielded data of even greater significance, The tap water in non-fluoridated Phillipsburg contained more calcium and magnesium than that of fluoridated Easton although both cities derived their water supplies from the same source, namely the Delaware River. The authors attributed this difference to the treatment of the water with fluorosilicic acid. Confirmation of the observation that the addition of fluorosilicic acid to municipal water supplies deprives the water of calcium and magnesium, would indeed be of importance in the evaluation of the effect of fluoridated water upon human health.

Two additional unexpected features were noted in this paper to which the authors failed to address themselves. Despite the fluoridation in Easton, the average levels of fluoride in the serum of the 41 subjects in the two cities showed no significant difference namely 0.46 µM/l (.00874 ppm)/liter in Phillipsburg and 0.41 µM/l (.00779 ppm)/liter in fluoridated Easton. This finding is in contrast to the data by Hodge and Smith (5) who upon comparing the serum levels for fluoride in individuals in fluoridated Newburgh, N.Y. with those in Rochester, New York, prior to fluoridation, found serum fluoride levels in Newburgh residents significantly higher than those in Rochester. It contradicts the data of Hanhijärvi who observed in Finland blood levels of fluoride of the order of 1.0 to 1.8 µM/l (.02 to .03 ppm) in fluoridated communities and 0.72 to 1 µM/l (.01 to .02 ppm) in nonfluoridated ones (6).
On the other hand, in the subjects of fluoridated Easton, levels of calcium, magnesium and inorganic phosphorus in their blood serum were significantly above those in non-fluoridated Phillipsburg (P<0.01).

It would be of interest to determine whether or not this increase is related to fluoridation of Easton's drinking water and to its relatively low calcium content.

The above-mentioned examples illustrate how casual incidental and unanticipated findings can lead to detection of important facts.

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INDUSTRIAL FLUOROSIS

by

J. Franke, F. Rath, H. Runge, F. Fengler, E. Auermann, and G. Lenart
Saale, G.D.R.

SUMMARY: This is a review of findings on workers in an aluminum plant with industrial fluorosis. Early signs of the disease are nocturnal back pains and restriction of the rotation of the trunk. Stage I of the disease usually occurs after 10 years, stage II after 15 years and stage III after 20 years. The diagnosis was established at an early stage through biopsies of the iliac crest by histological and microanalytical determinations of fluoride. A fluoride level exceeding 4000 ppm in the iliac crest ash was found to be associated with typical signs of fluorosis. The early histological changes including the microradiographic findings and typical foci of calcification in the corticalis are demonstrated.

Three necropsies in patients with fluorosis at different stages are reviewed. One of them showed a lesion in the cells of the anterior horn of the spinal cord which was believed to be related to fluorine. Crystallographic studies revealed that crystals of fluorotic bone mineral had become more slender. Increase in gastric acidity was associated with greater sensitivity toward fluoride. Prophylaxis and treatment of industrial fluorosis are discussed.

Industrial fluorosis is a rare occupational disease in workers of fluorine processing or manufacturing industries (factories for the production of aluminum, cryolite, hydrofluoric acid, fertilizers, insecticides, and glass. Industrial fluorosis was recognized for the first time in 1932 by Møller and Gudjonsson (1) in Danish cryolite workers. Roholm

From the Orthopedic Hospital of the Martin-Luther-University Halle, G.D.R.

* * * * * * *

Presented at the Sixth Annual Conference of I.S. E.R., Williamsburg, 11/7-9/7'
thoroughly described this disease in several monographs (2-4).

In 1944 Peperkorn and Kähling (5) described the first cases of industrial fluorosis in Germany. They found signs of fluorosis in 34 out of 47 workers in a hydrofluoric acid factory in Dohna (Saxony). In 1958, Fritz (6) extended the investigations in this factory to 156 persons and he found typical skeletal fluorosis in 57. Since then additional cases of industrial fluorosis were recorded from the U.S.A. (7-11) Great Britain (12-15), Soviet Union (16-18), Norway (18), France (20, 21), Switzerland (22, 23), and Germany (24-29).

We have also had the opportunity to investigate some patients who were suffering from industrial fluorosis, and we have reported about it in several communications (30-37). These patients are workers in smelters of an aluminum factory. Producing aluminum electrolytically, cryolite (Na₃AlF₆), aluminum fluoride (AlF₃) and soda (Na₂CO₃) are added to alumina (Al₂O₃, aluminum oxide) as fluxing agents. As a result the melting temperature is reduced from 2000° to 950° C. The anode-effect, the steam pressure of the salts, and the mechanic manipulations (breaking off the crusts, changing the anodes) cause the development of gas and dust which vapors contain hydrofluoric acid (HF), carbontetrafluoride (CF₄), cryolite (Na₃AlF₆), and aluminum fluoride (AlF₃). The fluorides are inhaled and swallowed. Because of the high temperatures the workers drink as much as 2 to 5 liters of liquid during one shift (29).

**Symptomatology**

In the initial stages, the complaints of the patients are not remarkable. At first they experience vague rheumatic pains, then the pains become localized in the spine, especially in the lumbosacral region. Later, a sensation of stiffness in the lumbar and cervical spine develop.

However, we also found patients with slight radiological changes (subtle signs or stage 0-1), who complained of intense pains in the spine and in the large joints. On the other hand, some patients whose fluorosis was radiologically distinct were almost without complaints.

A study of Domesle (29) showed that, of 400 aluminum workers, 44% had stiffness and pains in the back beginning in the lumbar and extending up to the cervical spine; 25% had pains in the large joints; 63% stinging and hypesthesia in the arms and legs after working hours. Many workers complained of pains at night and while resting, but movement caused them to disappear. In addition, attacks of vertigo, ringing and rushing in the ears, anorexia, constipation, nausea and, in 60%, cough and dyspnea appeared frequently.
Clinical Findings

Clinically one finds at first a restriction of movement of the spine, affecting eventually the cervical spine. As an early clinical sign of fluorosis we observed the restriction of rotation of the trunk (Fig. 1). This finding occurred when bone changes became demonstrable roentgenologically in the early stage.

Fig. 1

Restriction of Rotation of Trunk, An Early Sign of Fluorosis

Left: Normal    Right: Restricted rotation

Later on, complete stiffening of the spine (Fig. 2) and a marked restriction of the vital capacity and respiratory movement ensue. In the advanced stage, a more or less extensive restriction of movements of the large joints, especially of the hip-joints, supervenes. Therefore the clinical features resemble closely those of Bechterev's disease.

Laboratory Findings

Biochemically, calcium, phosphorus, and the acid phosphatase levels of the serum did not show any distinct changes; the erythrocyte sedimentation rate was normal, there was no evidence of anemia. The plasma alkaline phosphatase is sometimes increased. Domesle (29), however, did not find any correlation between the behavior of the alkaline phosphatase and the extent of the skeletal fluorosis.

Radiological Findings

In addition to the well-known radiological stage classification,
stage I to III according to Roholm (3), two prestages according to Fritz (6) have proved to be important in our investigations: the so-called Schwachzeichen (subtle signs) and the stage O-I. Concerning the subtle signs, which are only important in connection with a history of exposure to fluoride, a condensation of the bone-structure and an enlargement of the bone trabeculae in the lumbar spine are evident. In addition, there are subtle accompanying shadows along the tibia, fibula, radius, and ulna.

At the stage O-I (Fig. 3a, b) the structure of the thoracic spine has already increased in density, whereas in the lumbar region the normal structure of the bones begins to disappear. The periosteal appositions of new bone at the bones of the forearms and lower legs are more distinct.

For better proof of the periosteal appositions on these bones, we used slightly underexposed photographs similar to the kind of radiography employed for soft parts.
In distinction to Roholm's findings, we noted that a longer duration of exposure is required for the development of fluorosis. Subtle signs develop after an average period of 10.7 years (2 to 25 years), stage O-I after 12.2 years (5 to 33 years), stage I after 15.7 years (8 to 38 years), stage II after 17.6 years (11 to 21 years), stage III after 19.5 years (19 to 20 years) of duration of employment (Table 1).
TABLE 1

Average Duration of Fluoride Exposure for the Single Stages of Fluorosis (in years)

<table>
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<tr>
<th>Stage</th>
<th>Average Duration</th>
<th>Range</th>
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<tr>
<td>Vague symptoms (Schwachzeichen)</td>
<td>10.71 years</td>
<td>(2 - 25 years)</td>
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<tr>
<td>stage 0-I</td>
<td>12.15 years</td>
<td>(5 - 33 years)</td>
</tr>
<tr>
<td>stage I</td>
<td>15.70 years</td>
<td>(8 - 38 years)</td>
</tr>
<tr>
<td>stage II</td>
<td>17.6 years</td>
<td>(11 - 21 years)</td>
</tr>
<tr>
<td>stage III</td>
<td>19.5 years</td>
<td>(19 - 20 years)</td>
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The differences are due to different conditions of production: Roholm's data was concerned with a cryolite factory, whereas our experience was in connection with an aluminum factory where the fluoride concentration in the factory hall was lower.

Figures 4a and b present bones of a 56 year-old patient with a fluorosis stage III. An extreme marble-like sclerosis of the bones with ossification of the longitudinal ligaments of the spine are noted. The

![Image of X-ray showing fluorosis stage III] (4a. Marked sclerosis of lumbar spine; ossification of longitudinal ligaments.)
4b. Marked sclerosis of the pelvis; distinct prominence of the muscular attachments; ossification of ligaments and sacroiliac joints.

4c. Calcified interosseous ligament between radius and ulna.

bone structure is no longer discernible, the sacroiliac joints are ossified. The formation of outgrowths and spurs at the muscular insertions and the ossification of the ligaments of the pelvic floor complete this picture. Outgrowths like a saw blade develop also between radius and ulna (Fig. 4c).

Pathologic-Anatomical Findings

We obtained necropsy findings of three patients with industrial fluorosis, a fluorosis III, a 1-II, and an old fluorosis (3 years without any fluorine contact). The patients died from a traffic accident, a brain tumor, and a decompensated mitralinsufficiency respectively.

The pictures show the changes of the skeletal system in fluorosis stage III. Here we can see in the final stage a complete ossification of the longitudinal ligaments of the spine which has practically stiffened to a stick (Fig. 5a).

The small vertebral joints and the costovertebral joints are ankylosed by the ossification of the capsules, the muscular attachments protrude as exostoses. The spongy bone is condensed massively,
allowing hardly any space for bone marrow. The above-described changes are seen clearly on the pelvis (Fig. 5b); a projection of the muscular attachments on the iliac crest and pubic bone, ossification of the sacroiliac joints, of the pubic symphysis and of the ligaments of the pelvic floor. Peripherally, ossifications occur at muscular attachments. Saw-blade-like appositions are found at the inferior surface of the ribs between ulna and radius (Fig. 5c) and between the tibia and fibula. The long bones exhibit an increase in bone substance at the cross section with distinct thickening of the whole corticalis (Fig. 6).

Fig. 5

E. W., Fluorosis Stage III

5a. Macerated preparation of spine

5b. Macerated preparation of pelvis

FLUORIDE
5c. Macerated preparation of forearm

**Fig. 6**

**Extensive Thickening of Corticalis of Femur**

Fluorosis stage III (left) compared with two normal femora (center and right)

No pronounced narrowing of the intervertebral foramina and of the spinal canal in the cases with radiculomyelopathies such as was described by our Indian colleagues in endemic fluorosis (38-47) were encountered. We agree with Jolly (48) that in endemic fluorosis exostoses form in the canal of the cervical spine due to the custom in India of carrying heavy loads on the head. Changes in other organs which are not age-related such as damage to brain, liver, kidneys, and the vascular system were not found with one exception namely, the patient who experienced pathological changes in the nervous system which will be recorded later in another paper.

**Histological Findings**

Our histological findings are based on the analysis of 25 iliac crest needle biopsies and on 3 autopsied cases at different stages of
fluorosis, especially on the beginning stage of fluorosis. Since the details about the histological changes of industrial fluorosis were reported previously (32) the present discussion will be confined to a summary of what we observed: 1.) coarsening and condensation of the spongy bone, 2.) subperiosteal formation of fibrous bone with transformation into lamellar bone leading to the formation of exophytes, 3.) thickening and spongiosation of the corticais, 4.) enlarged osteocyte cavities, 5.) irregular matrix formation with a high turnover rate (Fig. 7), mosaic structure of the cement-lines, formation of chalky granules, and foci with a coarse fibrous structure, a high content of mucopolysaccharides, and with a trend to calcification (Fig. 8) which were described by us for the first time in 1972 (32,34).

**Fig. 7**
Microradiogram of Rib Showing a High Bone Turnover Rate

Fluorosis stage III (1:75)

**Fig. 8**
Typical Subperiosteal Focus with Coarsened Fibrous Structure

(H. E., 1:170)

FLUORIDE
These changes—subperiosteal formation of new bone, spongiosis of the corticalis as a symptom of endosteal bone resorption as well as disturbances of the matrix formation and of the mineralization—appear to be typical of fluorosis. Our most recent studies showed that the above-mentioned foci are situated, in most cases, in the corticalis near the periosteum and that the direction of their fibers does not correspond to the course of the surrounding osteons, but to that of the inserting tendinous fibers at the periosteum (Fig. 9). We consider them residues of connective tissue of former periosteum which were included in the bone formation and incrusted with calcium. The microradiogram, showing a high calcium content of these foci, supports this interpretation (Fig. 10)*. The bone structure did not reveal evidence of a secondary hyperparathyroidism.

The above-described findings become more distinct as the degree of fluoride intoxication advances with, however, wide individual variations.

Histochemically we observed distinct activities of the alkaline and acid phosphatase in some cases as well as of the \( \beta \)-glucuronidase in the endosteal cells and osteocytes which constitutes additional evidence of increased bone turnover during chronic fluoride intoxication.

**Fluorine Determination in the Bone Ash**

We (34) have developed a special method in order to confirm the diagnosis of "fluorosis" in doubtful cases in the early stage or in spora-

* I am grateful to Prof. Kuhlencordt, Hamburg, for the preparation of the microradiograms

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Typical focus of calcium accumulation (1:75)

dically occurring fluoroses: During the iliac crest biopsy a second bone cylinder is removed which is dried at a temperature of 105°C up to weight constancy and ashed for 2 hours at 450°C until the bone is white and porous. The fluorine determination is made according to a modified action of the method of Megregian (49) (determination of fluorine by distillation with perchloric acid and vapor and formation of a complex of circonerochromcyanine). Here the fluorine contents could be related to the single radiological stages. The normal value is 0.08% fluoride (800 ppm). We found the first distinct histological and radiological changes in bones containing approximately 0.35% (3500 ppm) to 0.40% fluorine in the ash of the iliac crest (Table 2). Nearly the same limits were recorded by Sankaram and Gadekar (44) in human beings and by Schmidt and Rand (50) in cattle. Jackson and Weidmann (51) found higher values, whereas Freitag et al. (52) reported lower ones.

**TABLE 2**

| Fluoride Content of the Iliac Crest Ashed at Various Stages of Fluorosis |
|-----------------------------|---------------------------|-----------|
|                             | Percentage | PPM        |
| normal individuals          | 0.05 - 0.11 | 500 - 1100 |
| Vague symptoms (Schwachzeichen) | 0.35 - 0.45 | 3500 - 4500 |
| stage 0 - I                 | 0.50 - 0.55 | 5000 - 5500 |
| stage I                     | 0.60 - 0.70 | 6000 - 7000 |
| stage II                    | 0.75 - 0.90 | 7500 - 9000 |
| stage III                   | > 1.0      | > 10,000   |
Special Observations

1. In 1939, Roholm (4) assumed that in fluorosis the degree of skeletal sclerosis declined after cessation of fluoride intake. Fritz (6, 27) made the same observation in 7 cases and Herbert and Francon in one (21). We confirmed this finding in 2 such cases. Their sclerosis decreased markedly within 2 years and 5 years respectively, whereas the ossifications in the ligaments persisted. In 1968, 63 year-old patient M. G., who had been working in an aluminum factory for 26 years, developed typical fluorosis, stage II. Following a change in occupation, the radiological check-up in 1973 showed a distinct decrease of the sclerosis (Fig. 11a, b). In 9 additional patients, the bone density remained unchanged for 5 years in spite of a change of employment.

Fig. 11a

Fluorosis Stage II Within Five Years

Note decrease of sclerosis in spine.

2. Whereas in general no serious neurological complications are reported in industrial fluorosis, as mentioned above, we nevertheless observed the following case. Patient E. N., 64 years-old, with fluorosis stage I-II died of a cerebral glioblastoma. In addition, the histological examination yielded distinct damage to the cells of the anterior horn of the spinal cord and localized destruction of muscle fibers. Whereas it appears that the brain tumor and fluorosis were coincidental, the damage to the spine and muscles could be related to the existing chronic fluoride intoxication.
Fig. 11b

Same Patient as in Fig. 11a

Note decrease of sclerosis in pelvis.

3. In several patients we failed to notice evidence of typical sclerosis in the radiogram. Instead, the picture of so-called "hypertrophic atrophy" was found as in the following case:

Patient G. M., 62 years old, had been working for 20 years in an aluminum smelter. X-rays showed typical hypertrophic atrophy with slight periosteal appositions on the forearms and lower legs (Fig. 12 a-c). The fluoride content in the ash of the iliac crest was 0.63%. Histologically a thin spongy compacta and narrow bone trabeculae as well as coarsening spongy and hyperostotic cortical structures were found. We observed similar findings following therapy with sodium fluoride for osteoporosis. It is likely that a previously existing osteoporosis is superimposed upon fluorosis or the predominance of the fluoride-induced bone resorption in conjunction with thickening of the statically loaded bone structure may be responsible.

Additional Special Studies

1. Gastric acid and the stage of fluorosis: As reported pre-
"Hypertrophic Atrophy" of Bone Structure

12a. Lumbar spine

12b. Pelvis

12c. Lower legs and forearms only slight periosteal appositions

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viously (32, 53-57) individual susceptibilities, particularly nutritional habits, the capacity of absorption of the gastrointestinal tract and the renal threshold for fluorides play an important role in the development and severity of fluorosis. We therefore studied the relationship of gastric acid in 150 aluminum workers to the degree of severity of fluorosis. The gastric acid was determined by the Acido-test. Figure 13 shows a distinct correlation namely, with increasing severity of fluorosis the percentage of hyperacid persons \((A_2 + A_3)\) increases and the proportion of hypo- or an- acid persons \((B_1 + B_2)\) decreases. The differences were statistically significant. These findings prove that fluoride resorption is obviously diminished by a deficiency of gastric acid and that it is enhanced by hyperacidity.

*Fig. 13*

**Correlation Between Gastric Acidity and Development of Fluorosis**

![Diagram showing correlation between gastric acidity and fluorosis stages]

2. Physical examinations: In the iliac crest biopsies and in the necropsies we noticed repeatedly an extreme hardness of the fluorotic bone. The studies of the physical properties of the fluorotic bone show the following (33, 58): a) An increase in the microhardness at the cut surface of a piece of the femur is more pronounced in fluorosis I-II than in fluorosis III; b) A threefold higher compressive strength per area of a fluorosis III vertebra; c) An increase of the module of elasticity of the femur slices, 2 cm long, and of the defined cylinders of the corticalis of the femur in moderate fluorosis. In severe fluorosis a decrease was observed; d) An increase of the breaking strength area of slices of femur in both cases of fluorosis. In fluo-
orosis III we found the breaking strength per area was impaired at the exactly defined cylinders of corticalis of the femur whereas there was a slight increase in strength in fluorosis I-II.

A moderate degree of fluorosis causes a real increase in bone strength, but severe fluorosis shows partly a static inferiority (cortex cylinder). This inferiority, explicable by the serious histological changes, might perhaps be compensated, at least partially, by the enormous quantity of bone.

3. Crystallographic studies: Material and Method - Fluorotic bones from a patient who had changed his job as an aluminum worker one year previously, fluorotic bones of two patients who had changed their job several years previously as well as bones of rats fed 20 mg NaF/day/kg for 12 months were studied. Diffractometric examinations were carried out on a diffractometer of the type Miller-Mikro 111 (radiation CuKα, 26 kV, 36 mA with nickel filter, goniometer speed: 1/2°/min. The intensities were integrated with a Dupa polar planimeter).

Results - The hydroxyapatite crystals were changed in the bone of the patient who had changed his job one year previously and also in the bones of rats fed with NaF inasmuch as their "a"-axis was shorter, i.e. they were more slender than the average (Fig. 14, curves 1 and 3).

![Curves of X-Ray-Diffraction Analysis](image)

- curve 1 - advanced fluorosis after one year without fluorine contact
- curve 2 - moderate fluorosis, 4 years without fluorine contact
- curve 3 - bones of rats fed 20 mg NaF/day/kg for 12 months
- curve 4 - slight fluorosis, 3 years without exposure to fluoride

The bones of the patients who had changed their job several years previously showed no crystal changes in spite of the sclerosis which is to be seen on the x-ray picture and of the higher than average fluoride level.
Our findings are similar to those of Baud and Bang (59, 60) and demonstrate that it is possible for the normal crystal forms to be restored after the patient has not been exposed to fluorides for several years.

**Therapy and Prophylaxis**

In the G.D.R., since 1950, industrial fluorosis has been recognized as an occupational disease which is reportable and for which compensation is required (Law Code of the G.D.R. 1950, 50, p. 389). By further decrees and laws of the G.D.R. government, industrial medical care of all workers has been markedly improved. Prophylactically, it is important to reduce the fluoride concentration of dust at the place of work, especially by improved ventilation of enclosed factory areas.

At the examination for employment, persons with the following diseases are considered totally unsuitable: liver and kidney changes, blood and thyroid gland diseases, post-traumatic or congenital skeletal damage, infectious and para-infectious diseases of the apparatus of locomotion (rheumatism, Bechterev's disease); also, workers with distinct degenerative changes of the spine and of the large joints are unsuitable.

Following the initial examination, the workers are examined once a year; at this examination, special attention is paid to the following points: pains in the spine and great joints, nausea, lack of appetite, constipation, headache, dyspnea, restriction of the movability of the spine (especially of rotation), of the respiratory chest expansion and of the vital capacity.

Biochemically, the following examinations are carried out: calcium, phosphorus and alkaline phosphatase of the serum, 24-hour-excretion of fluoride in the urine and a blood assay.

Every third year, at least, the following parts of the skeleton are x-rayed: thorax, pelvis, lumbar spine in two directions, one lower leg and one forearm in the anterior-posterior direction with the short exposure technique.

In doubtful cases, such as patients with distinct complaints and clinical findings but with slight roentgenological changes, we carry out an iliac crest needle biopsy. If there are distinct histological changes and if the fluoride values in the iliac crest ash are above 0.35% to 0.40%, such cases must also be recognized as an occupational disease in spite of the minimal degree of roentgenological changes.

Therapeutically, it is necessary to remove the worker from the fluoride-endangered place of employment as soon as fluorosis has been diagnosed. Physiotherapeutical measures like massage, short-
wave and ultrasonic therapy, balneotherapy, and a medicamentous treatment with indomethacin or phenylbutazone brings about an improvement of the condition but the patients will not become symptom-free.

Bibliography


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of Individuals from the Districts of Fort William and Kinlochleven, Medical Research Council Memorandum No. 22., His Majesty's Stationary Office, London, 1949, p. 47-75.


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Discussion

Dr. Sinclair: I note that you find very little osteoporosis and no evidence of secondary hyperparathyroidism, such as Dr. Teutia reported here. Could this be because your patients have a higher calcium intake than hers and thus do not require mobilization of calcium from their bones? Also, I am not clear why you see no anemia. You showed great diminution of the bone marrow due to osteosclerosis, but you observe no anemia.

Dr. Franke: My cases agree with those of Professor Jolly; he too encountered no osteoporosis. All exposed workers in my studies received a well-balanced diet and a normal intake of calcium.
(ca. 1 g/day). As to your second question, we have studied 400 aluminum workers afflicted with different stages of osteofluorosis and found no anemia. The cases I presented here showed a normal blood picture.

Dr. M. Teotia: To add to what Dr. Sinclair has said, in our cases osteoporosis could be correlated with lower calcium intake. In addition, because our patients live in the endemic areas from early childhood, their bones contain a larger amount of the less-soluble, more stable fluoroapatite from which ionized calcium is less available than from hydroxyapatite. This leads to a greater stimulation of the parathyroid glands and, therefore, we observe more evidence of secondary hyperparathyroidism. We have measured parathyroid hormone levels in the serum and have demonstrated hypertrophy of the parathyroid glands in a 63-year-old patient who developed tertiary hyperparathyroidism. This was reported in the British Medical Journal (17:637-40, 1973). We find that osteoporosis and secondary hyperparathyroidism are definitely related to deficiency in calcium intake and to the duration of exposure to fluoride.

Dr. Franke: With respect to the measurement of bone strength in industrial skeletal fluorosis, we repeatedly noticed extreme hardness of fluorosed bones in iliac crest biopsies and necropsies. Our studies revealed

a. an increase in the microhardness at the cut-surface of a piece of femur which is more pronounced in fluorosis stages I and II than in stage III,

b. a three-fold higher compression strength per unit area in stage III vertebrae,

c. an increase in the module of elasticity in sections of the femur 2 cm deep and 5 mm thick in moderate fluorosis (stages I and II) but a decrease in elasticity in severe fluorosis (stage III),

d. an increase in breaking strength per unit area in segments of femur in stages I and II but not in stage III. Moderate osteofluorosis gives rise to a real increase in bone strength but severe fluorosis causes a decrease for which, however, the enormous increase in the quantity of bone partially compensates.

Dr. Hanhijärvi: Did you measure urinary fluoride concentrations?

Dr. Franke: Yes, but we could not relate urinary fluoride levels with the degree of osteofluorosis. We often found severe fluorosis

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associated with low urinary fluoride levels and incipient fluorosis with very high levels.

Dr. Hahnjarvi: You stated that bone strength declines in stage III fluorosis. Was this bone substance from the surface or from the interior?

Dr. Franke: It was cortical bone.

***

INFLUENCE OF PROPAGATION MEDIA AND AMENDMENTS ON FLUORIDE TOXICITY OF CORDYLINE TERMINALIS 'BABY DOLL'

by

R. T. Poole and C. A. Conover
Apopka, Florida

SUMMARY: Cuttings of Cordyline terminalis 'Baby Doll', a popular foliage plant used extensively in dish gardens because of its attractive red coloration often exhibits tip necrosis in the propagation bed. This necrosis is caused by fluoride found in the soil-water solution. Proper selection of propagating medium and elevation of pH can alleviate the fluoride-induced necrosis.

Demand for plant materials in ornamental plant combinations (groups of different indoor foliage plants in a single container) has increased considerably in recent years. Foliage plants with good keeping quality and bright colors are highly prized in combinations with other plants because they provide a visual focal point. One foliage plant with excellent characteristics for combinations is Cordyline terminalis Kunth 'Baby Doll'. This plant grows upright, roots readily and possesses foliage of a maroon color with light rose margins.

From the Institute of Food and Agricultural Sciences, Agricultural Research Center, University of Florida.
Production of 'Baby Doll' is limited by leaf tip necrosis which usually occurs 2-3 weeks after terminal cuttings are placed in the propagational medium. Necrosis of 'Baby Doll' has been observed in the Apopka area for many years and was thought to be pathogenic; however, an active pathogen could not be isolated (1). Research by the authors indicated that fluoride was responsible for the toxicity (2, 3). Medium utilized during propagation and amendments added to the medium were found to influence necrosis severity.

The purpose of these experiments was to elucidate effects of various media and amendments on foliar necrosis.

**Influence of Medium**

Terminal cuttings approximately 15 cm long were placed under intermittent mist in various propagating media (Table 1) and graded two weeks later: 1 = no necrosis, 10 = complete necrosis (death) (Fig. 1). Soil fluoride was determined by stirring into 50 ml of water a 10 g sample of the dried medium. The sample was allowed to stand for 30 minutes with occasional stirring, filtered through Whatman 41 paper and analyzed for fluoride content utilizing a Technicon Auto Analyzer. Peat obtained from Louisiana which contained 0.6 ppm soluble fluoride, Turface, a calcined clay (0.5 ppm fluoride), and pine bark (0.9 ppm fluoride) all produced plants with little necrosis. Terragreen (8.4 ppm fluoride), Vermiculite (9.6 ppm fluoride) and Perlite (17.2 ppm fluoride) all caused severe necrosis (Table 1).

**TABLE 1**

<table>
<thead>
<tr>
<th>Medium</th>
<th>Rating*</th>
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<tr>
<td>Turface</td>
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<tr>
<td>Pine bark</td>
<td>2</td>
</tr>
<tr>
<td>Peace River Peat</td>
<td>3</td>
</tr>
<tr>
<td>Water Hyacinth</td>
<td>4</td>
</tr>
<tr>
<td>Fir bark</td>
<td>4</td>
</tr>
<tr>
<td>Bagasse</td>
<td>5</td>
</tr>
<tr>
<td>German Peat</td>
<td>5</td>
</tr>
<tr>
<td>Vermiculite</td>
<td>7</td>
</tr>
<tr>
<td>Perlite</td>
<td>8</td>
</tr>
<tr>
<td>Terragreen</td>
<td>9</td>
</tr>
</tbody>
</table>

*1 = no necrosis, 10 = complete necrosis (death)
Fig. 1

Ratings Used to Determine Fluoride Induced Damage of Cordyline terminalis 'Baby Doll'

A second experiment was conducted to determine effects of various media, intermittent mist and water restriction through cut stems on foliar necrosis (Table 2). Water uptake was restricted by placing paraffin wax on the cut portion of the stem.

Cuttings were placed in tap or deionized water in test tubes with a rubber obstruction at the top of the tube to prevent mist from entering the tube. Cuttings placed in peat or Surface were stuck in 10 cm pots and those not under mist were placed in 2.5 cm deep trays for sub-irrigation.

Data in Table 2 indicates importance of water restriction, water content and mist on foliar necrosis. Plants rooted in deionized water had no necrotic leaves while those in tap water, approximately 25 ppm fluoride (4) showed some necrosis (Fig. 2). Mist was not a factor when fluoride was not present. When water uptake through cut stems was greatly reduced by wax, necrosis was reduced, further implicating the water solution as a cause of necrosis. Mist was shown to be important in reducing necrosis, probably because of the cooling effect, thus reducing transpiration and reducing moisture uptake from the medium. Wiebe and Pooviah (5) report that moisture stress after fluoride fumigation markedly accentuates injury of soybeans. The importance of
TABLE 2

Effect of Medium, Mist and Wax on Basal End of Cutting on Necrosis of Cordyline Terminalis 'Baby Doll'

<table>
<thead>
<tr>
<th>Treatment</th>
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</tr>
<tr>
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<td>2</td>
</tr>
<tr>
<td>Tap water, mist</td>
<td>2</td>
</tr>
<tr>
<td>German peat, wax, mist</td>
<td>2</td>
</tr>
<tr>
<td>Turface, mist</td>
<td>3</td>
</tr>
<tr>
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</tr>
<tr>
<td>Tap water, no mist</td>
<td>4</td>
</tr>
<tr>
<td>Tap water, German peat, no mist</td>
<td>5</td>
</tr>
<tr>
<td>Tap water, Turface, no mist</td>
<td>6</td>
</tr>
<tr>
<td>Deionized water, German peat, no mist</td>
<td>7</td>
</tr>
<tr>
<td>German peat, mist</td>
<td>7</td>
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</table>

* 1 = no necrosis, 10 = complete necrosis (death)

Mist and wax can be seen by comparing necrosis of cuttings in German peat (Table 2). When cuttings were waxed and placed under mist, thus reducing water uptake and transpiration, plants had a low necrosis rating of 2, while those plants with no mist or no wax had ratings of 5 and 7. Turface, because of its large pore space conducts water by capillarity poorly thus causing a high necrotic rating when not placed under mist. All plants had satisfactory root systems at time of rating.

In a separate experiment, base of cuttings were waxed, placed in tap or deionized water and necrosis and tissue fluoride was determined. Plants had very little necrosis and tissue fluoride for both treatments was only 1.5 ppm. Leaf tissue fluoride was determined according to the procedure developed by Mandl et al (6).

Influence of Fluoride Concentration

To determine the influence of fluoride on necrosis, cuttings were placed in solutions of various fluoride concentrations. Toxicity was rated and tissue analyzed for fluoride. Necrosis and tissue fluoride increased with increasing concentrations of soluble fluoride (Table 3). A concentration of 0.15 ppm soluble fluoride produced a rating of 3.2 with a fluoride content of 6.5 ppm. This agrees with previous results of plants placed in solution (2), but is lower than that obtained from cuttings placed in various media under mist (3).
Fig. 2

Gradations of Fluoride Induced Damage to Dracaena Deremensis 'Janet Craig' (upper) Dracaena Deremensis 'Warneckii'

Soil Amendments

Cuttings were placed in either German peat or Turface with or without single superphosphate, which contains approximately 1.5 percent fluoride, and CaSO$_4$ or MgSO$_4$ at two levels (Table 4). Best plants were pro-
### TABLE 3

**Effect of Fluoride Concentration on Necrosis and Fluoride Content of Cordyline terminalis 'Baby Doll'**

<table>
<thead>
<tr>
<th>Fluoride (ppm) in solution</th>
<th>Rating*</th>
<th>Tissue Fluoride ppm</th>
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<td>0</td>
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<td>0.15</td>
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<td>6.2</td>
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<td>0.75</td>
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<td>17.2</td>
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</tbody>
</table>

*1 = no necrosis, 10 = complete necrosis (death)

### TABLE 4

**Effect of Medium and Soil Amendments on Necrosis and Fluoride Content of Cordyline terminalis 'Baby Doll'**

<table>
<thead>
<tr>
<th>Medium</th>
<th>Superphosphate lbs/yd</th>
<th>Sulfates lbs/yd</th>
<th>Rating*</th>
<th>Tissue F (ppm)</th>
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*1 = no necrosis, 10 = complete necrosis (death)
pagated in Turface without superphosphate. These plants were slightly less necrotic than cuttings placed in German peat without superphosphate. Tissue fluoride of plants was the same in both media when no superphosphate was added. Cuttings placed in German peat containing superphosphate were completely necrotic with tissue fluoride content of 200-300 ppm. Previous work by the authors indicate 100 ppm fluoride is sufficient to cause severe necrosis and more than 100 ppm will cause death of the plant (3). CaSO₄ and MgSO₄ had little effect on necrosis or tissue fluoride content. Previous work by the authors shows that an increase in pH caused by dolomite or Ca(OH)₂ will reduce necrosis. Neither CaSO₄ nor MgSO₄ affects pH of the medium suggesting that reduction in fluoride mobility rather than Ca or Mg ion competition causes the reduction in necrosis.

Bibliography


Discussion

Question: Dr. Poole mentioned that a pathologist has studied the necrosis. Did he find evidence that fluoride injury increases the susceptibility of ornamental plants to attack by pathogens?

Dr. Poole: Such secondary damage by pathogenic organisms, would be minor. We have not found any so far. Whatever the damage,
it would be due to fluoride and not a weakening in the plant by some other organism. I have several slides of quite a few additional plants which we have examined that are susceptible to fluoride. The problem is that the public has not been aware that soluble fluoride salts affect cut-flowers.

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FLUORIDE DISTRIBUTION IN DIFFERENT SEGMENTS OF THE FEMUR, METACARPUS AND MANDIBLE OF MULE DEER

by

C. E. Kay
Missoula, Montana

SUMMARY: The distribution of fluoride within the femur, metacarpus, and mandible of wild deer from contaminated, and control ecosystems was determined. Absolute fluoride concentrations were found to be highest in the cancellous portions of the bones and in sections with the largest surface area to weight ratio. The relationship of the relative fluoride levels within the various bones was in agreement with the published literature and showed no significant variation between normal and contaminated mule deer.

Introduction

Fluoride retention and distribution in the skeleton is a process dependent upon many factors. The cancellous, more metabolically active bones of the body, accumulate more fluoride than dense, compact bones; however limited information is available concerning the distribution of fluoride within a particular bone. Gardner et al. (1) have studied the fluoride distribution in the femurs of dogs given what they considered to be a normal diet; Zipkin and Scow (2) and Likens et al. (3) have shown variations of fluoride content along the shaft of the rat tibia; and Suttie and Phillips (4) have reported on the distribution of fluoride in the bovine metatarsus. No previous reports on wild animals from natural ecosystems were found in the literature.

From the Department of Environmental Studies, University of Montana, Missoula, Montana.
If different portions of the various bones of normal, control mule deer (Odocoileus hemionus) vary appreciably in fluoride content, as has been documented for experimental animals, considerable differences in reported skeletal fluoride values could be the result of different sampling methods. Analyses of various bones of the mule deer were undertaken by the author as part of a study designed to investigate the populational variation of fluoride parameters in wild ungulates of the Western United States (in preparation).

**Methods**

Bones were obtained from control mule deer collected by several sources (Table 1). A few mule deer were furnished by personnel of

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</tr>
</tbody>
</table>

the National Bison Range, Moiese, Montana, following a herd reduction program; others (T-106, T-111) were procured under personal hunting licenses, and the remainder were collected as highway kills by game wardens of the Montana Fish & Game Department. Mule deer from ecosystems experiencing industrial fluoride pollution were taken under specific collection permits by Montana Fish & Game biologists as part of other environmental studies (5, 6).

After the removal from the animals, bones were cleaned by boiling in a 5% Alconox detergent solution and air dried; one-half inch thick cross sections were then cut from the bones as depicted in Figure 1. The cross sections were then chipped using wire-cutter type
pliers, boiled again in the detergent solution and air dried. The samples were ether-extracted six times and ground in a Wiley mill to pass through a #40 mesh screen. To obtain an aliquot of the entire femur or metacarpus, a bone saw was used to bisect the bone perpendicular to the lateral aspect. The sawdust for the entire length of the bone was taken as a representative sample of the total bone and was considered as the original analysis of that tissue (4). Section B, from the opposite half of the mandible, was used as the original analysis for that bone.

A detailed description of the techniques employed in sample preparation for fluoride analysis is presented elsewhere (5). Fluoride activity was determined with an ORION Fluoride Specific Ion Electrode (7). For each segment, fluoride analyses were performed at two sample weights -- 0.05 and 0.10 grams -- hence the data represent the average of the two analyses.

Based on original fluoride measurement, bones were selected for cross-sectional analysis to represent a wide latitude of fluoride content. This technique was employed to determine if the relative dis-
tibution of fluoride within a bone — expressed as a percentage of segment C — was correlated with the absolute amount of fluoride in that bone.

Results and Discussion

From the analytical data for the various samples presented (Table 2), it is evident that these results are qualitatively similar to those obtained in other species in that they point out the lower fluoride concentration in the less metabolically active diaphyseal portion of the long bones. The distal portion of the metacarpus and the proximal portion of the femur, both composed largely of cancellous bone, were generally the highest in fluoride content; thereby what has been found with experimental species was demonstrated for control and contaminated wild mule deer (1–4).

Within the mandibles tested, fluoride concentrations were the highest in the thin, less dense bone segments. It is believed that this observed pattern has a dual causal mechanism: the cancellous bone structure of areas A and B and the large bone surface area to bone weight ratio of these thinner cross sections. It has been demonstrated that the surface layer of certain bones has a higher fluoride content than the inner tissues of the same bone (4). Hence it appears logical to assume that this factor is responsible, at least in part, for those portions of the mandible with the largest surface area having the correspondingly greater fluoride levels. However, the relationship of the variable controlling the distribution of fluoride within the mandible requires further clarification.

Variation between animals is such that the relative fluoride concentration within a particular bone does not appear to be correlated with the absolute amount of fluoride in that tissue. This suggests that the relative distribution of fluoride within skeletal structures is not dependent on the amount of fluoride ingested by the animal, and that other parameters may be influential. For example, of all the mule deer examined, DC-28 shows the greatest variation of fluoride content in femur, metacarpus, and mandible. The general pattern of fluoride distribution is consistent with that observed in the other individuals, but there is a several-fold increase in relative measurements. DC-28 was eight months old when collected and during this period the skeletal development of mule deer is at a stage where bone formation has not yet been completed (8). The highest fluoride content was found in portions of the growing bones with the greatest metabolic activity, indicating that maturation is a factor effecting the relative distribution of fluoride in skeletal tissue.
TABLE 2

The Distribution of Fluoride Within Cross-Sections of Various Bones of Mule Deer

(\text{ppm Fluoride on dry, fat-free weight})

<table>
<thead>
<tr>
<th>Bone</th>
<th>Sample Number</th>
<th>Original Analysis</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
</tr>
</thead>
<tbody>
<tr>
<td>Femur</td>
<td>T-106</td>
<td>139</td>
<td>205</td>
<td>141</td>
<td>127</td>
<td>191</td>
<td>189</td>
</tr>
<tr>
<td></td>
<td>T-136</td>
<td>187</td>
<td>243</td>
<td>159</td>
<td>130</td>
<td>193</td>
<td>197</td>
</tr>
<tr>
<td></td>
<td>T-148</td>
<td>296</td>
<td>542</td>
<td>268</td>
<td>247</td>
<td>321</td>
<td>414</td>
</tr>
<tr>
<td></td>
<td>DC-28</td>
<td>1079</td>
<td>2275</td>
<td>1433</td>
<td>420</td>
<td>1690</td>
<td>2175</td>
</tr>
<tr>
<td></td>
<td>DC-24</td>
<td>2550</td>
<td>3400</td>
<td>2775</td>
<td>2130</td>
<td>3205</td>
<td>3250</td>
</tr>
<tr>
<td></td>
<td>T-184</td>
<td>5850</td>
<td>7315</td>
<td>5551</td>
<td>5075</td>
<td>6232</td>
<td>7261</td>
</tr>
<tr>
<td>Metacarpus</td>
<td>T-145</td>
<td>124</td>
<td>121</td>
<td>97</td>
<td>60</td>
<td>65</td>
<td>148</td>
</tr>
<tr>
<td></td>
<td>T-32</td>
<td>189</td>
<td>240</td>
<td>182</td>
<td>180</td>
<td>206</td>
<td>269</td>
</tr>
<tr>
<td></td>
<td>T-58</td>
<td>262</td>
<td>275</td>
<td>201</td>
<td>175</td>
<td>233</td>
<td>345</td>
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<tr>
<td></td>
<td>DC-28</td>
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<td>2675</td>
<td>644</td>
<td>356</td>
<td>375</td>
<td>1045</td>
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<td></td>
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<td>2555</td>
<td>2305</td>
<td>2083</td>
<td>1533</td>
<td>1493</td>
<td>2328</td>
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<td>T-184</td>
<td>4440</td>
<td>4950</td>
<td>4375</td>
<td>2800</td>
<td>4327</td>
<td>4812</td>
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<tr>
<td>Mandible</td>
<td>T-111</td>
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<td>149</td>
<td>133</td>
<td>99</td>
<td>114</td>
<td>--</td>
</tr>
<tr>
<td></td>
<td>T-58</td>
<td>352</td>
<td>354</td>
<td>348</td>
<td>240</td>
<td>281</td>
<td>--</td>
</tr>
<tr>
<td></td>
<td>T-55</td>
<td>389</td>
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<td>236</td>
<td>212</td>
<td>--</td>
</tr>
<tr>
<td></td>
<td>DC-28</td>
<td>2550</td>
<td>2656</td>
<td>1924</td>
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</tr>
<tr>
<td></td>
<td>DC-24</td>
<td>2845</td>
<td>2617</td>
<td>2310</td>
<td>2446</td>
<td>2310</td>
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</tr>
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<td></td>
<td>DS 72-5</td>
<td>4005</td>
<td>4102</td>
<td>3679</td>
<td>3962</td>
<td>3285</td>
<td>--</td>
</tr>
<tr>
<td></td>
<td>T-184</td>
<td>6950</td>
<td>6724</td>
<td>5977</td>
<td>4952</td>
<td>4836</td>
<td>--</td>
</tr>
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</table>

Results Expressed as the Percentage of C1

<table>
<thead>
<tr>
<th>Bone</th>
<th>Sample Number</th>
<th>Original Analysis</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
</tr>
</thead>
<tbody>
<tr>
<td>Femur</td>
<td>T-106</td>
<td>162</td>
<td>111</td>
<td>100</td>
<td>119</td>
<td>149</td>
<td></td>
</tr>
<tr>
<td></td>
<td>T-136</td>
<td>187</td>
<td>123</td>
<td>100</td>
<td>148</td>
<td>152</td>
<td></td>
</tr>
<tr>
<td></td>
<td>T-148</td>
<td>228</td>
<td>109</td>
<td>100</td>
<td>130</td>
<td>148</td>
<td></td>
</tr>
<tr>
<td></td>
<td>DC-28</td>
<td>543</td>
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<td>100</td>
<td>403</td>
<td>518</td>
<td></td>
</tr>
<tr>
<td></td>
<td>DC-24</td>
<td>160</td>
<td>130</td>
<td>100</td>
<td>150</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>T-184</td>
<td>144</td>
<td>110</td>
<td>100</td>
<td>123</td>
<td>143</td>
<td></td>
</tr>
<tr>
<td>Metacarpus</td>
<td>T-145</td>
<td>218</td>
<td>162</td>
<td>100</td>
<td>108</td>
<td>247</td>
<td></td>
</tr>
<tr>
<td></td>
<td>T-32</td>
<td>133</td>
<td>101</td>
<td>100</td>
<td>115</td>
<td>149</td>
<td></td>
</tr>
<tr>
<td></td>
<td>T-58</td>
<td>157</td>
<td>116</td>
<td>100</td>
<td>134</td>
<td>197</td>
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</tr>
<tr>
<td></td>
<td>DC-28</td>
<td>750</td>
<td>181</td>
<td>100</td>
<td>105</td>
<td>299</td>
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<tr>
<td></td>
<td>DC-24</td>
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<td>134</td>
<td>100</td>
<td>98</td>
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<td></td>
<td>T-184</td>
<td>177</td>
<td>156</td>
<td>100</td>
<td>148</td>
<td>172</td>
<td></td>
</tr>
<tr>
<td>Mandible</td>
<td>T-111</td>
<td>149</td>
<td>133</td>
<td>100</td>
<td>114</td>
<td>--</td>
<td></td>
</tr>
<tr>
<td></td>
<td>T-58</td>
<td>136</td>
<td>134</td>
<td>100</td>
<td>108</td>
<td>--</td>
<td></td>
</tr>
<tr>
<td></td>
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<td>174</td>
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<td>100</td>
<td>132</td>
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<td></td>
</tr>
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<td>396</td>
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<td>100</td>
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</tr>
<tr>
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<td>100</td>
<td>94</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>DS 72-5</td>
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<td>100</td>
<td>100</td>
<td>96</td>
<td>--</td>
<td></td>
</tr>
<tr>
<td></td>
<td>T-184</td>
<td>135</td>
<td>120</td>
<td>100</td>
<td>97</td>
<td>--</td>
<td></td>
</tr>
</tbody>
</table>

The data also confirm that, to avoid confusion, it is extremely important that all reports of bone fluoride concentrations must be accompanied by a detailed description of the method of sampling.

Bibliography


* * * *
TOTAL FLUORIDE INTAKE AND FLUORIDE CONTENT 
OF COMMON FOODS: A REVIEW

by

C. S. Farkas
Waterloo, Ontario

SUMMARY: In current publications and textbooks most data regarding the fluoride content of common foods as well as tables showing the average daily intake of fluoride in various countries, are based upon work carried out up to thirty-seven years ago. Such work does not allow for the effect of fluoridated drinking water on fluoride levels of processed and cooked foods. Moreover, the accuracy of data due to early testing methods may be questioned. Work done internationally may raise questions regarding identification of foods and relevance to urban type diets. In one table, for example, the fluoride content of cereal is given as < .10 - 20 ppm fluoride based on a range of data compiled from eight sources namely, four from U.S.S.R., three from Germany, and one from Japan. One must question what is meant by "cereal" in this listing and how to relate it to processed products. Data in tables published in the 1970's, citing average fluoride ingestion, were found to be based upon a small sampling. Some figures presented were found to include misquoted data. It must therefore be concluded that data on fluoride content of foods should be updated.

In the monograph "Fluorides" published in 1971 by the National Research Council, National Academy of Sciences, a table on the fluoride content in food is accompanied by the following statement: "Little fluoride is consumed in the diet,... The daily dietary (including drinking water) fluoride consumption in several countries has been... found to be at least 0.2 mg, and in only three... greater than 1 mg" (1). The data from the NRC/NAS table, are presented in Table 1. Since they are also recorded in three other major books (2-4) on fluoride, they constitute the basis for the concept that little fluoride is ingested in foods and

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* * * * * *

Presented at the Sixth Annual Conference of I.S. F. R., Williamsburg, 11/7-9/74.
beverages.

Because of the importance of this question in assessing the health effects of fluoride, it was of interest to investigate the basis for the figures shown in this table, particularly in the light of the great increase in the number of fluoridated communities and of improved methods of fluoride analysis during recent years.

An attempt to ascertain the origin of the data in Table 1 revealed that the 1971 figures were adapted from a similar table utilized by Hodge and Smith (4) in 1970 who in turn adapted their table from work presented by Cholak in 1959 (5). Therefore most of the data in Table 1 originated in 1959.

**TABLE 1**

<table>
<thead>
<tr>
<th>Country</th>
<th>Fluoride ingested in Food and Water, mg</th>
<th>Fluoride in Drinking Water, ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canada</td>
<td>0.18 - 0.3</td>
<td>0.1</td>
</tr>
<tr>
<td>England</td>
<td>0.3 - 0.5</td>
<td>trace</td>
</tr>
<tr>
<td>Japan</td>
<td>0.47 - 2.66^b</td>
<td>0.01 - 0.08^c</td>
</tr>
<tr>
<td>Newfoundland</td>
<td>2.74^d</td>
<td>trace</td>
</tr>
<tr>
<td>Norway</td>
<td>0.22 - 0.31</td>
<td>0.01 - 0.07</td>
</tr>
<tr>
<td>Soviet Union</td>
<td>0.6 - 1.2</td>
<td>0.2 - 0.3</td>
</tr>
<tr>
<td>Sweden</td>
<td>0.9</td>
<td>-</td>
</tr>
<tr>
<td>Switzerland</td>
<td>0.5^e</td>
<td>-</td>
</tr>
<tr>
<td>United States</td>
<td>0.2 - 0.3^e</td>
<td>0.34 - 0.80</td>
</tr>
</tbody>
</table>

|                      |                                         |                                  |
|                      | ^a Adapted from Hodge and Smith (4)      |                                  |
|                      | ^b Including 0.07 - 0.86 mg from green tea |                                  |
|                      | ^c Milligrams of fluoride ingested       |                                  |
|                      | ^d Including 1 mg from tea              |                                  |
|                      | ^e Exclusive of that in drinking water   |                                  |

Table 2 presents the 1959 data of Cholak which included fluoride values in food consumed in the U.S.A. These data were derived from work done by Heyroth et al. in 1951-1954 (6), by Armstrong and Knowlton in 1942 (7) and by McClure in 1949 (8). It is of interest to note when these data were obtained in view of the fact that they appear in 1971.
TABLE 2
Quantities of Fluoride in the Food Consumed Daily by Adults
(According to Cholak, 1959)

<table>
<thead>
<tr>
<th>Location</th>
<th>ppm in drinking water</th>
<th>Fluoride in Food (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>United States of America</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cincinnati, Ohio</td>
<td>0.1</td>
<td>0.34 - 0.80</td>
</tr>
<tr>
<td>Galesburg, Ill.</td>
<td>2.0</td>
<td>0.94 - 1.16</td>
</tr>
<tr>
<td>Ennis, Texas</td>
<td>5.0 - 6.0</td>
<td>1.32 - 1.35</td>
</tr>
<tr>
<td>Lake Preston, S. Dak.</td>
<td>6.0</td>
<td>0.99 - 2.19</td>
</tr>
<tr>
<td>Bartlett, Texas</td>
<td>8.0</td>
<td>2.33 - 3.13</td>
</tr>
<tr>
<td>O’Donnell, Texas</td>
<td>18.0</td>
<td>1.41 - 1.49</td>
</tr>
<tr>
<td>(Average general diet)</td>
<td></td>
<td>0.2+ - 0.3+</td>
</tr>
<tr>
<td>Norway</td>
<td>0.22 - 3.1</td>
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</tr>
<tr>
<td>U.S.S.R.</td>
<td>0.6 - 1.2</td>
<td></td>
</tr>
<tr>
<td>Canada</td>
<td>0.18 - 0.3</td>
<td></td>
</tr>
<tr>
<td>Switzerland</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>England</td>
<td>0.6 - 1.8</td>
<td></td>
</tr>
</tbody>
</table>

For this table, the following original sources are cited for fluoride in food in countries other than the U.S.A.:

Norway - Danielsen et al., Chem. Abstr. 1957 (9)
U.S.S.R. - Gabovich 1951 (10)
Canada - Ham and Smith, 1950 (11)
Switzerland - Von Fellenberg, 1948 (12)
England - Longwell, 1957 (13)

When Hodge and Smith in 1970 utilized fluoride values in food from the 1959 Cholak table, they added values for Sweden, Newfoundland, and Japan but failed to update the figures for England. It is of interest to explore the source of these English figures.

Cholak had recorded a daily intake of 0.6 to 1.8 mg in 1959, a figure which was changed by Hodge and Smith to 0.3 - 0.5 mg in their 1970 paper, although the source for the data of both Cholak and Hodge and Smith was the same article, namely that by Longwell in 1957. The figure, 0.6-1.8 mg fluoride, recorded by Cholak represents the probable intake in non-fluoridated areas, whereas Longwell presents probable values for fluoridated areas as 1.2 - 3.2 mg fluoride daily. Cholak had chosen the lower of Longwell's two values. Hodge and Smith's figure, obtained from the work of Longwell, excluded beverages. With
beverages included, according to Longwell's work the figure would be 1.7 mg. The above analysis indicates the biased choice of data which constitute the basis for the conclusion that "diets are usually low in fluoride and remarkably uniform world wide" (14).

In the Hodge et al. 1970 table the data cited for Newfoundland were obtained from a 1960 publication by Elliot and Smith (15). These authors in turn utilized a 1945 survey (16) of Newfoundland dietary intake and compiled fluoride food values using McClure's 1949 figures. The last mentioned are actually a compilation of data on the fluoride content of food analyzed prior to 1949 (8).

Of further interest to Canadians is the entry in table 2 for Canada, namely 0.18 - 0.3 mg, as the daily fluoride intake from food, The data were obtained from work done in 1949 and reported in 1950 by Ham and Smith (11) at the University of Toronto and consisted of assays of four typical restaurant meals in Toronto, exclusive of tea. This work was carried out thirteen years prior to the fluoridation of Toronto's water supply. The meals consisted of: Breakfast - juice, cream of wheat, toast, jam; Lunch - fruit salad, rolls, butter, dessert; Dinner - #1 tomato juice, halibut, potatoes, spinach, bread, butter, dessert, #2 tomato juice, beef, potatoes, mixed vegetables, bread, butter, dessert. The food values recorded by Ham and Smith represent pre-fluoridation background levels. However their figures should not be considered typical of Canadian intake levels of fluoride in the 1970's.

In view of these facts, one cannot but question the reliability of older data in tables utilized in 1970 and later to indicate that little fluoride is consumed in the diet.

Prior to the research by Marier and Rose in 1966 (17) and by Kramer et al., in 1974 (18) little attention had been paid to the elevated fluoride levels in food and beverages due to food processing. Marier and Rose (17) reported on the fluoride content of several foods and beverages processed with fluoridated water. Although the Marier and Rose data were available in the literature, the 1970 WHO report on Fluorides and Human Health relied upon the 1949 figures by McClure (8) instead of the more recent data. An interesting case in point is the figure given for the fluoride content of beer in the WHO table, namely 0.20 ppm, a value derived from a paper by P. Clifford in 1945 (19), as recorded in McClure's 1949 table. For beer processed with fluoridated water Marier and Rose (17) obtained 0.88 ppm fluoride. Yet the WHO report in 1970 presented the lower 1945 data by McClure.

The extent of the use of fluoridated water in processing commercial food and beverages in Canada has recently been reported by
Farkas and Parsons (20). In this study it was shown that, of the fifteen plants in the Montreal-Quebec area manufacturing carbonated beverages, eleven were located in areas where the water supply is fluoridated and, of eight plants manufacturing soups in Canada, five were located in fluoridated areas. Thus many food products are processed in fluoridated areas. Other work by Farkas et al. (21) has shown that beverages made from concentrates, diluted with fluoridated water and sold as a liquid product, have surprisingly high fluoride levels. For instance, orange juice contained .9 ppm fluoride and an infant formula .9 ppm fluoride.

Also of interest to note is the origin of the data given for fluoride content of foods and beverages in fluoride food tables. Use of wide ranges of fluoride values in calculating a potential daily fluoride intake is difficult. The majority of the citations in table 3 were compiled from Chemical Abstracts and are of international origin. The use of international data for North American dietaries may be questioned. A case in point is the entry for cereals: cereal plus cereal products .10 to 20 ppm, .18 to 2.8 ppm.

### TABLE 3

Comparison of Fluoride Levels in Fresh Foods as Reported by Cholak (5) and Hodge et al. (4)

<table>
<thead>
<tr>
<th>Food, ppm</th>
<th>Cholak, 1959</th>
<th>Hodge, et al., 1970</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meats</td>
<td>0.01 - 7.7</td>
<td>0.14 - 2</td>
</tr>
<tr>
<td>Fish</td>
<td>0.10 - 24</td>
<td>0.8 - 40</td>
</tr>
<tr>
<td>Sardines</td>
<td>--</td>
<td>50*</td>
</tr>
<tr>
<td>Shrimp</td>
<td>--</td>
<td>186</td>
</tr>
<tr>
<td>Fish meal</td>
<td>--</td>
<td></td>
</tr>
<tr>
<td>Citrus fruits</td>
<td>0.04 - 0.36</td>
<td>0.07 - 0.17</td>
</tr>
<tr>
<td>Non-citrus fruits</td>
<td>0.02 - 1.32</td>
<td>0.03 - 0.84</td>
</tr>
<tr>
<td>Cereals and cereal products</td>
<td>0.10 - 20</td>
<td>0.18 - 2.8</td>
</tr>
<tr>
<td>Vegetables and tubers</td>
<td>1.10 - 3.0</td>
<td>0.02 - 0.9</td>
</tr>
</tbody>
</table>

*Shrimp meat, 0.4 ppm; shrimp shell, 18-48 ppm

The following references for this item are cited: 1956 Norwegian (22); 1955, 1961, 1962, 1963 U.S.S.R. (23-26); 1964 Japanese (27); 1963, 1965 German (28, 29). In other words, the data cited were compiled from work done on grains, flours and meals. In one U.S.S.R. FLUORIDE
study, the analysis of wheat, oats, and barley was made in a known endemic fluorosis area (23). One cannot but question the relevance of these outdated data to North American dietaries of 1970. The great import of the outdated fluoride values in food is brought to the fore by the fact that many recent texts rely on McClure's data obtained prior to 1948. Food tables which appear in Heinz Handbook of Nutrition (30); WHO, Fluorides and Human Health (2) and McClure's, Fluoridation, The Search and the Victory (3) cite these early values. Other food tables, presented in major works such as Fluorides (1) and Advanced Chemical Series, Dietary Chemicals vs. Dental Caries (4) are adapted mainly from Cholak's 1959 data much of which was also cited from earlier publications. It is obvious from the analysis presented here that current data on fluoride content of foods and beverages are needed in order to estimate the average daily dietary intake of fluoride in 1975.

Bibliography


14. Same as ref. 4., p. 98.


FLUORIDE
27. Iizuka, Y.: Studies on Fluoride from Hygienic Standpoint.
   2. Fluorine Contents in Human Teeth, in Foodstuffs and in Public


29. Grieser, N.: The Increase of the Fluoride Intake of Man by Con-
   sumption of Foods of Animal Origin. Medizin und Ernährung, 6:30-5,
   1965.

   p. 72.

* * * *

THE SAFE MAXIMUM DAILY INTAKE OF DIETARY FLUORIDES

by

C. S. Farkas
Waterloo, Ontario

SUMMARY: A survey questionnaire which was sent to
authorities in the fields of dentistry, nutrition and
medicine in order to establish a criterion for safe
daily maximum intake of fluoride yielded no consen-
sus. Many respondents to the questionnaire expressed
their answers in relative terms considering fluoride
intake in parts per million of fluoride ingested. For
any discussion of this subject it is desirable to em-
ploy absolute terms i.e., milligrams of fluoride ingest-
ed. If a criterion of mg/kg body weight is used as a
basis for recommending daily fluoride intake levels,
it is essential to know the level of fluoride in current
diets, and in foods and beverages. Little data is avail-
able in this regard.

From the Man-Environment Studies, University of Waterloo, Ontario, Canada.

* * * * *

Presented at the Sixth Annual Conference of I.S. F. R., Williamsburg, 11/7-9/74.

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Little agreement exists in the literature regarding the "safe" maximum intake of fluorides in milligrams per day. It was considered of interest, therefore, to obtain data on recommended daily intake levels of fluoride in order to develop a criterion for acceptable fluoride ingestion in absolute rather than relative terms. Such a criterion would be similar to those in existence or being developed for other substances such as lead and mercury which, like fluoride, are appearing in the environment in increasing amounts as a result of man's activities.

As a step in the ascertainment of a criterion, over 250 authorities in the fields of dentistry, medicine, and nutrition were surveyed. Names were selected from the list of reviewers of the World Health Organization monograph, "Fluorides and Human Health" (1), from editorial boards of various journals, and of other individuals recognized in the area of fluoride research.

Twenty-two replies were received to an original open-ended query: "In your opinion, what is considered to be a safe maximum daily intake in mg of fluorides in foods and beverages?" The replies to this question were compiled and resent to the original 250 individuals with the request that they indicate whether they agree (A) or disagree (DA).

The statements obtained from the first query tabulated in Table 1, were mailed for comments to the 250 original individuals. Forty-one useful responses were received from the second mailings. Several names were untraceable. Several individuals wrote that they considered other issues of greater importance than fluoride. Some judged themselves inadequate to answer the questionnaire. Several questionnaires were returned only partially answered or not answered at all. In the latter cases, letters were usually sent requesting additional comments.

Whether the correspondent agreed or disagreed with the four assertions has been recorded in Table 1.

Of interest is the following response to general statement #1: "I do not agree with the view of statement #1, since it can surely be decided what is safe maximum intake, not for the individual but, for the populace. This has been, in fact, established."

To statement #2, this same respondent commented: "General nutritional intake in civilized populations, apparently, is not influenced by fluoride intake. This assumption is sound one but far from being proven." Another respondent added the word "climate" to statement #2.
TABLE 1

Response to Original Query

<table>
<thead>
<tr>
<th>Statement</th>
<th>Agree</th>
<th>Disagree</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) It is difficult to decide on a safe maximum daily intake for fluorides. Instead, the acceptable daily intake (ADI) should be established, ADI being the amount of a substance that may be ingested daily without causing appreciable risk.</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>2) Safe Maximum fluoride intake is influenced by general nutritional intake, especially vitamin C and calcium.</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>3) Those daily doses are safe which do not cause objectionable mottling in children.</td>
<td>9</td>
<td>3</td>
</tr>
<tr>
<td>4) A healthy kidney function is important for maximum elimination of absorbed fluoride.</td>
<td>5</td>
<td>4</td>
</tr>
</tbody>
</table>

Statement #4 elicited this comment: "With impaired kidney function, a build-up of body wastes is more serious than fluoride-build up."

Several general observations were received from respondents: "... the safety of prolonged consumption of foods and water to which fluoride has been added even in small, rigorously controlled doses, does not appear sufficiently demonstrated (safety is not proven). If one wishes to utilize the preventive properties of fluoride vis-a-vis dental caries, the method to use is ingestion of fluoride tablets following dosage prescribed by physician and dentist, ... without exposing all the population to absorption of fluoride."

"Our opinion is that fluoride is only a palliative means for combatting caries and is not an etiological treatment; recourse to it must not disregard factors which can play a role such as abuse of carbohydrate, dental malposition leading to food deposits, and general constitutional factors."

"Further research on fluorine in nutrition, physiology, and toxicology is certainly indicated in view of the great importance of this element in several aspects of human health. Owing to the ever increasing water consumption in our cities and the psychological difficulties involved in water fluoridation, more research should be done particularly..."
on alternatives to water fluoridation. I regard domestic salt as the most promising alternative."

Table 2 is a compilation of replies to the second survey of opinion regarding Recommended Daily Intake Levels of Fluoride.

**TABLE 2**

**Recommended Daily Fluoride Intake Levels**

<table>
<thead>
<tr>
<th>Fluoride Intake Levels</th>
<th>No. that agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. 0.05 - 0.07 mg/kg body weight</td>
<td>5</td>
</tr>
<tr>
<td>2. 0.5 mg - children 2-3 years</td>
<td>10</td>
</tr>
<tr>
<td>1 mg - children over 3 years</td>
<td></td>
</tr>
<tr>
<td>3. 1.1 - 2 mg daily (children 5-15 years)</td>
<td>8</td>
</tr>
<tr>
<td>4. 2.1 - 3 mg daily</td>
<td>6</td>
</tr>
<tr>
<td>5. 3.1 - 4 mg daily</td>
<td>3</td>
</tr>
<tr>
<td>6. 4.1 - 5 mg daily</td>
<td>5</td>
</tr>
<tr>
<td>7. 5.1 - 6 mg daily</td>
<td>2</td>
</tr>
<tr>
<td>8. 6.1 - 7 mg daily</td>
<td>5</td>
</tr>
</tbody>
</table>

With respect to category 0.05 to 0.07 mg/kg body weight as a recommended maximum level of intake the following are excerpts of comments:

"I fully agree that the safe daily dosage varies between 0.05 to 0.07 mg/kg body weight. In the other dosages given (#2 to 8) no reference is made to body weight; they are not acceptable but may serve as a guide for an adult of approximately 70 kg as in the data given in #6."

Re the 3 to 4 mg/kg body weight: "For Singapore with a higher mean daily temperature probably lower supplementation of the public water supply can be recommended, but I do not see any reason to agree with the lower than necessary dosages given in #2, 3, 4 and 5. Perhaps the suggestion to increase daily intake to between 6 and 7 mg may be the upper permissible limit (for a 70 kg adult)."

"The recommendations (3 to 7 mg/day) given in #5 to 8 agree quite well and therefore might be accepted. Maybe the more moderate..."
recommendations (1 to 3 mg/day) in #3 and 4 should be employed. It will depend, of course, upon the basic content of fluoride in the drinking water."

"... Acceptable intake must vary with body weight and age. Many of your doses mention neither age nor the weight concerned."

"The safe maximal daily intake of fluoride varies with age. In infancy and children up to puberty, it would appear from the available data that an intake in the range of one to two mg of fluoride is not only safe but efficacious in reducing the incidence of dental caries. In adults, the data regarding the therapeutic necessity to fluoride ingestion has less documentation."

"The data presently are too limited to make an intelligent and knowledgeable recommendation for adults; however, it would appear that a level of 2 to 4 ppm is quite safe and probably efficacious in terms of maintaining a normally mineralized skeleton."

"The safe maximum daily intake of fluorides should be separately assessed for various population groups and the individual differences in man should be taken into consideration. ... the safe maximum daily intake for children 2 to 5 years should be placed somewhere between 0.6 and 1.2 mg. ... Safe maximum daily intake for adults might be in the limits of 1.2 to 2.4 mg of fluorides."

"There is an area in Turkey where 90% of the children show signs of fluorosis. In this area drinking water has 3.7 to 4.4 mg fluoride per liter. Therefore we recommend a maximum daily intake of 2.1 to 3.0 mg fluoride from foods and beverages."

"It is difficult to establish the safe daily intake of fluorides. The rate of intake cannot be the same for adults and children; there exist, further, individual reactions."

**Discussion**

This survey was an attempt to develop a criterion for acceptable fluoride ingestion in absolute terms of mg per person per day rather than relative terms of ppm in drinking water. No consensus was found.

It is of interest to note the number of respondents who stated that various levels of ingestion of fluoride in parts per million (ppm) were safe or recommended. This type of expression in relative terms...
is vague and misleading. Discussion of ingestion or intake should be expressed in absolute terms, i.e. milligrams of fluoride ingested. In other words, the average daily water intake is reported to be 4 glasses or 1 quart. Water fluoridated at 1 ppm thus provides an average of 1 mg, not including that ingested through food.

Work reported by Farkas, Burnie, Helmeute (2) has shown that preparation of tea (2-cup tea bag) with 1 ppm fluoridated water yields 0.5 mg fluoride per 6 oz. cup. Such calculations are rarely included in studies which cite the fluoride concentration of water exclusively.

Several respondents commented that Table 2 of the questionnaire failed to take into account the variation of fluoride intake because of age and/or weight. The first statement in the questionnaire took this aspect into account by suggesting intake on a mg/kg body weight basis. Few of the critics of the questionnaire checked this category. In connection with fluoride intake, many respondents seemed to disregard the importance of daily dose. They opted, instead, for the general dosage levels which were undefined as to whether they were for adults or children.

If one considers this criterion (mg/kg body weight) as a basis for recommending fluoride intake levels, then it is essential to know how much fluoride is present in current diets and, concurrently, how much fluoride is present in foods and beverages. The available data are not adequate to provide sufficient information on these points.

Bibliography


Discussion

Dr. Hanhijärvi: When we consider fluoride in the diet it is important to distinguish between total fluoride determinable by analysis and that which is physiologically available. The human gastrointestinal tract does not absorb food to remove all the fluoride which is present but absorbs only a part of it. Therefore it is the absorbable portion of fluoride in foodstuffs that should also be determined.
Prof. Burgstahler: Dr. H. Spencer of the Veteran's Administration Hospital in Hines, Illinois, has paid close attention to this question in her studies. She estimates that over 80 percent of fluoride in food and over 95 percent of that which is present in water, is absorbed.

Dr. Hanhijärvi: This is true, but as Professor Jolly noted yesterday, there are other factors in water which affect absorption. We must remember that the carbon-fluorine covalent bond is very strong and that, with few exceptions, it is not broken in the gastrointestinal tract or liver.

Prof, Burgstahler: You are raising another question. It is my impression that there is very little covalently bonded carbon-fluorine in food. Rather, much of the unabsorbed fluoride in food is present in ionic form tightly adsorbed to protein components or in highly insoluble mineral complexes, but not as covalently bonded organic fluoride. In connection with the intake of fluoride by infants and children, I should like to call attention to the recent Boston area study by R. Asendin and T. C. Peebles (Arch. Oral Biol., 19:321-326, 1974). These workers investigated the dental effects of 0.5 mg/day fluoride supplements administered shortly after birth to age 3 and then 1.0 mg/day to age 12. The incidence of enamel fluorosis in the permanent teeth was quite high: 67 percent with definite fluorosis and 14 percent in the "moderate" classification, giving an overall fluorosis index of 0.88. Among the 100 children in the study group, 5 or 6 were considered to have an "unacceptable" degree of moderate fluorosis. I believe these findings bear out the fluoride-intake fluorosis relationship found in children in India as reported at this session by Prof. Nanda.

Dr. Groth: Mrs. Farkas, did any respondents to your survey mention any possible toxic effects of low-level fluoride ingestion other than dental and skeletal fluorosis?

Mrs. Farkas: Only one respondent did so.

Prof. Patrick: We are still very much at sea in a storm of uncertainty with respect to determining actual fluoride intake and maximum safe levels of intake. From this discussion I see the following important problems which need to be resolved: (1) the extent of fluoride absorption versus dietary content; (2) the reliability of many of the older data on the fluoride content of foods; (3) the large variability in individual intake of flu-
oride and effects depending on diet, age, and state of health; (4) the physiological stability of the covalent carbon-fluoride bond; (5) the individual variability to both the chemical and biochemical challenge of fluoride. At present I see too many complications standing in the way of specifying a broadly permissible level of fluoride intake.

Mrs. Farkas: I wish to return to the matter of fluoride absorption from food and such sources as fish protein concentrate. Much of the criticism of Spencer's findings has been based on work done with rats, rabbits, and dogs. It is worth noting that these animals, in contrast to humans, synthesize ascorbic acid, and ascorbic acid tends to suppress fluoride absorption. Thus the results are not really comparable.

* * * *

CHEMICAL COMPOSITION AND STRUCTURE OF FLUOROTIC BONE

by

L. Singer, W. D. Armstrong, I. Zipkin, and P. D. Frazier
Minneapolis, Minnesota

(Abstracted from Clinical Orthopedics and Related Research, 99:303-12, 1974).

The authors investigated the composition of a markedly fluorosed human bone by chemical analytical methods, by X-ray diffraction, by microroentgenography and by density distribution of bone particles. The specimen was a portion of the seventh rib of a 45 year-old farmer with severe skeletal fluorosis who had been consuming water containing 9.5 ppm fluoride. His serum calcium was 9.4 mg/100 ml, serum inorganic phosphorus 3mg/100 ml, and serum alkaline phosphatase 8 KA units. The patient expired as the result of a urinary tract infection and a secondary infection from bed sores.

From the Department of Biochemistry (Medical School) University of Minnesota, Minneapolis, Minnesota.
The cation/anion relation in milli-equivalent (mEq) was 0.903 at the cortical region of the bone, 0.93 at the cancellous region and 0.963 in the exostoses compared with 1.02 in a "low" fluoride rib and 1.01 in the cortex of a bovine femur which served as controls. The calcium/phosphorus quotient was 1.59 for the cortical region, 1.62 for the cancellous region and 1.68 for the exostoses. The figures for the "low" fluoride rib and for the cortex of bovine femur were 1.72 and 1.65 respectively.

After being incinerated for 5 hours at 700° C, the ash content of the cortex, cancellous bone and exostoses of the fluorosed bones were 70.0, 69.1, and 67.8% respectively (dry fat-free). The collagen content of the fluorosed bone was 30.14%. The fluoride content of the fluorosed bone was 30 to 40% higher than that of the theoretical fluoride content of fluoroapatite. The three specimens of the fluorosed bone contained 1.15, 1.50 and 1.30% fluoride respectively which compared to 0.08% in the control human bone ash 0.103 in the bovine cortex. There was a decrease in citrate namely of 0.65 to 0.75% as compared to 1.08 to 1.92%. The carbon dioxide (carbonate) level of the fluorosed bone was considerably elevated.

Microscopograms of the fluorosed rib revealed hypercalcification and hyperossification of the cortex, of the medullary cavities and of the prominent exostoses. Resorption cavities and young osteons were virtually absent which suggested a failure of bone resorption. One of the lesions presented characteristic features of vitamin D resistant rickets.

The x-ray diffraction studies showed a high resolution at characteristic apatite reflection peaks, which indicated enhanced crystallinity of the bone mineral.

G.L.W.

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The International Society for Fluoride Research program committee is now soliciting abstracts of papers for presentation at its Seventh Conference to be held in Zandvoort, Holland, February 8-10, 1976. Abstracts up to 300 words should be submitted in triplicate to the Society's office, P.O. Box 692, Warren, Michigan 48090 no later than October 15, 1975.
EFFECT OF FLUORIDATED WATER UPON SERUM LIPIDS, IONS,
CARDIOVASCULAR DISEASE MORTALITY RATES

by

M. L. Bierenbaum, A. I. Fleischman, R. Stein, and T. Hayton
Montclair, New Jersey


This study compares the serum lipids and serum ions in two
groups of volunteers selected at random from two similar industrial
communities, Phillipsburg, N. J. and Easton, Pa. The subjects were
all males with a similar socio-economic and ethnic background. The
two communities, Phillipsburg and Easton are adjacent to each other
but on opposite sides of the Delaware River; they obtain their raw wa-
ter from the same source. Industrial activities in the two areas are
identical. The major difference with which residents of the two com-

munities are confronted is that Easton has been fluoridated for the
past 15 years whereas water in Phillipsburg is unfluoridated. The wa-
ter supply in Easton contains significantly less calcium and magnesium
namely, 18, 4 and 4, 3 respectively, as compared to that in Phillipsburg
namely, 26, 4 and 7, 2. This difference is attributed to the treatment
of the water with fluorosilicic acid. The total hardness of the water
is the same in the two cities.

The authors tabulated the mortality rates for the two cities
for the year 1968, and resident deaths for selective causes and age groups
for both communities. In Phillipsburg with a population of 18,510, there
were 131 deaths or a rate of 708 per 100,000; in Easton (population
30,000) 194 deaths occurred or 647 per 100,000. Of 50 randomly se-
lected subjects from each of the two cities, 41 participated in the study.
Their mean age was 43, 8 in Phillipsburg and 43, 0 in Easton. All 41 of
them had been residing and working in the two respective cities for at
least 5 years. Cases with diabetes, nephrosis, hypothyroidism and al-
coholism were eliminated since these diseases might alter lipid metabo-

lism. All specimens were collected within one month.

The serum cholesterol and triglycerides were slightly elevated
in Phillipsburg as compared to Easton but the differences were not sta-
tistically significant. The total number of lipid abnormalities were also
slightly higher in Phillipsburg. The serum fluoride levels in the two
cities showed no significant differences namely, 0.46 ± 0.01 μM/l in
Phillipsburg and 0.41 ± 0.02 μM/l in fluoridated Easton. The similar

From the Atherosclerosis Research Group, St. Vincent's Hospital, Mont-
cclair, N.J.

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Sem lithium levels were expected since both water and diet were essentially the same in the two areas. In Easton, which had the lower amount of calcium and magnesium in the water, there was a significantly higher serum calcium, serum magnesium and serum inorganic phosphorus. The authors explained this difference by assuming a possible synergistic effect of fluoride "in the absorption and transport of these ions". Based on the limited number of samples they concluded that "long term fluoridation does not appear to adversely affect cardiovascular disease mortality rates."

* * * * *

ENZYMES HISTOCHEMICAL STUDIES ON THE EFFECT OF SODIUM FLUORIDE UPON THE ORGAN OF CORTI

by

W. Schützle and B. von Westernhagen
Göttingen, Germany


This study was prompted by the fact that large doses of sodium fluoride have been used in the treatment of otosclerosis in order to increase the incorporation of calcium and counter resorption of bone as originally recommended by Shambaugh. The authors administered to 16 guinea pigs intraperitoneally, 0.1 mg sodium fluoride twice daily for a period of 10 days. Eight guinea pigs served as controls. Shortly after the final injection the animals were sacrificed. The cochlear bones were stained and studied histologically and histochemically. The following enzymes were studied: Peroxydase, succinic dehydrogenase, monoaminoxydase, nonspecific esterase, acid and alkaline phosphatases, galactosidase, glucuronidase and sulfutase. The morphological changes were sparse on surface preparations of the cochlea but the organ of Corti showed a decrease in the activity of several enzymes, especially of acid phosphatase. This enzyme was also diminished in the capsule of the osseous labyrinth.

The authors caution about prolonged use of fluoride: It might cause extensive damage to the ear although short-term doses may disclose damage in only a limited number of the hair cells.

* * * * *

From the Univ. HNO-Klinik, Göttingen, Germany.

G. L. W.

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THE HARDNESS OF HUMAN DENTIN IN RELATION TO THE CONTENT OF CALCIUM, PHOSPHORUS AND FLUORIDE

by

H. P. Worner
Tübingen, D.B.R.


The author explored the question whether or not caries-prone teeth are softer than caries-resistant teeth. He determined the degree of hardness by analyzing a fully developed 3rd molar tooth of a 23 year-old female patient for its calcium, phosphorus and fluoride content by means of electro-radio-microanalysis. He employed the "Durimet" instrument of Leitz-Wetzlar. Four different portions of a longitudinal section of the tooth ten microns in length were studied.

The calcium content is highest in the external portion of the enamel and remains constant at a distance of 1200 microns whereupon it decreases gradually to a minimum in the central portion of the enamel. In dentin close to the enamel, the values are about the same as those in the innermost portion of the enamel whence they increase towards the central zone of the dentin.

The concentration of phosphorus in the enamel also decreases gradually from the outer surface inward. On both sides of the enamel-dentin border the phosphorus content is about the same. In the central portion of the dentin, the phosphorus is irregularly distributed.

The maximum fluoride values are found about 400 microns below the external surface of the enamel. Toward the enamel-dentin border, the decrease in the fluoride concentration is so gradual that it is hardly noticeable but a second maximum is reached very close to the enamel-dentin border.

On the basis of a regression analysis the author observed a negative correlation between the calcium of the dentin and its hardness. In other words, as the calcium content of the dentin increases its hardness decreases. However, the phosphorus and fluoride content of the dentin is unrelated to its hardness. The author points out that the hardness of the tooth structure is dependent on the spaces between the apatite crystals i.e. on how closely together these crystals aggregate. He postulated that calcium is deposited in the tooth substance not only as hydroxylapatite and fluoroapatite but also as amorphous calcium carbonate.

From the Klinik für Zahn-, Mund- und Kieferkrankheiten der Universität Tübingen, D.B.R.
and that the hardness of the dentin decreases in relation to the increase of calcium carbonate in the spaces between the apatite.

G. L. W.

* * * *

NEPHROGENIC DIABETES INSIPIDUS WITH FLUOROSIS

by

L. W. Greenberg, C. E. Nelsen, and N. Kramer
Columbus, Ohio


The case histories of two white boys with nephrogenic diabetes insipidus were presented. One boy, age 10, had polydipsia in his early school years but had adjusted more recently to the situation. He had been residing throughout his entire life in a community with fluoridated water (1 ppm) and had also brushed his teeth with fluoride-containing toothpastes. Except for the presence of mottled teeth, the examination was unremarkable. The specific gravity of the urine was low; serum calcium 8.7 mg/100 ml, inorganic phosphorus 5.3 mg/100 ml, creatinine clearance 140 cc per minute. The analysis of a molar tooth showed 591 ppm of fluoride which was about 6 times the concentration of normal controls. After water deprivation and 5% dehydration, the urine osmolality remained below 100 mOsm per liter and the serum osmolality rose to 298 mOsm/liter. On hydrochlorothiazide, 50 mg twice daily, the urine excretion decreased by approximately 50%.

The second boy, age 11, had acute attacks of cyanosis and breathholding at 8 weeks of age. Other members of the family had polyuria and polydipsia. The serum calcium was low (8.8 mg/100 ml), phosphorus high (6.4 mg/100 ml) and blood urea nitrogen was 36 mg/100 ml. The specific gravity of the urine was in a low range (1.006-1.013). At seven months of age, the child had breath-holding episodes with unconsciousness which lasted from 24 to 36 hours. The EEG revealed a generalized arrhythmia and

From the Department of Pediatrics, College of Medicine, The Ohio State University, and The Children's Research Hospital Research Foundation, Columbus.
spiking at the right occipital area. Pitressin and arginine vasotocin did not improve the urinary osmolarity (160 mOsm/liter). The child also had one episode of hypokalemic alkalosis with tetany. His urinary output had been as high as 9 liters per day. He also had mottled teeth. Except for the first 4 years of his life he lived in a fluoridated community. His lateral deciduous incisor revealed a fluoride content of 285 ppm, nearly twice the control value.

The authors named the following diseases which give rise to polydipsia and polyuria: Central diabetes insipidus, psychogenic water ingestion, renal medullary disease including hypercalcemic nephropathy, hypokalemic nephropathy and anatomic and vascular disturbances, and diseases causing solute diuresis; they warn of fluoride toxicity from fluoridated water in such diseases.

G. L. W.

(Editor's note: Articles pertaining to polydipsia and polyuria due to fluoride intake were not cited in the bibliography.)

* * *

EFFECT OF FLUORIDE ON BONE DISEASE IN HEMODIALYSIS PATIENTS

by

P. E. Cordy, R. Gagnon, M. Kaye, and D. R. Taves
Montreal, Quebec and Rochester, New York


The authors compared two groups of kidney patients who had been undergoing dialysis for over one year with the KiiI dialyser single pass system, three times weekly for 24 to 30 hours. Thirty-four patients residing in non-fluoridated Montreal and seven in fluoridated communities; all but 8 of the Montreal patients were on home dialysis. Serum fluoride and bone fluoride were measured by Dr. D. R. Taves, University of Rochester, N. Y. X-rays, which were taken two years prior to the dialysis, were reviewed and new films were made at the end of the study: bone biopsies were analyzed at the beginning and at the end

From the Department of Medicine, Montreal General Hospital, Quebec, Canada and the University of Rochester, School of Medicine and Dentistry, Rochester, New York.
of the study. The average interval between biopsies was 3.6 years in the non-fluoride Montreal group and 2.9 in the fluoridated patients.

The two groups did not differ significantly either at the beginning or at the end of the study in regard to serum BUN, creatinine or bicarbonate. At the end of the study, the mean total serum calcium was 10 mg% in the non-fluoride and 9.6 mg% in the fluoride group, the mean phosphates were 5.5 mg% and 5.8 mg% respectively. The authors observed a significant elevation in the mean alkaline phosphatase in the fluoride group, namely 22 KA units due to a marked rise in four out of seven patients compared to 13.2 KA units in the non-fluoride group. There was also a significant increase in surface area covered by osteoid, namely 49.7% in the fluoride group compared to 12% in the control group. The increase in the fluoride group was accounted for by the fact that four patients developed a marked increase in osteoid as judged by bone biopsy. Twelve of the 34 non-fluoride patients exhibited progressive osteitis fibrosa verified by biopsy. Two of these underwent parathyroidectomy, the other ten were treated with dihydrotachysterol. Following this treatment the alkaline phosphatase and the percentage of osteitis fibrosa decreased. No significant difference was found in either group in the percentage of osteitis fibrosa at the time of the second biopsy compared with the first biopsy. In the non-fluoridated group no change in the demineralization and resorption was noted whereas in 5 patients the osteosclerosis decreased. On the other hand, in the fluoride group, osteosclerosis was more pronounced in over half of the patients at the end of the study.

In summary, 4 out of 7 nephritic patients using fluoridated water for hemodialysis developed fluoride osteomalacia which did not occur in the 34 patients residing in unfluoridated communities. Osteitis fibrosa was reversible in ten of twelve cases by dihydrotachysterol treatment. The authors concluded that the presence of fluoride in the dialysate is associated with an increased incidence of osteomalacia and that in the absence of fluoride, bone disease is largely controllable.

G. L. W.
To the Editor:

In my Editorial Review entitled "Fluoride and Down's Syndrome (Mongolism)" (January, 1975) the following changes should be made.

Page 2, paragraph 2 - After "... more than 800 urban cases" insert ref. 13. The tabulations in references 9 and 10 included 687 of these cases.

Page 5, paragraph 3 - The explanation proposed to account for the mean maternal age discrepancy is incorrect. Shortly after the review went to press I found out that an unstated statistical correction of 0.5 year was added to the arithmetical mean maternal ages in reference 24 to correct for the average time interval between the mother's recorded whole-number age and the date of the birth of her afflicted child. This was not done in reference 22 thus accounting for the apparent discrepancy.

Page 6, paragraph 2 - The total births figure should read 1,752,435 instead of 1,752,345.

Page 8 - The author of reference 1 is Down, J. Langdon II. (one name only).

In the condensed report by Gileva et al. (pp. 47-50 of the January, 1975 issue) the spelling of the words "mytotic" and "mytosis" should be changed to "mitotic" and "mitosis" throughout.

Professor Albert W. Burgstahler
Lawrence, Kansas