Toxicity of Fluorides in Dental Health

First Written Publication of Work on Fluorine Study at Indiana University


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The question may be asked, why is fluorine of interest to us now? How is it used. What are its main sources and compounds? An attempt will be made to answer these questions in the first part of this paper and the latter part will be used for the discussion of the toxicity of these materials.

Compounds of fluorine have important uses. The fluoride of calcium may play an important part in the building of teeth and bones. Fluorides are present, in small amounts, in the blood and have been suggested by some to be of importance in the mechanism of clotting. Fluorspar is used as a flux to combine with certain materials that cannot be melted readily, thus forming easily melting substances. The ammonium salt of fluorine is used as a disinfectant, and sodium fluoride as an insecticide, as a flux, and in treating wood to prevent the growth of fungi. Cryolite is used in the preparation of metallic aluminum. Also, fluoride compounds are used as refrigerants, in medicine, and in the fermentation industry.

Prevalence of Fluorine

Fluorine is approximately one half as abundant in the earth crust as chlorine, and about 10 times as plentiful as bromine and iodine. As compared to the other elements and compounds, it ranks about twentieth. It is never found free in nature because of its extreme activity. Its most widely distributed compounds are fluorspar, CaF₂, but it occurs also in cryolite, Na₃AlF₆, and in fluorapatite, CaF₂(Ca₃(PO₄)₂)₃. Very small traces are present in sea water. It is also present in the enamel of our teeth. The fourth member of the halogen family differs somewhat from the other. This difference is more apparent than real and is due mainly to the fact that fluorine itself is far more active than the other halogens and that its compounds are much more stable. Fluorine compounds are somewhat poisonous as is evident in the fact that they are used in large amounts in the manufacture of insect powders.

Fluorspar serves as the source...
of practically all fluorine compounds. It is a mineral which occurs as cubical crystals of many different colors. The crystals glow or “fluoresce” in a dark room after they have been exposed to bright sunlight; hence, the word fluorescence is derived from this property of fluor spar.

**Effect of Continued Administration of Fluorides**

Small quantities of fluoride that produce no apparent effects when administered singly, lead to marked changes when their administration is continued. The phenomena differ considerably according to the amounts administered. The smallest effective quantities, taken as drinking water or food, show only faulty tooth formation in children, “mottled enamel”; somewhat larger amounts, experimentally or in industrial exposure, may cause bone changes in adults, osteosclerosis in man, osteoporosis and osteomalacia in animals. Still larger amounts interfere with nutrition, growth, and reproduction.

Endemic fluorosis, characterized by “mottled enamel,” exists in various areas of the world; in the United States especially in regions of the Rocky Mountains and Mississippi Valley, but to some degree in practically every state. It was first described in 1916 by Black and McKay. Subsequent studies by McKay, 1926 and 1930, indicated its relation to the domestic water supply, and Church-

hill, 1931, showed spectroscopically that these waters contain fluorine. On the other hand, it is claimed that the incidence of dental caries varies inversely to the fluoride content of the water supply, regardless of the incidence of mottling.

Fluorine in food is at present of minor importance, unless the water content is also fairly high. Bone ash contains about 0.1 per cent of fluorine; this amount being sufficient to produce tooth degeneration when fed to rats. Rohom, 1939, therefore advises against the use of bone ash as a mineral diet supplement for children or pregnant or lactating women.

**Changes in Human Teeth**

The changes in human teeth consist of chalky white patches, often pitted and eroded. Identical changes had been observed by McCollum and associate, 1925, in the teeth of young rats receiving very small quantities of fluoride. The lower incisors are shortened by spontaneous fractures, leading to nonoclusion, and the upper incisors therefore continue to grow and curl backward. Changes, 1929, noted the dull, chalky color and roughening, and studied the histological changes. These have also been investigated in the teeth and jaw bones by Pachaly, 1932, and W. Dittrick, 1932. They consist in deposition of hypoplastic, faultily calcified enamel and bone tissue. The enamel-
forming cells are selectively vulnerable to fluoride, being injured by doses for which no other deleterious action has been demonstrated. Morphologic changes in the ameloblasts and their calcium globules may be seen an hour after injection of sodium fluoride (Schour and Smith, 1935). Dean, Sebrell, and Breaux, 1934, describe the progression of the changes with increasing concentrations of NaF in the drinking water, from minute transverse brown striations with 25 parts per million; passing to irregular brown patches with 150 p.p.m.; and becoming chalky and brittle at 300 p.p.m. These effects are not prevented by the administration of calcium, phosphorus, Na₂(HPO)₄ or parathyroid hormone (Sutro, 1935). Dogs develop mottled enamel, similar to the human (Greenwood, Hewitt and Nelson, 1935); cattle and pigs show marked changes in the mandibles, with increase of thickness, roughening of the surface and enlargement of the medullary spaces (G. E. T. Taylor, 1929; Bethke, Kick et. al., 1933).

The fluoride content of human teeth is normally about 0.02 and 0.03 per cent (Bowes and Murray, 1935).

Effect of Exposure to Cryolite

Bone changes are seen especially with industrial exposure to the dust of cryolite or phosphate rock, with larger fluoride income than would occur from water. With probable income of 15 to 25 mg. per day, the earliest roentgen changes are seen in about two and one-half years and become severe in about eleven years (Roholm, 1938). P. F. Moeller and Gudjonsson, 1932, found half of the workers exposed to cryolite dust affected. The changes consist in generalized osteosclerosis, involving all the bones, but especially spongy bone, including the spinal column. The density of the bone is increased, with preservation of the normal bone architecture but changes of the normal structure. The organic matrix is irregular, the calcium deposition is increased but irregular; calcareous deposits extend to the ligaments and muscles, osteocytes form between the vertebral bodies (P. A. Bishop, 1936).

Exposure to cryolite dust also develops other symptoms. Anorexia, nausea and vomiting appear early, but tolerance to these is soon established. Continued exposure leads to functional dyspepsia, rheumatic pain, constipation and the osteosclerosis, demonstrable by roentgen examination. Post-mortem examination of two workers exposed for many years revealed no visceral changes definitely attributable to the intoxication (Roholm, 1938).

Fluorosis

In young rats, fluorosis leads to generalized osteoporosis or osteomalacia, resembling rickets. The organic matrix and the calcium (Continued on page 60)
deposition are irregular. The ossification of the cartilages is retarded; the roentgen transparency of the bones is increased (Bergera, 1927). The bones become much more brittle (Christinani, 1939; Sutro, 1935). Many guinea-pigs with chronic fluoride poisoning show bony hypertrophic deformation of the tibia (Christinani, 1932). White mice have delayed ossification of the internal ear (A. Lewy, 1928). Fluoride administration of young dogs altered the calcium deposition similarly to rickets. Long continued administration led to sclerotic processes with abundant deposition of calcium in "calcium grains" (H. Kellner, 1930). Addition of fluoride to the diet of rachitic rats interferes with healing by vitamin D. The new bone being atypical (Morgareidge and Finn, 1940).

The cause of the bone changes is presumably through interference with the enzyme processes of ossification, but the details are not understood. Very dilute solutions of fluoride affect the deposition of calcium salts in the matrix profoundly in vitro. Monoiodoacetate has similar effects. Phosphatase does not seem to be materially concerned in chronic fluoride poisoning of rats. P. H. Phillips, 1932, reported rise of the plasma phosphatase.

Experimental Review
P. H. Phillips, 1933, found that


2. Bone marrow hyperplasia and atrophy and severe hypochromic anemia have been reported for long continued administration to dogs (Roholm, 1937). Goldemberg, 1921, reported that rats which received small doses of sodium fluoride (2 or 3 mg. per day for six to eight months), develop marked thyroid hyperplasia, and young rats showed the phenomena of cretinism. Similar effects were observed on rabbits. On this basis he suggested fluorosis as the cause of endemic goiter and cretinism. He also reported, 1930, that fluoride administration decreases the basal metabolic rate of rats and guinea-pigs. He concluded that it inactivates thyroxin and used it to treat the thyrotoxicosis of Basedow's disease (1932).

The thyroid glands store fluorine much more actively than other organs (Chang, Phillips, et al., 1934). R. J. Evans and Phillips, (Continued on page 62)