

EDITORIAL

THE PRE-SKELETAL PHASE OF CHRONIC FLUORIDE INTOXICATION

The two widely acknowledged characteristics of chronic fluoride poisoning in humans and animals are dental fluorosis (mottling of teeth) and skeletal fluorosis. Mottled teeth - an enamel defect consisting of a disturbance of the enamel building cells, the ameloblasts, and absence of cementing substance - develop only if excess fluoride intake occurs during the first 10 to 12 years of life while the teeth are being formed. Skeletal fluorosis, which is characterized by increased bone density and abnormal bone growth, is not likely to occur unless the subject has consumed excess fluoride for 10 to 30 years.

Similarly, chronic poisoning by many other toxic substances is characterized by one or two major features. For instance, the lead line or wrist drop are characteristic of lead poisoning; granulomatous lesions, of beryllium poisoning; keratosis of the skin, of arsenic poisoning; brownish acne-like lesions of the skin, of poisoning by biphenyl chlorides. In all the above-mentioned types of poisoning as well as in chronic fluoride poisoning, however, the action of the toxic agent is not confined to one or two target organs after its entry into the human body. Thus many additional manifestations accompany the above-described principal lesions.

In his classical description of fluoride intoxication, Roholm (1) has outlined a number of manifestations which are associated with skeletal fluorosis, mainly gastrointestinal and neuromuscular symptoms as well as such features as tachycardia, polydipsia, and allergic skin lesions. Yet, only a few subsequent investigators have paid attention to the systemic effects of fluoride in chronic poisoning.

In this issue Gründer (page 135) elucidates the fact that, in domestic animals, fluoride intoxication accounts for a wide variety of manifestations. They are dependent mainly on the kind of compound involved, its dose and the channels by which it enters the system. Long-term uptake of fluoroacetate, for instance, induces changes in the brains and heart. This condition is at variance with the generally recognized features of fluorosis.

In humans, Fradà et al. (2) reported gastrointestinal symptoms, gastroduodenitis, colitis, and acute abdominal episodes associated with liver disorders in 70% of the population of an area where the water contained fluoride naturally at a level of 5.2 ppm. He also noted a high incidence of degenerative arthritis and calcification of arteries. Rich (3) reported involvement of the gastrointestinal tract in conjunction with arthritis and visual disturbances in patients who received large therapeutic doses of fluoride for osteoporosis over extended periods of time. The

literature on the fluoride-containing anesthetic methoxyflurane is concerned particularly with its effect on the kidneys. Polyuria and polydipsia have been recorded in hydrofluorosis (4-6), a condition on which Taves (7, 8) has elaborated in several publications.

In infants, who are notably less resistant to toxic insults, administration of fluoride tablets has led to ulcers in the stomach and upper bowel (9).

Fluoride tablets administered to pregnant women and to young children caused stomach and bowel upsets as well as allergic skin lesions (10).

Duffy et al. (11) observed giant cells in the bone marrow of three patients who received large doses (16 to 150 mg daily for 1 to 36 months) of sodium fluoride for treatment of osteoporosis. These authors considered these cells suggestive of bone malignancy.

The significance of the non-skeletal phase of chronic fluoride poisoning which was originally brought into focus by Waldbott (12, 13) and more recently by Petraborg (14) is corroborated in the current issue of FLUORIDE (page 146) by Grimbergen in a preliminary study. These authors observed a typical syndrome early in the development of fluoride poisoning from such minute amounts of fluoride as are contained in fluoridated drinking water at the so-called optimal concentration. In this phase of the disease neither the teeth nor the bones are involved.

In contrast to acute fluoride intoxication from large doses of fluoride, such trace amounts can have a sustained effect on the gastrointestinal tract - the usual portal of entry of fluoride - in persons who are susceptible to poisoning by it. Symptoms such as nausea, vomiting, and bowel disturbances of the kind often described as "irritable colon" and frequent ulcers of the mouth (stomatitis) appear to be the most common feature. Excessive dryness in the mouth and throat are undoubtedly related to polydipsia and polyuria, which are indicative of an excess requirement of fluids due to damage to the kidneys by fluoride (3).

Of special interest are the neurological symptoms, mainly headaches, vertigo, ataxia and damage to the retina. Since these manifestations also occur in such diseases as multiple sclerosis, neurosyphilis and cerebral tumor a distinction must be made between them and fluoride poisoning in differential diagnosis. In this connection the recent observation by Franke et al. (page 168) acquires special significance. In a case of skeletal fluorosis these authors observed, for the first time, involvement of the cells of the anterior horn of the spinal cord. In their autopsied case they demonstrated incontrovertibly that damage to the ganglion cells of the spinal cord is not associated with pressure upon peripheral nerves nor upon the spinal cord due to proliferation of bone sub-

stance in the vertebral column. Direct involvement of nerve substance by fluoride can, therefore, not be excluded. Such a possibility would also explain the frequent findings of mental disturbances such as slow cerebration, inability to concentrate, loss of memory and mental depression described by Waldbott (12).

Another important feature in the case described by Franke et al, was the damage to muscle cells of the kind originally reported by Fasske in 1964 (15) who found similar changes in the musculature of the heart. Because this is the first and only report on a single individual, no final conclusion can be reached at this time. However, the unusual degree of muscular weakness and the pains in muscle frequently observed in such cases is suggestive of pathology in muscle tissue.

Arthritis of the spinal column develops early in the disease with or without demonstrable radiological changes. It often affects the small joints of the hands and fingers, not unlike the involvement of the metapalangeal joints in fluorosis in cattle as shown by Gr nder.

Lower urinary tract involvement is not uncommon in the more advanced stage of the pre-skeletal phase of fluoride poisoning. Muscular fibrillation, pains and paresthesias in arms and legs and even convulsions have been described during the course of the disease (16). Recently Waldbott and Cecilioni have pointed to the frequency of "Chizzola" Maculae, skin lesions attributed to fluoride in the early thirties in Italy (17) and encountered again in the same Italian area (18). The frequency of the occurrence of this condition in fluoridated communities or near fluoride-emitting industrial facilities is noteworthy. Yet, because of its close resemblance to traumatic suffusions which are often encountered, especially in children, this common skin disease is rarely recognized by physicians. Since the skin lesions constitute the first clue of intolerance to fluoride, they often lead to the detection of the systemic disease which might otherwise remain unrecognized.

It thus appears that fluorosis cannot be considered a disease of teeth or bones. It is a systemic disease liable to involve many, or perhaps all, organs of the system.

The development of clinical research on fluoride is relatively recent. It dates back to 1939 when Roholm presented the first comprehensive study on the subject. With the expanding role of fluoride in industry, with its special significance as an air pollutant and its increasing occurrence in food and drinks, an awakening to the clinical aspect of chronic fluoride poisoning is bound to occur in the not too distant future.

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