It has been shown on previous occasions (Spira, 1942 a, b, 1943 a, b) that lesions of the skin and its appendages, the teeth, nails and hair are a common occurrence in fluorosis. The action of fluorine is known to consist in its ability to precipitate calcium salts stored in the body, material indispensable for sustaining the vitality of most of the organic functions. The protracted ingestion of toxic amounts of this halogen may thus bring about the reduction of calcium in both blood and tissues to a dangerous level. Exactly how the lesions are produced in the various tissues must remain a matter of conjecture so long as no definite evidence is forthcoming. They may be produced by fluorine attacking predilected tissues in a direct manner; or they may be brought about through its interfering with the normal function of the parathyroids, as suggested by Spira (1942 a, b, 1943 a, b), who observed that the co-existent lesions concern organs which are regulated by these glands. Lachmann (1941) even believed that in hypoparathyroidism a calcium-regulating centre in the brain is involved.

The co-existence of the lesions of the skin, teeth, nails and hair in endocrine disturbances was pointed out by numerous writers, even before fluorine became the subject of closer investigation, to be remarkable because the organs involved are derived from the ectoderm. The purpose of this paper is to display the result of clinical observation on the action of fluorine upon other tissues known likewise to originate from the ectoderm. The tissues under discussion are the lining of the mouth, the epithelium of the salivary and other bucal glands, of the nostrils, and of the conjunctivae and lachrymal glands.

In describing the symptom complex caused by fluorine, one of the irritants contained in aluminium cooking utensils and in drinking water (Spira, 1928, 1933), it was pointed out that changes in the mouth occur frequently. The tongue loses its natural aspect of a flesh-coloured, moist, velvety surface, with its papillae only slightly elevated. Instead, the papillae are vividly red and enlarged. Later on, the edge of the tongue becomes indented by the teeth, raw and excoriated. Broekema (1933) found that the border of the tongue becomes atrophic. Deep fissures appear on the surface of the tongue, and they represent the condition of chronic superficial glossitis in a varying degree. Friedmann (1921), too, observed the presence of lingua geographica in such cases, and Mendes da Costa & Van der Valk (1919) reported the occurrence of keratosis of the tongue. Often the whole mucous membrane of the mouth is involved, presenting the complete picture of stomatitis (Gilford, 1904; Spira, 1928, 1933; Kazzelson, Reimann & Weiner, 1929; Broekema, 1933; Lachmann, 1941). Small vesicles which break after a few days to form shallow ulcers (ulcerative stomatitis), and to cause much discomfort and pain, especially when eating. In other cases linear tears or fissures of the mucous membrane occur on the floor of the mouth (aphthous stomatitis). Gingivitis is a frequent occurrence (Gaud, Charnot & Langlais, 1935; Dean, 1936; Dean & Elvove, 1936). Ainsworth (1933) found in as many as 60% of the children who exhibited 'mottled teeth', a dystrophy caused by the ingestion of toxic amounts of fluorine. Spira (19436) established the presence of 17% of cases of gingivitis, in a degree sufficient to produce bleeding of the gums, amongst 1700 men and women examined. When the affection is still further advanced, the gums appear red and spongy, with pus collecting under them, and a condition develops which is clinically identical with alveolar pyorrhoea. Lachmann (1941), too, found that paradentosis is a very common feature in hypoparathyroidism.

The affection of the mucous membrane of the nasopharynx, as part of the symptom complex in ectodermal dystrophy, has been observed by several writers. The often-cited Bébé of Nicolle & Halipré (1895) was suffering from perpetual coryza. Atrophic rhinitis and atrophy of the mucous membrane of the pharynx and larynx, the latter producing a distinct hoarseness, were amongst the signs and symptoms described by Goeckermann (1920). Woech (1929) reported ectodermal dysplasias accompanied by affections of the mucous membrane of the mouth and of the nasopharynx with frequent colds and infections of the throat in a patient whose voice had always been hoarse, and whose tonsils and adenoids had been removed. MacKee & Andrews (1924) found the presence of atrophic rhinitis; and Hill (1933) established both this and an atrophy of the mucous membrane of the pharynx and larynx in a patient who exhibited ectodermal dystrophies, and whose tonsils were very large and ragged. Spira (1928) observed that 'the absorption of the irritant also gives rise to catarrh of mucous membranes, producing conjunctivitis, frequent attacks of "common cold" with pharyngitis, bouts of frequent vehement sneezing and intense itching in the nose.' The co-existence of leukonychia with 'colds' led Josephson & Lerner (1934) to believe that both these conditions are of a common origin, which clinically they traced back to a disturbance of metabolism. It will be remembered that leukonychia is a nail dystrophy characterized by dull, opaque, chalky white specks, patches or transverse bands, familiar to everybody and attributed by Spira (1943a) to chronic fluorine poisoning. The 'colds' included infections of the upper respiratory tract, rhinitis, nasopharyngitis and enlarged tonsils with frequent attacks of tonsillitis. The hacking, unproductive cough accompanying chronic fluorine poisoning is similar in nature to that accompanying chronic arsenic poisoning, and points to the presence of trachitis. Wenner (1931) has shown that precipitation of calcium in the mucous membranes of the nose and sinuses by substances combining with calcium results in the disappearance of the cilia of the epithelium, stagnation and infection. 'Running nose', even without any other signs of a 'common cold', is often met with in hypoparathyroidism, and is lacrimation, even without conjunctivitis, as well as increased saliva-
complain of dryness in the mouth and throat, or of dryness alternating with excessive salivation. Increased salivation indicates a state of increased activity of the salivary glands. The fact that it has also been observed by Erdheim (1906) in his parathyroidectomized rats lends additional support to the conclusion that, in man, when co-existent with other signs and symptoms of fluorosis, increased salivation is likewise the result of a lowered function of the parathyroid glands. Similarly, increased lacrimation indicates increased activity of the lacrimal glands. In the case of Jacobsen (1928), however, there was absence of tears, and the patient of Thurnam (1848) has never been known to shed tears.

Increase in the activity of these organs, followed by its decrease is in perfect harmony with the fundamental physiological law, according to which a state of irritation brought about in any organ by the action of a noxin is followed by that of paralysis, if the noxin is allowed to continue to act upon it. The contradictory nature of the symptoms concerned is thus only apparent. It is this contradiction which helped the disease picture of fluorosis to escape our correct evaluation for so long. In fluorosis, the occurrence of symptoms opposite in character is not confined to the mouth, nasopharynx, tongue, and the salivary and lacrimal glands alone. In discussing the relationship between dermatoses and endocrine disturbances, and the reason why ‘dermatology is notoriously deficient in facts bearing on the causation of skin diseases’, McEwen (1916) seems to have referred to the same physiological law when he stated that ‘the rule holds that the pathologic factor causing the disturbance of function may sooner or later cause decrease or cessation of function, and thus bring to the fore symptoms more or less contrary to those first observed’.

In view of the close similarity between the signs and symptoms here described as forming part of the disease picture of fluorosis and those usually regarded as being caused by infection, the firmly established fact that fluorine acts by reducing the level of the calcium in blood and tissues seems to indicate that, in certain cases of infection, a causative relationship may exist between the two conditions. There can be no doubt that the body is less resistant to infection, both exogenous and endogenous, when appreciably deprived of its calcium content than is a body not exposed to toxic amounts of fluorine. Some micro-organisms which appear to be harmless under normal conditions might thus obtain a firm hold over the body when its calcium content falls below the normal level. Inoffensive, symptomless symbiosis (for which the term ‘abiotic symbiosis’ would be appropriate) gives way to disease, in which bacteria, no more resisted by a healthy soil, become pathogenic and able to play havoc.

The observations here described are borne out by the fact that the disturbed function of the tissues involved can be restored to a normal condition by the treatment directed against fluorosis. Moreover, it has been noted on numerous occasions that when prophylactic measures were taken against the onset of fluorosis, the above signs and symptoms were thereby also prevented.

**SUMMARY**

Like the skin and its appendages, the teeth, nails and hair, so also other tissues of ectodermal origin are here shown to be affected by fluorine. The action of fluorine consists in lowering the level of the calcium in the blood and tissues. The epithelia of the mouth and the salivary glands, of the nasopharynx, the conjunctivae and the lacrimal glands may be affected. Signs and symptoms are thus produced which are closely similar to those usually attributed primarily to infection. It is suggested that an infection accompanying chronic fluorine poisoning is of a secondary nature, and that it is brought about by the loss of calcium in the body.

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(MS. received for publication 28. v. 43.—Ed.)