HISTOPATHOLOGY OF THE MAXILLODENTAL SYSTEM IN EXPERIMENTAL FLUOROSIS

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UDC 616.314.13-02:546.16]-092.9-091.8

The dynamics of experimental fluorosis of the teeth and regression of the process were studied in albino rats. Fluorine was found to have a selective toxic action on the tissues of the permanently growing incisors, causing disturbances of dentine and enamel production and also of the microcirculation in the pulp. Changes in the bone tissue of the jaws were characterized by evidence of increasing porosity. Regression of the process was found to take place only after a recovery period of some considerable duration.

KEY WORDS: fluorosis of the teeth; fluorine poisoning.

The histopathology of fluorosis of the teeth has not yet been adequately discussed in the literature. In particular, the toxic effects of fluorine on the growing and fully formed teeth are not yet finally settled [3-5]. Accordingly, in the investigation described below the macroscopic and microscopic picture of experimental fluorosis of the teeth was studied in rats at various times after receiving various doses of sodium fluoride, and the possibility of regression of the changes so produced also were examined.

EXPERIMENTAL METHOD

Male rats (370) weighing initially 100 ± 20 g, were divided into 4 groups: The rats of group 1 received a solution of sodium fluoride by subcutaneous injection in a dose of 0.3 mg/kg daily, the rats of group 2 received the same solution in a dose of 1 mg/kg, the rats of group 3 in a dose of 12 mg/kg, and the rats of group 4 (control) were kept under identical conditions but received no sodium fluoride. The animals of the first two groups were investigated 5, 10, 15, 19, 24, and 30 weeks after the beginning of poisoning and 1, 2, 3, 4, 10, and 20 weeks after the beginning of the recovery period. The animals of group 3 were investigated 2 days and 1, 2, 4, 6, 7, 8, 10, and 12 weeks after the beginning of poisoning and 1, 4, 8, and 12 weeks after the end of sodium fluoride administration. At each time 10 animals (6 experimental and 4 control) were studied. The animals were killed by decapitation. Blocks of the upper and lower jaws were fixed in 10% formalin solution, decalcified in 5% nitric acid solution, and embedded in celloidin. Sections were stained with hematoxylin–eosin and picrofuchsin–fuchselin. To evaluate the effect of a toxic dose (12 mg/kg) of sodium fluoride on the enamel epithelium of the incisors quantitatively, a morphometric investigation of the thickness of the layer of ameloblasts was undertaken.

EXPERIMENTAL RESULTS

The character of the macroscopic changes in the lower and upper incisors of the rats receiving sodium fluoride in a dose of 12 mg/kg is shown in Table 1.

The lower incisors of the experimental rats were affected much sooner than the upper. The shape and size of the molars, and also the state of their enamel showed no appreciable macroscopic changes.

In 80% of animals of group 2, receiving sodium fluoride in a dose of 1 mg/kg, the enamel of the lower incisors by the 10th week of poisoning acquired an ill-defined "tigroid" appearance. In some animals of group 1, by the 11th-12th week of the experiment, very slight, thin, transverse strips of depigmentation could

Research Institute of Human Morphology, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR A. P. Avtsyn.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 82, No. 12, pp. 1506-1509, December, 1976. Original article submitted May 24, 1976.

TABLE 1. Character of Changes in Incisors of Rats of Group 3

Stages of experiments, weeks	Upper incisors	Lower incisors
Period of poisoning		
1	No change	Partial depigmentation
2—4	" "	"Tigering," i.e., alternation of transverse pigmented and depigmented stripes at base
5—6	"Tigering" extends to all teeth	"Tigering" covers half or more of incisor
7—12	Besides "tigering" areas of erosion and chalk spots of enamel, particularly well marked on lower incisors	
Recovery period		
1	Changes in enamel the same as during poisoning Increase in length	Compensatory grinding away
2—3	Ratio between length of upper and lower incisors inversely proportional to that in control	
4	Moderate growth, "tigering," erosions chalk spots	Sometimes grinding away to the base
5	Growth arrested	Changes the same
6—7	Decrease in length (grinding); enamel in neck region becomes normal in color	Growth of incisors but they are still smaller than in the control Enamel in neck region acquires normal color
8—9	Sometimes grinding away to the base	Sharp increase in length. "Tigering" sometimes still visible on crown of incisor
10—11	Moderate growth; enamel of usual color	No changes detected in enamel; compensatory decrease in length
12	As in control	As in control

be seen in a bright light on the lower incisors with the aid of a magnifying glass. The color of the enamel of the upper incisors of the rats of groups 1 and 2 was unchanged.

Histological examination of sections through the upper and lower jaws after 2 days of sodium fluoride posioning in a dose of 12 mg/kg revealed focal changes in the structural pattern of the enamel in the growth region of the lower incisors. Frequently the layer of ameloblasts was detached from the enamel and its structural pattern disorganized, whereas at other times hemorrhages could be seen. In the pulp congestion was conspicuous. In the molars and parodontium no differences from the control were found.

The first week of poisoning was accompanied by congestion of the pulp and the capillaries in the layer of odontoblasts were injected and sometimes showed signs of stasis. An increase in the quantity of interglobular dentine was observed and a band of it was particularly clearly visible close to the boundary between dentine and enamel. In the growth region of the incisor the enamel had become uneven because of focal destruction, with disturbance of the structure of the enamel prisms and greatly increased translucency of this region. Vacuolation of the basal part of the ameloblasts was observed, and this layer was sometimes deformed as a result of hemorrhages. In some cases focal marginal resorption of the root of the molar was found. Evidence of increased resorption also was observed in the bone tissue of the jaws. At the same time a moderate deposition of osteoid was noted.

After 2 to 4 weeks of poisoning marked changes were found in dentine and enamel production in the incisors, with disorganization of the layer of ameloblasts and the formation of crinkled structures and foci of necrobiosis in them. Instead of a uniform layer of enamel with regular structure, in these regions foci of clumps of enamel developed. The disturbance of dentine production was characterized by widening of the layer of predentine and a marked increase in the quantity of interglobular dentine. Evidence of osteolysis and osteoclastic absorption was strengthened.

After 6-8 weeks focal degenerative changes were observed in the ameloblasts, in the form of vacuolation and necrobiosis (Fig. 1a). Focal destruction and disorganization of the pattern of enamel prisms also were observed in the layer of enamel (Fig. 1b). The considerable congestion of the pulp, frequently with signs of stasis in the capillaries, should be noted (Fig. 1c). Sometimes capillaries could be seen to be entering the dentine from the pulp (Fig. 1d). Widening of the predentine layer was observed not only in the incisors, but also in the molars. Apposition of uncalcified cement to the root of the molar and stratification of poorly calcified tissue in the bony trabeculae of the jaws were visible.

Administration of sodium fluoride for 10-12 weeks led to increased apposition of uncalcified cement. The layer of predentine was wide and the pulp was grossly congested. The changes in the enamel of the incisors were similar in character to those at the preceding times.

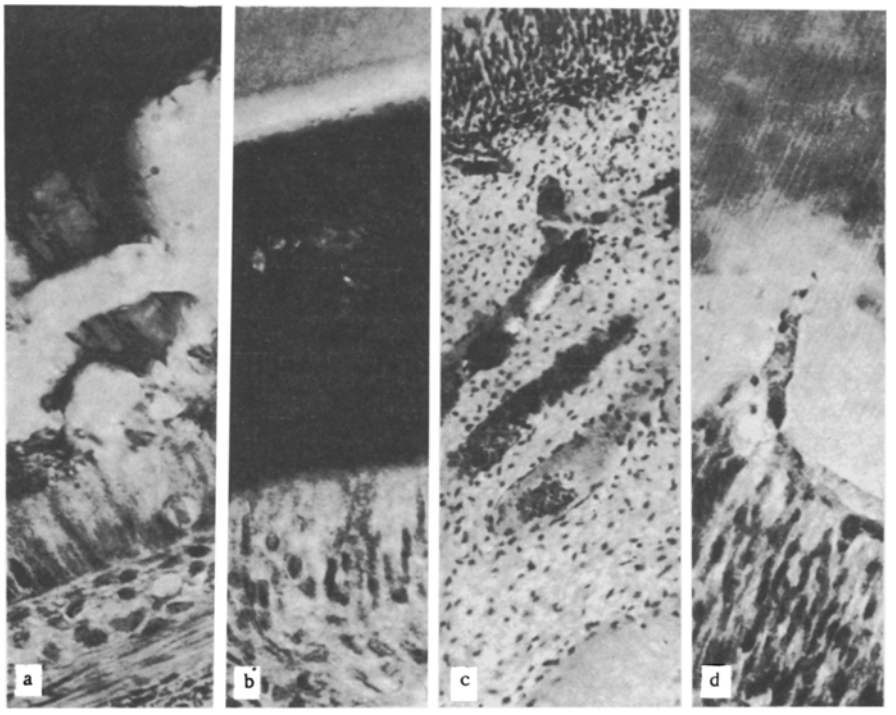

Fig. 1. Changes in tissue of incisors of rats receiving sodium fluoride in a dose of 12 mg/kg (hematoxylin–eosin): a) vacuolation and necrobiosis of layer of ameloblasts with its separation from enamel, and vacuolation and disturbance of structural pattern of enamel (6 weeks of poisoning, 500×); b) destruction of enamel and disturbance of structural pattern of enamel prisms (6 weeks of poisoning, 500×); c) congestion of pulp (8 weeks of poisoning, 120×); d) invasion of dentine by injected capillaries from layer of odontoblasts (6 weeks of poisoning, 250×).

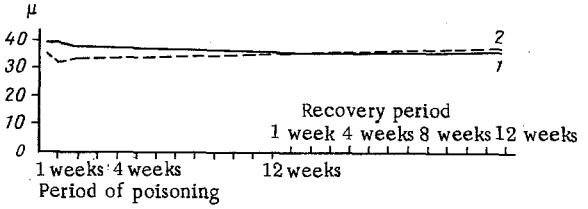

Fig. 2. Graph showing thickness of layer of ameloblasts of incisors in rats receiving sodium fluoride in a dose of 12 mg/kg: 1) control; 2) experiment. Ordinate, thickness of layer of ameloblasts (in μ); abscissa, duration of administration of sodium fluoride and of recovery period (in weeks).

Investigation of the thickness of the layer of enamel epithelium in the course of poisoning showed a significant decrease during the first 2 weeks of the experiment (Fig. 2). Later only a tendency toward a decrease was observed. In the recovery period no significant differences in the height of the epithelium could be found.

In the first week of the recovery period the changes observed were mainly the same as during poisoning. The only difference was some decrease in the apposition of uncalcified bone in the alveoli. After 4 weeks apposition of osteoid in the bone and of uncalcified cement in the root of the molars was no longer found. The gross disturbances of enamel formation observed previously in the root of the incisor could not be observed. The increase in the amount of interglobular dentine remained and the predentine layer was still widened. Later (8 and 12 weeks) no significant differences could be found between the experimental and control animals.

The character of the histological changes in the other two groups of the experiment (1 and 0.3 mg/kg sodium fluoride) was basically identical. The differences between the experimental and control animals were

clearest of all at the height of poisoning. For instance, after administration of these doses for 24 weeks a marked osteolytic reaction was observed in the bone tissue of the alveoli, where sometimes its integrity was disturbed by foci of replacement with fibrous tissue. By 30 weeks, in addition to the osteolytic changes in the bony alveoli, a disturbance of normal dentine production was observed in the region of the molars. It was characterized by interruption of the layer of odontoblasts by degenerative and sclerotic changes, by an irregular widening of the predentine layer, and by an increase in the amount of interglobular dentine. The last of these features was particularly well marked in the incisors. No gross disturbances of enamel production were found. At the last stage (20 weeks) of the recovery period no differences could be observed histologically between the experimental and control animals.

The "tigroid" striation of the enamel of the incisors is a pathognomonic sign of fluorosis of the teeth in rats and its severity and times of onset are directly dependent on the dose and duration of its action. The mechanism of onset of this lesion has not yet been explained [1, 6, 7]. "Tigering" of the enamel in fluorosis, in the present writer's opinion, must be associated with the direct harmful action of fluorine on the pigment-forming function of the ameloblasts and with the biological rhythm of the permanently growing incisors.

The structural changes discovered in this investigation in the maxillodental system confirm the observations of Kolesnik [2] pointing to a role of disturbances of phosphorus and calcium metabolism in the pathogenesis of experimental fluorosis.

Fluorine thus had a selective toxic action on the tissues of the permanently growing incisors of rats and caused disturbances of dentine and enamel production and also of the microcirculation in the pulp. Changes in the bone tissue of the jaws in this condition were characterized by increasing evidence of porosity as a result of the severity of the osteolytic and osteoclastic responses and a disturbance of the calcification process. The experiments showed that a sufficiently long recovery period is necessary for regression of the changes discovered in the period of poisoning to take place.

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