Odontogenic Hamartomas in an Inbred Strain of Mouse (STR/1N). (31686)

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STR/1N mice, fed a powdered diet, develop a hamartomatous lesion of the incisor teeth when they are about one year old. A comparable condition has not been described in previous accounts of the genetic or tumorous conditions of dental structures(1-5).

Materials and methods. The observations were made during other studies on the skeletal effects of fluoride on male STR/1N and A/LN mice(6). The experimental regimens, numbers of animals and ages are summarized in Table 1. The powdered diet (No. 303) contained 73% corn starch, 20% casein, 3% corn oil, 2% salts and 2% vitamin fortification mixtures, and had a low fluoride content. Half the mice in each strain drank distilled water; the others, water containing 50 parts per million (PPM) of fluoride (111 PPM NaF). The average fluoride concentration in the ashed pelvic bones of the former group was 0.185% in STR/1N and 0.200 in A/LN mice; and in the latter, 1.627 and 1.194 respectively. Observations were also made in STR/1N mice raised concurrently on commercial (Purina) chow pellets (19 PPM F) and tap water having 1 PPM of fluoride.

With the exception of eight STR/1N mice, in which the lesions were studied by serial histological sections, the observations were made grossly on jaws from which the soft tissues had been removed by dermestid beetles (7). The lesions were graded on a severity scale of 0 to 4 (Fig. 1) according to their greatest diameter (1 = 1 mm, 2 = 2 mm, etc.). Because maxillary lesions rarely presented externally, only mandibular ones have been recorded in the Table.

Results. All 4 incisors were affected and the degree of involvement usually was symmetrical. The lesions appeared as a bulbous or nodular enlargement of the root. The surfaces were bosselated. They were white, but sometimes contained patches of brown pigment. Although they were hard or gristly, the lesions also were brittle. Mandibular hamartomas expanded the cortex of the rami laterally in the vicinity of the insertion of the masseter muscle (Fig. 2). The bone here occasionally was perforated. Maxillary lesions enlarged superiorly into the antrum and sometimes the nasal passages. When the periodontal attachments were digested away with papain, the body of the incisor tooth was readily extracted in a distal direction from its socket.

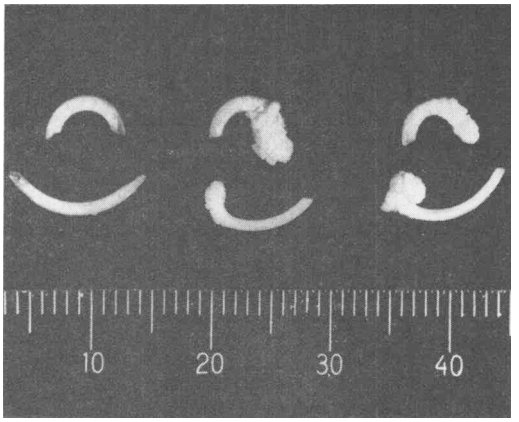

FIG. 1. Medial aspect of maxillary (upper row) and lateral aspect of corresponding mandibular (lower row) incisors. Left: normal. Center: grade 4, maxillary; grade 2, mandibular. Right: grade 1, maxillary; grade 4, mandibular.

By 16 months of age, the incisor teeth of the STR/1N mice, receiving the powdered diet and the distilled water, developed moderate hypoplastic changes: patchy depigmentation, ridged enamel and irregular, short or overgrown incisal edges. These abnormalities were not present in the A/LN mice or in the STR/1N mice fed pelleted chow. Marked hypoplasia appeared in the fluoride treated animals of both strains.

Histologically, most of the lesion consisted of well differentiated dentin. Patches of enamel epithelium and matrix and less of

TABLE I. Mandibular Hamartomas in Various Groups of Mice.

Strain	Diet	Fluoride (PPM H_2O)	Age (mo)	Hamartoma (grade)* 0	1	2	3	4	No. of mandibles
STR/1N	303	0	2	2					2
			4	4					4
			5	2					2
			6	2	2				4
			7	6					6
			8	6	2				8
			10	4					4
			11	6	2				8
			12	2		2		2	6
			16	12	30	10	4		56
		Total		46	36	12	4	2	100
STR/1N	303	50	2	2					2
			4		2	2			4
			5		4	2			6
			6			2	2		4
			7			3	1		4
			8		1	6	1		8
			10			3	2	3	8
			11			2			2
			12		2	1	3	2	8
			16	1	6	11	18	4	40
		Total		3	15	32	27	9	86
STR/1N	Stock	0	12	20					20
			16	2					2
		Total		22					22
A/LN	303	0	16	60					60
A/LN	303	50	16	56					56

* Figures represent numbers of individual mandibles, not mice.

cementum were present at the surface. Pulp mesenchyme and odontoblastic epithelium were sparse in the larger lesions and occasionally underwent focal coagulation necrosis. Isolated cementoclasts were present in periodontal connective tissue. The adjacent bone remodelled to conform to the contours of the hamartomas. There was no ankylosis. The crevicular epithelium of the incisors was atrophic. Old hemorrhage, manifest by hemosiderosis and xanthoma cell aggregation, was present beneath it but bore no constant relation to the hamartomas. The molar teeth, unlike the incisors, had a degree of hypercementosis like that of other old mice(8). The dentin of the hamartomas and adjacent bone of the mice receiving fluoride contained characteristic hematoxyphil or clear ovoid structures (9,10). Microscopic examination of young (3½ and 6 months old) STR/1N mice, prior to development of the hamartomas, disclosed no abnormality of the germinal tissues.

In STR/1N mice receiving distilled water, a few mild lesions were seen before one year of age; by 16 months, the mandibles were affected in 26 of 28 animals. In STR/1N mice receiving fluoride, the hamartomas appeared at an earlier age, were more frequent and larger than in the preceding group. Hamartomas were never seen in A/LN mice, whether they received fluoride or not; nor in STR/1N mice eating the pellets.

Discussion. The localization of the hamartomas to the roots of the incisors is related to the ever growing character of these teeth in rodents. We surmise that STR/1N mice have a proclivity, probably genetic, to develop these lesions because eruption of the incisors is inhibited by insufficient physiological stimulation from a hard diet. Although eruption is retarded, the germinal epithelium continues to grow and has nowhere else to go.

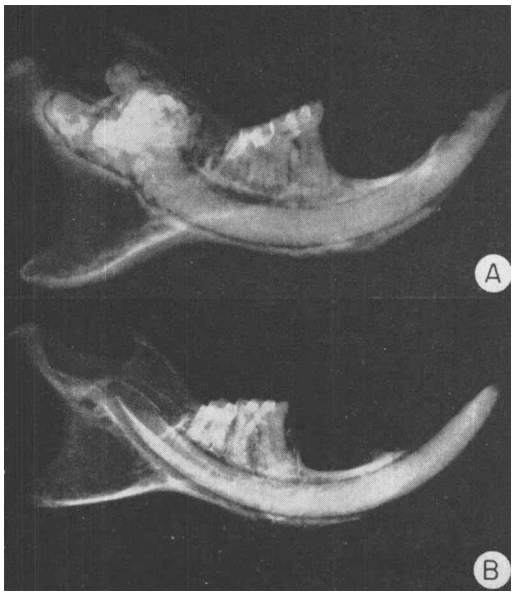

FIG. 2. Roentgenogram of mandibles, 16-month-old male mice, fluoride treated. A. STR/1N, with large hamartoma in the ramus. There is much hypercementosis about the molar teeth but no ankylosis of the incisor to its socket. B. A/LN, showing normal architecture of the incisor root.

The hamartomas thus bear an analogy to amputation neuromas rather than to true tumors. The incisor hypoplasia of STR/1N mice receiving the soft diet is somewhat similar to that induced by fluoride(11) and other agents. It is, therefore, not surprising that fluoride, in the large amounts administered here, should exaggerate hamartoma formation.

The lesion is to be distinguished from several "pseudo-odontomas" previously reported in rodents. In infant *gl* mice(12) and *ia* rats (13), redundant masses of germinating tooth tissue develop because eruption of teeth is prevented by a genetically governed failure of resorption of primary bone. STR/1N mice have an unusually heavy bone structure and develop late endosteal trabecular intrusions in their femoral shafts(6,14). There is, however, no reduction of the caliber of the alveolar sockets that might embarrass the continued eruption of the incisors.

The "odontomas" induced in hamsters by inoculation with rat RV virus differ from the present lesions in several respects. The former have considerable ankylosis, consist primarily of osteocementum, have little dentin or enamel, and affect molar as well as incisor teeth(15).

It should not be necessary to add that these observations do not constitute evidence that fluoridation of drinking water is hazardous. High levels (50 PPM) of fluoride have been employed. The lesions are not cancerous. They are a peculiarity of the STR/1N mouse when it is fed a soft diet.

Summary. Hamartomas of the incisor teeth develop in 48 of 62 mandibles of one-year or older STR/1N mice that had been fed a soft diet. Development of the lesions was further increased by incorporation of 50 PPM of NaF in the drinking water. Comparable growths were never seen in A/LN mice whether they received fluoride or not, nor in STR/1N mice eating a pelleted chow.

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