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Tongue Lesions Specific for Diagnosis of Myopathy in Inbred Syrian Hamsters (38586)

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Spontaneous muscular dystrophy in Syrian hamsters was first reported by Homburger *et al.* in 1962 (1) in one of their inbred strains. This dystrophy-like myopathic disease was found to be hereditary and transmitted by an autosomal recessive gene (designated cm, 1974) (2, 3). By selective breeding, it was possible to establish new dystrophic lines. These lines have been widely investigated, mainly because they present animal models in which to study the biochemistry and physiology of cardiomyopathy which might ultimately lead to clinical application (4–8).

In the present investigation, experiments have been designed to study the physiology and immunology of fetal heart transplants in cheek pouches of hamsters of the myopathic strains. These studies will be reported elsewhere. In the course of observing the buccal tissue of the BIO® 14.6 myopathic strain, careful oral examination revealed small (1–2 mm), indurated, white lesions embedded in the undersurface of the tongue, slightly anterior to the frenulum linguae.

Following the first observation, the oral cavities of other male and female hamsters of the stock BIO 14.6 strain were examined in age groups ranging from weanling to 6 mo. All of the observed hamsters of this strain showed tongue lesions beginning at 55 days. The lesions were not limited to the undersurface of the tongue, but were also apparent on both lateral surfaces and on the dorsum as well. The lesions were solitary or multiple and seemed to be confined to the anterior portion of the tongue. The findings of tongue lesions in the stock hamsters of BIO 14.6 strain confirmed the spontaneity of the lesions and indicated that their occurrence was in no way related to the transplantation experimentation.

These initial observations in the BIO 14.6 strain led us to examine other myopathic hamster strains and nonmyopathic strains of the Bio-Research Institute's breeding colony to ascertain whether the lesions were restricted to the myopathic disease groups. These examinations would also reveal the frequency of the occurrence of the lesions and the time of their onset.

Groups of 10 males and 10 females of each of four confirmed myopathic hamster strains, and 21 nonmyopathic strains with ages ranging from 55 days to 6 mo, were examined for the presence of tongue lesions (Table I). Additionally, whenever possible, litters ranging from neonates to weanlings were examined in the myopathic strains in order to detect the first indication of grossly visible tongue lesions. The techniques of performing the observations are relatively simple. The docile nature of the inbred hamsters precludes the necessity of using anesthesia. The investigator holds the animal in one hand and, tightening his grip on the loose skin from the scruff of the neck to the tail, immobilizes the head; then, using blunt forceps, he gently pulls the tongue forward for examination. In young hamsters prior to weaning, the tongue is carefully pulled forward with the fingers and rolled over the index finger for observation. The simplicity of the technique allows the investigator to examine large numbers of animals in a very short period of time.

All tongue lesions were excised for histopathologic examination. Tongues of some of the animals in which no lesion occurred were also examined microscopically as controls. Cardiac muscle and skeletal muscle of the leg, cheek pouch and pectoral region were studied histologically to determine whether the specific animals in which tongue lesions occurred were also myopathic.

Tissues prepared for histopathologic examination were fixed in Tellyesniczky's solution and stained with hematoxylin and eosin. Certain of the tongue and other muscle sections were stained with Von Kossas' solution for calcium.

TABLE I. INCIDENCE OF TONGUE LESIONS IN 25 BIO STRAINS OF INBRED HAMSTERS.[a]

Strain	Females		Males	
	Positive	Negative	Positive	Negative
Nonmyopathic strains				
1.26	1	9	0	10
1.5	1	9	0	10
2.4	0	10	0	10
4.22	2	8	0	10
4.24	0	10	0	10
7.88	0	10	0	10
12.14	0	10	0	10
15.16	0	10	0	10
41.56	0	10	0	10
45.5	0	10	0	10
54.7	0	10	0	10
65.67	0	10	0	10
72.79	0	10	0	10
82.73	0	10	0	10
84.9	0	10	0	10
86.93	1	9	0	10
87.20	0	10	0	10
X.3	0	10	0	10
X.68	0	10	0	10
X.XB	0	10	0	10
RB	0	10	0	10
Myopathic and cardiomyopathic strains (cm/cm)[b]				
14.6	10	0	10	0
40.54	10	0	10	0
53.58	10	0	10	0
82.62	10	0	10	0

[a] Ten females and ten males of each strain selected randomly from stock hamsters 55 days of age or older.

[b] cm = Cardiomyopathic.

A total of 500 male and female hamsters representing four myopathic strains and two nonmyopathic strains underwent oral examination for tongue lesions. Tongue lesions occurred in all 80 animals of the established myopathic strains, BIO 14.6, 40.54, 53.58 and 82.62 (Fig. 1). Of 420 hamsters of the nonmyopathic strains, tongue lesions occurred in only five females of four strains: 1.26, 1.5, 4.22 and 86.93, and in none of the animals of the other 17 strains (Table II). There were no tongue lesions apparent in any of the animals examined prior to 55 days of age.

Microscopically, tongue lesions vary in size and consist of deep, submucosal, Kossa-positive calcifications. The calcified areas are associated with varying amounts of acute and chronic inflammation and often include foreign body giant cell reactions. The overlying mucosa may appear normal or may show a moderate degree of epithelial hyperplasia. Throughout the submucosal muscle there may be foci of active myolysis with associated acute and chronic inflammation with areas of muscle atrophy and replacement by fibrous tissue. The deep muscle shows degenerative changes of varying severity ranging from minimal to advanced (Figs. 2 and 3).

Histopathologic examination of cardiac and skeletal muscle of hamsters of the various strains with tongue lesions revealed varying degrees of myopathy. Animals of the established myopathic strains showed slight, moderate or advanced cardiac muscular degeneration with focal chronic inflammation, myocardial calcification and organizing thrombi with calcification. The skeletal muscle also showed moderate to advanced myolytic changes. The myopathy and cardiomyopathy observed in these strains are consistent with the pathology reported by Homburger *et al.* (9). Hamsters of the nonmyopathic strains with confirmed tongue lesions showed minimal cardiac and skeletal muscular degenerative changes. In only one animal, a 100-day-old female of the BIO 4.22 strain, was there moderately advanced myolysis in the leg muscle.

The observations reported here are obviously important for the early diagnosis of myopathy in inbred strains of hamsters. The demonstration of tongue lesions in 100% of the animals examined in the myopathic strains indicates clearly that presence of the lesion correlates with onset of disease at *circa* 55 days as well as with more advanced stages.

The observation of tongue lesions in isolated cases of animals of nonmyopathic strains was of considerable interest. It suggests that selective inbreeding might develop new myopathic lines. That tongue lesions in nonmyopathic lines occurred only in females was also of interest.

In observing the sources of nonmyopathic

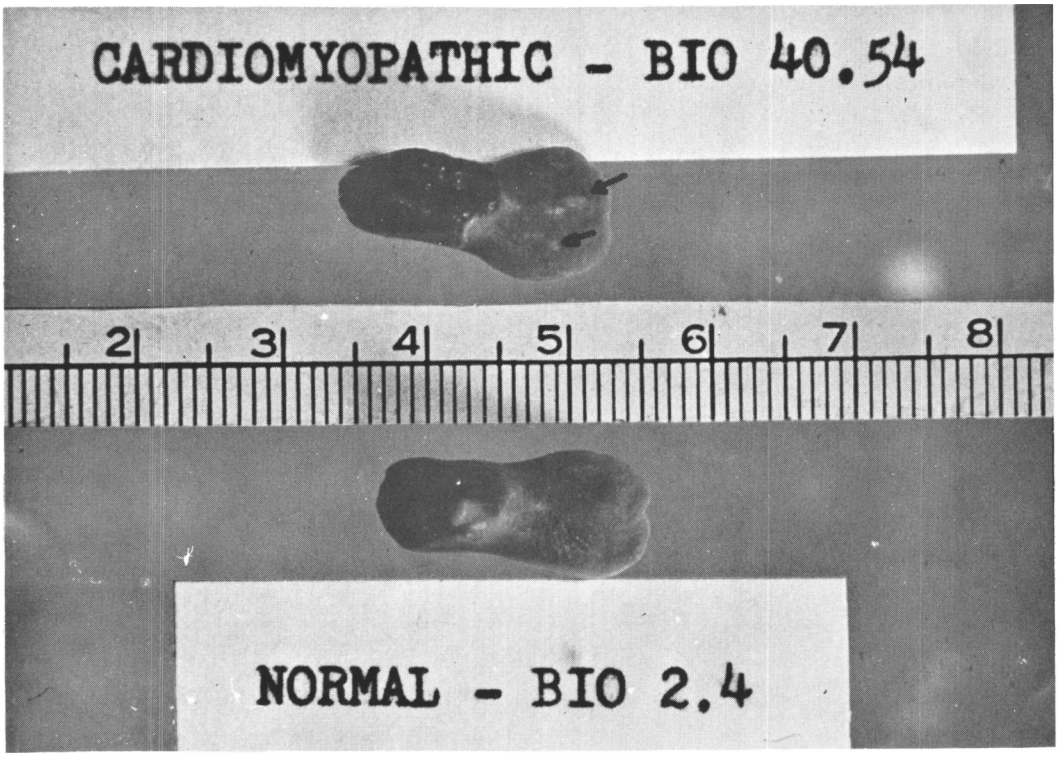

FIG. 1. Photograph of dissected tongues showing the lower surface with whitish lesions in top tongue (metric scale).

TABLE II. GENETIC BACKGROUND OF BIO[a] HAMSTER STRAINS SHOWING TONGUE LESIONS.

Line	Number of generations inbred	Coat color: Phenotype	Coat color: Genotype	Original source
		Myopathic and cardiomyopathic strains (cm/cm)[f]		
14.6	37	Acromelanic white	c^d/c^{d^c}	Schwentker, La Casse
40.54	19	Agouti	$+/+^b$	Schwentker, La Casse, Toolan, Gulf
53.58	11	Acromelanic white	c^d/c^d	Bio-Research line derived from Schwentker stock
82.62	22	Acromelanic white	c^d/c^d	Schwentker, La Casse, Toolan, Gulf
		Nonmyopathic strains (+/+)		
1.26	45	Acromelanic white	c^d/c^d	Schwentker, La Casse
1.5	30	Acromelanic white	c^d/c^d	NIH
4.22	54	Agouti	+/+	Schwentker
86.93	23	White	c^d/c^d, e/e,[d] b/b^e	Toth

[a] BIO, Bio-Research Consultants, Inc., Cambridge, MA 02141.
[b] + = Wild.
[c] c^d = Acromelanic white.
[d] e = Cream.
[e] b = Brown.
[f] cm = Cardiomyopathy.

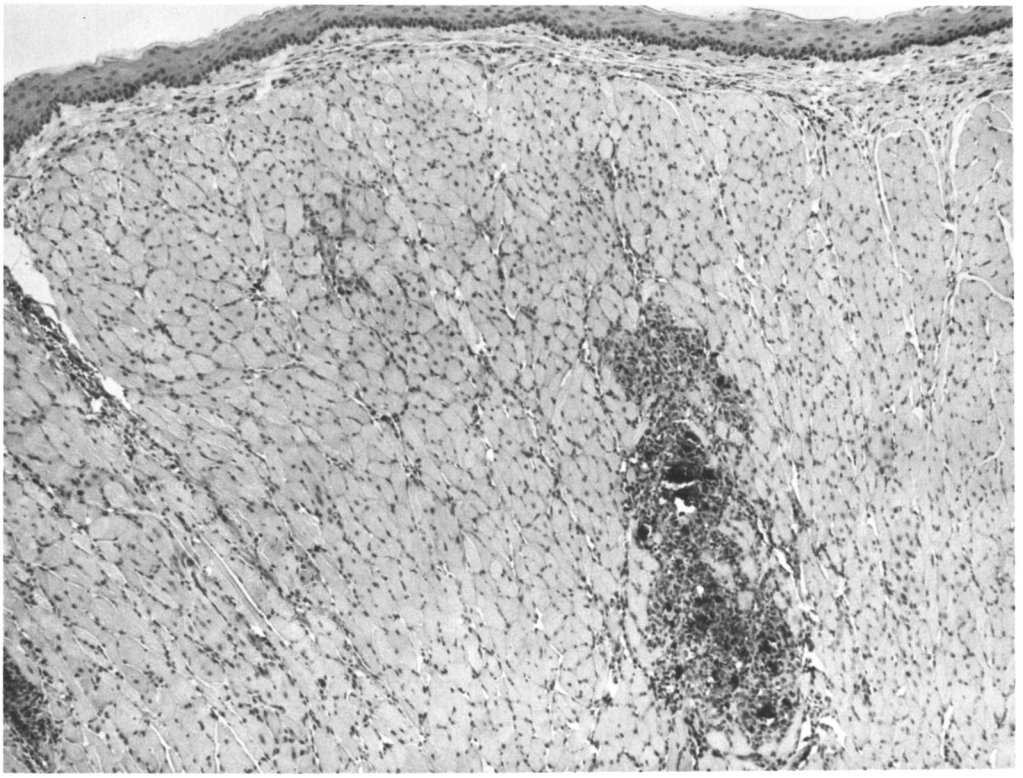

FIG. 2. Section of tongue of myopathic hamster showing early granulomatous lesion with very early calcification (X 60).

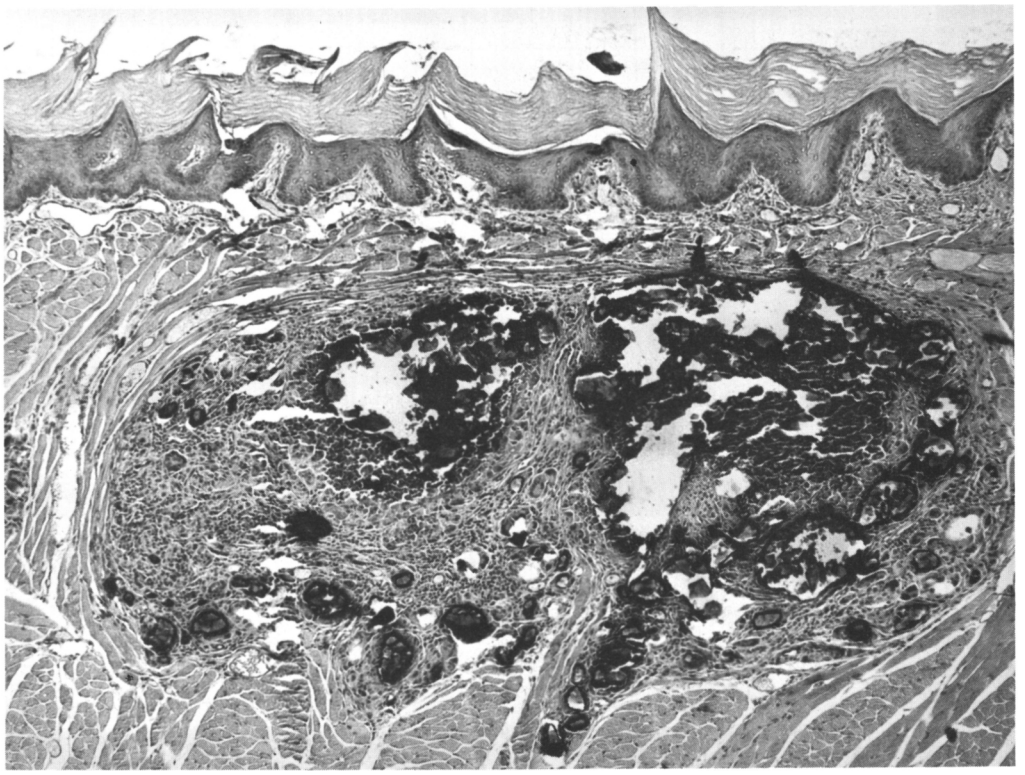

FIG. 3. Section of tongue of myopathic hamster showing well circumscribed submucosal granulomatous lesion with marked calcification (X 100).

hamster strains which developed tongue lesions, it was discovered that two of the strains, BIO 1.26 and 4.22, were derived from the Schwentker colony. This was the origin of the myopathic strains. Strains BIO 1.5 and 86.93 are listed in the TELACO (Trenton Experimental Laboratory Animal Company, Bar Harbor, Maine) Bulletin No. 4, as originating in the National Institutes of Health and in the colony of Dr. Bela Toth, respectively. At this point in our investigation, we have not yet been able to determine whether these animals originated also in the Schwentker colony or whether they are of different origin.

The observation of tongue lesions in these diseased hamsters, especially at the early age of 55 days, will be of great help in correlating the onset of disease with several physiological and biochemical parameters.

Following preparation of this manuscript, it was noted that dystrophic lesions were described in tongues of BIO 14.6 hamsters by K. S. Hartman and S. M. Standish (Arch. Pathol. **98**, 126–133, 1974).

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