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Carious Lesions in Cotton Rat Molars. II. Effect of Removal of Principal Salivary Glands.*

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An appreciable increase in susceptibility to dental caries has been observed in albino rats which were maintained on coarse particle diets after the removal of some or all of the principal salivary glands.¹⁻⁴ Similarly, a substantial increase in susceptibility to tooth decay has been observed in Syrian hamsters after the extirpation of the major salivary glands.⁵ The diets used in these investigations were composed primarily of natural foodstuffs. In the present experiments, the principal salivary glands of weanling cotton rats were removed prior to periods of maintenance on caries-producing, purified rations to determine if this procedure would result in a greater number and extent of carious lesions and a different distribution of the lesions with respect to the various tooth surfaces.

Experimental. The cotton rats to be used in this experiment were separated from their mothers at 14 days of age and divided into two groups, equal with respect to parentage, sex and weight. The individuals in the one group were kept as intact controls, while the principal salivary glands of the cotton rats in the other group were removed under ether anesthesia. After the operation, each animal was placed in an individual wire-bottom cage

with access to water and to either of 2 caries-producing purified rations *ad libitum*. Half of the cotton rats in each of the experimental and control groups were provided with ration 100.⁶ The basal composition of this ration was: sucrose 67%, casein 24%, salt mixture 4% and corn oil 5%, supplemented with adequate amounts of the fat-soluble vitamins, the B vitamins and liver concentrates to permit normal growth. The other half of the cotton rats in each of the intact and operated groups was fed a caries-producing ration of slightly lower caries-producing properties, ration 130, which was a slight variant of ration 100 attained through the isocaloric replacement of 18 of each 67 parts of sucrose by 8 parts of lard by weight. When rations comparable to ration 130 were fed after the development of the teeth was largely complete, the carbohydrate-protein-fat distribution has been shown previously to be borderline in its ability to reduce the susceptibility of the molar teeth of cotton rats to the initiation and development of carious lesions during a 14 week experimental period.⁷⁻⁹ At the end of 12 weeks after desalivation, all cotton rats were sacrificed and the number and extent of the carious lesions determined for each animal by previously described criteria.^{10,11}

Results. The average weight gain during

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⁴ Hukusima, M., *Tr. Soc. path. jap.*, 1940, **30**, 245.

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⁸ Schweigert, B. S., Potts, E., Shaw, J. H., Zepplin, M., and Phillips, P. H., *J. Nutrition*, 1946, **32**, 405.

⁹ Shaw, J. H., unpublished data.

¹⁰ Shaw, J. H., Schweigert, B. S., McIntire, J. M., Elvehjem, C. A., and Phillips, P. H., *J. Nutrition*, 1944, **28**, 333.

¹¹ Shaw, J. H., Schweigert, B. S., Elvehjem, C. A., and Phillips, P. H., *J. Dental Research*, 1944, **23**, 417.

TABLE I.
Effect of Extirpation of Principal Salivary Glands on Rate of Growth and Incidence and Extent
of Carious Lesions in the Cotton Rat.

Ration	Condition	No. of rats	Avg gain in g	Avg No. of carious lesions	S.E.M.*	C.R.†	Avg extent of carious lesions	S.E.M.*	C.R.†
100	Normal	7	50	22.1	2.0		50+	8+	
						5.1			5.6
"	"Desalivated"	9	28	33.9	1.1		109+	7+	
130	Normal	4	54	17.0	2.1		31+	9+	
						3.1			3.0
"	"Desalivated"	5	42	25.0	1.6		63+	6+	

* S.E.M., Standard error of means.

† C.R., Critical ratio.

the experimental period and the average number and extent of carious lesions developed in intact cotton rats and littermates from which the major salivary glands were removed are presented in Table I. Those cotton rats which had had their principal salivary glands removed prior to 12 weeks maintenance on ration 100 had a 53% higher average number of carious lesions and a 110% higher average extent of carious lesions than their intact littermates which had been fed ration 100 for the same period. Likewise, the desalivated animals which had been maintained on ration 130 had a 47% higher average number of carious lesions and a 100% increase in the average extent of carious lesions over that demonstrated by their normal littermates which had received ration 130. These increases in average number and average extent of carious lesions were sufficiently large to be judged statistically significant for both rations. As has been previously demonstrated, the intact cotton rats which were maintained on ration 130 for the 12 week experimental period had a slightly lower average number and average extent of carious lesions than their normal littermates which were maintained on ration 100. Likewise, the desalivated cotton rats which were maintained on ration 130 had an appreciably lower average number and average extent of carious

lesions than their desalivated littermates which were maintained on ration 100 throughout the experimental period. Thus the post-developmental caries-retarding effect of ration 130 occurred not only in normal but in desalivated cotton rats and to approximately the same degree in both the intact and operated animals.

Despite the fact that the average number and the average extent of the carious lesions were significantly higher in desalivated cotton rats than in their intact littermates, almost all carious lesions in intact and operated animals developed in the sulci of the molars except for a few lesions on the proximal surfaces of the molars. The increased occurrence of carious lesions in desalivated cotton rats was a result of the involvement of a higher percentage of the sulci and of the proximal surfaces than occurred in normal animals. No carious lesions were found on the smooth surfaces nor on the occlusal surfaces in either intact or desalivated animals.

At the end of the 12 week experimental period, the crowns of the molars in all 4 quadrants of the desalivated cotton rats which had received ration 100 had been considerably reduced in volume by the carious processes and the subsequent fracture of undercut cusps. The remaining areas of the smooth surfaces were heavily covered with food debris but no gross lesions were observable under this

material by the methods of detection used. In the cotton rats fed ration 130 much less of the molar crowns had been destroyed by the carious processes; thus the size of the smooth surfaces had not been reduced as much but were as heavily covered with food debris. Again no carious lesions were observed on the smooth surfaces. Thus the relative distribution of carious lesions on the various tooth surfaces in the desalivated cotton rat appeared to be identical with that in the normal cotton rat.

The rate of growth was approximately the same for normal cotton rats receiving rations 100 and 130. The rate of growth for the desalivated cotton rats was appreciably less

than for their intact littermates. This reduction in rate of growth was greatest in the animals which received ration 100 throughout the experimental period.

Summary. The removal of the principal salivary glands of cotton rats prior to maintenance on purified, caries-producing rations resulted in a significantly greater average number and average extent of carious lesions than was observed in their intact littermates maintained under otherwise identical experimental circumstances. No alteration in the relative distribution of the lesions with respect to the various tooth surfaces resulted from the removal of the major salivary glands.

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Inhibition of the Appearance of Phenol Red in Frog Kidney Tubules *in vitro*.

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4'-Carboxyphenylmethanesulfonanilide (caronamide) inhibits concentration of phenol red in the lumina of the tubules of frog kidney slices.[†] This observation suggested that it might be of interest to study the activity of various other substances as inhibitory agents. A number of compounds have been studied. These have been mainly carboxylic acids; however, the present communication is concerned only with derivatives of cinchoninic acid. A recent study in this laboratory has revealed that certain derivatives of cinchoninic acid inhibit a water diuresis in the dog.¹ Some of these compounds have been found to increase uric acid excretion in man.²⁻⁴ The

experiments described in this report show that the appearance of phenol red color in the lumina of the tubules in frog kidney slices is inhibited by certain of these substances.[‡]

Procedure. A modification of the method of Forster has been used.⁵ Both kidneys of a frog (*Rana pipiens*) were removed and sliced transversely into sections approximately 200 microns in thickness. The slices were mixed and distributed to 12 small Petri dishes each containing 5 ml of the solution described by Forster.⁵ The concentration of phenol red used was 0.03 millimoles per liter. The substances being tested were dissolved in this

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† Dr. E. K. Marshall, Jr., in conjunction with Dr. Roy P. Forster, made this observation on the fish kidney (flounder) in Maine in the summer of 1947.

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⁴ Impens, E., *Arch. de Pharmacodynamie*, 1911-12, **21-22**, 379.

[‡] We wish to thank Dr. K. C. Blanchard for supplying the cinchoninic acid derivatives.

⁵ Forster, Roy P., *Science*, 1948, **108**, 65.