

repeated bleedings exerted a more profound effect on rats than on rabbits, no explanation for this difference is apparent.

Summary. The turnover of serum protein

in the rat is unaffected by adrenalectomy, or by the administration of adrenal cortical lipo-extract (ACE) to adrenalectomized animals.

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Increased Dental Caries Activity in the Syrian Hamster Following Desalivation.*

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The Syrian hamster (*Cricetus auratus*) has been used in the study of experimental dental caries and appears well suited for such investigation since the disease process in this animal appears similar to that described in humans.¹ Furthermore, the administration of fluorine with a caries producing diet has been shown to reduce the caries incidence,² a finding which roughly parallels observations in man.³ It appeared of some importance to determine whether removal of the major salivary glands would be accompanied by increased caries activity since it is well known that removal, agenesis, or greatly reduced function of the salivary glands in humans is accompanied by rampant decay.⁴⁻⁵ Such a response might be expected since increased caries activity subsequent to salivary gland extirpation has been observed in the albino rat.⁶⁻⁹

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¹ Keyes, P. H., *J. D. Res.*, 1946, **25**, 341.

² Dale, P. P., Lazansky, J. P., and Keyes, P. H., *J. D. Res.*, 1944, **23**, 445.

³ Deatherage, C. F., *J. D. Res.*, 1943, **22**, 173.

⁴ Prinz, H., *D. Cosmos*, 1932, **74**, 129.

⁵ Faber, M., *Acta. Paediat.*, 1942, **30**, 148.

⁶ Kondo, S., Iehikawa, T., and Arai, M., *Tr. Soc. path. jap.*, 1938, **28**, 461.

⁷ Hukusima, M., *Tr. Soc. path. jap.*, 1940, **30**, 245.

⁸ Cheyne, V. D., *PROC. SOC. EXP. BIOL. AND MED.*, 1939, **42**, 587.

Experimental. The animals were of pure inbred stock and were raised on Purina Rabbit Checkers plus weekly supplements of fresh vegetables. They were kept in metal cages with wood shavings for bedding. When 42 days old ($\pm$ 4 days), the animals were separated into a control group (Group I) and an experimental group (Group II). A comparable supplementary group (Group Ia) was available for additional comparisons. The experimental animals were desalivated during a period of 2 weeks. The parotid, submaxillary, and major sublingual glands were removed, under ether anesthesia, through a single midline incision beginning about 5mm from the mandibular symphysis and extending to the manubrium. Control animals were not operated upon. One week after the last operation,‡ an experimental diet and tap water were provided *ad libitum* to Groups I and II. The diet consisted of whole wheat flour, 40%; whole powdered milk, 30%; glucose, C.P., 20%; alfalfa, 5% brewers yeast, 4%; and sodium chloride, 1%. The supplementary control animals (Group Ia), which were used for another study, were of the same age but had been started on the diet 25 days previously.

Animals were weighed at weekly intervals.

⁹ Weisberger, D., Nelson, C. T., and Boyle, P. E., *Am. J. Orthodontics and Oral Surg.*, 1940, **26**, 88.

‡ Four animals failed to survive the operation and, consequently, have not been included in the data.

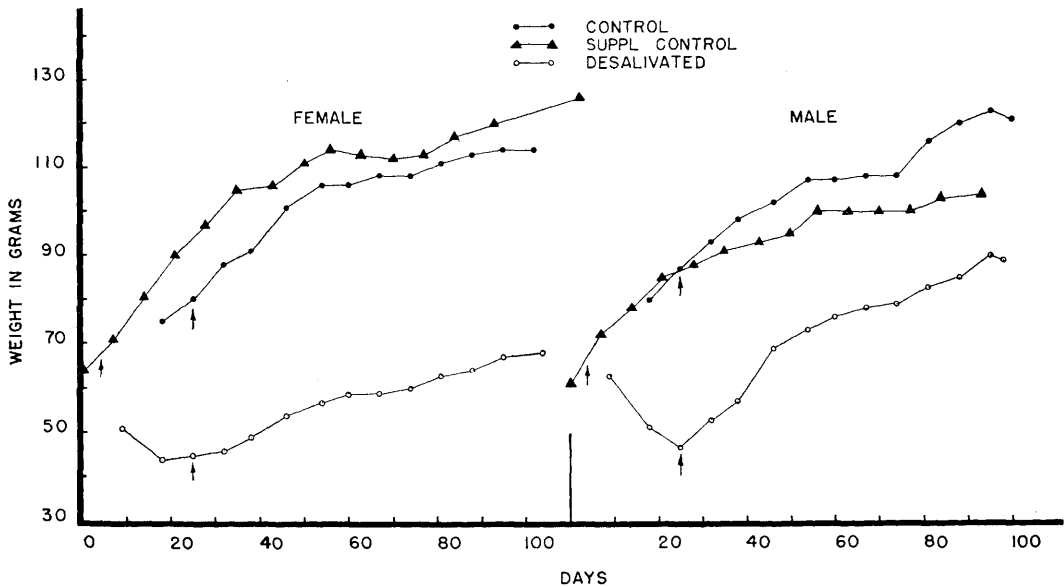


Fig. 1.

Average weight curves for the 3 groups. Arrows indicate the time at which the experimental diet was begun.

Group I and II animals were sacrificed over a 6 day period starting 73 days after the experimental diet had begun. An autopsy was done on each of these animals. Male animals in the supplementary group were killed after 93 days on the diet and female animals after 111 days. Heads were preserved in 10% formaldehyde, stripped of soft tissue, and scored;¹⁰ the number of carious teeth (M. A.), the number of cavities (C. N.), and the total score (T. S.) were recorded. Total score (T. S.) is an arbitrary figure which represents the amount of tooth structure destroyed. All teeth were scored by the same investigator. Data independently obtained for Group Ia animals by the co-author were in excellent agreement.

Differences among the means of average M. A., average C. N., and average T. S. for each of the groups compared were analyzed by the Student-t method.¹¹ Comparison was made between Group Ia ♂♂ and ♀♀; Group Ia and I ♂♂; Group Ia and I ♀♀; Group I and II ♂♂; and Group I and II ♀♀. An arbitrary level of significance of $p = .01$ was chosen; all results less than this value were

considered significant.

Differences among the groups were further compared by the calculation of "percentage of molars affected" and "average percentage of tooth destroyed" for each of the several types of molars. This method of calculation is illustrated beneath Table III.

Results. Average weight curves for the 3 groups are presented in Fig. 1. Desalivated animals lost weight following the operation and remained lighter than those of the control groups. Desalivated females were especially uniform in their weight response. Control animals were sleek, fat, and healthy in appearance. The experimental animals were noticeably emaciated, were more active, and showed at autopsy, a pronounced reduction in depot fat.

Inspection of the mouths prior to administration of the experimental diet disclosed a generalized dryness of the oral tissues in the case of the operated animals whereas the mucous membranes of Group I animals were bathed by copious amounts of salivary secretion.

Caries scores and statistical findings are presented in Tables I and II. **Control groups.** Despite the fact that Group Ia males had been maintained on the experimental diet

¹⁰ Keyes, P. H., *J. D. Res.*, 1944, **23**, 439.

¹¹ Fisher, R. A., *Statistical Methods for Research Workers*, 7th Ed., 1938, Chapt. 5.

DENTAL CARIES IN DESALIVATED HAMSTERS

TABLE I.
Effect of Desalivation on Caries Activity.

Group	Male				Female			
	Animal No.	Max. + Mand. scores			Animal No.	Max. + Mand. scores		
		M.A.	C.N.	T.S.		M.A.	C.N.	T.S.
Suppl. control	27	9	11	18	42	1	1	1 $\frac{1}{4}$
	82	9	10	31	12	3	3	1
	96	5	5	34	15	6	8	5
	69	10	12	59	57	5	6	7
	89	12	14	77	34	6	6	8
	32	11	11	104	75	6	6	9 $\frac{1}{4}$
	104	12	14	107	98	6	7	15
	51	12	14	132	122	8	9	29
					50	9	11	64
Avg		10	11	70		6	6	16
Control	123 ¹	5	5	2 $\frac{1}{4}$	71 ³	1	1	1 $\frac{1}{2}$
	112 ²	6	6	11	46	4	5	2
	124	12	12	73	100	8	8	13
	13	11	15	111	88 ⁴	4	4	13
					63 ⁵	7	8	29
Avg		9	10	49		5	5	12
Experimental	122 $\times$ ¹	11	15	72	68 ³	12	12	208
	113 ²	12	14	166	$\times$	12	13	239
	92	12	15	221	93 ⁴	12	12	257
					64 ⁵	12	12	278
Avg		12	15	153		12	12	246

M.A. = Molars affected.

C.N. = Cavity number.

T.S. = Total score.

Total scores of 138 and 144 indicate complete destruction of maxillary and mandibular molar teeth, respectively.

Animals indicated by same superscript are litter mates.

for 18 days less than the females, the average M. A., C. N., and T. S. were higher for male animals than for female. This difference was statistically significant. Differences between Groups Ia and I were not significant. *Experimental group.* The incidence of dental caries in both male and female animals was increased by desalivation. Average values for M. A., C. N., and T. S. are in every case higher for desalivated animals than for controls. Differences among the male hamsters (Groups I and II) were not statistically significant; differences among females of the same groups were highly significant. Several factors may have obscured statistical differences among the male animals; (1) high caries incidence among unoperated animals, (2) greater variability of response in the male and (3) the small number of animals employed. It is interesting to note that although male animals ordinarily accumulate more dental

decay, females experience a greater amount of tooth destruction subsequent to desalivation.

Considerable variation was observed among individual molar types with respect to percentage of teeth decayed and average percentage of tooth destroyed (Table III). However, in every case but one (δ , Group II, mand. 3rd molars) both measures of caries activity were greater for the desalivated group than for either control group. Every tooth of the experimental animals with one exception (as cited above) showed evidence of dental caries, while in several instances complete or almost complete destruction of all crowns was recorded, e. g. φ , Group II, max. molars.

Discussion. Under the conditions of this experiment, desalivation of hamsters was followed by a definite reduction in body weight especially in the female animals. Decreased food consumption may have contributed to this

TABLE II.
Statistical Evaluation of Caries Scores.

Comparison		Avg	t	p
Group Ia	♂ ♂ vs. ♀ ♀	M.A.	3.80	.002
		C.N.	3.50	.004
		T.S.	3.40	.004
♂ ♂	" " vs. Group I	M.A.	0.77	.45
		C.N.	0.73	.50
		T.S.	0.70	.50
♀ ♀	" " vs. " I	M.A.	0.55	.60
		C.N.	0.67	.50
		T.S.	0.46	.65
♂ ♂	" I vs. " II	M.A.	1.73	.14
		C.N.	2.10	.09
		T.S.	2.05	.10
♀ ♀	" I vs. " II	M.A.	5.90	.0006
		C.N.	5.27	.001
		T.S.	14.9	<.0002

$$t = \frac{m_1 - m_2}{\sqrt{\sigma_{m_1}^2 + \sigma_{m_2}^2}}$$

$$\sigma_m = \frac{\sigma}{\sqrt{N}}$$

$(N_1 + N_2 - 2) = \text{Degrees of freedom in } t$

where m_1 and $m_2 = \text{means compared}$

σ_{m_1} and $\sigma_{m_2} = \text{unbiased estimate of the standard deviation of the means}$

$\sigma = \text{unbiased estimate of standard deviation}$

$N = \text{No. of animals}$

TABLE III.
Caries Incidence as Found in Individual Molars.

		Group Ia (Suppl. control)		Group I (Control)		Group II (Experimental)	
Molar teeth		% molars affected	Avg % of tooth decayed	% molars affected	Avg % of tooth decayed	% molars affected	Avg % of tooth decayed
Max.	Female						
	1st	60.	1.6	40.	0.56	100.	97.
	2nd	40.	3.0	50.	8.4	100.	100.
Mand.	3rd	30.	2.2	00.	0.0	100.	100.
Max.	1	70.	7.0	80.	2.3	100.	93.
	2	60.	17.	60.	12.	100.	90.
	3	30.	1.3	10.	0.10	100.	55.
Max.	Male						
	1	90.	7.8	80.	2.0	100.	53.
	2	70.	21.	40.	13.	100.	61.
Mand.	3	80.	28.	80.	14.	100.	54.
Max.	1	90.	40.	90.	16.	100.	68.
	2	90.	34.	100.	49.	100.	75.
	3	80.	21.	50.	15.	80.	13.

Sample calculation (Maxillary 1st molar, Group Ia, female) :

Percentage of molars affected =

$$\frac{\text{No. of carious max. 1st molars}}{\text{Total No. of max. 1st molars}} \times 100 = \frac{11}{18} \times 100 = 60.6\%$$

Avg percentage of tooth destroyed =

$$\frac{\text{Sum of total scores of all carious max. 1st molars}}{\text{Sum of available total scores of all max. 1st molars}} \times 100 = \frac{7.75}{486} \times 100 = 1.6\%$$

effect for several measurements on group food intakes revealed a consistent reduction in the desalivated group. The effect of the operation, per se, cannot be stated since a sham operation was not performed on either of the control groups. Weight loss following operation has been observed in the rat.¹² Reports on the subsequent changes in weight after recovery of rats from comparable operations are not in agreement. Hukusima⁷ found a reduction in body weight; data presented by Cheyne¹² showed an appreciable reduction in 5 of the 8 groups studied although the animals remained in good health. Weisberger et al.⁹ reported no apparent ill effects on subsequent growth and development.

The higher incidence of decay observed in male hamsters (Group Ia) is in agreement with previous reports.^{1,13-16}

Since Group Ia was on the experimental regimen for appreciably longer periods of time than Group I, a higher incidence of decay would be expected in the former. This proved to be true although the differences were not large and were not shown to be significant. This finding tended to increase the number of control observations and strengthened the argument that changes observed in desalivated animals could not be explained on the basis of normal variation.

The increased caries incidence following salivary gland extirpation in the hamster conforms with observations made in the rat and in man. It is difficult to compare the response of the rat and hamster because of variable experimental conditions and dissimilar scoring technics. In the rat, there is a rise in number of animals⁶⁻⁷ and number of teeth⁸ affected as well as an increase in the number of carious lesions.⁸ With the hamster, large differences are noted only in the amount of tooth destruction, especially in the female. The rapidity of the carious

process may have obscured an increase in number of cavities formed.

The mechanism of increased caries activity cannot be explained by the present findings. Two possibilities suggest themselves: alteration in systemic factors and/or alteration in local factors. The latter explanation is probably more correct. Interference with salivary flow (as observed) would reduce the normal cleansing action of the saliva. In addition, it is not unlikely that the saliva of these rodents contains antibacterial agents and other compounds similar to those observed in human saliva, which are known to inhibit the growth¹⁷ or oppose the action of oral bacteria.¹⁸⁻¹⁹

Summary and conclusions. 1. Seven hamsters (3 ♂♂, 4 ♀♀) were desalivated and compared with a control group (4 ♂♂, 5 ♀♀) and a supplementary control group (8 ♂♂, 9 ♀♀). It has been found that the animal can be desalivated easily and that it will usually survive operations.

2. Under the experimental conditions, extirpation of the glands resulted in a sharp reduction in body weight. Subsequently, body weight remained below that of the control groups.

3. Dental caries activity following operation was increased in both male and female hamsters although the difference was not shown to be statistically significant in the case of male animals. It is probable that a comparable response does occur in males but that a larger group of animals would be necessary for an unequivocal demonstration. Response following desalivation was similar to that reported previously for albino rats and humans.

4. Unoperated male animals experienced more dental decay than did unoperated female animals.

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¹⁴ Dale, P. P., and Keyes, P. H., *J. D. Res.*, 1945, **24**, 194.

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¹⁶ Keyes, P. H., *J. D. Res.*, 1946, **25**, 469.

¹⁷ Bibby, B. G., Hine, M. K., and Clough, O. W., *J. A. D. A.*, 1938, **25**, 1290.

¹⁸ Stephan, R. M., *Science*, 1940, **92**, 578.

¹⁹ Kesel, R. G., O'Donnell, J. F., Kirch, E. R., and Wach, E. C., *J. A. D. A.*, 1946, **33**, 695.