sumption between solei from different animals and also between the two solei of single animals (Table I, I).

The tibial nerves of 19 animals were cut and the oxygen consumption measured 14 days later. It was found that the O_2 consumption of denervated muscles was on the average slightly higher than that of their unoperated controls (Table I, II), the statistical probability of the observed increase being significant lying between 95% and 98%. The oxygen consumption following a unilateral nerve crush was measured at time intervals ranging from 15 to 42 days after denervation. When the results were arrayed according to the degree of atrophy it was noticed that the muscles exhibiting greater weight loss tended to possess slightly higher metabolic rates than their unoperated controls (Table I, III A and B). Calculation of the correlation coefficient between the percentage of weight loss and the gain in Qo_2 showed that only a fair correlation existed ($r = .52 \pm .14$). To compare the oxygen uptake of totally denervated muscle with that of regenerating muscle, the left tibial nerve was crushed and the right tibial cut in another series of 110-days-old rats (Table I, IV A and B). When the weight losses of the contralateral muscles were of the same order, no significant difference in O_2 consumption between the regenerating and the completely denervated muscles was detectable.

Conclusions. Although in some instances statistical interpretation of the data was limited by the smallness of the sample size in relation to size of the mean differences and standard deviations, it may be concluded with reasonable certainty that regenerating muscle exhibits a slightly increased rate of oxygen consumption *in vitro* per gram of tissue, but that the rate of oxygen consumption of regenerating muscle does not differ significantly from that of completely denervated muscle which has undergone a similar degree of weight loss.

14295

Histamine Ineffective in the Rat as a Gastric Secretory Stimulant.

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In the course of a comparative study of gastric secretion it was observed that the rat did not respond to histamine when given in doses found effective in other mammals. This seemed of sufficient interest to warrant special study since in our experience the only animals found refractory to histamine are the elasmobranch fishes[1] and the lower amphibia.[2]

Young albino rats, from 180 to 240 g body weight, kept on a diet of Purina dog chow, were used. Because of the well known habit of coprophagy, the stomach ordinarily is found to be filled with ingestia even after withholding food for 48 hours. By enclosing the rat in a specially constructed jacket, Roe and Dyer[3] were able to obtain animals with empty stomachs. We used this method but later abandoned it in favor of a simpler one. Keeping the animals without food in specially constructed wide-mesh, false-bottom cages proved satisfactory. Water was allowed *ad lib.* Only 5 to 12% of more than 1000 rats were found to have stomachs containing ingested matter after 24 to 36 hours' fast.

The animal was anesthetized with nem-

[1] Babkin, B. P., Chaisson, A. F., and Friedman, M. H. F., *J. Biol. Board Canada*, 1934, **1**, 251.

[2] Friedman, M. H. F., *J. Cell. Comp. Physiol.*, 1942, **20**, 379.

[3] Roe, J. H., and Dyer, H. M., PROC. SOC. EXP. BIOL. AND MED., 1939, **41**, 603.

TABLE I.
Effect of Histamine on Gastric Secretion in the Rat. Following a Control Period of 30 Minutes All Animals (Except Those in the Control Series) Were Given Histamine in the Doses Indicated.

				Histamine								
	Control—65 rats			0.02 mg per kg—37 rats			0.2 to 0.4 mg per kg—29 rats			3.5 to 5.5 mg per kg—34 rats		
		m. eq/l. acid			m. eq/l. acid			m. eq/l. acid			m. eq/l. acid	
Time	vol. cc	free	total	vol. cc	free	total	vol. cc	free	total	vol. cc	free	total
Control 30 min	2.0	70	80	1.9	57	78	1.8	80	98	1.7	63	70
After histamine 30 min	1.5	88	98	1.5	76	92	1.8	84	98	1.9	76	90
90 "	1.4	64	81	1.5	61	79	1.2	71	90	1.7	88	101
150 "	0.9	54	66	0.4	57	70	0.7	52	68	0.8	90	113
210 "	0.7	50	54	0.6	55	68	0.8	50	60	0.4	70	86
Avg vol. for last 3½ hr	4.5	—	—	4.0	—	—	4.5	—	—	4.8	—	—
Max. avg acidity m. eq/l.	—	88	98	—	76	92	—	84	98	—	100	113
Total output of HCl during last 3½ hr, mg	—	11.13	13.05	—	9.53	11.86	—	11.39	13.87	—	14.38	17.06
Total output of acid as % of control group	—	100%	100%	—	85.6%	91.0%	—	102.3%	106.2%	—	129.0%	130.7%

butal or ether. In some instances gastric fistulas were established in the usual manner, but in most of the experiments samples of gastric juice were obtained by the method of Roe and Dyer.[3] The stomach was exposed through a small mid-line incision, the duodenum carefully ligated and a number 18 hypodermic needle inserted into the stomach in the region of the rumen. The needle served for withdrawing gastric contents. With care the stomach could be punctured repeatedly without contaminating the gastric contents with blood. Between periods of withdrawing gastric samples the abdomen was closed with small serrefines.

Histamine phosphate was given subcutaneously every 15 minutes, the first injection being made after an initial control period of 30 minutes. The doses used are shown in Table I. The acidities were determined with 0.01 N NaOH, using Topfer's reagent and phenolphthalein as indicators.

The results are summarized in Table I. The following conclusions may be drawn from the present study on 165 rats:

1. *The fasting rat continuously secretes small amounts of acid gastric juice.* While this secretion is greatest at the beginning, it still persists at a fairly steady rate during the 3rd and 4th hours and, as we have found in other experiments, even after 5 hours. Whether, as in the groundhog,[4] the continuous secretion is spontaneous and perhaps due to some innate properties of the secretory cells or, as in the dog,[5] the secretion is perhaps due to the presence of digestion products in the intestine, we do not know. In 12 rats, atropine in doses of 0.8 to 1.0 mg per kilo failed to inhibit this continuous secretion. The secretion probably was not due to operative trauma since further traumatizing the limbs and intestine 1 to 2 hours after the initial operation did not increase the secretion. That the gradual decrease in secretory rate from the initial high value was due to dehydration consequent to loss of gastric juice from the body[6] should be considered.

2. *Histamine does not stimulate in the rat an increased secretion of fluid.* The total

[4] Friedman, M. H. F., and Armour, J. C., *J. Cell. Comp. Physiol.*, 1936, **8**, 201.

[5] Babkin, B. P., *Emanuel Libman Anniversary Volumes*, 1932, **1**, 11, International Press, New York.

[6] Friedman, M. H. F., *J. Cell. Comp. Physiol.*, 1939, **13**, 219.

volume of gastric fluid secreted after 3½ hours of histamine injections was equal to that of the control series during the same period. With extremely large doses (3.5 to 5.5 mg per kg) the secretion appeared to be concentrated with respect to acid. However, the response was not uniform and the acidity values in this group were widely distributed. Further study would be required to determine whether a dissociation between acid and water secretion really does occur in the rat as these results might suggest. These results do not confirm those of Roe and Dyer[3] who found that 0.03 mg of histamine phosphate per kilo does stimulate an acid secretion. The curves of both the volume and acidity of their histamine-treated rats parallel closely those we obtained in our series that received no histamine. Polland[7] found no free acid secreted by the rat after huge unstated doses of histamine.

With respect to the effect of histamine on the gastric secretory cells, the rat behaves like the skate[1] and necturus[2] rather than other rodents (groundhogs,[4] guinea pig).[8] The extremely high tolerance of the rat to histamine is well known.[9] The ineffectiveness of histamine in the rat as a secretory stimulant may perhaps be related to the rapid rate of disappearance of injected histamine from the blood and the relatively small amount of histamine retained by the stomach.[10] Since histamine is a potent gastric secretory stimulant in the anesthetized groundhog,[4] guinea pig,[8] cat,[11] dog,[12] pigeon[6] and chicken,[6] it is unlikely that the ineffectiveness of histamine in the rat was due in these experiments to the use of anesthetics.

Conclusion. In the rat gastric secretion is continuous. Histamine has little if any effect on the gastric secretion of the (anesthetized) rat.

7 Polland, W. S., cited by Bloomfield and Polland, *Gastric Anacidity*, Macmillan, New York, 1933, p. 80.

8 Podolsky, H. M., and Friedman, M. H. F., in preparation for publication.

9 Best, C. H., and McHenry, E. W., *Physiol. Rev.*, 1931, **11**, 371.

10 Rose, B., and Brown, J. S. L., *Am. J. Physiol.*, 1938, **124**, 412.

11 Noble, R. L., and Robertson, J. D., *J. Physiol.*, 1938, **93**, 430.

12 Bowie, D. J., and Vineberg, A. M., *Quart. J. Exp. Physiol.*, 1935, **25**, 247.

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Return of Vision in Transplanted Adult Salamander Eyes After Several Days of Refrigeration.*

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It has been shown that adult salamander eyes can be transplanted successfully if they are grafted immediately after enucleation.[1,2] Return of vision 4 times in the same eye repeatedly transplanted demonstrates[3] how successful the results can be. The capacity of an adult salamander eye to recover is tested further in the following experiments by isolating it from its blood supply for a long period.

Fifty-nine enucleated adult *Triturus viridescens* eyes were refrigerated from 0°C to 8°C in sterile Ringer's solution for periods varying from 2 to 14 days and then transplanted into freshly denuded orbits of new

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1 Stone, L. S., and Zaur, I. S., *J. Exp. Zool.*, 1940, **85**, 243.

2 Stone, L. S., and Cole, C. H., *Yale J. Biol. and Med.*, 1943, **15**, 735.

3 Stone, L. S., and Farthing, T. E., *J. Exp. Zool.*, 1942, **91**, 265.