cago, and occasionally in wintertime, during a severe cold wave, the room temperature declined by several degrees. All heart rates taken during such periods were greatly elevated, even in rats which were resting quietly (Fig. 4c). In the investigation for which these heart rate studies were made,[10] one highly effective method used to accelerate the heart was chilling of the animal by depilation.

From these evidences it seems clear that dependable normal pulse rate determinations can be made in the unanesthetized rat, providing the extreme excitability of the animal and the great variability with temperature changes are recognized and steps taken accordingly. Early indications of studies in progress are that the training period may be cut to a week or two by the use of roomier cages than were formerly deemed necessary.

Summary. 1. A method is presented for accurate determination of the normal, conscious, resting heart rate in the albino rat. 2. The average value obtained on 113 adult males of 200-370 g body weight was 4.4 ± 0.30 beats per second, or 264 ± 18 per minute. 3. Emotional states were found to cause greater variation in heart rate than muscular activity. 4. Alterations in environmental temperature proved to exert a decided influence on the rat heart rate.

[10] Moses, L. E., *Am. J. Physiol.*, 1944, **142**, 686.

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Effect of Alloxan upon External Secretion of the Pancreas.

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The report of Goldner and Gomori[1] that in dogs made "diabetic" by alloxan injection the intralobular duct cells of the pancreas showed vacuolization suggested to us the possibility that this might serve as a means of investigating whether these duct cells perform a secretory function.

Methods and Results. A standard preparation of secretin concentrate designated S_1[2] was used in these experiments. It is known to contain both secretin and pancreozymin. The particular lot of material used for these experiments was tested on 2 normal dogs and the threshold dose[3] was found to be 0.3 and 0.5 mg respectively, indicating that the material had standard potency. In 4 dogs rendered "diabetic" for 18 to 30 days by the intravenous injection of 75 mg of alloxan per kg of body weight, the threshold dose of this same lot of secretin concentrate was found to be 2, 4, 5 and 10 mg. The "diabetic state" was attested by the strongly positive sugar reaction of the urine accompanied by moderate decline in body weight.

Two dogs which were similarly treated with alloxan but failed to become "diabetic" showed a threshold of 0.4 and 0.8 mg secretin concentrate, respectively. In the 2 normal dogs mentioned above, which were used to establish the potency of the secretin preparation, the injection of alloxan in a dose of 75 mg per kg of body weight after the threshold response had been determined did not significantly alter their response to a subsequently administered threshold dose of secretin concentrate within 3 hours.

Amylase determinations by the method of Schmidt[4] were performed on all samples of

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[1] Goldner, M. G., and Gomori, G., *Endocrin.*, 1943, **33**, 297.

[2] Greengard, H., and Ivy, A. C., *Am. J. Physiol.*, 1938, **124**, 427.

[3] Ivy, A. C., Kloster, G., Drewyer, G. E., and Lueth, H. C., *Am. J. Physiol.*, 1930, **95**, 35.

[4] Schmidt, C. R., Greengard, H., and Ivy, A. C., *Am. J. Digest. Dis.*, 1934, **1**, 618.

TABLE I.
Secretin Threshold Dose and Amylase Concentration of Pancreatic Juice in Control Dogs and Dogs Treated with Alloxan.

Dog No.	Alloxan (mg/kg)	Days after alloxan	Urine sugar	Amylase (mg glucose/cc)	Threshold dose of secretin (mg)
1	none	—	0	1460	0.3
2	"	—	0	1280	0.5
3	75	18	++	1760	2.0
4	75	24	++	1120	10.0
5	75	28	+++	1690	5.0
6	75	30	++	1430	4.0
7	75	22	0	1260	0.4
8	75	30	0	1740	0.8

pancreatic juice but revealed no remarkable differences between the juice obtained from alloxan-treated animals and that of normal dogs (Table I). In one animal with alloxan-induced diabetes in which the pancreas was examined histologically, the vacuolization of the intralobular ducts described by Goldner and Gomori[1] was found; the acinar cells were normal.

Discussion. The finding of decreased responsiveness to secretin accompanied by histological evidence of damage to the duct epithelium[1] suggests but does not prove that the small duct cells participate in the formation of pancreatic juice. It is generally taught that the entire pancreatic juice is produced by the acinar cells; no secretory function is ascribed to the duct cells. In the salivary glands the duct cells are believed to contribute most of the liquid portion of the saliva.[5]

Two separate hormones, namely secretin and pancreozymin, control the secretory activity of the pancreas. The type of activity engendered by each hormone (water and bicarbonate secretion in the case of secretin; enzyme secretion in the case of pancreozymin) can vary independently. These facts are compatible with the concept that each hormone acts predominantly upon a different cell type in the pancreas, the secretin upon the intralobular duct cells and the pancreozymin upon the acinar cells.

A similar situation obtains in the gastric glands where the parietal cells produce hydrochloric acid and most of the water of the gastric juice while the granulated body chief cells provide the pepsin. The analogy between the gastric and pancreatic glands can be extended to include a functional parallelism, *to-wit,* the relationship between the rate of secretion of the juice and the concentration of the acidic or basic constituent respectively. In the stomach as the rate of secretion increases the concentration of hydrochloric acid increases and approaches a limiting value, namely the concentration of acid in the pure parietal secretion.[6] Similarly, as the rate of pancreatic secretion increases the bicarbonate concentration increases and approaches a limiting value, which, as in the case of the acid of the stomach, is approximately equal to the osmolar concentration of blood plasma.[7]

This concept of participation in elaboration of secretion by the small duct epithelial cells is offered as an hypothesis; much more evidence is required to establish or disprove its validity.

(Scanlon, Catchpole and Gersh[8] have also found a decreased responsiveness to secretin in alloxan diabetic dogs).

[5] Babkin, B. P., *Secretory Mechanism of the Digestive Glands,* P. B. Hoeber, New York, 1944.

[6] Gray, J. S., *Gastroenterology,* 1945, **1**, 390.

[7] Hart, W. M., and Thomas, J. E., *Gastroenterology,* 1945, **4**, 409.

[8] Personal communication from J. H. Scanlon, H. R. Catchpole, and I. Gersh, Naval Medical Research Institute, Bethesda, Md.