(direct stimulation, by pressing the muscle together or by forcibly keeping the valves closed) it is found that this tone can be made to disappear by the same types of stimulation just described.

It has been possible to a certain extent to study the effect of simultaneous stimulation of the contraction and relaxation mechanisms of this muscle. It was found that small contractions can be completely suppressed. Stronger ones persist but are diminished in size and are slower in development. The relaxation of such contractions is faster than that of uninhibited ones, and after a purely inhibitory stimulation contractions are depressed for some time, showing that the inhibition mechanism outlasts the stimulus to a much greater extent than does the contraction mechanism. This may well be due to the presence in the muscle of a substance which disappears slowly and causes relaxation.

These results aid in clarifying the mechanism of contraction and relaxation of the slow muscle in Pecten. It now seems reasonable to conclude that some type of peripheral inhibitory nerve fibers exists.

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Effect of Anoxia on Blood Sugar in Adrenalectomized-Pancreatectomized Dogs.*

IRVINE MCQUARRIE, M. R. ZIEGLER AND L. J. HAY.

From the Departments of Pediatrics and Surgery, University of Minnesota, Minneapolis.

In a previous investigation by the authors and their associates,[1] it was found that the blood sugar of adrenalectomized dogs was progressively decreased, frequently to hypoglycemic levels, as a result of their being made to breathe an atmosphere with a low oxygen content (5% to 9% O_2). In contrast with this response, normal animals in the post-absorptive state develop a sustained hyperglycemia[2] (as the dogs used in our previous experiments did before

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1 McQuarrie, I., Ziegler, M. R., Stone, W. E., Wangensteen, O. H., and Dennis, C., (a) PROC. SOC. EXP. BIOL. AND MED., 1939, **42**, 513; (b) *Chinese Med. J.*, 1940, **58**, 26.

2 Kelloway, C. H., *J. Physiol.*, 1919, **53**, 211.

adrenalectomy[3]), when exposed to such an atmosphere. Since this latter reaction in the normal animal has been shown to be due to sympatho-adrenal stimulation with release of adrenalin into the blood stream and resultant mobilization of glucose from the liver, abolition of the hyperglycemic response to asphyxia would be expected to follow adrenalectomy. However, a well-defined hypoglycemic response, instead of a merely negative one, after adrenalectomy suggested the possibility of stimulation of the vago-insulin mechanism or a direct effect of anoxia on the islet cells of the pancreas with release of insulin. The experiments reported here were undertaken to obtain data bearing more directly upon this aspect of the problem.

Dogs were depancreatized and adrenalectomized in two stages. The pancreas and one adrenal were removed at the first operation. After the animal had recovered satisfactorily from this procedure and had become well adjusted to a suitable diabetic regimen, the remaining adrenal gland was extirpated. Adrenal cortical extract (Upjohn) was then given subcutaneously twice daily in doses varying between 10 cc and 5 cc to prevent adrenal insufficiency until the operative wounds had entirely healed. Thereafter from 2 to 4 cc of the extract per day sufficed to prevent the usual manifestations of adrenal insufficiency. The basic daily diet contained the following ingredients per kilogram of the animal's body weight: casein 3, sucrose 9, egg yolk 2, egg white 2, artificial bone ash 0.4 and NaCl 0.5 g. This was supplemented by 100 g of ground, raw beef pancreas (or 10 g of lecithin), 2.5 mg ascorbic acid, 5 mg nicotinic acid, 2 mg thiamine hydrochloride and 3 drops of percomorph liver oil daily.

Following removal of the second adrenal gland, the daily insulin requirement fell from between 8 and 15 units to 1 or 2 units. Food, insulin and cortin were all withheld for about 16 hours before each acute experiment was carried out. Throughout each period of observation the animal was kept loosely fastened to a board in a specially adapted clinical oxygen tent, whether breathing room air or a mixture of 5% O_2 and 95% N_2. The tent was constantly maintained at atmospheric pressure. Eight control blood sugar curves were obtained on two adrenalectomized-depancreatized dogs while they breathed ordinary room air. Blood sugar determinations were made at 30-minute intervals for 2.5 hours. An equal number of acute experiments to determine the effects of anoxia on blood sugar were carried out on the same operated animals at intervals of 6 to 8

[3] McQuarrie, I., and Ziegler, M. R., PROC. SOC. EXP. BIOL. AND MED., 1939, **39**, 525.

TABLE I.
Effect of Anoxia on Blood Sugar in Adrenalectomized-Depancreatized Dogs.

Dog No.	Blood sugar, mg per 100 cc				
	Initial sample	Time in tent			
		1 hr	1½ hr	2 hr	2½ hr
		Breathing room air.			
1	300	305	300	—	310
	355	346	—	300	330
	290	290	318	—	340
	320	250	—	260	270
2	265	240	—	240	250
	240	255	270	—	265
	305	250	—	265	246
	310	300	—	310	320
		Breathing 5% O_2 plus 95% N_2.			
1	360	380	—	340	345
	300	340	—	380	370
	352	348	348	—	355
2	252	280	—	320	300
	300	275	305	—	310
	300	345	380	—	360
	340	329	—	365	355

days, alternating with the control studies. In addition, the blood sugar responses to anoxia during periods of insulin hypoglycemia were determined in the animals before and again after removal of both the pancreas and the adrenals.

The results of the investigation may be summarized as follows (see Table I): There was no consistent rise or fall in the blood sugar levels of the adrenalectomized-pancreatectomized dogs, when they were exposed for 2.5 hours to an atmosphere containing but 5% O_2. The small fluctuations recorded did not differ significantly from those obtained for the same animals in room air. A composite curve representing the mean blood sugar values, determined at half-hour intervals throughout each of the 8 experiments, traversed an approximately straight horizontal line in the experiments involving anoxia as well as in those carried out in room air. Whereas sudden exposure to an atmosphere composed of 5% O_2 and 95% N_2 during a period of insulin hypoglycemia consistently caused a sharp rise in the blood sugar of normal dogs, no such alteration in the hypoglycemic curve resulted from anoxia in the depancreatized-adrenalectomized animals.

These results appear to indicate that anoxia normally stimulates both the vago-insulin and the sympatho-adrenal systems but that the former effect is masked under ordinary conditions by the more

pronounced response of the adrenals. The stimulating effect on the insulin-releasing mechanism becomes evident only after the latter effect has been abolished. A similar interpretation was given by Gellhorn and his collaborators[4] to results of their interesting study on the mutual relationship of the vago-insulin and sympatho-adrenal systems under conditions of central excitation induced by anoxia and by metrazol. These investigators confirmed the hypoglycemic response to anoxia in adrenalectomized rats and found in addition that denervation of the adrenals had an effect similar to that of adrenalectomy. Metrazol, like anoxia, produced a hyperglycemia in normal but a hypoglycemia in adrenalectomized rats. They then found that intraäbdominal section of the vagi of adrenalectomized rats abolished the hypoglycemic response to either anoxic anoxia or metrazol. The effect of pancreatectomy in the present experiments was practically identical with that of vagotomy in their study.

Conclusions. Since pancreatectomy has been shown to abolish the hypoglycemic response of the adrenalectomized animals to anoxic anoxia, it may be concluded with Gellhorn that anoxia normally stimulates the parasympathetic (insulin response) as well as the sympathetic (adrenal response) system.

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Distribution of Biotin and Avidin in Hen's Egg.

PAUL GYÖRGY AND CATHARINE S. ROSE.

From the Babies and Childrens Hospital, and the Department of Pediatrics, School of Medicine, Western Reserve University, Cleveland.

Identification, with biotin,[1] of the curative factor (vitamin H) for egg-white injury in rats, and the recognition that avidin,[2] a protein-like constituent of egg white, is the injury-producing principle[3] of raw egg white raised the question of the distribution of

[4] Feldman, J., Cortell, R., and Gellhorn, E., *Am. J. Physiol.*, 1940, **131**, 281.

[1] György, P., Melville, D. B., Burk, D., and du Vigneaud, V., *Science*, 1940, **91**, 243; du Vigneaud, V., Melville, D. B., György, P., and Rose, C. S., *Science*, 1940, **92**, 62.

[2] Eakin, R. E., Snell, E. E., and Williams, R. J., *J. Biol. Chem.*, 1940, **136**, 801; 1941, **140**, 535.

[3] György, P., Rose, C. S., Eakin, R. E., Snell, E. E., and Williams, R. J., *Science*, 1941, **93**, 477.