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The formation of lactic acid by depancreatized dogs.

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In seeking to extend our observations,[1] that the concentration of lactic acid is increased in the blood of normal dogs following the injection of insulin, we have studied the blood of depancreatized dogs during the violent exercise of strychnine convulsions. In an earlier investigation dealing with this problem Sass[2] came to the conclusion that, in contrast to normal animals, the titratable alkalinity of the blood of depancreatized dogs is decreased much less by strychnine convulsions, and that this is probably due to an impaired capacity to form acid (lactic) from carbohydrate.

Barr [3, 4] and his collaborators have recently published investigations showing that patients with a partial diabetes and completely phlorhizinized dogs form lactic acid as a result of exercise. Our experiments supply data on the same point for complete pancreatic diabetes in dogs and give additional information on the quantity of lactic acid precursor and glycogen in the muscles.

Experimental procedure: Male dogs were depancreatized and kept on insulin until the wound had healed. About ten days after the operation, the insulin was withdrawn. Within 4 to 6 days the urine generally showed a D:N ratio of about 2.8. A day or two later strychnine convulsions were induced and blood taken for comparison with a control sample. Since the blood specimens were generally taken from the femoral artery the figures given in the table are the concentrations in the arterial blood.

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[1] Briggs, A. P., Koechig, I., Doisy, E. A., and Weber, C. J., *J. Biol. Chem.*, 1924, lviii, 721.

[2] Sass, M., *Zt. f. exp. Path. u. Ther.*, 1914, xv, 370.

[3] Himwich, H. E., Loebel, R. O., and Barr, D. P., *J. Biol. Chem.*, 1924, lix, 265.

[4] Loebel, R. O., Barr, D. P., Tolstoi, E., and Himwich, H. E., *J. Biol. Chem.*, 1924, lxi, 9.

TABLE I.

Formation of Lactic Acid by Depancreatized Dogs.

Before strychnine			After strychnine				Remarks.
			First sample		Second sample		
Dog No.	Glucose	Lactic Acid	Glucose	Lactic Acid	Glucose	Lactic Acid	
1	170	26.	173	87.5	285	178.	No microscopic examination made.
2	337	31.	361	51.	364	42.	D/N 2.7 on day of experiment. No generalized convulsions.
	428	29.5	430	63.	418	89.5	D/N Apr. 13, 2.75; 14th, 2.72; 15th, 2.83; strychnine on Apr. 16th and again on Apr. 18th. Two small nodules of pancreas found on microscopic examination.
	403	37.5	389	71.	389	97.5	
3	345	35.5	345	81.	350	113.	D/N Apr. 13, 2.75; 14th, 2.86; 29th, 2.82; strychnine on Apr. 28th. Minute quantity of pancreas in duodenal wall.
	308	41.7	326	59.8	337	82.9	D/N for 4 days preceding strychnine convulsions varied between 2.76 and 2.30. No pancreatic tissue on microscopic examination. Post-mortem lactic acid in muscle 0.422 per cent.
4	263	42.4	267	62.8	270	82.7	
	500	41.6	500	63.0	550	94.4	D/N for 4 days preceding first strychnine convulsions varied between 2.86 and 2.23. No pancreatic tissue on microscopic examination. Post mortem lactic acid in muscle 0.437 per cent.
5	421	39.5	421	47.9	430	113.4	
6	359	27.8	326	66.8			Post mortem lactic acid in muscle 0.172 per cent.
8	265	16.0	292	39.	235	89.	Lactic acid maximum of muscle in $NaHCO_3$ 0.125 per cent. Second blood sample taken from heart 1 minute after death.
9	192	34.0	181	36.	176	36.	Lactic acid maximum of muscle 0.150 per cent. Contractions in response to strychnine poor.

After the death of each dog an examination of the abdomen for pancreas was made. All suspicious tissue fragments and the upper end of the duodenum were sectioned, stained and examined microscopically by the Pathology Department of St. Louis University. The experimental results reported in this paper were obtained on dogs that had only minute residues of pancreas or none at all. There seems to be no doubt about their ability to form lactic acid in response to strychnine convulsions.

In Table I we have given the results of 12 experiments performed on eight depancreatized dogs. Eleven of the 12 experiments show that lactic acid is formed during the convulsions induced by strychnine. Dog 9 differs from the others in that the blood sugar values were much lower, and that no increase in the lactic acid was observed. This dog had received several injections of adrenalin and was very weak. We believe that the convulsions were not severe enough to pile up the lactic acid in the arterial blood.

We are inclined to the belief that depancreatized or phlorhizinized dogs form lactic acid during muscular work so long as their muscles possess glycogen. As the store of glycogen is depleted, the animal becomes less able to produce lactic acid and perform work. (Compare experiments on Dogs 8 and 9 with 4 and 5).

Although the values of the lactic acid maximum of Dogs 8 and 9 are only about one-third of the value for a well nourished dog, they indicate the presence of glycogen. Direct determinations showed that some glycogen was still present even after the severe treatment given these dogs.

CONCLUSIONS.

Depancreatized dogs form easily detectable quantities of lactic acid during strychnine convulsions. Even though these animals may be unable to oxidize carbohydrate, still the production of lactic acid seems intimately concerned with muscular contractions.