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A Mechanism Maintaining the Hyperglycemia of Diabetes.

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In a previous report[1] it was shown that resting muscle of normal dogs may liberate lactic acid into the blood stream. The lactic acid may thus reach the liver where it is removed and converted to carbohydrate. It may be retained in the liver as glycogen or leave the liver, appearing in the blood as glucose. In the present study on diabetic dogs it was found that this lactic acid-glucose cycle involving muscle and liver was one of the mechanisms for maintaining hyperglycemia after the glycogen stores of the liver were reduced by fasting.

Fourteen large female dogs were fasted for 3 days or more and were then depancreatized under aseptic precautions. When the respiratory quotient and the D/N ratio indicated that the dogs had become completely diabetic, they were put under amytal anesthesia, the femoral vessels were exposed and the abdomen was opened by a longitudinal incision. Samples of blood were drawn practically simultaneously from the femoral artery, femoral vein, portal vein and hepatic vein. These blood samples were analyzed for glucose and lactic acid.

The results may be presented as 3 links in a chain of evidence: First as seen in Table I, both during rest and exercise there is greater concentration of lactic acid in the blood of the femoral vein than in that of the femoral artery. Taking differences of 5 mg. % or more as significant, this occurred in 13 of 25 observations. Only once did the muscles take out lactic acid from the blood.

[1] Himwich, H. E., Koskoff, Y. D., Nahum, L. H., PROC. SOC. EXP. BIOL. AND MED., 1928, XXV, 347.

TABLE I.

Lactic Acid of the Femoral Artery and the Femoral Vein.

	Lactic Acid mg. %	
	Femoral Artery	Femoral Vein
Resting blood	29	30
84 minutes of work	31	38
106 minutes of work	38	49

TABLE II.

Lactic Acid of the Blood Entering and Leaving the Liver.

	Lactic Acid mg. %		
	Femoral Artery	Portal Vein	Hepatic Vein
Resting blood	58	60	46
12 minutes of work	79	73	61
65 minutes of work	75	80	61

TABLE III.

Glucose of the Blood Entering and Leaving the Liver.

	Glucose mg. %		
	Femoral Artery	Portal Vein	Hepatic Vein
Resting blood	345	350	380
12 minutes of work	380	360	385
65 minutes of work	380	390	435

As shown in Table II, the second link in the chain of evidence, is the removal of lactic acid by the liver. In 16 of 22 observations the liver removed lactic acid from the blood and in but one instance did it add lactic acid.

The last link in the evidence (Table III) is the liberation of glucose by the liver. Despite the hyperglycemia, in 18 of 22 observations the liver added glucose to the blood passing through it. Only twice did the liver remove glucose from the blood stream.

In most instances the liver added more glucose to the blood than could be accounted for by the lactic acid entering that organ. This additional glucose is probably produced in the heightened processes of protein metabolism. However, our chief point is the fact that the liver forms carbohydrate from the lactic acid liberated by muscle. Since in diabetes this carbohydrate is not retained by the liver as glycogen it necessarily appears in the blood as glucose. This mechanism is therefore an important factor in maintaining the hyperglycemia of diabetes.