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The "Fat Sparing" Action of Glucose in the Absence of Insulin.*

I. Arthur Mirsky and Fanny A. Senior.

From the Department of Metabolism and Endocrinology, Institute for Medical Research, the Jewish Hospital, Cincinnati, Ohio.

It is generally acknowledged that the ketone bodies are intermediary products of fatty acid oxidation in the liver.[1, 2, 3] Hence, it is obvious that any procedure which results in a decrease of ketone body production must act by decreasing the rate at which fat is undergoing oxidation, *i. e.*, by sparing fat.

In a series of experiments[4] subsequently confirmed by Barker and Sweet,[5] we demonstrated that when the fasting depancreatized dog is treated with glucose intravenously in amounts adequate for glycogen deposition in the liver, a decrease in the ketone body content of the blood occurs even in the complete absence of insulin. Since it has been shown that this effect of glucose is not due to either an increased utilization[5] or an increased excretion of the ketone bodies,[4] it must be attributed to a decreased formation of these substances, or, in other words, to a decrease in fatty acid oxidation.

In a more recent report, Lichtman[6] demonstrated that while the administration of glucose *per os* results in a decrease in the blood fatty acids of normal dogs, it fails to produce this effect in animals deprived of their pancreas. From these observations, he draws the implication that glucose is "fat-sparing" only when insulin is present in the organism. If a decrease in the blood-fat level were a proper index of "fat-sparing", then when an inhibition of ketone body formation occurs in consequence of the intravenous administration of glucose, a diminution in the blood fatty acids should occur also. It became of interest to study this question.

Dogs were depancreatized, and in order to hasten the onset and aggravate the severity of the ketosis,[4] one gram of phlorhizin in oil and one gram of phlorhizin in sodium carbonate solution were administered subcutaneously 24 hours after pancreatectomy. After

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1 Quastel, J. H., and Wheatley, A. H. M., *Biochem. J.*, 1933, **27**, 1753.

2 Snapper, J., and Grunbaum, A., *Biochem. Z.*, 1927, **185**, 228.

3 Mirsky, I. A., and Broh-Kahn, R. H., *Am. J. Physiol.*, 1937, **119**, 734.

4 Mirsky, I. A., Heiman, J. D., and Broh-Kahn, R. H., *Am. J. Physiol.*, 1937, **118**, 290.

5 Barker, S. B., and Sweet, J. E., *Science*, 1937, **86**, 270.

6 Lichtman, A. L., *J. Biol. Chem.*, 1937, **120**, 35.

another interval of from 24 to 48 hours, the animals were anesthetized with sodium amytal† and a branch of the femoral artery was exposed. Two blood samples were drawn at hourly intervals, and then 2 gm. of glucose per kilo of body weight were administered intravenously every hour in a 30% solution. Blood samples were again drawn 2 and 4 hours after the onset of the glucose injections. The "total" ketone body content of the blood was determined by the Van Slyke and Fitz method,[7] and the total fatty acid content of the whole blood by Street's method.[8] As a control, glucose was administered to anesthetized normal dogs in the postabsorptive state, and the blood fatty acids were likewise determined.

TABLE I.
Influence of Intravenous Glucose Administration on Blood Fatty Acids and Blood "Total Ketones."

		Blood "Total Ketones" (Average)			Whole Blood Fatty Acids* (Average)		
Experiment	Dog	0 mg. %	2 hr. mg. %	4 hr. mg. %	0 mg. %	2 hr. mg. %	4 hr. mg. %
Normal	1	—	—	—	462	379	411
	2	—	—	—	565	509	536
	3	—	—	—	724	660	520
Depancreatized	1	19.9	10.4	7.2	489	491	553
	2	20.7	5.0	0.5	879	795	794
	3	38.0	20.3	0.0	924	959	918

* Total Lipids—Total Cholesterol.

Our results (Table I) are in accord with those of Lichtman in that a decrease in the blood fats occurs in the normal dog, following the administration of glucose and that no decrease occurs in the depancreatized animals. However, in all instances, the intravenous injection of glucose to depancreatized dogs, produces a marked fall in the blood ketone bodies. In view of the antiketogenic effect, it is obvious that a sparing of fat does occur in these animals even though simultaneously their blood fat level remains unchanged. Hence, it is probable that the response of the blood fatty acids to glucose administration in the presence of the pancreas is an indication of some effect on fat mobilization rather than on fat oxidation.

Conclusion. The intravenous administration of glucose to depancreatized dogs results in a "fat-sparing" action even in the absence of insulin. This is not associated with a decrease in the blood fatty

† We are indebted to the Eli Lilly Co. for generous supplies of sodium amytal.

7 Van Slyke, D. D., and Fitz, R., *J. Biol. Chem.*, 1917, **32**, 495.

8 Street, H. R., *J. Biol. Chem.*, 1936, **116**, 25.

acids. The action of glucose in depressing the level of the blood fats of normal dogs is attributed to some effect upon fat mobilization which is dependent upon the presence of a normal pancreas.

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Red Cell and Reticulocyte Counts in Guinea Pigs Following Exposure to Low Pressures.

ALBERT S. GORDON AND WILLIAM KLEINBERG. (Introduced by Harry A. Charipper.)

From Washington Square College, New York University.

Young adult guinea pigs (wgt. 350-400 gm.) were subjected for continuous periods, varying from 5 to 14 days, to pressures of 370-380 mm. Hg. in a specially made low pressure chamber (for details of the chamber, see Dubin[1]). This exposure is sufficient to cause an increase in red cell count of one to 2.5 million per cu. mm., and a reticulocyte count of 6% to 14%. Red cell counts were made from samples of blood drawn from the ear. The cells on 400 squares of a Levy-Hausser chamber were counted by each of us, and we were required to agree within 4%. Reticulocytes stained with brilliant cresyl blue were counted in wet smears according to the method described by Ramsey and Warren.[2] The behavior of the counts, following termination of the stimulus, in 4 representative animals exposed to the low pressures for different periods of time, is shown in Table I. The red cells are given in millions per cu. mm. and the reticulocytes as a percentage of the total reds.

The results obtained from experiments performed on 27 animals may be stated as follows. Soon after termination of the stimulus the counts begin to fall. The red cell counts attain normal values in 20-24 days and the reticulocytes in about 4 to 6 days. The red cell counts do not remain at this normal level but continue to drop, an anemia developing which reaches its maximum approximately a month after removal of the animals from the chamber. This anemia is similar to the one reported by Tyler and Baldwin[3] in rats after exposure to low oxygen tensions. Accompanying this drop below

[1] Dubin, M., *Quart. J. Exp. Physiol.*, 1934, **24**, 31.

[2] Ramsey, R., and Warren, C. O., *Quart. J. Exp. Physiol.*, 1932, **22**, 49.

[3] Tyler, D. B., and Baldwin, F. M., PROC. SOC. EXP. BIOL. AND MED., 1934, **31**, 823.