

rate of glucose uptake from the blood. Their teleological reasoning that glycogenolysis would not occur in the absence of a "need" for it is invalidated by a consideration of the hyperglycemia of asphyxia. Here, as is well known, the blood sugar is increased through the sympathetic glycogenolytic mechanism without there being any more immediate "need" for the glucose than there is following DNP administration. The close similarity of the means of production of the hyperglycemias of asphyxia and of DNP is striking. Although we¹ have shown that DNP evokes its hyperglycemia without producing an asphyxial state of the arterial blood, the possibility remains that the acceleration of the tissue metabolism in the sympathetic centers of the brain stem may result in local anoxia or acidosis and so set up the stimulus which activates the glycogenolytic mechanisms which are responsible for the hyperglycemia produced by the drug.

9518 P

Influence of Insulin on Amino Acid Utilization.*

I. ARTHUR MIRSKY, SAMUEL SWADESH AND JOSEPH RANSOHOFF.

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

During the course of an investigation on the endocrine control of nitrogen metabolism we found that insulin decreases the rate of protein catabolism. Our evidence suggested that this action of insulin may be due, in part, to an increased utilization of amino acids by the muscles. That insulin may have a proteinogenic action, was postulated by Wiechmann¹ and by Janney and Shapiro,² but neither group presented evidence to support this concept. On the other hand, Kiech and Luck³ concluded from their studies on rats that insulin increases the rate of amino acid catabolism and inhibits the compensatory process of protein hydrolysis by which the amino acids are generated. As was subsequently stated by Daniels and Luck,⁴ the possibility of an accompanying increase in the peripheral synthesis of protein from blood and tissue amino acids is not incompatible with their experimental findings.

* Aided by the David May Fund.

¹ Wiechmann, E., *Deutsch. Arch. Klin. Med.*, 1926, **150**, 186.

² Janney, N. W., and Shapiro, I., *Arch. Int. Med.*, 1926, **38**, 96.

³ Kiech, V. C., and Luck, J. M., *J. Biol. Chem.*, 1928, **78**, 257.

⁴ Daniels, A. C., and Luck, J. M., *J. Biol. Chem.*, 1931, **91**, 119.

In an attempt to obtain data of a more crucial nature, we performed a series of experiments which revealed that insulin stimulates the removal of amino acids from the blood by the muscles.

Normal fasting dogs were completely eviscerated under amytal anesthesia by a modification of the method of hepatectomy described by Markowitz, Yater and Burrows.⁵ The blood sugar subsequently was maintained at a normal level by a constant intravenous injection of glucose. The dose of glucose administered was 0.14 gm. per kilo of carcass weight per hour in the control groups and 0.28 gm. per kilo of carcass weight per hour in the insulin-treated group. Three groups of eviscerated dogs were studied: Group A consisted of 6 dogs receiving glucose alone; Group B, 6 dogs receiving glucose, and in addition, an intravenous injection of 600 mg. of glycine (in a 20% solution) per kilo of body weight; Group C, 6 dogs receiving glucose, glycine and in addition, an intravenous injection of 2 units insulin per kilo of body weight 15 minutes after the administration of the glycine and 0.1 unit insulin per kilo body weight at hourly intervals thereafter. Thirty minutes were allowed for the diffusion of the injected glycine before the first blood sample was drawn from an exposed branch of the femoral artery. Additional samples were drawn at 2-hourly intervals for from 4 to 6 hours. Further details will be published in a subsequent report. In this preliminary report, we wish to discuss the changes in the amino acid nitrogen of the blood which was determined by the method of Folin.⁶

The average initial amino acid nitrogen content of the arterial blood was 7.9 mg. % in Group A, 32.8 mg. % in Group B, and 36.4 mg. % in Group C. For illustrative purposes, the subsequent changes are depicted in Fig. 1 as mg. % deviation from the initial level. The data reveals that in the absence of the abdominal viscera, the amino acid nitrogen rises, presumably as a result of the cessation of deamination consequent to hepatectomy while the hydrolysis of muscle protein continues (A). When the initial blood amino acid level is raised, the spontaneous output of amino acids from the muscles ceases and hence the amino acid level remains fairly constant (B). When insulin is administered, a significant drop in blood amino acid nitrogen occurs (C). In view of the fact that the eviscerated preparation is essentially a muscle preparation, it is probable that the amino acids removed under the stimulus of insulin are utilized by the muscles for storage or for the synthesis of pep-

⁵ Markowitz, J., Yater, W. M., and Burrows, W. H., *J. Lab. and Clin. Med.*, 1933, **18**, 127.

⁶ Folin, O., *J. Biol. Chem.*, 1922, **51**, 377.

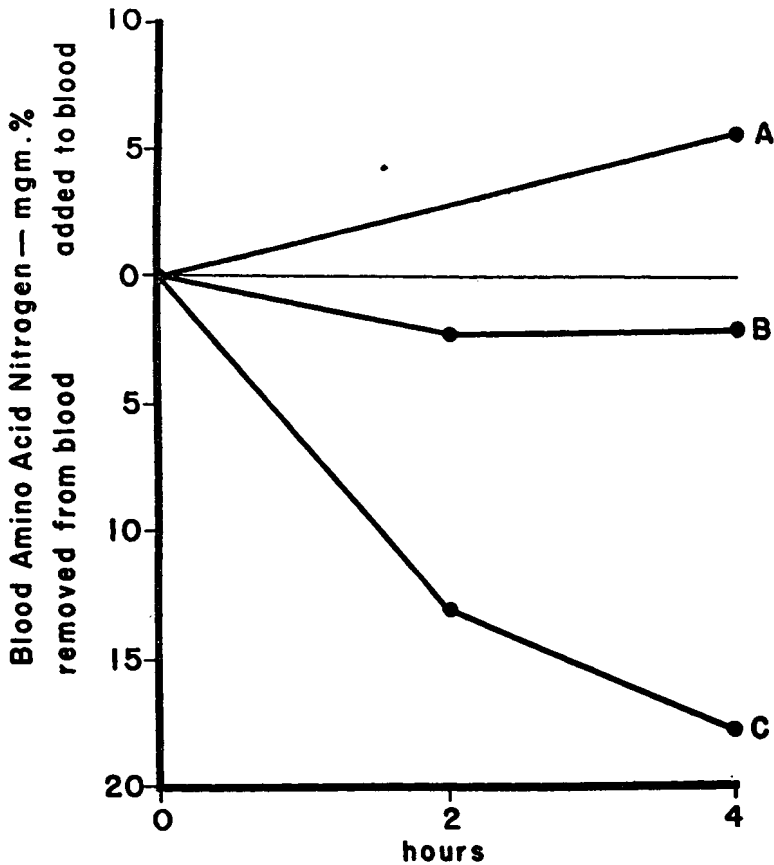


FIG. 1.

The average deviations from the initial level of the blood amino acid nitrogen in 6 eviscerated animals (A), 6 eviscerated animals which received glycine (B), and 6 eviscerated animals which received glycine plus insulin (C).

tides or proteins. The fate of these amino acids is now being investigated.

Conclusion. The spontaneous output of amino acid nitrogen by the muscles of the completely eviscerated dog is inhibited by the administration of glycine in amounts adequate to cause a hyperaminoacidemia. The administration of insulin to such animals results in an increased utilization of amino acids by the muscle. This action of insulin may be due to an increased storage of amino acids or to the synthesis of proteins in the muscles.