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Intravenous Glucose Transformation During Severe Muscular Exercise in Normal Dogs.

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Intravenous glucose is better assimilated during work than levulose, galactose or maltose,¹ when injected at a low rate. It was therefore thought advisable to examine the laws of its utilization in animals undergoing severe exercise (climbing a treadmill), thus complementing the similar study which has already been done for normal resting animals.² The purpose of the present research was to test the power of the body to transform this most utilizable foodstuff throughout the whole range of rates of constant supply and of its concentrations in the body fluids, obtainable in a living, working animal. As may be seen from the recent reviews,^{3,4,5,6} the knowledge on that subject is still nonexistent.

Dogs, kept on a constant high-carbohydrate diet, were made to perform work, during 5 hours, at two rates: either 1000 or 1250 kg/hr/kg body wt (causing a 4-6-fold increase in basal metabolism) and were injected with glucose at constant rates which varied from 20-230 g/sqm/hour (1-12 g/kg/hour)⁸ in different experiments, with proper regulation of water balance. When the animals performed work with saline added instead of glucose the level of blood glucose dropped a few mg%. Lactic acid in the blood increased above the resting level about 10 mg% and increased in the urine moderately. This intensity of work led therefore to some discharge of lactate from the contracting muscles.

Although utilization of injected glucose

rose greatly during work, the initial phase of lower assimilation⁷ was not abolished.* On the contrary it was relatively more marked and protracted. Still with an injection rate of 4 g/kg/hour, glucose elimination vanished towards the end of the experiment, whereas in resting animals even with a rate of 2 g/kg/hour, such an improvement of glucose transformation could never be achieved.²

The average values of glucose utilized* when plotted as ordinates against the increase of blood glucose concentration over the normal pre-injection level, as abscissa, showed an exponential rise of utilization with the rise of blood glucose, up to about 1000 mg%. At this concentration a peak of utilization was reached: at 1000 kg/hr/kg body wt, 107 g/sq m/hour were assimilated;⁸ at 1260 kg/hr/kg body wt, (128 g/sq m/hour.) The highest value obtained with the latter rate of work was about 150 g/sq m/hour (= 14 times the basal heat production = 6 g/kg/hour). In resting animals on the average the peak of transformation was reached at 750 mg% and amounted to 79 g/sq m/hour. In accordance with a previous communication, a shift to a higher level of utilization was accompanied by a shift to a higher blood glucose concentration.⁹ Both may depend to some extent on the rise of body temperature¹⁰ as a consequence of severe work.

No more increment in utilization was ob-

¹ Wierzechowski, M., Chmielewski, T., Gostyńska, A., and Fiszal, H., *Compt. Rend. Soc. de Biol.*, 1935, **119**, 433.

² Wierzechowski, M., *J. Physiol.*, 1936, **87**, 311.

³ Dill, D. B., *Physiol. Rev.*, 1936, **16**, 263.

⁴ Atzler, E., *Erg. Physiol.*, 1939, **41**, 164.

⁵ Gemmill, C. L., *Physiol. Rev.*, 1942, **22**, 32.

⁶ Keys, A., *Fed. Proc.*, 1943, **2**, 164.

⁷ Wierzechowski, M., *Biochem. Z.*, 1931, **237**, 103.

* Computed from blood and urine glucose curves, using the figure of 20% of body weight as body water, in which glucose was distributed.

⁸ Cowgill, G. R., and Drabkin, D. E., *Am. J. Physiol.*, 1927, **81**, 36.

⁹ Wierzechowski, M., *Abstracts of Comm. XVII International Physiological Congress, Oxford*, p. 256.

¹⁰ Wierzechowski, M., *Fed. Proc.*, 1948, **7**, 134.

tained when the blood glucose concentration was further raised. The whole surplus of glucose was rejected in the urine, presenting also during work the phenomena of overflow diabetes described for resting animals.² If 2500-3000 mg% of blood glucose were reached some extra amount of work was imposed upon the muscles by convulsive phenomena originating from stimulation of the segmental, motor nuclei across the whole neuraxis¹¹ and seemed to give some transitory further increase of glucose retention, before final weakness and failure of circulation took place.

Up to 1000 mg% of blood glucose, blood lactate was somewhat higher at work than at rest. At 1000 mg% a peak of lactate concentration was reached (35 mg% above basal value) almost exactly equal to the one observed for a resting animal. This concentration persisted up to 2500 mg% of

blood glucose, when convulsive phenomena began to augment the blood lactate formation intensely. In the urine at each value of blood glucose, lactate excretion was greater at work than at rest, the peak being reached at 1600 mg% of blood glucose; then the elimination decreased both at work and at rest with deterioration of circulation in the kidneys. It is evident that each value of blood glucose at work corresponded to a higher level of glucose transformation than at rest. Therefore, as expected, lactate, the rejection of which into the blood stream parallels glucose transformation, is formed in larger amounts during work at identical blood glucose levels, than at rest. The work itself also may contribute to its increased passage into the bloodstream.

Conclusion. Work does not increase to an unlimited extent the transformation of glucose supplied to the muscles in highest amounts. Its utilization at work, although even almost doubled, is governed by laws similar to those at rest.

¹¹ Wierzechowski, M., Toczyski, T., and Sysa, J., *Am. J. Med. Sc.*, 1948, **215**, 108.

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Stimulation of Gastric Secretion by Urticariogenic Wetting Agent (Tween 20) and Its Inhibition by Benadryl.

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The synthetic wetting agent Tween 20 (Atlas Powder Co.), which is a polyoxy-alkylene derivative of sorbitan monolaurate, has recently been shown to be capable of producing generalized urticaria when injected intravenously in dogs.¹

Several investigators^{2,3} have found that when whealing of the skin is produced by mechanical or thermal injury in the human, gastric acid secretion is stimulated. The

usual interpretation of this phenomenon is that injury to the skin causes the epidermal cells to release either histamine or a histamine-like substance (H-substance). This substance acts locally at the site of release to produce the whealing reaction and some of it is carried into the general circulation where it produces systemic effects similar to those produced by the injection of histamine, including stimulation of acid secretion by the stomach.

The present study was undertaken in order to determine whether the urticaria which occurs in dogs when Tween 20 is injected is accompanied by stimulation of gastric se-

¹ Ivy, A. C., Tanturi, C.A., Hernandez, R., and Baroso, E., *Arch. Derm.*, in press.

² Horton, B. T., Brown, G. E., and Roth, G. M., *J.A.M.A.*, 1936, **107**, 1263.

³ Kalk, H., *Klin. Wschr.*, 1929, **8**, 64.