

Morgan H E, Henderson M J, Regen D M & Park C R. Regulation of glucose uptake in muscle. I. The effects of insulin and anoxia on glucose transport and phosphorylation in the isolated, perfused heart of normal rats. *J. Biol. Chem.* 236:253-61, 1961.
[Dept. Physiology, Vanderbilt Univ. Sch. Medicine, Nashville, TN]

When rat hearts were perfused as Langendorff preparations, glucose transport limited the rate of glucose uptake and was accelerated by insulin and anoxia. After transport acceleration, glucose phosphorylation limited glucose uptake. Phosphorylation was increased by anoxia but not by insulin. [The SCI® indicates that this paper has been cited in over 515 publications since 1961.]

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"This paper was the first in a series of six papers published in the *Journal of Biological Chemistry* concerned with regulation of glucose metabolism in hearts from normal and diabetic rats.¹⁻⁵ This work was carried out in the laboratory of Charles R. Park. At the time, Margaret J. Henderson and I were postdoctoral fellows. I was attracted to this problem because of an interest in transport and its regulation rather than cardiac metabolism, *per se*. This work represented a career change for both David M. Regen and me and resulted from Park's enthusiasm and encouragement toward a career in physiology. I

had been trained as an obstetrician/gynecologist, while Regen was a medical student who had interrupted his training for a year to gain experience in research.

"The major findings of this study were that membrane transport was a major rate-limiting step for glucose utilization in the absence of insulin, and the rate of uptake conformed to Michaelis-Menten kinetics. Insulin increased glucose uptake because of an acceleration of the transport step. Under these conditions, glucose phosphorylation became the rate-limiting step. Anoxia accelerated glucose uptake by increasing rates of both glucose transport and phosphorylation. These studies confirmed earlier work in Levine's⁶ and Park's⁷ laboratories that showed an effect of insulin on glucose transport and work by Randle and Smith⁸ on the effect of anoxia on glucose transport.

"The other contribution of this paper and perhaps the reason for its frequent citation was the introduction of an easy and effective method for use of the isolated rat heart, perfused as a Langendorff preparation, for metabolic studies. Since this publication, a method for perfusion of the rat heart as a working preparation was developed in association with Neely, Liebermeister, and Battersby.⁹ In addition, a model of cardiac ischemia was introduced that employed the working rat heart.¹⁰ The isolated rat heart perfused as Langendorff, working, or ischemic preparations is a frequently used model for biochemical and physiological studies of carbohydrate, fat, protein, and RNA metabolism in cardiac muscle."¹¹

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