



EDITORIALS

THE GLUCOSE TOLERANCE TEST

The glucose tolerance test has been used for decades to help physicians establish the early diagnosis of diabetes mellitus and to distinguish nondiabetic glycosurias. In the majority of cases of diabetes, such a test is not needed for diagnosis; as Lukens points out, the indications are infrequent.¹ It is only when routine tests of the urine and blood sugar have been indecisive that it is now considered valuable.

According to Mosenthal, the old dictum that every diabetic has a high prolonged glucose tolerance curve but that every high prolonged curve is not indicative of diabetes still holds true. The variability of the results and the lack of specificity of the "positive" glucose tolerance test have become well known to clinicians, but the usefulness of the procedure under appropriate conditions continues to receive recognition. In recent years the studies of Mosenthal and Barry,² Lawrence,³ Blotner and Marble⁴ and others have confirmed the value of the test and have also shown its limitations.

Mosenthal and Barry pointed out the variable and unpredictable amounts of nonglucose substances included as glucose by the Folin-Wu determination and strongly favored the use of a blood sugar method determining the true blood glucose. They pointed out further that the use of venous blood is advantageous since the sugar content of arterial (or capillary) blood shows wide

fluctuations. The criteria for normal values of true glucose which they proposed are an upper limit of 100 mg. per 100 cc. in the fasting state, a maximum peak of 150 and a fall to 100 two hours after the ingestion of 100 Gm. of glucose. For the Folin-Wu determinations they gave values 20 mg. higher. This is in close agreement with, but not identical to, the information contained in the *Diabetes Guide Book* of the American Diabetes Association.⁵ Here it is stated that the normal results of the sugar tolerance test usually show a rise in the venous blood sugar not over 200, and a return below 120 in two hours.

Differences of opinion have developed in regard to the choice of route of administration of glucose in the tolerance test. For the sake of convenience, most physicians follow the traditional custom of giving it orally. Some prefer to give it intravenously. In a recent paper Soskin labeled the oral glucose tolerance test a "practically worthless" procedure.⁶ Soskin recommended the routine use of the glucose tolerance test by the intravenous method on the grounds of greater accuracy and also because of his opinion that such a test, performed in a standard manner, would permit differentiation of diabetes from a disorder of metabolism originating in the liver. On the other hand, Moyer and Womack⁷ concluded that "The intravenous test is inferior to the oral

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glucose tolerance test as an index of hepatic function and only under special circumstances is it of use as an adjunct to the oral method."

Soskin emphasized the fundamental role of the liver in the regulation of the blood sugar level and in its influence on the nature of the sugar tolerance blood sugar curve. Others have given special attention to the use of such tests in the study of various endocrine disorders affecting carbohydrate metabolism. In addition to the glucose tolerance test, the insulin tolerance test, the glucose-insulin tolerance test, and the insulin-followed-by-glucose tolerance test have been investigated.⁸ Each of these procedures can contribute to the study of carbohydrate metabolism, but it cannot be claimed with certainty that they can be applied with advantage in routine clinical practice. In fact, the claim that any pattern of blood sugar curve is specific for a disorder of the liver or any other disorder may be challenged.

To a large extent these adaptations of the tolerance test still represent technics of research. On the other hand, the confirmation of the diagnosis of diabetes or the exclusion of this condition by observation of the blood sugar curve is usually a simple matter, whether the glucose is given by mouth or by vein. For this limited purpose the oral glucose tolerance test is still a procedure of definite value in selected cases.

REFERENCES

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- ⁸ (a) Fraser, R. W., Albright, F., and Smith, P. H.: The value of the glucose tolerance test, insulin tolerance test and glucose-insulin tolerance test in the diagnosis of endocrinologic disorders of glucose metabolism. *J. Clin. Endocrinol.* 1:297, 1941.
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The importance of obesity in relation to diabetes has long been recognized. Information first came from a variety of clinical observations, including the common occurrence of diabetes in obese individuals, and the improvement in the diabetic state, even apparent remission, appearing after reduction of excess weight. Statistical studies have strengthened the evidence for this relationship. In a recent analysis of the weight of persons developing diabetes after the age of 40, it was found that approximately 60 per cent had previously been markedly overweight, and an additional 25 per cent had been moderately overweight. Only 15 per cent did not give a history of obesity preceding diabetes.¹

In spite of the clinical significance of obesity, the condition has been studied experimentally only to a limited extent. Nevertheless, information of a highly significant nature has been secured. Every stock and poultry raiser knows that animals can be fattened for the market by limited activity and liberal feeding. Ingle used this plan in the experimental production of obesity in rats.² He found that tremendous adiposity could be induced, a rat with restricted activities attaining a weight more than twice that of a normal active rat.

Long's report in this issue concerning obesity produced in rats and in monkeys is of unusual interest.³ As a result of bilateral lesions in the hypothalamus made by electrolysis, the animals acquired a voracious appetite resulting in the rapid development of extreme obesity. In certain cases, he noted progressive impairment of carbohydrate tolerance. He showed also that these animals became vulnerable to removal of a part of the pancreas. A partial pancreatectomy could be tolerated by the ordinary rat but was followed by glycosuria when the production of a brain lesion caused the development of obesity. These observations recall experiments conducted by Frederick M. Allen more than 30 years ago.⁴ He found that a partial pancreatectomy in dogs, which had no apparent effect when they were eating in the usual way, was followed by diabetes when the dogs were fattened by overfeeding.

The recent reports of hereditary obesity in mice represent a new approach to the problem. A strain has been produced with many adult mice weighing 38 to 56 Gm., compared with the average weight of non-obese mice, ranging from 16 to 26 Gm.⁵ In the limited number of cases in which tests could be made, it was found that the obese mice showed glycosuria and hyperglycemia indicating diabetes.⁶ The amount of sugar in the urine