LETTERS TO THE EDITOR

A NEW CARBOHYDRATE SOLUTION FOR TESTING GLUCOSE TOLERANCE

Leonards et al.[1] have recently described the preparation and evaluation of a cola-flavored product* for glucose tolerance testing. The solution consists of partially hydrolyzed cornstarch that is composed of 30 per cent glucose, 18 per cent maltose, 13 per cent maltotriose and 39 per cent higher saccharides. A 75 or 100 gm. dose of this carbohydrate material would contain an actual glucose concentration of 22.5 and 30 gm., respectively. It is stated, however, that the glucose equivalent of this carbohydrate mixture can be determined by boiling the

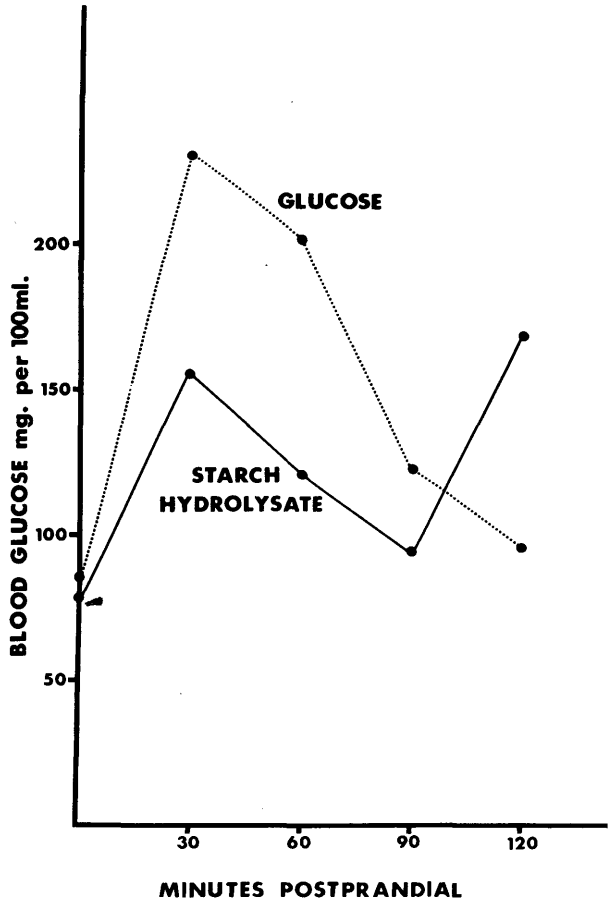

FIGURE 1

solution with 1.5 N hydrochloric acid for thirty minutes. Although no data on the glucose equivalents of the carbohydrate solution are presented by Leonards et al.,[1] presumably such treatment in vitro would completely hydrolyze all complex saccharides in the mixture to glucose. Similar digestion in vivo would depend upon the *p*H of the gastrointestinal content, the action of salivary and pancreatic amylase as well as the activity of the mucosal disaccharidases.

Some individuals, particularly those in the elderly age groups, are apt to digest carbohydrate at less than optimal rates.[2] In these cases, the glycemic response to a loading dose of carbohydrate might be significantly different from that noted after oral ingestion of glucose. The data on subject six presented by Leonards et al.[1] have been reproduced graphically to illustrate the tolerance curves with 100 gm. of glucose and a like dose of the partially hydrolyzed starch (figure 1). It is tempting to speculate that in this subject, perhaps, some factor in the process of carbohydrate digestion might have been responsible for the lessened degrees of hyperglycemia after challenge with the saccharide mixture as compared to glucose.

As early as 1920, Allen[3] reported that in diabetic patients, oral glucose produced greater degrees of hyperglycemia and glycosuria than more slowly absorbed starch. Some years later, Conn and Newberg[4] presented evidence of a more pronounced glycemic response after ingestion of glucose as compared to starch. Quite recently, Swan and co-workers[5] undertook a study of the effects of simple and complex carbohydrates on plasma glucose, insulin and unesterified fatty acids. Of particular interest is their finding that plasma insulin, after ingestion of 100 gm. of starch, was notably lower than following a 100 gm. dose of glucose. In addition, plasma glucose levels subsequent to a starch meal were neither as high during the first three hours nor as low in the next few hours as those obtained with a glucose challenge.

The possibility that variables in carbohydrate digestion are likely to influence the entry of glucose into the blood may serve to complicate interpretation of tolerance tests. Improved palatability is a highly desirable attribute of a tolerance test meal. However, this quality should be gained without altering the fundamental purpose of a glucose load, which is to reflect the insulin-secreting capacity of the pancreas. There appears to be little reason to doubt that test meals consisting of complex polysaccharides requiring digestion represent a challenge to both the exocrine and endocrine pancreas.

*Glucola, Ames Company, Elkhart, Indiana.

REFERENCES

1 Leonards, J. R., McCullagh, E. P., and Christopher, T. C.: A new carbohydrate solution for testing glucose tolerance. Diabetes *14*:96-99, Feb. 1965.

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[3] Allen, F. M.: Experimental studies on diabetes. II. Effect of carbohydrate diets. J. Exp. Med. *31*:395-402, April 1920.

[4] Conn, J. W., and Newberg, L. H.: The glycemic response to isoglucogenic quantities of protein and carbohydrate. J. Clin. Invest. *15*:665-71, Nov. 1936.

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To the Editor: Drs. Searcy and Low have presented a convincing review of the literature which showed that oral glucose produced greater degrees of hyperglycemia than did carbohydrate containing meals especially when these meals also contained protein and fat. The error in their theoretical argument against our published work is that although the above statement is correct, the digestion of these foods is entirely different from that of corn syrup—which is not starch—but a completely soluble partially hydrolyzed starch. They speculate that some individuals, particularly in the older age groups, digest carbohydrate at less than optimal rates but the reference quoted to substantiate this speculation does not contain such data. More important, however, are the actual experimental comparisons between glucose and the *partially hydrolyzed* starch solution (Glucola) in which the resulting blood glucose curves were shown to be virtually identical.[1]

It is of interest that this new carbonated glucose tolerance solution has now been used in 250,000 individuals in the detection program conducted by the Diabetes Association of Greater Cleveland. Of the individuals over the age of sixty, 15 per cent screened positive using the criterion of a blood glucose of 140 mg. per 100 ml. two hours after the loading dose.

REFERENCE

[1] Leonards, J. R., McCullagh, E. P., and Christopher, T.: Diabetes *14*:96-99, Feb. 1965.

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ABSTRACTS

Arquilla, Edward R.; Ooms, Henri; and Finn, Jack (Dept. of Pathology, Univ. of Calif., Sch. of Med., Los Angeles): GENETIC DIFFERENCES OF COMBINING SITES OF INSULIN ANTIBODIES AND IMPORTANCE OF C-TERMINAL PORTION OF THE A CHAIN TO BIOLOGICAL AND IMMUNOLOGICAL ACTIVITY OF INSULIN. Diabetologia 2:1-13, 1966.

Verbatim Summary. Using an insoluble insulin complex, it was possible to demonstrate that antibodies to insulin produced in individual animals are directed towards different portions of the insulin molecule. Furthermore, using the antisera from two different inbred strains of guinea pigs and their F_1 and F_2 offspring, evidence is presented for the genetic control of combining site configurations of antibodies to insulin produced in guinea pigs. The importance of different portions of the insulin molecule to biological and immunological activity was investigated. The attachment of I-125 to insulin (reportedly to the tyrosines at positions fourteen and/or nineteen of the A chain) seems to impair both the biological and immunological activity of insulin. The distribution of antibody-bound and free I-125-insulin was found to be different from the distribution of nonlabeled insulin. Relatively pure I-125-insulin was separated from nonlabeled insulin by acrylamide gel electrophoresis, and was found to have markedly reduced immunological reactivity in the immune hemolysis inhibition assay. It was concluded that antibodies to insulin exist which cannot react with iodinated insulin. Furthermore, when tested in the rat adipose tissue assay, purified I-125-insulin preparations had little or no biological activity. Conversely, mono-substituted fluorescein-labeled insulin (purified on acrylamide gel electrophoresis) appears to retain full immunological and biological competence. Fluorescein is thought to attach to the N-terminal phenylalanine of the B chain and/or to the N-terminal glycine of the A chain. It is concluded that these two residues contribute little to the biological and immunological integrity of insulin. Studies of this nature aid in elucidating the surface configuration of insulin, and thereby may contribute to an understanding of its tertiary structure.

Behrman, Simon (London, England): RETINAL CIRCULATION (Correspondence). Brit. Med. J. *1*:800, March 26, 1966.

The author takes issue with the argument that gradual reduction in arterial supply to the eye may be responsible for the classic ophthalmoscopic picture of central retinal vein obstruction (Editorial. "Retinal Circulation" Brit. Med. J. *1*: 562, 1966), and a recent review of changes in retinal veins in response to "chronic ischemia" is cited (Knox, D. L.: Amer. J. Ophthal. 60:995, 1965) in which the results of ischemia