Is the Oral Glucose Tolerance Test Obsolete?

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For several decades, the diagnosis of diabetes has been based on the blood glucose response to a standardized oral dose of glucose—the oral glucose tolerance test (OGTT). Before the report of the National Diabetes Data Group (NDDG) in 1979, the diagnostic criteria were a chaos of competing glucose response preferences based on inadequate data (1). That widely accepted report was the first step toward providing uniformity and consistency in the field. This position was further solidified in 1980 by the WHO Expert Committee on Diabetes Mellitus recommendations on diagnosis and classification with an update in 1985 (2,3). With some relatively minor alterations, it provided a very similar set of diagnostic criteria with the NDDG recommendations (1).

It is now 10 years since the diagnostic criteria for diabetes have been seriously revisited. We are pleased to present four manuscripts in this issue of *Diabetes Care* that bring the subject back to the "front burner." The past decade has seen remarkable advances in multiple research and clinical areas that impact the classification and diagnostic criteria of diabetes in a meaningful way. Immunological advances are providing increasingly sophisticated techniques for detecting β-cell inflammatory responses that usually reflect the autoimmune mechanisms associated with the development of insulin-dependent diabetes mellitus (IDDM). Increasing experience with and improvement in the methodology for determining glycosylated hemoglobin concentrations can provide a long-term view of glucose metabolism rather than the snapshot-like view provided by the OGTT. Advances in the genetic descriptors of both IDDM and non-insulin-dependent diabetes mellitus (NIDDM) provide increasing sophistication for classification and subclassification. Use of techniques to assess the state of insulin sensitivity and insulin resistance potentially provide another methodology for patient classification.

Has the OGTT lost its diagnostic usefulness? From a practical point of view, it appears that many if not most physicians have discarded it as the basis for diagnosis in favor of other simpler and more direct techniques. The three papers by Davidson et al. (4), McCance et al. (5), and Stolk et al. (6) come to remarkably similar conclusions derived from data on very different patient populations. Each of these groups of investigators challenge the continued use of the OGTT as the basis for the diagnosis of diabetes and propose that some combination of the fasting blood glucose and glycosylated hemoglobin should be officially substituted as the gold standard for diagnosis. The contribution by Zimmet (7), his Eli Lilly Award Lectureship given at the International Diabetes Federation in Kobe last November, takes a much broader and somewhat philosophical view of diabetes classification and diagnosis. Zimmet makes a plea for the introduction of other laboratory methodologies into the diagnosis and, most specifically, the classification of patients with diabetes. He feels that the state of the art is sufficiently advanced that we should begin using metabolic, immunologic, and genetic descriptors to subclassify patients. Zimmet and his coworkers have been remarkably productive in the application of studies of glutamic acid decarboxylase (GAD) antibodies in a variety of cultures and racial groups around the world. He takes a strong position that the presence of GAD antibodies is a highly reliable indicator of the immunologic process that leads to IDDM. His group has popularized a subdivision of IDDM appearing in the adult, referred to as latent autoimmune diabetes in adults (LADA), which they contend may be diagnosed by finding antibodies to GAD in adult-onset diabetic patients.

Are there identifiable drawbacks to the elimination of the OGTT from clinical medicine? Possibly. The NDDG interpretative criteria of the OGTT provides for an intermediate diagnostic category, referred to as impaired glucose tolerance. While some may view this intermediate status as a reflection of the imprecision of our knowledge and an element of confusion in the field, it has had practical utility. It has been used by many clinicians and investigators to identify individuals at increased risk for eventual development of diabetes who have then received increased supervision and even intervention. Indeed, a major collaborative multicentered National Institutes of Health–supported study is just getting underway

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GAD, glutamic acid decarboxylase; IDDM, insulin-dependent diabetes mellitus; NDDG, National Diabetes Data Group; NIDDM, non-insulin-dependent diabetes mellitus; OGTT, oral glucose tolerance test.

across the U.S. (Diabetes Prevention Program—DPPII), which is directed toward identifying adults at high risk for the eventual development of NIDDM and developing intervention strategies that will hopefully prevent or reduce the progression to overt disease. One of the major selection criteria for this investigation may be individuals with impaired glucose tolerance. Of possible special significance, both to this study and to clinical medicine in general, is the combination of the plasma glucose response to OGTT with the simultaneously determined plasma insulin level, thus producing an index of insulin sensitivity. What might the elimination of the OGTT do to the reliability and clinical applicability of this important study?

The issues addressed in the four manuscripts making up this mini-diagnostic symposia are extremely timely. The American Diabetes Association has recently appointed an expert panel to take a fresh look at the diagnostic criteria and classification systems for diabetes. We look forward to the report of this committee. In the meantime, it is our hope that this series of publications will provoke active discourse within our pages. Let's hear from you.

References

1. National Diabetes Data Group: Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. *Diabetes* 28:1039–1057, 1979
2. World Health Organization: *WHO Expert Committee on Diabetes Mellitus. Second report.* Geneva, World Health Org., 1980, p. 9–14 (Tech. Rep. Ser., no. 646)
3. World Health Organization Expert Committee on Diabetes Mellitus: *Diabetes Mellitus: Report of a WHO Study Group.* Geneva, World Health Org., 1985 (Tech. Rep. Ser., no. 727)
4. Davidson MB, Peters AL, Schriger DL: An alternative approach to the diagnosis of diabetes with a review of the literature (Review). *Diabetes Care* 18:1049–1055, 1995
5. McCance DR, Hanson RL, Charles M-A, Jacobsson LTH, Pettitt DJ, Bennett PH, Knowler WC: Which test for diagnosing diabetes? (Commentary) *Diabetes Care* 18: 1066–1068, 1995
6. Stolk RP, Orchard TJ, Grobbee DE: Why use the oral glucose tolerance test? *Diabetes Care* 18:1069–1073, 1995
7. Zimmet PZ: The pathogenesis and prevention of diabetes in adults: genes, autoimmunity, and demography. *Diabetes Care* 18:1034–1048, 1995