Response to Fajans

Dr. Fajans (1) raises relevant and important issues with regard to maturity-onset diabetes of the young. His suggestions are well taken, and in the next printing of the Expert Panel Report (January 1998), the appropriate changes in the document will be made.

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Response to the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus

The landmark report of the American Diabetes Association's Expert Committee on the Diagnosis and Classification of Diabetes Mellitus (1) is welcomed. It recommends a shift from the present phenotypic classification to one based on etiology and emphasizes earlier detection and possible prevention.

The diagnosis of undifferentiated gestational diabetes mellitus (GDM) is reviewed in detail and included as a single diagnosis in group IV of the proposed classification. Pregnancy provides a free stress test for latent diabetes, but it is the underlying mechanism that determines the type for the individual patient. Since there are two definite etiologic types of GDM, each of which carries different implications for the prevention and for the management of diabetes, we suggest that they be recognized in the classification as the following:

IV. Gestational Diabetes Mellitus (GDM)
   A. Type 1 associated, leading to absolute insulin deficiency
   B. Type 2 associated, with predominantly insulin resistance

A wide range of islet cell and anti-GAD antibodies has been reported in patients during and after pregnancy complicated by GDM, varying with population and geography (2,3). The timing of the test may be important. However, the reliability of autoantibody testing in pregnancy remains unknown because of the alterations in maternal immune status to prevent rejection of the fetus and placenta. The timing of the test may be important, and testing after the pregnancy may prove more reliable. However, long-term (2–11 years) clinical studies (4) have reported that in specific populations, up to 20% of women with previous GDM have type 1 diabetes because of markedly decreased plasma C-peptide response to glucose infusion. Further work is clearly needed in this area. Thus, general screening with tests for anti-islet antibodies may not be cost-effective for all pregnant women with GDM. However, a case can be made for testing those subjects with risk factors for this type of diabetes, particularly a family history of type 1 diabetes or autoimmune disease, and without those for type 2. Methods of arresting type 1 diabetes are effective in mice, but not yet in humans. There are now, however, ongoing trials of prevention to which patients may be referred. These issues and other recommendations for women with GDM are discussed in more detail in the report of the recent 4th International Workshop Conference on Gestational Diabetes to be published shortly in *Diabetes Care*.

It seems equally important to recognize GDM associated with type 2 diabetes. Presumptive diagnosis may be made on the basis of risk factors such as a family history, central obesity, particularly visceral abdominal, and the various aspects of the metabolic syndrome of insulin resistance. Measurement of the insulin/glucose (I/G) ratio may be useful in differentiating from type 1–associated GDM.

Thus, all in all, it seams reasonable to us to include the distinction of the two etiologic types of GDM, even though we do not yet have all the answers.

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Response to Sims and Catalano

Drs. Sims and Catalano (1), who have contributed much to our understanding of the pathophysiology of gestational diabetes mellitus (GDM), have proposed that the classification for GDM include two separate types, indicating whether the woman who has had GDM is more likely to go on to develop type 1 or type 2 diabetes later in life. Certainly, most women with GDM are at greatest risk for the development of type 2 diabetes. The detection of autoantibodies during and after pregnancies complicated by GDM seems to be associated with an increased risk for type 1 diabetes in the years following pregnancy, as shown in several studies, including the recent publication by Füchtenbusch et al. (2). However, as implied by Drs. Sims and Catalano, this body of knowledge is still evolving. Hopefully, increasing information

in this important field will allow us to better understand processes leading to GDM.

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Screening for Diabetes in Obese Patients Using the New Diagnostic Criteria

The introduction of the new diagnostic criteria for diabetes, recently proposed by the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus of the American Diabetes Association (ADA) (1) may considerably affect prevalence estimates. The proposed classification of diabetes and related metabolic abnormalities also includes a new category, impaired fasting glucose (IFG), the prevalence of which is unknown.

A consecutive series of 350 obese patients (BMI >30 kg/m^2), aged ≥25 years and with no previous history of diabetes, who attended the Outpatient Clinic of the Section of Metabolic Diseases and Diabetology of the University of Florence (Florence, Italy) after 1 September 1996 was studied. The patients (286 women, 64 men) had an age of 45.8 ± 11.9 years (mean ± SD), a BMI of 37.3 ± 7.1 kg/m^2, and a waist-to-hip ratio of 0.85 ± 0.05 for women and 0.92 ± 0.06 for men. In all patients, fasting plasma glucose (FPG) was determined at 8:00 A.M. after an overnight fast. On the following day, FPG was measured again, and a standard oral glucose tolerance test (OGTT) was performed, determining plasma glucose 30, 60, 90, and 120 min after the administration of a 75-g oral glucose load (2).

Using the previous (1979) criteria of the National Diabetes Data Group (3), 69 patients (55 women, 13 men) could be classified as being affected by diabetes and 54 patients (41 women, 13 men) by impaired glucose tolerance (IGT). Applying criteria issued by the World Health Organization (WHO) in 1985 (2), the number of cases of diabetes did not change, while the number of patients classified as affected by IGT increased to 100 (79 women, 21 men).

Using the new diagnostic criteria proposed by the ADA (1), 83 cases (67 women, 16 men) of diabetes and 92 cases (72 women, 20 men) of IGT were identified. The prevalence of diabetes was 23.7 vs. 19.7% with WHO criteria (an increase of 20.3%), while the prevalence of IGT was 26.2 vs. 28.5%. The diagnosis of IFG (without IGT or diabetes at the OGTT) could be established in 17 patients (14 women, 3 men), with a prevalence of 4.8%. The overall prevalence of diabetes and related abnormalities was 48.2% using WHO criteria (diabetes plus IGT), and 54.7% using the new criteria (diabetes plus IGT and IFG), with a relative increase of 59.0%. If the results of the OGTT had not been considered, the diagnosis of diabetes could have been established in only 47 patients (13.4%) who had a FPG ≥126 mg/dl at both determinations instead of 83 patients (23.7%).

Although this clinical sample of obese patients is not representative of the general population, the present results allow some considerations about the impact of the new diagnostic criteria and screening methods proposed (1). The adoption of the new criteria determines a substantial rise in the estimates of prevalence of diabetes, which could have a relevant impact on management of resources for health care. In fact, the classification of a patient as being affected by diabetes has legal consequences on reimbursement issues in several countries, and a rise of >20% in the number of diabetic individuals can modify considerably provisions of public expenditures.

To simplify screening procedures, it has been recommended that FPG be used for diagnosis of diabetes in unaffected individuals in clinical settings (1). It should be observed that only 56.6% of cases can be identified with this procedure; the standard OGTT could therefore retain its relevance as a screening method in high-risk groups. If the OGTT is applied, the prevalence of IFG appears to be substantially lower than that of diabetes and IGT.

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Response to Mannucci et al.

The observations of Mannucci et al. (1) are important and appreciated. They highlight some of the difficulties of defining precise cutoff points for the diagnosis of a clinically heterogeneous disease in which the damaging effects of the offending etiologic agent (glucose) occur along a continuum.

It should be noted that the new recommendations do not presume to "considerably affect prevalence estimates." In fact, should there be more widespread use of a single test (i.e., fasting plasma glucose [FPG] ≥126 mg/dl, with confirmation) rather than multiple tests, overall prevalence rates of newly diagnosed disease might decrease (1). However, the use of a single simpler test might indeed greatly increase the number of high-risk individuals tested and result in