TABLE 417-2 CRITERIA FOR THE DIAGNOSIS OF DIABETES MELLITUS

- Symptoms of diabetes plus random blood glucose concentration ≥11.1 mmol/L (200 mg/dL)[a] *or*
- Fasting plasma glucose ≥7.0 mmol/L (126 mg/dL)[b] *or*
- Hemoglobin A_{1c} ≥ 6.5%[c] *or*
- 2-h plasma glucose ≥11.1 mmol/L (200 mg/dL) during an oral glucose tolerance test[d]

[a]Random is defined as without regard to time since the last meal. [b]Fasting is defined as no caloric intake for at least 8 h. [c]Hemoglobin A_{1c} test should be performed in a laboratory using a method approved by the National Glycohemoglobin Standardization Program and correlated to the reference assay of the Diabetes Control and Complications Trial. Point-of-care hemoglobin A_{1c} should not be used for diagnostic purposes. [d]The test should be performed using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water, not recommended for routine clinical use.

Note: In the absence of unequivocal hyperglycemia and acute metabolic decompensation, these criteria should be confirmed by repeat testing on a different day.

Source: Adapted from American Diabetes Association: Diabetes Care 37(Suppl 1):S14, 2014.

DIAGNOSIS

Glucose tolerance is classified into three broad categories: normal glucose homeostasis, DM, or impaired glucose homeostasis. Glucose tolerance can be assessed using the fasting plasma glucose (FPG), the response to oral glucose challenge, or the hemoglobin A_{1c} (HbA_{1c}). An FPG <5.6 mmol/L (100 mg/dL), a plasma glucose <140 mg/dL (11.1 mmol/L) following an oral glucose challenge, and an HbA_{1c} <5.7% are considered to define normal glucose tolerance. The International Expert Committee with members appointed by the ADA, the European Association for the Study of Diabetes, and the International Diabetes Federation have issued diagnostic criteria for DM **(Table 417-2)** based on the following premises: (1) the FPG, the response to an oral glucose challenge (oral glucose tolerance test [OGTT]), and HbA_{1c} differ among individuals, and (2) DM is defined as the level of glycemia at which diabetes-specific complications occur rather than on deviations from a population-based mean. For example, the prevalence of retinopathy in Native Americans (Pima Indian population) begins to increase at an FPG >6.4 mmol/L (116 mg/dL) **(Fig. 417-3)**.

An FPG ≥7.0 mmol/L (126 mg/dL), a glucose ≥11.1 mmol/L (200 mg/dL) 2 h after an oral glucose challenge, or an HbA_{1c} ≥6.5% warrants the diagnosis of DM (Table 417-2). A random plasma glucose concentration ≥11.1 mmol/L (200 mg/dL) accompanied by classic symptoms of DM (polyuria, polydipsia, weight loss) is also sufficient for the diagnosis of DM (Table 417-2).

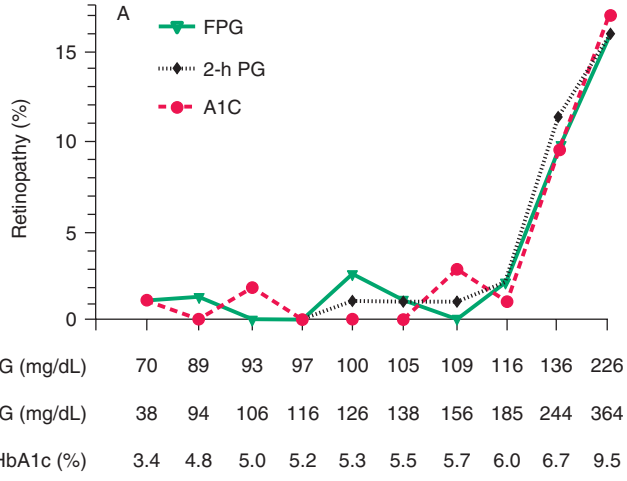

FIGURE 417-3 Relationship of diabetes-specific complication and glucose tolerance. This figure shows the incidence of retinopathy in Pima Indians as a function of the fasting plasma glucose (FPG), the 2-h plasma glucose after a 75-g oral glucose challenge (2-h PG), or the hemoglobin A_{1c} (HbA_{1c}). Note that the incidence of retinopathy greatly increases at a fasting plasma glucose >116 mg/dL, a 2-h plasma glucose of 185 mg/dL, or an HbA_{1c} >6.5%. (Blood glucose values are shown in mg/dL; to convert to mmol/L, divide value by 18.) *(Copyright 2002, American Diabetes Association. From Diabetes Care 25[Suppl 1]: S5–S20, 2002.)*

Abnormal glucose homeostasis (Fig. 417-1) is defined as (1) FPG = 5.6–6.9 mmol/L (100–125 mg/dL), which is defined as *impaired fasting glucose* (IFG); (2) plasma glucose levels between 7.8 and 11 mmol/L (140 and 199 mg/dL) following an oral glucose challenge, which is termed *impaired glucose tolerance* (IGT); or (3) HbA_{1c} of 5.7–6.4%. An HbA_{1c} of 5.7–6.4%, IFG, and IGT do not identify the same individuals, but individuals in all three groups are at greater risk of progressing to type 2 DM, have an increased risk of cardiovascular disease, and should be counseled about ways to decrease these risks (see below). Some use the terms *prediabetes*, *increased risk of diabetes*, or *intermediate hyperglycemia* (World Health Organization) for this category. These values for the fasting plasma glucose, the glucose following an oral glucose challenge, and HbA_{1c} are continuous variables and not discrete categories. The current criteria for the diagnosis of DM emphasize the HbA_{1c} or the FPG as the most reliable and convenient tests for identifying DM in asymptomatic individuals (however, some individuals may meet criteria for one test but not the other). OGTT, although still a valid means for diagnosing DM, is not often used in routine clinical care.

The diagnosis of DM has profound implications for an individual from both a medical and a financial standpoint. Thus, abnormalities on screening tests for diabetes should be repeated before making a definitive diagnosis of DM, unless acute metabolic derangements or a markedly elevated plasma glucose are present (Table 417-2). These criteria also allow for the diagnosis of DM to be withdrawn in situations when the glucose intolerance reverts to normal.

SCREENING

Widespread use of the FPG or the HbA_{1c} as a screening test for type 2 DM is recommended because (1) a large number of individuals who meet the current criteria for DM are asymptomatic and unaware that they have the disorder, (2) epidemiologic studies suggest that type 2 DM may be present for up to a decade before diagnosis, (3) some individuals with type 2 DM have one or more diabetes-specific complications at the time of their diagnosis, (4) treatment of type 2 DM may favorably alter the natural history of DM, diagnosis of prediabetes should spur efforts for diabetes prevention. The ADA recommends screening all individuals >45 years every 3 years and screening individuals at an earlier age if they are overweight (BMI >25 kg/m^2 or ethnically relevant definition for overweight) and have one additional risk factor for diabetes **(Table 417-3)**. In contrast to type 2 DM, a long asymptomatic period of hyperglycemia is rare prior to the diagnosis of type 1 DM. A number of immunologic markers for type 1 DM are becoming available (discussed below), but their routine use outside a clinical trial is discouraged, pending the identification of clinically beneficial interventions for individuals at high risk for developing type 1 DM.

TABLE 417-3 RISK FACTORS FOR TYPE 2 DIABETES MELLITUS

Family history of diabetes (i.e., parent or sibling with type 2 diabetes)
Obesity (BMI ≥25 kg/m^2 or ethnically relevant definition for overweight)
Physical inactivity
Race/ethnicity (e.g., African American, Latino, Native American, Asian American, Pacific Islander)
Previously identified with IFG, IGT, or an hemoglobin A_{1c} of 5.7–6.4%
History of GDM or delivery of baby >4 kg (9 lb)
Hypertension (blood pressure ≥140/90 mmHg)
HDL cholesterol level <35 mg/dL (0.90 mmol/L) and/or a triglyceride level >250 mg/dL (2.82 mmol/L)
Polycystic ovary syndrome or acanthosis nigricans
History of cardiovascular disease

Abbreviations: BMI, body mass index; GDM, gestational diabetes mellitus; HDL, high-density lipoprotein; IFG, impaired fasting glucose; IGT, impaired glucose tolerance.

Source: Adapted from American Diabetes Association: Diabetes Care 37(Suppl 1):S14, 2014.