

# Diabetes Mellitus, Hypoglycemia

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## DIABETES MELLITUS

### Definition and Diagnostic Criteria

Diabetes mellitus is not a single disease but a group of disorders that develop as a consequence of absolute or relative deficiency of the hormone insulin. Inadequate actions of insulin in stimulating the uptake of glucose by body tissues and regulating the metabolism of carbohydrate, fat, and protein result in *hyperglycemia*. Other metabolic disturbances in addition to hyperglycemia typically occur in uncontrolled diabetes, including altered lipoprotein dynamics and elevated free fatty acid levels. These abnormalities contribute to the acute and chronic clinical consequences of diabetes.

The criteria used to diagnose diabetes mellitus in nonpregnant individuals are summarized in [Table 66-1](#). The diagnosis can be made on the basis of a fasting blood glucose level of 126 mg/dL or higher, a random blood glucose concentration (i.e., determined at any time in association with meals or fasting) of 200 mg/dL or higher, or a 2-hour glucose level of 200 mg/dL or higher as part of a 75-g oral glucose tolerance test. Alternatively, diabetes can be diagnosed if the hemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>) level is 6.5% or higher. HbA<sub>1c</sub>, a measure of the percentage of hemoglobin in circulating erythrocytes that is glycosylated, correlates with mean circulating glucose levels. HbA<sub>1c</sub> provides an index of the average blood glucose level over the preceding 2 to 3 months. Because HbA<sub>1c</sub> accumulates progressively throughout the lifespan of an erythrocyte, spurious values may occur in states of altered erythrocyte turnover (e.g., with various anemias) or with certain hemoglobinopathies that increase or decrease the susceptibility of hemoglobin to glycosylation. In patients with marked elevations in blood glucose or HbA<sub>1c</sub> and coincident symptoms typical for hyperglycemia (e.g., polyuria and polydipsia), the

diagnosis can be made based on a single test result. With less marked glucose elevations in the absence of symptoms, the diagnosis should be confirmed by repeat testing on a separate day.

Patients who have mild elevations in plasma glucose levels that do not reach the threshold for diagnosis of diabetes (e.g., HbA<sub>1c</sub> levels between 5.7% and 6.4%) are at increased risk for progression to diabetes and therefore are considered to have *prediabetes*. Prediabetes patients with fasting blood glucose levels between 100 and 125 mg/dL are more specifically labeled as having *impaired fasting glucose*, and those with 2-hour postprandial plasma glucose levels between 140 and 199 mg/dL (most reliably measured after a standardized 75-g oral glucose load) have *impaired glucose tolerance* (see [Table 66-1](#)). Although not all individuals with prediabetes will become diabetic, the mean progression rate to overt diabetes is approximately 6% per year. There also is evidence from observational studies that the prediabetic state is associated with an increased risk of cardiovascular disease.

*Gestational diabetes mellitus* (GDM) is a term applied to diabetes first recognized during pregnancy. The most widely accepted thresholds for diagnosis of GDM are a fasting plasma glucose level of 92 mg/dL or higher at any gestational stage and values on a 75-g oral glucose tolerance test at 24 to 28 weeks' gestation of 92 mg/dL or higher fasting, 180 mg/dL or higher at 1 hour, or 153 mg/dL or higher at 2 hours after glucose loading ([Table 66-2](#)). Untreated diabetes in pregnancy is associated with increased fetal malformations, problems in delivery, and possibly more frequent diabetes complications in the mother.

### Etiologic Classification

Once the diagnosis is made based on elevated blood glucose or HbA<sub>1c</sub> values, it is important to establish the specific subtype of diabetes based on a combination of clinical and molecular pathophysiological features [Table 66-3](#).

**TABLE 66-1** CRITERIA FOR THE DIAGNOSIS OF DIABETES MELLITUS

MEASUREMENT	NORMAL	PREDIABETES	DIABETES MELLITUS
Plasma glucose (mg/dL)			
Fasting*	<100	100-125 <sup>†</sup>	≥126
2-hr Postload <sup>‡</sup>	<140	140-199 <sup>§</sup>	≥200
Random <sup>  </sup>			≥200
Hemoglobin A <sub>1c</sub> (%)	≤5.6	5.7-6.4	≥6.5

Data from the American Diabetes Association clinical practice recommendations 2013, *Diabetes Care* 36(Suppl 1):S11-S66, 2013.

\*Fasting: no caloric intake for ≥8 hr.

<sup>†</sup>Impaired fasting glucose.

<sup>‡</sup>Postload: Following a standardized 75-g oral glucose load or after a meal.

<sup>§</sup>Impaired glucose tolerance.

<sup>||</sup>Random: any time of day, unrelated to meals.