TABLE 66-2 CRITERIA FOR THE DIAGNOSIS OF GESTATIONAL DIABETES MELLITUS

MEASUREMENT	DIAGNOSTIC THRESHOLD (mg/dL)
Plasma glucose	
Fasting*	≥92
After 75-g oral glucose load	
1 hr	≥180
2 hr	<153

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.

TABLE 66-3 ETIOLOGIC CLASSIFICATION OF DIABETES MELLITUS

TYPE 1 DIABETES MELLITUS
Immune-mediated (type 1a)
Idiopathic (type 1b)
TYPE 2 DIABETES MELLITUS
OTHER SPECIFIC TYPES
Genetic defects of beta-cell function
Maturity-onset diabetes of the young (MODY) and other disorders
Genetic defects in insulin action
Insulin receptor mutations and other disorders
Diseases of the exocrine pancreas
Endocrinopathies
Cushing's syndrome, acromegaly, and other disorders
Drug- or chemical-induced
Glucocorticoids most common
Infections
Uncommon forms of immune-mediated diabetes
Insulin receptor–blocking antibodies and other disorders
Other genetic syndromes sometimes associated with diabetes
GESTATIONAL DIABETES MELLITUS

Data from the American Diabetes Association clinical practice recommendations 2013, Diabetes Care 36(Suppl 1):S67–S74, 2013.

Type 1 diabetes (T1DM) is characterized by extensive destruction of the insulin-producing beta cells within the islets of Langerhans in the pancreas and dependence on insulin therapy for survival. In previous medical literature, the terms *juvenile-onset diabetes* or *insulin-dependent diabetes* were used for T1DM. This terminology is no longer used, because T1DM not uncommonly has its onset in adulthood, and multiple other forms of diabetes often require treatment with insulin. T1DM accounts for 5% to 10% of all diabetes in the United States. In most patients, it involves autoimmune mechanisms leading to beta cell destruction (the *type 1A* form). Rare individuals have no markers for autoimmunity and are classified as having *type 1B (idiopathic) diabetes*. Most patients with T1DM progress to marked insulin deficiency over a period of several weeks to months after initial presentation. A smaller number of individuals with evidence of beta cell autoimmunity but much slower disease progression have a variant form of T1DM that is designated *latent autoimmune diabetes of adulthood* (LADA).

In patients with marked elevations in glucose and accompanying ketoacidosis, particularly if they are young and nonobese, the diagnosis of T1DM is highly probable. This can be confirmed by measuring autoantibodies, often as a panel including insulin, anti-IA2 (anti–tyrosine phosphatase), anti-insulin, and glutamic acid decarboxylase (GAD or GAD65) antibodies, and also by a clinical course demonstrating an ongoing need for insulin to control hyperglycemia. A fasting C-peptide level can be measured later in the disease to confirm marked deficiency in insulin secretion. C-peptide is a fragment of the insulin precursor proinsulin, which is cleaved during the synthesis of insulin. It is secreted and circulates in proportion to endogenous insulin production but is absent from injected exogenous insulin preparations.

Type 2 diabetes (T2DM) is a heterogeneous, clinically defined subtype that accounts for more than 90% of all diabetes in the United States. It typically has a gradual onset with progression over multiple years or even decades. There is often prolonged preservation of at least partial insulin secretory capacity together with evidence of insulin resistance. Most patients have associated obesity (80% to 90%), although a subset of patients with a clinical picture otherwise typical for T2DM are nonobese. T2DM usually can be presumptively distinguished from T1DM by its indolent course in the presence of risk factors such as obesity and by the milder hyperglycemia and absence of ketoacidosis due to residual insulin secretion. If there is clinical suspicion of T1DM based on earlier age at onset, degree of hyperglycemia, absence of obesity, or presence of ketoacidosis, an autoantibody panel (which should be negative) and a C-peptide level (which should be positive) can be measured.

An expanding number of diabetes etiologies distinct from T1DM and T2DM are classified under a broad category designated *other specific types*. Although these forms of diabetes are uncommon (1% to 2% of all diabetes), it is important to recognize them in clinical practice. They include a group of inherited, autosomal dominant disorders historically designated *maturity-onset diabetes of the young (MODY)*; many of these patients have clinical features similar to those of T2DM but onset typically before 25 years of age. Patients with MODY3 (hepatocyte nuclear factor-1alpha mutations) are particularly sensitive to sulfonylureas, whereas those with MODY2 (glucokinase mutations) have mild, nonprogressive blood glucose elevations and often require no treatment except during pregnancy. For this reason, patients with early-onset diabetes, lack of autoimmune markers, and family histories suggestive of autosomal dominant inheritance should be considered for MODY gene sequencing.

Much less common genetic defects include mutations in insulin receptors or various other genes involved in insulin action. Exocrine pancreatic disease from causes such as chronic pancreatitis or surgery results in loss of the glucagon-producing islet alpha-cells as well as the insulin-producing beta cells. These patients often exhibit greater sensitivity to insulin and more of a propensity for hypoglycemia than T1DM patients because of the absent insulin counter-regulatory effects of glucagon. Endocrine disorders with excess production of hormones that counteract insulin, such as growth hormone in acromegaly or glucocorticoids in Cushing's syndrome, are important to recognize as causes of diabetes because removal of the source of excess hormone can lead to resolution of the diabetic state. Many drugs have been associated with diabetes, most notably glucocorticoids.

The category GDM includes any woman in whom diabetes is first recognized during pregnancy and usually represents T2DM.