glycemia, the use of the term NIDDM generated considerable confusion. A second difference is that age or treatment modality is not a criterion. Although type 1 DM most commonly develops before the age of 30, an autoimmune beta cell destructive process can develop at any age. It is estimated that between 5 and 10% of individuals who develop DM after age 30 years have type 1 DM. Although type 2 DM more typically develops with increasing age, it is now being diagnosed more frequently in children and young adults, particularly in obese adolescents.

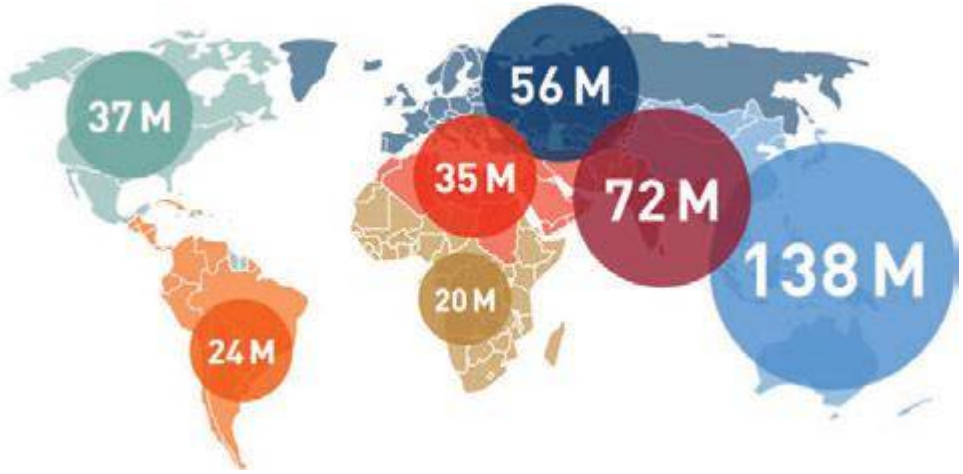

FIGURE 417-2 **Worldwide prevalence of diabetes mellitus.** Global estimate is 382 million individuals with diabetes. Regional estimates of the number of individuals with diabetes (20–79 years of age) are shown (2013). *(Used with permission from the IDF Diabetes Atlas, the International Diabetes Federation, 2013.)*

OTHER TYPES OF DM

Other etiologies for DM include specific genetic defects in insulin secretion or action, metabolic abnormalities that impair insulin secretion, mitochondrial abnormalities, and a host of conditions that impair glucose tolerance (Table 417-1). *Maturity-onset diabetes of the young* (MODY) and *monogenic diabetes* are subtypes of DM characterized by autosomal dominant inheritance, early onset of hyperglycemia (usually <25 years; sometimes in neonatal period), and impaired insulin secretion (discussed below). Mutations in the insulin receptor cause a group of rare disorders characterized by severe insulin resistance.

DM can result from pancreatic exocrine disease when the majority of pancreatic islets are destroyed. Cystic fibrosis–related DM is an important consideration in that patient population. Hormones that antagonize insulin action can also lead to DM. Thus, DM is often a feature of endocrinopathies such as acromegaly and Cushing's disease. Viral infections have been implicated in pancreatic islet destruction but are an extremely rare cause of DM. A form of acute onset of type 1 diabetes, termed *fulminant diabetes*, has been noted in Japan and may be related to viral infection of islets.

GESTATIONAL DIABETES MELLITUS

Glucose intolerance developing during pregnancy is classified as gestational diabetes mellitus (GDM). Insulin resistance is related to the metabolic changes of late pregnancy, and the increased insulin requirements may lead to IGT or diabetes. GDM occurs in ~7% (range 1–14%) of pregnancies in the United States; most women revert to normal glucose tolerance postpartum but have a substantial risk (35–60%) of developing DM in the next 10–20 years. The International Association of the Diabetes and Pregnancy Study Groups and the American Diabetes Association (ADA) recommend that diabetes diagnosed at the initial prenatal visit should be classified as "overt" diabetes rather than GDM. With the rising rates of obesity, the number of women being diagnosed with GDM or overt diabetes is rising worldwide.

EPIDEMIOLOGY AND GLOBAL CONSIDERATIONS

The worldwide prevalence of DM has risen dramatically over the past two decades, from an estimated 30 million cases in 1985 to 382 million in 2013 (Fig. 417-2). Based on current trends, the International Diabetes Federation projects that 592 million individuals will have diabetes by the year 2035 (see *http://www.idf.org/*). Although the prevalence of both type 1 and type 2 DM is increasing worldwide, the prevalence of type 2 DM is rising much more rapidly, presumably because of increasing obesity, reduced activity levels as countries become more industrialized, and the aging of the population. In 2013, the prevalence of diabetes in individuals from age 20–79 ranged from 23 to 37% in the 10 countries with the highest prevalence (Tuvalu, Federated States of Micronesia, Marshall Islands, Kiribati, Vanuatu, Cook Islands, Saudi Arabia, Nauru, Kuwait, and Qatar, in descending order of prevalence). The countries with the greatest number of individuals with diabetes in 2013 are China (98.4 million), India (65.1 million), United States (24.4 million), Brazil (11.9 million), and the Russian Federation (10.9 million). Up to 80% of individuals with diabetes live in low-income or medium-income countries. In the most recent estimate for the United States (2012), the Centers for Disease Control and Prevention (CDC) estimated that 9.3% of the population had diabetes (~28% of the individuals with diabetes were undiagnosed; globally, it is estimated that 50% of individuals may be undiagnosed). The CDC estimated that the incidence and prevalence of diabetes doubled from 1990–2008, but appears to have plateaued from 2008–2012. DM increases with age. In 2012, the prevalence of DM in the United Sates was estimated to be 0.2% in individuals age <20 years and 12% in individuals age >20 years. In individuals age >65 years, the prevalence of DM was 26.9%. The prevalence is similar in men and women throughout most age ranges (14% and 11%, respectively, in individuals age >20 years). Worldwide, most individuals with diabetes are between the ages of 40 and 59 years.

There is considerable geographic variation in the incidence of both type 1 and type 2 DM. Scandinavia has the highest incidence of type 1 DM; the lowest incidence is in the Pacific Rim where it is 20- to 30-fold lower. Northern Europe and the United States have an intermediate rate. Much of the increased risk of type 1 DM is believed to reflect the frequency of high-risk human leukocyte antigen (HLA) alleles among ethnic groups in different geographic locations. The prevalence of type 2 DM and its harbinger, IGT, is highest in certain Pacific islands and the Middle East and intermediate in countries such as India and the United States. This variability is likely due to genetic, behavioral, and environmental factors. DM prevalence also varies among different ethnic populations within a given country, with indigenous populations usually having a greater incidence of diabetes than the general population of the country. For example, the CDC estimated that the age-adjusted prevalence of DM in the United States (age >20 years; 2010–2012) was 8% in non-Hispanic whites, 9% in Asian Americans, 13% in Hispanics, 13% in non-Hispanic blacks, and 16% in American-Indian and Alaskan native populations. The onset of type 2 DM occurs, on average, at an earlier age in ethnic groups other than non-Hispanic whites. In Asia, the prevalence of diabetes is increasing rapidly, and the diabetes phenotype appears to be somewhat different from that in the United States and Europe, with an onset at a lower body mass index (BMI) and younger age, greater visceral adiposity, and reduced insulin secretory capacity.

Diabetes is a major cause of mortality, but several studies indicate that diabetes is likely underreported as a cause of death. In the United States, diabetes was listed as the seventh leading cause of death in 2010. A recent estimate suggested that diabetes was responsible for almost 5.1 million deaths or 8% of deaths worldwide in 2013. In 2013, it was estimated that $548 billion or 11% of health care expenditures worldwide were spent on individuals with diabetes.