usually recommended for secondary prevention of cardiovascular disease (supported by clinical trial evidence) or for primary prevention in patients with a 10-year cardiovascular risk greater than 10% (based on expert opinion). Influenza vaccination should be provided yearly; pneumococcal immunization should be given once and then repeated after age 65.

Management of Diabetes during Intercurrent Illness

Diabetes often requires changes in the blood glucose management regimen during an intercurrent illness to accommodate potential decreases in nutrient intake and increases in insulin resistance secondary to disease-related release of stress hormones. Patients with T1DM require exogenous insulin administration at all times to prevent marked hyperglycemia and DKA, even if they are unable to consume nutrients during an illness (e.g., with gastroenteritis). Depending on the degree and duration of interruption of food intake, they may require a transient, partial reduction in insulin dosage as well as more frequent glucose monitoring. Alternatively, if they are consuming a normal diet, they may require a modest increase in insulin dose because of insulin resistance related to the stress of illness. T2DM patients taking oral agents who are undergoing surgical procedures or are hospitalized for serious illness often require discontinuation of the oral agents and use of insulin to control blood glucose until normal eating patterns are resumed.

For hospitalized patients, blood glucose target goals are adjusted to prevent marked hyperglycemia and at the same time protect against hypoglycemia. For noncritical illness, typical blood glucose targets include lowest levels of 90 to 100 mg/dL, premeal levels lower than 140 mg/dL, and random levels lower than 180 mg/dL. For critically ill patients, intravenous insulin infusion may be needed to allow for rapid adjustments in dosage, and the blood glucose range recommended by most expert panels is 140 to 180 mg/dL.

Gestational Diabetes

The hormonal environment of pregnancy results in insulin resistance and therefore predisposes to the development or unmasking of diabetes during pregnancy. GDM occurs in 2% to 5% of all pregnancies and is associated with consequences for both mother and fetus if untreated. For this reason, screening for GDM is routinely performed between 24 and 28 weeks of gestation in women older than 25 years of age and in younger women who fulfill one or more of the risk criteria in Table 66-6 (2a through 2d and 2g). Women who are at high risk (i.e., those who are obese, have a personal history of GDM, glycosuria, or have a first-degree relative with diabetes) should be screened earlier, at their initial obstetric or prenatal visit. A broadly accepted approach to screening is a 2-hour 75-g oral glucose tolerance test with cutoff values as specified in Table 66-2.

A detailed discussion of the approach to managing GDM and also preexisting diabetes during pregnancy is beyond the scope of this chapter. The fundamental principles include diet, exercise, and glucose-lowering oral agents or insulin as needed. Blood glucose goals are set lower than in nonpregnant individuals because of the importance of minimizing exposure of the fetus to hyperglycemia: fasting, 95 mg/dL (5.3 mmol/L) or lower; 1-hour postprandial, 140 mg/dL (7.8 mmol/L) or lower; and 2-hours postprandial, 120 mg/dL (6.7 mmol/L) or lower. HbA_{1c} levels may be useful in establishing the presence of hyperglycemia before its discovery during pregnancy, but they have limited value in managing GDM. Women with GDM should be reevaluated with a 75-g glucose tolerance test 6 to 12 weeks after delivery, at which point approximately 10% will still have overt diabetes. Up to 40% of women with GDM go on to develop diabetes in the subsequent 20 years, with this risk varying substantially depending on ethnic background and obesity. Pregnancy serves as a provocative test and not as a risk factor for the future development of diabetes.

Management of Severe Metabolic Decompensation in Diabetes

Diabetic Ketoacidosis

Diabetic ketoacidosis (DKA) develops most commonly in patients with T1DM (approximately 2.5 cases per 100 T1DM patients per year). It also can occur in those with T2DM, especially during acute illness (severe infection, medical illness, or trauma), and in a subset of *ketosis-prone* T2DM patients. DKA is present in approximately 25% of T1DM patients at diagnosis and otherwise most often develops when patients with known T1DM stop taking prescribed insulin. It is a potentially life-threatening condition that has an overall mortality rate of approximately 2.5%, with most deaths resulting from complicating or precipitating medical conditions rather than the metabolic disturbances of DKA itself.

The pathophysiology of DKA results from the combined effects of insulin deficiency and increased levels of *insulin counter-regulatory (stress) hormones*. With insulin deficiency, glucose levels rise as a consequence of decreased uptake and metabolism by body tissues, the breakdown of hepatic glycogen stores *(glycogenolysis)*, and net glucose production by the liver and kidney *(gluconeogenesis)*. Catabolism of muscle proteins as a result of low insulin levels leads to the release of amino acids, which provide substrate that further drives gluconeogenesis. Because glucose is being synthesized endogenously, blood glucose levels rise markedly, even in the fasted state. Blood glucose levels greater than 170 mg/dL result in glycosuria. Excretion of glucose in the urine necessitates the co-excretion of large amounts of water and electrolytes (Na^+ and K^+). Patients experience polyuria but cannot compensate adequately and become progressively more fluid and electrolyte depleted. The osmotic diuresis is characterized by greater losses of water than electrolytes, and this leads to progressively increasing hyperosmolality. Because of insulin deficiency, there is decreased *lipogenesis* and accelerated *lipolysis* leading to increased levels of circulating free fatty acids, which serve as a substrate for the hepatic synthesis of ketone bodies (β-hydroxybutyrate, acetoacetate, and acetone). β-Hydroxybutyrate and acetoacetate are acids, and their rising plasma levels contribute to the development of a metabolic acidosis.

These processes can result from simple insulin deficiency, but often they are exacerbated by an underlying or precipitating illness, such as an infection. Infection results in insulin resistance secondary to increased levels of *stress hormones* (cortisol,