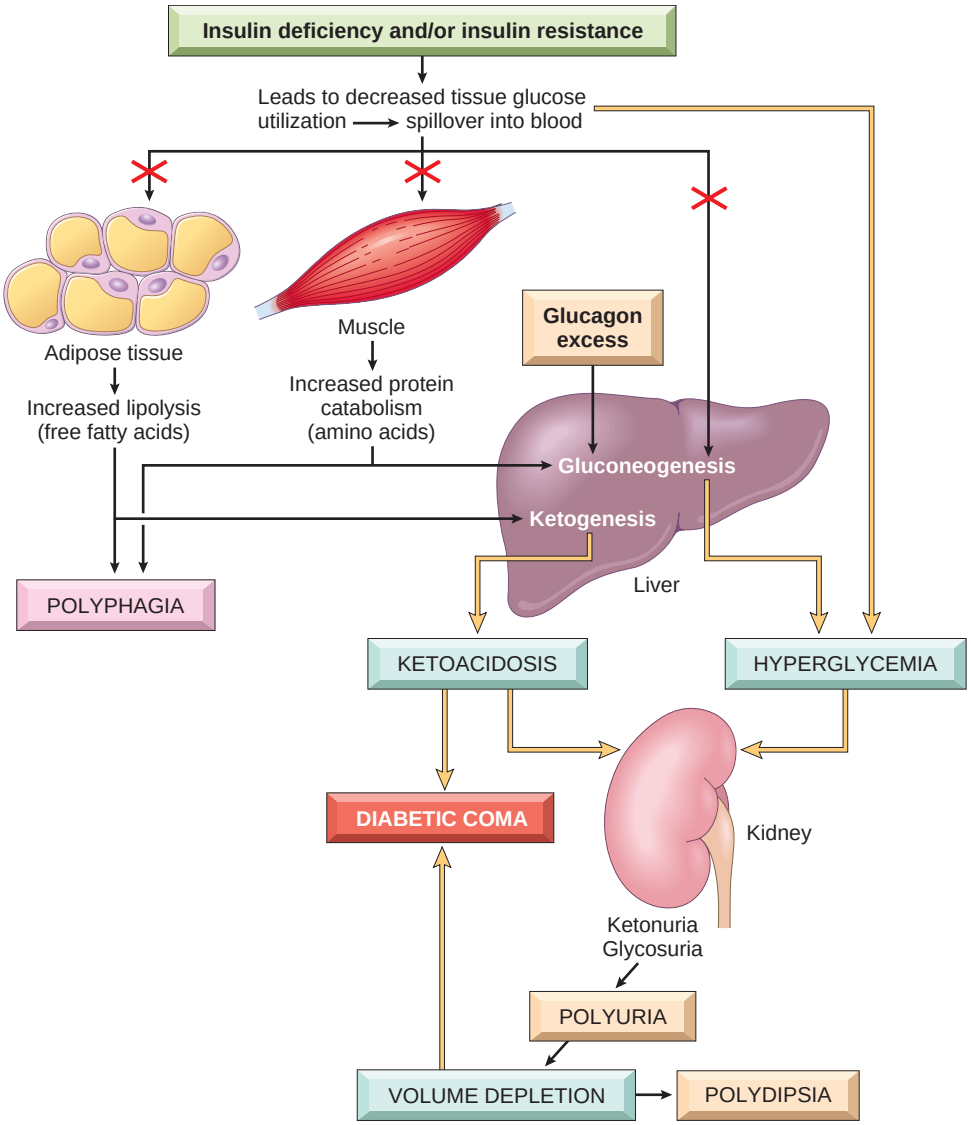

Figure 24-33 Sequence of metabolic derangements underlying the clinical manifestations of diabetes. An absolute insulin deficiency leads to a catabolic state, culminating in ketoacidosis and severe volume depletion. These cause sufficient central nervous system compromise to lead to coma and eventual death if left untreated.

extent. The most common precipitating factor is a failure to take insulin, although other stressors such as intercurrent infections, illness, trauma and certain drugs might also lead to this complication. Many of these factors are associated with the release of the catecholamine *epinephrine*, which blocks any residual insulin action and stimulates the secretion of glucagon. The insulin deficiency coupled with glucagon excess decreases peripheral utilization of glucose while increasing gluconeogenesis, severely exacerbating hyperglycemia (the plasma glucose levels are usually in the range of 250 to 600 mg/dL). The hyperglycemia causes an osmotic diuresis and dehydration characteristic of the ketoacidotic state.

The second major effect of insulin deficiency is activation of the ketogenic machinery. Insulin deficiency stimulates lipoprotein lipase, with resultant breakdown of adipose stores and an increase in levels of free fatty acids. When these free fatty acids reach the liver, they are esterified to fatty acyl coenzyme A. Oxidation of fatty acyl coenzyme A molecules within the hepatic mitochondria produces *ketone bodies* (acetoacetic acid and β-hydroxybutyric acid). The rate at which ketone bodies are formed may exceed the rate at which acetoacetic acid and β-hydroxybutyric acid can be utilized by peripheral tissues, leading to *ketonemia* and *ketonuria*. If the urinary excretion of ketones is compromised by dehydration, the result is a systemic *metabolic ketoacidosis*. Release of ketogenic amino acids by protein catabolism aggravates the ketotic state.

The clinical manifestations of diabetic ketoacidosis include fatigue, nausea and vomiting, severe abdominal pain, a characteristic fruity odor, and deep, labored breathing (also known as *Kussmaul breathing*). Persistence of the ketotic state eventually leads to depression in cerebral consciousness and coma. Reversal of ketoacidosis requires

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