catecholamines, glucagon, and growth hormone). A series of positive feedback loops are thus generated and lead to ever-accelerating hyperglycemia, fluid and electrolyte depletion, ketosis, and metabolic acidosis. More than simple restoration of insulin dosing is required, and patients usually need hospital admission and multicomponent interventions.

Common presenting symptoms in DKA include polyuria, thirst and polydipsia, recent weight loss (especially in new-onset diabetes), blurred vision, weakness, anorexia, nausea and vomiting, abdominal pain (which can mimic acute abdomen), and mental status changes varying from somnolence to coma. DKA and these associated symptoms usually evolve over 2 to 4 days but can have an onset of less than 12 hours in patients using insulin pumps. On physical examination, patients typically have evidence of dehydration including decreased skin turgor, hypotension, and tachycardia. The skin may be warm and dry from the vasodilating effects of acidosis, and marked hypotension should generate concern for impending vascular collapse. Patients often have deep, rapid respirations (Kussmaul breathing) as respiratory compensation for the metabolic acidosis, together with a characteristic fruity odor on their breath from exhaled acetone. The diagnosis is made in patients who have (1) a high blood glucose concentration (>250 mg/dL), (2) moderate to severe ketonemia (β-hydroxybutyrate >5 mmol/L or positive ketone levels by Ketostix at a serum dilution of 1 : 2 or higher), and (3) acidosis (pH <7.3 or plasma bicarbonate ≤15 mEq/L). Measurements of urine ketones may be misleading, because urinary ketones can be positive during fasting in the absence of DKA.

Additional evaluation besides the diagnostic tests already mentioned should include electrolytes, blood urea nitrogen, creatinine, phosphate, liver function tests, and amylase; arterial or mixed venous blood gases (including pH); complete blood count; urinalysis; electrocardiogram; and chest radiographs. The serum anion gap, which is usually greater than 12 mEq/L in DKA, should be calculated (anion gap = $[Na^+] - [Cl^- + HCO_3^-]$). Serum osmolality should be measured directly or calculated: estimated osmolality = $(2 \times [Na^+]) + ([\text{glucose in mg/dL}]/18)$.

Precipitating causes of DKA include infection (most common), myocardial infarction (including silent infarction), inflammatory processes (appendicitis, pancreatitis), and medications (especially glucocorticoids).

Treatment of DKA should start promptly with institution of measures to correct life-threatening abnormalities, including insulin deficiency, fluid and electrolyte depletion, potassium (K^+) depletion, and metabolic acidosis. In a typical regimen, insulin is administered as a regular insulin bolus (0.1 U/kg) followed by a continuous intravenous infusion at 0.1 U/kg/hour. Plasma glucose is monitored hourly until it is less than 250 mg/dL, and the rate of insulin infusion is adjusted as needed to target a rate of blood glucose decline of 75 to 100 mg/dL/hour to avoid potential complications of rapid shifts in osmolality.

At the time of starting insulin, it is essential to begin fluid and electrolyte replacement. The initial fluid deficit should be estimated based on the magnitude of weight loss (if known), mucous membrane dryness, skin turgor, and whether or not there is postural hypotension, with the knowledge that losses in DKA usually range from 3 to 8 L. A typical program for intravenous fluid replacement starts with 1 L of normal saline in the first hour. Normal saline may then be continued at 15 mL/minute for a second hour depending on the estimated severity of initial fluid depletion. This then may be changed to 0.45% (half-normal) saline at 7.5 mL/minute for the next 2 hours and gradually tapered thereafter to achieve full replacement of the estimated fluid deficit in approximately 8 hours. During that time, there should be frequent monitoring for jugular venous distention and chest auscultation to ensure early detection of fluid overload. Central venous pressure should be monitored in patients who are at risk for congestive heart failure.

Potassium repletion is needed in all patients, and there should be careful monitoring and replacement to ensure that patients do not develop potentially harmful hypokalemia or hyperkalemia. Urine output should be verified with the use of a Foley catheter if necessary before K^+ replacement is started. Unless patients are anuric, K^+ replacement should be initiated within 1 to 2 hours after starting insulin. A key goal is to maintain serum K^+ at all times higher than 3.5 mEq/L, and it is especially important to administer K^+ early in the course of treatment if there is initial hypokalemia or if bicarbonate is administered to correct acidosis, because the latter action promotes a shift of extracellular K^+ into cells. Potassium typically is withheld if the serum K^+ is 5 mEq/L or higher; otherwise, it is administered as part of the intravenous fluid regimen at 10 to 40 mEq/hour depending on the measured serum level. Serum K^+ should be monitored every 2 hours if it is less than 4 or greater than 5 mEq/L.

Bicarbonate infusion in general should be avoided but needs to be considered for patients who have a pH lower than 7, a serum bicarbonate level lower than 5.0 mEq/L, a K^+ concentration greater than 6.5 mEq/L, hypotension unresponsive to fluid replacement, severe left ventricular failure, or respiratory depression. Under these circumstances, 50 to 100 mEq (1 to 2 ampules) of bicarbonate may be infused intravenously over 2 hours.

As DKA resolves, it is important to continue providing adequate insulin to effectively resolve the ketosis, which may correct more slowly than the other abnormalities. This can be accomplished by adding glucose to the intravenous regimen (e.g., 5% glucose in half-normal saline) when blood glucose levels decrease to less than 200 to 250 mg/dL and continuing insulin infusion at 1 to 2 U/hour.

In patients with resolved DKA, transition to subcutaneous insulin can be made when the patient is clinically stable with normal vital signs, the acidosis is fully corrected, the patient is able take fluids orally without nausea or vomiting, and any precipitating conditions (e.g., infection) are controlled.

Hyperglycemic Hyperosmolar State

A hyperglycemic hyperosmolar state (HHS) occurs almost exclusively in patients with T2DM, one third of whom have not been previously diagnosed. Patients often are elderly and frequently have compromised renal function. Insulin deficiency, often exacerbated by insulin resistance resulting from the stress, leads to hyperglycemia, glucosuria, and an osmotic diuresis. However, the presence of some endogenous insulin secretion suppresses lipolysis and ketogenesis enough to prevent ketoacidosis. Patients with HHS typically develop more marked hyperglycemia, fluid and electrolyte deficits, and hyperosmolality compared to those with DKA. HHS usually develops insidiously over days to weeks,