

# Overview of the Diagnosis and Management of Diabetic Ketoacidosis

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**ABSTRACT:** Diabetic ketoacidosis is an acute complication of diabetes mellitus that can be life-threatening if not treated properly. Once thought to occur only in patients with type 1 diabetes, diabetic ketoacidosis has been also observed in patients with type 2 diabetes under certain conditions. The basic underlying mechanism for diabetic ketoacidosis is insulin deficiency coupled with elevated levels of counter-regulatory hormones, such as glucagon, cortisol, catecholamines, and growth hormone. Diabetic ketoacidosis can be the initial presentation of diabetes mellitus or precipitated in known diabetic patients by many factors, most com-

monly infection. The management of diabetic ketoacidosis involves careful clinical evaluation, correction of metabolic abnormalities, identification and treatment of precipitating and comorbid conditions, appropriate long-term treatment of diabetes, and plans to prevent recurrence. Certain areas need further research, such as indications for the use of bicarbonate and phosphates and the use of intravenous rapid-acting insulin. **KEY INDEXING TERMS:** Diabetes; Ketoacidosis; Insulin; Fluid management. [*Am J Med Sci* 2006;331(5):243–251.]

**D**iabetic ketoacidosis (DKA) is a metabolic derangement that, as the name implies, consists of three concurrent abnormalities: high concentration of blood glucose, high levels of ketone bodies, and metabolic acidosis.<sup>1</sup> The original description of DKA dates to 1886, more than 3 decades before the discovery of insulin.<sup>2</sup>

It is estimated that 2% to 8% of hospital admissions for children with diabetes are due to DKA, with about 160,000 hospital admissions per year in the United States.<sup>3</sup>

The annual incidence rate for DKA in the pediatric population ranges from 4.6 to 8 episodes per 1000 patients with diabetes, with a trend toward an increased hospitalization rate in the past two decades.<sup>4</sup>

Before the discovery and use of insulin in 1922, the mortality rate in patients with DKA was almost 100%. By 1932, the mortality rate dropped to 29%,<sup>5</sup> and the current mortality rate is less than 5% in

experienced centers.<sup>1</sup> The prognosis of DKA is worsened at the extremes of age and in the presence of coma and hypotension.<sup>1</sup>

## Pathophysiology

Diabetic ketoacidosis comprises three elements: marked hyperglycemia, ketosis, and acidosis. This clinical syndrome is accompanied by volume and electrolyte depletion. The main underlying pathophysiologic mechanism in DKA is insulin deficiency, either relative or absolute, combined with excess of insulin counter-regulatory hormones, including glucagon, catecholamines, cortisol, and growth hormone and elevation of proinflammatory cytokines (tumor necrosis factor- $\alpha$ , interleukin-6, interleukin-1 $\beta$ , and interleukin-8), free fatty acids, and plasminogen activator inhibitor-1.<sup>6</sup> These hormonal abnormalities lead to alterations in the metabolism of carbohydrates, proteins, and lipids. The following section briefly discusses those metabolic disturbances.

## Hyperglycemia

In normal conditions, insulin suppresses hepatic glucose production and lipolysis. In DKA, insulin deficiency and high levels of counter-regulatory hormones lead to marked hyperglycemia and increased free fatty acids and amino acids. Insulin deficiency leads to hepatic glucose overproduction while elevated concentrations of glucagon and catecholamines result in in-

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creased glycogenolysis and gluconeogenesis.<sup>7</sup> Insulin deficiency can be absolute or insufficient relative to the effect of counter-regulatory hormones causing impaired insulin action. Elevated cortisol levels stimulate protein catabolism with a consequent increase in circulating levels of amino acids, which provide a source for further glucose production through gluconeogenesis in the liver. The high concentrations of catecholamines, cortisol, and growth hormone along with the resulting ketosis and acidosis lead to reduction in glucose uptake by the tissues and impaired insulin action and secretion; this further worsens hyperglycemia.<sup>8,9</sup>

### *Ketosis and Acidosis*

Insulin deficiency and elevated levels of counter-regulatory hormones stimulate lipolysis and inhibit lipogenesis, resulting in high circulating levels of free fatty acids. These free fatty acids are taken up by the liver and oxidized to ketone bodies (beta-hydroxybutyrate and acetoacetate). Ketone bodies are relatively strong acids that dissociate at physiologic pH, producing a large hydrogen ion load. Metabolic acidosis ensues as the body's alkali reserves are depleted in an attempt to buffer hydrogen ions and ketone anions accumulate accounting for the elevated plasma anion gap.<sup>10</sup> In addition, there is decreased peripheral use of ketone bodies, which further aggravates hyperketonemia and metabolic acidosis.<sup>11</sup>

### *Volume and Electrolyte Depletion*

Hyperglycemia raises extracellular fluid osmolality, which leads to the shift of water from the intracellular to the extracellular compartment; this causes cellular dehydration and the movement of electrolytes out of the cells. With marked hyperglycemia, the renal threshold for glucose reabsorption is exceeded and glucose appears in the urine (glucosuria). This results in osmotic diuresis, with loss of water and electrolytes in the urine, causing hypovolemia and electrolyte depletion. Ketone bodies exert additional osmotic diuresis along with excretion of positively charged electrolytes, such as sodium, potassium, magnesium, and calcium, to maintain electrical neutrality.<sup>12</sup>

### **Precipitating Factors**

The most common precipitating factor in the development of DKA is infection,<sup>1</sup> most commonly urinary tract infections and pneumonia. In addition, new-onset type 1 diabetes, inadequate insulin doses, or insulin pump malfunction can lead to the development of DKA. Poor compliance with insulin therapy as a cause of DKA is commonly observed in young populations as well as patients belonging to ethnic minority groups and inner-city patients.<sup>13,14</sup> Other precipitating factors include myocardial in-

farction, cerebrovascular accident, acute pancreatitis, trauma, severe burns, alcohol abuse, and drugs (such as corticosteroids). Psychological factors complicated by eating disorders are implicated in about 20% of recurrent episodes of DKA in young patients with type 1 diabetes.<sup>1</sup> Factors that may lead to omission of insulin in young women include fear of weight gain with the use of insulin, fear of hypoglycemia, rebellion from authority, and stress of chronic disease.<sup>15</sup> In a minority of patients (about 5%), no precipitating factor can be identified.<sup>16</sup>

## **Diagnosis**

### *Clinical Presentation*

The symptoms of poorly controlled diabetes leading to DKA are usually of short duration (few days) and typically last less than 24 hours.<sup>1</sup> The history generally includes polyuria, polydipsia, polyphagia, weight loss, vomiting, abdominal pain, weakness, and drowsiness. Symptoms of precipitating factor may include fever, chest pain, shortness of breath, dysuria, abdominal pain, and neurologic deficits. Physical signs can include dehydration, dry mucous membranes, decreased skin turgor, tachycardia, Kussmaul respirations (rapid and deep breathing) with acetone smell, hypotension, alteration in mental status, shock, and coma. Clinical indicators of dehydration (blood pressure, pulse, capillary refill, tissue turgor, moistness of oral mucous membranes, and degree of weight loss) may not provide an accurate assessment of hydration status in children<sup>17</sup>; therefore, frequent monitoring of hemodynamic status is important.

Upper gastrointestinal hemorrhage, most commonly due to erosive esophagitis, occurred in 9% of patients hospitalized with DKA in one series and correlated with blood glucose levels, admission to the intensive care unit, duration of diabetes, and the presence of diabetic complications and signify a high non-bleeding-related death. Bleeding is generally self-limited, but blood transfusion may be required.<sup>18</sup>

Diabetic ketoacidosis can cause significant abdominal pain that resolves with appropriate measures of treatment; however, caution should be taken, as the pain could be a result or an indication of a precipitating cause of DKA. Further evaluation is needed if abdominal pain does not resolve with resolution of dehydration and metabolic acidosis. Although infection is a common precipitant of DKA, normothermia or even hypothermia can occur because of peripheral vasodilatation. The American Diabetes Association<sup>1</sup> classifies DKA into mild, moderate, and severe according to specific criteria (Table 1 shows the distinguishing features of each degree).

**Table 1.** Classification of Diabetic Ketoacidosis

	Mild	Moderate	Severe
Serum bicarbonate (mEq/L)	15–18	10–15	> 15
Arterial pH	7.25–7.30	7.0–7.24	< 7.0
Anion gap	> 10	> 12	> 12
Mental status	Alert	Alert/drowsy	Stupor/coma

### Laboratory Findings

For the acutely ill patient, quick bedside testing for capillary glucose and urine or serum ketones is appropriate. The initial laboratory evaluation should include plasma glucose, electrolytes (including bicarbonate), serum beta-hydroxybutyrate (if not available, check serum ketones), arterial or venous pH, osmolality, complete blood cell count with differential, urinalysis, and urine ketones. Further testing depends on the clinical examination findings and can include electrocardiography, bacterial cultures (e.g., of urine, blood, and throat), and imaging studies such as chest radiographs and computed tomography scans of the head.

To establish the diagnosis of DKA, the three following components should be present: 1) elevated plasma glucose (>250 mg/dL), 2) the presence of ketones (in serum or urine), and 3) the presence of acidosis (serum bicarbonate <18 mEq/L and/or arterial pH <7.30).<sup>1</sup> The anion gap [calculated as Sodium – (chloride + bicarbonate)] (normal  $10 \pm 2$  mmol/L) is typically elevated. Leukocytosis is common and has been attributed to dehydration and stress. Serum sodium level is usually decreased because of osmotic flux of water to the intravascular space due to hyperglycemia, and, less commonly, sodium concentration may be falsely lowered by severe hypertriglyceridemia. Serum sodium can be normal or high due to osmotic diuresis that results in excess loss of water compared to sodium.

The following formula is used to calculate the corrected serum sodium: Serum Sodium +  $1.6 \times$  [glucose in mg/dL] – 100/100.

Serum potassium concentration is generally elevated due to the extracellular shift of potassium caused by insulin deficiency, acidemia, and hypertonicity. Low-normal or low serum potassium concentration indicates severe total body potassium deficiency and should be managed vigorously. The occurrence of stupor or coma in the absence of high serum osmolality (>320 mOsm/L) should alert the clinician to consider other causes of altered mental status. Effective serum osmolality can be calculated as follows:  $[2 \times \text{serum sodium (mEq/L)}] + \text{glucose (mg/dL)}/18$ . Blood urea nitrogen is not included in the formula because it is freely permeable through the intracellular compartment.<sup>19</sup> Other biochemical abnormalities associated with DKA include high

concentrations of serum amylase, serum lipase, and liver enzymes.

### Differential Diagnosis

Diabetic ketoacidosis should be distinguished from alcoholic ketoacidosis, starvation ketosis, and conditions causing metabolic acidosis such as lactic acidosis, chronic renal failure and ingestion of drugs such as salicylate, methanol, ethylene glycol, and paraldehyde. Alcoholic ketoacidosis can be identified by clinical history and low to mildly elevated plasma glucose concentration. Starvation ketosis can be recognized by history and absence of significant acidosis. History of drug ingestion should always be elicited. Measurement of blood levels of lactate, salicylate, and ethanol can be helpful. Ethylene glycol (antifreeze) is expected by the presence of calcium oxalate and hippurate crystals in the urine. Paraldehyde ingestion is indicated by the characteristic odor of vinyl on breath. Because these intoxicants are low molecular weight organic compounds, they can produce an osmolar gap in addition to the anion gap.<sup>20</sup>

### Management

The initial management of DKA can be divided into the following categories:

1. Fluid and electrolyte therapy
2. Insulin therapy
3. Treatment of precipitating causes
4. Monitoring of therapy and complications

Successful management of DKA requires frequent monitoring of the patient's condition and response to treatment. Algorithms of management are presented in Figures 1 and 2.

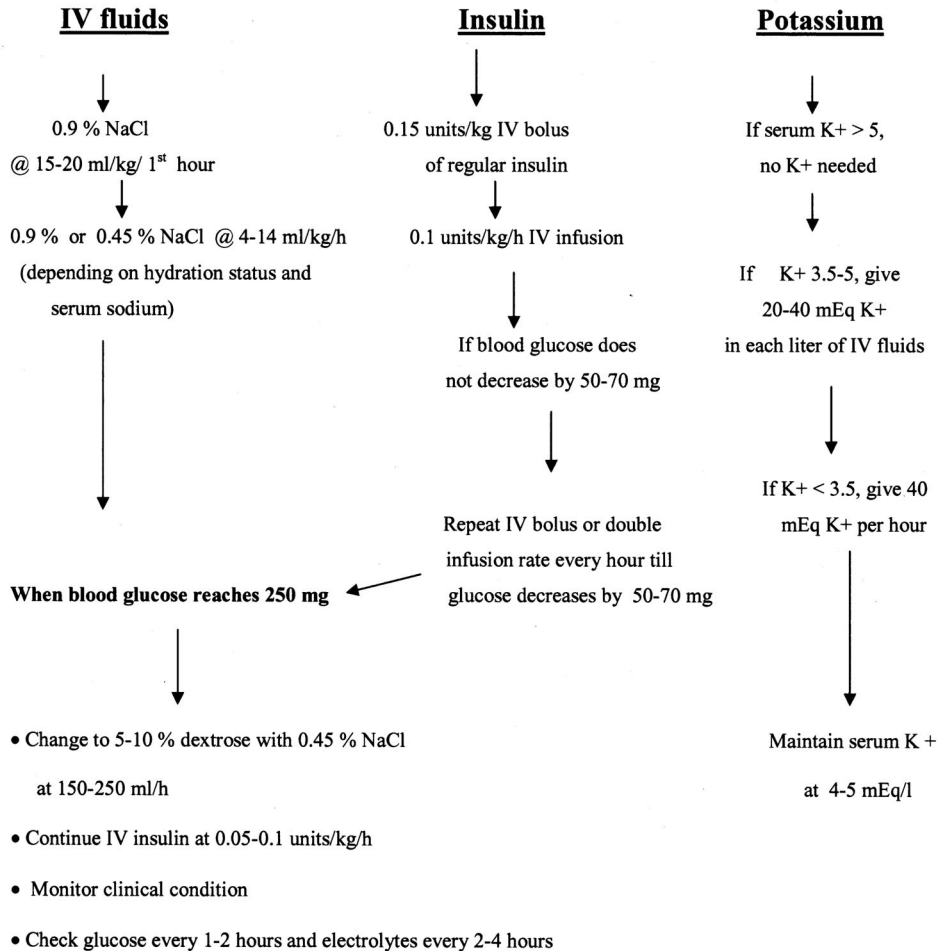
#### Fluid and Electrolyte Therapy

**Fluids.** Because patients with DKA are invariably dehydrated and sodium depleted, fluid therapy should be initiated immediately. The goal of fluid resuscitation is expansion of the intravascular and extravascular volume that improves renal perfusion, facilitates the excretion of glucose, and reduces the concentration of counter-regulatory hormones.

The total body water deficit can be estimated from the following formula:  $0.6 \times \text{weight} \times [1 - 140/\text{serum sodium}]$  and is generally 5 to 8 L in DKA.

## Diabetic Ketoacidosis

- Perform history & physical examination
- Evaluate for precipitating factors of diabetic ketoacidosis



**Figure 1.** Management of diabetic ketoacidosis in adult patients.

Limited data are available to guide fluid therapy. Most of the literature is extracted from consensus guidelines and expert opinions. The approach depends on the patient's age group as follows:

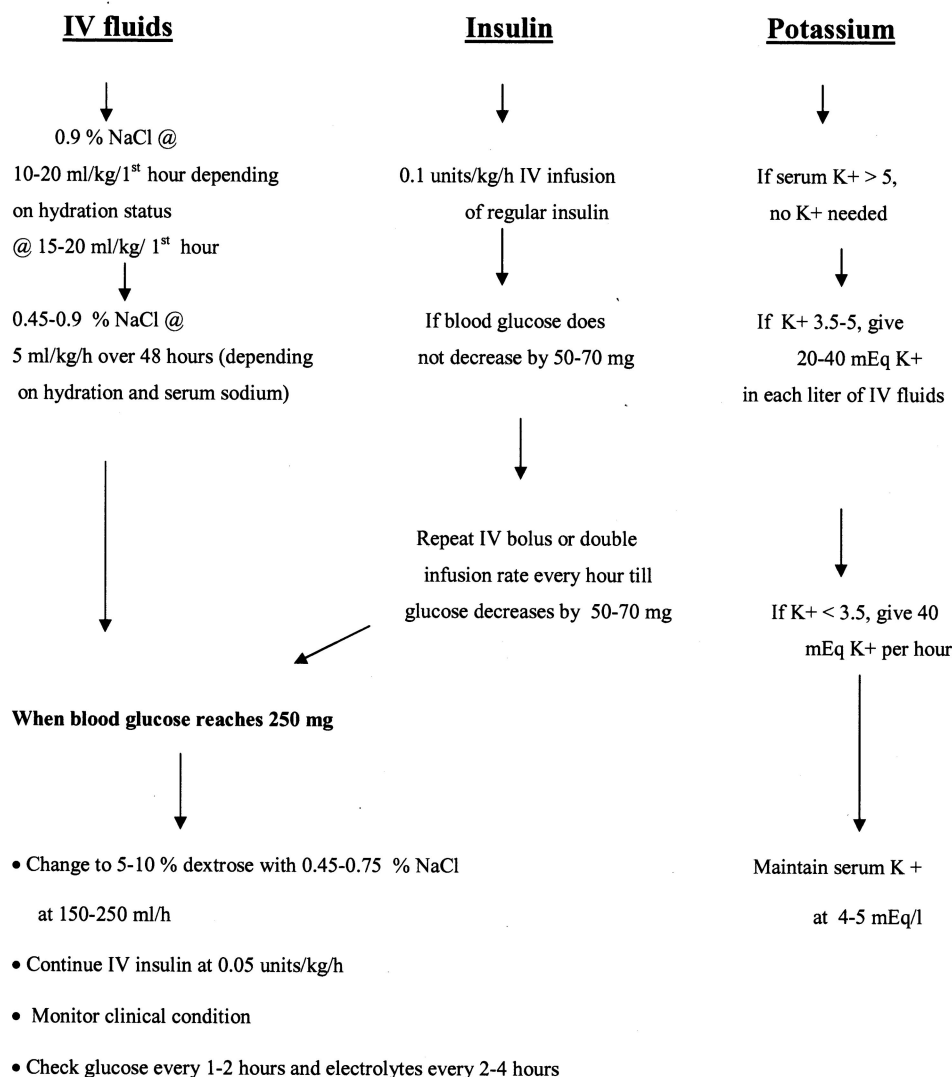
**Adult Patients.** Initial fluid replacement starts with isotonic saline (0.9 % NaCl) at a rate of 15 to 20 mL/kg (about 1–1.5 L) over the first hour then 4 to 14 mL/kg per hour, depending on the hydration status.<sup>1</sup> The goal is to replace 50% of the estimated total body water deficit over the first 8 hours and the rest by 16 to 24 hours. After the initial resuscitation phase, the choice of fluids will depend on hemodynamic monitoring (blood pressure, pulse), clinical examination, electrolyte concentrations, and urinary output. Isotonic saline is continued in patients with hypovolemic shock as well as those with low corrected serum sodium, and 0.45% NaCl is used in patients who respond by showing stable blood pressure and adequate urine output and those with high

or normal corrected serum sodium. For critically ill patients such as those with cardiac compromise or neurologic deficits, close monitoring and frequent assessment of hemodynamic, cardiac, renal, and mental status should be performed to avoid iatrogenic fluid overload. When serum glucose reaches 14 mmol/L (250 mg/dL), 5% to 10% dextrose (depending on glucose levels) should be added with 0.45% NaCl at 150 to 250 mL/hour to maintain glucose concentration at 150 to 250 mg/dL.

**Pediatric Patients.** Accurate assessment and management of dehydration in pediatric patients with DKA remains an essential part of the management. Fluid requirement should be determined and assessed carefully, as rapid fluid administration may lead to cerebral edema.<sup>21</sup> Clinical estimates of fluid deficit are usually in the range of 7% to 10%<sup>17</sup>. The first hour of fluid therapy consists of isotonic saline at the rate of 10 to 20 mL/kg per hour; this can



- Perform history & physical examination
- Evaluate for precipitating factors of diabetic ketoacidosis



**Figure 2.** Management of diabetic ketoacidosis in pediatric patients.

be repeated in cases of severe dehydration, but the initial total fluid amount should not exceed 50 mL/kg during the first 4 hours of therapy. Continued fluid therapy is calculated to replace the fluid deficit evenly over the next 48 hours. Isotonic or hypotonic (0.45%) saline is infused, depending on serum sodium levels, at a rate of 5 mL/kg (which is about 1.5 times the daily maintenance). There are no data to support the use of colloids in preference to crystalloids or the use of solutions more dilute than 0.45% NaCl in the treatment of DKA; the use of these solutions, which contain a large amount of electrolyte free water, is likely to lead to a rapid osmolar change and movement of fluid into the intracellular fluid compartment.<sup>22</sup> Once serum glucose concentra-

tion reaches 250 mg/dL, the fluid should be changed to 5% to 10% dextrose with 0.45% to 0.75% NaCl (depending on hydration status and serum sodium levels). Monitoring should include frequent assessment of fluid input and output and mental status to identify signs that might indicate fluid overload, which can lead to cerebral edema.<sup>23</sup>

**Electrolytes.** Measurement of serum electrolytes is crucial in the management of DKA, as there is significant total-body deficit of these molecules, particularly sodium (7–10 mmol/kg), chloride (3–5 mmol/kg), potassium (3–5 mmol/kg), and phosphorus (1–1.5 mmol/kg).<sup>24</sup>

It is very important to measure serum potassium before starting insulin and if the potassium level is

less than 3.5 mEq/L, supplemental potassium should be given and serum potassium monitored closely, as insulin therapy can further lower potassium levels. Despite total body potassium depletion, patients with DKA frequently have normal or high serum potassium levels. Hypokalemia at presentation may be related to prolonged duration of disease, whereas hyperkalemia primarily results from reduced renal function. Vomiting or nasogastric tube suction and significant dehydration can further decrease total body potassium levels. Volume expansion, correction of acidosis, and insulin therapy will facilitate potassium entry in the cells and decrease serum potassium concentration. The amount of potassium supplement should depend on the serum potassium level, with a goal to keep serum potassium concentration at 4 to 5 mEq/L. If serum potassium is more than 5 mEq/L, no supplement is required, but potassium levels should be monitored closely for possible need for replacement. If potassium is less than 3.5 mEq/L, potassium chloride 40 mEq/hour is given until potassium level rises to more than 3.5 mEq/L. For levels between 3.5 to 5.0 mEq/L, potassium replacement can be started using 20 to 40 mEq potassium in each liter of intravenous fluids. Replacement and follow-up of serum potassium is slightly different in pediatric patients and is outlined in Figure 2.

Serum phosphate concentration is usually normal or elevated at presentation. Phosphate levels may decrease with insulin therapy. Phosphate therapy should not be administered routinely to patients with DKA, as severe hypocalcemia can occur.<sup>25</sup> Phosphate therapy in the form of potassium phosphate 20 to 30 mEq/L can be considered when serum phosphorus is less than 1 mg/dL and for patients with cardiac compromise, anemia, or respiratory depression.<sup>1</sup>

### *Insulin Therapy*

Insulin treatment is a cornerstone in the management of DKA. Insulin therapy in adults starts by administering an intravenous bolus of regular insulin at 0.15 units per kilogram body weight, followed by a continuous infusion of regular insulin at a dose of 0.1 units per kilogram per hour. In pediatric patients, the insulin bolus dose is not required; a continuous infusion of regular insulin at 0.1 units per kg body weight per hour is recommended.<sup>1,22</sup>

Plasma glucose should be measured hourly and if it did not decrease by 50 to 75 mg/dL from the initial value in the first hour, hydration status must be evaluated; if acceptable, the insulin infusion rate can be doubled every hour until glucose falls at a steady hourly rate of 50 to 75 mg/dL.<sup>1</sup> When the plasma glucose level reaches 250 mg/dL, dextrose (5–10%) should be added to maintain glucose concentration at 150 to 250 mg/dL. Insulin is sometimes

mistakenly discontinued when plasma glucose concentration reaches the acceptable range. Insulin infusion should be continued at a rate of 0.05 to 0.1 units/kg/hour and the rate is adjusted, aiming at resolving the ketoacidosis; this requires the achievement of a serum bicarbonate level of greater than 18 mEq/L or a venous pH of greater than 7.3.<sup>1</sup> Rapid-acting insulin (Lispro and Aspart) has been used in the subcutaneous form in a small number of patients with uncomplicated DKA and was found to be safe and effective.<sup>26,27</sup>

### *Bicarbonate Therapy*

Bicarbonate use in DKA remains controversial. Prospective randomized studies have showed no beneficial or deleterious effects in patients with DKA who have pH between 6.9 and 7.1.<sup>28,29</sup> There are potential arguments against the use of bicarbonate.<sup>30,31</sup> Administration of insulin stops further ketone synthesis and allows excess ketoacids to be metabolized, resulting in the regeneration of bicarbonate and spontaneous correction of acidemia.<sup>1,12</sup> Also, treatment of hypovolemia will improve tissue perfusion and renal function, thus increasing the excretion of organic acids. Of concern is that bicarbonate therapy may cause paradoxical central nervous system acidosis and that rapid correction of acidosis caused by bicarbonate will result in hypokalemia, may accentuate sodium load, and will contribute to serum hypertonicity. In addition, alkali therapy can increase hepatic ketone production, thus slowing the rate of recovery from the ketosis. Therefore, the use of bicarbonate is not recommended in patients with a pH greater than 7.0.<sup>1,22</sup> No prospective randomized studies regarding the use of bicarbonate in patients with DKA with pH values less than 6.9 have been reported. Some authorities such as the American Diabetes Association, the Pediatric Endocrine Society, and the European Society of Pediatric Endocrinology<sup>1,22</sup> recommend bicarbonate administration when the pH is less than 7.0. In adult patients with a pH of 6.9 to 7.0, sodium bicarbonate in an amount of 50 mmol is diluted in 200 mL sterile water and infused at a rate of 200 mL per hour. If the pH is less than 6.9, 100 mmol sodium carbonate is added to 400 mL sterile water and given at a rate of 200 mL per hour. In pediatric patients, bicarbonate is administered if the pH remains less than 7.0 after the initial hour of hydration; this is given as sodium bicarbonate at a dose of 1 to 2 mEq/kg added to sodium chloride, to produce a solution that does not exceed 155 mEq/L sodium. Since bicarbonate therapy, as well as insulin, lowers potassium concentration, serum potassium should be monitored and potassium supplementation should be maintained in intravenous fluids (see electrolytes section).

### *Treatment of Precipitating Causes*

The precipitating cause of DKA should be identified as soon as possible and treatment initiated, as this will facilitate the management process. As stated earlier, infection (commonly urinary tract infections and pneumonias) is the most common precipitating cause of DKA. When infection is suspected, appropriate laboratory tests, imaging modalities, and cultures should be performed and treatment started. It is very important for the clinician to recognize the other precipitating factors that may be masked by the clinical presentation, such as myocardial infarction (as adults can have silent ischemia), gastrointestinal bleeding, acute pancreatitis, stroke, pulmonary embolism, and trauma.

### *Monitoring of Therapy and Complications*

The patient's clinical condition should be monitored frequently depending on the initial evaluation. Monitoring should include follow-up of blood pressure, pulse, hydration, mental status, fluid input, and urinary output. Measurement and follow-up of laboratory tests along with adjustment of fluid and electrolyte therapy accordingly (as discussed above) is paramount in the management of DKA. Blood glucose level should be checked every hour at the beginning of therapy until it reaches 250 mg/dL and when the patient's condition is stable, then it can be checked every 2 hours. Electrolytes and venous pH (repeat arterial blood gases are not necessary) can be checked every 2 to 4 hours. Using a data flow sheet that includes parameters of the patient's clinical condition, results of laboratory data and records of fluid, electrolyte, and insulin given is helpful. Resolution of DKA is indicated by a glucose level less than 200 mg/dl, serum bicarbonate level of 18 mEq/L or greater, and venous pH of greater than 7.3.<sup>12</sup> The clearance of ketone bodies takes a longer time than the resolution of hyperglycemia and acidosis. Ketones in the blood or urine are generally measured by the nitroprusside method, which only measures acetoacetic acid and acetone and not beta-hydroxybutyrate (which is the strongest and most prevalent acid in DKA). During therapy, beta-hydroxybutyrate is converted to acetoacetic acid, which may lead the clinician to believe that acidosis has worsened. Therefore, assessment of serum or urinary ketones by the nitroprusside method should not be used as an indicator of response to therapy; direct measurement of beta-hydroxybutyrate in the blood is the preferred method for monitoring ketones during the management of DKA.<sup>32</sup>

Careful monitoring for the occurrence of complications is an important aspect in the management of DKA. The most common complications are hypoglycemia due to high doses of insulin, hypokalemia due to insulin administration and treatment of acidosis, and hyperglycemia due to interruption or discontinuation of insulin therapy after resolution of DKA

without administering subcutaneous insulin. This can be treated with appropriate replacement of glucose (some patients may need dextrose 10% to keep glucose in the acceptable range) and potassium; management and initiation of insulin will be discussed under the next section (post DKA management).

Hyperchloremic metabolic acidosis is commonly observed during the treatment of DKA.<sup>10</sup> The main mechanism is loss of ketoanions in the urine that are necessary for bicarbonate regeneration; other mechanisms include 1) intravenous fluids containing chloride concentrations exceeding that of plasma, 2) volume expansion with bicarbonate-free fluids, and 3) intracellular shift of sodium bicarbonate during correction of DKA.<sup>33,34</sup> These abnormalities are transient and are not clinically significant except in patients with acute renal failure or severe oliguria.<sup>12</sup>

Cerebral edema is a rare (0.5–1.0%) complication that primarily occurs in children with DKA.<sup>31,35</sup> The clinical presentation includes change in the level of consciousness, decrease in arousal, behavioral changes, and headache. With worsening of the condition, brain stem herniation occurs, with seizures, incontinence, papillary changes, bradycardia, and respiratory distress. The pathophysiologic mechanism of cerebral edema appears to be multifactorial, including cerebral ischemia/hypoxia, the generation of various inflammatory mediators, and increased cerebral blood flow.<sup>22,36</sup> Reported mortality rates from cerebral edema in population-based studies ranged between 21% and 25%.<sup>22,31,37</sup> Significant morbidity is evident in up to 26% of survivors.<sup>37</sup> This catastrophic complication may be prevented by gradual correction of water and sodium deficits, especially in patients with high serum osmolality, avoidance of rapid decline in blood glucose concentration, and the addition of dextrose to fluids once blood glucose reaches 250 mg/dL.<sup>20,38</sup>

Hypoxemia and rarely noncardiogenic pulmonary edema may complicate the treatment of DKA.<sup>1</sup> Hypoxemia is attributed to a reduction in colloid osmotic pressure that causes increased lung water content and decreased lung compliance.<sup>12</sup> Patients with DKA who have a widened alveolo-arteriolar oxygen gradient or with rales on lung examination seem to be at an increased risk for the development of pulmonary edema.

### **Post-DKA Management**

Once DKA is resolved, further management depends on the patient's condition. If the patient cannot tolerate oral intake, intravenous insulin and fluid replacement should be continued according to blood glucose and electrolyte levels.<sup>12</sup> When the patient is able to eat, intravenous fluids can be discontinued and a subcutaneous insulin regimen in mul-



tiple daily injections should be initiated using a split-mixed regimen that uses a combination of short- or rapid-acting insulin and intermediate- or long-acting insulin. The half-life of intravenous regular insulin in the blood is less than 10 minutes. Therefore, it is important to continue intravenous insulin infusion for at least an hour after the subcutaneous insulin regimen is begun to ensure adequate blood insulin levels.<sup>8</sup> Doses of insulin are adjusted based on blood glucose monitoring. Most patients will need intensive insulin management, with three to four injections per day.

### Prevention

Prevention of subsequent episodes of DKA and recurrent admissions is an important element in managing this condition. Many cases of DKA can be prevented by better access to medical care, proper education, and effective communication with the members of the medical team. Omission of insulin is a common precipitant of DKA; this can be due to an underlying disorder such as psychiatric conditions or economic restraints.<sup>13,14</sup> This fact emphasizes the need for the health care system to address this problem, which is clinically serious and costly.

Adolescents and young patients who have recurrent episodes of DKA should undergo psychiatric evaluation to uncover disorders that can contribute to these episodes. Examples of these disorders include depression, eating disorders, and sexual or physical abuse.

If DKA occurs as a result of mechanical failure of continuous subcutaneous insulin infusion therapy (insulin pump), arrangement with the diabetes team should be undertaken to ensure proper education to identify pump malfunction and use of alternative insulin route when necessary and easy access to medical and technical support.

The first phase of preventing future episodes of DKA starts from the first hospital admission. Patients should receive proper education on the importance of compliance with all aspects of diabetes care, with clear guidelines for sick-day management. These should include specific information on 1) early recognition of the symptoms and signs of DKA, 2) home blood glucose goals and the use of supplemental insulin during illness, 3) a sick-day management diary, and 4) when to contact the health care provider.<sup>8</sup>

Successful sick-day management depends on the active involvement of the patients and family members. A proper educational program should include measuring pulse, temperature, blood pressure, respiratory rate, blood glucose, and urine or blood ketone, identifying the manifestations of infection, and the use of a liquid diet containing carbohydrates and salts. Most importantly, the patient should be advised to never discontinue insulin and to seek

medical assistance early in the course of the illness. Appropriate adherence to sick-day rules could decrease the incidence and severity of DKA.<sup>7</sup> In addition, a prevention program directed toward the education of primary care providers and school personnel to recognize the manifestations of uncontrolled diabetes and new-onset diabetes was shown to decrease the incidence of DKA in children.<sup>4,39</sup>

In conclusion, despite major advances in the understanding of the pathogenesis and a more uniform agreement on the diagnosis and treatment of DKA, it continues to be an important cause of morbidity and mortality among patients with diabetes mellitus. Early diagnosis and treatment of precipitating causes, provision of coordinate care, intensive patient education programs, and improved access to medical care are likely to reduce the development of DKA-associated complications. Because most cases of admissions for DKA occur in previously known diabetics, prevention remains an important approach to decrease the occurrence of this condition.

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