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Diabetic ketoacidosis is characterized by a biochemical triad of hyperglycemia, ketonemia, and acidemia, with rapid symptom onset.

Common symptoms and signs include polyuria, polydipsia, polyphagia, weakness, weight loss, tachycardia, dry mucous membranes, poor skin turgor, hypotension, and, in severe cases, shock.

Successful treatment includes correction of volume depletion, hyperglycemia, electrolyte imbalances, and comorbid precipitating events, with frequent monitoring.

Complications of treatment include hypoglycemia, hypokalemia, hypoxemia, and rarely pulmonary edema.

Cerebral edema, a rare but potentially rapidly fatal complication, occurs mainly in children. It may be prevented by avoiding overly rapid fluid and electrolyte replacement.
Diabetic ketoacidosis (DKA) is an acute metabolic complication of diabetes that is potentially fatal and requires prompt medical attention for successful treatment. It is characterized by absolute insulin deficiency and is the most common acute hyperglycemic complication of type 1 diabetes mellitus.\[1\]

### Definition

Diabetic ketoacidosis (DKA) is an acute metabolic complication of diabetes that is potentially fatal and requires prompt medical attention for successful treatment. It is characterized by absolute insulin deficiency and is the most common acute hyperglycemic complication of type 1 diabetes mellitus.\[1\]

### Other hyperglycemic states

- Diabetes mellitus
- Hyperosmolar hyperglycemic state (HHS)
- Impaired glucose tolerance
- Stress hyperglycemia

### Other ketotic states

- Ketotic hypoglycemia
- Alcoholic ketosis
- Starvation ketosis

### Other metabolic acidotic states

- Lactic acidosis
- Hyperchloremic acidosis
- Salicylism
- Uremic acidosis
- Drug-induced acidosis

### Triad of DKA


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### Epidemiology

In the US from 2000-2009, the rate of hospitalizations for DKA decreased overall, from 21.9 to 19.5 in 1000 persons with diabetes, but then increased from 2009-2014 to 30.2 in 1000 persons with diabetes.\[7\] In 2014, rates of hospitalization for DKA were highest among people aged <45 years (44.3 in 1000 persons with diabetes) and decreased with age (5.2 in 1000 persons with diabetes aged 45-64 years; 1.6 in 1000 65-74 years; and 1.4 in 1000 ≥75 years).\[7\] From 2000-2014, in-hospital mortality rates among people with DKA consistently decreased, from 1.1% to 0.4%.\[7\] In 2014 in the US, about 207,000 emergency department visits for people aged ≥18 years were for hyperglycemic crises (e.g., DKA, hyperglycemic hyperosmolar state).\[8\]

### Etiology

In DKA, there is a reduction in the net effective concentration of circulating insulin along with an elevation of counter-regulatory hormones (glucagon, catecholamines, cortisol, and growth hormone). These alterations lead to extreme manifestations of metabolic derangements that can occur in diabetes. The two most common
Diabetic ketoacidosis precipitating events are inadequate insulin therapy or infection. Underlying medical conditions such as myocardial infarction or stroke that provoke the release of counter-regulatory hormones are also likely to result in DKA in patients with diabetes. Drugs that affect carbohydrate metabolism, such as corticosteroids, thiazides, pentamidine, sympathomimetic agents (e.g., dobutamine and terbutaline), second-generation antipsychotic agents, and immune checkpoint inhibitors may contribute to the development of DKA. The use of sodium-glucose cotransporter 2 (SGLT-2) inhibitors has also been implicated in the development of euglycemic DKA in patients with both type 1 and type 2 diabetes.

Pathophysiology

Reduced insulin concentration or action, along with increased insulin counter-regulatory hormones, leads to the hyperglycemia, volume depletion, and electrolyte imbalance that underlie the pathophysiology of DKA. Hormonal alterations in DKA lead to increased gluconeogenesis, hepatic and renal glucose production, and impaired glucose utilization in peripheral tissues, which result in hyperglycemia and hyperosmolarity. Insulin deficiency leads to release of free fatty acids from adipose tissue (lipolysis), hepatic fatty acid oxidation, and formation of ketone bodies (beta-hydroxybutyrate and acetacetate), which result in ketonemia and acidosis. Studies have demonstrated the elevation of proinflammatory cytokines and inflammatory biomarkers (e.g., CRP), markers of oxidative stress, lipid peroxidation, and cardiovascular risk factors with hyperglycemic crises. All of these parameters return to normal following insulin and hydration therapies within 24 hours of hyperglycemic crises. Elevation of proinflammatory cytokines, and markers of lipid peroxidation and oxidative stress, have also been demonstrated in non-diabetic patients with insulin-induced hypoglycemia. The observed proinflammatory and procoagulant states in hyperglycemic crises and hypoglycemia may be the result of adaptive responses to acute stress and not hyperglycemia or hypoglycemia per se. It has also been postulated that ketosis-prone diabetes comprises different syndromes based on autoantibody status, human leukocyte antigen (HLA) genotype, and beta-cell functional reserve.
**Classification**

**Clinical DKA classification[1]**

Diagnostic criteria and classification:

**Mild DKA**
- Plasma glucose: >250 mg/dL
- Arterial pH: 7.25 to 7.30
- Serum bicarbonate: 15-18 mEq/L
- Urine ketone: positive
- Serum ketone: positive
- Effective serum osmolality: variable
- Anion gap: >10
- Mental status: alert.

**Moderate DKA**
- Plasma glucose: >250 mg/dL
- Arterial pH: 7.00 to <7.24
Diabetic ketoacidosis

Basics

• Serum bicarbonate: 10 to <15 mEq/L
• Urine ketone: positive
• Serum ketone: positive
• Effective serum osmolality: variable
• Anion gap: >12
• Mental status: alert and/or drowsy.

Severe DKA

• Plasma glucose: >250 mg/dL
• Arterial pH: <7.00
• Serum bicarbonate: <10 mEq/L
• Urine ketone: positive
• Serum ketone: positive
• Effective serum osmolality: variable
• Anion gap: >12
• Mental status: stupor and/or coma.
Primary prevention

Patient education about management of their diabetes during periods of mild illness (sick-day management) is vital for preventing DKA. This should include information on when to contact a healthcare professional, blood glucose monitoring, use of insulin, and initiation of appropriate nutrition during illness. This information should be reinforced with patients periodically. Patients should be advised to continue insulin and to seek professional advice early in the course of the illness. Close follow-up is very important, as it has been shown that 3-month visits to the endocrine clinic will reduce the number of emergency department admissions for DKA.[1] [33] [34] Self-monitoring of ketones is also emerging as a potential strategy.[35]

SGLT-2 inhibitor-associated DKA in patients with type 2 diabetes is typically precipitated by insulin omission or significant dose reduction, severe acute illness, dehydration, extensive exercise, surgery, low-carbohydrate diets, or excessive alcohol intake. DKA prevention strategies should include withholding SGLT-2 inhibitors when precipitants are present, and avoiding insulin omission or large insulin dose reduction.[36] [37]

Many cases can be prevented by better access to medical care, proper education, and effective communication with a healthcare provider during an intercurrent illness. Adequate supervision by family and healthcare provider may decrease the rates of hospitalization and mortality.[1] [38] Hospital admission with DKA, and recurrent admissions in particular, may be considered a "red flag" for triggering psychiatric assessment so that mental health problems can be addressed and further admissions with DKA prevented.[19]

Screening

If a patient is brought to the emergency department with signs and symptoms of hyperglycemia (polyuria, polydipsia, and abdominal pain), volume depletion, acetone breath, and changes in mental status (even without a history of diabetes), then plasma glucose and urine ketones should be checked. In the presence of high plasma glucose and/or positive urine ketones, full diagnostic laboratory evaluations for DKA and hyperosmolar hyperglycemic state should be performed.[1]
Case history

Case history #1

A 20-year-old man is brought to the emergency department with abdominal pain, nausea, and vomiting with increasing polyuria, polydipsia, and drowsiness since the day before. He was diagnosed with type 1 diabetes 2 years previously. He mentions that he ran out of insulin 2 days ago. Vital signs at admission are: BP 106/67 mmHg, heart rate 123 beats per minute, respiratory rate 32 breaths per minute, temperature 98.8°F (37.1 °C). On mental status examination, he is drowsy. Physical examination reveals Kussmaul breathing (deep and rapid respiration due to ketoacidosis) with acetone odor and mild generalized abdominal tenderness without guarding and rebound tenderness. Initial laboratory data are: blood glucose 450 mg/dL, arterial pH 7.24, pCO₂ 25 mmHg, bicarbonate 12 mEq/L, WBC count 18,500/microliter, sodium 128 mEq/L, potassium 5.2 mEq/L, chloride 97 mEq/L, BUN 32 mg/dL, creatinine 1.7 mg/dL, serum ketones strongly positive.

Other presentations

It is now well recognized that new-onset type 2 diabetes can manifest with DKA. These patients are obese and have undiagnosed hyperglycemia, impaired insulin secretion, and insulin resistance. However, after treatment of the acute hyperglycemic episode with insulin, beta-cell function and insulin effects improve so these patients are able to discontinue insulin therapy and may be treated orally or by diet alone, with 40% remaining insulin-independent 10 years following the initial episodes of DKA. These patients do not have the typical autoimmune laboratory findings of type 1 diabetes.[2] This type of diabetes has been labeled as "type 1 and ½" or "type 1 and a half" diabetes, "Flatbush" diabetes, or "ketosis-prone" diabetes. Conversely, an extreme hyperosmolar state similar to hyperosmolar hyperglycemic state (HHS) has been reported in combination with DKA in type 1 diabetes.[3] [4] [5] [6]

Step-by-step diagnostic approach

The symptoms of DKA usually develop rapidly over 1 day or less. DKA may be the initial presentation in up to 25% of people with newly diagnosed diabetes. Hyperglycemia is a key diagnostic criterion for DKA; however, a wide range of plasma glucose levels can be present on admission, and approximately 10% of DKA patients present with glucose <250 mg/dL (“euglycemic DKA”).[1] Hyperosmolar hyperglycemic state (HHS) is often discussed as a separate condition. However, DKA and HHS represent two points on the spectrum of metabolic derangements in diabetes. In contrast to DKA, HHS may evolve insidiously over days to weeks. Symptoms of hyperglycemia in both DKA and HHS include polyuria, polydipsia, weakness, and weight loss.

Important factors to consider in the patient’s past or current medical history include infection, myocardial infarction, pancreatitis, stroke, acromegaly, hyperthyroidism, and Cushing syndrome, as these may be precipitants or risk factors for DKA. In euglycemic DKA, pregnancy, starvation, concomitant alcohol use, and sodium-glucose cotransporter 2 (SGLT-2) inhibitors have all been implicated in its etiology.[12] [39]

It is essential to take a full medication history, in particular looking for corticosteroids, thiazides, pentamidine, sympathomimetics, second-generation antipsychotic agents, and immune checkpoint inhibitors, as these affect carbohydrate metabolism and may participate in the development of hyperglycemic crises.[1] [25] [11]
Diabetic ketoacidosis

Diagnosis

Cocaine abuse may be an independent risk factor associated with recurrent DKA. SGLT-2 inhibitors (e.g., canagliflozin, dapagliflozin, empagliflozin), used for glycaemic control of type 2 diabetes, have been the subject of an FDA warning about a risk for DKA.

Physical exam

Physical signs of volume depletion include dry mucous membranes, poor skin turgor, tachycardia, hypotension, and, in severe cases, shock. DKA patients may exhibit nausea, vomiting, Kussmaul respiration, acetone breath, and, occasionally, abdominal pain. Abdominal pain may correlate with the degree of acidosis in patients with DKA, and it may be confused with an acute abdominal crisis. Mild hypothermia may be observed in some patients, due to peripheral vasodilation. Hyperthermia is not usual, even in the presence of infection. Mental status may be altered in DKA, varying from alert in mild DKA to stupor and/or coma in severe DKA. In HHS, mental obtundation and coma are more frequent. Focal neurologic signs (hemianopia and hemiparesis) and seizures may also be features in HHS.

Initial laboratory evaluation

Plasma glucose

- Plasma glucose is typically >250 mg/dL with presence of acidosis and ketonemia. However, a wide range of plasma glucose levels can be present on admission, and approximately 10% of DKA patients present with glucose <250 mg/dL (euglycemic DKA).

Urinalysis

- Positive for glucose and ketones. Other potential findings include leukocytes and nitrates in the presence of infection, and myoglobinuria and/or hemoglobinuria in rhabdomyolysis.

Arterial and venous blood gases

- Arterial blood gas (ABG) shows a metabolic acidosis, which is essential for the diagnosis of DKA. Arterial pH measurement is necessary for diagnosis of DKA, but venous pH is recommended for monitoring treatment, due to the pain and risk of infection in obtaining frequent arterial samples. A venous pH sample is usually 0.03 units lower than arterial pH, and this difference should be considered.
- The pH varies from 7.00 to 7.30, and the arterial bicarbonate ranges from <10 mEq/L in severe DKA to >15 mEq/L in mild DKA.

Capillary or serum ketones (beta-hydroxybutyrate)

- There are three main ketones that are produced in DKA that can be measured: acetone, acetoacetate, and beta-hydroxybutyrate (BOHB).
- In early DKA, the acetoacetate concentration is low, but it is a major substrate for ketone measurement by many laboratories (nitroprusside reaction method). Therefore, serum ketone measurement by usual laboratory techniques has a high specificity, but low sensitivity for the diagnosis of DKA; hence a negative test for serum ketones does not exclude DKA. Acetone is rarely measured due to its volatile nature. Conversely, BOHB is an early and abundant ketoacid that can be the first signal of the development of DKA. Point-of-care BOHB testing is widely available and is highly sensitive and specific for the diagnosis of DKA.
Diabetic ketoacidosis

Diagnosis

• During the treatment of DKA, BOHB is converted to acetoacetate, which is detected by the nitroprusside method. Therefore, the increase in acetoacetate during the treatment of DKA may mistakenly indicate a worsening of ketonemia.

• Another potential source of error in detecting ketone bodies is the patient's medications. Some drugs, such as the ACE inhibitor captopril, contain sulfhydryl groups that can react with the reagent in the nitroprusside test and give a false-positive result. Therefore, clinical judgement and other biochemical tests will be required in patients who are receiving such medications.[1]

BUN

• Typically increased due to volume depletion.

Serum electrolytes[1][18]

• Sodium: serum sodium is usually low due to osmotic reflux of water from the intracellular to extracellular space in the presence of hyperglycemia. Total sodium deficit is 7 to 10 mEq/kg. Hypernatremia in the presence of hyperglycemia indicates profound volume depletion. Alternately, in the presence of high serum chylomicron concentration, pseudonormoglycemia and pseudohyponatremia may occur.

• Calculation of the corrected sodium: the corrected serum sodium level should be evaluated as this is used to guide appropriate fluid replacement. The equation for conventional units is: corrected sodium (mEq/L) = measured sodium (mEq/L) + 0.016 (glucose [mg/dL] - 100).

• Potassium: total potassium deficit is 3 to 5 mEq/kg. Serum potassium is usually elevated due to extracellular shift of potassium caused by insulin insufficiency, hypertonicity, and acidemia, but the total body potassium concentration is low due to increased diuresis. Therefore, low potassium level on admission indicates severe total-body potassium deficit.

• Chloride: usually low. The total chloride deficit is 3 to 5 mEq/kg.

• Magnesium: usually low. The total body deficit of magnesium is usually 1 to 2 mEq/kg.

• Calcium: usually low. Total body calcium deficit is usually about 1 to 2 mEq/kg.

• Phosphate: despite the total body phosphate deficit averaging 1.0 mmol/kg, serum phosphate is often normal or increased at presentation, but decreases with insulin therapy.

Anion gap

• The calculated serum anion gap in mEq/L (serum sodium - [serum chloride + bicarbonate]) gives an estimate of the unmeasured anions in plasma, which in DKA are ketoacids. The anion gap is typically more than 10 to 12 mEq/L in DKA.

• Normalization of the anion gap reflects correction of the ketoacidosis as these anions are removed from the blood.

Creatine phosphokinase

• Rhabdomyolysis is common in cocaine users with concurrent DKA, and creatine phosphokinase levels should be assessed in known or suspected cocaine users who present with DKA.[28]

• In rhabdomyolysis, pH and serum osmolality are usually mildly elevated and plasma glucose and ketones are normal. Myoglobinuria and/or hemoglobinuria are detected on urinalysis.

Serum lactate

• Measured to exclude lactic acidosis. Lactate levels are normal in DKA but elevated in lactic acidosis.
Diabetic ketoacidosis

**Diagnosis**

**Liver function tests (LFTs)**

- Usually normal, and are used to screen for an underlying hepatic precipitant. Abnormal LFTs indicate underlying liver disease such as fatty liver, or other conditions such as congestive heart failure.

**Serum amylase and lipase**

- Amylase is elevated in the majority of patients with DKA, but this may be due to nonpancreatic sources such as parotid glands.
- Serum lipase is usually normal and may be beneficial in differentiating pancreatitis in patients with elevated amylase level. However, mildly elevated serum lipase level in the absence of pancreatitis has also been reported in patients with DKA.[1]

**Plasma osmolality**

- This is variable in DKA.

**CBC with differential**

- Leukocytosis is present in hyperglycemic crises and correlates with blood ketone levels. However, leukocytosis >25,000/microliter may indicate infection and requires further evaluations.[1]

**Additional tests**

**ECG**

- Used to exclude myocardial infarction (MI) as a precipitant or to look for cardiac effects of electrolyte disturbances (usually of potassium). Evidence of MI includes Q waves or ST segment changes. Evidence of hypokalemia (U waves) or hyperkalemia (tall T waves) may be present.
- A high index of suspicion for MI should be maintained as diabetic patients often present with atypical symptoms.

**Chest x-ray**

- Indicated to exclude pneumonia. In pneumonia, may show typical changes of pneumonia including infiltration, consolidation, effusions, and cavitation.

**Blood, urine, or sputum cultures**

- Should be obtained if there are signs of infection such as chills, constitutional upset (e.g., fatigue, confusion, anxiety), or symptoms and signs of specific infections. The most common precipitating infections are pneumonia and urinary tract infections. Patients are usually normothermic or hypothermic due to peripheral vasodilation so fever may not be seen.

**Cardiac biomarkers**

- Usually normal, but are elevated if MI is the precipitant. A high index of suspicion should be maintained as diabetic patients often present with atypical symptoms.

**Typical deficits in mild DKA**

Typical deficits[18]
Diabetic ketoacidosis

Diagnosis

Mild DKA:

- Total water (L): 6
- Water (mL/kg): 100
- Na+ (mEq/kg): 7 to 10
- Cl- (mEq/kg): 3 to 5
- K+ (mEq/kg): 3 to 5
- PO4 (mmol/kg): 5 to 7
- Mg++ (mEq/kg): 1 to 2
- Ca++ (mEq/kg): 1 to 2.

Notes: Deficits based on per kg of body weight.

Risk factors

Strong

inadequate or inappropriate insulin therapy

- Reduction in the net effective concentration of insulin leads to impaired carbohydrate, lipid, and ketone metabolism in DKA. Decreased insulin results in increased gluconeogenesis, accelerated glycogenolysis, and impaired glucose utilization by peripheral tissues.[1]
- Non-compliance with insulin therapy has been found to be the leading precipitating factor in black people and is present in over 30% of patients with DKA.[18][9] Psychological and social factors may impact on glycemic control, and low socio-economic status is correlated with a higher risk for DKA.[19][20]

infection

- The most common precipitating factor in DKA is infection. Increased counter-regulatory hormones, particularly epinephrine, as a systemic response to infection lead to insulin resistance, increased lipolysis, ketogenesis, and volume depletion, which may contribute to the development of hyperglycemic crises in patients with diabetes.[1]

myocardial infarction#

- Underlying cardiovascular events, particularly myocardial infarction, provoke the release of counter-regulatory hormones that are likely to result in DKA in patients with diabetes.[1][21]

Weak

pancreatitis

- Medical conditions such as pancreatitis, characterized by increased levels of counter-regulatory hormones and compromised access to water and insulin, may contribute in the development of hyperglycemic crises.[1][22]

stroke

- Acute medical events such as stroke, with increased levels of counter-regulatory hormones and compromised access to water and insulin, may contribute to the development of hyperglycemic crises.[1]
Diabetic ketoacidosis

Diagnosis

**Diagnosis**

**acromegaly**
- Hormonal derangements in some endocrine glands lead to increased counter-regulatory hormones and development of DKA in patients with concomitant diabetes.[23]

**hyperthyroidism**
- Hormonal derangements in some endocrine glands lead to increased counter-regulatory hormones and development of DKA in patients with concomitant diabetes.[24]

**drugs (e.g., corticosteroids, thiazides, pentamidine, sympathomimetics, second-generation antipsychotics, cocaine, immune checkpoint inhibitors, or SGLT-2 inhibitors)**
- Drugs that affect carbohydrate metabolism may precipitate hyperglycemic crises.[25] [11] [26] [27] Cocaine abuse may be an independent risk factor associated with recurrent DKA.[28] [10]
- Sodium-glucose cotransporter-2 (SGLT-2) inhibitors (e.g., canagliflozin, dapagliflozin, empagliflozin), used for glycemic control of type 2 diabetes, have been the subject of an FDA warning about a risk for DKA.[29] Immune checkpoint inhibitor therapy for cancer (PD-1 and PD-L1 blocking antibodies such as nivolumab, pembrolizumab, and avelumab) appears to be associated with a risk for DKA and type 1 diabetes mellitus.[30] [31]

**Cushing syndrome**
- Hypercortisolism leads to insulin resistance and may occasionally precipitate DKA in patients with concomitant diabetes; it more commonly precipitates hyperosmolar hyperglycemic state.

**Hispanic or black ancestry**
- Ancestry plays a role in ketosis-prone diabetes, with DKA a presenting manifestation of undiagnosed type 2 diabetes in young adults. Approximately 80% of obese black patients with DKA have type 2 diabetes, characterized by higher insulin secretion, the absence of autoimmune markers, and a lack of human leukocyte antigen (HLA) genetic association compared with lean patients with type 1 diabetes.[3]

**bariatric surgery**
- DKA has been reported in patients with type 1 diabetes who have had bariatric surgery.[32]

**History & examination factors**

**Other diagnostic factors**

**polyuria (common)**
- Symptom of hyperglycemia.

**polyphagia (common)**
- Symptom of hyperglycemia.

**polydipsia (common)**
- Symptom of hyperglycemia.
Diabetic ketoacidosis

**Diagnosis**

- **weight loss (common)**
  - Symptom of hyperglycemia.

- **weakness (common)**
  - Symptom of hyperglycemia.

- **nausea or vomiting (common)**
  - Abdominal pain, nausea, and vomiting in DKA correlate with the degree of acidosis and may be confused with acute abdominal crisis.[1]

- **abdominal pain (common)**
  - Abdominal pain, nausea, and vomiting in DKA correlate with the degree of acidosis and may be confused with acute abdominal crisis.[1]

- **dry mucous membranes (common)**
  - Sign of volume depletion.

- **poor skin turgor (common)**
  - Sign of volume depletion.

- **sunken eyes (common)**
  - Sign of volume depletion.

- **tachycardia (common)**
  - Sign of volume depletion.

- **hypotension (common)**
  - Sign of volume depletion.

- **Kussmaul respiration (common)**
  - Rapid and deep respiration due to acidosis. Common in DKA.

- **acetone breath (common)**
  - Sign of ketosis. Common in DKA.

- **altered mental status (common)**
  - Mental status may be altered, and varies from alert in mild DKA to stupor/coma in severe DKA. Studies have shown that acidosis is independently associated with altered sensorium in DKA patients, but hyperosmolarity and serum ketone levels are not. Combination of hyperosmolarity and acidosis predicts altered sensorium with good sensitivity (61%) and specificity (87%) in DKA patients.[43]

- **hypothermia (uncommon)**
  - Although concomitant infection is common, patients usually are normothermic or hypothermic due to peripheral vasodilation. Severe hypothermia is a poor prognostic sign.[44]
**Diagnostic tests**

### 1st test to order

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>plasma glucose</strong></td>
<td></td>
</tr>
<tr>
<td>• A plasma glucose test should be performed as an initial laboratory evaluation. In DKA, it is usually &gt;250 mg/dL with acidosis and ketonemia.</td>
<td>elevated</td>
</tr>
<tr>
<td>• However, 10% of DKA patients present with blood glucose &lt;250 mg/dL, which is termed euglycemic DKA.[1]</td>
<td></td>
</tr>
<tr>
<td><strong>ABG</strong></td>
<td></td>
</tr>
<tr>
<td>• Acidosis is essential for the diagnosis of DKA. Arterial pH measurement is necessary for diagnosis of DKA, but venous pH is recommended for monitoring treatment, due to the pain and risk of infection in obtaining frequent arterial samples. A venous pH sample is usually 0.03 units lower than arterial pH, and this difference should be considered.</td>
<td>pH varies from 7.00 to 7.30 in DKA; arterial bicarbonate ranges from &lt;10 mEq/L in severe DKA to &gt;15 mEq/L in mild DKA</td>
</tr>
<tr>
<td>• In hyperosmolar hyperglycemic state, the arterial pH is usually &gt;7.30 and the arterial bicarbonate is &gt;15 mEq/L.[1]</td>
<td></td>
</tr>
<tr>
<td><strong>capillary or serum ketones</strong></td>
<td></td>
</tr>
<tr>
<td>• There are three main ketones that are produced in DKA that can be measured: acetone, acetoacetate, and beta-hydroxybutyrate (BOHB).</td>
<td>beta-hydroxybutyrate elevated ≥3.8 mmol/L in adults or ≥3.0 mmol/L in children</td>
</tr>
<tr>
<td>• In early DKA, acetoacetate concentration is low, but it is a major substrate for ketone measurement by many laboratories (nitroprusside reaction method). Therefore, serum ketone measurement by usual laboratory techniques has a high specificity, but low sensitivity for the diagnosis of DKA; hence a negative test for serum ketones does not exclude DKA. Acetone is rarely measured due to its volatile nature.[41] Conversely, BOHB is an early and abundant ketoacid that can be the first signal of the development of DKA. Point-of-care BOHB testing is widely available and is highly sensitive and specific for the diagnosis of DKA.[42]</td>
<td></td>
</tr>
<tr>
<td>• During the treatment of DKA, BOHB is converted to acetoacetate, which is detected by the nitroprusside method. Therefore, the increase in acetoacetate during the treatment of DKA may mistakenly indicate a worsening of ketonemia.</td>
<td></td>
</tr>
<tr>
<td>• Another potential source of error in detecting ketone bodies is the patient’s medications. Some drugs, such as the ACE inhibitor captopril, contain sulfhydryl groups that can react with the reagent in the nitroprusside test and give a false-positive result. Therefore, clinical judgement and other biochemical tests will be required in patients who are receiving such medications.[1]</td>
<td></td>
</tr>
<tr>
<td><strong>urinalysis</strong></td>
<td></td>
</tr>
<tr>
<td>• Glucose and ketones are typical findings in DKA.[1]</td>
<td>positive for glucose and ketones; positive for leukocytes and nitrites in the presence of infection</td>
</tr>
<tr>
<td><strong>serum BUN</strong></td>
<td></td>
</tr>
<tr>
<td>• Increased due to volume depletion.[1]</td>
<td>elevated</td>
</tr>
<tr>
<td><strong>serum creatinine</strong></td>
<td></td>
</tr>
<tr>
<td>• Increased due to volume depletion.[1]</td>
<td>elevated</td>
</tr>
<tr>
<td>Test</td>
<td>Result</td>
</tr>
<tr>
<td>----------------------</td>
<td>-------------------------</td>
</tr>
<tr>
<td><strong>serum sodium</strong></td>
<td>usually low</td>
</tr>
</tbody>
</table>
| • Serum sodium is usually low due to osmotic reflux of water from the intracellular to extracellular space in the presence of hyperglycemia. Total sodium deficit is 7 to 10 mEq/kg. Hypernatremia in the presence of hyperglycemia in DKA indicates profound volume depletion. Alternately, in the presence of high serum chylomicron concentration, pseudonormoglycemia and pseudohyponatremia may occur in DKA. • The corrected serum sodium level should be evaluated as this is used to guide appropriate fluid replacement. The equation for conventional units is: corrected sodium (mEq/L) = measured sodium (mEq/L) + 0.016 (glucose [mg/dL] - 100).
| **serum potassium**  | usually elevated        |
| • Total potassium deficit is 3 to 5 mEq/kg. Serum potassium is usually elevated due to extracellular shift of potassium caused by insulin insufficiency, hypertonicity, and acidemia, but the total body potassium concentration is low due to increased diuresis. Therefore, low potassium level on admission indicates severe total-body potassium deficit.[1] [18] |
| **serum chloride**   | usually low             |
| • Total chloride deficit is 3 to 5 mEq/kg.[1] [18] |
| **serum magnesium**  | usually low             |
| • Total body deficit of magnesium is usually 1 to 2 mEq/kg.[1] [18] |
| **serum calcium**    | usually low             |
| • Total body calcium deficit is usually about 1 to 2 mEq/kg.[1] [18] |
| **serum phosphate**  | normal or elevated      |
| • Despite the total body phosphate deficit averaging 1.0 mmol/kg, serum phosphate is often normal or increased at presentation, but decreases with insulin therapy.[1] [18] |
| **anion gap calculation** | elevated anion gap (>10-12 mEq/L) |
| • Anion gap is calculated by subtracting the sum of serum chloride and bicarbonate from measured sodium concentration. [1] |
| **serum creatine phosphokinase** | elevated in rhabdomyolysis |
| • In patients with history of cocaine abuse and DKA, rhabdomyolysis is common; therefore, checking creatine phosphokinase level can be initially assessed in patients with DKA if clinically indicated. • In rhabdomyolysis, pH and serum osmolality are usually mildly elevated and plasma glucose and ketones are normal. Myoglobinuria and/or hemoglobinuria are detected in urinalysis.[1] [18] |
| **serum lactate**    | elevated in lactic acidosis |
| • Plasma glucose and serum ketones are normal in lactic acidosis. Serum lactate is >5 mmol/L in lactic acidosis.[1] |
| **LFT**              | usually normal          |
| • Used to identify underlying diseases such as fatty liver or congestive heart failure.[1] |
| **serum amylase**    | usually elevated due to extrapancreatic sources |
| • Amylase is elevated in majority of patients with DKA, but this may be due to nonpancreatic sources such as parotid glands.[1] |
### Test

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>serum lipase</td>
<td>serum lipase may be beneficial in differentiating pancreatitis in patients with elevated amylase level. However, mildly elevated serum lipase level in the absence of pancreatitis has also been reported in patients with DKA. [1]</td>
</tr>
<tr>
<td>serum osmolality</td>
<td>The serum osmolality is variable in DKA but is &gt;320 mOsm/kg in hyperosmolar hyperglycemic state. [1]</td>
</tr>
<tr>
<td>CBC</td>
<td>Leukocytosis is present in hyperglycemic crises and correlates with blood ketone levels. However, leukocytosis &gt;25,000/microliter may indicate infection and requires further evaluations. [1]</td>
</tr>
</tbody>
</table>

### Other tests to consider

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>chest x-ray</td>
<td>The most common infections are pneumonia and urinary tract infections. [1]</td>
</tr>
<tr>
<td>ECG</td>
<td>If clinically indicated, should be performed for identification of the precipitating cardiovascular diseases, such as myocardial infarction (MI) or severe electrolyte abnormalities. [1]</td>
</tr>
<tr>
<td>cardiac biomarkers</td>
<td>MI is a common precipitant of DKA in diabetic patients. [1]</td>
</tr>
<tr>
<td>blood, urine, or sputum cultures</td>
<td>If indicated clinically, further sepsis workup should be performed. [1]</td>
</tr>
</tbody>
</table>
## Differential diagnosis

<table>
<thead>
<tr>
<th>Condition</th>
<th>Differentiating signs / symptoms</th>
<th>Differentiating tests</th>
</tr>
</thead>
</table>
| **Hyperosmolar hyperglycemic state (HHS)** | • Patients are typically older than patients with DKA and are usually patients with type 2 diabetes. Older nursing home residents with poor fluid intake are at high risk.  
• Symptoms evolve insidiously over days to weeks.  
• Mental obtundation and coma are more frequent. Focal neurologic signs (hemianopia and hemiparesis) and seizures are also seen. Seizures may be the dominant clinical features.[1] | • Serum glucose is >600 mg/dL. Serum osmolality is usually >320 mOsm/kg.  
• Urine ketones are normal or only mildly positive. Serum ketones are negative.  
• Anion gap is variable but typically <12 mEq/L.  
• Total chloride deficit is 5 to 15 mEq/kg.  
• ABG: arterial pH is typically >7.30, whereas in DKA it ranges from 7.00 to 7.30. Arterial bicarbonate is >15 mEq/L. |
| **Lactic acidosis** | • The presentation is identical to that of DKA. In pure lactic acidosis, the serum glucose and ketones should be normal and the serum lactate concentration should be elevated. | • Serum lactate >5 mmol/L.[1] |
| **Starvation ketosis** | • Starvation ketosis results from inadequate carbohydrate availability resulting in physiologically appropriate lipolysis and ketone production to provide fuel substrates for muscle. | • The blood glucose is usually normal. Although the urine can have large amounts of ketones, the blood rarely does. Arterial pH is normal and the anion gap is at most mildly elevated.[1] |
| **Alcoholic ketoacidosis** | • Classically, these are people with long-standing alcohol use disorder for whom ethanol has been the main caloric source for days to weeks. The ketoacidosis occurs when for some reason alcohol and caloric intake decreases. | • In isolated alcoholic ketoacidosis, the metabolic acidosis is usually mild to moderate in severity. The anion gap is elevated. Serum and urine ketones are always present. Blood alcohol may be undetectable and the patient may be hypoglycemic.[1] |
| **Salicylate poisoning** | • Can be differentiated by history and laboratory investigation. Salicylate intoxication produces an anion gap metabolic acidosis usually with a respiratory alkalosis. | • The plasma glucose is normal or low, ketones are negative, osmolality is normal, and salicylates are positive in blood and/or urine. It should be noted that salicylates may cause false-positive or false-
Diabetic ketoacidosis

**Condition** | **Differentiating signs / symptoms** | **Differentiating tests**
--- | --- | ---
**Ethylene glycol/methanol intoxication** | • Methanol and ethylene glycol also produce an anion gap metabolic acidosis without hyperglycemia or ketones. | • Methanol/ethylene glycol serum levels are elevated. They can produce an increase in the measured serum osmolality.[1]

**Uremic acidosis** | • This is characterized by markedly elevated BUN and creatinine with normal plasma glucose. The pH and anion gap are usually mildly abnormal. | • Elevated BUN usually >200 mg/dL and elevated creatinine usually >10 mg/dL.[1]

---

**Diagnostic criteria**

**Hyperglycemic crises in adult patients with diabetes: a consensus statement from the American Diabetes Association[1]**

**Plasma glucose (mg/dL)**

• >250 in DKA.

**Arterial pH**

• 7.25 to 7.3 in mild DKA  
• 7.00 to <7.24 in moderate DKA  
• <7.00 in severe DKA.

**Serum bicarbonate (mEq/L)**

• 15-18 in mild DKA  
• 10-15 in moderate DKA  
• <10 in severe DKA.

**Urine and serum ketones (nitroprusside reaction method)**

• + in DKA.

**Effective serum osmolality (mOsm/kg)**

• variable in DKA.

**Anion gap (mEq/L)**

• >10 in mild DKA  
• >12 in moderate and severe DKA.

**Mental status**
Diabetic ketoacidosis

Diagnosis

• alert in mild DKA
• alert/drowsy in moderate DKA
• stupor/coma in severe DKA.[1]

The most widely used diagnostic criteria for DKA are plasma glucose >250 mg/dL, arterial pH <7.3, and presence of ketonemia and/or ketonuria. However, severity of DKA or the required number of criteria for diagnosis have not been officially stated, and the above-mentioned classification has been based heavily on prospective studies of DKA.[1]
Step-by-step treatment approach

The main goals of treatment are:

- Restoration of volume deficits
- Resolution of hyperglycemia and ketosis/acidosis
- Correction of electrolyte abnormalities (potassium level should be >3.3 mEq/L before initiation of insulin therapy; use of insulin in a patient with hypokalemia may lead to respiratory paralysis, cardiac arrhythmias, and death)
- Treatment of the precipitating events and prevention of complications.

It must be emphasized that successful treatment requires frequent monitoring of clinical and laboratory parameters to achieve resolution criteria. A treatment protocol and a flow sheet for recording the treatment stages and laboratory data should be maintained.[1] [46] [47] [48]

Initial and supportive treatment

The majority of patients present to the emergency department, where treatment should be initiated. There are several important steps that should be followed in early management:

- Fluid therapy should be started immediately after initial laboratory evaluations.
- Infusion of isotonic solution of 0.9% sodium chloride at a rate of 1.0 to 1.5 L/hour should be used for the first hour of fluid therapy.

Indications for admission to the intensive care unit (ICU) are hemodynamic instability or cardiogenic shock, altered mental status, respiratory insufficiency, severe acidosis, and hyperosmolar state with coma.

The diagnosis of hemodynamic instability should be made by observing for hypotension and clinical signs of poor tissue perfusion, including oliguria, cyanosis, cool extremities, and altered mental state. After admission to ICU, central venous and arterial lines are required, with continuous percutaneous oximetry. Oxygenation and airway protection are critical. Intubation and mechanical ventilation are commonly required, with constant monitoring of respiratory parameters. Nasogastric suctioning is always performed because of frequent ileus and danger of aspiration.

Initial management in hemodynamically unstable patients includes fluid resuscitation to correct hypovolemia and hypotension, close monitoring, and vasopressor therapy. Dopamine is the vasopressor of choice, given in an intravenous infusion whose rate is adjusted according to blood pressure and other hemodynamic parameters. If the patient remains hypotensive despite moderate doses of dopamine, a direct vasoconstrictor (e.g., norepinephrine) should be started and titrated to maintain a mean arterial pressure of 60 mmHg.[1] [52]

Fluid therapy

Fluid deficit averages 6 liters.[53] After the initial management, continuous fluid therapy should be started. The goal is the restoration of fluid loss. Correction of fluid deficits should be undertaken gradually over 12-24 hours, as overly rapid correction can result in the patient developing cerebral edema.[54] [55]

After initial therapy with 1.0 to 1.5 L of isotonic solution (0.9% NaCl) for the first hour of admission in all patients, hydration status should be evaluated clinically. The presence of orthostatic hypotension or supine hypotension with dry mucous membranes and poor skin turgor indicates severe volume depletion, which should be treated by infusion of 0.9% NaCl at the rate of 1.0 L/hour until signs of severe volume
Diabetic ketoacidosis

Depletion are resolved. These patients then continue to receive fluid therapy as for mild volume depletion, based on the corrected serum sodium level.

In patients with mild volume depletion (characterized by an absence of hypotension), corrected serum sodium level should be evaluated (corrected sodium [mEq/L] = measured sodium [mEq/L] + 0.016 [glucose (mg/dL) - 100]).

- In hyponatremic patients: 0.9% NaCl should be started at 250-500 mL/hour and when the plasma glucose reaches 200 mg/dL, fluid therapy should be changed to 5% dextrose with 0.45% NaCl at 150-250 mL/hour.[1] [52]
- In hypernatremic or eunatremic patients, 0.45% NaCl at 250-500 mL/hour is recommended and when plasma glucose reaches 200 mg/dL, it should be changed to 5% dextrose with 0.45% NaCl at 150-250 mL/hour.[1] [40] [52] [56]

Insulin therapy

The goal is the steady but gradual reduction of serum glucose and plasma osmolality by low-dose insulin therapy, in order to reduce the risk of treatment complications including hypoglycemia and hypokalemia.

Patients should receive a continuous intravenous infusion of regular insulin after exclusion of hypokalemia (i.e., potassium level should be >3.3 mEq/L before initiation of insulin therapy). Two alternative low-dose regimens are recommended by current guidelines.[1] [45] The first option is a continuous intravenous infusion of regular insulin at a dose of 0.14 units/kg/hour (approximately 10 units/hour in a 70 kg patient) with no initial bolus.[1] This is based on studies that show the use of low-dose regular insulin administered by intravenous infusion is sufficient for the treatment of DKA, provided the dose is above 0.1 units/kg/hour. The alternative regimen involves an initial intravenous bolus dose of 0.1 units/kg followed by a continuous infusion at a dose of 0.1 units/kg/hour.[53] These low-dose insulin therapy protocols decrease plasma glucose concentration at a rate of 50 to 75 mg/dL/hour.[1]

If plasma glucose does not fall by at least 10% or 50 mg/dL in the first hour of insulin infusion, then a dose of 0.14 units/kg of regular insulin should be administered as an intravenous bolus and the continuous insulin infusion rate should be continued (either 0.1 units/kg/hour or 0.14 units/kg/hour depending on the regimen selected).[1] [53] Insulin injection by a sliding scale is no longer recommended. When serum glucose is <200 mg/dL, the infusion can be reduced to 0.02 to 0.05 units/kg/hour, at which time dextrose may be added to the intravenous fluids.[1] [53] The rate of insulin infusion (or the dextrose concentration) should then be adjusted to maintain a plasma glucose level of between 150-200 mg/dL.[1]

Patients with severe DKA (plasma glucose >250 mg/dL, arterial pH <7.00, serum bicarbonate <10 mEq/L), hypotension, anasarca (severe generalized edema), or associated severe critical illness should be managed with intravenous regular insulin in the ICU using the regimen described above.[1] [57] [58] [59] Patients with mild to moderate DKA (plasma glucose >250 mg/dL, arterial pH 7.00 to 7.30, serum bicarbonate 10-18 mEq/L) that is not complicated by acute myocardial infarction, congestive heart failure, end-stage renal or hepatic failure, steroid use, or pregnancy, may be given rapid-acting insulin subcutaneously as an alternative to intravenous regular insulin.[60] [61] [62] This has been demonstrated to be safe and effective from studies in adults in one center.[1] A suggested protocol would be an initial subcutaneous injection of rapid-acting insulin at a dose of 0.3 units/kg, followed 1 hour later by another subcutaneous injection of 0.2 units/kg. Thereafter, they should receive 0.2 units/kg every 2 hours until blood glucose becomes <250 mg/dL. At this point, the insulin dose should be decreased by half to 0.1 units/kg every 2 hours until the resolution of DKA.[58] Until the results of these studies are replicated in
multicenter trials, the administration of continuous intravenous infusion of regular insulin should remain the preferred route because of its short half-life and easy titration (compared with the delayed onset of action and prolonged half-life of subcutaneously administered insulin). However, in places where there are increased waiting times for ICU admission or with limited medical resources, the use of insulin analogs for the treatment of mild uncomplicated DKA episodes can be considered in outpatient, general wards, or emergency departments.

Management of adult DKA. Abbreviations: blood glucose (BG); diabetic ketoacidosis (DKA); hour (h); intravenous (IV); subcutaneous (SC)


Potassium therapy

Insulin therapy and correction of acidemia and hyperosmolality will drive potassium into cells, which may cause serious hypokalemia. The goal, therefore, is to correct the actual potassium deficits and thereby prevent fatal complications of hypokalemia, including respiratory paralysis and cardiac dysrhythmia.

Insulin therapy should be withheld until the serum potassium level reaches 3.3 mEq/L. Likewise, if plasma potassium falls below 3.3 mEq/L at any point during therapy, insulin should be stopped and potassium replaced intravenously. In all patients with a serum potassium level <5.3 mEq/L and an adequate urine output of >50 mL/hour, 20-30 units (mEq) of potassium should be added to each liter of infusion fluid to prevent hypokalemia caused by insulin therapy. If potassium level is >5.3 mEq/L, replacement is not needed but potassium level should be checked every 2 hours.[1]
**Bicarbonate therapy**

Bicarbonate use in DKA remains controversial. At arterial blood pH >7.0, administration of insulin blocks lipolysis and resolves ketoacidosis without the need to add bicarbonate. Administering bicarbonate therapy in these patients may result in increased risk of hypokalemia, decreased tissue oxygen uptake, and cerebral edema.

Bicarbonate therapy may be used in adult patients with an arterial blood pH <7 in DKA, although data are limited.[63] Based on studies in adult patients with an arterial blood pH of 6.9 to 7.0, 50 mmol sodium bicarbonate in 200 mL sterile water with 10 mEq potassium chloride (KCl) may be administered over 1 hour until pH is >7.0.

In adult patients with pH <6.9, it is recommended that 100 mmol sodium bicarbonate in 400 mL sterile water (an isotonic solution) with 20 mEq KCl be administered at a rate of 200 mL/hour for 2 hours until pH >7.0. For monitoring of treatment, venous pH is sufficient and should be checked at least each hour in this setting. Treatment should be repeated every 2 hours until pH >7.0.

Bicarbonate therapy as well as insulin therapy lowers serum potassium; therefore, KCl is added to isotonic bicarbonate infusion.[1] [64]
**Phosphate therapy**

Despite total body phosphate deficits in DKA that average 1.0 mmol/kg of body weight, serum phosphate is often normal or increased at presentation, but decreases with insulin therapy. Previous studies have failed to show any beneficial effects of phosphate replacement in DKA patients. Therefore, routine replacement of phosphate is not recommended.

However, to avoid cardiac, respiratory, and skeletal muscle dysfunction, careful phosphate therapy may be indicated in patients with cardiac dysfunction (e.g., with signs of left ventricular dysfunction), symptomatic anemia, or respiratory depression (e.g., decreased oxygen saturation), and in those with confirmed hypophosphatemia (serum phosphate concentration <1.0 mg/dL).[1]
**Monitoring of therapy**

Monitoring of respiratory parameters and hemodynamic status are essential in hemodynamically unstable patients.

Subsequent to initial laboratory evaluation, serum glucose and electrolytes are measured at least hourly; calcium, magnesium, and phosphate are checked every 2 hours, and BUN, creatinine, and ketones every 2-6 hours, depending on the patient’s clinical condition and response to therapy.

Serial beta hydroxybutyrate (BOHB) measurements may aid monitoring of the response to treatment in DKA. However, measurement of ketone bodies, in the absence of a meter with capacity to measure BOHB, is not recommended. BOHB is converted to acetoacetate, which is detected by the nitroprusside method, during the treatment of DKA. Therefore, the increase in acetoacetate during DKA treatment may mistakenly indicate a worsening of ketonemia.

Present evidence suggests monitoring bicarbonate, anion gap, and pH to reflect the response to therapy. A flow sheet classifying these findings as well as mental status, vital signs, insulin dose, fluid and electrolytes therapies, and urine output allows easy analysis of response to therapy and resolution of crises. Metabolic panel measurement during DKA therapy provides dynamic information on the changes in renal function and sodium level.

Management and monitoring should continue until resolution of DKA. The criteria for resolution are:[1]

- plasma glucose is <200 mg/dL (at this point, insulin can be decreased by 50%)
- serum bicarbonate is >18 mEq/L
- venous pH is >7.3
- anion gap is <10.

**Treatment details overview**

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: see disclaimer
## Treatment

### Acute

<table>
<thead>
<tr>
<th>Severe Volume Depletion</th>
<th>Serum Potassium</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3.3 mEq/L</td>
<td>1st intravenous fluids</td>
<td>plus supportive care + ICU admission, plus potassium therapy, plus intravenous insulin once serum potassium reaches 3.3 mEq/L, adjunct vaspressors, adjunct bicarbonate therapy, adjunct phosphate therapy</td>
</tr>
<tr>
<td>3.3 to 5.3 mEq/L</td>
<td>1st intravenous fluids</td>
<td>plus supportive care + ICU admission, plus intravenous insulin, plus potassium therapy, adjunct vaspressors, adjunct bicarbonate therapy, adjunct phosphate therapy</td>
</tr>
<tr>
<td>&gt;5.3 mEq/L</td>
<td>1st intravenous fluids</td>
<td>plus supportive care + ICU admission, plus intravenous insulin, adjunct vaspressors, adjunct bicarbonate therapy, adjunct phosphate therapy</td>
</tr>
</tbody>
</table>

### Mild to Moderate Volume Depletion: Hyponatremic

<table>
<thead>
<tr>
<th>Serum Potassium</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3.3 mEq/L</td>
<td>1st intravenous fluids</td>
</tr>
</tbody>
</table>
### Acute

#### (summary)

<table>
<thead>
<tr>
<th>Serum Potassium</th>
<th>1st</th>
<th>1st</th>
<th>Adjunct</th>
<th>Adjunct</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.3 to 5.3 mEq/L</td>
<td>Intravenous fluids</td>
<td>Supportive care ± ICU admission</td>
<td>Insulin</td>
<td>Potassium therapy</td>
</tr>
<tr>
<td>1st</td>
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<tr>
<td></td>
<td>Supportive care ± ICU admission</td>
<td>Insulin</td>
<td>Potassium therapy</td>
<td>Bicarbonate therapy</td>
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<td></td>
<td>Phosphate therapy</td>
</tr>
<tr>
<td>5.3 mEq/L</td>
<td>Intravenous fluids</td>
<td>Supportive care ± ICU admission</td>
<td>Insulin</td>
<td>Bicarbonate therapy</td>
</tr>
<tr>
<td></td>
<td></td>
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<td>Phosphate therapy</td>
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<tr>
<td>&gt;5.3 mEq/L</td>
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<td>Bicarbonate therapy</td>
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<td></td>
<td></td>
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<td>Phosphate therapy</td>
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</tbody>
</table>

#### Mild to Moderate Volume Depletion: Eunatremic or Hypernatremic

<table>
<thead>
<tr>
<th>Serum Potassium</th>
<th>1st</th>
<th>1st</th>
<th>Adjunct</th>
<th>Adjunct</th>
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</thead>
<tbody>
<tr>
<td>&lt;3.3 mEq/L</td>
<td>Intravenous fluids</td>
<td>Supportive care ± ICU admission</td>
<td>Potassium therapy</td>
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<tr>
<td>1st</td>
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<td></td>
<td>Supportive care ± ICU admission</td>
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<td>Potassium therapy</td>
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<tr>
<td></td>
<td>Supportive care ± ICU admission</td>
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<td>Bicarbonate therapy</td>
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</tr>
<tr>
<td>3.3 to 5.3 mEq/L</td>
<td>Intravenous fluids</td>
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<tr>
<td>1st</td>
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<td></td>
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</tbody>
</table>
### Acute Treatment

- **adjunct bicarbonate therapy**
- **adjunct phosphate therapy**

### Ongoing Treatment

**Summary**

DKA resolved and patient able to tolerate oral intake

1st establish regular subcutaneous insulin regime
Treatment options

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: see disclaimer.
Diabetic ketoacidosis

**TREATMENT**

**Acute**

**severe volume depletion**

- **serum potassium** <3.3 mEq/L

  **1st intravenous fluids**

  » Severe volume depletion is indicated by the presence of orthostatic hypotension or supine hypotension, dry mucous membranes, and poor skin turgor. Extreme cases may be hemodynamically unstable.

  » The goal of initial fluid therapy is to restore tissue perfusion. The initial choice of fluid is isotonic saline infused at a rate of 1.0 to 1.5 L (or 15-20 mL/kg body weight) for the first hour. In patients with severe volume depletion or cardiogenic shock, isotonic fluid therapy and hemodynamic monitoring should continue in the intensive care unit until the patient becomes stable.

  » Electrolytes should be checked at least hourly (to monitor potassium levels) and BUN, venous pH, creatinine, and glucose should be checked every 2-4 hours until the resolution of DKA.

  » When plasma glucose reaches 200 mg/dL, fluid therapy should be changed to 5% dextrose with 0.45% NaCl at 150-250 mL/hour in order to avoid hypoglycemia.[1]

**plus supportive care + ICU admission**

Treatment recommended for ALL patients in selected patient group

» Indications for intensive care unit (ICU) admission include hemodynamic instability or cardiogenic shock, altered mental status, respiratory insufficiency, and severe acidosis.

» After admission to ICU, central venous and arterial lines are required as well as Swan-Ganz catheterization and continuous percutaneous oximetry.

» Intubation and mechanical ventilation are commonly required, with constant monitoring of respiratory parameters.

» Nasogastric suctioning is always performed because of frequent ileus and danger of aspiration.[1]

**plus potassium therapy**

Treatment recommended for ALL patients in selected patient group

**Primary options**
**Acute**

- **potassium phosphate**: 20-30 mEq added to each liter of infusion fluid initially, adjust dose according to serum potassium level. If potassium is <3.3 mEq/L at any point of therapy, insulin should be discontinued.

  OR

- **potassium chloride**: 20-30 mEq added to each liter of infusion fluid initially, adjust dose according to serum potassium level. If potassium is <3.3 mEq/L at any point of therapy, insulin should be discontinued.

- Insulin therapy and correction of hyperosmolarity and acidemia decrease plasma concentration of potassium. For this reason, insulin therapy should be withheld until the serum potassium level reaches 3.3 mEq/L.

- Likewise, if plasma potassium falls <3.3 mEq/L at any point of therapy, insulin should be discontinued.

- The dose of potassium replacement is 20-30 mEq added to each liter of infusion fluid.[1]

- Choices are potassium phosphate or potassium chloride. One third of the potassium replacement should be administered as potassium phosphate to avoid excessive chloride administration.

- The serum potassium level should be monitored at least hourly and replacement adjusted accordingly.

  plus **intravenous insulin once serum potassium reaches 3.3 mEq/L**

  Treatment recommended for ALL patients in selected patient group

**Primary options**

- **insulin regular**: consult local protocols for dosing guidelines

- Insulin therapy should not be commenced until serum potassium reaches 3.3 mEq/L.

- Patients should receive a continuous intravenous infusion of regular insulin after exclusion of hypokalemia (i.e., potassium level should be >3.3 mEq/L before initiation of insulin therapy). Two alternative low-dose regimens are recommended by current guidelines.[1][45] The first option is a continuous intravenous infusion of regular insulin at a dose of 0.14 units/kg/hour.
### Acute

(approximately 10 units/hour in a 70 kg patient) with no initial bolus.[1] This is based on studies that show the use of low-dose regular insulin administered by intravenous infusion is sufficient for the treatment of DKA, provided the dose is >0.1 units/kg/hour. The alternative regimen involves an initial intravenous bolus dose of 0.1 units/kg followed by a continuous infusion at a dose of 0.1 units/kg/hour.[53] These low-dose insulin therapy protocols decrease plasma glucose concentration at a rate of 50-75 mg/dL/hour.[1]

> If plasma glucose does not fall by at least 10% or 50 mg/dL in the first hour of insulin infusion, then a dose of 0.14 units/kg of regular insulin should be administered as an intravenous bolus and the continuous insulin infusion rate should be continued (either 0.1 units/kg/hour or 0.14 units/kg/hour depending on the regimen selected).[1] [53] Insulin injection by a sliding scale is no longer recommended. When serum glucose reaches 200 mg/dL, the infusion can be reduced to 0.02 to 0.05 units/kg/hour, at which time dextrose may be added to the intravenous fluids.[1] [53] The rate of insulin infusion (or the dextrose concentration) should then be adjusted to maintain a plasma glucose level of between 150-200 mg/dL.[1]

> This regimen should be followed until all remaining criteria for resolution are met: serum bicarbonate >18 mEq/L, venous pH >7.3, and anion gap <10.[1]

### Adjunct vasopressors

Treatment recommended for SOME patients in selected patient group

#### Primary options

> **dopamine**: 5-10 micrograms/kg/min intravenously initially, adjust rate according to blood pressure and other hemodynamic parameters

#### Secondary options

> **norepinephrine**: 0.5 micrograms/kg/min intravenously initially, titrate to maintain a mean arterial pressure of 60 mmHg

> In hemodynamically unstable patients, vasopressor therapy (dopamine therapy) may also be required. Often these patients require high doses of dopamine, in the order of 20 micrograms/kg/minute. If the patient remains hypotensive despite moderate doses
Diabetic ketoacidosis

Treatment

### Acute

**adjunct bicarbonate therapy**

Treatment recommended for SOME patients in selected patient group

**Primary options**

- **Sodium bicarbonate:** serum pH 6.9 to 7.0: 50 mmol intravenous infusion over 1 hour until pH >7.0; serum pH <6.9: 100 mmol intravenous infusion at a rate of 200 mL/hour for 2 hours or until pH >7.0

- Bicarbonate therapy may be used in adult patients with pH <7 or a bicarbonate level <5 mEq/L, although data are limited.

- In adults with pH 6.9 to 7.0, 50 mmol sodium bicarbonate (1 ampule) in 200 mL sterile water with 10 mEq KCl may be administered over 1 hour until pH is >7.0.

- In adults with pH <6.9, we recommend that 100 mmol sodium bicarbonate in 400 mL sterile water with 20 mEq KCl be administered at a rate of 200 mL/hour for 2 hours or until pH >7.0. Treatment should be repeated every 2 hours until pH >7.0. Bicarbonate therapy, like insulin therapy, lowers serum potassium; therefore, KCl is added to isotonic bicarbonate.

**adjunct phosphate therapy**

Treatment recommended for SOME patients in selected patient group

**Primary options**

- **Potassium phosphate:** 20-30 mEq added to each liter of infusion fluid

- Routine replacement of phosphate is not recommended.

- However, to avoid cardiac, respiratory, and skeletal muscle dysfunction, careful phosphate therapy may be indicated in patients with cardiac dysfunction (e.g., with signs of left ventricular dysfunction), symptomatic anemia, or respiratory depression (e.g., decreased oxygen saturation), and in those with confirmed hypophosphatemia (serum phosphate concentration <1.0 mg/dL).

- The dose is 20-30 mEq/L potassium phosphate added to replacement fluids.
Diabetic ketoacidosis

Treatment

### Acute

<table>
<thead>
<tr>
<th>serum potassium 3.3 to 5.3 mEq/L</th>
<th>intravenous fluids</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Phosphate therapy above the recommended dose may result in severe hypocalcemia.[1] [75] [76]</td>
</tr>
<tr>
<td></td>
<td>Severe volume depletion is indicated by the presence of orthostatic hypotension or supine hypotension, dry mucous membranes, and poor skin turgor. Extreme cases may be hemodynamically unstable.</td>
</tr>
<tr>
<td></td>
<td>The goal of initial fluid therapy is to restore tissue perfusion. The initial choice of fluid is isotonic saline infused at a rate of 1.0 to 1.5 L (or 15-20 mL/kg body weight) for the first hour. In patients with severe volume depletion (i.e., orthostatic or supine hypotension, dry mucous membranes, and poor skin turgor) or cardiogenic shock, isotonic fluid therapy and hemodynamic monitoring should continue in the intensive care unit until the patient becomes stable.</td>
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<td>Electrolytes should be checked at least hourly (to monitor potassium levels) and BUN, venous pH, creatinine, and glucose should be checked every 2-4 hours until the resolution of DKA.</td>
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<td>When plasma glucose reaches 200 mg/dL, fluid therapy should be changed to 5% dextrose with 0.45% NaCl at 150-250 mL/hour in order to avoid hypoglycemia.[1]</td>
</tr>
</tbody>
</table>

**plus** supportive care + ICU admission

Treatment recommended for ALL patients in selected patient group

- Indications for intensive care unit (ICU) admission include hemodynamic instability or cardiogenic shock, altered mental status, respiratory insufficiency, and severe acidosis.
- After admission to ICU, central venous and arterial lines are required as well as Swan-Ganz catheterization and continuous percutaneous oximetry.
- Intubation and mechanical ventilation are commonly required, with constant monitoring of respiratory parameters.
- Nasogastric suctioning is always performed because of frequent ileus and danger of aspiration.

**plus** intravenous insulin

Treatment recommended for ALL patients in selected patient group
### Primary options

- **insulin regular**: consult local protocols for dosing guidelines

- Patients should receive a continuous intravenous infusion of regular insulin after exclusion of hypokalemia (i.e., potassium level should be >3.3 mEq/L before initiation of insulin therapy). Two alternative low-dose regimens are recommended by current guidelines. The first option is a continuous intravenous infusion of regular insulin at a dose of 0.14 units/kg/hour (approximately 10 units/hour in a 70 kg patient) with no initial bolus. This is based on studies that show the use of low-dose regular insulin administered by intravenous infusion is sufficient for the treatment of DKA, provided the dose is above 0.1 units/kg/hour. The alternative regimen involves an initial intravenous bolus dose of 0.1 units/kg followed by a continuous infusion at a dose of 0.1 units/kg/hour. These low-dose insulin therapy protocols decrease plasma glucose concentration at a rate of 50 to 75 mg/dL/hour.

- If plasma glucose does not fall by at least 10% or 50 mg/dL in the first hour of insulin infusion, then a dose of 0.14 units/kg of regular insulin should be administered as an intravenous bolus and the continuous insulin infusion rate should be continued (either 0.1 units/kg/hour or 0.14 units/kg/hour depending on the regimen selected). Insulin injection by a sliding scale is no longer recommended. When serum glucose reaches 200 mg/dL, the infusion can be reduced to 0.05 units/kg/hour, at which time dextrose may be added to the intravenous fluids. The rate of insulin infusion (or the dextrose concentration) should then be adjusted to maintain a plasma glucose level of between 150-200 mg/dL.

- This regimen should be followed until all remaining criteria for resolution are met: serum bicarbonate >18 mEq/L, venous pH >7.3, and anion gap <10.

- If plasma potassium falls below 3.3 mEq/L at any point, insulin should be discontinued and potassium replaced intravenously. Insulin therapy can be restarted when the potassium level returns to 3.3 mEq/L.

**plus potassium therapy**

Treatment recommended for ALL patients in selected patient group
Diabetic ketoacidosis

Treatment

**Acute**

**Primary options**

- **potassium phosphate**: 20-30 mEq added to each liter of infusion fluid initially, adjust dose according to serum potassium level. If potassium is <3.3 mEq/L at any point of therapy, insulin should be discontinued and potassium replaced intravenously. OR

- **potassium chloride**: 20-30 mEq added to each liter of infusion fluid initially, adjust dose according to serum potassium level. If potassium is <3.3 mEq/L at any point of therapy, insulin should be discontinued and potassium replaced intravenously.

- Insulin therapy and correction of hyperosmolarity and acidemia decrease the plasma concentration of potassium. Concurrent potassium replacement is recommended if the serum potassium is in the range 3.3 to 5.3 mEq/L, to prevent cardiac arrhythmias due to hypokalemia. The dose is 20-30 mEq added to each liter of infusion fluid. If potassium is <3.3 mEq/L at any point of therapy, insulin should be discontinued and potassium replaced intravenously.[1]

- Choices are potassium phosphate or potassium chloride. One third of the potassium replacement should be administered as potassium phosphate to avoid excessive chloride administration.

- The serum potassium level should be monitored at least hourly and replacement adjusted accordingly.

**adjunct vasopressors**

Treatment recommended for SOME patients in selected patient group

**Primary options**

- **dopamine**: 5-10 micrograms/kg/min intravenously initially, adjust rate according to blood pressure and other hemodynamic parameters

**Secondary options**

- **norepinephrine**: 0.5 micrograms/kg/min intravenously initially, titrate to maintain a mean arterial pressure of 60 mmHg
Diabetic ketoacidosis

### Acute

» In hemodynamically unstable patients, vasopressor therapy (dopamine therapy) may also be required. Often these patients require high doses of dopamine, in the order of 20 micrograms/kg/minute. If the patient remains hypotensive despite moderate doses of dopamine, a direct vasoconstrictor (e.g., norepinephrine) should be started.[1] [52]

**adjunct bicarbonate therapy**

Treatment recommended for SOME patients in selected patient group

**Primary options**

» **sodium bicarbonate**: serum pH 6.9 to 7.0: 50 mmol intravenous infusion over 1 hour until pH >7.0; serum pH <6.9: 100 mmol intravenous infusion at a rate of 200 mL/hour for 2 hours or until pH >7.0

» Bicarbonate therapy may be used in adult patients with pH <7 or a bicarbonate level <5 mEq/L, although data are limited.[1] [63]

» In adults with pH 6.9 to 7.0, 50 mmol sodium bicarbonate (1 ampule) in 200 mL sterile water with 10 mEq KCl may be administered over 1 hour until pH is >7.0.

» In adults with pH <6.9, we recommend that 100 mmol sodium bicarbonate in 400 mL sterile water with 20 mEq KCl be administered at a rate of 200 mL/hour for 2 hours or until pH >7.0. Treatment should be repeated every 2 hours until pH >7.0. Bicarbonate therapy, like insulin therapy, lowers serum potassium; therefore, KCl is added to isotonic bicarbonate.[64]

**adjunct phosphate therapy**

Treatment recommended for SOME patients in selected patient group

**Primary options**

» **potassium phosphate**: 20-30 mEq added to each liter of infusion fluid

» Routine replacement of phosphate is not recommended.

» However, to avoid cardiac, respiratory, and skeletal muscle dysfunction, careful phosphate therapy may be indicated in patients with cardiac dysfunction (e.g., with signs of left ventricular dysfunction), symptomatic anemia, or respiratory depression (e.g., decreased oxygen saturation), and in those with confirmed hypophosphatemia (serum phosphate concentration <1.0 mg/dL).[1]
Acute

- serum potassium >5.3 mEq/L

1st intravenous fluids

- Severe volume depletion is indicated by the presence of orthostatic hypotension or supine hypotension, dry mucous membranes, and poor skin turgor. Extreme cases may be hemodynamically unstable.

- The goal of initial fluid therapy is to restore tissue perfusion. The initial choice of fluid is isotonic saline infused at a rate of 1.0 to 1.5 L (or 15-20 mL/kg body weight) for the first hour. In patients with severe volume depletion (i.e., orthostatic or supine hypotension, dry mucous membranes, and poor skin turgor) or cardiogenic shock, isotonic fluid therapy and hemodynamic monitoring should continue in the intensive care unit until the patient becomes stable.

- Electrolytes should be checked at least hourly (to monitor potassium levels), and BUN, venous pH, creatinine, and glucose should be checked every 2-4 hours until the resolution of DKA.

- When plasma glucose reaches 200 mg/dL, fluid therapy should be changed to 5% dextrose with 0.45% NaCl at 150-250 mL/hour in order to avoid hypoglycemia.[1]

plus supportive care + ICU admission

Treatment recommended for ALL patients in selected patient group

- Indications for intensive care unit (ICU) admission include hemodynamic instability or cardiogenic shock, altered mental status, respiratory insufficiency, and severe acidosis.

- After admission to ICU, central venous and arterial lines are required as well as Swan-Ganz catheterization and continuous percutaneous oximetry.

- Intubation and mechanical ventilation are commonly required, with constant monitoring of respiratory parameters.

- Nasogastric suctioning is always performed because of frequent ileus and danger of aspiration.

plus intravenous insulin
Diabetic ketoacidosis

Treatment

**Acute**

<table>
<thead>
<tr>
<th>Treatment recommended for ALL patients in selected patient group</th>
</tr>
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</table>

**Primary options**

- **insulin regular**: consult local protocols for dosing guidelines

- Patients should receive a continuous intravenous infusion of regular insulin after exclusion of hypokalemia (i.e., potassium level should be >3.3 mEq/L before initiation of insulin therapy). Two alternative low-dose regimens are recommended by current guidelines.[1] [45] The first option is a continuous intravenous infusion of regular insulin at a dose of 0.14 units/kg/hour (approximately 10 units/hour in a 70 kg patient) with no initial bolus.[1] This is based on studies that show the use of low-dose regular insulin administered by intravenous infusion is sufficient for the treatment of DKA, provided the dose is above 0.1 units/kg/hour. The alternative regimen involves an initial intravenous bolus dose of 0.1 units/kg followed by a continuous infusion at a dose of 0.1 units/kg/hour.[53] These low-dose insulin therapy protocols decrease plasma glucose concentration at a rate of 50-75 mg/dL/hour.[1]

- If plasma glucose does not fall by at least 10% or 50 mg/dL in the first hour of insulin infusion, then a dose of 0.14 units/kg of regular insulin should be administered as an intravenous bolus and the continuous insulin infusion rate should be continued (either 0.1 units/kg/hour or 0.14 units/kg/hour depending on the regimen selected).[1] [53] Insulin injection by a sliding scale is no longer recommended. When serum glucose reaches 200 mg/dL, the infusion can be reduced to 0.02 to 0.05 units/kg/hour, at which time dextrose may be added to the intravenous fluids.[1] [53] The rate of insulin infusion (or the dextrose concentration) should then be adjusted to maintain a plasma glucose level of between 150-200 mg/dL.[1]

- This regimen should be followed until all remaining criteria for resolution are met: serum bicarbonate >18 mEq/L, venous pH >7.3, and anion gap <10.[1]

- Potassium replacement is not required, but potassium levels should be checked every 2 hours.

**adjunct vasopressors**

Treatment recommended for SOME patients in selected patient group
### Treatment

#### Acute

<table>
<thead>
<tr>
<th><strong>Primary options</strong></th>
</tr>
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<td><strong>dopamine</strong>: 5-10 micrograms/kg/min intravenously initially, adjust rate according to blood pressure and other hemodynamic parameters</td>
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<th><strong>Secondary options</strong></th>
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<td><strong>norepinephrine</strong>: 0.5 micrograms/kg/min intravenously initially, titrate to maintain a mean arterial pressure of 60 mmHg</td>
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*In hemodynamically unstable patients, vasopressor therapy (dopamine therapy) may also be required. Often these patients require high doses of dopamine, in the order of 20 micrograms/kg/minute. If the patient remains hypotensive despite moderate doses of dopamine, a direct vasoconstrictor (e.g., norepinephrine) should be started.*

**adjunct bicarbonate therapy**

Treatment recommended for SOME patients in selected patient group

<table>
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<tr>
<td><strong>sodium bicarbonate</strong>: serum pH 6.9 to 7.0: 50 mmol intravenous infusion over 1 hour until pH &gt;7.0; serum pH &lt;6.9: 100 mmol intravenous infusion over 2 hours or until pH &gt;7.0</td>
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*Bicarbonate therapy may be used in adult patients with pH <7 or a bicarbonate level <5 mEq/L, although data are limited.*

*In adults with pH 6.9 to 7.0, 50 mmol sodium bicarbonate (1 ampule) in 200 mL sterile water with 10 mEq KCl may be administered over 1 hour until pH is >7.0.*

*In adults with pH <6.9, we recommend that 100 mmol sodium bicarbonate in 400 mL sterile water with 20 mEq KCl be administered at a rate of 200 mL/hour for 2 hours or until pH >7.0. Treatment should be repeated every 2 hours until pH >7.0. Bicarbonate therapy, like insulin therapy, lowers serum potassium; therefore, KCl is added to isotonic bicarbonate.*

**adjunct phosphate therapy**

Treatment recommended for SOME patients in selected patient group

<table>
<thead>
<tr>
<th><strong>Primary options</strong></th>
</tr>
</thead>
</table>
### Acute

- **potassium phosphate**: 20-30 mEq added to each liter of infusion fluid

- Routine replacement of phosphate is not recommended.

- However, to avoid cardiac, respiratory, and skeletal muscle dysfunction, careful phosphate therapy may be indicated in patients with cardiac dysfunction (e.g., with signs of left ventricular dysfunction), symptomatic anemia, or respiratory depression (e.g., decreased oxygen saturation), and in those with confirmed hypophosphatemia (serum phosphate concentration <1.0 mg/dL).[1]

- The dose is 20-30 mEq/L potassium phosphate added to replacement fluids.

- Phosphate therapy above the recommended dose may result in severe hypocalcemia.[1] [75] [76]

### mild to moderate volume depletion: hyponatremic

- **serum potassium <3.3 mEq/L**

- **1st intravenous fluids**

  - Mild to moderate volume depletion is indicated by the absence of orthostatic hypotension or supine hypotension, dry mucous membranes, and poor skin turgor. The goal is to gradually replace half of the fluid deficit over 12-24 hours, to prevent complications such as cerebral edema.

  - The initial choice of fluid is isotonic saline infused at a rate of 1.0 to 1.5 L (or 15-20 mL/kg body weight) for the first hour.

  - Following the initial fluid replacement, corrected serum sodium level should be evaluated (corrected sodium [mEq/L] = measured sodium [mEq/L] + 0.016 [glucose (mg/dL) - 100]). In patients found to be hyponatremic, 0.9% NaCl should be started at 250-500 mL/hour.

  - Electrolytes should be checked at least hourly (to monitor potassium levels), and BUN, venous pH, creatinine, and glucose should be checked every 2-4 hours until the resolution of DKA.

  - When plasma glucose reaches 200 mg/dL, fluid therapy should be changed to 5% dextrose with 0.45% NaCl at 150-250 mL/hour in order to avoid hypoglycemia.[1]

- **plus supportive care ± ICU admission**
Treatment recommended for ALL patients in selected patient group

» Indications for intensive care unit (ICU) admission include altered mental status, respiratory insufficiency, and severe acidosis.

» After admission to ICU, central venous and arterial lines are required as well as Swan-Ganz catheterization and continuous percutaneous oximetry. Intubation and mechanical ventilation are commonly required, with constant monitoring of respiratory parameters. Nasogastric suctioning is always performed because of frequent ileus and danger of aspiration.

» Mild cases of DKA may be managed without ICU admission.[1]

plus potassium therapy

Treatment recommended for ALL patients in selected patient group

Primary options

» potassium phosphate: 20-30 mEq added to each liter of infusion fluid initially, adjust dose according to serum potassium level. If potassium is <3.3 mEq/L at any point of therapy, insulin should be discontinued and potassium replaced intravenously.

OR

» potassium chloride: 20-30 mEq added to each liter of infusion fluid initially, adjust dose according to serum potassium level. If potassium is <3.3 mEq/L at any point of therapy, insulin should be discontinued and potassium replaced intravenously.

» Insulin therapy and correction of hyperosmolality and acidemia decrease plasma concentration of potassium. For this reason, insulin therapy should be withheld until the serum potassium level reaches 3.3 mEq/L.

» Likewise, if plasma potassium falls <3.3 mEq/L at any point of therapy, insulin should be discontinued.

» The dose is 20-30 mEq added to each liter of infusion fluid.[1]

» Choices for potassium therapy are potassium phosphate or potassium chloride. One third of the potassium replacement should be
Diabetic ketoacidosis

**Treatment**

**Acute**

administered as potassium phosphate to avoid excessive chloride administration.

**plus**

insulin once serum potassium reaches 3.3 mEq/L

Treatment recommended for ALL patients in selected patient group

**Primary options**

- insulin regular: consult local protocols for dosing guidelines

**Secondary options**

- insulin aspart: consult local protocols for dosing guidelines

**OR**

- insulin lispro: consult local protocols for dosing guidelines

Insulin therapy should not be commenced until serum potassium reaches 3.3 mEq/L.

Patients should receive a continuous intravenous infusion of regular insulin after exclusion of hypokalemia (i.e., potassium level should be >3.3 mEq/L before initiation of insulin therapy). Two alternative low-dose regimens are recommended by current guidelines.[1][45] The first option is a continuous intravenous infusion of regular insulin at a dose of 0.14 units/kg/hour (approximately 10 units/hour in a 70 kg patient) with no initial bolus.[1] This is based on studies that show the use of low-dose regular insulin administered by intravenous infusion is sufficient for the treatment of DKA, provided the dose is above 0.1 units/kg/hour. The alternative regimen involves an initial intravenous bolus dose of 0.1 units/kg followed by a continuous infusion at a dose of 0.1 units/kg/hour.[53] These low-dose insulin therapy protocols decrease plasma glucose concentration at a rate of 50-75 mg/dL/hour.[1]

If plasma glucose does not fall by at least 10% or 50 mg/dL in the first hour of insulin infusion, then a dose of 0.14 units/kg of regular insulin should be administered as an intravenous bolus and the continuous insulin infusion rate should be continued (either 0.1 units/kg/hour or 0.14 units/kg/hour depending on the regimen selected).[1][53] Insulin injection by a sliding scale is no longer recommended. When serum glucose reaches 200 mg/dL, the infusion can be reduced to 0.02 to 0.05 units/kg/hour, at which
## Treatment

<table>
<thead>
<tr>
<th>Acute</th>
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</table>

| **time** dextrose may be added to the intravenous fluids.\[1\] \[53\] The rate of insulin infusion (or the dextrose concentration) should then be adjusted to maintain a plasma glucose level of 150-200 mg/dL.\[1\] |

| Patients with mild to moderate DKA (plasma glucose >250 mg/dL, arterial pH 7.00-7.30, serum bicarbonate 10-18 mEq/L) that is not complicated by acute MI, congestive heart failure, end-stage renal or hepatic failure, steroid use, or pregnancy, may be given rapid-acting insulin subcutaneously as an alternative to intravenous regular insulin.\[60\] \[61\] \[62\] This has been demonstrated to be safe and effective from studies in adults in one center.\[1\] A suggested protocol would be an initial subcutaneous injection of rapid-acting insulin at a dose of 0.3 units/kg, followed 1 hour later by another subcutaneous injection of 0.2 units/kg. Thereafter, they should receive 0.2 units/kg every 2 hours until blood glucose becomes <250 mg/dL. At this point, the insulin dose should be decreased by half to 0.1 units/kg every 2 hours until the resolution of DKA.\[58\] Until the results of these studies are replicated in multicenter trials, the administration of continuous intravenous infusion of regular insulin should remain the preferred route because of its short half-life and easy titration. This is compared with the delayed onset of action and prolonged half-life of subcutaneously administered insulin. However, in places where there are increased waiting times for intensive care unit (ICU) admission or with limited medical resources, the use of insulin analogs for the treatment of mild uncomplicated DKA episodes can be considered in outpatient, general wards, or emergency departments. Patients with severe DKA (plasma glucose >250 mg/dL, arterial pH <7.00, serum bicarbonate <10 mEq/L), hypotension, anasarca (severe generalized edema), or associated severe critical illness should be managed with intravenous regular insulin in the ICU using the regimen described above.\[1\] \[58\] \[57\] \[59\] This regimen should be followed until all remaining criteria for resolution are met: serum bicarbonate >18 mEq/L, venous pH >7.3, and anion gap <10.\[1\] |

**adjunct** bicarbonate therapy

Treatment recommended for SOME patients in selected patient group

**Primary options**
**Diabetic ketoacidosis**

**Treatment**

**Acute**

» **sodium bicarbonate**: serum pH 6.9 to 7.0: 50 mmol intravenous infusion over 1 hour until pH >7.0; serum pH <6.9: 100 mmol intravenous infusion at a rate of 200 mL/hour for 2 hours or until pH >7.0

» Bicarbonate therapy may be used in adult patients with pH <7 or a bicarbonate level <5 mEq/L, although data are limited.[1] [63]

» In adults with pH 6.9 to 7.0, 50 mmol sodium bicarbonate (1 ampule) in 200 mL sterile water with 10 mEq KCl may be administered over 1 hour until pH is >7.0.

» In adults with pH <6.9, we recommend that 100 mmol sodium bicarbonate in 400 mL sterile water with 20 mEq KCl be administered at a rate of 200 mL/hour for 2 hours or until pH >7.0. Treatment should be repeated every 2 hours until pH >7.0. Bicarbonate therapy, like insulin therapy, lowers serum potassium; therefore, KCl is added to isotonic bicarbonate.[1] [64]

**adjunct phosphate therapy**

Treatment recommended for SOME patients in selected patient group

**Primary options**

» **potassium phosphate**: 20-30 mEq added to each liter of infusion fluid

» Routine replacement of phosphate is not recommended.

» However, to avoid cardiac, respiratory, and skeletal muscle dysfunction, careful phosphate therapy may be indicated in patients with cardiac dysfunction (e.g., with signs of left ventricular dysfunction), symptomatic anemia, or respiratory depression (e.g., decreased oxygen saturation), and in those with confirmed hypophosphatemia (serum phosphate concentration <1.0 mg/dL).[1]

» The dose is 20-30 mEq/L potassium phosphate added to replacement fluids.

» Phosphate therapy above the recommended dose may result in severe hypocalcemia.[1] [75] [76]

**serum potassium 3.3 to 5.3 mEq/L**

**1st intravenous fluids**

» Mild to moderate volume depletion is indicated by the absence of orthostatic hypotension or supine hypotension, dry mucous membranes, and poor skin turgor. The goal is to gradually replace half of the fluid deficit over 12-24 hours,
## Acute

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</tr>
<tr>
<td></td>
<td>» <strong>insulin aspart</strong>: consult local protocols for dosing guidelines</td>
</tr>
</tbody>
</table>
Diabetic ketoacidosis

Treatment

**Acute**

**OR**

- **insulin lispro**: consult local protocols for dosing guidelines

- Patients should receive a continuous intravenous infusion of regular insulin after exclusion of hypokalemia (i.e., potassium level should be >3.3 mEq/L before initiation of insulin therapy). Two alternative low-dose regimens are recommended by current guidelines.\[1\] \[45\] The first option is a continuous intravenous infusion of regular insulin at a dose of 0.14 units/kg/hour (approximately 10 units/hour in a 70 kg patient) with no initial bolus.\[1\] This is based on studies that show the use of low-dose regular insulin administered by intravenous infusion is sufficient for the treatment of DKA, provided the dose is above 0.1 units/kg/hour. The alternative regimen involves an initial intravenous bolus dose of 0.1 units/kg followed by a continuous infusion at a dose of 0.1 units/kg/hour.\[53\] These low-dose insulin therapy protocols decrease plasma glucose concentration at a rate of 50-75 mg/dL/hour.\[1\]

- If plasma glucose does not fall by at least 10% or 50 mg/dL in the first hour of insulin infusion, then a dose of 0.14 units/kg of regular insulin should be administered as an intravenous bolus and the continuous insulin infusion rate should be continued (either 0.1 units/kg/hour or 0.14 units/kg/hour depending on the regimen selected).\[1\] \[53\] Insulin injection by a sliding scale is no longer recommended. When serum glucose reaches 200 mg/dL, the infusion can be reduced to 0.02 to 0.05 units/kg/hour, at which time dextrose may be added to the intravenous fluids.\[1\] \[53\] The rate of insulin infusion (or the dextrose concentration) should then be adjusted to maintain a plasma glucose level of 150-200 mg/dL.\[1\]

- Patients with mild to moderate DKA (plasma glucose >250 mg/dL, arterial pH 7.00 to 7.30, serum bicarbonate 10-18 mEq/L) that is not complicated by acute MI, congestive heart failure, end-stage renal or hepatic failure, steroid use, or pregnancy, may be given rapid-acting insulin subcutaneously as an alternative to intravenous regular insulin.\[60\] \[61\] \[62\] This has been demonstrated to be safe and effective from studies in adults in one center.\[1\] A suggested protocol would be an initial subcutaneous injection of rapid-acting insulin at a dose of 0.3 units/kg, followed 1 hour later by another subcutaneous injection...
Diabetic ketoacidosis

TREATMENT

Acute

of 0.2 units/kg. Thereafter, they should receive 0.2 units/kg every 2 hours until blood glucose becomes <250 mg/dL. At this point, the insulin dose should be decreased by half to 0.1 units/kg every 2 hours until the resolution of DKA.[58]

Until the results of these studies are replicated in multicenter trials, the administration of continuous intravenous infusion of regular insulin should remain the preferred route because of its short half-life and easy titration. This is compared with the delayed onset of action and prolonged half-life of subcutaneously administered insulin. However, in places where there are increased waiting times for intensive care unit (ICU) admission or with limited medical resources, the use of insulin analogs for the treatment of mild uncomplicated DKA episodes can be considered in outpatient, general wards, or emergency departments. Patients with severe DKA (plasma glucose >250 mg/dL, arterial pH <7.00, serum bicarbonate <10 mEq/L), hypotension, anasarca (severe generalized edema), or associated severe critical illness should be managed with intravenous regular insulin in the ICU using the regimen described above.[1] [58] [57] [59]

» The intravenous or subcutaneous regimens should be followed until all remaining criteria for resolution are met: serum bicarbonate >18 mEq/L, venous pH >7.3, and anion gap <10.[1]

plus potassium therapy

Treatment recommended for ALL patients in selected patient group

Primary options

» potassium phosphate: 20-30 mEq added to each liter of infusion fluid initially, adjust dose according to serum potassium level If potassium is <3.3 mEq/L at any point of therapy, insulin should be discontinued and potassium replaced intravenously.

OR

» potassium chloride: 20-30 mEq added to each liter of infusion fluid initially, adjust dose according to serum potassium level If potassium is <3.3 mEq/L at any point of therapy, insulin should be discontinued and potassium replaced intravenously.

Insulin therapy and correction of hyperosmolarity and acidemia decrease the plasma concentration of potassium. Concurrent
Diabetic ketoacidosis

**Acute**

Potassium replacement is recommended if the serum potassium is in the range 3.3 to 5.3 mEq/L, to prevent cardiac arrhythmias due to hypokalemia. The dose is 20-30 mEq added to each liter of infusion fluid. If potassium is <3.3 mEq/L at any point of therapy, insulin should be discontinued.[1]

- Choices are potassium phosphate or potassium chloride. One third of the potassium replacement should be administered as potassium phosphate to avoid excessive chloride administration.

- The serum potassium level should be monitored at least hourly and replacement adjusted accordingly.

**Adjunct bicarbonate therapy**

Treatment recommended for some patients in selected patient group

**Primary options**

- **sodium bicarbonate**: serum pH 6.9 to 7.0: 50 mmol intravenous infusion over 1 hour until pH >7.0; serum pH <6.9: 100 mmol intravenous infusion at a rate of 200 mL/hour for 2 hours or until pH >7.0

- Bicarbonate therapy may be used in adult patients with pH <7 or a bicarbonate level <5 mEq/L, although data are limited.[1] [63]

- In adults with pH 6.9 to 7.0, 50 mmol sodium bicarbonate (1 ampule) in 200 mL sterile water with 10 mEq KCl may be administered over 1 hour until pH is >7.0.

- In adults with pH <6.9, we recommend that 100 mmol sodium bicarbonate in 400 mL sterile water with 20 mEq KCl be administered at a rate of 200 mL/hour for 2 hours or until pH >7.0. Treatment should be repeated every 2 hours until pH >7.0. Bicarbonate therapy, like insulin therapy, lowers serum potassium; therefore, KCl is added to isotonic bicarbonate.[1] [64]

**Adjunct phosphate therapy**

Treatment recommended for some patients in selected patient group

**Primary options**

- **potassium phosphate**: 20-30 mEq added to each liter of infusion fluid

- Routine replacement of phosphate is not recommended.
<table>
<thead>
<tr>
<th>Acute</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>serum potassium &gt;5.3 mEq/L</td>
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<td>» However, to avoid cardiac, respiratory, and skeletal muscle dysfunction, careful phosphate therapy may be indicated in patients with cardiac dysfunction (e.g., with signs of left ventricular dysfunction), symptomatic anemia, or respiratory depression (e.g., decreased oxygen saturation), and in those with confirmed hypophosphatemia (serum phosphate concentration &lt;1.0 mg/dL).[1] The dose is 20-30 mEq/L potassium phosphate added to replacement fluids. Phosphate therapy above the recommended dose may result in severe hypocalcemia.[1] [75] [76]</td>
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<td>» Following the initial fluid replacement, corrected serum sodium level should be evaluated (corrected sodium [mEq/L] = measured sodium [mEq/L] + 0.016 [glucose (mg/dL) - 100]). In patients found to be hyponatremic, 0.9% NaCl should be started at 250-500 mL/hour.</td>
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<td>» Electrolytes, BUN, venous pH, creatinine, and glucose should be checked every 2-4 hours until the resolution of DKA.</td>
</tr>
<tr>
<td></td>
<td>» When plasma glucose reaches 200 mg/dL, fluid therapy should be changed to 5% dextrose with 0.45% NaCl at 150-250 mL/hour in order to avoid hypoglycemia.[1]</td>
</tr>
<tr>
<td></td>
<td>plus supportive care ± ICU admission</td>
</tr>
<tr>
<td></td>
<td>Treatment recommended for ALL patients in selected patient group</td>
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<tr>
<td></td>
<td>» Indications for intensive care unit (ICU) admission include altered mental status, respiratory insufficiency, and severe acidosis.</td>
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</table>
**Acute**

- After admission to ICU, central venous and arterial lines are required as well as Swan-Ganz catheterization and continuous percutaneous oximetry. Intubation and mechanical ventilation are commonly required, with constant monitoring of respiratory parameters. Nasogastric suctioning is always performed because of frequent ileus and danger of aspiration.

- Mild cases of diabetic ketoacidosis may be managed without ICU admission.\(^1\)

**plus insulin**

Treatment recommended for ALL patients in selected patient group

**Primary options**

- **insulin regular**: consult local protocols for dosing guidelines

**Secondary options**

- **insulin aspart**: consult local protocols for dosing guidelines

**OR**

- **insulin lispro**: consult local protocols for dosing guidelines

**Patients should receive a continuous intravenous infusion of regular insulin after exclusion of hypokalemia (i.e., potassium level should be >3.3 mEq/L before initiation of insulin therapy). Two alternative low-dose regimens are recommended by current guidelines.\(^1\)\(^45\) The first option is a continuous intravenous infusion of regular insulin at a dose of 0.14 units/kg/hour (approximately 10 units/hour in a 70 kg patient) with no initial bolus.\(^1\) This is based on studies that show the use of low-dose regular insulin administered by intravenous infusion is sufficient for the treatment of DKA, provided the dose is above 0.1 units/kg/hour. The alternative regimen involves an initial intravenous bolus dose of 0.1 units/kg followed by a continuous infusion at a dose of 0.1 units/kg/hour.\(^53\) These low-dose insulin therapy protocols decrease plasma glucose concentration at a rate of 50-75 mg/dL/hour.\(^1\)

- If plasma glucose does not fall by at least 10% or 50 mg/dL in the first hour of insulin infusion, then a dose of 0.14 units/kg of regular insulin should be administered as an intravenous bolus and the continuous insulin infusion rate should be continued (either 0.1 units/kg/hour or
TREATMENT

Acute

Insulin injection by a sliding scale is no longer recommended. When serum glucose reaches 200 mg/dL, the infusion can be reduced to 0.02 to 0.05 units/kg/hour, at which time dextrose may be added to the intravenous fluids. The rate of insulin infusion (or the dextrose concentration) should then be adjusted to maintain a plasma glucose level of between 150 and 200 mg/dL.

Patients with mild to moderate DKA (plasma glucose >250 mg/dL, arterial pH 7.00 to 7.30, serum bicarbonate 10-18 mEq/L) that is not complicated by acute MI, congestive heart failure, end-stage renal or hepatic failure, steroid use, or pregnancy, may be given rapid-acting insulin subcutaneously as an alternative to intravenous regular insulin. This has been demonstrated to be safe and effective from studies in adults in one center. A suggested protocol would be an initial subcutaneous injection of rapid-acting insulin at a dose of 0.3 units/kg, followed 1 hour later by another subcutaneous injection of 0.2 units/kg. Thereafter, they should receive 0.2 units/kg every 2 hours until blood glucose becomes <250 mg/dL. At this point, the insulin dose should be decreased by half to 0.1 units/kg every 2 hours until the resolution of DKA.

Until the results of these studies are replicated in multicenter trials, the administration of continuous intravenous infusion of regular insulin should remain the preferred route because of its short half-life and easy titration. This is compared with the delayed onset of action and prolonged half-life of subcutaneously administered insulin. However, in places where there are increased waiting times for intensive care unit (ICU) admission or with limited medical resources, the use of insulin analogs for the treatment of mild uncomplicated DKA episodes can be considered in outpatient, general wards, or emergency departments. Patients with severe DKA (plasma glucose >250 mg/dL, arterial pH <7.00, serum bicarbonate <10 mEq/L), hypotension, anasarca (severe generalized edema), or associated severe critical illness should be managed with intravenous regular insulin in the ICU using the regimen described above.

The intravenous or subcutaneous regimens should be followed until all remaining criteria for resolution are met: serum bicarbonate >18 mEq/L, venous pH >7.3, and anion gap <10.
**Acute**

**adjunct bicarbonate therapy**

Treatment recommended for SOME patients in selected patient group

**Primary options**

- **sodium bicarbonate**: serum pH 6.9 to 7.0: 50 mmol intravenous infusion over 1 hour until pH >7.0; serum pH <6.9: 100 mmol intravenous infusion at a rate of 200 mL/hour for 2 hours or until pH >7.0

- Bicarbonate therapy may be used in adult patients with pH <7 or a bicarbonate level <5 mEq/L, although data are limited.[1] [63]

- In adults with pH 6.9 to 7.0, 50 mmol sodium bicarbonate (1 ampule) in 200 mL sterile water with 10 mEq KCl may be administered over 1 hour until pH is >7.0.

- In adults with pH <6.9, we recommend that 100 mmol sodium bicarbonate in 400 mL sterile water with 20 mEq KCl be administered at a rate of 200 mL/hour for 2 hours or until pH >7.0. Treatment should be repeated every 2 hours until pH >7.0. Bicarbonate therapy, like insulin therapy, lowers serum potassium; therefore, KCl is added to isotonic bicarbonate.[1] [64]

**adjunct phosphate therapy**

Treatment recommended for SOME patients in selected patient group

**Primary options**

- **potassium phosphate**: 20-30 mEq added to each liter of infusion fluid

- Routine replacement of phosphate is not recommended.

- However, to avoid cardiac, respiratory, and skeletal muscle dysfunction, careful phosphate therapy may be indicated in patients with cardiac dysfunction (e.g., with signs of left ventricular dysfunction), symptomatic anemia, or respiratory depression (e.g., decreased oxygen saturation), and in those with confirmed hypophosphatemia (serum phosphate concentration <1.0 mg/dL).[1]

- The dose is 20-30 mEq/L potassium phosphate added to replacement fluids.

- Phosphate therapy above the recommended dose may result in severe hypocalcemia.[1] [75] [76]
**Acute**

**mild to moderate volume depletion:**
- eunatremic or hypernatremic

<table>
<thead>
<tr>
<th>Serum potassium &lt;3.3 mEq/L</th>
<th>1st intravenous fluids</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>» Mild to moderate volume depletion is indicated by the absence of orthostatic hypotension or supine hypotension, dry mucous membranes, and poor skin turgor. The goal is to gradually replace half of the fluid deficit over 12-24 hours, to prevent complications such as cerebral edema.</td>
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<td>» The initial choice of fluid is isotonic saline infused at a rate of 1.0 to 1.5 L (or 15-20 mL/kg body weight) for the first hour.</td>
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<td>» Following the initial fluid replacement, corrected serum sodium level should be evaluated (corrected sodium [mEq/L] = measured sodium [mEq/L] + 0.016 [glucose (mg/dL) - 100]). In patients found to be hypernatremic or eunatremic, 0.45% NaCl at 250 to 500 mL/hour is recommended.</td>
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<td>» Electrolytes should be checked at least hourly (to monitor potassium levels), and BUN, venous pH, creatinine, and glucose should be checked every 2-4 hours until the resolution of DKA.</td>
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</table>

**plus supportive care ± ICU admission**

Treatment recommended for ALL patients in selected patient group

» Indications for intensive care unit (ICU) admission include altered mental status, respiratory insufficiency, and severe acidosis.

» After admission to ICU, central venous and arterial lines are required as well as Swan-Ganz catheterization and continuous percutaneous oximetry. Intubation and mechanical ventilation are commonly required, with constant monitoring of respiratory parameters. Nasogastric suctioning is always performed because of frequent ileus and danger of aspiration.

» Mild cases of DKA may be managed without ICU admission.[1]

**plus potassium therapy**

Treatment recommended for ALL patients in selected patient group

Primary options
**Acute**

- **potassium phosphate**: 20-30 mEq added to each liter of infusion fluid initially, adjust dose according to serum potassium level.
  If potassium is <3.3 mEq/L at any point of therapy, insulin should be discontinued and potassium replaced intravenously.

**OR**

- **potassium chloride**: 20-30 mEq added to each liter of infusion fluid initially, adjust dose according to serum potassium level.
  If potassium is <3.3 mEq/L at any point of therapy, insulin should be discontinued and potassium replaced intravenously.

- Insulin therapy and correction of hyperosmolarity and acidemia decrease plasma concentration of potassium. For this reason, insulin therapy should be withheld until the serum potassium level reaches 3.3 mEq/L.

- Likewise, if plasma potassium falls <3.3 mEq/L at any point of therapy, insulin should be discontinued.

- The dose is 20-30 mEq added to each liter of infusion fluid.[1]

- Choices for potassium therapy are potassium phosphate or potassium chloride. One third of the potassium replacement should be administered as potassium phosphate to avoid excessive chloride administration.

- The serum potassium level should be monitored at least hourly and replacement adjusted accordingly.

**plus**  
**insulin once serum potassium reaches 3.3 mEq/L**

Treatment recommended for ALL patients in selected patient group

**Primary options**

- **insulin regular**: consult local protocols for dosing guidelines

**Secondary options**

- **insulin aspart**: consult local protocols for dosing guidelines

**OR**

- **insulin lispro**: consult local protocols for dosing guidelines
Diabetic ketoacidosis

**Treatment**

**Acute**

» Insulin therapy should not be commenced until serum potassium reaches 3.3 mEq/L.

» Patients should receive a continuous intravenous infusion of regular insulin after exclusion of hypokalemia (i.e., potassium level should be >3.3 mEq/L before initiation of insulin therapy). Two alternative low-dose regimens are recommended by current guidelines.[1] [45] The first option is a continuous intravenous infusion of regular insulin at a dose of 0.14 units/kg/hour (approximately 10 units/hour in a 70 kg patient) with no initial bolus.[1] This is based on studies that show the use of low-dose regular insulin administered by intravenous infusion is sufficient for the treatment of DKA, provided the dose is >0.1 units/kg/hour. The alternative regimen involves an initial intravenous bolus dose of 0.1 units/kg followed by a continuous infusion at a dose of 0.1 units/kg/hour.[53] These low-dose insulin therapy protocols decrease plasma glucose concentration at a rate of 50 to 75 mg/dL/hour.[1]

» If plasma glucose does not fall by at least 10% or 50 mg/dL in the first hour of insulin infusion, then a dose of 0.14 units/kg of regular insulin should be administered as an intravenous bolus and the continuous insulin infusion rate should be continued (either 0.1 units/kg/hour or 0.14 units/kg/hour depending on the regimen selected).[1] [53] Insulin injection by a sliding scale is no longer recommended. When serum glucose reaches 200 mg/dL, the infusion can be reduced to 0.02 to 0.05 units/kg/hour, at which time dextrose may be added to the intravenous fluids.[1] [53] The rate of insulin infusion (or the dextrose concentration) should then be adjusted to maintain a plasma glucose level of between 150-200 mg/dL.[1]

» Patients with mild to moderate DKA (plasma glucose >250 mg/dL, arterial pH 7.00 to 7.30, serum bicarbonate 10-18 mEq/L) that is not complicated by acute MI, congestive heart failure, end-stage renal or hepatic failure, steroid use, or pregnancy, may be given rapid-acting insulin subcutaneously as an alternative to intravenous regular insulin.[60] [61] [62] This has been demonstrated to be safe and effective from studies in adults in one center.[1] A suggested protocol would be an initial subcutaneous injection of rapid-acting insulin at a dose of 0.3 units/kg, followed 1 hour later by another subcutaneous injection of 0.2 units/kg. Thereafter, they should receive 0.2 units/kg every 2 hours until blood glucose
Diabetic ketoacidosis

Treatment

Acute

becomes <250 mg/dL. At this point, the insulin dose should be decreased by half to 0.1 units/kg every 2 hours until the resolution of DKA.[58] Until the results of these studies are replicated in multicenter trials, the administration of continuous intravenous infusion of regular insulin should remain the preferred route because of its short half-life and easy titration. This is compared with the delayed onset of action and prolonged half-life of subcutaneously administered insulin. However, in places where there are increased waiting times for intensive care unit (ICU) admission or with limited medical resources, the use of insulin analogs for the treatment of mild uncomplicated DKA episodes can be considered in outpatient, general wards, or emergency departments. Patients with severe DKA (plasma glucose >250 mg/dL, arterial pH <7.00, serum bicarbonate <10 mEq/L), hypotension, anasarca (severe generalized edema), or associated severe critical illness should be managed with intravenous regular insulin in the ICU using the regimen described above.[1] [58] [57] [59]

» This regimen should be followed until all remaining criteria for resolution are met: serum bicarbonate >18 mEq/L, venous pH >7.3, and anion gap <10.[1]

adjunct bicarbonate therapy

Treatment recommended for SOME patients in selected patient group

Primary options

» sodium bicarbonate: serum pH 6.9 to 7.0: 50 mmol intravenous infusion over 1 hour until pH >7.0; serum pH <6.9: 100 mmol intravenous infusion at a rate of 200 mL/hour for 2 hours or until pH >7.0

» Bicarbonate therapy may be used in adult patients with pH <7 or a bicarbonate level <5 mEq/L, although data are limited.[1] [63]

» In adults with pH 6.9 to 7.0, 50 mmol sodium bicarbonate (1 ampule) in 200 mL sterile water with 10 mEq KCl may be administered over 1 hour until pH is >7.0.

» In adults with pH <6.9, we recommend that 100 mmol sodium bicarbonate in 400 mL sterile water with 20 mEq KCl be administered at a rate of 200 mL/hour for 2 hours or until pH >7.0. Treatment should be repeated every 2 hours until pH >7.0. Bicarbonate therapy, like insulin
<table>
<thead>
<tr>
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<th>Treatment</th>
</tr>
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<tbody>
<tr>
<td>adjunct phosphate therapy</td>
<td>Treatment recommended for SOME patients in selected patient group</td>
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</table>

**Primary options**

- **potassium phosphate**: 20-30 mEq added to each liter of infusion fluid

- Routine replacement of phosphate is not recommended.

- However, to avoid cardiac, respiratory, and skeletal muscle dysfunction, careful phosphate therapy may be indicated in patients with cardiac dysfunction (e.g., with signs of left ventricular dysfunction), symptomatic anemia, or respiratory depression (e.g., decreased oxygen saturation), and in those with confirmed hypophosphatemia (serum phosphate concentration <1.0 mg/dL).

  - The dose is 20-30 mEq/L potassium phosphate added to replacement fluids.

  - Phosphate therapy above the recommended dose may result in severe hypocalcemia.

**serum potassium 3.3 to 5.3 mEq/L**

**1st intravenous fluids**

- Mild to moderate volume depletion is indicated by the absence of orthostatic hypotension or supine hypotension, dry mucous membranes, and poor skin turgor. The goal is to gradually replace half of the fluid deficit over 12 to 24 hours, to prevent complications such as cerebral edema.

  - The initial choice of fluid is isotonic saline infused at a rate of 1.0 to 1.5 L (or 15-20 mL/kg body weight) for the first hour.

  - Following the initial fluid replacement, corrected serum sodium level should be evaluated (corrected sodium [mEq/L] = measured sodium [mEq/L] + 0.016 [glucose (mg/dL) - 100]). In patients found to be hypernatremic or eunatremic, 0.45% NaCl at 250-500 mL/hour is recommended.

  - Electrolytes should be checked at least hourly (to monitor potassium levels), and BUN, venous pH, creatinine, and glucose should be checked every 2-4 hours until the resolution of DKA.

**plus supportive care ± ICU admission**
Acute

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**plus** insulin

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» Patients should receive a continuous intravenous infusion of regular insulin after exclusion of hypokalemia (i.e., potassium level should be >3.3 mEq/L before initiation of insulin therapy). Two alternative low-dose regimens are recommended by current guidelines.[1] [45] The first option is a continuous intravenous infusion of regular insulin at a dose of 0.14 units/kg/hour (approximately 10 units/hour in a 70 kg patient) with no initial bolus.[1] This is based on studies that show the use of low-dose regular insulin administered by intravenous infusion is sufficient for the treatment of DKA, provided the dose is above 0.1 units/kg/hour. The alternative regimen involves an initial intravenous bolus dose of 0.1 units/kg followed by a continuous infusion at a dose of 0.1 units/kg/hour.[53] These low-dose insulin therapy protocols decrease plasma glucose concentration at a rate of 50-75 mg/dL/hour.[1]
Acute

» If plasma glucose does not fall by at least 10% or 50 mg/dL in the first hour of insulin infusion, then a dose of 0.14 units/kg of regular insulin should be administered as an intravenous bolus and the continuous insulin infusion rate should be continued (either 0.1 units/kg/hour or 0.14 units/kg/hour depending on the regimen selected).[1] [53] Insulin injection by a sliding scale is no longer recommended. When serum glucose reaches 200 mg/dL, the infusion can be reduced to 0.02 to 0.05 units/kg/hour, at which time dextrose may be added to the intravenous fluids.[1] [53] The rate of insulin infusion (or the dextrose concentration) should then be adjusted to maintain a plasma glucose level of between 150-200 mg/dL.[1]

» Patients with mild to moderate DKA (plasma glucose >250 mg/dL, arterial pH 7.00 to 7.30, serum bicarbonate 10-18 mEq/L) that is not complicated by acute MI, congestive heart failure, end-stage renal or hepatic failure, steroid use, or pregnancy, may be given rapid-acting insulin subcutaneously as an alternative to intravenous regular insulin.[60] [61] [62] This has been demonstrated to be safe and effective from studies in adults in one center.[1] A suggested protocol would be an initial subcutaneous injection of rapid-acting insulin at a dose of 0.3 units/kg, followed 1 hour later by another subcutaneous injection of 0.2 units/kg. Thereafter, they should receive 0.2 units/kg every 2 hours until blood glucose becomes <250 mg/dL. At this point, the insulin dose should be decreased by half to 0.1 units/kg every 2 hours until the resolution of DKA.[58] Until the results of these studies are replicated in multicenter trials, the administration of continuous intravenous infusion of regular insulin should remain the preferred route because of its short half-life and easy titration. This is compared with the delayed onset of action and prolonged half-life of subcutaneously administered insulin. However, in places where there are increased waiting times for intensive care unit (ICU) admission or with limited medical resources, the use of insulin analogs for the treatment of mild uncomplicated DKA episodes can be considered in outpatient, general wards, or emergency departments. Patients with severe DKA (plasma glucose >250 mg/dL, arterial pH <7.00, serum bicarbonate <10 mEq/L), hypotension, anasarca (severe generalized edema), or associated severe critical illness should be managed with intravenous regular insulin in the ICU using the regimen described above.[1] [58] [57] [59]
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<td>plus</td>
<td><strong>potassium therapy</strong></td>
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<tr>
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<td><strong>Primary options</strong></td>
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<td>- Insulin therapy and correction of hyperosmolarity and acidemia decrease the plasma concentration of potassium. Concurrent potassium replacement is recommended if the serum potassium is in the range 3.3 to 5.3 mEq/L, to prevent cardiac arrhythmias due to hypokalemia. The dose is 20-30 mEq added to each liter of infusion fluid. If potassium is &lt;3.3 mEq/L at any point of therapy, insulin should be discontinued.[1]</td>
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<td><strong>Primary options</strong></td>
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<td></td>
<td>- <strong>sodium bicarbonate</strong>: serum pH 6.9 to 7.0: 50 mmol intravenous infusion over 1 hour until pH &gt;7.0; serum pH &lt;6.9: 100 mmol</td>
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### Acute

<table>
<thead>
<tr>
<th>Treatment</th>
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</tr>
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<tbody>
<tr>
<td>intravenous infusion at a rate of 200 mL/hour for 2 hours or until pH &gt;7.0</td>
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- Bicarbonate therapy may be used in adult patients with pH <7 or a bicarbonate level <5 mEq/L, although data are limited.[1] [63]

- In adults with pH 6.9 to 7.0, 50 mmol sodium bicarbonate (1 ampule) in 200 mL sterile water with 10 mEq KCl may be administered over 1 hour until pH is >7.0.

- In adults with pH <6.9, we recommend that 100 mmol sodium bicarbonate in 400 mL sterile water with 20 mEq KCl be administered at a rate of 200 mL/hour for 2 hours or until pH >7.0. Treatment should be repeated every 2 hours until pH >7.0. Bicarbonate therapy, like insulin therapy, lowers serum potassium; therefore, KCl is added to isotonic bicarbonate.[64]

### Adjunct phosphate therapy

- Treatment recommended for SOME patients in selected patient group

### Primary options

- **potassium phosphate:** 20-30 mEq added to each liter of infusion fluid

- Routine replacement of phosphate is not recommended.

- However, to avoid cardiac, respiratory, and skeletal muscle dysfunction, careful phosphate therapy may be indicated in patients with cardiac dysfunction (e.g., with signs of left ventricular dysfunction), symptomatic anemia, or respiratory depression (e.g., decreased oxygen saturation), and in those with confirmed hypophosphatemia (serum phosphate concentration <1.0 mg/dL).[1]

- The dose is 20-30 mEq/L potassium phosphate added to replacement fluids.

- Phosphate therapy above the recommended dose may result in severe hypocalcemia.[1] [75] [76]

### Serum potassium >5.3 mEq/L

- 1st intravenous fluids

- Mild to moderate volume depletion is indicated by the absence of orthostatic hypotension or supine hypotension, dry mucous membranes, and poor skin turgor. The goal is to gradually replace half of the fluid deficit over 12-24 hours, to prevent complications such as cerebral edema.
Diabetic ketoacidosis

**Treatment**

### Acute

- The initial choice of fluid is isotonic saline infused at a rate of 1.0 to 1.5 L (or 15-20 mL/kg body weight) for the first hour.

- Following the initial fluid replacement, corrected serum sodium level should be evaluated (corrected sodium [mEq/L] = measured sodium [mEq/L] + 0.016 [glucose (mg/dL) - 100]). In patients found to be hypernatremic or eunatremic, 0.45% NaCl at 250 to 500 mL/hour is recommended.

- Potassium replacement is not required, but potassium levels should be checked every 2 hours.

- Electrolytes, BUN, venous pH, creatinine, and glucose should be checked every 2-4 hours until the resolution of DKA.

**plus** supportive care ± ICU admission

Treatment recommended for ALL patients in selected patient group

- Indications for intensive care unit (ICU) admission include altered mental status, respiratory insufficiency, and severe acidosis.

- After admission to ICU, central venous and arterial lines are required as well as Swan-Ganz catheterization and continuous percutaneous oximetry. Intubation and mechanical ventilation are commonly required, with constant monitoring of respiratory parameters. Nasogastric suctioning is always performed because of frequent ileus and danger of aspiration.

- Mild cases of DKA may be managed without ICU admission.[1]

**plus** insulin

Treatment recommended for ALL patients in selected patient group

**Primary options**

- insulin regular: consult local protocols for dosing guidelines

**Secondary options**

- insulin aspart: consult local protocols for dosing guidelines

**OR**

- insulin lispro: consult local protocols for dosing guidelines
## Acute

<table>
<thead>
<tr>
<th>Treatment</th>
</tr>
</thead>
</table>
| Patients should receive a continuous intravenous infusion of regular insulin after exclusion of hypokalemia (i.e., potassium level should be >3.3 mEq/L before initiation of insulin therapy). Two alternative low-dose regimens are recommended by current guidelines.\[1\] \[45\] The first option is a continuous intravenous infusion of regular insulin at a dose of 0.14 units/kg/hour (approximately 10 units/hour in a 70 kg patient) with no initial bolus.\[1\] This is based on studies that show the use of low-dose regular insulin administered by intravenous infusion is sufficient for the treatment of DKA, provided the dose is above 0.1 units/kg/hour. The alternative regimen involves an initial intravenous bolus dose of 0.1 units/kg followed by a continuous infusion at a dose of 0.1 units/kg/hour.\[53\] These low-dose insulin therapy protocols decrease plasma glucose concentration at a rate of 50-75 mg/dL/hour.\[1\]  

| If plasma glucose does not fall by at least 10% or 50 mg/dL in the first hour of insulin infusion, then a dose of 0.14 units/kg of regular insulin should be administered as an intravenous bolus and the continuous insulin infusion rate should be continued (either 0.1 units/kg/hour or 0.14 units/kg/hour depending on the regimen selected).\[1\] \[53\] Insulin injection by a sliding scale is no longer recommended. When serum glucose reaches 200 mg/dL, the infusion can be reduced to 0.02 to 0.05 units/kg/hour, at which time dextrose may be added to the intravenous fluids.\[1\] \[53\] The rate of insulin infusion (or the dextrose concentration) should then be adjusted to maintain a plasma glucose level of 150-200 mg/dL.\[1\]  

| Patients with mild to moderate DKA (plasma glucose >250 mg/dL, arterial pH 7.00 to 7.30, serum bicarbonate 10-18 mEq/L) that is not complicated by acute MI, congestive heart failure, end-stage renal or hepatic failure, steroid use, or pregnancy, may be given rapid-acting insulin subcutaneously as an alternative to intravenous regular insulin.\[60\] \[61\] \[62\] This has been demonstrated to be safe and effective from studies in adults in one center.\[1\] A suggested protocol would be an initial subcutaneous injection of rapid-acting insulin at a dose of 0.3 units/kg, followed 1 hour later by another subcutaneous injection of 0.2 units/kg. Thereafter, they should receive 0.2 units/kg every 2 hours until blood glucose becomes <250 mg/dL. At this point, the insulin dose should be decreased by half to 0.1 units/kg every 2 hours until the resolution of DKA.\[58\] |
## Treatment

### Acute

Until the results of these studies are replicated in multicenter trials, the administration of continuous intravenous infusion of regular insulin should remain the preferred route because of its short half-life and easy titration. This is compared with the delayed onset of action and prolonged half-life of subcutaneously administered insulin. However, in places where there are increased waiting times for intensive care unit (ICU) admission or with limited medical resources, the use of insulin analogs for the treatment of mild uncomplicated DKA episodes can be considered in outpatient, general wards, or emergency departments. Patients with severe DKA (plasma glucose >250 mg/dL, arterial pH <7.00, serum bicarbonate <10 mEq/L), hypotension, anasarca (severe generalized edema), or associated severe critical illness should be managed with intravenous regular insulin in the ICU using the regimen described above.[1] [58] [57] [59]

- The intravenous or subcutaneous regimens should be followed until all remaining criteria for resolution are met: serum bicarbonate >18 mEq/L, venous pH >7.3, and anion gap <10.[1]

- Potassium replacement is not required, but potassium levels should be checked every 2 hours.

### adjunct bicarbonate therapy

Treatment recommended for SOME patients in selected patient group

#### Primary options

- **sodium bicarbonate**: serum pH 6.9 to 7.0: 50 mmol intravenous infusion over 1 hour until pH >7.0; serum pH <6.9: 100 mmol intravenous infusion at a rate of 200 mL/hour for 2 hours or until pH >7.0

- Bicarbonate therapy may be used in adult patients with pH <7 or a bicarbonate level <5 mEq/L, although data are limited.[1] [63]

- In adults with pH 6.9 to 7.0, 50 mmol sodium bicarbonate (1 ampule) in 200 mL sterile water with 10 mEq KCl may be administered over 1 hour until pH is >7.0.

- In adults with pH <6.9, we recommend that 100 mmol sodium bicarbonate in 400 mL sterile water with 20 mEq KCl be administered at a rate of 200 mL/hour for 2 hours or until pH >7.0. Treatment should be repeated every 2 hours until pH >7.0. Bicarbonate therapy, like insulin
Diabetic ketoacidosis

Treatment

**Acute**

**adjunct phosphate therapy**

Treatment recommended for SOME patients in selected patient group

**Primary options**

- **potassium phosphate:** 20-30 mEq added to each liter of infusion fluid

- Routine replacement of phosphate is not recommended.

- However, to avoid cardiac, respiratory, and skeletal muscle dysfunction, careful phosphate therapy may be indicated in patients with cardiac dysfunction (e.g., with signs of left ventricular dysfunction), symptomatic anemia, or respiratory depression (e.g., decreased oxygen saturation), and in those with confirmed hypophosphatemia (serum phosphate concentration <1.0 mg/dL).

- The dose is 20-30 mEq/L potassium phosphate added to replacement fluids.

- Phosphate therapy above the recommended dose may result in severe hypocalcemia.

therapy, lowers serum potassium; therefore, KCl is added to isotonic bicarbonate.[1] [64] [75]
Diabetic ketoacidosis

Treatment

Ongoing

<table>
<thead>
<tr>
<th>DKA resolved and patient able to tolerate oral intake</th>
</tr>
</thead>
</table>

1st establish regular subcutaneous insulin regime

- When DKA has resolved and the patient is able to tolerate oral intake, transition to subcutaneous insulin needs to be initiated. Patient should be given subcutaneous insulin 1-2 hours before the termination of insulin infusion to allow sufficient time for subcutaneous insulin to start work at this time. Intermediate or long-acting insulin is recommended for basal requirements and short-acting insulin for prandial glycemic control.

- If a patient used insulin as their diabetes treatment prior to DKA, the same dose can be started; otherwise, the following regimen is recommended: total daily insulin dose of 0.5 to 0.8 units/kg/day, with 30% to 50% of the total daily dose given as basal long-acting insulin, usually at night as a single dose, and the remainder of the total daily dose given as divided doses of fast-acting insulin before each meal.\[1\] [58] [59]
**Recommendations**

**Monitoring**

It is possible to manage mild DKA without admission to the intensive care unit (ICU); however, many cases will require ICU care.

After admission to ICU, central venous and arterial lines are usually required. Swan-Ganz catheterization and continuous percutaneous oximetry are needed in patients with hemodynamic instability. Monitoring of respiratory parameters is also required to ensure adequate oxygenation and airway protection.

Initially, serum glucose, electrolytes, BUN, creatinine, calcium, magnesium, phosphate, ketones, lactate, creatine phosphokinase, LFTs, urinalysis, ECG, upright chest radiograph, CBC, and ABGs are obtained. Subsequently, glucose and electrolytes are measured at least hourly; calcium, magnesium, and phosphate are checked every 2 hours and BUN, creatinine, and ketones every 2 to 6 hours, depending on the patient's clinical condition and response to therapy.

Serial beta hydroxybutyrate (BOHB) measurements may aid monitoring of the response to treatment in DKA. However, measurement of ketone bodies, in the absence of a meter with capacity to measure BOHB, is not recommended. BOHB is converted to acetoacetate, which is detected by the nitroprusside method, during the treatment of DKA. Therefore, the increase in acetoacetate during DKA treatment may mistakenly indicate a worsening of ketonemia.

Monitoring bicarbonate, anion gap, and pH has also been shown to reflect the response to therapy. A flow sheet classifying these findings as well as mental status, vital signs, insulin dose, fluid and electrolytes therapies, and urine output allows easy analysis of response to therapy and resolution of crises.[1] [38] [83] [84]

**Patient instructions**

Management should be reviewed periodically with all patients. This should include:

- When to contact the healthcare provider
- Blood glucose goals and the use of supplemental short- or rapid-acting insulin during illness
- Means to suppress fever and treat infection
- Initiation of an easily digestible fluid diet containing electrolytes and glucose during illness.

Patients should be advised to always continue insulin during illness and to seek professional advice early.

Sodium-glucose cotransporter 2 (SGLT-2) inhibitor-associated DKA in patients with type 2 diabetes is typically precipitated by insulin omission or significant dose reduction, severe acute illness, dehydration, extensive exercise, surgery, low-carbohydrate diets, or excessive alcohol intake. DKA prevention strategies should include withholding SGLT-2 inhibitors when precipitants are present, and avoiding insulin omission or large insulin dose reduction.[36] [37]

The patient (or family member or carer) must be able to accurately measure and record blood glucose, insulin administration, temperature, respiratory rate, and pulse. Blood ketone (BOHB) should be checked when blood glucose is >300 mg/dL and, if it is high, the patient should present to the hospital for further evaluation. The frequency of blood glucose monitoring depends on the patient's clinical condition: in uncontrolled diabetes (HbA1c >7.0%), it is recommended to check blood glucose before each meal, plus at bedtime.[1] [85]
## Complications

<table>
<thead>
<tr>
<th>Complications</th>
<th>Timeframe</th>
<th>Likelihood</th>
</tr>
</thead>
<tbody>
<tr>
<td>hypoglycemia</td>
<td>short term</td>
<td>high</td>
</tr>
<tr>
<td>This iatrogenic complication can occur with excessive high-dose insulin therapy. It can be prevented by following current treatment protocols with frequent monitoring of plasma glucose and use of glucose-containing intravenous fluids.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>hypokalemia</td>
<td>short term</td>
<td>high</td>
</tr>
<tr>
<td>This iatrogenic complication can occur with excessive high-dose insulin therapy and bicarbonate therapy. It can be prevented by following current treatment protocols with frequent monitoring of potassium levels and appropriate replacement.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>arterial or venous thromboembolic events</td>
<td>short term</td>
<td>medium</td>
</tr>
<tr>
<td>Standard prophylactic low-dose heparin is certainly reasonable in these patients. Applying prophylactic treatment is based on clinical evaluation by the physician of risk factors for thromboembolic events. Currently no evidence exists for full anticoagulation.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>nonanion gap hyperchloremic acidosis</td>
<td>short term</td>
<td>low</td>
</tr>
<tr>
<td>This occurs due to urinary loss of ketoanions that are needed for bicarbonate regeneration, and also increased reabsorption of chloride secondary to intensive administration of chloride-containing fluids. This acidosis usually resolves and should not affect the treatment. It is more likely in pregnant women.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>cerebral edema/brain injury</td>
<td>short term</td>
<td>low</td>
</tr>
<tr>
<td>This occurs in 0.7% to 10% of children with DKA and is rare in adults with DKA. Children at ages under 5 years are at increased risk. It is manifested by headache, lethargy, papillary changes, and seizure. Mortality is high. Mannitol infusion and mechanical ventilation should be used to treat this condition. Prevention may be achieved by avoidance of overzealous hydration and by maintaining the glucose level at 150-200 mg/dL in DKA. Results of the first prospective randomised study to evaluate fluid regimens in children with DKA found that neither the sodium chloride content nor the speed of delivery of intravenous fluids affected the short- and long-term neurologic outcomes.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>acute respiratory distress syndrome (ARDS)</td>
<td>short term</td>
<td>low</td>
</tr>
<tr>
<td>Treatment-related reduction in colloid osmotic pressure may lead to accumulation of water in the lungs, decreased lung compliance and possibly hypoxemia in DKA. Management includes the monitoring of blood oxygen levels with pulse oximetry and lowering the fluid intake with addition of colloid replacement.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## Prognosis

The mortality rate is 5% in experienced centers. Death is rarely caused by the metabolic complications of hyperglycemia or ketoacidosis but rather relates to the underlying illness. The prognosis is substantially worsened at the extremes of age and in the presence of coma and hypotension.
## Diagnostic guidelines

### International

**Standards of medical care in diabetes - 2020**

[https://professional.diabetes.org/content-page/standards-medical-care-diabetes]

[45]

**Published by:** American Diabetes Association  
**Last published:** 2020

**Hyperglycemic crises in adult patients with diabetes**

[https://care.diabetesjournals.org/content/32/7.toc]  
[1]

**Published by:** American Diabetes Association  
**Last published:** 2009

## Treatment guidelines

### International

**Standards of medical care in diabetes - 2020**

[https://professional.diabetes.org/content-page/standards-medical-care-diabetes]

[45]

**Published by:** American Diabetes Association  
**Last published:** 2020

**Hyperglycemic crises in adult patients with diabetes: a consensus statement from the American Diabetes Association**

[https://care.diabetesjournals.org/content/32/7.toc]  
[1]

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Diabetic ketoacidosis

Key articles


References


Diabetic ketoacidosis

References


Diabetic ketoacidosis


Diabetic ketoacidosis

**Images**

**Other hyperglycemic states**
- Diabetes mellitus
- Hyperosmolar hyperglycemic state (HHS)
- Impaired glucose tolerance
- Stress hyperglycemia

**Hyperglycemia**

**Ketosis**

**Acidosis**

**Other ketotic states**
- Ketotic hypoglycemia
- Alcoholic ketosis
- Starvation ketosis

**Other metabolic acidotic states**
- Lactic acidosis
- Hyperchloremic acidosis
- Salicylism
- Uremic acidosis
- Drug-induced acidosis

**Figure 1: Triad of DKA**

Figure 2: Pathogenesis of DKA and HHS; triggers include stress, infection, and insufficient insulin. FFA: free fatty acid; HHS: hyperosmolar hyperglycemic state

From: Kitabchi AE, Umpierrez GE, Miles JM, et al. Diabetes Care. 2009;32:1335-43; used with permission
Figure 3: Management of adult DKA. Abbreviations: blood glucose (BG); diabetic ketoacidosis (DKA); hour (h); intravenous (IV); subcutaneous (SC)

Figure 4: Algorithm for the management of potassium and bicarbonate

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BMJ accepts no responsibility for misinterpretation of numbers which comply with this stated numerical separator standard.

This approach is in line with the guidance of the International Bureau of Weights and Measures Service.

Figure 1 – BMJ Best Practice Numerical Style
Contributors:

// Authors:

Aidar R. Gosmanov, MD, PhD, FACE
Associate Professor of Medicine
Division of Endocrinology, Albany Medical College, Chief, Endocrinology Section, Albany VAMC, Albany, NY
DISCLOSURES: ARG declares that he has no competing interests.

Laleh Razavi Nematollahi, MD
Assistant Professor of Medicine
Case Western Reserve University, Cleveland, OH
DISCLOSURES: LRN declares that she has no competing interests.

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DISCLOSURES: AEK is an author of a number of references in this topic.

// Peer Reviewers:

David Jenkins, DM, FRCP
Consultant Physician
Worcestershire Royal Hospital, Worcester, UK
DISCLOSURES: DJ declares that he has no competing interests.

Udaya M. Kabadi, MD, FRCP(C), FACP, FACE
Professor of Medicine
University of Iowa, Iowa City, IA
DISCLOSURES: UMK declares that she has no competing interests.