

in the clinic

Diabetic Ketoacidosis

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CME Objective: To provide information about the prevention, diagnosis, and management of diabetic ketoacidosis.

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Diabetic ketoacidosis (DKA), the complication of diabetes mellitus that causes the greatest risk for death, is characterized by hyperglycemia and metabolic acidosis due to the accumulation of ketones from the breakdown of free fatty acids. Treatment requires hospitalization to correct hyperglycemia as well as serious volume depletion and electrolyte abnormalities. DKA occurs primarily in patients with type 1 diabetes mellitus but can also occur in those with type 2 diabetes. In a multicenter study of nearly 15 000 children and adolescents, DKA was the initial presentation of type 1 diabetes for 21.1%, and this proportion did not change substantially from 1997 to 2007 (1). The number of persons with diabetes is increasing rapidly, but the number of hospitalizations for DKA has increased at a slower pace (2). This relative reduction in the incidence of DKA is probably due to improvements in diabetes management. The risk for death with DKA has typically been about 4% (3, 4), but some studies report lower mortality rates in recent years (5). Deaths are concentrated primarily in elderly persons (3). Patient education and self-monitoring tools can prevent DKA. When it does occur, management that follows evidence-based treatment principles, which include hydration, insulin therapy, potassium repletion, and correction of the precipitating factor, can prevent DKA-related morbidity and mortality.

Prevention

1. Neu A, Hofer SE, Karges B, et al; DPV Initiative and the German BMBF Competency Network for Diabetes Mellitus. Ketoacidosis at diabetes onset is still frequent in children and adolescents: a multicenter analysis of 14,664 patients from 106 institutions. *Diabetes Care*. 2009;32:1647-8. [PMID: 19549730]
2. Wild S, Roglic G, Green A, et al. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes Care*. 2004;27:1047-53. [PMID: 15111519]
3. Henriksen OM, Røder ME, Prahj JB, et al. Diabetic ketoacidosis in Denmark: Incidence and mortality estimated from public health registries. *Diabetes Res Clin Pract*. 2007;76:51-6. [PMID: 16959363]
4. Freire AX, Umpierrez GE, Afessa B, et al. Predictors of intensive care unit and hospital length of stay in diabetic ketoacidosis. *J Crit Care*. 2002;17:207-11. [PMID: 12501147]
5. Lin SF, Lin JD, Huang YY. Diabetic ketoacidosis: comparisons of patient characteristics, clinical presentations and outcomes today and 20 years ago. *Chang Gung Med J*. 2005;28:24-30. [PMID: 15804145]

Who is at risk for DKA?

Although most patients with DKA have type 1 diabetes, 10% to 30% have type 2 diabetes (3, 6). Therefore, all patients with diabetes need to be provided with educational materials and the tools to self-monitor glucose and urine ketone levels or blood 3- β -hydroxybutyrate levels (7). Physicians and other clinicians who manage the care of persons with diabetes need to educate their patients about the many conditions that can precipitate DKA, including infections (for example, pneumonia or urinary tract infection); alcohol misuse; psychological stress; pregnancy; cardiovascular events; trauma; and medications, such as corticosteroids (8) (Box). The most prevalent contributing factor to DKA is poor adherence to diabetes treatment program (9–10). Patients may discontinue diabetes medications or monitoring for many reasons, such as cost, poor understanding of the disease, or weight control. In adolescents, psychological disorders, such as depression and eating disorders, are frequently underlying episodes of DKA. In addition to

medication nonadherence, patients may not monitor their blood sugar levels and may, therefore, be unaware of increasingly poor control.

Patient education and reminders that promote adherence to prescribed diabetes monitoring, diet, and medication are important means to prevent DKA. Because DKA is often the initial presentation of diabetes in minority communities (11), community-based education about the warning signs of diabetes is particularly important. The same patients can present

Factors That Can Precipitate DKA

- Infection (for example, pneumonia, urinary tract infection, sepsis)
- Alcohol misuse
- Psychological stress
- Pregnancy
- Cardiovascular events
- Trauma
- Medications (such as corticosteroids)
- Cushing disease
- Acute gastrointestinal disease (for example, pancreatitis, obstruction, mesenteric thrombosis)

repeatedly with DKA until the underlying contributory factors are identified and addressed. These patients need to understand that they are at risk for repeated episodes and need a program of self-monitoring and changes in medication, diet, and hydration well-defined for them (Box). Social support may be needed for patients with psychological or social issues that make adherence difficult. The patient must understand whom and when to call if symptoms and signs (blood glucose and urine or blood ketones)

Sick-Day Protocol*

Examples of sick days

- Feeling sick or have had a fever for a couple of days and not getting better
- Vomiting or having diarrhea for more than 6 hours

Management

- Check blood sugars at least every 4 hours, but, when changing quickly, check more often
- Check urine or blood ketones
- Modify usual insulin regimen according to a plan developed by the diabetes physician or team
- Maintain adequate food and fluid intake. If poor appetite: aim for 50 g of carbohydrate every 3–4 hours. If you are nauseated, consume high-carbohydrate liquids, such as regular (not diet) soft drinks, juice, frozen juice bars, sherbet, pudding, creamed soups, and fruit-flavored yogurt. Broth is also a good alternative.

Examples of when to call physician or diabetes team:

- If glucose levels are >13.3 mmol/L (>240 mg/dL) despite taking extra insulin according to a sick-day plan
- If you take diabetes pills and blood sugar is still >13.3 mmol/L (>240 mg/dL) before meals and remains there for more than 24 hours
- If symptoms develop that might signal DKA or dehydration, such as dizziness, trouble breathing, fruity breath, or dry and cracked lips or tongue

* From American Diabetes Association. Living with diabetes. Accessed at www.diabetes.org/living-with-diabetes/treatment-and-care/my-healthcare-team/when-youre-sick.html on 16 November 2009.

suggest impending DKA (Box). Both primary and secondary prevention of DKA are critical to reduce morbidity and mortality.

Can patients with type 2 diabetes develop DKA?

In an analysis of admissions to a large academic center for moderate-to-severe DKA, 21.7% were for patients with type 2 diabetes who were also significantly more likely to be Latino or African American (12). Most persons with ketosis-prone type 2 diabetes are also more likely to be middle aged and obese and to have newly diagnosed diabetes (13). In contrast to the predominance of girls and women with type 1 diabetes who develop DKA, men are more likely to have type 2 diabetes complicated by DKA (Box).

Patients with newly diagnosed ketosis-prone type 2 diabetes often have classic symptoms of poorly controlled diabetes, including polyuria, polydipsia, and weight loss for at least 1 month. These persons often have multiple risk factors for diabetes, including family history of diabetes. The hemoglobin A_{1c} level at presentation is usually greater than 13%. Improved access to medical care and monitoring of the development of these symptoms in patients at risk for diabetes may reduce the prevalence of DKA.

According to systematic review of ketosis-prone type 2 diabetes, features that are associated with near-euglycemic remission after an episode of DKA include minority

Clinical Characteristics of Persons With Type 2 Diabetes and DKA

- African American or Latino
- Male
- Middle aged
- Overweight or obese (body mass index, 27 to 28 kg/m²)
- Family history of diabetes
- With newly diagnosed diabetes

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7. Laffel LM, Wentzell K, Loughlin C, et al. Sick day management using blood 3-hydroxybutyrate (3-OHB) compared with urine ketone monitoring reduces hospital visits in young people with T1DM: a randomized clinical trial. *Diabet Med*. 2006;23:278-84. [PMID: 16492211]
8. Kitabchi AE, Umpierrez GE, Murphy MB, et al. Management of hyperglycemic crises in patients with diabetes. *Diabetes Care*. 2001;24:131-53. [PMID: 11194218]
9. Ko SH, Lee WY, Lee JH, et al. Clinical characteristics of diabetic ketoacidosis in Korea over the past two decades. *Diabet Med*. 2005;22:466-9. [PMID: 15787674]
10. Morris AD, Boyle DI, McMahon AD, et al. Adherence to insulin treatment, glycaemic control, and ketoacidosis in insulin-dependent diabetes mellitus. The DARTS/MEMO Collaboration. *Diabetes Audit and Research in Tayside Scotland. Medicines Monitoring Unit. Lancet*. 1997;350:1505-10. [PMID: 9388398]
11. Nyenwe E, Loganathan R, Blum S, et al. Admissions for diabetic ketoacidosis in ethnic minority groups in a city hospital. *Metabolism*. 2007;56:172-8. [PMID: 17224329]
12. Umpierrez GE, Smiley D, Kitabchi AE. Narrative review: ketosis-prone type 2 diabetes mellitus. *Ann Intern Med*. 2006;144:350-7. [PMID: 16520476]
13. Newton CA, Raskin P. Diabetic ketoacidosis in type 1 and type 2 diabetes mellitus: clinical and biochemical differences. *Arch Intern Med*. 2004;164:1925-31. [PMID: 15451769]

race, obesity, family history of diabetes, newly diagnosed diabetes, and negative autoantibodies (islet cells or glutamic acid decarboxylase). C-peptide levels also help distinguish these patients. The fasting C-peptide level is greater than 0.33 nmol/L within 1 week after resolution of DKA and greater than 0.5 nmol/L on follow-up after 6 to 8 weeks. The glucagon-stimulated C-peptide level is greater than 0.5 nmol/L at presentation with DKA and greater than 0.75 nmol/L on follow-up after 6 to 8 weeks. Glucagon-stimulated C-peptide test is administered after a 10-hour overnight fast with blood samples taken at baseline and at 3 or 6 minutes after injection of glucagon (1 mg) to measure levels of glucose and C-peptide (12).

What advice should be given to patients with diabetes regarding management of sick days?

Because DKA is often precipitated by concurrent acute infection, it is important that patients know how to monitor and manage diabetes when they develop symptoms of an infection. Specifically, adherence to self-monitoring of blood glucose levels with a plan for treatments in specific ranges offers an important defense against DKA. Sick-day instructions should include information on how often to check glucose and urinary ketone levels, how to treat glucose levels in specific ranges, diet to maintain adequate nutrition, hydration with fluids that will not worsen the hyperglycemia, and the avoidance of exercise if ketosis is present (Box). When illness or other stressors occur, patient education should emphasize increasing the frequency of monitoring to at least every 4 hours. An infection or other illness should be expected to increase insulin requirements. Instructions should clearly indicate when to consult the physician or other clinician managing diabetes care. The self-management plan needs to include maintenance of adequate nutrition and hydration with appropriate fluids that will not worsen the hyperglycemia.

The sick-day program is demanding and requires advance preparation with clear, low-literacy educational materials for patients and their caregivers.

However, patients should be counseled that persons with type 1 diabetes mellitus need to take insulin even during periods of starvation because of the effects of counter-regulatory hormones that produce hyperglycemia, such as glucagon, cortisol, growth hormone, and catecholamines. These effects can be worsened by nausea and vomiting or when the patient has a poor appetite because of feeling poorly. The sick day protocol gives instructions about use of supplemental short-acting insulin in addition to usual insulin and management of infections. Patients who use an insulin-infusion pump should change to insulin injections until they confirm that the pump is functioning properly.

Some groups recommend that physicians also have patients check serum ketone levels in those with type 1 diabetes. Elevation of urine or serum ketones or β -hydroxybutyrate level should prompt the patient to contact the provider or go to an emergency department. Similarly, the patient should seek care when unable to tolerate food or liquid or if they have changes in mental status. The severity of the precipitating illness influences morbidity and mortality from DKA. Special precautions are necessary during pregnancy. Patients who are pregnant should check ketones for any glucose readings greater than 11.1 mmol/L (200 mg/dL). They should contact their physician after several high glucose readings with positive ketones, several high readings without the ability to keep fluids down, or continued high glucose readings despite negative ketones.

14. Reichel A, Rietzsch H, Köhler HJ, et al. Cessation of insulin infusion at nighttime during CSII-therapy: comparison of regular human insulin and insulin lispro. *Exp Clin Endocrinol Diabetes*. 1998;106:168-72. [PMID: 9710355]
15. Kitabchi AE, Umpierrez GE, Miles JM, et al. Hyperglycemic crises in adult patients with diabetes. *Diabetes Care*. 2009;32:1335-43. [PMID: 19564476]

Prevention... DKA occurs in both type 1 and 2 diabetes. Patients at risk for DKA with type 2 diabetes are more likely to be men, middle-aged, obese, and with a family history of diabetes and newly diagnosed diabetes. DKA can result from infections or other stressors, such as cardiovascular disease, but is most commonly due to nonadherence to the diabetes-care program, including treatment and self-monitoring. DKA can also be the first presentation of diabetes. A sick-day management plan should be established for all patients with diabetes but especially those with a history of DKA to avoid repeated episodes.

CLINICAL BOTTOM LINE

Diagnosis

Who should be evaluated for potential DKA?

All patients with positive ketones, constitutional symptoms, or suspicion of DKA and significantly elevated blood glucose levels (>13.9 mmol/L [>250 mg/dL]) should have electrolytes and blood gases checked to look for an anion gap metabolic acidosis. Especially in type 1 diabetes, DKA can develop within hours if insulin injections are stopped or an insulin pump malfunctions (14). The new American Diabetes Association (ADA) definition of DKA includes a blood glucose level of 13.9 mmol/L (250 mg/dL) (15) and reflects many studies that have shown that DKA is infrequent at lower levels except in situations with poor oral intake or pregnancy (16). It is also important to consider DKA in the differential diagnoses for a patient who has an anion gap metabolic acidosis. The calculation of the anion gap is $\text{Na}^+ - (\text{Cl}^- + \text{HCO}_3^-)$ (Table 1). The serum glucose should be checked even when the patient has no history of diabetes. DKA must be considered if the serum glucose

is greater than 13.9 mmol/L (250 mg/dL), but an elevated glucose level alone is insufficient to diagnose DKA.

DKA should be considered in patients with diabetes who have a concurrent infection, stroke, myocardial infarction, or other serious illness. These intercurrent illnesses should be sought and treated aggressively. Similarly, it is important to consider DKA when patients with diabetes experience nausea and vomiting, even if the blood glucose level is less than 13.9 mmol/L (250 mg/dL). Euglycemic DKA occurs more often in patients who have not eaten but who continue to take insulin. A blood glucose level less than 13.9 mmol/L (250 mg/dL) occurs in 1% to 7% of reported DKA cases (17) and seems to be more common in patients with hepatic dysfunction or in those who are hospitalized.

Several drugs, such as glucocorticoids or thiazides, are well-known causes of hyperglycemia that may lead to DKA. Clinicians should

Table 1. Serum Chemistry Calculations Relevant to Diabetic Ketoacidosis

Serum Chemistry Value	Calculation	Normal Range
Anion gap	$\text{Na}^+ - (\text{Cl}^- + \text{HCO}_3^-)$	7–13 mmol/L
Δ Anion gap	(Patient gap – 12)	<10 mmol/L*
Total serum osmolality	$2 \times (\text{serum Na}^+) + (\text{glucose} / 18) + (\text{blood urea nitrogen} / 2.8)^\dagger$	290 ± 5 mOsm/kg H_2O

*Varies by institution.

† Serum Na^+ measured in mmol/L, glucose and blood urea nitrogen measured in mg/dL.

16. Delaney MF, Zisman A, Kettyle WM. Diabetic ketoacidosis and hyperglycemic hyperosmolar non-ketotic syndrome. *Endocrinol Metab Clin North Am*. 2000;29:683-705. V. [PMID: 11149157]
17. Lebovitz HE. Diabetic ketoacidosis. *Lancet*. 1995;345:767-72. [PMID: 7891491]

also consider DKA in patients taking atypical antipsychotic drugs who present with hyperglycemia. Atypical antipsychotic drugs have been linked to increased frequency of diabetes, glucose intolerance, and DKA (18, 19). The anion gap and ketone levels should be measured in such patients. Another type of antipsychotic drug must be chosen to help resolve this complication.

What are key elements of the history and physical examination in DKA?

The presentation of a patient with DKA varies substantially depending on the severity of the episode. Mild or moderately ill patients may describe vague symptoms of fatigue, lethargy, poor appetite, or headache. In type 1 diabetes, the history of polyuria and polydipsia may be relatively recent, but in type 2 diabetes, these symptoms may have been building for weeks to months. Nausea, vomiting, and abdominal pain are commonly seen in DKA and may be related to the combined effects of dehydration, hypokalemia, ketonemia, and delayed gastric emptying.

Signs of dehydration, including poor skin turgor, decreased axillary sweat, or postural hypotension, may be present on physical examination. Kussmaul respirations (a pattern of deep breathing and hyperventilation in response to metabolic acidosis) may be present. Patients' breath may smell fruity due to increased acetone from ketonemia, but the absence of this finding does not rule out DKA. One aspect of the examination that can be confusing is abdominal tenderness, which may resolve as the DKA is treated or may reflect a more acute abdominal process that precipitated DKA. Abdominal pain correlates with the level of acidosis. The physical examination should focus on identifying potential precipitating factors, such as infections or cardiovascular events. Patients may

have mental status changes ranging from mild lethargy to delirium or coma. The most-severe cases are characterized by hypotension, tachycardia, and coma.

Is measurement of capillary blood ketones helpful in the diagnosis of DKA?

Capillary blood ketone measurement is a relatively new quantitative and enzymatic test that determines levels of 3- β -hydroxybutyrate, 1 of the 3 ketone bodies. The equipment is similar to that used by patients for home blood glucose determination, but it requires specific strips. In 1 small study, the levels of 3- β -hydroxybutyrate were more closely related to the bicarbonate level than to the serum ketones (20). However, checking capillary blood ketones is much more expensive than checking urine ketones, and further clinical studies are needed to define the most appropriate role for β -hydroxybutyrate monitoring.

A prospective study of the utility of point-of-care blood ketone testing in patients with diabetes presenting to the emergency department found that a rapid, bedside capillary blood ketone test for β -hydroxybutyrate measures this blood ketone better than urine ketones. The sensitivity and specificity of urine ketone dipstick testing and capillary blood ketone testing in determining DKA were 66% and 78% and 72% and 82%, respectively; and in determining hyperketonemia were 82% and 54% and 91% and 56%, respectively (21).

Are low levels of ketones in blood or urine diagnostic of DKA?

If clinical suspicion of DKA is high, a negative urine dipstick for ketones does not exclude DKA. Clinicians should be aware that urine test sticks do not measure β -hydroxybutyrate, which is the predominant ketone. Acetoacetate measured on the dipstick may not be elevated until later in the course of the illness (22).

18. Wilson DR, D'Souza L, Sarkar N, et al. New-onset diabetes and ketoacidosis with atypical antipsychotics. *Schizophr Res.* 2003;59:1-6. [PMID: 12413635]
19. Ananth J, Venkatesh R, Burgoyne K, et al. Atypical antipsychotic drug use and diabetes. *Psychother Psychosom.* 2002;71:244-54. [PMID: 12207104]
20. Vanelli M, Chiari G, Capuano C, et al. The direct measurement of 3-beta-hydroxybutyrate enhances the management of diabetic ketoacidosis in children and reduces time and costs of treatment. *Diabetes Nutr Metab* 2003;16:312-6

What laboratory tests are used to evaluate for DKA?

Table 2 shows recommended laboratory and other studies for DKA. DKA is diagnosed when the blood glucose level is greater than 13.9 mmol/L (250 mg/dL), arterial pH is less than 7.3, serum bicarbonate is less than 15 mmol/L, and a moderate degree of ketonemia or ketonuria is present. A total body deficit of potassium frequently complicates DKA, so initial measurement and frequent monitoring of potassium is required to determine replacement need. Because of the metabolic acidosis, hyperkalemia may initially be present.

Are arterial blood gases required to make the diagnosis of DKA?

Arterial blood gas (ABG) assessment is generally considered to be the most reliable method to evaluate the degree of acidosis in DKA, but a venous pH may be a more practical alternative. The normal anion gap is 7 to 9 mmol/L, but is approximately 25 mmol/L in DKA. Rarely, patients with DKA have a mixed acidosis and alkalosis with a pH that is close to normal. However, treatment of DKA

should not be affected by this unexpected laboratory result. Determination of the ABG may be less essential than originally thought.

A prospective, observational study examined emergency physicians' decision making for 200 consecutive patients with suspected DKA. Venous pH, chemistry panel, and ABGs were obtained for all patients, but the physicians based their decisions only on the venous pH or the ABG. The additional information obtained from the ABG changed: diagnosis for only 1%; management for 3.5%; and disposition for 1%. The venous pH was closely correlated with the arterial pH ($r = 0.951$), so the authors concluded that it could serve as a substitute (23).

How does DKA differ from hyperosmolar hyperglycemic state?

Patients with type 1 diabetes are at greater risk for DKA than patients with type 2 diabetes, but patients with type 2 diabetes are at greater risk for hyperosmolar hyperglycemic state (HHS), which has a similar presentation to DKA. In DKA, the serum glucose level is generally less than 33.3 mmol/L (600 mg/dL), whereas in the ADA definition of HHS, the

Table 2. Laboratory and Other Studies for Diabetic Ketoacidosis

Test	Notes
Plasma glucose	Usually >13.9 mmol/L (>250 mg/dL)
Arterial blood gas	pH is usually <7.3
Serum ketones	Usually 7–10 mmol/L in DKA or >1:2 dilution
Anion gap (electrolytes)	Usually >15 in DKA
Serum sodium	Usually low
Serum potassium	May be high, normal, or low. Potassium level will guide management
Serum phosphate	May be normal or high initially but usually decreases with insulin therapy
Serum amylase/lipase	May be high in DKA, unrelated to pancreatitis. Diagnosis of pancreatitis in DKA should be based on clinical judgment and imaging
Blood urea, creatinine levels	Usually elevated due to dehydration and decreased renal perfusion
CBC count and differential	Leukocytosis is common and may not represent infection. Levels $>25 \times 10^9$ cells/L should warrant diligent search for infection
Urine and blood cultures	If suspicion of infection is present
Chest radiography	If suspicion of pneumonia or pulmonary disorder
ECG	Should be done in all patients to assess effect of potassium status and rule out ischemia or myocardial infarction

CBC = complete blood cell; DKA = diabetic ketoacidosis; ECG = electrocardiography.

21. Bektas F, Eray O, Sari R, et al. Point of care blood ketone testing of diabetic patients in the emergency department. *Endocr Res.* 2004;30:395-402. [PMID: 15554356]
22. Koul PB. Diabetic ketoacidosis: a current appraisal of pathophysiology and management. *Clin Pediatr* 2009; 48: 135-44.
23. Ma OJ, Rush MD, Godfrey MM, et al. Arterial blood gas results rarely influence emergency physician management of patients with suspected diabetic ketoacidosis. *Acad Emerg Med.* 2003;10:836-41. [PMID: 12896883]

Table 3. Diabetic Ketoacidosis Versus Hyperosmolar Hyperglycemic State*

Value	Mild DKA	Moderate DKA	Severe DKA	HHS
Plasma glucose				
mmol/L	>13.9	>13.9	>13.9	33.3
mg/dL	>250	>250	>250	>600
Arterial pH	7.25 to 7.30	7.00 to <7.24	<7.00	>7.30
Serum bicarbonate, mmol/L	15 to 18	10 to <15	<10	18
Urine ketones	Positive	Positive	Positive	Small
Serum ketones (β -hydroxybutyrate)	High	High	High	Normal or elevated
Effective serum osmolality, mOsm/kg [†]	Variable	Variable	Variable	>320
Anion gap [‡]	>10	>12	>12	Variable
Alteration in sensoria or mental obtundation	Alert	Alert/drowsy	Stupor/coma	Stupor/coma

DKA = diabetic ketoacidosis; HHS = hyperosmolar hyperglycemic state.

* Adapted from Kitabchi AE, Umpierrez GE, Miles JM, et al. Hyperglycemic crises in adult patients with diabetes. *Diabetes Care*. 2009;32:1335-43. [PMID: 19564476]

[†] Effective serum osmolality = $2 \times (\text{measured Na [mmol/L]}) + (\text{glucose [mg/dL]} \div 18)$.

[‡] Anion gap = $\text{Na}^+ - (\text{Cl}^- + \text{HCO}_3^-)$ [mmol/L].

glucose level is greater than 33.3 mmol/L (600 mg/dL) and often greater than 55.5 mmol/L (1000 mg/dL) but with minimal ketone accumulation and only mild reduction in the arterial pH (Table 3) (15). As the main metabolite of ketones, β -hydroxybutyrate levels are elevated in DKA but are usually normal in HHS. The increased serum osmolality in HHS reflects serious dehydration and often produces mental status changes, including coma in 25% to 50% of cases. However, DKA and HHS can overlap and have many similarities. Like DKA,

HHS usually results from a precipitating factor, such as an infection or poor adherence to diabetes medications.

What conditions should be considered in the differential diagnosis of DKA?

If the blood glucose level is less than 13.9 mmol/L (250 mg/dL), another cause of the metabolic acidosis needs to be considered (Table 4). Other conditions, such as starvation, can increase ketones, but this elevation is usually mild. DKA can co-occur with other causes of metabolic acidosis, including lactic acidosis.

Diagnosis... Patients with DKA may present with a wide variety of nonspecific symptoms; therefore, it is important to have a high index of suspicion. The physical examination can yield clues to the diagnosis, such as a fruity-smelling breath from ketonemia, or to the severity of the episode, such as signs of significant dehydration. Laboratory assessment typically shows a blood glucose level greater than 13.9 mmol/L (250 mg/dL), arterial pH less than 7.3, serum bicarbonate less than 15 mmol/L, and a moderate degree of ketonemia or ketonuria. Patients with type 2 diabetes are at greater risk for HHS, in which glucose level is often greater than 55.5 mmol/L (1000 mg/dL) but the ketones are minimally elevated and the pH is only mildly depressed. The venous pH may offer an alternative to the arterial pH in the emergency department.

CLINICAL BOTTOM LINE

Table 4. Differential Diagnosis of Diabetic Ketoacidosis

<i>Disease</i>	<i>Characteristics</i>	<i>Notes</i>
Starvation ketosis	Patients may have intercurrent illness and quite ill, usually a clear history of not eating, and possibly nausea or vomiting.	Blood glucose can be normal, low or somewhat elevated. Starvation ketosis does not lead to acidosis; bicarbonate levels usually >18 mmol/L.
Alcoholic ketoacidosis	History of excessive alcohol intake in patients with long-term alcohol abuse.	Blood glucose is key: if normal or low with ketonemia and metabolic acidosis, alcoholic ketoacidosis is likely. An osmolar gap occur (difference between measured and calculated osmolality).
Lactic acidosis	Serum lactate is usually about 5 mmol/L	Can co-occur with diabetic ketoacidosis. Measure lactate if lactic acidosis suspected or history of metformin use.
Salicylate intoxication	Anion gap metabolic acidosis, but often with primary respiratory alkalosis.	Blood glucose level is usually not elevated and may be low. Measure the salicylate level.
Methanol intoxication	Ketones not significantly elevated, symptoms include blurry vision and abdominal pain.	Blood glucose level is normal to elevated. Measure methanol level.
Ethylene glycol intoxication	Ketones not usually increased, but anion gap and osmolar gap are typically high.	Blood glucose level is variable. Calcium oxalate and hippurate crystals can be seen in the urine. Measure ethylene glycol.
Chronic renal failure	Mild acidosis with slight increase in anion gap, but ketones not elevated.	History of increased serum creatinine.
Pseudoketosis	Paraldehyde or isopropyl alcohol ingestion.	Normal pH and normal anion gap.
Rhabdomyolysis	Creatine kinase is usually very high. Causes of rhabdomyolysis, such as statins, trauma, or heat stroke, may be present.	pH low, glucose level normal, ketones normal with anion gap and myoglobinuria.

Treatment

Do all patients with DKA require hospitalization?

In some cases, patients with uncomplicated mild-to-moderate DKA can be treated and discharged from the emergency department if they are stable, able to adhere to treatment, and have good support at home. Rapid-acting insulin analogs, such as lispro, glulisine, and aspart, can be used subcutaneously in these patients. Although patients may respond to therapy quickly, they can relapse if they do not monitor themselves or use sufficient doses of insulin.

Patients with moderate-to-severe DKA should be hospitalized, often in the intensive care unit or in an intermediate care unit. Following of practice guidelines, frequent monitoring, and continuous insulin infusion are associated with mortality rates of less than 1%. Patients with an arterial pH level less than 7.25,

a bicarbonate level less than 15, or a significant precipitating illness should be treated in care units that are experienced with DKA management and associated diseases. Some patients may require specialized therapy, such as treatment for a myocardial infarction at a coronary care unit.

What is the role of hydration in the management of DKA?

Rehydration alone will replace the fluid deficit, lower the glucose level, and improve insulin sensitivity and renal function. It should be started immediately after the diagnosis of DKA. Serum sodium should be corrected for hyperglycemia (for each 5.55 mmol/L [100 mg/dL] of glucose more than 5.55 mmol/L [100 mg/dL], add 1.6 mmol to sodium value for corrected serum sodium value). Begin with normal saline (0.9% sodium chloride), and reassess fluid-replacement hourly

(Figure). Switch to 0.45% sodium chloride after an initial bolus if the serum sodium is high or normal. The initial rate should be 15 to 20 mL/kg per hour depending on the fluid deficit. Switch to dextrose-containing fluids once the blood sugar level is approximately 11.1 mmol/L (200 mg/dL). Patients with severe hypovolemia or shock require more aggressive hydration, hemodynamic monitoring, and possibly vasopressor therapy. Assess patients for such underlying medical conditions before initiating fluid resuscitation. Renal insufficiency and congestive heart failure put

patients at risk for complications from fluid overload. Use extra caution when hydrating children, who have higher incidence of cerebral edema associated with DKA therapy. Children are also at risk for pulmonary edema.

How should clinicians administer insulin and potassium during the treatment of DKA?

The approach to managing DKA with insulin and potassium replacement is the same regardless of the type of diabetes. Insulin is required to treat the hyperglycemia and ketosis, but can

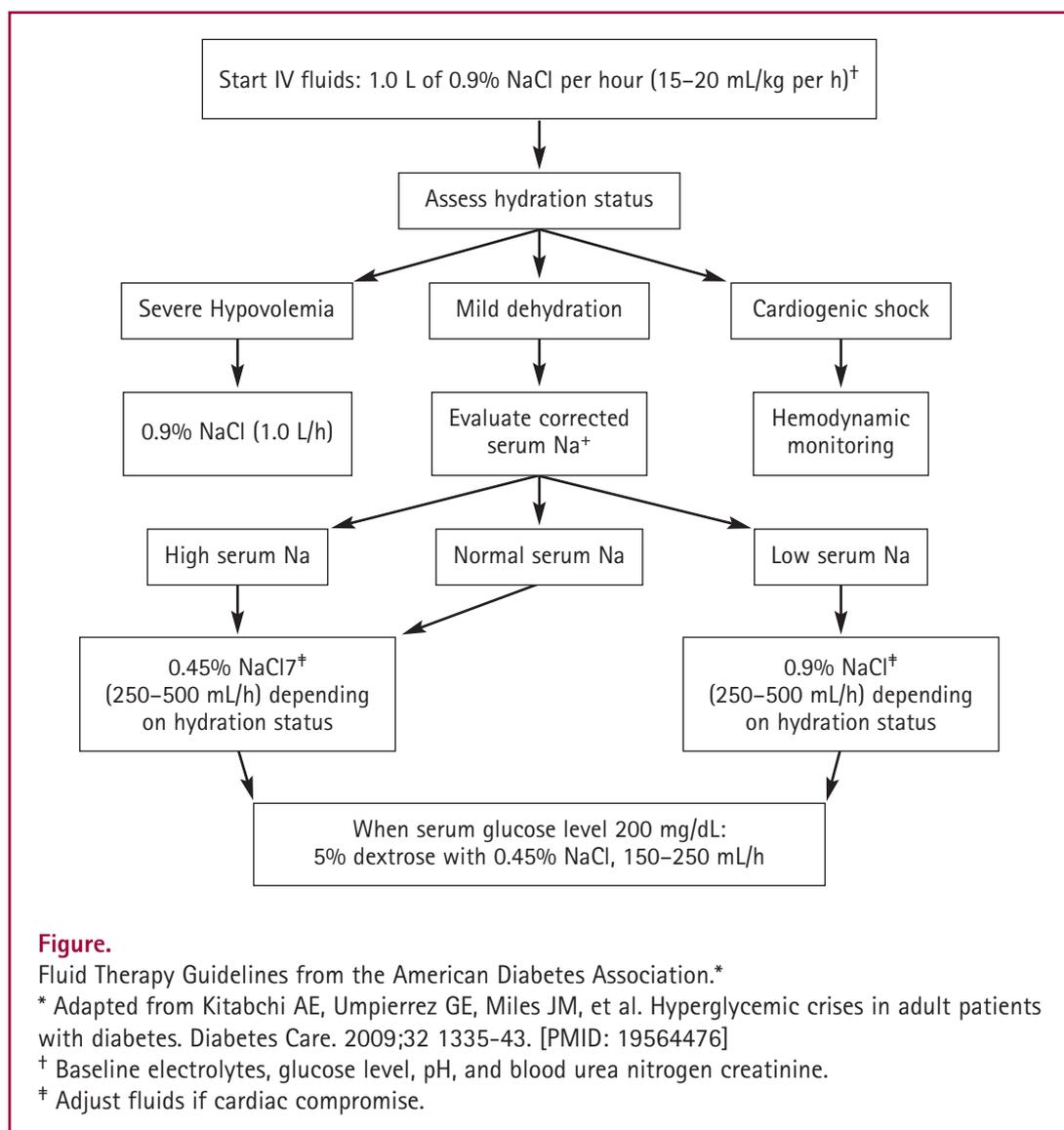


Figure.

Fluid Therapy Guidelines from the American Diabetes Association.*

* Adapted from Kitabchi AE, Umpierrez GE, Miles JM, et al. Hyperglycemic crises in adult patients with diabetes. *Diabetes Care*. 2009;32:1335-43. [PMID: 19564476]

† Baseline electrolytes, glucose level, pH, and blood urea nitrogen creatinine.

‡ Adjust fluids if cardiac compromise.

24. Kitabchi AE, Murphy MB, Spencer J, et al. Is a priming dose of insulin necessary in a low-dose insulin protocol for the treatment of diabetic ketoacidosis? *Diabetes Care*. 2008;31:2081-5. [PMID: 18694978]
25. Umpierrez GE, Cervo R, Karabell A, et al. Treatment of diabetic ketoacidosis with subcutaneous insulin aspart. *Diabetes Care*. 2004;27:1873-8. [PMID: 15277410]

result in profound hypokalemia that can produce serious cardiac arrhythmias. Both metabolic acidosis and insulin deficiency cause potassium to shift from the intracellular to the extracellular space. Insulin therapy reverses this process and moves potassium back into the intracellular space but can seriously deplete extracellular potassium levels. Many patients with DKA have a total body deficit of potassium despite normal or elevated potassium levels at baseline. The Box explains how to manage potassium while treating DKA. Clinicians should check serum electrolytes before administering insulin and should measure serum potassium at baseline, at 1 hour, then every 2 hours during initial therapy. Insulin is not given initially when the potassium level is less than 3.3 mmol/L because of the risk for life-threatening arrhythmias (Box).

After treatment with intravenous fluids has been started and the potassium level is greater than 3.3 mmol/L, an initial bolus of regular insulin is usually given intravenously or as a subcutaneous or intramuscular injection (Table 5). As an alternative, start regular insulin infusion at a rate of 0.14 U/kg per hour without initial bolus (about 10 U/h in a 70-kg patient) (24). Then the infusion

rate is adjusted until the glucose level decreases by 10% or by 2.8 to 4.2 mmol/L (50 to 75 mg/dL). When the blood glucose is less than 11.1 mmol/L (200 mg/dL), the insulin dose may then be reduced to 0.02 to 0.05 U/kg per hour. Therapy should be monitored on the basis of changes in the anion gap and serum ketones. The insulin dose or the dextrose concentration should be adjusted to keep the glucose between 8.3 to 11.1 mmol/L (150 to 200 mg/dL).

As an alternative to an intravenous infusion of regular insulin, adults with uncomplicated mild-to-moderate DKA can be treated with subcutaneous rapid-acting insulin analogs (for example, lispro or aspart) (25). In a small randomized, controlled trial, subcutaneous insulin lispro administered on the floor resulted in similar outcomes but lower costs than intravenous insulin administered in the intensive care unit (26). In DKA, correction of hyperglycemia is faster than ketoacidosis. It is ill-advised to reduce intravenous insulin therapy too quickly after normalization of blood glucose level, because this can prolong the duration of DKA. When DKA resolves, a multiple-dose insulin regimen should be initiated.

Guidelines for Initial Potassium Replacement from the American Diabetes Association*

- Serum K⁺ <3.3 mmol/L: No insulin; give 20–30 mmol K⁺ per h
- Serum K⁺ ≥3.3 to <5.2 mmol/L: Give 20–30 mmol/L to keep K⁺ between 4–5 mmol/L
- Serum K⁺ ≥5.2 mmol/L: Check K⁺ q 2 h but do not give K⁺ replacement

* Adapted from Kitabchi AE, Umpierrez GE, Miles JM, et al. Hyperglycemic crises in adult patients with diabetes. *Diabetes Care*. 2009;32:1335–43. [PMID: 19564476]

Table 5. American Diabetes Association Guidelines for Insulin Replacement*

Condition	IV Administration
Initial bolus	Regular at 0.1 U/kg as IV bolus
Infusion	0.1 U/kg per h as continuous IV infusion
If glucose level does not decrease by at least 10% in first hour	0.14 U/kg as IV bolus, then continue previous IV infusion
Serum glucose level reaches 11.1 mmol/L (<200 mg/dL)	Reduce insulin to 0.02–0.05 U/kg per h; or give rapid-acting insulin, 0.1 U/kg SC every 2 h, to keep glucose between 8.3–11.1 mmol/L (150–200 mg/dL) until metabolic control achieved

IV = intravenous; SC = subcutaneous.

* Adapted from Kitabchi AE, Umpierrez GE, Miles JM, et al. Hyperglycemic crises in adult patients with diabetes. *Diabetes Care*. 2009;32:1335–43. [PMID: 19564476]

26. Umpierrez GE, Latif K, Stoeber J, et al. Efficacy of subcutaneous insulin lispro versus continuous intravenous regular insulin for the treatment of patients with diabetic ketoacidosis. *Am J Med*. 2004;117(5):291–6.

What are the indications for phosphate therapy and bicarbonate therapy in the treatment of DKA?

Phosphate replacement is not typically needed when treating DKA, because low phosphate levels usually correct when the patient resumes eating. However, for patients with cardiac disease, anemia, respiratory depression, or profound hypophosphatemia (<0.0555 mmol/L [<1.0 mg/dL]), 20 to 30 mmol/L of potassium phosphate may be warranted, with close monitoring for hypocalcemia.

Bicarbonate therapy is more controversial because of potential risks, including worsening hypokalemia and intracellular acidosis. Many studies have failed to show improved clinical outcomes with bicarbonate therapy in patients with DKA (27, 28). The ADA recommends bicarbonate therapy if pH is less than 6.9 (15). Administer 100 mmol NaHCO_3 in 400 mL of water with 20 mmol KCL at 200 mL/h. Repeat every 2 hours until the pH is 7.0 or greater and check serum K^+ every 2 hours.

Do all cases of DKA require consultation with a diabetes specialist?

A diabetes specialist consultation is warranted if the DKA is severe, recurrent, or unresponsive to treatment. Outcomes of DKA are similar whether internists, emergency physicians, or specialists manage DKA, but the time to discharge can be shortened when a diabetologist is involved (29). Other specialists may need to be involved; for example, a timely nephrologist consultation is necessary for severe renal impairment that may require dialysis.

How should clinicians handle patients with recurrent episodes of DKA?

Recurrent DKA is a red flag that puts patients at high risk for future

recurrence. Repeated admissions for DKA consume an estimated one quarter of all health care dollars spent on adults with type 1 diabetes (8). Patients must be closely monitored by an experienced diabetes care team to ensure that the patient is treated with an optimal insulin regimen. Recurrent DKA is often associated with nonadherence to insulin (30); therefore, adherence barriers need to be addressed, such as ensuring that the medications are covered and affordable. Patients should use reminders to promote adherence to checking blood glucose and may use multiple insulin doses.

A randomized, controlled trial of an educational manual was conducted in 119 patients from a multidisciplinary diabetes clinic. All the participants had a hemoglobin A_{1c} level of 8.0 or greater, and 35% had type 1 diabetes. The manual aimed to improve patient understanding of how to perform and use blood glucose monitoring results. Over 6 months of follow-up, blood glucose monitoring increased in the intervention group (1.9 [SD, 1.3] to 2.8 [SD, 1.5] times daily; $P < 0.001$) and hemoglobin A_{1c} level decreased (-0.13 [SD, 1.28] vs. standard care (0.04 [SD, 1.10])). The intervention group also showed better knowledge about hemoglobin A_{1c} ($P = 0.04$). The authors concluded that an educational manual similar to the one they developed could serve as a useful adjunct to standard diabetes education and support to optimize blood glucose monitoring and glycemic control (31).

Psychosocial and other barriers to adherence must also be addressed. For example, urine drug screening may be warranted, because cocaine use is an independent risk factor for recurrent DKA (32). The management plan must be well established for when the patient begins to develop signs and symptoms of DKA. Health insurance and access to diabetes care is a basic requisite for the management of diabetes and avoidance of DKA.

In nearly 400 children with recently diagnosed type 1 diabetes, the uninsured children were 6 times more likely to present with DKA (odds ratio, 6.19 [95% CI, 3.04 to

27. Viallon A, Zeni F, Lafond P, et al. Does bicarbonate therapy improve the management of severe diabetic ketoacidosis? *Crit Care Med.* 1999;27:2690-3. [PMID: 10628611]
28. Green SM, Rothrock SG, Ho JD, et al. Failure of adjunctive bicarbonate to improve outcome in severe pediatric diabetic ketoacidosis. *Ann Emerg Med.* 1998;31:41-8. [PMID: 9437340]
29. Levetan CS, Passaro MD, Jablonski KA, et al. Effect of physician specialty on outcomes in diabetic ketoacidosis. *Diabetes Care.* 1999;22:1790-5. [PMID: 10546009]
30. Polonsky WH, Anderson BJ, Lohrer PA, et al. Insulin omission in women with IDDM. *Diabetes Care.* 1994;17:1178-85. [PMID: 7821139]

12.60)) than were those with insurance. The uninsured children also had a 6-fold increase in the odds of presenting with severe DKA (pH <7.10) (odds ratio, 6.09 [CI, 3.21 to 11.56]) compared with insured children (33).

When can treatment with subcutaneous insulin therapy resume?

When patients can eat adequate carbohydrates, they should resume rapid-acting insulin at meals and intermediate- or long-acting insulin. Intravenous insulin should continue for several hours after resumption of subcutaneous insulin to avoid recurrent hyperglycemia and a possible return to ketosis. Resolution of DKA is marked by a glucose level less than 11.1 mmol/L (200 mg/dL) and 2 of the following: serum bicarbonate level greater than 15 mmol/L, venous pH greater than 7.3, and anion gap less than 12. The typical duration of DKA therapy is about 48 hours. Obese patients with type 2 diabetes, especially minority patients, may be transitioned from insulin to oral medications after a period of improved diabetes control.

Patients with known diabetes can usually restart with the dose they were using before the onset of DKA. In patients with newly diagnosed diabetes, clinicians need to calculate the insulin regimen. For these patients, an initial insulin dose of 0.5 to 0.8 U/kg per day is usually adequate

to achieve metabolic control. The mainstay regimen is human insulin (NPH and regular) usually given in 2 or 3 doses per day. Frequently recommended alternatives are insulin analogs of basal (glargine or detemir) and preprandial rapid insulin analogs (aspart, lispro, glulisine). Patients with type 2 diabetes who have an episode of DKA do not automatically require long-term insulin therapy.

When should patients who have recovered from DKA receive follow-up care after discharge from hospital?

Patients, their families, and their caregivers should receive education about diabetes, the early signs of DKA, and sick-day management while still in the hospital. This can prevent recurrence of DKA. Referral to a diabetes center for intensive education may be appropriate. After discharge, patients require close follow-up with their physician. Patients with newly diagnosed diabetes should visit with their physician 7 to 10 days after discharge. This visit allows for a follow-up history and physical examination and for assessment of whether dosing adjustments or prescription changes are necessary. It also allows for further patient education and gives patients the opportunity to address any concerns with their doctor. Subsequent monitoring needs to be tailored to the patient's needs and ability to address the factors that precipitated the episode of DKA.

Treatment... The therapeutic goals of treating an episode of DKA involve hydration, correcting electrolyte imbalances, reducing the serum glucose level, eliminating ketones (both serum and urine), identifying the underlying precipitating factor, and managing or treating that factor. Treatment requires close monitoring in a setting in which laboratory testing can be assessed every few hours, including electrolytes, venous or arterial pH, and glucose determination. Patients may also need to have their phosphate levels checked periodically. Protocols can help ensure that patients have their significant metabolic and electrolyte abnormalities corrected at a safe, sustainable rate. Postdischarge management must focus on addressing the factors that precipitated the episode of DKA. Patient education and adherence supports are critical to preventing further episodes.

CLINICAL BOTTOM LINE

31. Moreland EC, Volkening LK, Lawlor MT, et al. Use of a blood glucose monitoring manual to enhance monitoring adherence in adults with diabetes: a randomized controlled trial. *Arch Intern Med.* 2006;166:689-95. [PMID: 16567610]
32. Nyerwe EA, Loganathan RS, Blum S, et al. Active use of cocaine: an independent risk factor for recurrent diabetic ketoacidosis in a city hospital. *Endocr Pract.* 2007;13:22-9. [PMID: 17360297]
33. Maniatis AK, Goehrig SH, Gao D, et al. Increased incidence and severity of diabetic ketoacidosis among uninsured children with newly diagnosed type 1 diabetes mellitus. *Pediatr Diabetes.* 2005; 6: 79-83. [PMID: 15963034]

Practice Improvement

What do professional organizations recommend regarding the management of DKA?

In 2009, the ADA updated their consensus statement on DKA, which addresses prevention, diagnosis, and treatment (15). The ADA defines DKA as blood glucose level >13.9 mmol/L (>250 mg/dL), arterial pH <7.3 , bicarbonate <15 mmol/L, and moderate ketonuria or ketonemia. Criteria for resolution of DKA are a glucose level <11.1 mmol/L (<200 mg/dL), serum bicarbonate ≥ 18 mmol/L, and a venous pH of >7.3 .

The ADA recommends fluid replacement as the first step in DKA treatment (Figure) (15). Frequent monitoring of fluid input/output and clinical examination are needed, with the goal of correcting estimated fluid deficits within the first 24 hours. If the K^+ is <3.3 mmol/L, give K^+ at 20 to 30 mmol/h but no insulin until the K^+ is >3.3 mmol/L. If K^+ is 3.3 to 5.2 mmol/L, give 20 to 30 mmol K^+ in each liter of fluid to maintain a normal K^+ . If K^+ >5.2 mmol/L, no K^+ supplement is given, but the level should be checked every 2 hours. Bicarbonate therapy is limited to patients with a pH <6.9 who should receive 100 mmol of bicarbonate in 400 mL water with 20 mmol KCl over 2 hours until pH >7 .

The ADA recommends 2 options for low-dose regular insulin in DKA. One is to give an insulin bolus dose of 0.1 U/kg, then a continuous infusion of 0.1 U/kg per hour. Based on a recent randomized trial (24), the second option is to give a continuous intravenous insulin infusion of 0.14 U/kg per hour without an initial bolus. If serum glucose does not decrease by at least 10% in the first hour, give an insulin bolus of 0.14 U/kg, then continue the previous insulin infusion until the glucose reaches 200 mg/dL. Then the regular insulin infusion is reduced to 0.02 to 0.05 U/kg per hour or 0.1 U/kg rapid-acting insulin given subcutaneously every 2 hours, aiming for a glucose of 8.3 to 11.1 mmol/L (150 to 200 mg/dL) until DKA resolves.

What measures do U.S. stakeholders use to evaluate the quality of DKA management?

The 2010 Physician Quality Reporting Initiative (PQRI) includes 179 measures, none of which are specifically related to the care of patients with DKA. However, most patients with DKA have a hemoglobin A_{1c} level $>9\%$ which is addressed in 1 quality measure.

in the clinic Tool Kit

Diabetic Ketoacidosis

PIER Module

pier.acponline.org

Access the PIER model on diabetic ketoacidosis. PIER modules provide evidence-based, updated information on current diagnosis and treatment in an electronic format designed for rapid access at the point of care.

Physician Resources

http://professional.diabetes.org/News_Display.aspx?TYP=9&CID=74814

Abstract of new study on the use of insulin analogues and human insulin for DKA

www.ncbi.nlm.nih.gov/pubmed/17079764?dopt=AbstractPlus

Citation of a clinical practice article from the New England Journal of Medicine on hyperglycemia in the hospital setting.

www.aafp.org/afp/20050501/1705.html

Full text of a narrative review in American Family Medicine on DKA management

www.annals.org/content/144/5/350/full

Abstract of narrative review from the Annals of Internal Medicine on ketosis-prone type 2 diabetes.

http://care.diabetesjournals.org/content/27/suppl_1/s94.full

Summary of the contrasting laboratory and clinical characteristics of DKA and HHS from the American Diabetes Association.

Patient Education Resources

www.annals.org/intheclinic/toolkit-dka.html

Access the patient information located on the above link to download and distribute to your patients.

www.diabetes.org/living-with-diabetes/complications/ketoacidosis-dka.html

Patient information on DKA from the American Diabetes Association.

in the clinic

THINGS YOU SHOULD KNOW ABOUT DIABETIC KETOACIDOSIS

What is diabetic ketoacidosis?

- Insulin helps the sugar in your bloodstream go into cells, where it is used for energy.
- Diabetic ketoacidosis (DKA) happens when your blood sugar (glucose) goes up too high because you are low on insulin. A high blood sugar can make you pass a lot of urine, which leads to dehydration.
- In DKA, the body burns fat, which increases a toxic acid (called ketones) in the blood.
- DKA happens mostly in children or adults with type 1 diabetes, but people (mostly adults) with type 2 diabetes or with diabetes during pregnancy can also get DKA.
- DKA is usually brought on by an illness, such as pneumonia, or by missing doses of diabetes medication.
- DKA is sometimes the first sign of having diabetes but can be prevented if you can recognize the signs of getting diabetes or DKA.



- Treatment is giving you fluids by vein, giving medication to lower your blood sugar, and correcting problems with the salt and potassium in your body.

How does a person know that they might have DKA?

- The clues to getting DKA are feeling thirsty all the time, urinating a lot, and feeling very tired or sleepy.
- Blood sugars over 250 mg/dL can be a sign of DKA as well as finding an acid (ketones) on a home blood or urine test.

How is DKA treated?

- DKA is successfully treated more than 95% of the time, but if untreated, can lead to coma and even death. People with DKA are usually hospitalized.

Is DKA preventable?

- Your doctor should make a plan for when you are sick (called a Sick Day Plan) to help keep you from getting DKA.
- On sick days, you make frequent blood sugar checks and take extra insulin depending on the sugar level as well as do home tests of urine or blood ketones. You drink extra fluid and eat specific foods.
- Call your doctor if your blood sugar stays over 240 mg/dL even though you have been following your sick day plan.

For More Information

Web Sites With Good Information About DKA

www.diabetes.org/type-1-diabetes/ketoacidosis.jsp
American Diabetes Association

<http://diabetes.niddk.nih.gov/dm/pubs/type1and2/specialtimes.htm#sick>
National Diabetes Information Clearinghouse

www.aafp.org/afp/20050501/1721ph.html
American Academy of Family Physicians

ACP
AMERICAN COLLEGE OF PHYSICIANS
INTERNAL MEDICINE | Doctors for Adults®

1. A 43-year-old alcoholic man with type 1 diabetes mellitus for 21 years is admitted from the emergency department for vomiting and diabetic ketoacidosis apparently caused by missing 2 days of insulin treatment. His initial metabolic values included a pH of 7.02, a blood carbon dioxide level of 8 mmol/L, a serum potassium level of 5.6 mmol/L, large ketones, and a plasma glucose level of 22.9 mmol/L (412 mg/dL). After several hours of treatment with intravenous fluids, insulin, and potassium, the glucose level decreases to 7.2 mmol/L (130 mg/dL). Intravenous therapy is changed to a subcutaneous twice-daily intermediate-acting insulin plus a sliding-scale short-acting insulin regimen. After 8 hours, the patient is again vomiting. His metabolic values are a pH of 7.09, large ketones, a blood carbon dioxide level of 12 mmol/L, a serum potassium level of 5.2 mmol/L, and a serum glucose level of 9/7 mmol/L (175 mg/dL).

Which of the following is not a reason for the persistent acidosis?

- A. Alcohol withdrawal syndrome
 - B. Volume expansion acidosis
 - C. Premature discontinuation of intravenous insulin administration
 - D. Failure to administer sodium bicarbonate
 - E. Lack of absorption of subcutaneous insulin
2. A 26-year-old woman with type 1 diabetes mellitus presents to the emergency department because of abdominal pain for the past 24 hours. Her temperature is 38°C (101°F).
- Laboratory studies: blood urea nitrogen, 7.14 mmol/L (20 mg/dL); serum creatinine, 106.1 μmol/L (1.2 mg/dL); serum sodium, 133 mmol/L; serum potassium, 3.9 mmol/L; serum chloride, 97 mmol/L; serum bicarbonate, 10 mmol/L; serum

glucose, 25.0 mmol/L (450 mg/dL); arterial blood gases: pH, 7.2, Pco₂, 23 mm Hg; blood cultures were negative; whole-blood lactate, 0.6 mmol/L.

What condition best explains the patient's acid-base status?

- A. Diabetic ketoacidosis alone
 - B. Diabetic ketoacidosis complicated by a proximal renal tubular acidosis
 - C. Diabetic ketoacidosis complicated by sepsis
 - D. Diabetic ketoacidosis complicated by respiratory acidosis
3. An 89-year-old woman is evaluated in a nursing home. She has had diabetes for more than 15 years; she was treated with a sulfonylurea for 1 year, but subsequently required insulin therapy. She has recently been experiencing labile control, with blood glucose levels fluctuating widely between 2.78 mmol/L (50 mg/dL) and more than 16.65 mmol/L (300 mg/dL). She takes 70/30 NPH/regular insulin, 22 U in the morning and 18 U at night. During a recent episode of gastroenteritis, her morning insulin was withheld because of concern that she would consume few calories that day. At 4 p.m. that day, her glucose level was 28.47 mmol/L (513 mg/dL). Her medical history is notable for stroke, coronary artery disease, and colon cancer. Examination shows a thin woman (BMI, 21 mg/kg of body weight) who looks her stated age. Dipstick urinalysis shows glucose and ketones.

Which of the following is the appropriate categorization of this patient's diabetes?

- A. Type 1 diabetes mellitus
- B. Type 2 diabetes mellitus
- C. Secondary diabetes
- D. Latent autoimmune diabetes of adulthood

4. A 20-year-old man with history of type 1 diabetes treated with human insulin 70/30 twice a day before meals presents to the emergency department with nausea, vomiting, and a few episodes of watery diarrhea of about 6 hours duration. He stopped his insulin injection because he could not tolerate any food. He seemed conscious, alert, and afebrile but was tachypneic. Initial laboratory studies showed serum glucose level, 33.3 mmol/L (600 mg/dL); creatinine level, 106.08 μmol/L (1.2 mg/dL); sodium, 130 mmol/L; potassium, 3.1 mmol/L; chloride, 95 mmol/L; bicarbonate, 12; anion gap, 28; and pH, 7.01.

Which of the following is the best initial treatment?

- A. Immediate volume repletion with intravenous normal saline
- B. Correction of hyperglycemia and ketosis with low-dose infusion of regular insulin
- C. Concurrent administration of insulin and normal saline infusion
- D. Administration of normal saline with 40 mmol/L of potassium added to the infusion
- E. Concurrent infusion of both low-dose insulin and potassium

Questions are largely from the ACP's Medical Knowledge Self-Assessment Program (MKSAP). Go to www.annals.org/intheclinic/ to obtain up to 1.5 CME credits, to view explanations for correct answers, or to purchase the complete MKSAP program.