

PEDIATRIC EMERGENCY MEDICINE PRACTICE

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Acute Hyperglycemic Crisis In The Pediatric Patient

A four-year-old boy presents to the emergency department with chief complaints of abdominal pain and nausea. A history reveals that the progressive abdominal pain and new-onset nausea, as well as polyuria, have lasted for several weeks. On further questioning, the parents indicate their son has lost several pounds in recent weeks. The physical examination reveals a generally uncomfortable boy who is holding his belly and is in obvious pain. He appears moderately dehydrated, with tacky lips and decreased skin turgor but adequate perfusion. A pulmonary examination reveals a deep and labored breathing pattern with no other focal abnormalities. His abdomen is diffusely tender, but there are no peritoneal signs.

You've seen this syndrome before. It is most likely diabetic ketoacidosis. A reading of "unmeasurable" on a finger stick confirms your suspicion. But now comes the hard part. You recall a similar patient a few months ago who developed sudden neurologic deterioration upon transfer to the pediatric intensive care unit. The intensivists diagnosed cerebral edema and felt it could have been avoided with better initial management. As you think about management options for this patient, you begin to question yourself: Was I responsible for the other patient's poor outcome? Are there clear right and wrong choices when it comes to fluids, insulin, and electrolyte supplementation?

Acute hyperglycemic crisis is the most common and most serious reason for emergency department (ED) evaluation of diabetic children.¹⁻⁴ In patients who are eventually diagnosed with type 1 diabetes mellitus (also called juvenile diabetes or insulin-dependent diabetes mellitus), approximately 25% to 30% initially present with diabetic ketoacidosis (DKA), one form of acute hyperglycemic crisis.⁵ In patients with known type 1 diabetes, DKA and DKA-related illnesses comprise the majority of acute presentations.⁶ While many of these

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CME Objectives

Upon completion of this article, you should be able to:

1. Identify key features of the history and physical examination that may predispose patients to acute hyperglycemic crises.
2. Describe the evidence for and against an association between cerebral edema and therapeutic decisions.
3. Determine appropriate indications for electrolyte supplementation.
4. Identify a method for early recognition and treatment of cerebral edema.

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patients do well, DKA carries an estimated mortality rate of 0.15% to 0.30%.^{7,8} The most common cause of mortality is cerebral edema.^{1,7,9} While the mechanism of cerebral edema is not well understood, evidence suggests it occurs early in the course of DKA,^{1,10} emphasizing the vital role of the ED clinician in the initial management of the disorder.

The correction of hyperglycemia and the prevention of morbidity and mortality in patients with DKA begin in the ED. In recent years, a large body of evidence has helped to elucidate the pathophysiology of the disorder and the appropriate management options for children with this and related illnesses. This issue of *Pediatric Emergency Medicine Practice* provides the most up-to-date guidelines and the results of evidence-based studies in order to assist the pediatric emergency clinician in caring for patients presenting with acute hyperglycemic crises.

Note: Acute hyperglycemic crisis refers to both diabetic ketoacidosis (DKA) and hyperglycemic hyperosmolar state (HHS). Although the term collectively describes the 2 disorders, the majority of this article will focus on DKA, as it is the more common disease process. A special section is also dedicated to the understanding of HHS.

Critical Appraisal Of The Literature

Population-Based Data

Patient demographics, admission rates, and risk factors for the initial presentation and severity of DKA have come largely from population-based studies. The majority of these studies have been conducted in European countries with access to national databases or registry systems. Only a few have been prospective in nature,^{6,11-13} but the majority were well designed, with large samples and excellent study-to-study reliabilities.

Treatment And Outcomes Data

The highest estimated incidence of cerebral edema in children with DKA is approximately 0.9%,¹⁰ emphasizing the need for large prospective controlled studies to determine the true differences between treatment and outcome measures. Support for consensus guidelines has also been hindered by the lack of such trials. Unfortunately, most prospective studies of DKA to date have not used control groups.²⁸⁻³⁸ Large retrospective studies have also lacked controls,¹⁴⁻²¹ while those studies that have used them have been notably small.²²⁻²⁷

There have been some exceptions. For example, support for insulin therapy, now recommended in consensus guidelines for the treatment of DKA, is supported by multiple prospective controlled trials.³⁹⁻⁴³ In addition to literature on insulin administration, there have been some prospective studies with control groups^{44,45} and large retrospective stud-

ies with control groups involving other aspects of DKA management.^{46,47}

Literature Search

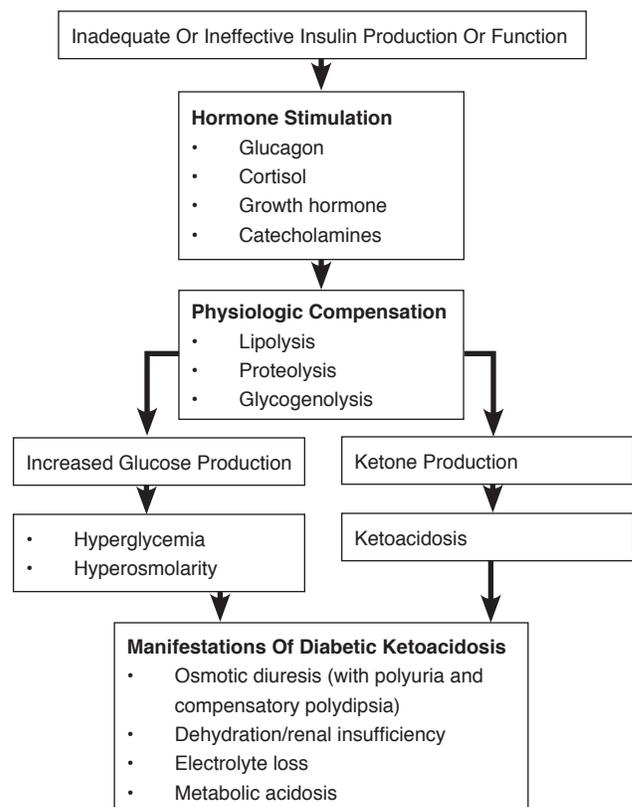
Ovid MEDLINE® and PubMed® were searched for literature on hyperglycemia and pediatrics published from 1950 to the present. Terms used in the search included hyperglycemia, DKA, pediatric, child, guideline, and cerebral edema. More than 200 articles were analyzed, providing the background for further review. The Cochrane Database of Systematic Reviews and the National Guideline Clearinghouse™ (www.guidelines.gov) were also consulted.

Table 1 lists guidelines related to hyperglycemia that are helpful for the practicing emergency clinician.

Pathophysiology

Diabetic ketoacidosis is the cumulative consequence of inadequate insulin production/function, the upregulation of counter-regulatory hormones, and the production of byproducts leading to the characteristic findings of hyperglycemia, ketonemia, and metabolic acidosis.¹ The consensus definition of DKA includes blood glucose level greater than 200 mg/dL, venous pH less than 7.3, and/or serum bicarbonate concentration below 15 mmol/L.^{1,48} A summary of the pathophysiologic mechanisms is represented in the Figure 1.

Figure 1. Pathophysiology Of Diabetic Ketoacidosis



Epidemiology

Between 1% and 5% of patients with type 1 diabetes present with an episode of DKA each year,⁵⁰ at an estimated cost of \$11,000 per hospitalization.⁵ As is the case with many other chronic diseases, a minority of patients represent the majority of these presentations.⁷ Most recurrent admissions occur secondary to missed insulin doses or the underdosing of prescribed insulin.^{1,12,48,51,54} As a result, there is great interest in identifying those patients at risk for DKA, and more importantly, those at risk for severe episodes.

Risk Factors For DKA

A wealth of literature has been published on DKA, and several important risk factors have consequently been identified:^{2-5,11,12,52-54}

1. Markers of poor glycemic control (eg, high hemoglobin A_{1c} [HbA_{1c}] level)^{12,52,54}
2. Young age (< 5 years) at severe or initial presentation^{5,8,11,53}
3. Older age (> 13 years) at recurrent admissions^{4,11,12,54}
4. Female sex¹¹
5. Lack of first-degree relative with diabetes mellitus⁸
6. Social characteristics (minority status, underinsured or receiving public insurance, poor family support)^{2,4,12,54}
7. Larger home insulin dosing^{12,54}

Prehospital Treatment

Prehospital care of the pediatric patient with DKA should focus on diagnosis and the management of potentially life-threatening issues, with particular attention given to the ABCs of basic life support. Once hyperglycemia is confirmed through a finger stick, patients should receive nothing by mouth. Peripheral venous access should be established, and cardiac monitors should be placed to evaluate for arrhythmias secondary to electrolyte imbalances. For patients in shock, oxygen should be placed, and 0.9% normal saline 10- to 20-mL/kg bolus may be given.⁵⁵

ED Evaluation

Important History Questions

The type of history obtained will depend on whether the patient has confirmed diabetes. With new diagnoses, it is imperative to rule out other causes of hyperglycemia and/or abdominal pain, especially intoxications, infection, and surgical processes.

Once laboratory evidence has confirmed the diagnosis of DKA, the evaluation should focus on historical indicators of severity. Population studies have evaluated markers of severity and patient histories leading to initial presentations of DKA^{6,13} and found that subtle symptoms often existed for weeks prior to presentation.⁶ A large prospective population study in Europe demonstrated that polyuria, weight loss, and fatigue were the most common presenting symptoms in patients newly diagnosed with type 1

Table 1. Evidence-Based Consensus Guidelines

Organization	Topic	Recommendations
American Diabetes Association ⁴⁸	Evaluation and management of acute hyperglycemic crisis	<ol style="list-style-type: none"> 1. Initial rehydration should use 0.9% normal saline at 10-20 mL/kg/h to maintain renal perfusion. 2. Initial insulin bolus should NOT be administered in pediatric patients. 3. Complications can be minimized by decreasing serum osmolality by 3 mOsm/kg/h and glucose level by 50-75 mg/dL/h.
European Society for Paediatric Endocrinology/Lawson Wilkins Pediatric Endocrine Society ¹	<p>Management of acute diabetic ketoacidosis in children and adolescents</p> <p>Prevention, recognition, and treatment of cerebral edema</p>	<ol style="list-style-type: none"> 1. Recognition of early cerebral edema can be achieved by rigorous use of a flow sheet. 2. Mannitol or 3% normal saline should be administered as soon as cerebral edema is suspected. 3. Electrolyte replacement: Onset of potassium replacement depends on the patient's potassium level on arrival in the emergency department; there is no evidence for replacement of other electrolytes.
International Society for Pediatric and Adolescent Diabetes ⁴⁹	Diabetic ketoacidosis	<ol style="list-style-type: none"> 1. Criteria for hyperglycemic hyperosmolar state include the following: <ol style="list-style-type: none"> a. Blood glucose > 600 mg/dL b. pH > 7.3 c. Serum bicarbonate > 15 mmol/L d. Small ketones e. Serum osmolality > 320 mOsm/kg f. Coma or stupor 2. Fluid estimation: Dehydration of 5%-7% is considered to be moderate; dehydration of 7%-10% is considered to be severe. 3. Insulin administration should be withheld for 1-2 hours after initiation of rehydration.

diabetes.^{6,13} Patients should still be asked about other classic symptoms including abdominal pain, nausea, and vomiting, although these are significantly less common at the initial presentation.⁶ The duration of the illness should also be determined, as this has been shown in some studies to be an important indicator of DKA severity.^{6,9,13,7} New-onset DKA can present with abdominal pain; therefore, the emergency clinician should consider the disorder as a differential diagnosis when evaluating patients with this chief complaint.

Historical markers shown to be independent risk factors for severe DKA on initial presentation are displayed in **Table 2**.

A large body of evidence suggests that in patients with known type 1 diabetes, the majority of cases of DKA are the result of missed or suboptimal insulin delivery.^{1,12,47,50,53} Thus, the patient history should also address the home insulin regimen (including dosage as well as delivery system), the method and frequency of blood glucose measurements, the number of missed doses, the baseline HbA_{1c} level (if known), and the strategy for sick-day management. Recurrent DKA is often triggered by an acute illness coupled with mismanaged insulin therapy during the illness period. Despite nothing-by-mouth status, a proper sick-day management plan should include maintenance insulin therapy in consultation with the patient's endocrinologist.^{12,50,53} If the patient is stable, the clinician may also focus on aggravating factors such as social stressors and psychological or psychiatric conditions.¹ Body image issues are particularly common among female adolescents who present with recurrent DKA and may be related to failure to take insulin in order to lose weight.¹

Important Physical Findings

The physical examination of the pediatric patient should concentrate on 5 general areas:⁴⁷

Table 2 Independent Risk Factors For Severe DKA

Marker	Rationale For Association
Age < 5 years ^{6,7,13,55}	<ul style="list-style-type: none"> Less likely to describe polyuria = longer duration before presentation Less well-developed B cells = increased likelihood of sudden, severe onset
Absence of relative with type 1 diabetes mellitus ^{6,13}	<ul style="list-style-type: none"> Less knowledge of presenting symptoms = longer duration before presentation
Greater proportion/longer duration of body weight loss ^{6,13}	<ul style="list-style-type: none"> Longer disease duration

1. **Airway/Breathing** – In addition to a standard assessment of the ABCs, any suspicious breathing patterns should be identified.^{47,48} A Kussmaul sign, which is highly indicative of DKA severity, may mimic impending respiratory failure and should be promptly investigated.^{47,48}
2. **Mentation** – The Glasgow Coma Scale should be used to determine the need for airway support,⁴⁸ but it is an inaccurate measure of elevated intracranial pressure.⁴⁵ A criteria-based scale similar to the Jones criteria for rheumatic fever has been used to identify impending neurologic compromise.⁴⁵ In one study, this scale demonstrated greater than 90% sensitivity and specificity in retrospectively distinguishing patients who later experienced neurologic deterioration.⁴⁵ Recent guidelines and review articles reflect the results of this study, and consensus support for use of the scale has been established.^{1,47,48,57} The criteria are listed in **Table 3**.⁴⁵
3. **Cardiovascular system**– Diastolic blood pressure (BP) monitoring in particular was indicative of severe disease in one retrospective study,⁴⁶ and heart rate and diastolic BP level are major and minor criteria, respectively,⁴⁵ of the neurologic compromise scale shown in **Table 3**.
4. **Infection** – All potential sources of infection should be evaluated, as infection is a common precipitating factor of acute illness.^{1,47,58} Evidence gained from retrospective analyses demonstrates the importance of the physical examination over laboratory markers such as white blood cell (WBC) count in detecting infection.⁵⁸ An

Table 3. Criteria To Identify Neurologic Compromise⁴⁵

Diagnostic Criteria	Major Criteria	Minor Criteria
Abnormal motor or verbal response to pain	Altered or fluctuating consciousness	Emesis
Posturing (either decorticate or decerebrate)	Sustained heart rate decelerations unrelated to other etiologies such as sleep or improved volume	Headache
Cranial nerve palsy (especially nerve III, IV, or VI)	Age-inappropriate incontinence	Lethargy or decreased arousability
Neurologic respiratory pattern		Diastolic blood pressure > 90 mm Hg
		Age < 5 years

The evaluation is considered positive for neurologic compromise if ANY of the following are present: 1 diagnostic criterion; 2 major criteria; or 1 major criterion and 2 minor criteria.

elevated WBC count is a nonspecific test result because the count is often elevated regardless of infectious status.⁵⁸

- Fluid balance – The pediatric patient should be assessed for degree of dehydration and signs of impending shock. According to results of a large systematic review, estimates of fluid balance are most reliable when assessed by capillary refill, skin turgor, and respiratory pattern.⁵⁹ It can be difficult to accurately estimate dehydration during DKA, however, as clinical signs of dehydration reflect the extracellular volume. With osmolar shifts from intracellular to extracellular volumes in DKA, the clinical signs may not present until late in the disease process, when total body water volume is significantly depleted. Perhaps because of this, clinicians are generally poor at estimating the extent of dehydration.^{34,47,60} Thus, most consensus guidelines recommend use of broad categorizations such as moderate (5%-7%) or severe (7%-10%) dehydration.^{47,48,56}

Diagnostic Studies

Flow Sheet

After the patient history and physical examination are completed, a diabetic flow sheet should be initiated.^{1,47,48} A flow sheet is a useful tool for tracking progress throughout a patient's hospitalization. Although flow sheet components differ from one institution to another, most forms include the following information:^{1,47}

Table 4. Initial Laboratory Tests

Diagnostic Test	Reason For Test
Serum glucose	Extent of hyperglycemia
Arterial blood gas	Acid-base status
Electrolytes with anion gap calculation	Assessment of hypokalemia/hyperkalemia
Calcium, magnesium, and phosphorus	Assessment of hypophosphatemia and baseline levels of calcium and magnesium, which may be affected by phosphate supplementation ⁶²
Serum urea nitrogen and creatinine	Extent of pre-renal impairment
Serum ketones	Measurement of ketonemia
Serum osmolality	Determination of severity classification and possibly fluid management ⁵⁶
Complete blood cell count with differential cell count	Measurement of white blood cell elevation, which can indicate the severity of ketoacidosis (not infection) ^{7,58}
Urinalysis	Assessment of dehydration and ketonuria

- Vital signs, every hour
- Neurologic assessment, every hour
- Input/output, every hour
- Insulin dose, every hour
- Capillary blood glucose level, every hour
- Laboratory values, every 2 to 4 hours (see the following section for specific laboratory tests)

Initial Laboratory Tests

The laboratory values shown in **Table 4** should be obtained for all patients with suspected DKA on presentation to the ED.^{1,47,48,61}

Table 5 contains laboratory tests that should also be considered depending on the patient's clinical presentation.

Classification Of Disease Severity

Early stratification of DKA severity can help to distinguish those patients who are at greatest risk for morbidity and mortality. Robust studies support the classification systems used by most hospitals today.^{10,16,21,28,31,32,43,46} Not surprisingly, prospective and retrospective studies have shown the degree of acidosis to be the most sensitive and specific predictor of disease severity.^{10,28,43,46} Hyponatremia⁴⁶ and elevated serum urea nitrogen levels^{10,43} have also been shown to correlate with severity in some studies.

The identification of acidosis as the preferred indicator of DKA severity has led to the establishment of treatment parameters in multiple consensus guidelines.^{1,48,61} The classification scheme listed in **Table 6 (page 6)** provides the ED clinician with evidence-based criteria to support treatment and disposition choices.^{1,48,61}

Follow-up Laboratory Evaluation

The resolution of DKA is a long process that requires frequent laboratory evaluations to minimize the risk of complications.⁴⁷ The recommended frequency of follow-up testing is based strictly on consensus guidelines, as no studies to date have evaluated the timing of follow-up testing. Of special note, the consensus guidelines recommend venous blood draws for all follow-up measurements including blood gas

Table 5. Additional Laboratory Testing

Diagnostic Test	Reason For Test
Blood and urine cultures, chest radiograph	Evaluation for infectious etiologies ^{1,47,48,61} and increased risk of serious bacterial infection due to impaired immune response ⁵⁸
Hemoglobin A _{1c}	Assessment of long-term control if patient has confirmed diabetes ^{1,47,48,61}
Electrocardiogram	T-wave assessment if patient is found to be hypokalemic or hyperkalemic ^{1,47,48,61}

values. The authors emphasize that venous draws give a relatively accurate assessment of pH and that arterial puncture is unnecessary and painful provided an adequate venous line can be placed.^{1,47,48,61} Current guidelines recommend the reassessment schedule shown in **Table 7**.^{1,61}

Head Computed Tomography Scan

Because severe DKA is associated with a high risk of cerebral edema, the astute emergency clinician might think it wise to order a head computed tomography (CT) scan for patients presenting with the disorder. However, current research indicates this test is a low-yield venture and may delay important initial therapies. On admission, the majority of pediatric patients with DKA do have significantly narrowed ventricles suggestive of brain swelling.²⁸ On presentation, more than 50% have brain swelling; by 8 hours into the hospital course, more than 75% show significant swelling on CT scans.²⁸ However, these radiographic findings do not necessarily correlate with a more severe course and instead likely reflect a more pervasive pathologic process in all patients with DKA.^{28,29,45} Therefore, it may be more prudent to rely on frequent neurologic assessments and to consider a head CT scan as supportive evidence only for patients who show clinical evidence of neurologic deterioration.⁵⁶

Treatment

The introduction of insulin in the early 20th century led to a marked reduction in morbidity and mortality from DKA.⁶³ In the early stages of treatment, insulin was given in large boluses, and fluid protocols were not considered. While this initial treatment regimen was highly successful, case reports of unexpected death during treatment began to emerge in the literature. At autopsy, researchers noted cerebral edema in children who were seemingly doing well in their treatment course before a sudden, profound neurologic deterioration ultimately led to significant impairment or death.⁶³

With highly successful treatment in most patients with DKA, the research focus turned to

identifying the causes of unexpected sequelae in this small number of patients. Case reports led to retrospective analyses, and eventually a link was found in several treatment modalities. As a result, a new emphasis was placed on determining which patients are at high risk of developing cerebral edema and finding a treatment regimen to help minimize this risk. The current DKA treatment protocol maintains this focus, with the goals of reversing detrimental pathophysiologic processes in concert with minimizing the risk of iatrogenic morbidity and mortality.

Fluids

Goals

Fluid administration should be based on 2 goals: the rapid identification and treatment of hypovolemic shock and the gradual replacement of the remaining fluid deficit.^{18,19,32,34,60} Although these goals can overlap, thinking of them separately emphasizes the importance of assessing each patient for volume status. In some centers, fluid boluses are given to patients regardless of evidence suggesting shock.¹⁹ In one retrospective series, 84% of patients received boluses even though fewer than 15% of them demonstrated clinical evidence of shock.¹⁹

Initial Treatment

Patients suffering from hypovolemic shock should be resuscitated immediately upon arrival at the ED.^{1,18,32} Consensus guidelines and expert opinions suggest the use of 0.9% normal saline or lactated ringers (LR) solution IV bolus at 10 mL/kg over a 1-hour period, with an additional 10-mL/kg bolus if the patient is still showing clinical evidence of shock.^{1,18,32}

Maintenance Treatment

While emergency clinicians are involved primarily in the initial treatment of DKA, patients often remain in the ED for part of the maintenance phase (ie, while they await appropriate placement for continued management). It is during this phase that fluid administration is most controversial and hotly debated because of a possible link to cerebral edema.

The argument for fluid involvement in the development of cerebral edema stems from the hyper-

Table 6. Classification of Disease Severity^{1,48, 61}

Class	Laboratory Values
Hyperglycemia without ketoacidosis	pH > 7.3; bicarbonate concentration > 15 mmol/L
Mild diabetic ketoacidosis	pH 7.2-7.3 or bicarbonate concentration 10-15 mmol/L
Moderate diabetic ketoacidosis	pH 7.1-7.2 or bicarbonate concentration 5-10 mmol/L
Severe diabetic ketoacidosis	pH < 7.1 or bicarbonate concentration < 5 mmol/L

Table 7. Reassessment Guidelines

Frequency	Test
Every hour	• Finger stick capillary blood glucose
Every 2-4 hours	• Venous blood gas • Serum electrolytes • Serum urea nitrogen/creatinine • Serum osmolality • Serum ketones
With every void	• Urine ketones

osmolar explanation of cerebral edema pathophysiology. According to this theory, during DKA the intracellular environment within the brain slowly equilibrates with the extracellular environment by producing inorganic osmoles. This process prevents the rapid fluid shifts that normally occur in the hyperglycemic state. It is theorized that during rapid correction, the combination of fluid overload and a brisk decline in extracellular glucose concentration leads to a disruption of the osmolar balance. This disruption causes a massive influx of fluid into the brain cells, resulting in cerebral edema.⁵⁷

Support for this theory has been demonstrated in the literature. Multiple retrospective studies have shown a link between the rate of serum osmolarity decrease^{22,31} or total volume of fluids administered and the risk for cerebral edema.^{27,46} Based on these analyses, the subsequent movement was toward development of a “safe” model of fluid administration. Multiple prospective studies showed reduced risk of cerebral edema when fluid deficits were corrected over a 36- to 48-hour period.^{27,32-34,43} These results led to recommendations for a relatively conservative time course for fluid replacement.^{1,47,48}

Although conceptually strong and supported by promising evidence, the hyperosmolar theory and the role of fluids in the development of cerebral edema have come under scrutiny. Arguments against the theory cite the absence of control groups or cases of cerebral edema in prospective studies.^{43,64,65} With an incidence of less than 1% in DKA, cerebral edema can be elusive. In even the largest prospective studies, the samples may not have been large enough to detect this condition.³² Additional evidence indicates that despite changes in fluid management, rates of cerebral edema have remained relatively stable.^{10,65,66}

The most damaging evidence against the hyperosmolar theory concerns the proposed cause and effect relationship. If excess fluid administration causes osmolar shifts leading to cerebral edema, all cases of cerebral edema would be expected to occur well into the treatment course. However, this has not been the case. Glaser et al¹⁰ found several cases of cerebral edema that were apparent on presentation. Follow-up studies have shown similar occurrences, with support from imaging studies demonstrating significant cerebral edema prior to the initiation of treatment.^{28,29,45,65}

Taking all the evidence into account, many experts now think the development of cerebral edema may be multifactorial. Administration of fluids may have an impact, but it is clear that it is not the sole determinant of morbidity. Clear evidence indicates that hypotonic fluids can be harmful,^{1,57} but most other options are also based on controversial evidence.

Until further data can be obtained, emergency clinicians are prudent to be relatively conservative

with their treatment choices, with the knowledge that evidence in all directions is clearly weak.⁵⁷ A conservative model for fluid replacement that takes guidelines and simplicity into account is described in **Table 8**.

Sodium And Pseudohyponatremia

During acute hyperglycemic crises, serum sodium levels often decrease secondary to osmolar fluid shifts, resulting in dilution of the measured extracellular sodium concentration. Common practice is to correct for this dilutional effect in order to determine the likely serum sodium concentration following reversal of hyperglycemia.⁶⁷ The common correction factor of 1.6 is represented in the equation below.⁶⁸

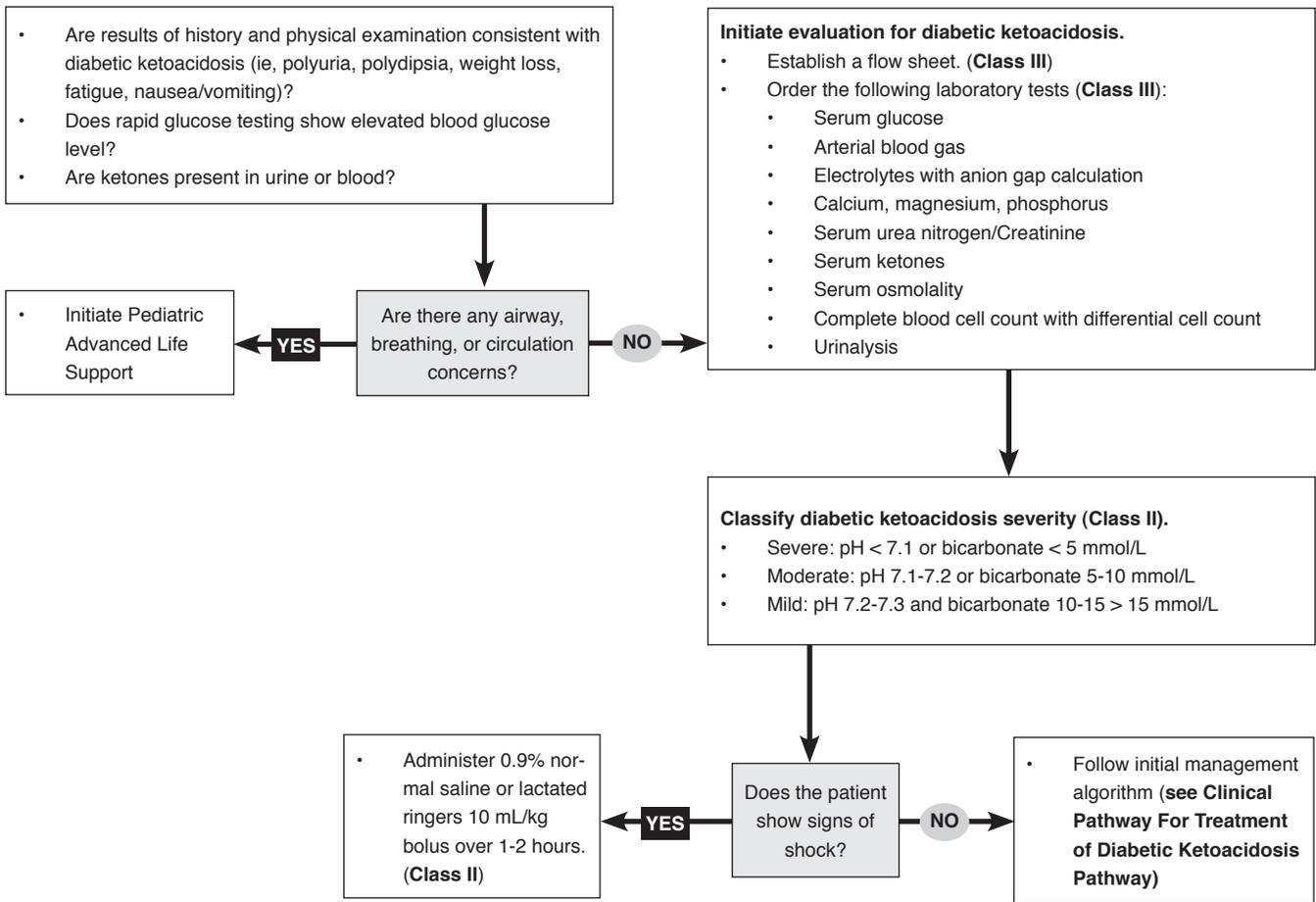
$$\text{Sodium}_{\text{cor}} (\text{mEq/L}) = \text{Sodium}_{\text{obs}} (\text{mEq/L}) + 0.016 \times [\text{Serum Glucose}_{\text{obs}} (\text{mg/dL}) - 100]$$

The basis for this correction factor is largely theoretical, with no clinical trials to confirm its accuracy.⁶⁷ Only one clinical trial has examined pseudohyponatremia secondary to acute hyperglycemia. This trial demonstrated a nonlinear association

Table 8. Fluid Guidelines

Phase Of Treatment	Treatment Plan
Initial	<ul style="list-style-type: none"> Administer 0.9% normal saline or lactated ringers 10 mL/kg bolus over 1 hour for “shocky” patients.^{1,47,61} Consider additional 10-mL/kg bolus if examination reveals that poor perfusion persists.^{1,47,61}
Deficit	<ul style="list-style-type: none"> Estimate the fluid deficit. <ul style="list-style-type: none"> Calculate 1.5-2.0 times maintenance fluid requirements.^{1,47,61} Calculate percentage of dehydration on admission; some experts advise using an estimation of 5%-7% for moderate dehydration and 7%-10% for severe dehydration.^{47,48} Add percentage of dehydration to maintenance requirements.¹
Maintenance fluids	<ul style="list-style-type: none"> Subtract fluid given in the bolus(es) from the total.^{1,47} Replace remaining deficit plus requirements with 0.9% normal saline, 0.45% normal saline, or lactated ringers administered evenly over the course of 36-48 hours.^{1,47,48,61} Consider supplementation with potassium and/or phosphorus (see following sections).^{1,47,48,61} Add dextrose to fluids if ketones are still present and blood glucose level approaches 250 mg/dL or less (see Insulin section).^{1,47,48}

Clinical Pathway For Initial Evaluation Of Diabetic Ketoacidosis



Class Of Evidence Definitions

Each action in the clinical pathways section of *Pediatric Emergency Medicine Practice* receives a score based on the following definitions.

Class I

- Always acceptable, safe
- Definitely useful
- Proven in both efficacy and effectiveness

Level of Evidence:

- One or more large prospective studies are present (with rare exceptions)
- High-quality meta-analyses
- Study results consistently positive and compelling

Class II

- Safe, acceptable
- Probably useful

Level of Evidence:

- Generally higher levels of evidence
- Non-randomized or retrospective studies: historic, cohort, or case control studies
- Less robust RCTs
- Results consistently positive

Class III

- May be acceptable
- Possibly useful
- Considered optional or alternative treatments

Level of Evidence:

- Generally lower or intermediate levels of evidence
- Case series, animal studies, consensus panels
- Occasionally positive results

Indeterminate

- Continuing area of research
- No recommendations until further research

Level of Evidence:

- Evidence not available
- Higher studies in progress
- Results inconsistent, contradictory
- Results not compelling

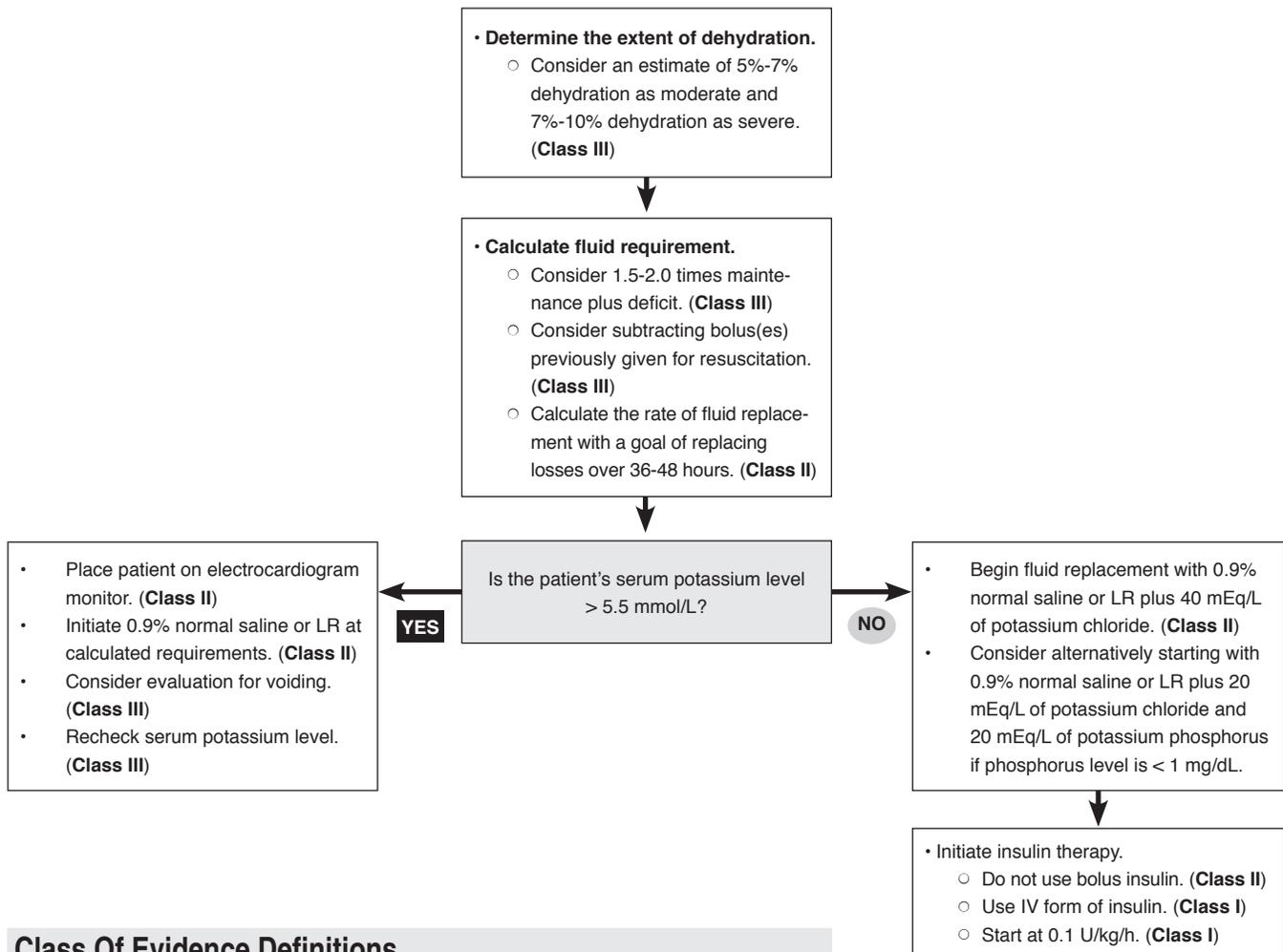
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tatives from the resuscitation councils of ILCOR: How to Develop Evidence-Based Guidelines for Emergency Cardiac Care: Quality of Evidence and Classes of Recommendations; also: Anonymous. Guidelines for cardiopulmonary resuscitation and emergency cardiac care. Emergency Cardiac Care Committee and Subcommittees, American Heart Association. Part IX. Ensuring effectiveness of community-wide emergency cardiac care. *JAMA*. 1992;268(16):2289-2295.

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Clinical Pathway For Treatment Of Diabetic Ketoacidosis



Class Of Evidence Definitions

Each action in the clinical pathways section of *Pediatric Emergency Medicine Practice* receives a score based on the following definitions.

Class I

- Always acceptable, safe
- Definitely useful
- Proven in both efficacy and effectiveness

Level of Evidence:

- One or more large prospective studies are present (with rare exceptions)
- High-quality meta-analyses
- Study results consistently positive and compelling

Class II

- Safe, acceptable
- Probably useful

Level of Evidence:

- Generally higher levels of evidence
- Non-randomized or retrospective studies: historic, cohort, or case

Control Studies

- Less robust RCTs
- Results consistently positive

Class III

- May be acceptable
- Possibly useful
- Considered optional or alternative treatments

Level of Evidence:

- Generally lower or intermediate levels of evidence
- Case series, animal studies, consensus panels
- Occasionally positive results

Indeterminate

- Continuing area of research
- No recommendations until further research

Level of Evidence:

- Evidence not available
- Higher studies in progress
- Results inconsistent, contradictory
- Results not compelling

Significantly modified from: The Emergency Cardiovascular Care Committees of the American Heart Association and representatives from the resuscitation councils of ILCOR: How to Develop Evidence-Based Guidelines for Emergency Cardiac Care: Quality of Evidence and Classes of Recommendations; also: Anonymous. Guidelines for cardiopulmonary resuscitation and emergency cardiac care. Emergency Cardiac Care Committee and Subcommittees, American Heart Association. Part IX. Ensuring effectiveness of community-wide emergency cardiac care. *JAMA*. 1992;268(16):2289-2295.

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between sodium and hyperglycemia, suggesting the commonly used correction factor may grossly underestimate the degree of dilutional sodium decreases, especially in cases of severe hyperglycemia. The results of this study suggest a correction factor of 2.4, with the acknowledgment that even this figure may underestimate the dilutional effect when the blood glucose level is greater than 400 mg/dL.⁶⁷ The modified equation is shown below.

$$\text{Sodium}_{\text{cor}} (\text{mEq/L}) = \text{Sodium}_{\text{obs}} (\text{mEq/L}) + 0.024 \times [\text{Serum Glucose}_{\text{obs}} (\text{mg/dL}) - 100]$$

Insulin

Goal

Insulin therapy is the driving force for reduction of extracellular hyperglycemia/hyperosmolarity and ketolysis. Administration is tailored to meet this goal while balancing common adverse consequences including hypoglycemia and hypokalemia.

Initial Treatment

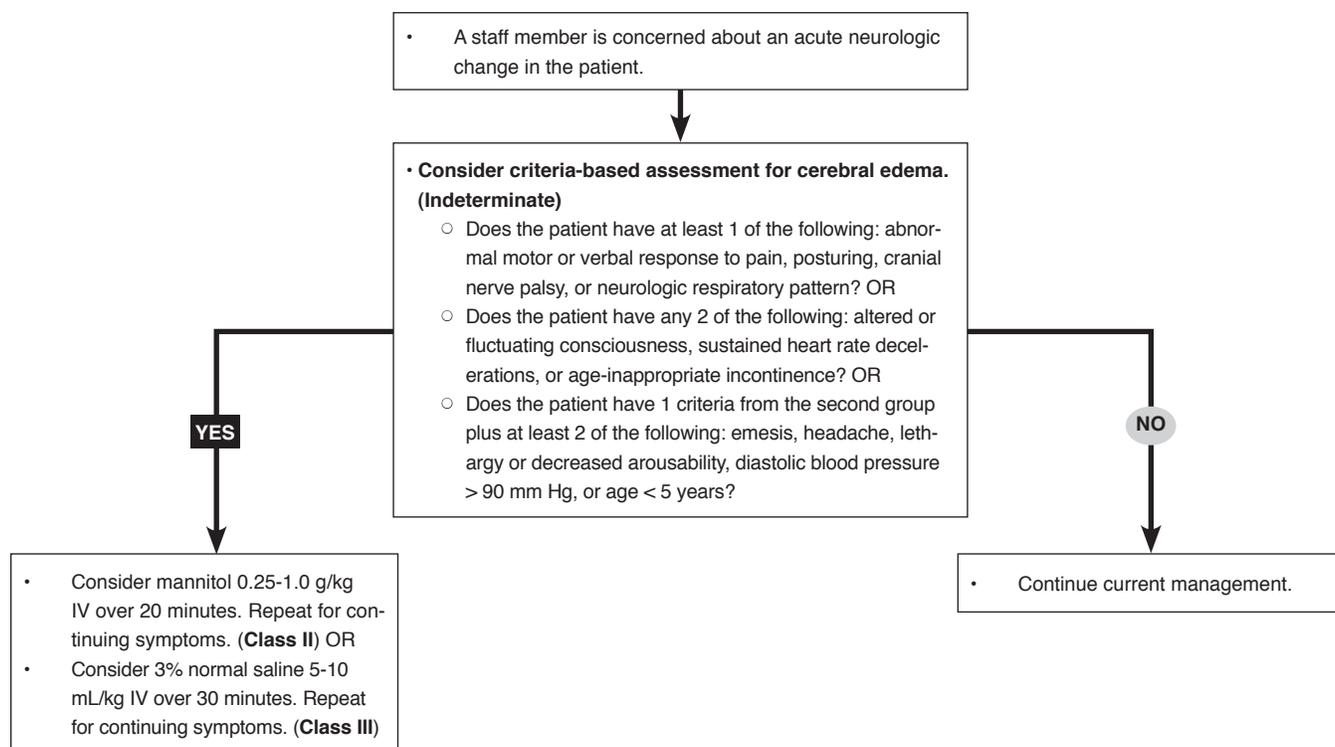
After fluid management, initial insulin administration is the second most controversial aspect of DKA care. Debates in the literature involve both the dosage and timing of insulin administration.

Whereas bolus insulin therapy is common in the management of adult DKA, its use in pediatric patients is argued in the literature. From a theoretical perspective, the use of bolus insulin makes sense.

If the goal is to drive down blood sugar levels and decrease ketone production, more rapid administration should lead to a quicker response. However, this is not always the case. Multiple studies, including several prospective controlled trials, have demonstrated no additional benefits from bolus insulin therapy when compared with the use of continuous infusions.⁴⁰⁻⁴² Although patients receiving bolus insulin therapy typically respond with a faster drop in blood glucose levels in the first 1 to 2 hours of therapy,^{41,42} the ultimate goal of reaching normoglycemia usually occurs within the same time frame. With continuous insulin infusion, this goal is reached with a steady, predictable decrease in serum glucose concentration.⁴¹ Additionally, the effectiveness of bolus insulin therapy in clearing ketones from the blood is similar to or no better than that of continuous insulin infusion.^{41,42}

Although there does not appear to be a clear advantage to bolus insulin therapy, there are several potential disadvantages associated with its use. First, the risk of hypokalemia is increased with larger doses of insulin.^{7,35} Second, there is a potential relationship between rapid declines in blood glucose levels and the development of cerebral edema, though this is poorly supported in the literature.^{1,43,57} Overall, bolus insulin therapy does not appear to be superior to continuous insulin infusion, and the risk for adverse consequences with its use should not be ignored.

Clinical Pathway For Evaluation And Treatment Of Cerebral Edema



A more recent concern regarding initial insulin administration involves the timing of therapy. Conventional wisdom suggests that if bolus therapy is not indicated, early continuous infusion is still a benefit. Recent study results appear to suggest otherwise.⁴⁴ Fluid administration alone can have dramatic effects on the reduction of serum glucose concentrations by increasing renal perfusion.^{1,43,47} Recent recommendations, based on admittedly poor data correlating early insulin administration with cerebral edema, suggest holding insulin administration until the patient has received an hour of fluid therapy.⁴³ While the data are not strong, they appear to depict a philosophy in DKA management that emphasizes fluid administration as the most important initial step and suggests that insulin therapy, while necessary, be used only after the fluid status has been addressed.

Maintenance Treatment

Maintenance insulin therapy is an area of DKA management that has been largely immune from controversy. A large body of evidence supports low-dose continuous intravenous (IV) therapy (0.1 U/kg/h).^{1,32,35,42,47,48,57} Higher doses lead to adverse side effects, with no appreciable benefits.³⁵ On the basis of this evidence, patients should be given IV insulin infusions at a rate of 0.1 U/kg/h. Therapy may continue at this rate until the patient's blood glucose level normalizes, acidosis resolves, and serum ketones have cleared. Failure of ketoacidosis to resolve should prompt the clinician to assess for common complicating factors including inadequate insulin delivery due to mechanical failure, incorrect insulin preparation, and severe resistance secondary to infection.

For patients who have not yet cleared ketones but have a blood glucose level of less than 250 mg/dL, dextrose should be added to fluids to prevent hypoglycemia while a continuous insulin infusion is maintained.^{1,47,48} This allows continued administration of insulin, which is often necessary to correct the residual ketoacidosis. The saline infusion should be changed to dextrose 5% in isotonic saline or LR when the serum glucose concentration decreases to 250 to 300 mg/dL (13.9-16.7 mmol/L). If the serum glucose level falls below 100 mg/dL before complete resolution of the ketoacidosis, the concentration of dextrose in the IV solution should be increased by up to 10%. Any adjustments in insulin dosage to manage rapid declines in blood glucose levels (ie, decreasing insulin infusion to 0.05 U/kg/h) should be based on the potential association with cerebral edema.^{1,43,57}

Resolution

Therapy is considered complete when the patient's blood glucose level is less than 200 mg/dL, the

serum bicarbonate concentration is greater than 18 mmol/L, and the venous pH is greater than 7.3.⁶¹ With resolution, a transition to a home glucose regimen may be made after consultation with the institution's endocrinology service.⁶¹

Potassium

Pathophysiology

Potassium losses during DKA are estimated at 3 to 6 mmol/kg in adult patients.¹ These losses often reflect disease severity, as studies have demonstrated distinct correlations between low levels of potassium and other markers of severity.⁶⁹

Intracellular potassium is lost secondary to a combination of factors including intracellular fluid shifts, the buffering of hydrogen ions, and the absence of insulin-stimulated cell entry.^{1,69}

At the time of presentation, a patient may have a low, normal, or even high serum potassium level.¹ Early in the process of DKA, potassium is moved from the intracellular environment to the extracellular environment by the mechanisms described previously. As the disease continues, additional processes can contribute to the variety of potassium levels observed in the ED. For example, if the patient becomes significantly dehydrated such that renal impairment ensues, an elevated serum potassium concentration will result.¹ If renal perfusion is maintained, potassium will be excreted, eventually resulting in low serum potassium levels.¹ It is important to remember that the total body potassium level is decreased in all cases. With adequate treatment, a patient presenting with an elevated serum potassium value will inevitably become hypokalemic and require supplementation.

Monitoring

Prior to treatment, all patients should be placed on cardiac monitoring so they can be evaluated for arrhythmias secondary to disease-related or iatrogenic potassium disturbances.^{1,47,61}

Replacement

Prospective clinical trials have evaluated the extent and rapidity of potassium loss during treatment for DKA and found significant and immediate decreases upon initiation of insulin and rehydration.⁷⁰ Although all patients will have a large decrease in potassium levels, the timing of potassium supplementation should be determined by the presenting serum concentration in order to limit the risk of life-threatening arrhythmias.^{1,7,47,61}

All consensus guidelines recommend immediate supplementation for patients presenting with low serum potassium levels.^{1,56,61} Guidance on when to initiate therapy for patients with normal or elevated serum potassium levels is less clear.^{1,47,61} One consensus guideline recommends the initiation of potas-

sium replacement when renal perfusion is restored and a documented void has occurred,¹ while another consensus statement recommends waiting for documentation of a normal serum potassium level.⁴⁷ Because laboratory values are reassessed often in the treatment of DKA, it may be best to wait for a documented value to minimize the risk of inducing iatrogenic cardiac arrhythmias.

The recommended method for replacement, on the other hand, has strong support in the literature.^{1,47,69} Based on prospective studies⁶⁹ and consensus guidelines,^{1,47} appropriate replacement is approximately 30 to 40 mEq/L. Traditionally, replacement is in the form of potassium chloride; however, potassium phosphorus may sometimes be used for reasons discussed in the next section.

Phosphorus

Theoretical Benefit

Phosphorus depletion during treatment for DKA has been well described in the literature.^{23,36,44} Depletion results in decreased levels of 2,3-diphosphoglycerate (DPG), which consequently shifts the oxygen saturation curve to the left, resulting in increased oxygen binding and subsequent tissue anoxia.³⁶ Theoretically, phosphorous supplementation should alleviate this potentially harmful side effect.³⁶ At this time, however, the data do not support the theoretical claim.

Multiple well-designed studies have looked into phosphorus replacement because of concerns about tissue injury.^{23,24,36,62} Only modest improvements in phosphorus and 2,3-DPG levels were seen in these studies, and those improvements did not demonstrate statistical or clinical significance.^{23,24} Of greater concern is the potential for induction of hypocalcemia and hypomagnesemia with phosphorus repletion.^{23,24,37,62} Statistically significant decreases in calcium were found in 2 prospective studies,^{24,37} and hypomagnesemia was found in 1 study.³⁷

Replacement

Based on the limited benefits demonstrated in these studies, phosphorus replacement is somewhat controversial. Consensus guidelines acknowledge the lack of demonstrated benefits and concerns about the induction of hypocalcemia.^{1,47,61} As a result of these concerns, most guidelines agree that replacement should be initiated in cases of significantly low phosphorus levels (< 1 mg/dL),^{1,47,61} with cardiac monitoring and frequent evaluation of serum calcium levels to anticipate iatrogenic hypocalcemia.^{1,47} Phosphorus is typically supplemented in the form of potassium phosphorus at 20 mEq/L.⁶¹ If this form is administered, it can replace some of the potassium chloride used for potassium replacement.

Bicarbonate

Theoretical Benefit

The appeal of bicarbonate is related to the notions that profound acidosis appears to be a risk factor for DKA severity and cerebral edema^{10,31,43,46,47} and that correction of acidosis could therefore eliminate a major cause of morbidity and mortality. However, in multiple studies of bicarbonate use, the medication was not helpful in restoring acid-base balance and in some cases may have caused significant harm.^{1,10,20,25,26,47,56,57}

Lack of Benefits

Retrospective analyses have examined the potential benefits of bicarbonate use in the treatment of DKA in pediatric patients.^{1,7,20,47,57} The studies found no benefits in clinical outcome, time to improvement, or length of hospital stay.²⁰ Patients appeared to improve independently of bicarbonate administration.¹

Potential Harm

Several studies have elucidated the risks involved in the administration of bicarbonate.^{25,26} Animal models have demonstrated lactic acidosis and cerebral injury during administration of the drug,²⁵ and a paradoxical worsening of acidosis during administration has been suggested.¹ Whether this is a direct result of bicarbonate use or part of a multifactorial process is unclear.^{43,47,57}

Use

Despite its theoretical benefit, bicarbonate does not appear to have a role in the current management of DKA.^{1,47,61}

Special Circumstances

Management of Cerebral Edema

Even with strict adherence to treatment guidelines, a number of pediatric patients who present with DKA will ultimately develop cerebral edema.^{1,45,57} Although many of these patients will deteriorate long after leaving the ED, a substantial number will develop signs and symptoms early in the course of the disease,^{10,45} making it imperative that ED clinicians know their options for management.

Unfortunately, data on best practices for treatment of cerebral edema are limited. Proposed options have included mannitol or hypertonic saline diuresis, steroids, and hyperventilation. Mannitol has received the strongest backing, with several studies showing benefits and with consensus guidelines supporting consideration of its use.^{1,10,14,15,45,57,71} Hypertonic saline should also be considered because of its similar physiologic effects, although recommendations for its use are based largely on theory rather than on well-supported studies.^{1,17,45,57} Hyperventilation was thought to be helpful given its utility

in similar situations of increased intracranial pressure; however, it was shown to be potentially detrimental and is no longer recommended.^{1,16,57} Steroids have a theoretical use but have been supported by only one study.⁵⁷

The low rate of cerebral edema is fortuitous for the pediatric emergency clinician. However, the low incidence means that experience with the disorder and literature on the subject are limited. According to current evidence, in the case of impending cerebral edema, the ED clinician should consider the use of mannitol (0.25-1.0 g/kg IV over 20 minutes) or hypertonic saline (3% normal saline 5-10 mL/kg IV given over 30 minutes) along with fluid restriction with repeated dosing for continuing symptoms.^{1,17,71} Cerebral edema with significant neurologic manifestations is the main reason for providing airway protection in the form of intubation in patients with DKA. Caution should be used if sedation is provided, as sedatives may dampen the Kussmaul respiratory sign and aggravate acidosis.

Hyperosmolar Hyperglycemic State

Definition

Hyperosmolar hyperglycemic state (HHS), also referred to as hyperosmolar nonketotic state or hyperosmolar coma, warrants specific attention as it differs from DKA in several important ways. Characteristics of the disease include the following:^{1,72,73}

1. Blood glucose level > 600 mg/dL
2. Serum osmolality > 320 mOsm/kg
3. PCO₂ > 15 mm Hg
4. Urinary ketones absent or small
5. Serum ketones absent or low
6. Mental status change

Epidemiology/Pathophysiology

HHS is significantly less common than DKA in the pediatric population.^{72,73} As a result, literature on the disorder is limited, consisting of a few case reports,⁷² review articles,⁷³ and consensus guidelines.¹ In addition to being older than patients with DKA, patients with HHS typically have type 2 diabetes.^{1,72,73}

Although HHS has been rare in the pediatric age group, evidence suggests it is becoming more common, perhaps because of increased rates of childhood obesity with subsequent development of type 2 diabetes.⁷² Changes in the demographics of patients with type 2 diabetes may indicate that some young patients have been incorrectly classified as having type 1 diabetes strictly because of their age. This point was illustrated in one case series in which 7 patients originally classified with DKA retrospectively met criteria for HHS.⁷²

In pediatric HHS, the classic presentation is an obese male adolescent of African American descent.^{72,73} The marked elevations in glucose and

osmolality levels with the absence of ketosis are thought to be secondary to the preserved function of beta-cells.⁷³ Insulin production is intact, preventing the promotion of ketosis. However, with peripheral insulin resistance, glucose remains outside the cell, initiating shifts of fluids and electrolytes and the subsequent alteration of the osmolar gradient.⁷³

Clinical Presentation

These extracellular shifts result in the characteristic presentation of severe dehydration with mental status changes and often severe abnormalities in electrolyte levels.^{72,73} Patients often present late in the course of HHS, as abdominal features are typically absent because of the relatively preserved acid-base status.⁷³ Retrospective analyses often show nonspecific complaints such as headache and fatigue early in the disease course.⁷² Recognition of early stage HHS requires familiarity with the epidemiology of the disease (an obese teenager with signs of peripheral insulin resistance),⁷² but it can be lifesaving, as the mortality rate in late stages of the disease is extremely high, approaching 15%.^{72,73} The pediatric ED clinician should always consider a rapid glucose check in an obese adolescent patient who complains of headache and fatigue.

Treatment

Treatment of HHS is similar to treatment of DKA, with several important distinctions.

- Hypovolemia is typically profound and is the leading cause of mortality. Thus, particular attention should be paid to early recognition and treatment of hypovolemic shock.⁷³
- Hypokalemia affects all patients with HHS. Electrolyte levels should be closely monitored, and replacement should begin immediately upon diagnosis.⁷³
- Insulin is often required but should be held pending fluid and electrolyte replacement, as early use of the drug may result in rapid electrolyte shifts.⁷³ The characteristic absence of ketosis and infrequency of profound acid-base disturbances may also limit its use.

Cutting Edge

In this era of growing ED use, emergency clinicians are under pressure to appropriately and promptly treat their patients. In the context of DKA, clinicians must be able to rapidly distinguish those patients requiring urgent intervention from those with less crucial needs. To this end, research efforts have focused on finding an efficient and accurate measurement device that can be used on initial presentation. One option under study involves tests of β-hydroxybutyrate levels in the capillary blood system. Interest in this concept grew from observations that traditional

measurements (urine ketones, serum bicarbonate, and serum pH) are either user dependent, slow, or painful for the patient.⁷⁴ In addition, β -hydroxybutyrate is the first ketone to become elevated in DKA,

and it often stays elevated long after a patient's serum glucose level has normalized.⁴⁹ This makes the enzyme a perfect candidate for a point-of-care test. Initial study results have been very promising.

Risk Management Pitfalls For Pediatric Acute Hyperglycemic Crisis

- 1. "All of my pediatric patients with DKA have high WBC counts. How can I tell which patients to work up and treat for infection?"**

Elevated WBC counts are common in patients with DKA and can be caused by the DKA process itself rather than by a true infection. The clinician should base the evaluation and treatment on clinical findings suggestive of infection rather than on an isolated WBC count.
- 2. "This child is always here for DKA. It's clear the parents are incapable of properly caring for her."**

In addition to parental neglect, there are other important reasons for patients to present with frequent DKA. Insulin pump failure is a common reason for readmission among patients with known diabetes. Inability to access proper medication can be a treatment barrier that is difficult to overcome. Finally, some teenage patients may be skipping insulin doses in order to lose weight.
- 3. "The patient had a normal score on the Glasgow coma scale. I don't understand how I missed cerebral edema."**

The Glasgow coma scale is not a sensitive marker for cerebral edema. The key to prevention is frequent reevaluation, with focus on ANY neurologic changes. A potential diagnostic strategy is shown in the **ED Evaluation** section of this article.
- 4. "I have been treating this patient for hours, and his blood glucose level will not budge."**

In this situation, it is important to consider comorbidities such as infection that may prevent appropriate lowering of glucose levels despite adequate insulin dosing. Alternatively, pharmacy errors or errors in administration may be the cause of static serum glucose levels.
- 5. "My pediatric patient with DKA is hyponatremic."**

DKA causes a pseudohyponatremia. Fluid shifts from the cell cause dilution of the serum sodium concentration, leading to the impression of a low serum sodium level. With correction of the serum glucose level, the serum sodium value will likely increase.
- 6. "My patient's head CT scan shows narrowing of the ventricles."**

Ventricular narrowing is very common during treatment for DKA. It does not appear to correlate with disease severity and most likely reflects a pathophysiologic mechanism of DKA. Treatment for cerebral edema should be initiated on the basis of clinical change as opposed to findings on a CT scan.
- 7. "My patient decompensated but did not show signs or symptoms of cerebral edema."**

It is important to consider other etiologies of decompensation in DKA. Known causes of death in patients presenting with DKA include infection, electrolyte abnormalities, hypoglycemia, thrombosis, pneumonia, renal failure, and pancreatitis.
- 8. "I never worry about cerebral edema in my adult patients."**

It is unclear why children are uniquely susceptible to cerebral edema; nevertheless, the disease does not occur in adults. Various mechanisms have been proposed, but they are strictly theoretical at this time. The important take-home point for the emergency clinician is that DKA management in children requires more rigor and attention to detail to minimize a risk that is unique to this age group.
- 9. "My patient decompensated prior to therapy."**

There have been several documented incidences of cerebral edema occurring prior to initiation of therapy. These cases appear to undermine theories related to fluid administration and insulin dosing and to point instead toward a multifactorial etiology.
- 10. "My patient has a severely elevated blood glucose level but no ketones."**

The patient likely has HHS. This disorder is distinguished by higher glucose levels than those typically found in DKA as well as the absence of ketonemia. These patients benefit from early recognition of the condition and intensive focus on rehydration and electrolyte balances.

Several prospective studies have compared capillary β -hydroxybutyrate levels with standard measures for identifying DKA in adult patients.^{49,74,75} Results indicate that sensitivities, specificities, and negative predictive values approach 100% when cutoff values of less than 1.5 to 1.8 mmol/L are used.^{49,74} Although further studies are needed to assess the cost-effectiveness of β -hydroxybutyrate measurement and its crossover to the pediatric population, this area of research may dramatically improve the speed and accuracy of DKA diagnosis.

Disposition

Pediatric patients meeting the criteria for severe DKA warrant hospitalization in an intensive care unit or on a floor with personnel specifically trained in the management of DKA and the identification of impending cerebral edema.^{1,47} At a minimum, these patients require a location where telemetry, a low nurse to patient ratio, and hourly neurologic and glucose checks can be provided and a strict hourly fluid balance can be maintained. On the other end of the spectrum, patients who fall within the criteria for mild DKA or hyperglycemia without acidosis can likely be discharged to home after consultation with an endocrinologist.^{1,46,47} Patients meeting the criteria for moderate DKA are typically hospitalized; however, this protocol may soon change.

Some recent studies have examined methods for determining the disposition of patients with mild or moderate DKA (ie, either a low level of in-hospital care or discharge to home) based on their response to initial therapy.^{76,77} Results indicate a patient's level of improvement within the first 6 hours of therapy may be useful in identifying patients with mild DKA.^{76,77} With subsequent study, it may be feasible to observe patients for a set amount of time and, pending resolution of acidosis and clinical improvement, discharge them once adequate follow-up with a reliable primary medical doctor is guaranteed.⁷⁶ Until more studies are conducted, however, all pediatric patients who meet the criteria for moderate to severe DKA should be admitted to the hospital. Additionally, all patients with newly diagnosed dia-

betes should be admitted because of increased risk of cerebral edema and the need for education about this significant lifestyle change.

Summary

Few disorders in pediatric emergency medicine challenge the fine line between treatment and harm as clearly as acute hyperglycemic crisis does. On one hand, there is a clear need to reverse the precipitating insult. On the other, there is a desire to limit the potential for injury related to therapy. As this article has made clear, the effective treatment of DKA relies on the clinician's ability to rapidly assess the severity of the illness and make appropriate decisions regarding treatment modalities based on the available evidence. By using the information presented here, clinicians can hopefully limit the morbidity and mortality associated with this challenging disease process and improve the care of those children with diabetes who seek their help.

Case Conclusion

The initial laboratory test results come back. With a venous pH of 7.07, a serum bicarbonate level of 4 mmol/L, a serum glucose value of 650 mg/dL, and large ketones, your patient clearly meets the criteria for severe DKA. You immediately obtain IV access and give the patient 0.9% NS 10 mL/kg bolus over 1 hour for moderate dehydration with concern for impending shock. You connect the patient to cardiac and pulmonary monitors and continue to follow him closely.

After the bolus is complete, additional laboratory test results are delivered. Significant values include a serum potassium level of 6.3 mmol/L, a serum sodium level of 123 mmol/L, a serum osmolality of 340 mOsm/kg and serum urea nitrogen and creatinine values of 36 mg/dL and 0.8 mg/dL, respectively. A repeated finger stick shows that the bolus alone has decreased the serum glucose level to 575 mg/dL. You reassess the patient to find that he is somewhat less dehydrated but otherwise still uncomfortable. You initiate insulin 0.1 U/kg/h IV and 0.9% NS at 1.5 times maintenance plus deficits. In your calculation for fluid, you subtract the bolus you gave before starting maintenance therapy.

Cost-Effective Strategies

- **Resist the urge to pursue infectious workups on all patients with DKA.** Nearly all patients with DKA will have elevated WBC counts on admission. The elevation of this single value is likely a sign of the disease state as opposed to a sign of underlying infection that requires evaluation and treatment. Patients with an active infection will manifest other symptoms that, along with an elevated WBC count, support concern.
- **Arterial access may not be required in all patients with DKA.** Acid-base status in DKA can be determined by venous blood draws, as bicarbonate is largely unaffected by drawing from the venous side. Management of arterial access is unnecessary if a patient does not have hemodynamic instability and is expected to have a relatively short hospital stay.

You continue to reassess the patient frequently, looking for subtle neurologic changes. Fortunately, the patient appears to be doing quite well. His potassium level begins to trend down, and you now add KCl 40 mEq/L to his fluid in anticipation of a rapid decline. As you review other potential treatment options, you recall the risks/benefits of using bicarbonate or phosphorus and decide to continue your current therapy without adding either.

Your patient continues to do well, and you arrange for transportation to the PICU. During your next shift, you check in with your PICU colleagues and find that your patient is on his way home after completing the management therapy you successfully initiated.

References

Evidence-based medicine requires a critical appraisal of the literature based upon study methodology and number of subjects. Not all references are equally robust. The findings of a large, prospective, randomized, and blinded trial should carry more weight than a case report.

To help the reader judge the strength of each reference, pertinent information about the study, such as the type of study and the number of patients in the study, will be included in bold type following the reference, where available. In addition, the most informative references cited in this paper, as determined by the authors, will be noted by an asterisk (*) next to the number of the reference.

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CME Questions



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1. Which is NOT a risk factor for DKA on initial presentation of type 1 diabetes?
 - a. Age less than 5 years
 - b. Age > 13 years
 - c. Multiple relatives with diabetes
 - d. Female sex
2. The degree of acidosis is the most sensitive and specific predictor of disease severity.
 - a. True
 - b. False
3. What is the most appropriate technique for fluid resuscitation in a patient with moderate DKA who is not showing signs of hypovolemic shock?
 - a. Initiate maintenance fluids with 0.9% normal saline at 1.5 to 2.0 times maintenance requirements, with a plan to replace losses over 48 hours.
 - b. Initiate maintenance fluids with 0.9% normal saline at 1.5 to 2.0 times maintenance requirements, with a plan to replace losses over 24 hours.
 - c. Initiate maintenance fluids with ¼ normal saline at 1.5 to 2.0 times maintenance requirements, with a plan to replace losses over 48 hours.
 - d. Initiate maintenance fluids with ¼ normal saline at 1.5 to 2.0 times maintenance requirements, with a plan to replace losses over 24 hours.
4. Which of the following tests should be obtained for patients with suspected DKA on presentation to the ED?
 - a. Serum glucose
 - b. Arterial blood gas
 - c. Urinalysis
 - d. Serum ketones
 - e. All of the above
5. Fluids are harmful in all cases and should be avoided.
 - a. True
 - b. False
6. Which dose is the most appropriate for initiation of insulin therapy in pediatric DKA?
 - a. 0.05 U/kg/h continuous IV infusion
 - b. 0.1 U/kg/h continuous IV infusion
 - c. 0.5 U IV push × 1
 - d. 1.0 U IV push × 1

7. How should suspected DKA-related cerebral edema be treated?
 - a. With dexamethasone 0.5 mg/kg per day IV
 - b. With hyperventilation to achieve $\text{PCO}_2 \sim 35$ mm Hg
 - c. By increasing fluids to 2.5 times maintenance requirements
 - d. With mannitol 0.25 to 1.0 g/kg IV over 20 minutes

8. What is the appropriate method for replacement of bicarbonate in patients with DKA?
 - a. Bicarbonate should be replaced for all patients with a venous pH below 7.2.
 - b. Bicarbonate should be infused slowly to decrease the risk of cerebral edema.
 - c. Bicarbonate should be given by IV bolus to decrease the risk of cerebral edema.
 - d. Bicarbonate should not be given to patients with DKA.

9. How does the management of HHS differ from that of DKA?
 - a. Blood glucose levels seen in HHS are relatively high compared with those seen in DKA; therefore, insulin should be given immediately to patients with HHS.
 - b. Potassium replacement is contraindicated in HHS.
 - c. Electrolyte abnormalities occur with greater frequency in HHS and should be monitored more closely.
 - d. Patients with HHS rarely require fluid replacement.

10. Which laboratory value is NOT considered necessary for a diagnosis of HHS?
 - a. Absent or small urinary ketones
 - b. Blood glucose level > 600 mg/dL
 - c. $\text{PCO}_2 < 15$ mm Hg
 - d. Serum osmolality > 320 mmol/kg

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EVIDENCE-BASED PRACTICE RECOMMENDATIONS

Acute Hyperglycemic Crisis In The Pediatric Patient

Tothy A, Ryan, M. August 2009; Volume 6 Number 8

This issue of *Pediatric Emergency Medicine Practice* provides the most up-to-date guidelines and the results of evidence-based studies in order to assist the pediatric emergency clinician in caring for patients presenting with acute hyperglycemic crises. For a more detailed and systematic look at the latest evidence on acute hyperglycemic crisis in the pediatric patient as well as other considerations such as the physical examination, clinical pathways, and other laboratory tests not noted here, see the full text article at www.ebmedicine.net.

Key Points	Comments
Include ABCs, mental status, evaluation for infection, and assessment of fluid status in your initial evaluation of a patient with suspected DKA.	Initial laboratory assessment should include: plasma glucose, ABG, electrolytes, Ca/Mg/Phos, BUN and creatinine, serum and urine ketones, serum osms, and CBC with differential. Disease severity should be classified on the basis of acid/base balance status. ^{1,47,48,61}
Focus fluid administration in patients with DKA on accurate assessment of fluid balance, treatment of impending shock, and slow replacement of remaining losses. ^{18,19,32,34,60}	The proposal that fluid resuscitation is related to cerebral edema is supported by potential pathophysiologic explanations, retrospective studies, and a few prospective studies. A correlation has been shown in some studies, but a cause and effect has not been demonstrated. ^{1,47,48, 57}
Consider a criteria-based assessment for cerebral edema.	In cases of suspected or proven cerebral edema, mannitol is the therapy of choice. There is some evidence to suggest hypertonic saline may also be beneficial. ^{1,10,14,15, 17, 45,57,71}
Continue insulin therapy for patients with glucose levels of <250 if ketones are still present. To decrease risk of hypoglycemia, add dextrose to fluids when serum glucose approaches 250. ^{1,47,48}	Bolus insulin therapy should be avoided in pediatric patients. Initial dosing should start at 0.1 units/kg/hr. ⁴⁰⁻⁴²
Determine the timing of potassium supplementation by the presenting serum concentration in order to limit the risk of life-threatening arrhythmias. ^{1,7,47,61}	Although theoretically logical, the replacement of phosphorous and bicarbonate are not supported by literature. ^{1,20,47,61}
It is important to recognize Hyperglycemic Hyperosmolar State (HHS) as a unique and often missed entity which can manifest with significant disturbances in electrolytes and fluid status.	HHS is also known as hyperosmolar nonketotic state or hyperosmolar coma. Treatment of HHS is largely similar to DKA with several important distinctions.
Admit patients that meet the criteria for severe DKA to a pediatric intensive care unit or a floor with personnel specifically trained in the management of DKA and identification of impending cerebral edema. ^{1,47}	Some recent studies have looked at methods to determine low risk patients who may warrant either lower levels of in-hospital care or potential discharge to home depending on initial improvement with therapy. Until more studies are conducted, it is advisable to admit all patients who meet criteria for moderate to severe DKA. Additionally, it is advisable to admit all newly diagnosed diabetics for reasons including increased risk of cerebral edema and need for education for this significant lifestyle change. ^{76,77}

* See reverse side for reference citations.

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