**Definition:** Diabetic ketoacidosis (DKA) is a decrease in effective circulating insulin associated with increases in counter regulatory hormones (e.g., glucagon, catecholamines, cortisol, and growth hormone). Hyperglycemia and acidosis result in osmotic diuresis, dehydration, and obligate loss of electrolytes. (1)

Biochemical Criteria: blood glucose >200 mg/dL; venous pH <7.25 (arterial pH <7.3) and/or bicarbonate <15 mmol/L with ketones in blood or urine. (1)

**Pathophysiology:** (11) Insulin deficiency is the initial primary event in progressive β-cell failure, its exogenous omission in a patient with established disease, or its relative ineffectiveness when insulin action is provoked by physiological stress (e.g., sepsis) and in the context of counterregulatory hormone excess. These hormonal changes augment glucose production from glycolysis and gluconeogenesis while limiting glucose utilization. This process results in hyperglycemia (>11 mmol/L, approximately 200 mg/dL), osmotic diuresis, electrolyte loss, dehydration, decreased glomerular filtration, and hyperosmolality. Simultaneously, lipolysis provides increased free fatty acids. The oxidation of free fatty acids facilitates gluconeogenesis and generates acetoacetic and β-hydroxybutyric acids (ketones) that overwhelm buffering capacity, resulting in metabolic acidosis (pH 7.3). This is compounded by lactic acidosis from poor tissue perfusion. Progressive dehydration, hyperosmolality, acidosis, and electrolyte disturbances exaggerate stress hormone secretion and establish a self-perpetuating cycle of progressive metabolic decompensation.

**Epidemiology:** DKA occurs in 26% of children with new onset type 1 diabetes (T1DM). (2) DKA is the leading cause of morbidity and mortality in children with diabetes. (3,4) Mortality rates are less than 1% with the majority (62-87%) of these caused by cerebral edema.

Risk Factors for Cerebral Edema (CE): (5-10)
- Age <5 years
- New onset diabetes
- High initial serum urea
- Low initial partial pressure of arterial carbon dioxide
- Rapid administration of hypotonic fluid
- Failure of corrected serum sodium to rise during treatment
- Treatment with bicarbonate (HCO₃⁻)

**Inclusion Criteria**
Neonates to 18 years
Clinical findings of DKA

**Exclusion Criteria**
Hyperglycemia without acidosis

**Differential Diagnosis**
- Sepsis
- Stress-induced or steroid-related hyperglycemia
- Inborn errors of metabolism
- Hyperosmolar coma

**Diagnostic Evaluation**

**History:** Assess for
- Diabetes
- Polyuria, polydipsia, polyphagia
- Estimated weight loss
- Abdominal pain, vomiting
- Concurrent illness or infections
- Kussmaul respiration (rapid and/or deep sighing)
- Inadequate insulin therapy (e.g., non-adherence, inappropriate dosing)
- Altered sensorium 
- Steroid use
- The recording of conscious level is a vital assessment in the management of children with DKA as CE is rare but potentially devastating. (1)

**Physical Examination**
Degree of acidosis (mild, moderate, severe) is an important marker for determining the severity of DKA and is a risk factor for CE. Clinical assessment of dehydration can be imprecise. It’s important to treat children with DKA based on a moderate level of dehydration.
- Airway, breathing, circulation
- Weight (actual), height, m²
- Age <5 years
- Blood pressure, heart rate, respiratory rate, temperature
- Fruity breath
- Kussmaul respiration (rapid and/or deep sighing)
- Neurological status† (e.g., level of consciousness, fundal exam, pupils, Babinski reflex)

Degree of Acidosis: (11)
- Mild/Moderate - venous pH 7.0-7.30
- Severe - venous pH <7.0

**Laboratory Tests** (12)
Obtain immediately by bedside meter:
- Blood glucose
- β-hydroxybutyrate

Additional tests:
- K, HCO₃⁻, Cl, glucose
- BUN, Cr
- β-hydroxybutyrate
- Blood gas

For new onset diabetes:
- Diabetes panel
- Celiac panel
- Thyroglobulin antibodies panel

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Evidence Supports

- The use of potassium values from the venous blood gas to guide decisions regarding potassium supplementation. (12) – Strong recommendation, moderate quality evidence
- The use of 0.9% sodium chloride solution (normal saline) for rehydration in children age five years or older. Give one 20 mL/kg normal saline bolus, assess need for a second 20 mL/kg bolus, and subsequent fluid management should amount to 2500 mL per meter squared per day (subtract boluses; do not subtract boluses if rate dips below maintenance). If concerned for hyperchloremic acidosis (Cl level >110 mEq/L), consider changing fluid to LR. (13-21) – Strong recommendation, moderate quality evidence
- Remarks: In the studies reviewed, there appeared to be no clinically significant differences between types of fluids nor rate.
- The use of intravenous insulin to correct diabetic ketoacidosis when the patient has a pH <7.3. (22-25) – Strong recommendation, very low quality evidence

Remarks: In light of the equivocal evidence, the team decided to standardize and use IV insulin as the preferred approach. In circumstances where continuous IV administration is not possible for patients with uncomplicated DKA, serial subcutaneous insulin administration every 3 hours are safe and may be as effective as IV regular insulin infusion, but ideally should not be used in patients whose peripheral circulation is impaired.
- The administration of mannitol as the preferred agent in pediatric patients with diabetic ketoacidosis and cerebral edema. If mannitol is unavailable, give hypertonic saline. (26) – Strong recommendation, very low quality evidence
- The use of clinical judgment to determine if treatment is needed for cerebral edema. (27) – Strong recommendation, very low quality evidence

Evidence Lacking/Inconclusive

- Use of bicarbonate reported from the venous blood gas to guide the decision to start intravenous insulin therapy in patients whose bicarbonate values are <13 mmol/L; in patients whose bicarbonate levels are ≥13 mmol/L, wait for the laboratory values to confirm before initiating treatment. – Consensus recommendation
- To treat patients with diabetic ketoacidosis and hypokalemia with IV potassium. Consider oral supplementation after continuous intravenous insulin is discontinued and patient is able to tolerate oral medications. – Consensus recommendation
- To NOT decrease the insulin infusion if the blood glucose concentration decreases too quickly (greater than 100 mg/dL/hr) or falls too low (below 150 mg/dL) before DKA has resolved; rather, increase the amount of dextrose administered unless maximum already reached. Increase the amount of dextrose if patient is on less than 100% D10. – Consensus recommendation

Remarks: With equivocal evidence, the team felt that any additional time used to prepare could potentially delay treatment.
- The administration of lower-dose insulin infusions to children with DKA under the age of 5 and higher-dose insulin infusions to children aged 5 and older. (32-34) – Strong recommendation, low quality evidence

Remarks: Though there is evidence that a lower-dose concentration of insulin is safe and effective, there is no evidence to suggest that the higher-dose concentration is harmful.

Condition-Specific Elements of Clinical Management

General: Children with DKA present with signs and symptoms that are related to the degree of hyperosmolality, volume depletion and acidosis. The severity of DKA should determine the appropriate clinical setting in which to treat the child.

Treatment Recommendations: For children being transferred from an outside hospital (OSH), please see Clinical Algorithm for Transport of Children with DKA on page 6.

Fluid and Electrolyte Therapy
Initiate fluid replacement therapy BEFORE insulin therapy. Normal saline should be administered at 20 mL/kg and if clinically indicated, repeat once. For subsequent fluids, administer 2.5 L/m²/DAY and never exceed 4 L/m²/DAY (including the initial bolus), unless discussed with Attending Physician.

Insulin Therapy
For all children who have a pH <7.3 an insulin infusion should be administered. The decision to administer subcutaneous insulin should be made in consideration of the child’s hydration status.

Insulin Infusion- Administer continuous low dose IV infusions. Mix regular insulin, 100 units in 100 mL of Normal Saline (1 mL/h = 1 unit/h). Dose at 0.1 units/kg/h.

Maintain glucose between 100-200 mg/dL by titrating Bag A and Bag B. See Table I.

Subcutaneous Insulin- Administer insulin as determined by Diabetes Service.

Phosphate
Administration of phosphate bolus is not routinely recommended.

Bicarbonate
Administration of bicarbonate is not recommended.

Potassium (K⁺)
Potassium replacement is required if K⁺ is ≤5.5. See Table I.
**Admission Criteria**
- Admission criteria to DCU/TCU
  - DCU: pH 7.0 to 7.3
  - TCU: Overflow
- Admission criteria to Critical Care
  - Severe DKA with pH <7
  - Age <5 years
  - Altered mental status
  - DKA and received >40 mL/kg of fluid
  - Sepsis/SIRS
  - NaHCO₃ treatment
- West Campus/Woodlands admission criteria to critical care
  - Confirmed DKA

**Consults/Referrals/Follow-up Care**
Consultation and follow up with a Diabetes specialist is appropriate for all children with diabetes. Consultation with Psychology, Registered Dietician, Social Work, and Child Life for children with new onset or as determined by Endocrine.

**Measures**
**Process**
- Medical length of stay in Critical Care
- Medical length of stay in Diabetes Care Unit or Transitional Care Unit
- Total hospital medical length of stay
- # readmissions within one week of discharge

**Outcome**
- Time to administer subcutaneous insulin
- Incidence of cerebral edema after beginning therapy
- Time to correction of acidosis (e.g., normal anion gap <15; β-hydroxybutyrate <2; HCO₃ >15)
- pH level on arrival
- Glucose on arrival
- GCS on arrival
- # deaths with DKA diagnosis

**Special Care Monitoring**
Blood glucose every 1 h
Chem 10 every 12 h
Electrolytes every 2 h x 3, then every 6 h with improving anion gap (Normal anion gap <15)
Strict I&O
β-hydroxybutyrate every 6 h

**Cerebral Edema**
Consider administering mannitol at 0.5 grams/kg and restricting fluids. If mannitol given and patient stable, consider computed tomography (CT) scan.

**Diabetes Care Unit/Progressive Care Unit Admission Criteria**
Children who have mild or moderate DKA (pH 7.0 - 7.30).

**Intensive Care Unit Admission Criteria**
All children with one or more of the indicators below:
- Severe DKA (pH <7.0)
- Aged <5 years in DKA
- Altered mental status (AMS)
- >40 mL/kg of volume resuscitation
- Treatment with HCO₃
- Associated with sepsis/systemic inflammatory response syndrome (SIRS)

---

**Table I. 2 Bag System**

<table>
<thead>
<tr>
<th>Blood Glucose</th>
<th>A</th>
<th>B</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;300 mg/dL</td>
<td>0 mL/h (100%)</td>
<td>0 mL/h</td>
</tr>
<tr>
<td>251-300 mg/dL</td>
<td>0 mL/h (75%)</td>
<td>0 mL/h (25%)</td>
</tr>
<tr>
<td>201-250 mg/dL</td>
<td>0 mL/h (50%)</td>
<td>0 mL/h (50%)</td>
</tr>
<tr>
<td>151-200 mg/dL</td>
<td>0 mL/h (25%)</td>
<td>0 mL/h (75%)</td>
</tr>
<tr>
<td>≤150 mg/dL</td>
<td>0 mL/h</td>
<td>0 mL/h (100%)</td>
</tr>
</tbody>
</table>

If <100 mg/dL Notify practitioner while on IV therapy

NOTE: The goal is to obtain a blood glucose of 150 mg/dL. However, if rate of drop is ≥100 mg/dL or if the patient becomes hypoglycemic, please consult Diabetes Team for reconsideration of fluid rate or type.

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Initial history/clinical findings suggestive of DKA

Evidence of shock:
- Yes: Place O₂, administer normal saline 20 mL/kg bolus (repeat as needed)
- No: Place O₂, obtain and send STAT lab: HbA₁C, POC venous blood gas with metabolites, BHBA, Chem 10

Evidence of Cerebral Edema?
- Yes: Room immediately, place O₂, administer normal saline 20 mL/kg bolus, or obtain or calculate serum osmolality
- No: Place O₂, obtain or calculate serum osmolality, consider mannitol 0.5 grams/kg

Low Risk of DKA
- Room patient per routine
- Ask if long acting insulin has been administered in last 12-24 hours or patient is on insulin pump
- Send routine DM labs: HbA₁C, BHBA, Chem 10, POC Venous Blood Gas with metabolites
- Page Diabetes On Call Physician if new onset DM or if blood glucose > 250 mg/dL to order insulin in Epic or assist EC provider in order entry

Suspected DKA
- Room patient as soon as possible
- Administer normal saline 20 mL/kg bolus unless contraindicated (i.e., evidence of cerebral edema)
- Obtain and send STAT lab: HbA₁C, POC venous blood gas with metabolites, BHBA, Chem 10

pH < 7.3?
- No: Update Diabetes On Call Physician on lab results & Dispo per ER
- Yes: Confirmed Diagnosis of DKA
  Refer to “Continuing Treatment for DKA” Algorithm (link)
Inclusion Criteria: Neonates to 18 years; clinical findings of DKA.
Exclusion Criteria: Hyperglycemia without acidosis; pregnancy.

Risk Factors for Cerebral Edema (CE):
- Age < 5 years
- New onset diabetes
- High initial serum urea
- Low initial pCO₂
- Failure of corrected serum sodium to rise during treatment
- Use of bicarbonate

Clinical Signs of CE:
- Altered sensorium, headache
- Inappropriate slowing of the pulse rate
- Increase in BP

NOTE: CE typically occurs 4-12 h after treatment is activated; however, it can be present before treatment has begun.

Clinical Algorithm for Continuing Treatment of Diabetic Ketoacidosis

DKA confirmed

Contact Diabetes On Call Physician
Determine appropriate level of care

Treatment
- Initiate 2 bag system
- Administer insulin infusion (0.1 units/kg/h if ≥ 5 years old, 0.05 units/kg/hr if < 5 years)
- Continuous pulse oximetry and cardiac monitoring
- Neurological vital signs per unit policy
- POC Glucose q 1 h
- Chem 10 every 12 h
- Electrolytes every 2 h x 3, then every 6 h with improving anion gap (Normal anion gap < 15 mEq/L)
- B-hydroxybutyrate every 6 h
- Strict I&O

Worsening labs; changes in mental status; AND/OR concerning vital signs

No
- Continue to manage as appropriate to clinical findings
- Contact Diabetes On Call Physician with changes in patient’s status AND/OR patient’s readiness to transition to subcutaneous insulin

Yes
- Consider transferring to higher level of care if in DCU
- Update Diabetes On Call Physician with changes in patient’s status

2 bag system
- If K⁺ ≤ 5.5 mEq/L: (Adjust IVF rates based on finger stick glucoses)
  - Bag A: NS + KCl 1.5 mEq/100 mL + KPO₄ 2 mmol/100 mL
  - Bag B: D10NS + KCl 1.5 mEq/100 mL + KPO₄ 2 mmol/100 mL

- If K⁺ > 5.5 mEq/L: (Adjust IVF rates based on fingerstick glucoses)
  - Bag A: NS
  - Bag B: D10NS

Total IVF mL/h = Bag A mL/h + Bag B mL/h

<table>
<thead>
<tr>
<th>Blood glucose</th>
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<td>mL/h (25%)</td>
<td>mL/h (75%)</td>
</tr>
<tr>
<td>≤ 150 mg/dL</td>
<td>mL/h</td>
<td>mL/h (100%)</td>
</tr>
<tr>
<td>&lt; 100 mg/dL</td>
<td>Notify practitioner while on IV therapy</td>
<td></td>
</tr>
</tbody>
</table>

Clinical standards are developed for 80% of the patient population with a particular disease. Each practitioner must use his/her clinical judgment in the management of any specific patient.

May 23, 2019
Clinical Algorithm for Transport of Children with DKA

**Inclusion Criteria:**
- Neonates to 18 years
- Clinical findings of DKA

**Exclusion Criteria:**
- Hyperglycemia without acidosis
- Pregnancy

**Risk Factors for Cerebral Edema (CE):**
- Age < 5 years
- New onset diabetes
- High initial serum urea
- Low initial pCO₂
- Rapid administration of hypotonic fluids
- Failure of serum sodium to rise during treatment
- Use of bicarbonate

**Clinical Signs of CE**
- Altered sensorium, headache
- Inappropriate slowing of the pulse rate
- Increase in BP

**Emergency Center MD to obtain from Outside Hospital (OSH):**
- Brief history/clinical findings
- Lab values (blood gas, electrolytes, blood glucose)

**NOTE:** Consider OSH lab values when confirming DKA.

**DKA confirmed based on OSH history/clinical findings/lab values:***

**OFF algorithm**
Manage as appropriate to clinical findings

**Absence of signs and symptoms of shock?**

**Shock**
- Place O₂
- Administer normal saline 20 mL/kg bolus
- Consider Kangaroo Crew® for transport

**NOTE:** Repeat bolus as needed.

**Shock resolved?**

**OFF algorithm**
Manage as appropriate to clinical findings

**Evaluate for Cerebral Edema**

**Cerebral Edema**
- Place O₂
- Obtain or calculate serum osmolality
- Consider mannitol 0.5 gram/kg
- Consider restriction of fluids
- If mannitol given and patient stable, consider CT scan
- Consider Kangaroo Crew® for transport

**No signs and symptoms of cerebral edema?**

**Referring Provider decides mode of transport**

**Mission Control to contact Kangaroo Crew® for transfer to TCH or local EMS for transfer to the EC**

**Fluid Bolus**
- Administer normal saline 20 mL/kg over 1 h unless contraindicated.

**Maintenance Fluids**
- Administer normal saline without dextrose. Calculate IV fluid rate at 2500 mL/m²/day.

**Insulin**
- If transporting by Kangaroo Crew® or other pediatric specialty team, initiate insulin infusion at 0.05 units/kg/hour using short acting insulin.
- If IV insulin is not initiated during transport, consider giving a subcutaneous dose of insulin prior to transport
- If glucose <300 mg/dL, change IVF to DSNF at 2500 mL/m²/day.

**Treatment Recommendations for OSH and During Transport**

**Monitoring During Transport**
- Continuous pulse oximetry
- Neurological vital signs every 1 h
- Glucose every 1 h and on arrival
- Electrolytes should be drawn at OSH, or once by transport team. Notify medical control if K⁺<4.0
- Strict I&O

Clinical standards are developed for 80% of the patient population with a particular disease. Each practitioner must use his/her clinical judgment in the management of any specific patient.
References

34. Puttha, R., Codd, A., Subbarayan, A., Odeka, E., Ariyawansa, I., Bone, M., ... & Amin, R. (2010). Low dose (0.05 units/kg/h) intravenous insulin infusion for the initial treatment of diabetic ketoacidosis in children with type 1 diabetes—an observational study. *Pediatric Diabetes, 11*(1), 12-17.
Clinical Standards Preparation
This clinical standard was prepared by the Evidence-Based Outcomes Center (EBOC) team in collaboration with content experts at Texas Children's Hospital. Development of this clinical standard supports the TCH Quality and Patient Safety Program initiative to promote clinical standards and outcomes that build a culture of quality and safety within the organization.

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No relevant financial or intellectual conflicts to report.

Development Process
This clinical standard was developed using the process outlined in the EBOC Manual. The literature appraisal documents the following steps:

1. Review Preparation
   - PICO questions established
   - Evidence search confirmed with content experts

2. Review of Existing External Guidelines
   - American Diabetes Association “Standards of Medical Care in Diabetes”
   - National Institute of Clinical Excellence “Diabetes (type 1 and type 2) in children and young people: diagnosis and management”
   - Ministry of Health, Social Services and Equality (Spain) “Clinical Practice Guideline for Diabetes Mellitus Type 1”

3. Literature Review of Relevant Evidence
   - Searched: Cochrane, PubMed,

4. Critically Analyze the Evidence
   - Eight randomized controlled trials, and thirteen nonrandomized studies

5. Summarize the Evidence
   - Materials used in the development of the clinical standard, literature appraisal, and any order sets are maintained in a Diabetic Ketoacidosis review manual within EBOC.

Evaluating the Quality of the Evidence
Published clinical guidelines were evaluated for this review using the AGREE II criteria. The summary of these guidelines are included in the literature appraisal. AGREE II criteria evaluate Guideline Scope and Purpose, Stakeholder Involvement, Rigor of Development, Clarity and Presentation, Applicability, and Editorial Independence using a 4-point Likert scale. The higher the score, the more comprehensive the guideline.

This clinical standard specifically summarizes the evidence in support of or against specific interventions and identifies where evidence is lacking/inconclusive. The following categories describe how research findings provide support for treatment interventions.

"Evidence Supports" provides evidence to support an intervention “Evidence Against” provides evidence against an intervention. “Evidence Lacking/Inconclusive” indicates there is insufficient evidence to support or refute an intervention and no conclusion can be drawn from the evidence.

The GRADE criteria were utilized to evaluate the body of evidence used to make practice recommendations. The table below defines how the quality of the evidence is rated and how a strong versus weak recommendation is established. The literature appraisal reflects the critical points of evidence.

<table>
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<th>Recommendation</th>
<th>High</th>
<th>Moderate</th>
<th>Low</th>
<th>Very Low</th>
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<td>Quality</td>
<td>Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies</td>
<td>Evidence from RCTs with important limitations (e.g., inconsistent results, methodological flaws, indirect evidence, or imprecise results) or unusually strong evidence from unbiased observational studies</td>
<td>Evidence for at least 1 critical outcome from observational studies, RCTs with serious flaws or indirect evidence</td>
<td>Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence</td>
</tr>
</tbody>
</table>

| Type of Evidence | Desirable effects clearly outweigh undesirable effects or vice versa | Desirable effects closely balanced with undesirable effects |

Recommendations
Practice recommendations were directed by the existing evidence and consensus amongst the content experts. Patient and family preferences were included when possible. The Content Expert Team and EBOC team remain aware of the controversies in the diagnosis/management of diabetic ketoacidosis in children. When evidence is lacking, options in care are provided in the clinical standard and the accompanying order sets (if applicable).

Approval Process
Clinical standards are reviewed and approved by hospital committees as deemed appropriate for its intended use. Clinical standards are reviewed as necessary within EBOC at Texas Children’s Hospital. Content Expert Teams are involved with every review and update.

Disclaimer
Practice recommendations are based upon the evidence available at the time the clinical standard was developed. Clinical standards (guidelines, summaries, or pathways) do not set out the standard of care and are not intended to be used to dictate a course of care. Each physician/practitioner must use his or her independent judgment in the management of any specific patient and is responsible, in consultation with the patient and/or the patient’s family, to make the ultimate judgment regarding care.
## Version History

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<td>Nov 2009</td>
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<tr>
<td>Oct 2014</td>
<td>Algorithm modifications</td>
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<td>Jun 2015</td>
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<tr>
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