DIAGNOSIS OF DKA

• hyperglycemia: glucose ≥11.1 mmol/L
• acidosis: pH <7.3 or HCO$_3^-$ <15 mmol/L
• ketones in blood and/or urine

• ~10–20% of kids with new-onset T1D present in DKA
• DDx: hyperglycemic hyperosmolar state
SEVERITY OF DKA

<table>
<thead>
<tr>
<th></th>
<th>pH</th>
<th>HCO₃⁻</th>
</tr>
</thead>
<tbody>
<tr>
<td>mild</td>
<td>&lt;7.3</td>
<td>&lt;15</td>
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<tr>
<td>moderate</td>
<td>&lt;7.2</td>
<td>&lt;10</td>
</tr>
<tr>
<td>severe</td>
<td>&lt;7.1</td>
<td>&lt;5</td>
</tr>
</tbody>
</table>
DKA: PATHOPHYSIOLOGY

• metabolic effects of insulinopenia
• ↓ glucose uptake into muscle, fat, liver
• ↑ gluconeogenesis, ↑ glycogenolysis, ↑ lipolysis, ↑ ketogenesis
• hyperglycemia, obligate diuresis
• ↑ stress hormones aggravate situation
• metabolic acidosis: ketones, lactate
• huge losses of H2O, Na+, K+, HCO3−, Pi
**Pathophysiology of Diabetic Ketoacidosis**

- Absolute insulin deficiency
- or
- Stress, infection or insufficient insulin

**Counterregulatory Hormones**
- ↑ Glucagon
- ↑ Cortisol
- ↑ Catecholamines
- ↑ Growth Hormone

**Upward Flows**

- ↑ Lipolysis
- ↑ Glucose utilization
- ↑ Proteolysis
- ↑ Glycogenolysis

**Downward Flows**

- ↓ FFA to liver
- ↓ Ketogenesis
- ↓ Glucose utilization
- ↓ Proteolysis
- ↓ Glycogenolysis

**Acidosis**
- ↑ Lactate
- ↑ Ketogenesis
- ↓ Alkali reserve

**Hyperglycemia**
- ↑ Gluconeogenic substrates
- ↑ Gluconeogenesis

**Dehydration**
- Glucosuria (osmotic diuresis)
- Loss of water and electrolytes
- Impaired renal function

**Decreased fluid intake**
- Hyperosmolarity

*Diabetes Care 2006;29:1150–1159*
RATIONALE FOR 2019 REVISION

• The PECARN FLUID Trial demonstrated that fast vs slow rehydration for DKA seems to be equivalent with respect to:
  o brain injury (0.9%)
  o short-term memory
  o post-event memory
  o IQ
  o serious adverse events

• some suggestion (not significant) that faster rehydration:
  o led to less ↓ in GCS
  o led to faster ↑ in short-term memory scores in sickest patients
DKA PROTOCOL 2019: GENERAL PRINCIPLES

• 10–20 mL/kg fluid push up front, repeat if CV status not improved
• assume 5–10% dehydration (7% for most)
• even rehydration over 24–36 h
• use of 0.45–0.9% NaCl-containing fluids
• avoid use of bicarbonate
• no insulin in the 1–2 h of treatment
• continuous insulin infusion, glucose to match
• continued use of the “two-bag” method

adapted from: Pediatric Diabetes 2019;20(1):10–14
MODIFICATIONS FROM 2015 PROTOCOL

• more-aggressive fluid boluses are suggested at the start of therapy:
  o all patients with DKA should receive a 10-mL/kg bolus of normal saline at the beginning
  o the majority will receive a second 10-mL/kg bolus to follow
• fluid infusion rate calculations have been simplified
• fluid rehydration rates will reflect a goal to correct losses over a 36-h period (previously this was 48 h)
DKA PROTOCOLS: DISCLAIMER

• **no** DKA protocol has been shown to eliminate the risk of cerebral injury

• current gold standard: ISPAD *Clinical Practice Consensus Guidelines 2018*

• guidelines should not replace intelligent thought and should be tailored to meet the needs of each individual patient

• involve Pediatric Endocrinology early!
ISPAD CLINICAL PRACTICE CONSENSUS GUIDELINES

ISPAD Clinical Practice Consensus Guidelines 2018: Diabetic ketoacidosis and the hyperglycemic hyperosmolar state

Joseph L. Wolfsdorf1 | Nicole Glaser2 | Michael Aguas3,5 | Maria Fritsch6 | Ragnh Hana7 | Areta Reeves8 | Mark A. Sperling7 | Ethel Codner9

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2Division of Endocrinology, Section of Endocrinology, Children’s Hospital, Boston, Massachusetts
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4Division of Diabetes, Endocrinology, and Metabolism, University of California, San Francisco, California
5Division of Clinical Care: Pediatrics, Boston Children’s Hospital, Boston, Massachusetts
6Department of Pediatrics and Adolescent Medicine, University of Miami Miller School of Medicine, Miami, Florida
7Department of Pediatrics, University of Southern California, Los Angeles, California
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9Department of Pediatrics, University of California, San Diego, California

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1 | SUMMARY OF WHAT IS NEW/DIFFERENT

Recommendations concerning fluid management have been modified to reflect recent findings from a randomized controlled clinical trial showing no difference in clinical injury in patients randomized at different times with either 0.45% or 0.9% saline.

2 | EXECUTIVE SUMMARY

The biochemical criteria for the diagnosis of diabetic ketoacidosis (DKA) are:

- Hyperglycemia (plasma glucose >11 mmol/L [200 mg/dL])
- Venous pH <7.3 or bicarbonate <15 mmol/L
- Ketonemia (acetoacetate + β-hydroxybutyrate >3 mmol/L) or moderate or large ketonuria.

The clinical signs of DKA include: dehydration, tachypnea, tachycardia, deep sighing respiration, taut necks of anterior, sweating and/or sweating, abdominal pain. Many vital signs, confusion, drowsiness, progressive decrease in level of consciousness and, eventually, loss of consciousness.

Risk factors for DKA in newly diagnosed patients include younger age, delayed diagnosis, lower socioeconomic status, and residence in a country with low prevalence of type 1 diabetes mellitus (T1DM).

Risk factors for DKA in patients with known diabetes include: omission of insulin for various reasons, limited access to medical services, and uncontrolled interruption of insulin delivery in patients using an insulin pump.

The following recommendations are based on currently available evidence and are intended to be a general guide to DKA management. Because there is considerable individual variability in the presentation of DKA (ranging from mild with only minimal dehydration to severe with profound dehydration), some patients may require specific treatment that is the judgment of the treating physician, may be variable, or, occasionally, outside the range of options presented here. Clinical judgment should always be used to determine optimal treatment for the individual patient, and timely adjustments to treatment (glucose and electrolyte compensation) are also influenced by the fluid replacement. Insulin delivery should be based on regular, careful clinical and biochemical monitoring of the patient’s response.

Emergency measures should follow the general guidelines for Pediatric Advanced Life Support (PALS) and include: immediate measurement of blood glucose, blood or urine ketones, serum electrolytes, blood gases and complete blood counts; assessment of severity of dehydration, and level of consciousness.
Diabetes Canada’s 2018 Clinical Practice Guidelines
**DKA Algorithm**

**Recognition of DKA**
- Can occur in existing or new onset type 1 or type 2 diabetes.
- Diagnostic criteria: Diabetes w/ elevated glucose (~15 mmol/L).
- Clinical features: Polyuria, polydipsia, weight loss, dehydration, hyperglycemia, Kussmaul breathing, heart rate decreased level of consciousness, delirium, and vomiting.

**Alert Pediatric Referral Center**

**Initial Management**
- Assess ABCs, vital signs (including EKG), neurologic status, and skin turgor.
- Rapid bolus saline.
- SC bolus 0.5 mg/kg regular insulin.
- IV access if more than 12 years old.
- Insulin at <12, bolus 1 U/kg bolus and continue at 0.1 U/kg/h.
- Hypokalemia: 4.0 mmol/L or lower.
- Monitor potassium levels and adjust insulin doses accordingly.
- Insulin is given at a slow infusion rate (0.1 U/kg/h).
- Follow up in 2 hours.

**CAUTION!**
- Insulin and IV fluids are given at a slow rate.
- Monitor the patient closely.
- Check vital signs and glucose levels frequently.

**DKA Severity**
- **Type 1:** Severe DKA: Blood glucose >20 mmol/L, high anion gap, ketoacidosis.
- **Type 2:** Severe DKA: Blood glucose >20 mmol/L, high anion gap, ketoacidosis.

**DKA: Ongoing Fluid Management**

**Insulin**
- Infuse regular insulin at 0.1 U/kg/h.
- Monitor glucose levels closely.
- Adjust insulin doses as needed.

**DKA with Suspected Cerebral Edema**

**Immediate Management – High Suspicion of Cerebral Edema**
- Start therapy for hyperosmolar state.
- Monitor serum glucose levels.
- Administer mannitol or other osmotic diuretics.

**DKA: Monitoring**

**CPEG Pediatric DKA Algorithm: Ongoing Management**

**Insulin**
- Infuse regular insulin at 0.1 U/kg/h.
- Monitor glucose levels closely.
- Adjust insulin doses as needed.

**DKA: Ongoing Fluid Management**

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**DKA: Ongoing Fluid Management**

**Insulin**
- Infuse regular insulin at 0.1 U/kg/h.
- Monitor glucose levels closely.
- Adjust insulin doses as needed.
0. ABCs, vital signs (with BP), neurovascular signs. Place large-bore IV. Draw labs. Confirm DKA: plasma glucose (PG) >11 mmol/L, moderate-large ketonuria or β-hydroxybutyrate ≥2.0 mmol/L, and venous pH <7.3, or serum HCO₃⁻ <15 mmol/L.¹ Consider possibility of an element of hyperglycemic hyperosmolar state.⁴

1. Measure body weight (BW) in kilograms: .................................................. (i) _______ kg

2. Give 0.9% saline (normal saline, NS) rehydration bolus²
   • recommended amount: 10 mL/kg BW over 30 minutes: .................................. (ii) _______ mL

3. Repeat with second bolus of NS if persistent tachycardia, prolonged cap refill (>2 sec), cool extremities:
   • recommended amount: 10 mL/kg BW over 30 minutes: .................................. (iii) _______ mL

4. Begin rehydration, calculated for even correction over 36 hours, based on admission BW:²
   • 5–10 kg BW: .......................... 6.5 mL/kg/h
   • 10–20 kg BW: ......................... 6 mL/kg/h
   • 20–40 kg BW: ......................... 5 mL/kg/h
   • >40 kg BW: ............................. 4 mL/kg/h, maximum 250 mL/h: ........................................... (iv) _______ mL/kg/h

5. Calculate total hourly fluid rate to be given for 36 hours: multiply (i) and (iv): ................. (v) _______ mL/h

6. Use NS with KCl 40 mEq/L (Bag A) as initial rehydration fluid, at rate determined in (5), ensuring that patient has voided and has plasma K⁺ <5 mmol/L, before adding potassium to the IV fluids.

7. At 60–120 minutes after starting the first fluid bolus, make up and start a piggyback insulin drip at 0.05–0.1 units/kg BW/h (Bag C):³
   • 50 units insulin regular (Humulin® R or Novolin® Toronto) in 500 mL NS or D50/NS
   • run at 0.5–1 mL/kg/BW/h: ............................................................................... (vi) _______ mL/h

8. Begin “2-bag method”⁴. Y together (Bag A) NS with 40 mEq/L KCl and (Bag B) D50–D3/2.5/NS with 40 mEq/L KCl.
   Decrease replacement fluid rate to adjust for insulin drip rate:
   subtract (7) from (5): ................................................................. (vii) _______ mL/h

9. Aim to keep PG ≤8–12 mmol/L, by titrating the rates of these two solutions, keeping the combined rate at (vii).² Continue this for the next 8–12 hours, monitoring as below.

10. At 4–6 hours after initial fluids and if corrected plasma Na⁺ <145 mmol/L, stable or increasing, switch Bag A to 0.45% saline w/ 40 mEq/L KCl and Bag B to D50–D12.5/0.45% saline w/ 40 mEq/L KCl at the rate as in (vii).³

Rationale & Notes:

1. Please note that this protocol is designed as an algorithm for treating the majority of cases of DKA in infants, children and adolescents. It cannot replace careful clinical observation and judgment in treating this potentially very dangerous condition.

2. If you have questions or problems related to the management of DKA or diabetes, please feel free to contact the BCCH Pediatric Endocrinologist on call.

3. Hyperglycemic hyperosmolar state (HHHS) should be suspected when there is significant hyperglycemia (>33 mmol/L) and hyper-osmolality (>350 mOsm/L) without ketosis or acidosis (bicarbonate >15 mmol/L, venous pH >7.3). A mixed picture of DKA and HHHS is possible. Mild hyperglycemia, even with ketosis and mild acidosis, can often be managed without IV fluids or IV insulin.

4. Rapid, deep mouth-breathing (Kussmaul respiration) often dries out the oral mucosa, making the child appear more dehydrated than s/he really is. The hematocrit and other clinical signs (decreased capillary refill) are more accurate measures of dehydration.

5. Recent research shows that most children with moderate-severe DKA will require a 20 mL/kg rehydration fluid bolus to restore perfusion, prior to the rehydration phase.

6. Recent research shows that DKA can be safely corrected over a 4–6 h period. This protocol is designed to correct a 10% fluid deficit (100 mL/kg) every 30 h.

7. IV insulin boluses are always contraindicated. Insulin given in the first 1–2 h of DKA repair is thought to increase mortality. This insulin rate fully inhibits ketogenesis and gluconeogenesis and should be maintained if possible. If unable to keep PG ≤8 mmol/L, drop the insulin rate by 25–50%.
2019 BCCH DKA PROTOCOL

THROUGHOUT

11. Re-evaluate appropriateness of replacement fluid type frequently, anticipating the need to add or increase Na⁺, K⁺, dextrose, etc.
   - dextrose²: aim to keep the PG “9–12 mmol/L range
   - sodium³: corrected Na⁺ <145 mmol/L, or falling regardless of level: continue NS
   - potassium⁴: patient urinating and K⁺ remains <5: continue KCl 40 mmol/L, may give 50% of K⁺ as acetate or phosphate
   - bicarbonate⁵: NaHCO₃ is not generally recommended

12. Children with DKA have high risk for acute kidney injury (AKI). Use Schwartz formula to calculate expected baseline creatinine (EBC)¹.

13. Close neurological observation and frequent rousing of the child with finger-pokes to detect any changes consistent with cerebral edema. Follow Glasgow Coma Scale. Severe headache, change in sensorium or BP, dilated pupils, bradycardia, irritable breathing, posturing and incontinence are signs of impending deterioration. Rapid intervention is imperative:
   - airway / breathing / circulation
   - elevate head of bed
   - decrease all fluid bags to 5 mL/h pending physician reassessment
   - mannitol 20% (0.5–1 g/kg, 2.5–5 mL/kg IV over 15 min) or NaCl 3% (2.5–6 mL/kg IV over 15 min)²³
   - consider intubation and mild hyperventilation (keep pCO₂ <22 mg Hg) for impending respiratory failure
   - arrange CT when stable

14. Follow laboratory parameters (use of a flowsheet is highly recommended):
   - follow PG by meter every 30–60 min: does child respond to the poke?
   - follow Na⁺, K⁺, CI⁻, HCO₃⁻, anion gap, urea, creatinine, venous pH every 2–4 hours²⁰⁴¹: Ca²⁺, Mg²⁺ and Pi every 2–4 hours if giving phosphate²⁰
   - follow (preferably) plasma β-hydroxybutyrate every 2–4 hours or urine ketones with each void

15. Re-evaluate appropriateness of replacement fluid type frequently, anticipating the need to increase or decrease Na⁺, K⁺, dextrose, etc.

"Keeping the PG in the “9–12 mmol/L range allows for a buffer against hypoglycemia and a too-rapid fall in plasma osmolality". The "two-bag method" (see our DKA Nursing Protocol) is a handy way to adjust the glucose without altering the Na⁺ or K⁺ delivery. It also allows for a faster response to PG changes, and it decreases nursing and pharmacy workload and costs.

"The introduction of hypertonic fluids must be considered carefully. The corrected Na⁺ should be calculated and followed closely: corrected Na⁺ = (measured Na⁺ × 0.58) + (PG – 4). If corrected Na⁺ falls or fails to rise as the PG falls, this could indicate excess free-water administration. It is also helpful to monitor the active osmolality (PG – 2H₂O × Na⁺ × 1.5), which should not fall >0.5 mmol/kg/h. If the corrected sodium is ≥145 mmol/L and stable and the active osmolality has been dropping slowly, switching to NS can be considered after 4–6 h of fluids. An elevated measured Na⁺ in the face of hyperglycemia indicates severe dehydration and an element of the hyperglycemic-hyperosmolar state. Such patients should be rehydrated using fluids with higher osmolar content (e.g., NS) for longer time periods (10–12 h).

"Serum K⁺ levels are usually normal at diagnosis and fall precipitously with treatment. An IV fluid containing 20–40 mmol/L K⁺ is required to keep the serum K⁺ ≥3.0 mmol/L. Begin K⁺ and insulin together. Oral/nasogastric KCl boluses (0.5–1 mmol/kg/BW) may also be administered.

"While there is no proven benefit to using potassium phosphate or acetate, it does have the theoretical advantage of replenishing the severe phosphate deficit of DKA and ameliorating the hyperchloremia which inevitably occurs during DKA treatment if phosphate is given. Serum calcium, magnesium and phosphate levels should be monitored closely.

"The acidosis of DKA is due to both lactate and lactic acid, and therefore is treated with fluid and insulin replacement. There is no evidence that NaHCO₃ is either necessary or safe in DKA, but its use has a number of deleterious effects: paradoxical CNS acidosis, hypokalemia, hyperchloremia, delayed clearance of ketones, and cerebral edema. NaHCO₃ in DKA should only be considered if pH <6.8 or cardiac failure.

"EBC (μmol/L) = (36.5 + 3.5 × height [cm]/120) × measured creatinine 1.3×1.98 × B/E Stage 3, 2.2×2.98 × B/E Stage 2, 3.1×2.98 × B/E Stage 1 AD²⁴

"Subclinical brain swelling is common in children with DKA. Cerebral edema (CE) accounts for more than half of the ~1–5% mortality rate of DKA in children. AKI and high risk are newly diagnosed patients, those aged <5 years, and those with initial pH <7.1 or pCO₂ >18. The exact etiology of CE remains unclear. Reevaluation is successful in only 50% of cases.

Accompanying documents on our website:
   - DKA flowsheet and DKA Simple Pediatric Input Sheet
   - DKA Protocol, Fluid and Insulin Management
   - DKA Nursing Protocol (including the "two-bag" method)
   - DKA Brushes for Mixing Solutions

BC CHILDREN'S HOSPITAL ENDOCRINOLOGY & DIABETS UNIT
DIABETES CLINIC: 604-875-2868
DIABETES CLINIC FAX: 604-875-3231
TOLL-FREE PHONE: 1-888-300-3088
WWW.BCCHILDREN.CA/ENDOCRINOLOGY-DIABETES-SITE/DOWNLOADS/DIABETS.pdf
FEBRUARY 8, 2020
24-H-PAGES: 604-875-2161
PAGE 2 OF 2

14
2019 BCCH DKA PROTOCOL – FILLABLE

SEVERITY OF DKA

DKA vs. HHS

ESTIMATE DECOMAL SYMPTOMS

GLASGOW COMA SCALE

TIME = 60 MIN – 36 HOURS

FIRST 60 MIN

0. ABCs, vital signs (with BP), neurovital signs. Place large-bore IV. Draw labs. Confirm DKA: plasma glucose (PG) >11 mmol/L, moderate–large ketonuria or β-hydroxybutyrate ≥2.0 mmol/L, and venous pH <7.3 or serum HCO₃⁻ <15 mmol/L. Consider possibility of an element of hyperglycemic hyperosmolar state.¹

1. Measure body weight (BW) in kilograms._______________________________(i)_______ kg

2. Give 0.9% saline (normal saline, NS) resuscitation bolus³:

   • recommended amount: 50 ml/kg BW over 30 minutes________________________(ii)_______ mL

3. Repeat with second bolus of NS if persistent tachycardia, prolonged cap refill (>2 sec), cool extremities:

   • recommended amount: 10 ml/kg BW over 30 minutes________________________(iii)_______ mL

4. Begin rehydration, calculated for even correction over 36 hours, based on admission BW:⁶

   • 5–10 kg BW: 6.5 ml/kg/h
   • 10–20 kg BW: 6 ml/kg/h
   • 20–40 kg BW: 5 ml/kg/h
   • >40 kg BW: 4 ml/kg/h, maximum 250 mL/h______________________________(iv)_____ mL/h

5. Calculate total hourly fluid rate to be given for 36 hours: multiply (i) and (iv)_______ mL/h

6. Use NS with KCl 40 mEq/L (Bag A) as initial rehydration fluid, at rate determined in (5), ensuring that patient has voided and has plasma K⁺ < 5 mmol/L, before adding potassium to the IV fluids.

7. At 60–120 minutes after starting the first fluid bolus, make up and start a piggyback insulin drip at 0.05–0.1 units/kg BW/h (Bag C)³:

   • 50 units insulin regular (Humulin® R or Novolet® Toronto) in 500 ml NS or D5NS
   • run at 0.5–1 ml/kg BW/h______________________________(v)_____ ml/h

8. Begin “2-bag method”⁴. Y together (Bag A) NS with 40 mEq/L KCl and (Bag B) 0.10–0.125% NS with 40 mEq/L KCl. Decrease replacement fluid rate to adjust for insulin drip rate:

   • subtract (7) from (5)______________________________(vi)_____ ml/h

9. Aim to keep PG 8–12 mmol/L, by titrating the rates of these two solutions, keeping the combined rate at 8 ml/h. Continue this for the next 6–12 hours, monitoring as below.

10. At 4–6 hours after initial fluids and if corrected plasma Na⁺ is ≤145 mmol/L, stable or increasing, switch Bag A to 0.45% saline w/v 40 mEq/L, KCl and Bag B to 0.10–0.125% 0.45% saline w/v 40 mEq/L, KCl at the rate as in (8)².

BC CHILDREN’S HOSPITAL DIABETIC KETOACIDOSIS PROTOCOL⁵

FOR CHILDREN AGES 1 MONTH TO 19 YEARS

Rationale & Notes:

¹Please note that this protocol is designed as an algorithm for treating the majority of cases of DKA in infants, children and adolescents. It cannot replace careful clinical observation and judgment in treating potentially very serious conditions. If you have questions or problems related to the management of DKA or diabetes, please feel free to contact the BCH Pediatric Endocrinologist on call.

²Hyperglycemic hyperosmolar state (HHS) should be suspected when there is significant hyperglycemia (>33 mmol/L) and hyper-osmolality (>350 mOsm/L) without ketosis or acidosis (bicarbonate >15 mmol/L, venous pH >7.3). A mixed picture of DKA and HHS is possible. Mild hyperglycemia, even with ketones and mild acidosis, can often be managed without IV fluids or IV insulin.

³Rapid, deep mouth-breathing (kussmaul respiration) often dries out the oral mucosa, making the child appear more dehydrated than she really is. The hematocrit and other clinical signs (decreased capillary refill) are more accurate measures of dehydration.

⁴Recent research shows that most children with moderate-severe DKA will require a 20 ml/kg resuscitation fluid bolus to restore perfusion, prior to the rehydration phase.

⁵Recent research shows that DKA can be safely corrected over a 24 to 48-hour period. This protocol is designed to correct a 10% fluid deficit (100 mL/kg) evenly over 56.

⁶IV insulin rates are always contraindicated. Insulin given in the first 1–2 h of DKA repair is thought to increase mortality. This insulin rate fully inhibits ketogenesis and glucoseogenesis and should be maintained if possible. If unable to keep PG <8 mmol/L, drop the insulin rate by 20–50%.
# BCCH DKA GLUCOSE, INSULIN AND FLUID MANAGEMENT

## 2019 REVISIONS TO BCCH DKA PROTOCOL

The 2019 revisions to the BCCH DKA Protocol are based on the results of recent research findings on rehydration protocols. These revisions bring the BCCH DKA Protocol into alignment with the Clinical Practice Consensus Guidelines 2019 from the International Society for Pediatric and Adolescent Diabetes (ISPAD) and with the 2018 DKA resources from TREK Canada (references below).

### INITIAL FLUID REPLACEMENT

Results from the PICARN DKA FLUID Study (reference below) have demonstrated that fluid replacement can safely be achieved using more-aggressive regimens than have been in place over the past two decades. It is now recommended that all patients in moderate-to-severe DKA receive a 10-ml/kg bolus of 0.9% sodium chloride (normal saline, NS) over 30 minutes. These patients with persistent tachycardia, prolonged capillary refill (>2 sec), and cool extremities should receive a second 10-ml/kg fluid push as well. Once the fluid push(es) have been delivered, and assuming the patient has adequate urine output and a normal serum potassium, fluid replacement is continued using NS + 40 mEq/L KCl (Bag A, see next section), until the patient has been receiving fluids for 2 hours; at that point, intravenous insulin is started. Fluid replacement rates are now calculated for a 36-hour period of rehydration, compared to the 48-h period used in the past.

### THE "TWO-BAG SYSTEM"

The "two-bag system" (reference below) consists of two IV bags (A and B) with equal electrolyte concentration, one containing no dextrose, the other 10-12.5% dextrose. They are administered simultaneously. The total rate is determined by the child’s degree of dehydration, according to the BCCH DKA Medical Protocol (see 5). The insulin infusion (Bag C) will eventually be Yd into these bags (see below).

In the "two-bag system", Bag A is generally NS + 40 mEq/L KCl, and Bag B is usually D10/NS + 40 mEq/L KCl (or D12.5/NS + 40 mEq/L KCl, if your institution makes this). The BCCH Pharmacy has prepared a "recipe book" for preparing these solutions from.

### TABLE: BCCH DKA MEDICAL DOCUMENTS

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<tr>
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<th>Time</th>
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<th>Respiratory Rate</th>
<th>Blood Pressure</th>
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October 9, 2018

December 30, 2018
# Sample Prescriber Orders for DKA

## Prescriber’s Orders

### For Diabetic Ketoacidosis (DKA)

#### Inpatient and Outpatient

<table>
<thead>
<tr>
<th>Date</th>
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<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Instructions

- **On Admission Stat:**
  - Vital signs and mental status on admission and then hourly
  - Urine output
  - Urinary and venous blood gas and lactate
  - Oxygen saturation and cardiac monitor
  - Insert large bore intravenous cannula
  - Capillary blood glucose by fingerstick
  - Use for ketones
  - Venous blood gas, whole blood sodium, potassium, chloride, bicarbonate, anion gap, arterial lactate, arterial pH, urine electrolytes
  - Venous creatinine, phosphorus, complete blood count, blood urea nitrogen, Na+, K+, Cl-
  - Other labs

#### Fluid Resuscitation (Reckless) (initial 30–60 minutes)

<table>
<thead>
<tr>
<th>Initial sodium chloride</th>
<th>mL</th>
<th>IV over 30 minutes</th>
<th>10% NaCl</th>
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#### Fluid Resuscitation (Reckless) (initial 1–2 hours)

<table>
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</tr>
</tbody>
</table>

#### Fluid Resuscitation (Reckless) (after initial 30–60 minutes)

<table>
<thead>
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#### Insulin Infusion (after initial 1–2 hours)

<table>
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<tr>
<th>Initial insulin infusion</th>
<th>mL/h</th>
</tr>
</thead>
</table>

#### Insulin Infusion (after initial 1–2 hours)

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<tr>
<th>Initial insulin infusion</th>
<th>mL/h</th>
</tr>
</thead>
</table>

### Monitoring

- Capillary glucose every .... minutes (suggested 30–60 minutes)
- Venous blood glucose, whole blood sodium, potassium, chloride, bicarbonate, white blood cell, total calcium, glucose, AKP, Na+K+/H2O, ABG, creatinine, and phosphorus every .... hours (suggested 2–4 hours)
- ECG and laboratory tests if significant metabolic abnormalities or complications
- Insulin infusion and glucose levels monitored every 15 minutes

### Signature

- Signature: [Signature]
- Date: [Date]
- Time: [Time]
- Signature: [Signature]
- Date: [Date]
- Time: [Time]

### Notes

- Noted by: [Noted by]
- Date: [Date]
- Time: [Time]

### Pharmacy

- Use only if prescribed

---

*BC Children’s Hospital*

**Design:** [Design]

**Date:** October 9, 2019

**Page:** 1 of 1
**EPOPS DKA ORDERS: POLICYANDORDERS.CW.BC.CA**

### Endocrinology | Diabetic | Ketoacidosis | DKA
---|---|---|---
**Inpatient and Outpatient**

#### Patient Care

**Due admission:**
- **Measure weight STAT**
- **Strictly monitor intake and output**
- Insert large-bore intravenous catheter STAT
- **Blood glucose, point-of-care measurement STAT:** then q 4-6 h (range 32 to 60 minutes)
- **Ketone, urine/glucose STAT**

- **If patient develops severe headache or alteration in vital signs or Glasgow Coma Scale (GCS):**
  - Notify physician STAT
  - **Place head of bed 30°**
  - Decrease d/v fluid bags to 0 mL/hr pending MD assessment

#### Vital Signs

**Vital signs STAT on admission, then q 4 h**
- **Heart rate, blood pressure, respiratory rate, temperature, urine output,** then q 4 h.
  - Continuous cardioscapal monitoring

#### IV Infusions

**Fluid Resuscitation Boluses (initiated 30 to 60 minutes):**
- **First:** Sodium Chloride 0.9% 1 mL/kg IV over 30 min (10 mL/kg)
- **Second:** Sodium Chloride 0.9% 1 mL/kg IV over 30 min (10 mL/kg)

**Fluid Repair:**
- After initial 30 to 60 minutes:
  - **Bag A:** Sodium Chloride 0.9% with 0.8% with Potassium Chloride 40 mEq IV at 1 mL/kg / min (rate determined from DKA protocol, line 6).
- After initial 4 to 2 hours:
  - **Bag B:**
    - Sodium Chloride 0.9% with 0.8% with Potassium Chloride 40 mEq IV at 1 mL/kg / min (rate determined from DKA protocol, line 6).

**Medications:**
- **If patient develops severe headache or alteration in vital signs or GCS:**
  - **Vomited 10% dextrose IV STAT over 15 min (8.3 to 1 g/kg, 2.5 to 5 mL/kg)**
  - **Sodium Chloride 3% en, IV STAT over 15 min (2.5 to 5 mL/kg)**

---

**Signature:**

**Print Name:**

**College:**

**Department:**

**Date:**

**Page:**

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DKA NURSING DOCUMENTS

BCCH DKA RECIPES FOR MAKING SOLUTIONS

<table>
<thead>
<tr>
<th>Item #</th>
<th>Dextrose solution to prepare:</th>
<th>1 Dextrose solution and size of IV bag to use:</th>
<th>2 Withdraw &amp; discard from bag:</th>
<th>3 Add to bags:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.5W NaCl 0.9% with 40 mmol KCl/L</td>
<td>1000 mL 0.5W NaCl 0.9% with 40 mmol KCl/L</td>
<td>100 mL</td>
<td>100 mL 0.5W</td>
</tr>
<tr>
<td>2</td>
<td>D10W NaCl 0.9% with 40 mmol KCl/L</td>
<td>1000 mL D10W NaCl 0.9% with 40 mmol KCl/L</td>
<td>100 mL</td>
<td>100 mL D10W</td>
</tr>
<tr>
<td>3</td>
<td>D10.5W NaCl 0.9% with 40 mmol KCl/L</td>
<td>1000 mL D10.5W NaCl 0.9% with 40 mmol KCl/L</td>
<td>100 mL</td>
<td>150 mL D10W</td>
</tr>
<tr>
<td>4</td>
<td>D5W NaCl 0.45% with 40 mmol KCl/L</td>
<td>1000 mL D5W NaCl 0.45% with 40 mmol KCl/L</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>D10W NaCl 0.45% with 40 mmol KCl/L</td>
<td>1000 mL D10W NaCl 0.45% with 40 mmol KCl/L</td>
<td>100 mL</td>
<td>100 mL D10W</td>
</tr>
<tr>
<td>6</td>
<td>D12.5W NaCl 0.45% with 40 mmol KCl/L</td>
<td>1000 mL D12.5W NaCl 0.45% with 40 mmol KCl/L</td>
<td>100 mL</td>
<td>150 mL D10W</td>
</tr>
</tbody>
</table>

Note: these results in approximate concentrations and is to be used only when pharmacy mixing is not available.

Prepared by G&W Pharmacy Department; contact 604-875-2059 for questions.

ENDOCRINOLOGY & DIABETES UNIT
Diabetes Clinic: 604-875-2068
Toll-free Phone: 1-888-300-3088, x2868
Fax: 604-875-3231
http://endocrinob.chbc.ca

BCCH DIABETIC KETOCIDOSIS NURSING PROTOCOL

Diabetic ketoacidosis (DKA) involves a combination of hyperglycemia, acidosis, and ketones. It is diagnosed when (1) the blood glucose is >11 mmol/L, (2) capillary pH is <7.3 and/or capillary bicarbonate is <15 mmol/L, and (3) ketones are present in the blood and/or urine (see below). It usually takes days to develop DKA, but it can take hours in children with acute illness, insulin omission, or insulin pump site problems.

Causes of DKA Include:
- undiagnosed type 1 diabetes
- insulin omission or manipulation
- inadequate insulin dosing and monitoring periods of increased insulin needs
- illness, infection, major stress, puberty, pregnancy
- insulin pump misfire or infusion site disconnection, kinking or failure

Signs and Symptoms of DKA Include:
- polyuria
- polydipsia
- dehydration
- weight loss
- nausea, vomiting and abdominal pain
- fruity or acetone-smelling breath
- flushed face
- confusion
- hyperventilation and Kussmaul breathing (rapid, deep, sighing mouth-breathing)
- ↑ heart rate and ↑ respirations, and possibly ↓ blood pressure

Acute dehydration must be treated with 2L fluid replacement. Overhydration, correcting the hyperglycemia too quickly, the use of insulin in the first 1 to 2 hours of fluid therapy, and the use of bicarbonate have been implicated in causing cerebral edema in DKA, which can be fatal. Hydration should be cautious, according to the BCCH DKA Protocol.

November 28, 2019
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http://endocrinob.chbc.ca
BCCH DKA PROTOCOL 2019: TIMELINE

- on admission: weight, vitals, assessment and stabilization
- first 30–60 minutes: fluid resuscitation
- 60 min–36 h:
  - fluid replacement
  - insulin infusion
  - addition of glucose
- throughout:
  - careful monitoring, reassessment
  - titration of fluids, electrolytes, glucose, insulin
INITIAL ER MANAGEMENT

• ABC’s and GCS
• weigh patient
• insert large-bore IV
• check chemistries, venous pH, urine/blood ketones
• evaluate dehydration
• think about underlying illness (infection, etc.)
EVALUATING DEHYDRATION

• best:
  o prolonged capillary refill (>1.5–2 sec)
  o abnormal skin turgor
  o abnormal respiratory pattern

• also:
  o no tears
  o weak pulses
  o cool extremities
  o HR

• poor:
  o dry mouth
  o urine output
  o BP
  o weight
### ESTIMATING DEHYDRATION (% BODY WEIGHT)

<table>
<thead>
<tr>
<th></th>
<th>INFANTS</th>
<th>KIDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>MILD</td>
<td>5%</td>
<td>3%</td>
</tr>
<tr>
<td>MODERATE</td>
<td>10%</td>
<td>6%</td>
</tr>
<tr>
<td>SEVERE</td>
<td>15%</td>
<td>9 (10)%</td>
</tr>
</tbody>
</table>
CAUTIONS IN APPROACH

• fluid and electrolyte imbalances in patients presenting in DKA can be quite disparate:
  o kid has been drinking only water all day
  o kid has been drinking juice all day
  o kid has been vomiting all day
  o kid has been having chicken soup all day

• some kids may have insulin on board

• many patients present with an element of hyperglycemic hyperosmolar state and/or hypernatremic dehydration
BCCH PROTOCOL: 1\textsuperscript{st} 60 MINUTES

• give 1\textsuperscript{st} bolus of NS 10 mL/kg IV over 30 min
• most sicker patients require a 2\textsuperscript{nd} NS bolus of 10 mL/kg IV over 30 min
• the sickest patients may require even more NS to stabilize HR and peripheral perfusion
BCCH PROTOCOL: 60 MINUTES–36 HOURS

• begin even rehydration over 36 h, estimating 10% dehydration:
  o 5–10 kg BW: 6.5 mL/kg/h
  o 10–20 kg BW: 6 mL/kg/h
  o 20–40 kg BW: 5 mL/kg/h
  o >40 kg BW: 4 mL/kg/h, max 250 mL/h

• start with NS + 40 mEq KCl/L, assuming patient is urinating
BCCH PROTOCOL: 60 MINUTES–36 HOURS

• at 60–120 min after start of 1st fluid bolus, begin insulin infusion:
  o 0.05–0.1 Units/kg/h
  o 0.5–1 mL/kg/h of 50 units Regular insulin in 500 mL NS

• when BG is <25 mmol/L and falling >5 mmol/L/h, add dextrose to IV fluids using the “two-bag” method
“TWO-BAG” METHOD

BCCH PROTOCOL: 60 MINUTES–36 HOURS

• aim to keep BG in the ~8–12 mmol/L range by titrating the rates of the two Bags A and B

• a general rule is to make changes of approximately 10–20% of the total rate every hour

• if the patient’s BG is lower than desired, despite maximal dextrose infusion from Bag B, you may (in order of safety):
  o cut the insulin infusion rate by ~25%, provided the acidosis is correcting
  o give the patient a small amount (1–2 mL/kg) of juice or 2–4 dextrose tablets (being mindful of the overall fluid balance)
  o change the insulin Bag C to D10/NS
  o in institutions with intensive-care capabilities, consider placing a central line and using a higher concentration of dextrose (e.g. D20) in Bag B
BCCH PROTOCOL: 60 MINUTES–36 HOURS

• at 4–6 h after initial fluids and if corrected Na⁺ is ≥145 mmol/L, stable or increasing:
  o switch Bag A to ½NS + 40 mEq/L KCl
  o switch Bag B to D10/½NS + 40 mEq/L KCl
• if unable to get K⁺ >3.5 mmol/L with IV fluids: consider PO/NG KCl
• may give 50% of K⁺ as phosphate (order by the mmol of K⁺)
  o may prevent ensuing hyperchloremia, but no clear evidence of benefit
• bicarbonate: rarely if ever needed
ONGOING MONITORING

• BG by meter q30–60 min (may need lab BG if >30 mmol/L)
• Na\(^+\), K\(^+\), Cl\(^-\), HCO\(_3\)\(^-\), anion gap, urea, creatinine, venous pH q2–4 h
• Ca\(^{2+}\), Mg\(^{2+}\), P\(_i\) q2–4 h if giving phosphate
• β-hydroxybutyrate (preferably) or urine ketones q2–4 h
• neurovital signs/GCS q30–60 min

• corrected Na\(^+\) = [measured Na\(^+\) + 0.36×(BG−5.6)]
• active osmolality = [BG + 2×(Na\(^+\)+K\(^+\))]
## URINE vs BLOOD KETONES

<table>
<thead>
<tr>
<th>URINE KETONES</th>
<th>β-HYDROXYBUTYRATE</th>
</tr>
</thead>
<tbody>
<tr>
<td>negative</td>
<td>≤0.5 mmol/L</td>
</tr>
<tr>
<td>trace (&lt;0.5 mmol/L)</td>
<td>0.6–0.9 mmol/L</td>
</tr>
<tr>
<td>small (1+, 0.5 mmol/L)</td>
<td>1.0–1.4 mmol/L</td>
</tr>
<tr>
<td>moderate (2+, 1.5 mmol/L)</td>
<td>1.5–2.4 mmol/L</td>
</tr>
<tr>
<td>large (3+, 4 mmol/L)</td>
<td>2.5–2.9 mmol/L</td>
</tr>
<tr>
<td>very large (4+, 8 mmol/L)</td>
<td>≥3.0 mmol/L</td>
</tr>
</tbody>
</table>
FALL IN BLOOD VS. URINE KETONES IN DKA

blood $\beta$-hydroxybutyrate

urine ketones
ACUTE KIDNEY INJURY

• DKA should be considered a multiple organ dysfunction syndrome
• kids in DKA have a high risk (64%) of acute kidney injury (AKI)
• use Schwartz formula to calculate expected baseline creatinine:
  o $\text{EBC (µmol/L)} = 36.5 \times \text{height (cm)}/120$
  o measured creatinine $1.5–1.99 \times \text{EBC} = \text{Stage 1}$
  o measured creatinine $2–2.99 \times \text{EBC} = \text{Stage 2}$
  o measured creatinine $\geq 3 \times \text{EBC} = \text{Stage 3}$
• some creatinine assays have cross-reactivity with ketones!
MECHANISMS OF CEREBRAL INJURY

• vasogenic edema: leakage across altered BBB
  o hypoxia
  o cerebral hypoperfusion/reperfusion
  o neuroinflammation (IL-6, etc.)
  o ketones (altered BBB)
  o hypocapnia (↓ cerebral blood flow)

• other possible factors:
  o role of Na\(^+\)–H\(^+\) antiporter-3 (insulin) and Na\(^+\)–K\(^+\)–Cl\(^-\) cotransporter-1
  o continued absorption of H\(_2\)O from GI tract
  o vasopressin, atrial natriuretic peptide
  o cellular edema: osmotic shifts across cell membrane
CEREBRAL INJURY: MORTALITY

- can be present at diagnosis before treatment
- usually occurs in first 12–24 hours of treatment
- DKA still has ~0.5–1% risk of cerebral injury
- ~25% mortality rate, ~35% serious morbidity rate
- 70–80% of diabetes-related deaths in kids <12
- greatest contributor (~50%) to mortality of DKA, not hyperglycemia or shock
- subclinical CI with subtle sequelae may be frequent in DKA
BASELINE RISK FACTORS FOR CI

- infants and young children
- new-onset (3.3% vs. 0.23% in known pts)
- long-standing symptoms
- $\uparrow$ serum Na$^+$, $\downarrow$ serum Na$^+$
- $\downarrow$ $p_a$CO$_2$ (even adjusting for pH), $\downarrow$ pH (most acidic)
- $\uparrow$ plasma urea, $\uparrow$ serum K$^+$, $\uparrow$ hematocrit (most dehydrated)
- “sickest looking”?
TREATMENT-RELATED RISK FACTORS FOR CI

• too-rapid fall in “corrected Na⁺”
  o Na⁺ + [0.36 \times (\text{glucose} - 5.6)]

• failure of uncorrected Na⁺ to rise

• too-rapid fall in “active osmolality”
  o \text{glucose} + [2 \times (\text{Na}^+ + K^+)]

• bicarbonate therapy

• early (<60 min) insulin Rx or large insulin boluses

• ? fluids ≥4 L/m²/24 h or ≥50 mL/kg in 1st 4 h
CEREBRAL INJURY: SYMPTOMS

• severe headache
• change in sensorium: irritability, confusion, inability to arouse
• dilated pupils, papilledema, cranial nerve palsies
• posturing, incontinence
• decreased \( \text{O}_2 \) saturation
• Cushing’s triad
  o  bradycardia
  o  hypertension
  o  irregular respirations
CEREBRAL INJURY: TREATMENT

• elevate head of bed
• reduce fluid rate by $\frac{1}{3}$
• mannitol 20% 0.5–1 g/kg (2.5–5 mL/kg) IV over 15 min
• NaCl 3% 2.5–5 cc/kg IV over 15 min
• intubate if pending respiratory failure
• mild hyperventilation
• no known role for dexamethasone
• early Dx and Rx improve outcome
OTHER COMPLICATIONS OF DKA

- hypokalemia*, hypocalcemia, hypomagnesemia, hypophosphatemia*
- hyperchloremic acidosis
- hypoglycemia
- peripheral venous*, dural sinus, basilar artery thrombosis
- pulmonary embolism*, pulmonary edema*, pneumothorax, aspiration pneumonia*, ARDS
- rhabdomyolysis*
- acute pancreatitis*
- intracranial hemorrhage, cerebral infarction
- acute kidney injury*

*HHS > DKA
HYPERGLYCEMIC HYPEROSMOLAR STATE

• hyperglycemia: glucose >33.3 mmol/L
• hyperosmolality: osmolality >320 mOsm/kg
• small ketonuria, absent-to-small ketonemia
• absence of significant acidosis: $\text{pH}_{\text{art}} > 7.30$, $\text{pH}_{\text{ven}} > 7.25$, $\text{HCO}_3^- > 15$
• obtundation, combativeness, seizures (~50%)
• seen in T2D, obese, blacks
• also seen in T1D drinking lots of pop
• can have mixture of DKA and HHS
HHS vs. DKA

- ↑ hyperosmolality, ↑ hyperglycemia
- ↑ dehydration, ↑ fluid Rx needed
- ↑ electrolyte loss
- ↓ acidosis, ↑ HCO$_3^-$
- may not need much or any insulin
- ↑ risk of shock, thrombosis, rhabdomyolysis
- ↓ risk of cerebral injury
TREATING HHS

• assume 12–15% dehydration
• fluids: 20 cc/kg NS, then balance Na⁺ content:
  o intravascular needs vs. lowering osmolality
• K⁺: 20 mEq/L KCl + 20 mEq/L KPhos
• insulin: 0.025 U/kg/h if BG won’t ↓ with fluids
• lower Na⁺ by ~0.5 mmol/L/h
• lower glucose by ~3–5 mmol/L/h
HHS ALGORITHM

- Bolus 0.9% saline 20 cc/kg, repeat until perfusion established
- Maintenance fluids plus deficit replacement over 24-48 hours; 0.45-0.75% saline
- Replace urine output
- Monitor electrolytes, calcium, magnesium, phosphate every 2-4 hours
- Frequent assessment of circulatory status
- Adjust rate and electrolyte composition of fluids as needed

HHS
- When serum K⁺ <5 mEq/L, start replacement with K 40 mEq/L
- Start insulin infusion when BG no longer decreases with fluid alone
- IV regular insulin 0.025-0.05 unit/kg/hr

Hyperosmolar DKA
- Start insulin after initial fluid bolus
- IV regular insulin 0.05-0.1 unit/kg/hr depending on degree of acidosis
- Titrate insulin dose to decrease blood glucose 4-5.5 mmol/L (75-100 mg/dL) per hour

ISPAD 2018
RECURRENT DKA

• most often seen in:
  o very small kids with GI illness
  o unsupervised kids
  o non-compliant teens
  o insulin pump site problems

• nearly all cases of recurrent DKA are preventable!

• get an A1C!
DKA PREVENTION (BC PEDIATRIC SOCIETY)

beyonddtype1.org/dkacampaign
Endocrinology & Diabetes

The Endocrinology & Diabetes Unit is a diagnostic, treatment and education centre for children and families affected with diabetes and other endocrine conditions.

The endocrine conditions that we care for include variations and abnormalities of normal growth and puberty, as well as both over- and under-production of thyroid, parathyroid, adrenal, and antidiuretic hormones.

http://endodiab.bcchildrens.ca
REFERENCES


• BC Children’s Hospital ePOPS (Electronic Policies, Order Sets, Procedures and Standards): [http://policyandorders.cw.bc.ca](http://policyandorders.cw.bc.ca).