DIABETIC KETOACIDOSIS PROTOCOL

2019 REVISION

www.bcchildrens.ca/endocrinology-diabetes-site/documents/dkaslides.pptx
DIAGNOSIS OF DKA

- hyperglycemia: glucose ≥11.1 mmol/L
- acidosis: pH < 7.3 or $\text{HCO}_3^- < 15$ 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>HCO$_3^-$</th>
</tr>
</thead>
<tbody>
<tr>
<td>mild</td>
<td>&lt;7.3</td>
<td>&lt;15</td>
</tr>
<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 $\text{H}_2\text{O}$, $\text{Na}^+$, $\text{K}^+$, $\text{HCO}_3^-$, $\text{P}_i$
Pathophysiology of Diabetic Ketoacidosis

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

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

↑ Lipolysis
- ↑ FFA to liver
- ↑ Ketogenesis
- ↓ Alkali reserve

↑ Glucose utilization
- ↓ Protein synthesis

↑ Proteolysis
- ↑ Gluconeogenic substrates
- ↑ Gluconeogenesis

- Hyperglycemia
- Glucosuria (osmotic diuresis)
- Loss of water and electrolytes
- Decreased fluid intake
- Impaired renal function

- Dehydration
- Hyperosmolarity
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 2018

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

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1 SUMMARY OF WHAT IS NEW/DIFFERENT

Recommendations concerning trial management have been modified to reflect recent findings from a randomized controlled clinical trial showing a difference in cerebral 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 (fasting glucose >15 mmol/L) or (200 mg/dL)
- 
- 
- 
- 
- 

- Nausea, vomiting, turbid or thick blood</text>
Diabetes Canada’s 2018 Clinical Practice Guidelines
BC CHILDREN’S HOSPITAL DIABETIC KETOACIDOSIS PROTOCOL

FOR CHILDREN AGES 1 MONTH TO 19 YEARS

This protocol is also available in a printable format.

0. ABCs, vital signs (with BP), neurovitals 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. 8

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

2. Give 0.9% saline (normal saline, NS) resuscitation bolus: 7
   • recommended amount: 10 ml/kg BW over 30 minutes: __________________________ ml

3. Repeat with second bolus of NS if persistent tachycardia, prolonged cap refill (>2 sec), cool extremities: 7
   • recommended amount: 10 ml/kg BW over 30 minutes: __________________________ ml

4. Begin rehydration, calculated for even correction over 36 hours, based on admission BW: 7
   • 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: __________________________ ml/h

5. Calculate total hourly fluid rate to be given for 36 hours: multiply (1) and (4): __________________________ 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 60–130 minutes after starting the first fluid bolus, make up and start a piggyback insulin drip at 0.05–0.1 units/kg/h BW (Bag CI): 7
   • 50 units insulin regular (Humulin® R or Novolin® Toronto) in 500 ml NS or D5NS
   • run at 0.5–1 ml/kg/h BW: __________________________ ml/h

8. Begin “2-bag method”: 7 Y together (Bag A) NS with 40 meq/L KCl and (Bag B) D10-12.5%NS with 40 meq/L KCl. Decrease replacement fluid rate to adjust for insulin drip rate: subtract (1) from (5): __________________________ 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). 7  Continue this for the next 5–6 hours, monitoring as below.

10. At 4–6 hours after initial fluids and if corrected plasma Na+ is 1345 mmol/L, stable or increasing, switch Bag A to 0.45% saline w/ 40 meq/L KCl and Bag B to D10–12.5% 0.45% saline w/ 40 meq/L KCl at the rate as in (8). 7

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

2. Hyperglycemic hyperosmolar state (HHS) should be suspected when there is significant hyperglycemia (>15 mmol/L) and hyper-osmolality (>300 mOsm/L) without ketoacidosis (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.

3. Rapid, 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 noted are more accurate.

4. Recent 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.

5. Recent research shows that DKA can be safely corrected over a 24- to 48-hour period. This protocol is designed to correct a 1% fluid deficit (100 ml/kg) evenly over 36 h.

6. Insulin boluses are always continued initiated. Insulin given in the first 1–2 h of DKA repair is thought to increase mortality. This insulin rate typically inhibits ketogenesis and gluconeogenesis and should be maintained if possible. If unable to keep PG >6 mmol/L, drop the insulin rate by 25–50%.
11. Re-evaluate appropriateness of replacement fluid type frequently, anticipating the need to add or increase Na+, K+, dextrose, etc.
- dextrose 2:
- aim to keep the PG "8-12 mmoL/L range
- sodium 3:
- corrected Na+ <145 mmoL/L, or falling regardless of level: continue NS
- corrected Na+ >145, stable or increasing, switch to 0.5NS after 4-6 h
- potassium 4:
- patient urinating and K+ remains <5 continue KCI 40 mmoL/L, may give 50% of K+ as acetate or phosphate
- bicarbonate 5:
- 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). 6

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, irregular 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 mls/h pending physician reassessment
- mannitol 20% (0.5-1.0 g/kg, 2.5-5.0 ml/kg i/v over 15 min) or NaCl 3% (2.5-5.0 ml/kg i/v over 15 min)
- consider intubation and mild hyperventilation (keep PCO2 >22 mgHg) 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 7 : does child respond to the poke?
- follow Na+, K+, Cl-, HCO3-, anion gap, urea, creatinine, venous pH every 2-4 hours, etc. 8
- 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 “8-12 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 hypotonic fluids must be considered carefully. The corrected Na+ should be calculated and followed closely: corrected Na+ = 140 actual Na+ + 0.3×[HCO3- - 6.8]. If corrected Na+ falls or fails to rise as the PG falls, this would indicate excess free-water administration. It is also helpful to monitor the active osmolality [PG = 2×[Na+ + K+]], which should not fall more than 10 mOsm/kg/h. If the corrected sodium is <134 mmoL/L, and stable and the active osmolality has been dropping slowly, switching to 0.5NS can be considered after 6-8 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 osmol content (e.g. KCl) for longer time periods (12-24 h).**

**Serum K+ levels are usually normal at diagnosis and fall precipitously with treatment. An i/v fluid containing 20-40 mmoL/L K+ is usually required to keep the serum K+ >3.0 mmoL/L. Begin K+ and insulin together. Oral/intragastric KCl loads (0.5-1.0 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 repleniting the severe phosphate deficit of DKA and/or 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 ketoads and lactic acid, and these resolve 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: peripheral CNS acidosis, hypokalemia, hyperglycemia, delayed clearance of ketones, and cerebral edema. NaHCO3 in DKA should only be considered if pH <6.9 or cardiac failure.**

**EBC (mmol/L) = 36.5 + height (cm)/2.0. Measured creatinine 1.5-3.5 mmol/ecl/1.5 Stage 1, 2-3.5 mmol/ecl/1.5 Stage 2, >3.5 mmol/ecl/1.5 Stage 3/IV.**

**Subclinical brain swelling is common in children with DKA. Cerebral edema (C2) accounts for more than half of the 1%-5% mortality rate of DKA in children. At highest risk are newly diagnosed patients, those aged <5 years, and those with initial pH <7.1 or HCO3 <20. The exact etiology of CE remains unclear. Resuscitation is successful in only 50% of cases.**

Accompanying documents on our website:
- DKA flowsheet and DKA Summary: Diagnosis, Order Sheet
- DKA Nursing Protocol (including the "two-bag" method)
- DKA Resident Guide (including the "two-bag" method)
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 serious condition. 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.

2. Hyperglycemic hyperosmolar state (HHS) should be suspected when there is significant hyperglycemia (>13 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 intravenous fluids or insulin.

3. Rapid, deep mouth breathing (Kussmaul respiration) often dries out the oral mucosa, making the child appear more dehydrated than they really is. The hemogram and other clinical signs noted are more accurate.

4. A recent 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.

5. Insulin is not always contraindicated. Insulin given in the first 1-2 hours of DKA repair is thought to increase mortality. This insulin rate must inhibit ketogenesis and gluconeogenesis and should be maintained if possible. If unable to keep P5 < 18 mmol/L, drop the insulin rate by 25-50%.
**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 brings 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 TREDX Canada (references below).

**INITIAL FLUID REPLACEMENT**

Results from the PECAH1 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 50 mL/kg bolus of 0.9% sodium chloride (normal saline, NS) over 30 minutes. Those 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-hour 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 10-15.5% 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 can make this). The BCCH Pharmacy has prepared a "recipe book" for preparing these solutions from...
**SAMPLE PRESCRIBER ORDERS FOR DKA**

<table>
<thead>
<tr>
<th>Prescriber's Orders for Diabetic Ketoacidosis (DKA)</th>
<th>Inpatient and Outpatient</th>
</tr>
</thead>
</table>

**On Admission STAT:**
- Vital signs and rectal temperature on admission and then hourly
- Weight
- Venous blood gas input and initial 
- Nothing by mouth
- Order telemetry and ward monitor
- Insert large bore intravenous cannula
- Replace dextrose by fructose
- Time for laboratory
- Venous blood gas, arterial blood gas, potassium, chloride, bicarbonate, anion gap, lactate, and complete blood count
- Labs: leukocyte, platelet, complete blood cell count/differential, Hgb/Hct

**Fluid Resuscitation (Drip bag):** Start 30-45 minutes

<table>
<thead>
<tr>
<th>Bag A</th>
<th>Dextrose 5% 1/2 N, 10 mL/kg/hr</th>
</tr>
</thead>
</table>

**Fluid Repair (after initial 30-45 minutes): begin at __________ h**

| Bag A | Sodium chloride 0.9% 10 mL/kg/hr, potassium chloride at __________ mL/hr IV rate determined from CA algorithm, line 5 |

**Fluid Repair and Insulin Infusion (after initial 1-2 hours): begin at __________ h**

<table>
<thead>
<tr>
<th>Bag B</th>
<th>Insulin 0.1 units/kg/hr, 10 mL/kg/hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bag C</td>
<td>Dextrose 5% 1/2 N, sodium chloride 0.9% 10 mL/kg/hr, potassium chloride at __________ mL/hr IV rate determined from CA protocol, line 5</td>
</tr>
<tr>
<td>Bag D</td>
<td>Dextrose 5% 1/2 N, sodium chloride 0.9% 10 mL/kg/hr, insulin 0.1 units/kg/hr, 10 mL/kg/hr</td>
</tr>
</tbody>
</table>

**Electrolytes Monitoring:**
- Sodium-glucose-every-____ minutes (suggested 30-40 minutes)
- Venous blood gas, arterial blood gas, potassium, chloride, bicarbonate, anion gap, lactate, glucose, electrolytes, plasma urea, creatinine, and prothrombin activity every 2 hours (suggested 2-4 hours)
- Patients with severe nausea or vomiting in vital signs of Glasgow Coma Scale (GCS) < 9, systolic blood pressure < 90 mmHg, and heart rate > 100 beats per minute, MD review

**Signature:**

- **Date:**______________
- **Time:**______________
- **HRS:**______________
- **Weight:**______________
- **Height:**______________
- **Allergy Status:** sheet removed
- **Written by:** Name

---

**Prescriber's Orders for Diabetic Ketoacidosis (DKA) Inpatient and Outpatient**

- Date: __________
- Time: __________
- HRS: __________
- Weight: __________
- Height: __________
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- Written by: Name

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**Signature:**

- **Date:**______________
- **Time:**______________
- **HRS:**______________
- **Weight:**______________
- **Height:**______________
- **Allergy Status:** sheet removed
- **Written by:** Name

---

**Please note:** The information provided is a sample and should not be used as a substitute for professional medical advice. Always consult a healthcare professional for accurate and personalized medical advice.
**EPOPS DKA ORDERS:** POLICYANDORDERS.CW.BC.CA

### Endocrinology Diabetic Ketoadcinosis (DKA) Inpatient and Outpatient

#### (Page 1 of 2)

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<th>Refer to BCCH Diabetic Ketoadcinosis Nursing Protocol on ePOPS</th>
<th>Refer to BCCH Diabetic Ketoadcinosis Recipes for Making Solutions on ePOPS</th>
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#### Patient Care

- **(on admission)**
  - Measure weight **STAT**
  - Check serum electrolytes **STAT**
  - Check base deficit
  - Monitor serum bicarbonate
  - Monitor urine output
  - Monitor blood glucose

- **Hypokalemia or hypomagnesium, omit electrolyte**

#### If patient develops severe headache or alteration in vital signs or Glasgow Coma Scale (GCS):

- Notify physician **STAT**
- Raise head of bed **30°**
- Decrease IV fluid to 0.5 ml/kg per hour and reassess

#### VITAL SIGNS

- **Vitals signs **STAT** on admission, then q4h
- **Headache, neck stiffness, altered level of consciousness, then q4h
- **Continuous cardiovascular monitoring

#### IV Infusions

- **Initial Fluid Resuscitation (Initial 30 to 90 minutes)
  - Intravenous Dextrose 5% in 0.9% saline at 100 ml/hr for 1 hour (15 ml/kg)
  - Intravenous 10% Calcium Gluconate 1 ml/kg over 10 minutes (15 ml/kg)
- Fluid Resuscitation (Initial 30 to 90 minutes)
  - Intravenous Dextrose 5% in 0.9% saline at 100 ml/hr for 1 hour (15 ml/kg)
- Fluid Resuscitation (Initial 30 to 90 minutes)
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#### Blood Work

- **(on admission)**
  - Hematocrit
  - Hemoglobin
  - Electrolytes
  - Creatinine
  - BUN
  - Sodium
  - Potassium
  - Glucose
  - Calcium
  - Phosphorus
  - Lactate
  - Total Protein
  - albumin
  - Total Cholesterol
  - Triglycerides
  - Lipids

### Endocrinology Diabetic Ketoadcinosis (DKA) Inpatient and Outpatient

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### BCCH DKA RECIPES FOR MAKING SOLUTIONS

<table>
<thead>
<tr>
<th>Item #</th>
<th>Dextrose solution to prepare</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Dextrose solution and size of IV bag to use</td>
<td>Withdraw &amp; discard from bag</td>
<td>Add to bag</td>
</tr>
<tr>
<td>1</td>
<td>commercial available</td>
<td>0.5W-NaCl 0.9% with 40 mEq KC1/L</td>
<td>1000 ml 0.5W-NaCl 0.9% with 40 mEq KC1/L</td>
<td>100 ml 100 ml 0.05W</td>
</tr>
<tr>
<td>2</td>
<td>0.10W-NaCl 0.9% with 40 mEq KC1/L</td>
<td>1000 ml 0.5W-NaCl 0.9% with 40 mEq KC1/L</td>
<td>100 ml 100 ml 0.05W</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>0.125W-NaCl 0.9% with 40 mEq KC1/L</td>
<td>1000 ml 0.5W-NaCl 0.9% with 40 mEq KC1/L</td>
<td>100 ml 100 ml 0.05W</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>commercial available</td>
<td>0.5W-NaCl 0.45% with 40 mEq KC1/L</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>0.10W-NaCl 0.45% with 40 mEq KC1/L</td>
<td>1000 ml 0.5W-NaCl 0.45% with 40 mEq KC1/L</td>
<td>100 ml 100 ml 0.05W</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>0.125W-NaCl 0.45% with 40 mEq KC1/L</td>
<td>1000 ml 0.5W-NaCl 0.45% with 40 mEq KC1/L</td>
<td>100 ml 100 ml 0.05W</td>
<td></td>
</tr>
</tbody>
</table>

Note: These results in appropriate concentration and is to be used only when Pharmacy mixing is not available.

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

### BCH DKA RECIPE DOCUMENTS

**Diabetic Ketoacidosis (DKA) involves a combination of hyperglycemia, acidosis, and ketonemia. 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.
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 during 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
- Lethargy
- Nausea, vomiting, and abdominal pain
- fruity or acetone-smelling breath
- Flushed face
- Confusion
- Hyperventilation and Kussmaul breathing (rapid, deep, sighing mouth-breathing)
- T. heart rate and T. respirations, and possibly T. blood pressure

Acute dehydation must be treated with IV 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.
BCCH DKA PROTOCOL 2019: TIMELINE

• on admission: weight, vitals, assessment and stabilization

• first 30–60 minutes: fluid resuscitation

• 60 min–36 h:
  o fluid replacement
  o insulin infusion
  o addition of glucose

• throughout:
  o careful monitoring, reassessment
  o titration of fluids, electrolytes, glucose, insulin
INITIAL ER MANAGEMENT

- ABC’s and GCS
- weigh patient
- insert large-bore IV
- check chemistries, CBG, 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: 1st 60 MINUTES

- give 1st bolus of NS 10 mL/kg IV over 30 min
- most sicker patients require a 2nd 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

adapted from *Journal of Pediatrics* 1999;134(3):376–378
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\(^+\) = \([\text{measured Na}^+ + 0.36\times(BG-5.6)]\)
• active osmolality = \([BG + 2\times(Na^++K^+)]\)
# 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>
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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 EBC (µmol/L) = 36.5 × height (cm)/120
  o measured creatinine 1.5–1.99× EBC = Stage 1
  o measured creatinine 2–2.99× EBC = Stage 2
  o measured creatinine ≥3× EBC = Stage 3
• some creatinine assays have cross-reactivity with ketones!

JAMA Pediatrics 2017;171(5):e170020
MECHANISMS OF CEREBRAL INJURY

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

• other possible factors:
  - role of Na⁺–H⁺ antiporter-3 (insulin) and Na⁺–K⁺–Cl⁻ cotransporter-1
  - continued absorption of H₂O from GI tract
  - vasopressin, atrial natriuretic peptide
  - 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
• ↑ serum Na\(^+\), ↓ serum Na\(^+\)
• ↓ \(p_a\)CO\(_2\) (even adjusting for pH), ↓ pH (most acidotic)
• ↑ plasma urea, ↑ serum K\(^+\), ↑ hematocrit (most dehydrated)
• “sickest looking”? 
TREATMENT-RELATED RISK FACTORS FOR CI

• too-rapid fall in “corrected Na⁺”
  o Na⁺ + [0.36 × (glucose – 5.6)]

• failure of uncorrected Na⁺ to rise
• too-rapid fall in “active osmolality”
  o glucose + [2 × (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 O₂ saturation
- Cushing’s triad
  - bradycardia
  - hypertension
  - irregular respirations
CEREBRAL INJURY: TREATMENT

• elevate head of bed
• reduce fluid rate by ⅓
• 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: $pH_{\text{art}} > 7.30$, $pH_{\text{ven}} > 7.25$, $\text{HCO}_3^- > 15$
• 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

When serum K⁺ <5 mEq/L, start replacement with K 40 mEq/L

Monitor electrolytes, calcium, magnesium, phosphate every 2-4 hours

Start insulin infusion when BG no longer decreases with fluid alone

IV regular insulin 0.025-0.05 unit/kg/hr

Tritrate insulin dose to decrease blood glucose 4.5.5 mmol/L (75-100 mg/dL) per hour

Frequently assess circulatory status
Adjust rate and electrolyte composition of fluids as needed

Start insulin after initial fluid bolus

IV regular insulin 0.05-0.1 unit/kg/hr depending on degree of acidosis

Hyperosmolar DKA

HHS

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)

beyondtype1.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.

In this section

- Endocrinology & Diabetes
- Atypical Antipsychotics
- DKA Protocol
- Professional Resources
- Tools & Calculators

http://endodiab.bcchildrens.ca
REFERENCES


• Translating Emergency Knowledge for Kids (TREKK Canada): http://trekk.ca.


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