DIABETIC KETOACIDOSIS PROTOCOL

2024 REVISION

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

DIAGNOSIS OF DKA

- hyperglycemia: blood glucose >11.1 mmol/L
- acidosis: venous pH <7.3 or HCO_3^- <18 mmol/L
- ketones:
  - plasma β-hydroxybutyrate ≥3 mmol/L
  - moderate–large ketonuria (≥2+)

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

SEVERITY OF DKA

	pH	HCO_3^-
mild	<7.3	<18
moderate	<7.2	<10
severe	<7.1	<5

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 H_2O, Na^+, K^+, HCO_3^-, P_i

RATIONALE FOR 2024 REVISION

- The PECARN FLUID Trial demonstrated that fast *vs* slow rehydration for DKA seems to be equivalent with respect to:
  - brain injury (0.9%)
  - short-term memory
  - post-event memory
  - IQ
  - serious adverse events
- some suggestion (not significant) that faster rehydration:
  - led to less ↓ in GCS
  - led to faster ↑ in short-term memory scores in sickest patients

New England Journal of Medicine 2018;378(24):2275–2338

DKA PROTOCOL 2024: GENERAL PRINCIPLES

- 20 mL/kg fluid push over 30 min, 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* 2022;23(7):835--856

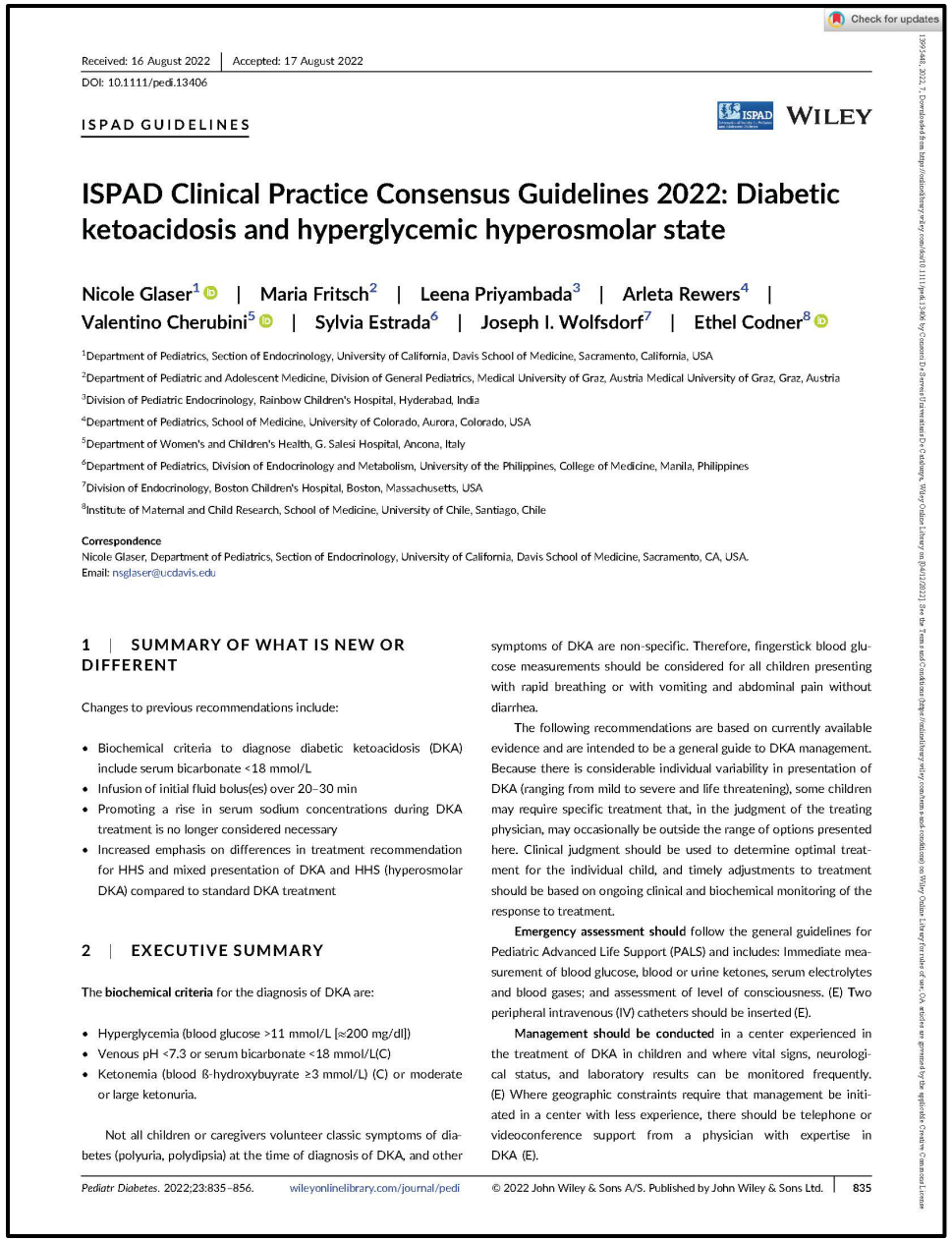
MODIFICATIONS FROM 2019 PROTOCOL

- a plasma HCO_3^- <18 mmol/L is now diagnostic of DKA (previously, the cut-off was 15 mmol/L)
- more-aggressive fluid boluses are suggested at the start of therapy:
  - most patients with DKA should receive a 20-mL/kg bolus of normal saline over 30 min at the initiation of treatment
  - repeated 20-mL/kg boluses may be required for circulatory compromise
- notation is added not to begin KCl unless patient is urinating and has plasma K^+ ≤5.5 mmol/L
- notation is added not to begin insulin unless plasma K^+ ≥3.5 mmol/L
- an insulin infusion rate of 0.05 U/kg/h is suggested when pH >7.15

DKA PROTOCOLS: DISCLAIMER

- **no** DKA protocol has been shown to eliminate the risk of cerebral injury
- current gold standard: ISPAD *Clinical Practice Consensus Guidelines 2022*
- guidelines should not replace intelligent thought and should be tailored to meet the needs of each individual patient
- involve Pediatric Endocrinology early!

ISPAD 2022



Received: 16 August 2022 | Accepted: 17 August 2022
DOI: 10.1111/pedi.13406

ISPAD GUIDELINES

ISPAD WILEY

ISPAD Clinical Practice Consensus Guidelines 2022: Diabetic ketoacidosis and hyperglycemic hyperosmolar state

Nicole Glaser[1] | Maria Fritsch[2] | Leena Priyambada[3] | Arleta Rewers[4] | Valentino Cherubini[5] | Sylvia Estrada[6] | Joseph I. Wolfsdorf[7] | Ethel Codner[8]

[1]Department of Pediatrics, Section of Endocrinology, University of California, Davis School of Medicine, Sacramento, California, USA
[2]Department of Pediatric and Adolescent Medicine, Division of General Pediatrics, Medical University of Graz, Austria Medical University of Graz, Graz, Austria
[3]Division of Pediatric Endocrinology, Rainbow Children's Hospital, Hyderabad, India
[4]Department of Pediatrics, School of Medicine, University of Colorado, Aurora, Colorado, USA
[5]Department of Women's and Children's Health, G. Salesi Hospital, Ancona, Italy
[6]Department of Pediatrics, Division of Endocrinology and Metabolism, University of the Philippines, College of Medicine, Manila, Philippines
[7]Division of Endocrinology, Boston Children's Hospital, Boston, Massachusetts, USA
[8]Institute of Maternal and Child Research, School of Medicine, University of Chile, Santiago, Chile

Correspondence
Nicole Glaser, Department of Pediatrics, Section of Endocrinology, University of California, Davis School of Medicine, Sacramento, CA, USA.
Email: nsglaser@ucdavis.edu

1 | SUMMARY OF WHAT IS NEW OR DIFFERENT

Changes to previous recommendations include:

- Biochemical criteria to diagnose diabetic ketoacidosis (DKA) include serum bicarbonate <18 mmol/L
- Infusion of initial fluid bolus(es) over 20–30 min
- Promoting a rise in serum sodium concentrations during DKA treatment is no longer considered necessary
- Increased emphasis on differences in treatment recommendation for HHS and mixed presentation of DKA and HHS (hyperosmolar DKA) compared to standard DKA treatment

2 | EXECUTIVE SUMMARY

The **biochemical criteria** for the diagnosis of DKA are:

- Hyperglycemia (blood glucose >11 mmol/L [≈200 mg/dl])
- Venous pH <7.3 or serum bicarbonate <18 mmol/L(C)
- Ketonemia (blood ß-hydroxybuyrate ≥3 mmol/L) (C) or moderate or large ketonuria.

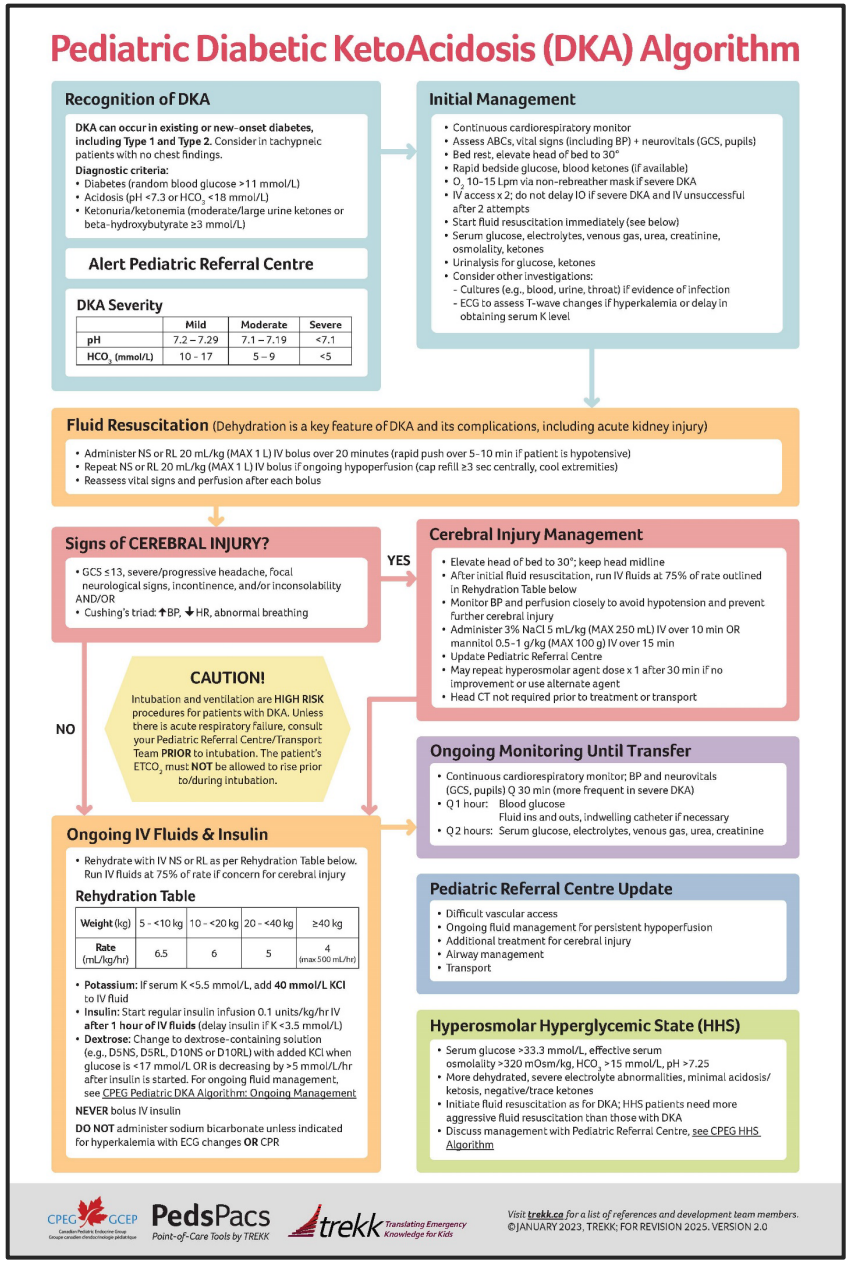
Not all children or caregivers volunteer classic symptoms of diabetes (polyuria, polydipsia) at the time of diagnosis of DKA, and other symptoms of DKA are non-specific. Therefore, fingerstick blood glucose measurements should be considered for all children presenting with rapid breathing or with vomiting and abdominal pain without diarrhea.

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 presentation of DKA (ranging from mild to severe and life threatening), some children may require specific treatment that, in the judgment of the treating physician, may occasionally be outside the range of options presented here. Clinical judgment should be used to determine optimal treatment for the individual child, and timely adjustments to treatment should be based on ongoing clinical and biochemical monitoring of the response to treatment.

Emergency assessment should follow the general guidelines for Pediatric Advanced Life Support (PALS) and includes: Immediate measurement of blood glucose, blood or urine ketones, serum electrolytes and blood gases; and assessment of level of consciousness. (E) Two peripheral intravenous (IV) catheters should be inserted (E).

Management should be conducted in a center experienced in the treatment of DKA in children and where vital signs, neurological status, and laboratory results can be monitored frequently. (E) Where geographic constraints require that management be initiated in a center with less experience, there should be telephone or videoconference support from a physician with expertise in DKA (E).

TREKK 2023



Pediatric Diabetic KetoAcidosis (DKA) Algorithm

Recognition of DKA

DKA can occur in existing or new-onset diabetes, including Type 1 and Type 2. Consider in tachypneic patients with no chest findings.

Diagnostic criteria:
- Diabetes (random blood glucose >11 mmol/L)
- Acidosis (pH <7.3 or HCO_3 <18 mmol/L)
- Ketonuria/ketonemia (moderate/large urine ketones or beta-hydroxybutyrate ≥3 mmol/L)

Alert Pediatric Referral Centre

DKA Severity

	Mild	Moderate	Severe
pH	7.2 – 7.29	7.1 – 7.19	<7.1
HCO_3 (mmol/L)	10 - 17	5 – 9	<5

Initial Management

- Continuous cardiorespiratory monitor
- Assess ABCs, vital signs (including BP) + neurovitals (GCS, pupils)
- Bed rest, elevate head of bed to 30°
- Rapid bedside glucose, blood ketones (if available)
- O_2 10-15 L pm via non-rebreather mask if severe DKA
- IV access x 2; do not delay IO if severe DKA and IV unsuccessful after 2 attempts
- Start fluid resuscitation immediately (see below)
- Serum glucose, electrolytes, venous gas, urea, creatinine, osmolality, ketones
- Urinalysis for glucose, ketones
- Consider other investigations:
  - Cultures (e.g., blood, urine, throat) if evidence of infection
  - ECG to assess T-wave changes if hyperkalemia or delay in obtaining serum K level

Fluid Resuscitation (Dehydration is a key feature of DKA and its complications, including acute kidney injury)

- Administer NS or RL 20 mL/kg (MAX 1 L) IV bolus over 20 minutes (rapid push over 5–10 min if patient is hypotensive)
- Repeat NS or RL 20 mL/kg (MAX 1 L) IV bolus if ongoing hypoperfusion (cap refill ≥3 sec centrally, cool extremities)
- Reassess vital signs and perfusion after each bolus

Signs of CEREBRAL INJURY?

- GCS ≤13, severe/progressive headache, focal neurological signs, incontinence, and/or inconsolability AND/OR
- Cushing's triad: ↑BP, ↓HR, abnormal breathing

YES

NO

CAUTION!

Intubation and ventilation are **HIGH RISK** procedures for patients with DKA. Unless there is acute respiratory failure, consult your Pediatric Referral Centre/Transport Team **PRIOR** to intubation. The patient's $ETCO_2$ must **NOT** be allowed to rise prior to/during intubation.

Cerebral Injury Management

- Elevate head of bed to 30°; keep head midline
- After initial fluid resuscitation, run IV fluids at 75% of rate outlined in Rehydration Table below
- Monitor BP and perfusion closely to avoid hypotension and prevent further cerebral injury
- Administer 3% NaCl 5 mL/kg (MAX 250 mL) IV over 10 min OR mannitol 0.5–1 g/kg (MAX 100 g) IV over 15 min
- Update Pediatric Referral Centre
- May repeat hyperosmolar agent dose x 1 after 30 min if no improvement or use alternate agent
- Head CT not required prior to treatment or transport

Ongoing Monitoring Until Transfer

- Continuous cardiorespiratory monitor; BP and neurovitals (GCS, pupils) Q 30 min (more frequent in severe DKA)
- Q 1 hour: Blood glucose; Fluid ins and outs, indwelling catheter if necessary
- Q 2 hours: Serum glucose, electrolytes, venous gas, urea, creatinine

Ongoing IV Fluids & Insulin

- Rehydrate with IV NS or RL as per Rehydration Table below. Run IV fluids at 75% of rate if concern for cerebral injury

Rehydration Table

Weight (kg)	5 - <10 kg	10 - <20 kg	20 - <40 kg	≥40 kg
Rate (mL/kg/hr)	6.5	6	5	4 (max 500 mL/hr)

- **Potassium:** If serum K <5.5 mmol/L, add **40 mmol/L KCl** to IV fluid
- **Insulin:** Start regular insulin infusion 0.1 units/kg/hr IV **after 1 hour of IV fluids** (delay insulin if K <3.5 mmol/L)
- **Dextrose:** Change to dextrose-containing solution (e.g., D5NS, D5RL, D10NS or D10RL) with added KCl when glucose is <17 mmol/L OR is decreasing by >5 mmol/L/hr after insulin is started. For ongoing fluid management, see CPEG Pediatric DKA Algorithm: Ongoing Management

NEVER bolus IV insulin

DO NOT administer sodium bicarbonate unless indicated for hyperkalemia with ECG changes **OR** CPR

Pediatric Referral Centre Update

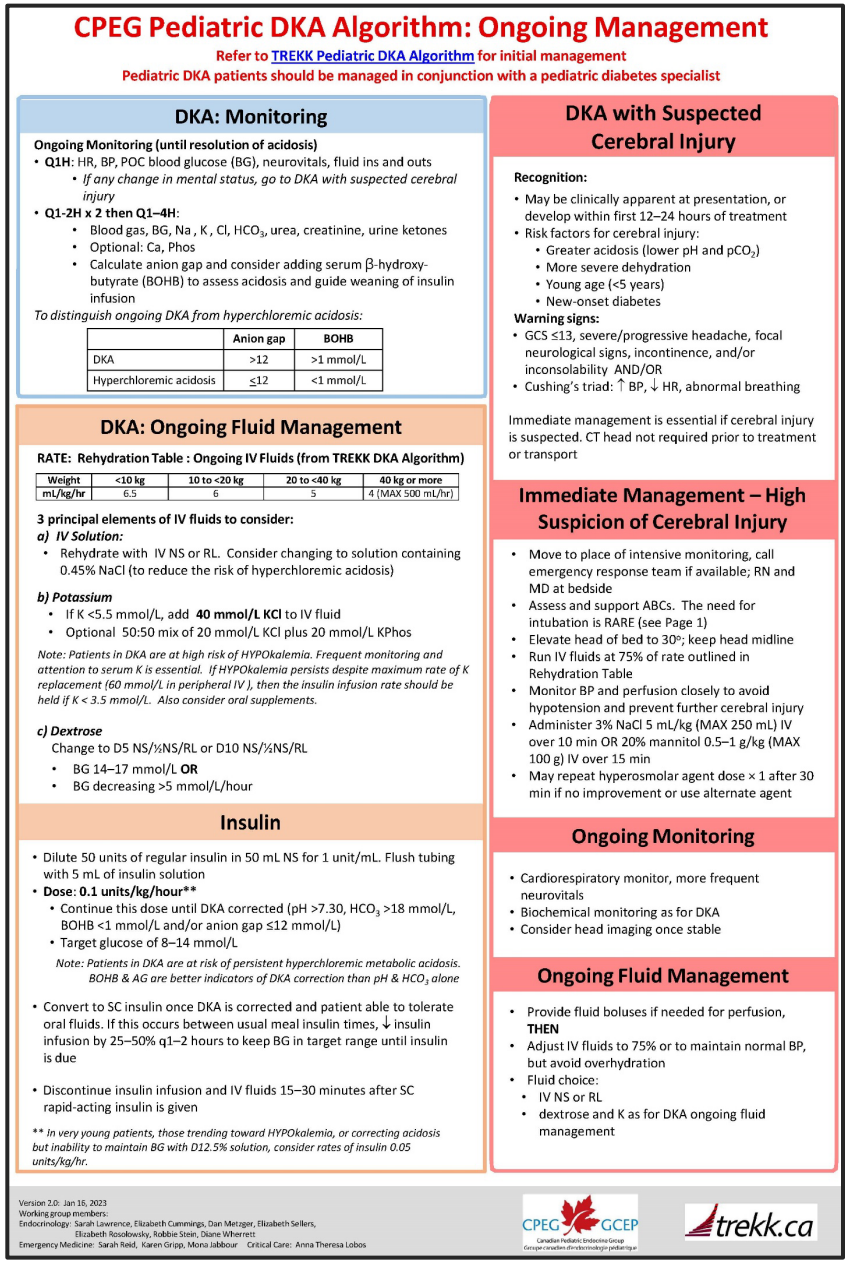
- Difficult vascular access
- Ongoing fluid management for persistent hypoperfusion
- Additional treatment for cerebral injury
- Airway management
- Transport

Hyperosmolar Hyperglycemic State (HHS)

- Serum glucose >33.3 mmol/L, effective serum osmolality >320 mOsm/kg, HCO_3 >15 mmol/L, pH >7.25
- More dehydrated, severe electrolyte abnormalities, minimal acidosis/ketosis, negative/trace ketones
- Initiate fluid resuscitation as for DKA; HHS patients need more aggressive fluid resuscitation than those with DKA
- Discuss management with Pediatric Referral Centre, see CPEG HHS Algorithm

CPEG GCEP PedsPacs Point-of-Care Tools by TREKK trekk Translating Emergency Knowledge for Kids

Visit trekk.ca for a list of references and development team members.
©JANUARY 2023, TREKK; FOR REVISION 2025. VERSION 2.0



CPEG Pediatric DKA Algorithm: Ongoing Management

Refer to TREKK Pediatric DKA Algorithm for initial management

Pediatric DKA patients should be managed in conjunction with a pediatric diabetes specialist

DKA: Monitoring

Ongoing Monitoring (until resolution of acidosis)
- **Q1H:** HR, BP, POC blood glucose (BG), neurovitals, fluid ins and outs
  - *If any change in mental status, go to DKA with suspected cerebral injury*
- **Q1-2H x 2 then Q1–4H:**
  - Blood gas, BG, Na , K , Cl, HCO_3, urea, creatinine, urine ketones
  - Optional: Ca, Phos
  - Calculate anion gap and consider adding serum β-hydroxy-butyrate (BOHB) to assess acidosis and guide weaning of insulin infusion

To distinguish ongoing DKA from hyperchloremic acidosis:

	Anion gap	BOHB
DKA	>12	>1 mmol/L
Hyperchloremic acidosis	≤12	<1 mmol/L

DKA: Ongoing Fluid Management

RATE: Rehydration Table : Ongoing IV Fluids (from TREKK DKA Algorithm)

Weight	<10 kg	10 to <20 kg	20 to <40 kg	40 kg or more
mL/kg/hr	6.5	6	5	4 (MAX 500 mL/hr)

3 principal elements of IV fluids to consider:

a) IV Solution:
- Rehydrate with IV NS or RL. Consider changing to solution containing 0.45% NaCl (to reduce the risk of hyperchloremic acidosis)

b) Potassium
- If K <5.5 mmol/L, add **40 mmol/L KCl** to IV fluid
- Optional 50:50 mix of 20 mmol/L KCl plus 20 mmol/L KPhos

Note: Patients in DKA are at high risk of HYPOkalemia. Frequent monitoring and attention to serum K is essential. If HYPOkalemia persists despite maximum rate of K replacement (60 mmol/L in peripheral IV), then the insulin infusion rate should be held if K < 3.5 mmol/L. Also consider oral supplements.

c) Dextrose

Change to D5 NS/½NS/RL or D10 NS/½NS/RL
- BG 14–17 mmol/L **OR**
- BG decreasing >5 mmol/L/hour

Insulin

- Dilute 50 units of regular insulin in 50 mL NS for 1 unit/mL. Flush tubing with 5 mL of insulin solution
- **Dose: 0.1 units/kg/hour****
  - Continue this dose until DKA corrected (pH >7.30, HCO_3 >18 mmol/L, BOHB <1 mmol/L and/or anion gap ≤12 mmol/L)
  - Target glucose of 8–14 mmol/L

Note: Patients in DKA are at risk of persistent hyperchloremic metabolic acidosis. BOHB & AG are better indicators of DKA correction than pH & HCO_3 alone

- Convert to SC insulin once DKA is corrected and patient able to tolerate oral fluids. If this occurs between usual meal insulin times, ↓ insulin infusion by 25–50% q1–2 hours to keep BG in target range until insulin is due
- Discontinue insulin infusion and IV fluids 15–30 minutes after SC rapid-acting insulin is given

*** In very young patients, those trending toward HYPOkalemia, or correcting acidosis but inability to maintain BG with D12.5% solution, consider rates of insulin 0.05 units/kg/hr.*

DKA with Suspected Cerebral Injury

Recognition:
- May be clinically apparent at presentation, or develop within first 12–24 hours of treatment
- Risk factors for cerebral injury:
  - Greater acidosis (lower pH and pCO_2)
  - More severe dehydration
  - Young age (<5 years)
  - New-onset diabetes

Warning signs:
- GCS ≤13, severe/progressive headache, focal neurological signs, incontinence, and/or inconsolability AND/OR
- Cushing's triad: ↑ BP, ↓ HR, abnormal breathing

Immediate management is essential if cerebral injury is suspected. CT head not required prior to treatment or transport

Immediate Management – High Suspicion of Cerebral Injury

- Move to place of intensive monitoring, call emergency response team if available; RN and MD at bedside
- Assess and support ABCs. The need for intubation is RARE (see Page 1)
- Elevate head of bed to 30°; keep head midline
- Run IV fluids at 75% of rate outlined in Rehydration Table
- Monitor BP and perfusion closely to avoid hypotension and prevent further cerebral injury
- Administer 3% NaCl 5 mL/kg (MAX 250 mL) IV over 10 min OR 20% mannitol 0.5–1 g/kg (MAX 100 g) IV over 15 min
- May repeat hyperosmolar agent dose × 1 after 30 min if no improvement or use alternate agent

Ongoing Monitoring

- Cardiorespiratory monitor, more frequent neurovitals
- Biochemical monitoring as for DKA
- Consider head imaging once stable

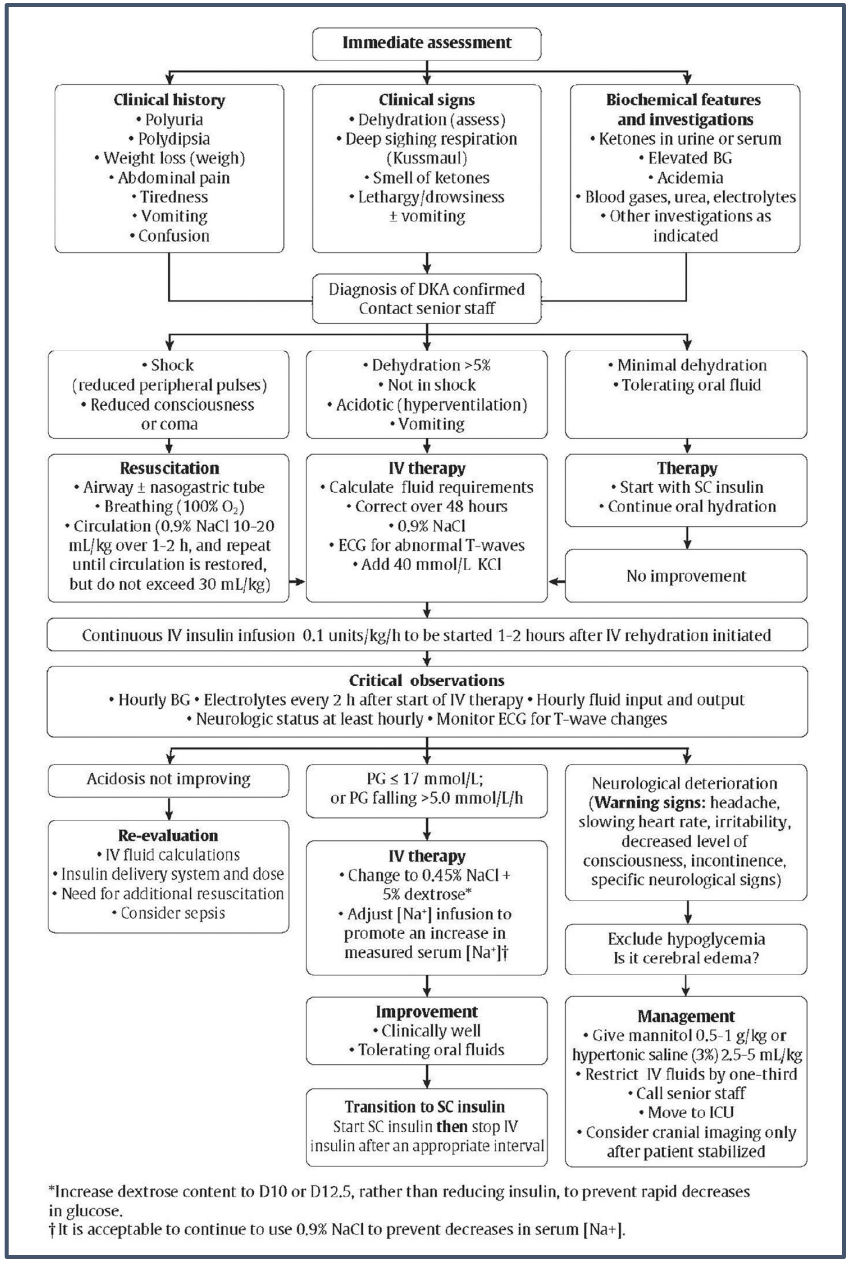
Ongoing Fluid Management

- Provide fluid boluses if needed for perfusion, **THEN**
- Adjust IV fluids to 75% or to maintain normal BP, but avoid overhydration
- Fluid choice:
  - IV NS or RL
  - dextrose and K as for DKA ongoing fluid management

Version 2.0: Jan 16, 2023
Working group members:
Endocrinology: Sarah Lawrence, Elizabeth Cummings, Dan Metzger, Elizabeth Sellers, Elizabeth Rosolowsky, Robbie Stein, Diane Wherrett
Emergency Medicine: Sarah Reid, Karen Gripp, Mona Jabbour Critical Care: Anna Theresa Lobos

CPEG GCEP trekk.ca

DIABETES CANADA 2018



Diabetes Canada's *2018 Clinical Practice Guidelines*

2024 BCCH DKA PROTOCOL

BC CHILDREN'S HOSPITAL DIABETIC KETOACIDOSIS PROTOCOL[A]

FOR CHILDREN AGES 1 MONTH TO 19 YEARS

THIS PROTOCOL IS ALSO AVAILABLE IN FILLABLE PDF FORMAT

BC Children's Hospital
Provincial Health Services Authority

FIRST 30 MIN

0. ABCs, vital signs (with BP), neurovital signs. Place large-bore IV. Draw labs. Confirm DKA: blood glucose ≥11.1 mmol/L, moderate–large ketonuria (≥2+) or plasma β-hydroxybutyrate ≥3.0 mmol/L, and venous pH <7.3 or plasma HCO_3^- <18 mmol/L.[C] Consider possibility of an element of hyperglycemic hyperosmolar state.[B]
1. Measure body weight in kilograms ..... (1) _____ kg
2. Give 0.9% saline (normal saline, NS) resuscitation bolus[D]
   - recommended amount: 20 mL/kg over 30 min, max 1000 mL ..... (2) _____ mL
3. Give rapid repeated boluses of NS if persistent tachycardia, prolonged cap refill (>2 sec), cool extremities:
   - 20 mL/kg boluses, repeated until stable; total **extra** given: ..... (3) _____ mL

TIME = 30 MIN–36 HOURS

4. Begin rehydration, calculated for even correction over 36 hours, based on admission body weight:[E]
   - 5–10 kg: 6.5 mL/kg/h
   - 10–20 kg: 6 mL/kg/h
   - 20–40 kg: 5 mL/kg/h
   - >40 kg: 4 mL/kg/h, maximum 500 mL/h ..... (4) _____ mL/kg/h
5. Calculate **total** hourly fluid rate to be given for 36 hours: multiply (1) and (4) ..... (5) _____ 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 a plasma K^+ ≤5.5 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/h (Bag C). Ensure plasma K^+ ≥3.5 mmol/L first. Consider 0.5 mL/kg/h if pH >7.15.[F]
   - 50 units insulin regular (Humulin® R or Novolin® Toronto) in 500 mL NS or D10/NS
   - run at 0.5–1 mL/kg BW/h ..... (7) _____ mL/h
8. Begin "2-bag method"[G]. Y together (Bag A) NS with 40 mEq/L KCl and (Bag B) D10–D12.5/NS with 40 mEq/L KCl. Decrease replacement fluid rate to adjust for insulin drip rate: subtract (7) from (5) ..... (8) _____ 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)[G]. 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 ≥140 mmol/L, stable or increasing, switch Bag A to 0.45% saline w/ 40 mEq/L KCl and Bag B to D10–D12.5/0.45% saline w/ 40 mEq/L KCl at the rate as in (8)[H].

Rationale & Notes:

[A]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, please feel free to contact the BCCH Pediatric Endocrinologist on call.

[B]Hyperglycemic hyperosmolar state (HHS) should be suspected when there is significant hyperglycemia (>33 mmol/L) and hyper-osmolality (>330 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.

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

[D]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.

[E]Recent research shows that DKA can be safely corrected over a 24- to 48-h period. This protocol is designed to correct a 10% fluid deficit (100 mL/kg) evenly over 36 h.

[F]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[G], drop the insulin rate by 25–50%. Consider 0.05 U/kg/h for pH >7.15. Ensure plasma K^+ ≥3.5 mmol/L before starting insulin.

BC Children's Hospital UBC

2024 BCCH DKA PROTOCOL

THROUGHOUT

11. Re-evaluate appropriateness of replacement fluid type frequently, anticipating the need to add or increase Na^+, K^+, dextrose, etc.
    - dextrose[G]: aim to keep the PG ~8–12 mmol/L range
    - sodium[H]: corrected Na^+ <140 mmol/L, or falling regardless of level: continue NS
      corrected Na^+ ≥140, stable or increasing, switch to ½NS after 4–6 h
    - potassium[I,J]: patient urinating and K^+ remains ≤5.5: continue KCl 40 mmol/L may give 50% of K^+ as phosphate
    - bicarbonate[K]: $NaHCO_3$ 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).[L]
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 mL/h pending physician reassessment
    - mannitol 20% (0.5–1 g/kg, 2.5–5 mL/kg IV over 15 min) or NaCl 3% (2.5–5 mL/kg IV over 15 min)[M]
    - consider intubation and mild hyperventilation (avoid hypocapnia) 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[G]: does child respond to the poke?
    - follow Na^+, K^+, Cl^-, HCO_3^-, anion gap, urea, creatinine, venous pH every 2–4 hours[H, I, K]; Ca^{2+}, Mg^{2+} and P_i every 2–4 hours if giving phosphate[J]
    - 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.

[G]Keeping the PG in the ~8–12 mmol/L range allows for a buffer against hypoglycemia and a too-rapid fall in plasma osmolality[H]. 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.

[H]At some point, the patient will require a switch to the use of hypotonic fluids. The corrected Na^+ should be calculated and followed closely: corrected Na^+ = [measured Na^+ + 0.36×(PG–5.6)]. It is also helpful to monitor the active osmolality [PG + 2×(Na^+ + K^+)], which should not fall >0.5 mOsm/kg/h. If the corrected sodium is ≥140 mmol/L and stable or rising and the active osmolality has been dropping slowly, switching to ½NS should 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).

[I]Serum K^+ levels are usually normal at diagnosis and fall precipitously with treatment. An IV fluid containing 20–40 mmol/L K^+ is usually required to keep the serum K^+ ≥3.5 mmol/L. Begin K^+ and insulin together. Oral/nasogastric KCl boluses (0.5–1 mmol/kg BW) may also be administered.

[J]While there is no proven benefit to using potassium phosphate, it does have the theoretical advantage of repleting the severe phosphate deficit of DKA and/or ameliorating hyperchloremia which inevitably occurs during DKA treatment. A phosphate <0.32 mmol/L should be treated. If phosphate is given, serum calcium, magnesium and phosphate levels should be monitored closely.

[K]The acidosis of DKA is due to both ketoacids and lactic acid, and these resolve with fluid and insulin replacement. There is no evidence that $NaHCO_3$ is either necessary or safe in DKA, but its use has a number of deleterious effects: paradoxical CNS acidosis, hypokalemia, hyperosmolality, delayed clearance of ketones, and cerebral edema. $NaHCO_3$ in DKA should only be considered if pH <6.9 or cardiac failure.

[L]EBC (µmol/L) = 36.5 × height (cm)/120. Measured creatinine 1.5–1.99× EBC = Stage 1, 2–2.99× EBC = Stage 2, ≥3× EBC = Stage 3 AKI.

[M]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. At highest risk are newly diagnosed patients, those aged <5 years, and those with initial pH <7.1 or pCO_2 <18. The exact etiology of CE remains unclear. Resuscitation is successful in only 50% of cases.

Accompanying documents on our website:
- *DKA Flowsheet* and *DKA Sample Physician Order Sheet*
- *DKA Glucose, Fluid and Insulin Management*
- *DKA Nursing Protocol* (including the "two-bag" method)
- *DKA Recipes for Making Solutions*

2024 BCCH DKA PROTOCOL – FILLABLE

SEVERITY OF DKA | DKA vs. HHS | ESTIMATE DEHYDRATION | GLASGOW COMA SCALE

PRINT FORM | RESET FORM

BC CHILDREN'S HOSPITAL DIABETIC KETOACIDOSIS PROTOCOL[A]

FOR CHILDREN AGES 1 MONTH TO 19 YEARS

THIS PROTOCOL IS ALSO AVAILABLE IN FILLABLE PDF FORMAT

BC Children's Hospital
Provincial Health Services Authority

FIRST 30 MIN

0. ABCs, vital signs (with BP), neurovital signs. Place large-bore IV. Draw labs. Confirm DKA: blood glucose ≥11.1 mmol/L, moderate–large ketonuria (≥2+) or plasma β-hydroxybutyrate ≥3.0 mmol/L, and venous pH <7.3 or plasma HCO_3^- <18 mmol/L.[C] Consider possibility of an element of hyperglycemic hyperosmolar state.[B]
1. Measure body weight in kilograms ..... (1) _____ kg
2. Give 0.9% saline (normal saline, NS) resuscitation bolus[D]
   - recommended amount: 20 mL/kg over 30 min, max 1000 mL ..... (2) _____ mL
3. Give rapid repeated boluses of NS if persistent tachycardia, prolonged cap refill (>2 sec), cool extremities:
   - 20 mL/kg boluses, repeated until stable; total **extra** given: ..... (3) _____ mL

TIME = 30 MIN–36 HOURS

4. Begin rehydration, calculated for even correction over 36 hours, based on admission body weight:[E]
   - 5–10 kg: 6.5 mL/kg/h
   - 10–20 kg: 6 mL/kg/h
   - 20–40 kg: 5 mL/kg/h
   - >40 kg: 4 mL/kg/h, maximum 500 mL/h ..... (4) _____ mL/kg/h
5. Calculate **total** hourly fluid rate to be given for 36 hours: multiply (1) and (4) ..... (5) _____ 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 a plasma K^+ ≤5.5 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/h (Bag C). Ensure plasma K^+ ≥3.5 mmol/L first. Consider 0.5 mL/kg/h if pH >7.15.[F]
   - 50 units insulin regular (Humulin® R or Novolin® Toronto) in 500 mL NS or D10/NS
   - run at 0.5–1 mL/kg BW/h ..... (7) _____ mL/h
8. Begin "2-bag method"[G]. Y together (Bag A) NS with 40 mEq/L KCl and (Bag B) D10–D12.5/NS with 40 mEq/L KCl. Decrease replacement fluid rate to adjust for insulin drip rate: subtract (7) from (5) ..... (8) _____ 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)[G]. 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 ≥140 mmol/L, stable or increasing, switch Bag A to 0.45% saline w/ 40 mEq/L KCl and Bag B to D10–D12.5/0.45% saline w/ 40 mEq/L KCl at the rate as in (8)[H].

Rationale & Notes:

[A]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, please feel free to contact the BCCH Pediatric Endocrinologist on call.

[B]Hyperglycemic hyperosmolar state (HHS) should be suspected when there is significant hyperglycemia (>33 mmol/L) and hyper-osmolality (>330 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.

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

[D]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.

[E]Recent research shows that DKA can be safely corrected over a 24- to 48-h period. This protocol is designed to correct a 10% fluid deficit (100 mL/kg) evenly over 36 h.

[F]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[G], drop the insulin rate by 25–50%. Consider 0.05 U/kg/h for pH >7.15. Ensure plasma K^+ ≥3.5 mmol/L before starting insulin.

BC Children's Hospital | UBC

DKA MEDICAL DOCUMENTS

BC Children's Hospital

BCCH ENDOCRINOLOGY & DIABETES UNIT
DIABETIC KETOACIDOSIS FLOWSHEET

DATE: TIME:											
HEART RATE											
RESPIRATORY RATE											
BLOOD PRESSURE											
GLASGOW COMA SCALE											
NEURO ✓ DONE?											
BLOOD GLUCOSE	METER										
	LAB										
URINE KETONES											
NURSE'S INITIALS											
VENOUS pH											
BICARBONATE: HCO_3^-	VENOUS										
	SERUM										
BASE DEFICIT											
SODIUM: Na^+											
POTASSIUM: K^+											
CHLORIDE: Cl^-											
ANION GAP: $[Na^+ + K^+ - Cl^- - HCO_3^-]$											
β-HYDROXYBUTYRATE											
"CORRECTED" SODIUM: $Na^+ + 0.36 \times [Glucose - 5.6]$											
"ACTIVE" OSMOLALITY: GLUCOSE + $2 \times [Na^+ + K^+]$											
UREA											
CREATININE											
CALCIUM											
PHOSPHATE											
PHYSICIAN'S INITIALS											

BC Children's Hospital

ENDOCRINOLOGY & DIABETES UNIT
Diabetes Clinic: 604-875-2868
Toll-free Phone: 1-888-300-3088, x2868
Fax: 604-875-3231
http://endodiab.bcchildrens.ca

BCCH DKA GLUCOSE, INSULIN AND FLUID MANAGEMENT

2024 REVISIONS TO THE BCCH DKA PROTOCOL

The 2024 revisions to the *BCCH DKA Medical Protocol* are based on the results of recent research findings on rehydration protocols. These revisions bring the *BCCH DKA Medical Protocol* into alignment with the *Clinical Practice Consensus Guidelines 2022* from the International Society for Pediatric and Adolescent Diabetes (ISPAD) and with the 2023 DKA resources from TREKK Canada (references below).

INITIAL FLUID REPLACEMENT

Results from the PECARN 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 most patients in moderate-to-severe DKA receive a 20-mL/kg bolus of 0.9% sodium chloride (normal saline, NS), maximum 1000 mL, over 30 minutes. Those patients with persistent tachycardia, prolonged capillary refill (>2 sec), and cool extremities should receive rapid repeated 20-mL/kg fluid pushes to restore peripheral circulation. Once the fluid push(es) have been delivered, and having ensured that the patient has adequate urine output and a plasma potassium ≤5.5 mmol/L, fluid replacement is continued using NS + 40 mEq/L KCl (Bag A, see next section), until the patient has been receiving fluids for 1–2 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 fluid replacement rate calculated includes both the fluid deficit and maintenance fluids; ongoing urinary losses are generally not replaced.

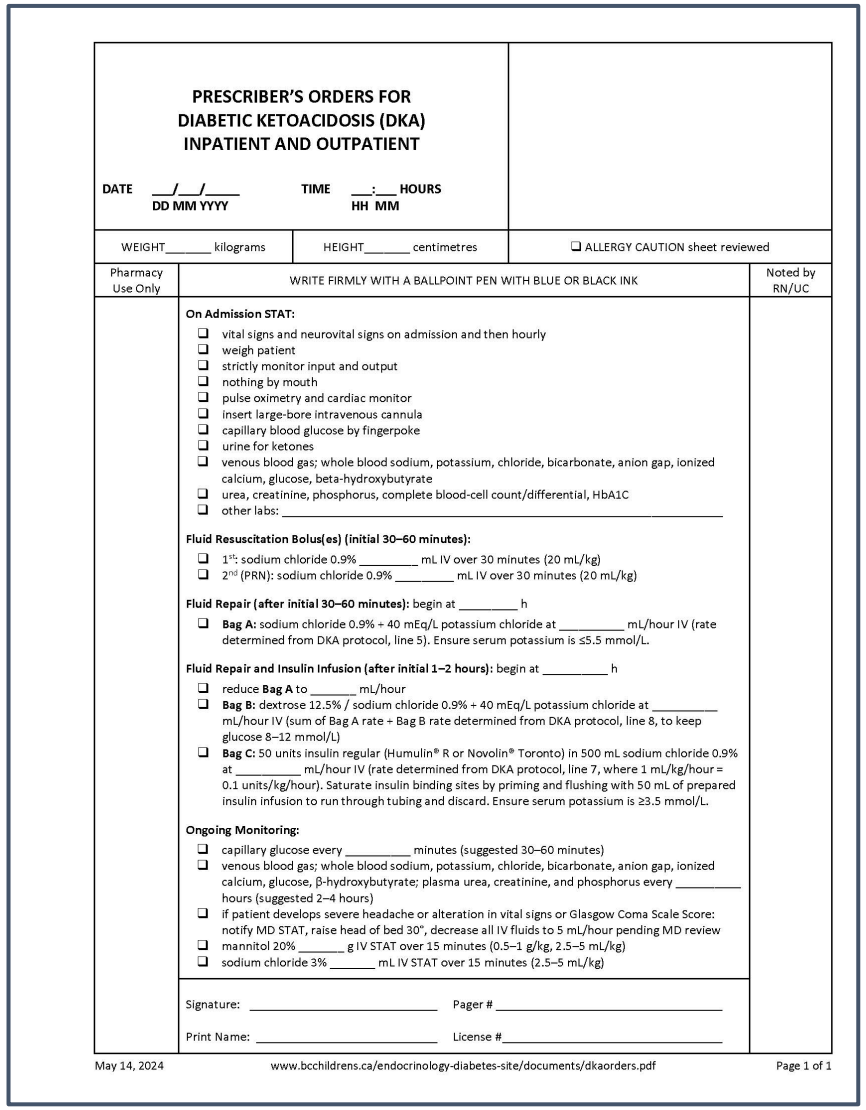
For obese children, adult fluid rates are used: 1000 mL for a resuscitation bolus and a rate of 500 mL/h for ongoing fluid infusions.

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 (line 5). The insulin infusion (**Bag C**) will eventually be Y'd into these bags (see below).

BC Children's Hospital UBC

SAMPLE PRESCRIBER ORDERS FOR DKA



PRESCRIBER'S ORDERS FOR DIABETIC KETOACIDOSIS (DKA) INPATIENT AND OUTPATIENT

DATE ___/___/____ (DD MM YYYY) TIME ___:___ HOURS (HH MM)

WEIGHT_____ kilograms | HEIGHT_____ centimetres | ❑ ALLERGY CAUTION sheet reviewed

Pharmacy Use Only | WRITE FIRMLY WITH A BALLPOINT PEN WITH BLUE OR BLACK INK | Noted by RN/UC

On Admission STAT:

- ❑ vital signs and neurovital signs on admission and then hourly
- ❑ weigh patient
- ❑ strictly monitor input and output
- ❑ nothing by mouth
- ❑ pulse oximetry and cardiac monitor
- ❑ insert large-bore intravenous cannula
- ❑ capillary blood glucose by fingerpoke
- ❑ urine for ketones
- ❑ venous blood gas; whole blood sodium, potassium, chloride, bicarbonate, anion gap, ionized calcium, glucose, beta-hydroxybutyrate
- ❑ urea, creatinine, phosphorus, complete blood-cell count/differential, HbA1C
- ❑ other labs: _____

Fluid Resuscitation Bolus(es) (initial 30–60 minutes):

- ❑ 1st: sodium chloride 0.9% _____ mL IV over 30 minutes (20 mL/kg)
- ❑ 2nd (PRN): sodium chloride 0.9% _____ mL IV over 30 minutes (20 mL/kg)

Fluid Repair (after initial 30–60 minutes): begin at _____ h

- ❑ **Bag A:** sodium chloride 0.9% + 40 mEq/L potassium chloride at _____ mL/hour IV (rate determined from DKA protocol, line 5). Ensure serum potassium is ≤5.5 mmol/L.

Fluid Repair and Insulin Infusion (after initial 1–2 hours): begin at _____ h

- ❑ reduce **Bag A** to _____ mL/hour
- ❑ **Bag B:** dextrose 12.5% / sodium chloride 0.9% + 40 mEq/L potassium chloride at _____ mL/hour IV (sum of Bag A rate + Bag B rate determined from DKA protocol, line 8, to keep glucose 8–12 mmol/L)
- ❑ **Bag C:** 50 units insulin regular (Humulin® R or Novolin® Toronto) in 500 mL sodium chloride 0.9% at _____ mL/hour IV (rate determined from DKA protocol, line 7, where 1 mL/kg/hour = 0.1 units/kg/hour). Saturate insulin binding sites by priming and flushing with 50 mL of prepared insulin infusion to run through tubing and discard. Ensure serum potassium is ≥3.5 mmol/L.

Ongoing Monitoring:

- ❑ capillary glucose every _____ minutes (suggested 30–60 minutes)
- ❑ venous blood gas; whole blood sodium, potassium, chloride, bicarbonate, anion gap, ionized calcium, glucose, β-hydroxybutyrate; plasma urea, creatinine, and phosphorus every _____ hours (suggested 2–4 hours)
- ❑ if patient develops severe headache or alteration in vital signs or Glasgow Coma Scale Score: notify MD STAT, raise head of bed 30°, decrease all IV fluids to 5 mL/hour pending MD review
- ❑ mannitol 20% _____ g IV STAT over 15 minutes (0.5–1 g/kg, 2.5–5 mL/kg)
- ❑ sodium chloride 3% _____ mL IV STAT over 15 minutes (2.5–5 mL/kg)

Signature: _____ Pager # _____

Print Name: _____ License #_____

May 14, 2024 www.bcchildrens.ca/endocrinology-diabetes-site/documents/dkaorders.pdf Page 1 of 1

DKA NURSING DOCUMENTS

ENDOCRINOLOGY & DIABETES UNIT
Diabetes Clinic: 604-875-2868
Toll-free Phone: 1-888-300-3088, x2868
Fax: 604-875-3231
http://endodiab.bcchildrens.ca

BCCH DKA RECIPES FOR MAKING SOLUTIONS

Item #		Dextrose solution to prepare:	1 Dextrose solution and size of IV bag to use:	2 Withdraw & discard from bag:	3 Add to bag:
1	commercially available	**D5W**-NaCl 0.9% with 40 mmol KCl /L			
2		**D10W**-NaCl 0.9% with 40 mmol KCl /L	1000 mL D5W-NaCl 0.9% with 40 mmol KCl /L	100 mL	100 mL **D50W**
3		**D12.5W**-NaCl 0.9% with 40 mmol KCl /L	1000 mL D5W-NaCl 0.9% with 40 mmol KCl /L	100 mL	150 mL **D50W**
4	commercially available	**D5W**-NaCl 0.45% with 40 mmol KCl /L			
5		**D10W**-NaCl 0.45% with 40 mmol KCl /L	1000 mL D5W-NaCl 0.45% with 40 mmol KCl /L	100 mL	100 mL **D50W**
6		**D12.5W**-NaCl 0.45% with 40 mmol KCl /L	1000 mL D5W-NaCl 0.45% with 40 mmol KCl /L	100 mL	150 mL **D50W**
Note: this results in approximate concentrations and is to be used only when Pharmacy mixing is not available					
Prepared by **C&W Pharmacy Department; contact 604-875-2059 for questions**					

ENDOCRINOLOGY & DIABETES UNIT
Diabetes Clinic: 604-875-2868
Toll-free Phone: 1-888-300-3088, x2868
Fax: 604-875-3231
http://endodiab.bcchildrens.ca

BCCH DIABETIC KETOACIDOSIS 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 <18 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 during periods of increased insulin needs: (illness, infection, major stress, puberty, pregnancy)
- insulin pump misuse 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)
- ↑ heart rate and ↑ respirations, and possibly ↓ blood pressure

Acute dehydration 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 Medical Protocol*.

BCCH DKA PROTOCOL 2024: TIMELINE

- on admission: weight, vitals, assessment and stabilization
- first 20–30 minutes: fluid resuscitation
- 30 min–36 h:
  - fluid replacement
  - insulin infusion (no sooner than 60 min)
  - 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, CBG, urine/blood ketones
- evaluate dehydration
- think about underlying illness (infection, etc.)

EVALUATING DEHYDRATION

- best:
  - prolonged capillary refill (>1.5–2 sec)
  - abnormal skin turgor
  - abnormal respiratory pattern
- also:
  - no tears
  - weak pulses
  - cool extremities
  - ↓ HR
- poor:
  - dry mouth
  - urine output
  - BP
  - weight

ESTIMATING DEHYDRATION (% BODY WEIGHT)

	INFANTS	KIDS
MILD	5%	3%
MODERATE	10%	6%
SEVERE	15%	9 (10)%

CAUTIONS IN APPROACH

- fluid and electrolyte imbalances in patients presenting in DKA can be quite disparate:
  - kid has been drinking only water all day
  - kid has been drinking juice all day
  - kid has been drinking pop all day
  - kid has been vomiting all day
  - 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 20–30 MINUTES

- give 1st bolus of NS 20 mL/kg (max 1000 mL) IV over 20–30 min
- patients with persistent tachycardia, prolonged capillary refill (>2 sec), and cool extremities should receive rapid repeated 20-mL/kg fluid pushes to restore peripheral circulation

BCCH PROTOCOL: 30 MINUTES–36 HOURS

- begin even rehydration over 36 h, estimating 10% dehydration:
  - 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, max 500 mL/h

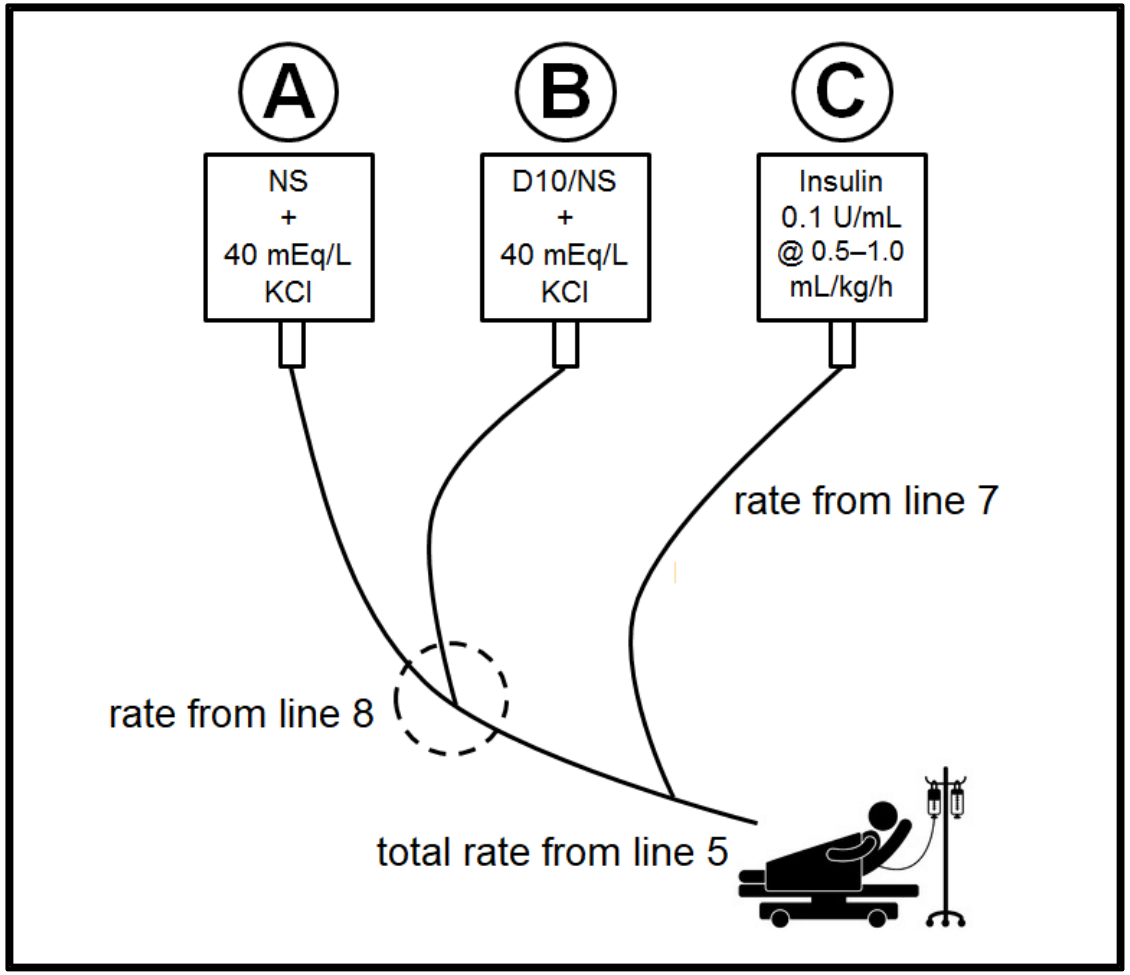
- start with NS + 40 mEq KCl/L, assuming patient is urinating and plasma K^+ is ≤5.5 mmol/L

BCCH PROTOCOL: 30 MINUTES–36 HOURS

- at 60–120 min after start of 1st fluid bolus, begin insulin infusion:
  - ensure plasma K^+ is ≥3.5 mmol/L
  - 0.05–0.1 Units/kg/h
  - consider 0.05 U/kg/h for pH >7.15
  - 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: 30 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):
  - cut the insulin infusion rate by ~25%, provided the acidosis is correcting
  - give the patient a small amount (1–2 mL/kg) of juice or 2–4 dextrose tablets (being mindful of the overall fluid balance)
  - change the insulin Bag **C** to D10/NS
  - 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: 30 MINUTES–36 HOURS

- at 4–6 h after initial fluids and if corrected Na^+ is ≥140 mmol/L, stable or increasing:
  - switch Bag **A** to ½NS + 40 mEq/L KCl
  - 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^+)
  - may prevent ensuing hyperchloremia, but no clear evidence of benefit
- bicarbonate: rarely if ever needed

ONGOING MONITORING

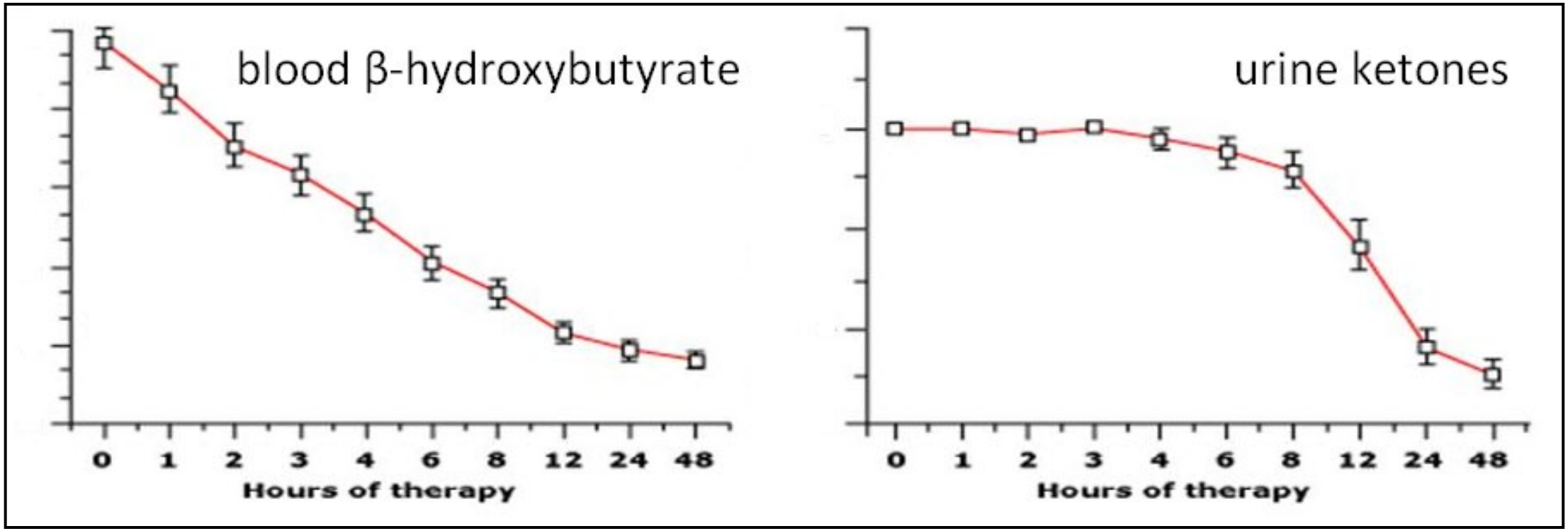
- BG by meter q30–60 min (may need lab BG if >30 mmol/L)
- Na^+, K^+, Cl^-, HCO_3^-, anion gap, urea, creatinine, venous pH q2–4 h
- Ca^{2+}, Mg^{2+}, P_i q2–4 h if giving phosphate
- β-hydroxybutyrate (preferably) or urine ketones q2–4 h
- neurovital signs/GCS q30–60 min

- corrected Na^+ = [measured Na^+ + 0.36×(BG−5.6)]
- active osmolality = [BG + 2×(Na^++K^+)]

URINE *vs* BLOOD KETONES

URINE KETONES	β-HYDROXYBUTYRATE
negative	≤0.5 mmol/L
trace (<0.5 mmol/L)	0.6–0.9 mmol/L
small (1+, 0.5 mmol/L)	1.0–1.4 mmol/L
moderate (2+, 1.5 mmol/L)	1.5–2.4 mmol/L
large (3+, 4 mmol/L)	2.5–2.9 mmol/L
very large (4+, 8 mmol/L)	≥3.0 mmol/L

FALL IN BLOOD VS. URINE KETONES IN DKA



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:
  - EBC (µmol/L) = 36.5 × height (cm)/120
  - measured creatinine 1.5–1.99× EBC = Stage 1
  - measured creatinine 2–2.99× EBC = Stage 2
  - 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 H_2O 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
- ↑ plasma Na^+, ↓ plasma Na^+
- ↓ p_aCO_2 (even adjusting for pH), ↓ pH (most acidotic)
- ↑ plasma urea, ↑ plasma K^+, ↑ hematocrit (most dehydrated)
- “sickest looking”?

TREATMENT-RELATED RISK FACTORS FOR CI

- too-rapid fall in "corrected Na^+"
  - $Na^+ + [0.36 \times (glucose - 5.6)]$
- failure of uncorrected Na^+ to rise
- too-rapid fall in "active osmolality"
  - $glucose + [2 \times (Na^+ + K^+)]$
- bicarbonate therapy
- early (<60 min) insulin Rx or large insulin boluses
- ? fluids ≥4 $L/m^2/24$ h or ≥50 mL/kg in 1st 4 h

CEREBRAL INJURY: DIAGNOSIS 1

- 92% sensitivity, 4% false-positive:
  - 1 diagnostic criterion
  - 2 major criteria
  - 1 major and 2 minor criteria
- neuroimaging not required

- diagnostic criteria:
  - abnormal motor or verbal response to pain
  - decorticate or decerebrate posture
  - cranial nerve palsy (especially III, IV, and VI)
  - abnormal neurogenic respiratory pattern (e.g., grunting, tachypnea, Cheyne–Stokes respiration, apneusis)

CEREBRAL INJURY: DIAGNOSIS 2

- major criteria:
  - altered mentation, confusion, fluctuating level of consciousness
  - sustained heart rate deceleration (decrease more than 20 beats per minute) not attributable to improved intravascular volume or sleep state
  - age-inappropriate incontinence
- minor criteria:
  - vomiting
  - headache
  - lethargy or not easily arousable
  - diastolic BP >90 mm Hg
  - age <5 years

CEREBRAL INJURY: TREATMENT

- elevate head of bed
- reduce fluid rate by ⅓, but avoid hypotension
- administer hyperosmolar agent:
  - mannitol 20% 0.5–1 g/kg (2.5–5 mL/kg) IV over 15 min
  - NaCl 3% 2.5–5 mL/kg IV over 15 min
- intubate if pending respiratory failure
- mild hyperventilation, avoid hypocapnia
- 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

- diagnosis:
  - hyperglycemia: glucose >33.3 mmol/L
  - hyperosmolality: effective plasma osmolality >320 mOsm/kg
  - small ketonuria (0–1+) or β-hydroxybutyrate <1.5 mmol/L
  - no significant acidosis: pH_{art} >7.30 or pH_{ven} >7.25 or HCO_3^- >15 mmol/L
- obtundation, combativeness, seizures (~50%)
- seen in T2D, obese, blacks
- also seen in T1D drinking lots of pop
- can have mixture of DKA and HHS

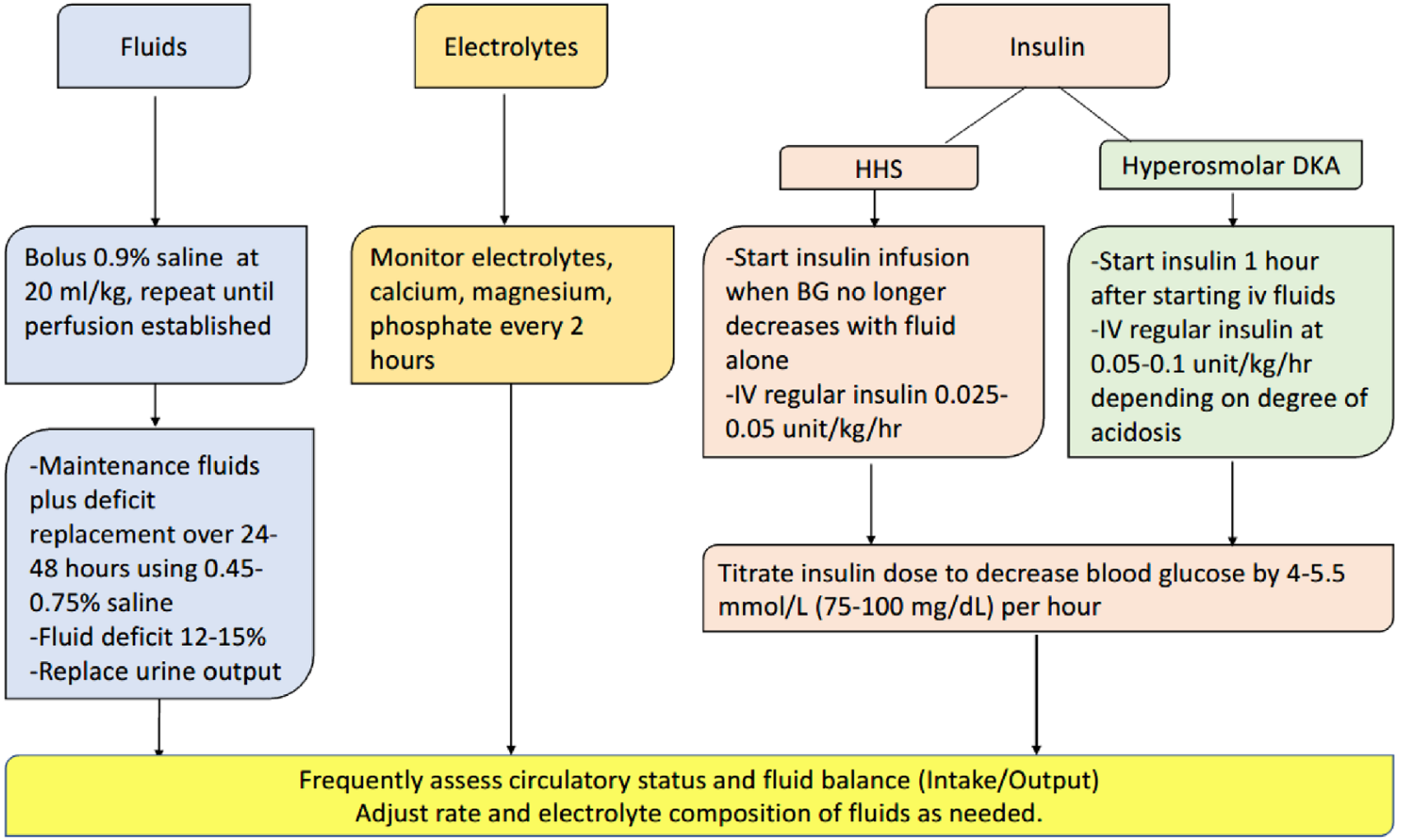
HHS vs. DKA

- ↑ 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

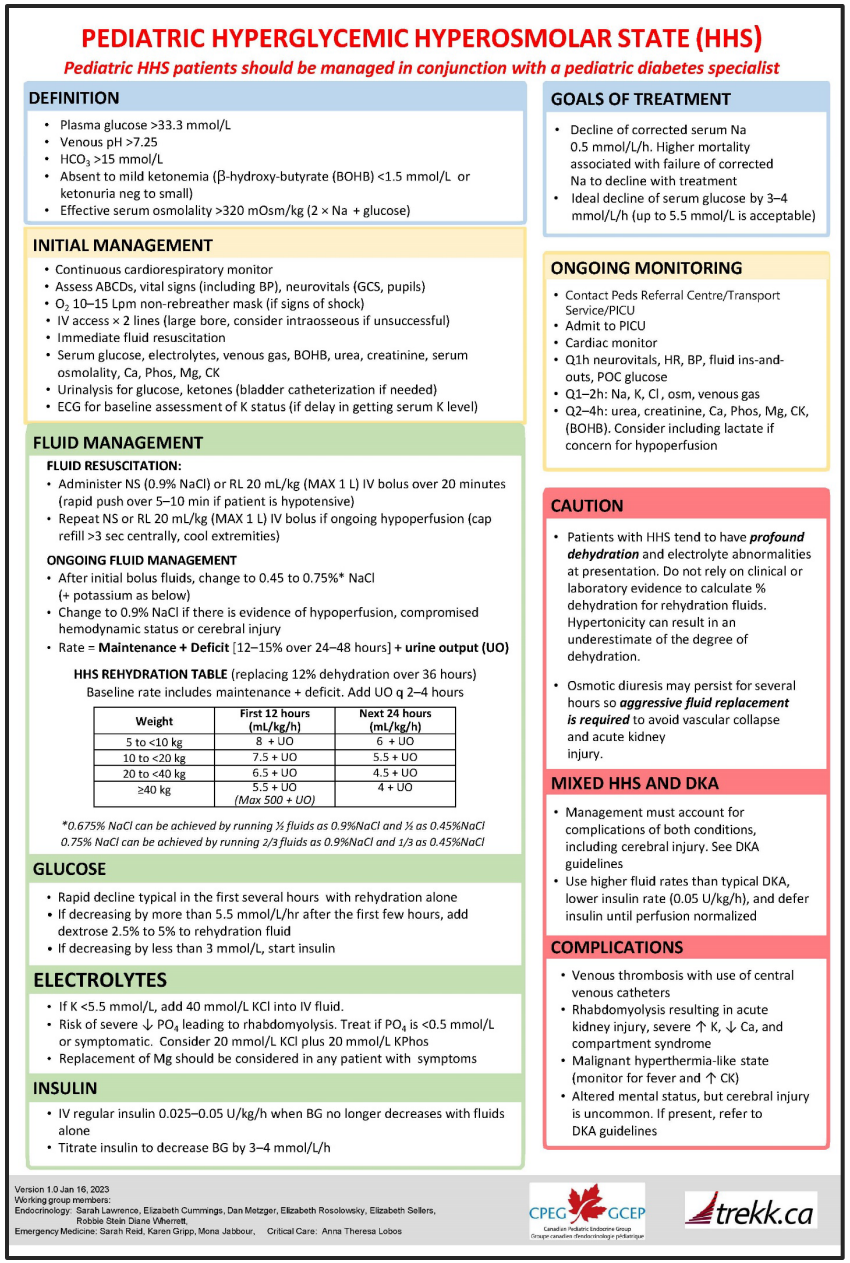
TREATING HHS

- assume 12–15% dehydration
- fluids: 20 mL/kg NS, then balance Na^+ content:
  - 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

ISPAD HHS ALGORITHM



CPEG HHS ALGORITHM 2023



PEDIATRIC HYPERGLYCEMIC HYPEROSMOLAR STATE (HHS)

Pediatric HHS patients should be managed in conjunction with a pediatric diabetes specialist

DEFINITION

- Plasma glucose >33.3 mmol/L
- Venous pH >7.25
- HCO_3 >15 mmol/L
- Absent to mild ketonemia (β-hydroxy-butyrate (BOHB) <1.5 mmol/L or ketonuria neg to small)
- Effective serum osmolality >320 mOsm/kg (2 × Na + glucose)

INITIAL MANAGEMENT

- Continuous cardiorespiratory monitor
- Assess ABCDs, vital signs (including BP), neurovitals (GCS, pupils)
- O_2 10–15 Lpm non-rebreather mask (if signs of shock)
- IV access × 2 lines (large bore, consider intraosseous if unsuccessful)
- Immediate fluid resuscitation
- Serum glucose, electrolytes, venous gas, BOHB, urea, creatinine, serum osmolality, Ca, Phos, Mg, CK
- Urinalysis for glucose, ketones (bladder catheterization if needed)
- ECG for baseline assessment of K status (if delay in getting serum K level)

FLUID MANAGEMENT

FLUID RESUSCITATION:

- Administer NS (0.9% NaCl) or RL 20 mL/kg (MAX 1 L) IV bolus over 20 minutes (rapid push over 5–10 min if patient is hypotensive)
- Repeat NS or RL 20 mL/kg (MAX 1 L) IV bolus if ongoing hypoperfusion (cap refill >3 sec centrally, cool extremities)

ONGOING FLUID MANAGEMENT

- After initial bolus fluids, change to 0.45 to 0.75%* NaCl (+ potassium as below)
- Change to 0.9% NaCl if there is evidence of hypoperfusion, compromised hemodynamic status or cerebral injury
- Rate = **Maintenance + Deficit** [12–15% over 24–48 hours] **+ urine output (UO)**

HHS REHYDRATION TABLE (replacing 12% dehydration over 36 hours)
Baseline rate includes maintenance + deficit. Add UO q 2–4 hours

Weight	First 12 hours (mL/kg/h)	Next 24 hours (mL/kg/h)
5 to <10 kg	8 + UO	6 + UO
10 to <20 kg	7.5 + UO	5.5 + UO
20 to <40 kg	6.5 + UO	4.5 + UO
≥40 kg	5.5 + UO *(Max 500 + UO)*	4 + UO

**0.675% NaCl can be achieved by running ⅔ fluids as 0.9%NaCl and ⅓ as 0.45%NaCl*
0.75% NaCl can be achieved by running 2/3 fluids as 0.9%NaCl and 1/3 as 0.45%NaCl

GLUCOSE

- Rapid decline typical in the first several hours with rehydration alone
- If decreasing by more than 5.5 mmol/L/hr after the first few hours, add dextrose 2.5% to 5% to rehydration fluid
- If decreasing by less than 3 mmol/L, start insulin

ELECTROLYTES

- If K <5.5 mmol/L, add 40 mmol/L KCl into IV fluid.
- Risk of severe ↓ PO_4 leading to rhabdomyolysis. Treat if PO_4 is <0.5 mmol/L or symptomatic. Consider 20 mmol/L KCl plus 20 mmol/L KPhos
- Replacement of Mg should be considered in any patient with symptoms

INSULIN

- IV regular insulin 0.025–0.05 U/kg/h when BG no longer decreases with fluids alone
- Titrate insulin to decrease BG by 3–4 mmol/L/h

GOALS OF TREATMENT

- Decline of corrected serum Na 0.5 mmol/L/h. Higher mortality associated with failure of corrected Na to decline with treatment
- Ideal decline of serum glucose by 3–4 mmol/L/h (up to 5.5 mmol/L is acceptable)

ONGOING MONITORING

- Contact Peds Referral Centre/Transport Service/PICU
- Admit to PICU
- Cardiac monitor
- Q1h neurovitals, HR, BP, fluid ins-and-outs, POC glucose
- Q1–2h: Na, K, Cl , osm, venous gas
- Q2–4h: urea, creatinine, Ca, Phos, Mg, CK, (BOHB). Consider including lactate if concern for hypoperfusion

CAUTION

- Patients with HHS tend to have ***profound dehydration*** and electrolyte abnormalities at presentation. Do not rely on clinical or laboratory evidence to calculate % dehydration for rehydration fluids. Hypertonicity can result in an underestimate of the degree of dehydration.
- Osmotic diuresis may persist for several hours so ***aggressive fluid replacement is required*** to avoid vascular collapse and acute kidney injury.

MIXED HHS AND DKA

- Management must account for complications of both conditions, including cerebral injury. See DKA guidelines
- Use higher fluid rates than typical DKA, lower insulin rate (0.05 U/kg/h), and defer insulin until perfusion normalized

COMPLICATIONS

- Venous thrombosis with use of central venous catheters
- Rhabdomyolysis resulting in acute kidney injury, severe ↑ K, ↓ Ca, and compartment syndrome
- Malignant hyperthermia-like state (monitor for fever and ↑ CK)
- Altered mental status, but cerebral injury is uncommon. If present, refer to DKA guidelines

Version 1.0 Jan 16, 2023
Working group members:
Endocrinology: Sarah Lawrence, Elizabeth Cummings, Dan Metzger, Elizabeth Rosolowsky, Elizabeth Sellers, Robbie Stein Diane Wherrett,
Emergency Medicine: Sarah Reid, Karen Gripp, Mona Jabbour, Critical Care: Anna Theresa Lobos

cpeg-gcep.net/content/dka-hhs-management-resources

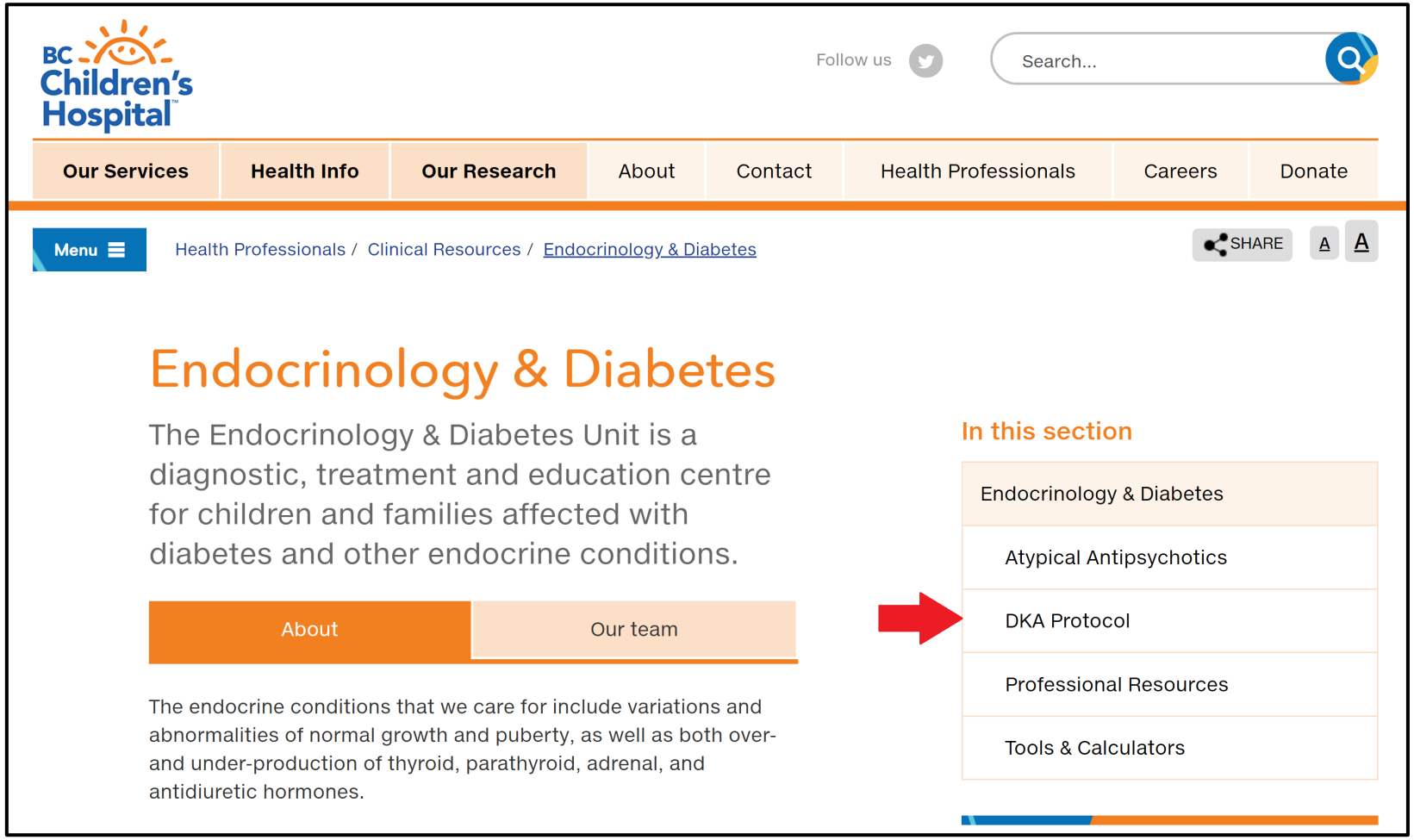
RECURRENT DKA

- most often seen in:
  - very small kids with GI illness
  - unsupervised kids
  - non-compliant teens
  - insulin pump site problems
- nearly all cases of recurrent DKA are preventable!
- get an A1C!

DKA PREVENTION (BC PEDIATRIC SOCIETY)

beyondtype1.org/dkacampaign

EDU WEBSITE



http://endodiab.bcchildrens.ca

REFERENCES

- Wherrett DK, Ho J, Huot C, Legault L, Nakhla N, Rosolowsky E. Diabetes Canada Clinical Practice Guidelines Expert Committee. Diabetes Canada 2018 Clinical practice guidelines for the prevention and management of diabetes in Canada: Type 1 diabetes in children and adolescents. *Can J Diabetes* 2018;42(Suppl 1):S234-S246.
- Glaser N, Fritsch M, Priyambada L, Rewers A, Cherubini V, Estrada S, Wolfsdorf JI, Codner E. ISPAD Clinical Practice Consensus Guidelines 2022: Diabetic ketoacidosis and hyperglycemic hyperosmolar state. *Pediatric Diabetes* 2022:23(7):835–856.
- Kuppermann N, Ghetti S, Schunk JE, Stoner MJ, Rewers A, McManemy JK, Myers SR, Nigrovic LE, Garro A, Brown KM, Quayle KS, Trainor JL, Tzimenatos L, Bennett JE, DePiero AD, Kwok MY, Perry CS 3rd, Olsen CS, Casper TC, Dean JM, Glaser NS; PECARN DKA FLUID Study Group. Clinical trial of fluid infusion rates for pediatric diabetic ketoacidosis. *NEJM* 2018;378(24):2275-2287.
- Grimberg A, Cerri RW, Satin-Smith M, Cohen P. The “two bag system” for variable intravenous dextrose and fluid administration: Benefits in diabetic ketoacidosis management. *J Pediatr* 1999;134(3):376–378.
- Translating Emergency Knowledge for Kids (TREKK Canada): http://trekk.ca.
- Glaser N, Kuppermann N. Fluid treatment for children with diabetic ketoacidosis: how do the results of the PECARN FLUID Trial change our perspective? *Pediatr Diabetes* 2019;20(1):10–14.
- BC Children’s Hospital ePOPS (Electronic Policies, Order Sets, Procedures and Standards): http://policyandorders.cw.bc.ca.