DIABETIC KETOACIDOSIS

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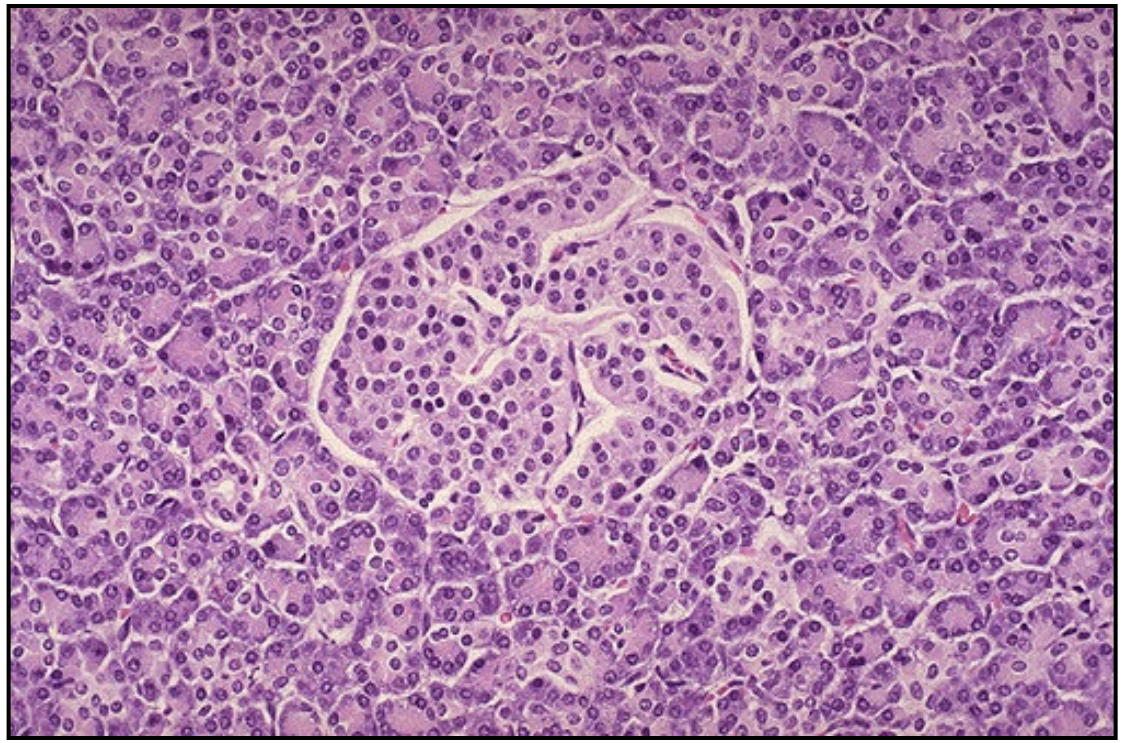
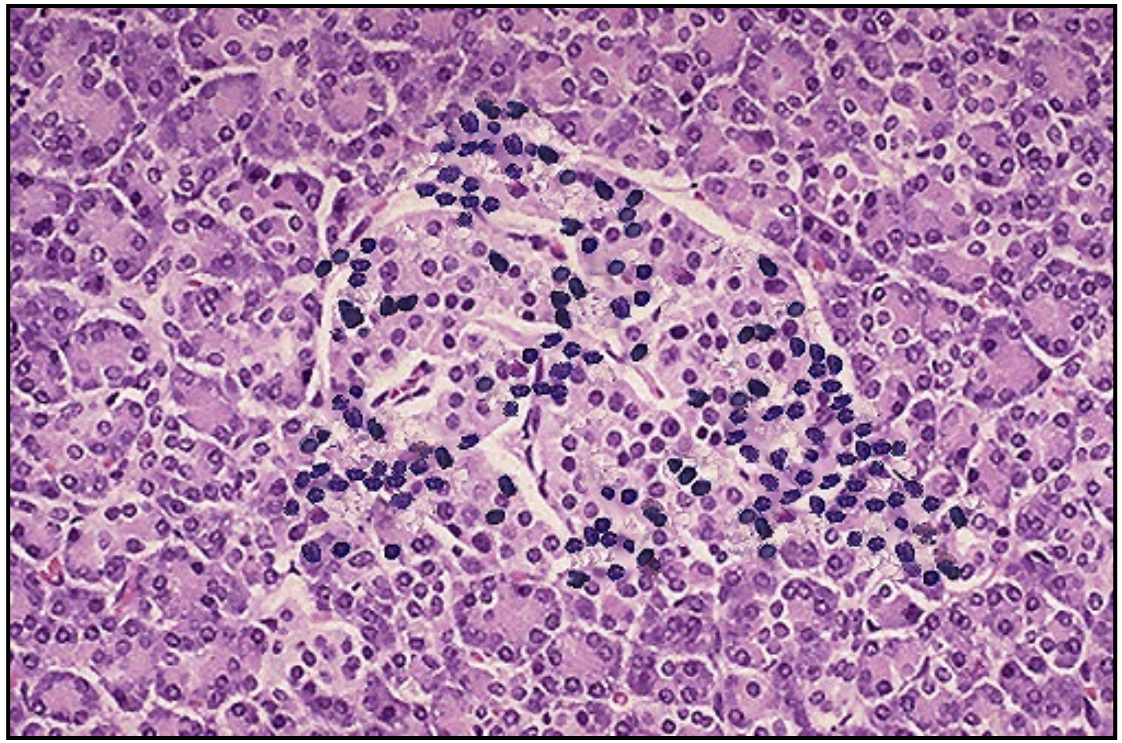
TYPE 1 DIABETES

- prevalence
  - ~1 in 400 children <20 years affected
  - lifetime risk ~1 in 250
- incidence
  - 1 new case per ~5,000 children per year
  - incidence appears to be rising ~3%/year
  - most affected: 0–5 year range
- ~10–20% of new-onset T1D presents in DKA

T-CELL INFILTRATION

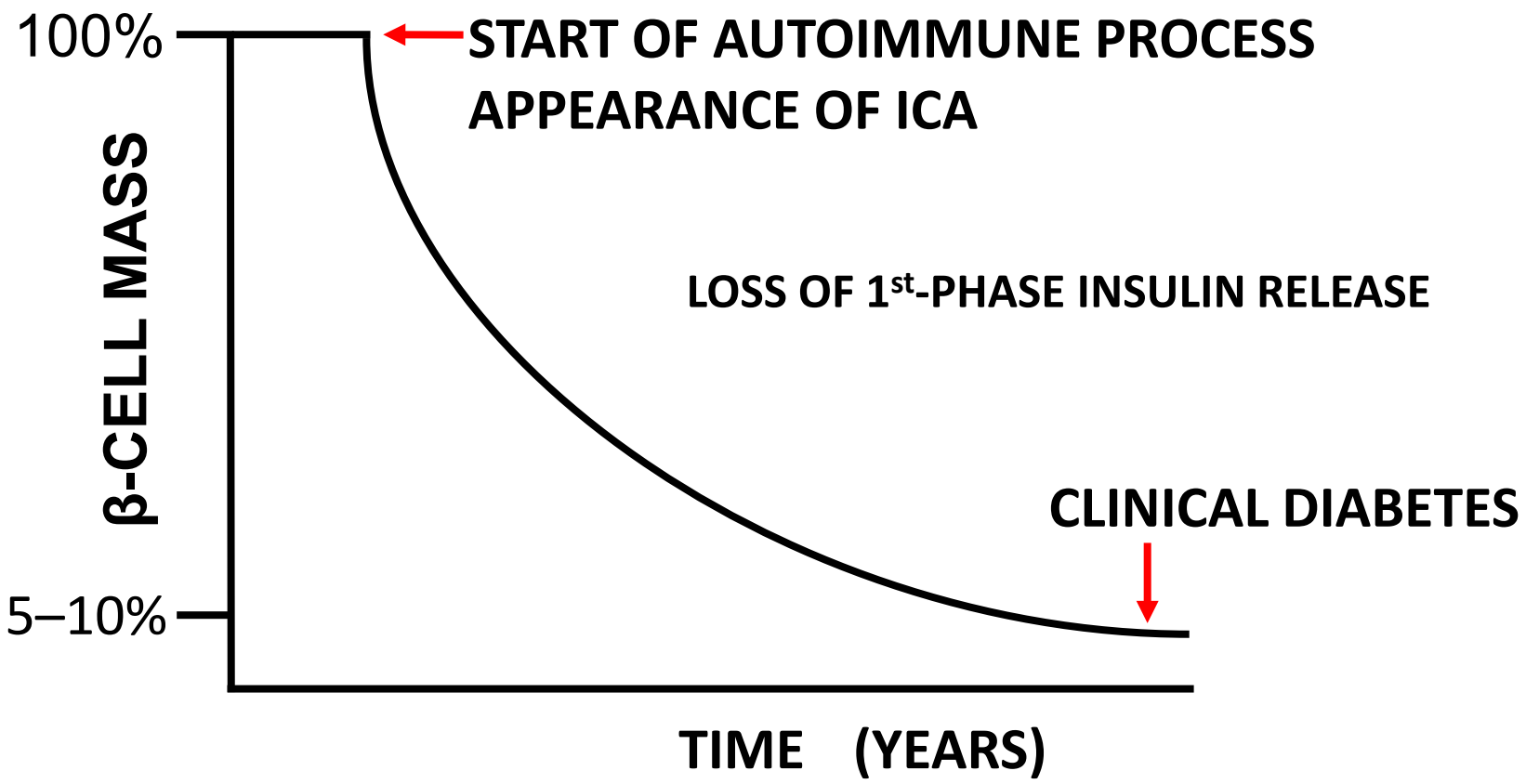




ETIOLOGY OF T1D

- T cell–mediated autoimmune destruction of β cells
- both islet-cell (GAD65, IA2, ZnT8A) and insulin autoantibodies present in the blood
- gradual development of insulinopenia
- diabetes clinically apparent when <5–10% of β-cell function left
- process may take years

EVOLUTION OF T1D



CONTRIBUTORS TO T1D

- genetic
  - 5% in 1st-degree relatives, 50% in identical twins
  - HLA-DR3 and -DR4, others
- environmental
  - viruses (Coxsackie, rubella)
  - feeding (breast milk, cow's milk, Vitamin D)
  - antigen mimicry
- accelerator and hygiene hypotheses
- bad luck

PHYSIOLOGIC ROLES OF INSULIN

- muscle
  - ↑ uptake amino acids, anabolism
  - ↓ catabolism, gluconeogenesis
- fat
  - ↑ uptake FFA, lipogenesis
  - ↓ lipolysis, ketone bodies (β-hydroxybutyrate)
- liver
  - ↑ uptake glucose, glycogen synthesis
  - ↓ glycogenolysis

GLUCOSE SENSING

- insulin required for glucose entry into “glucostat” cells in the hypothalamus
- w/o insulin, body senses it’s hypoglycemic
- defence: stress hormones
  - epinephrine
  - glucagon
  - growth hormone
  - cortisol
- ↑ ketones and ↑ gluconeogenesis

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

- DDx: hyperglycemic hyperosmolar state

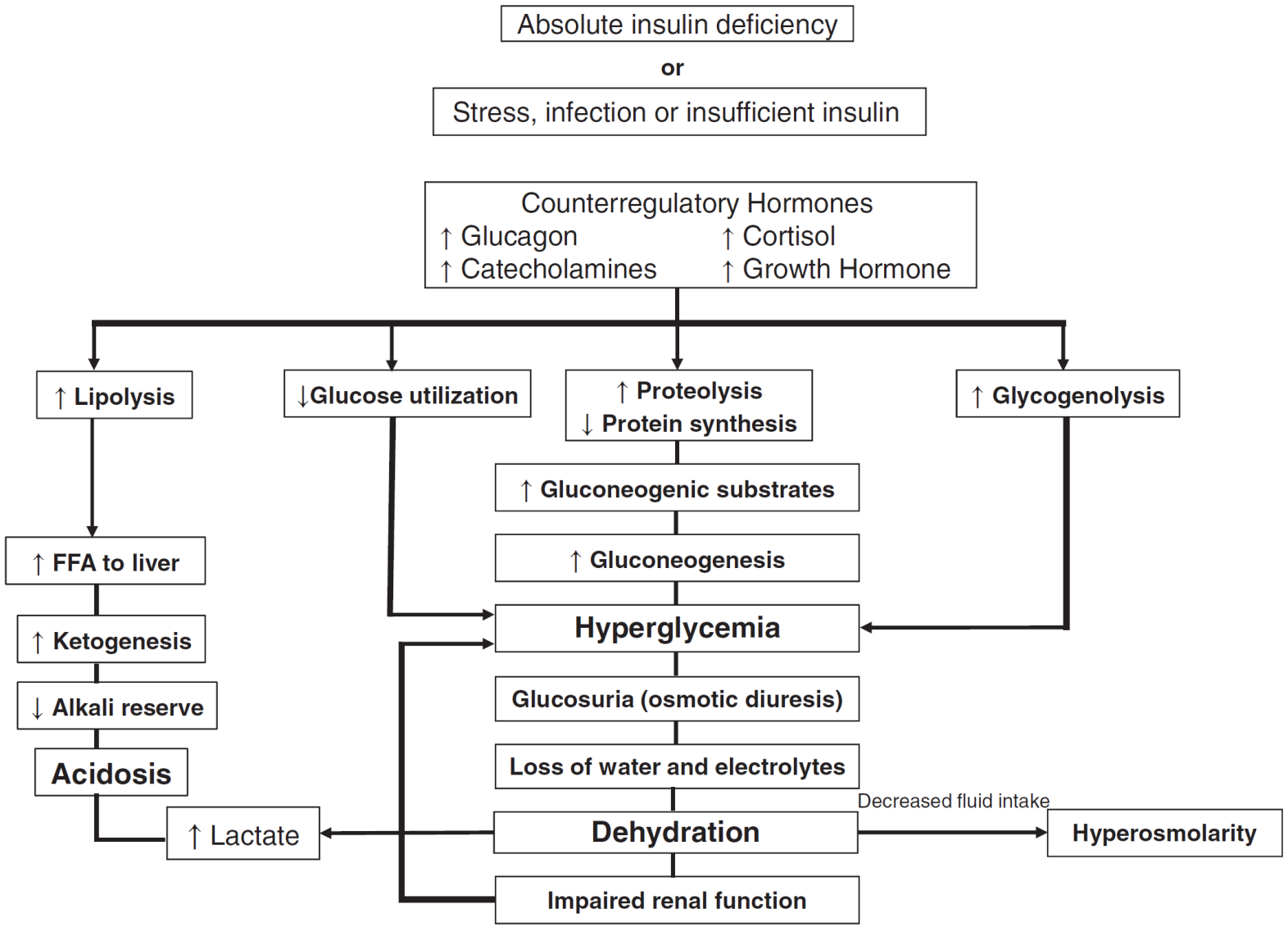
SEVERITY OF DKA

	pH	HCO_3^-
mild	<7.3	<15
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

Pathophysiology of Diabetic Ketoacidosis



Diabetes Care 2006;29:1150–1159

DKA PROTOCOLS: DISCLAIMER

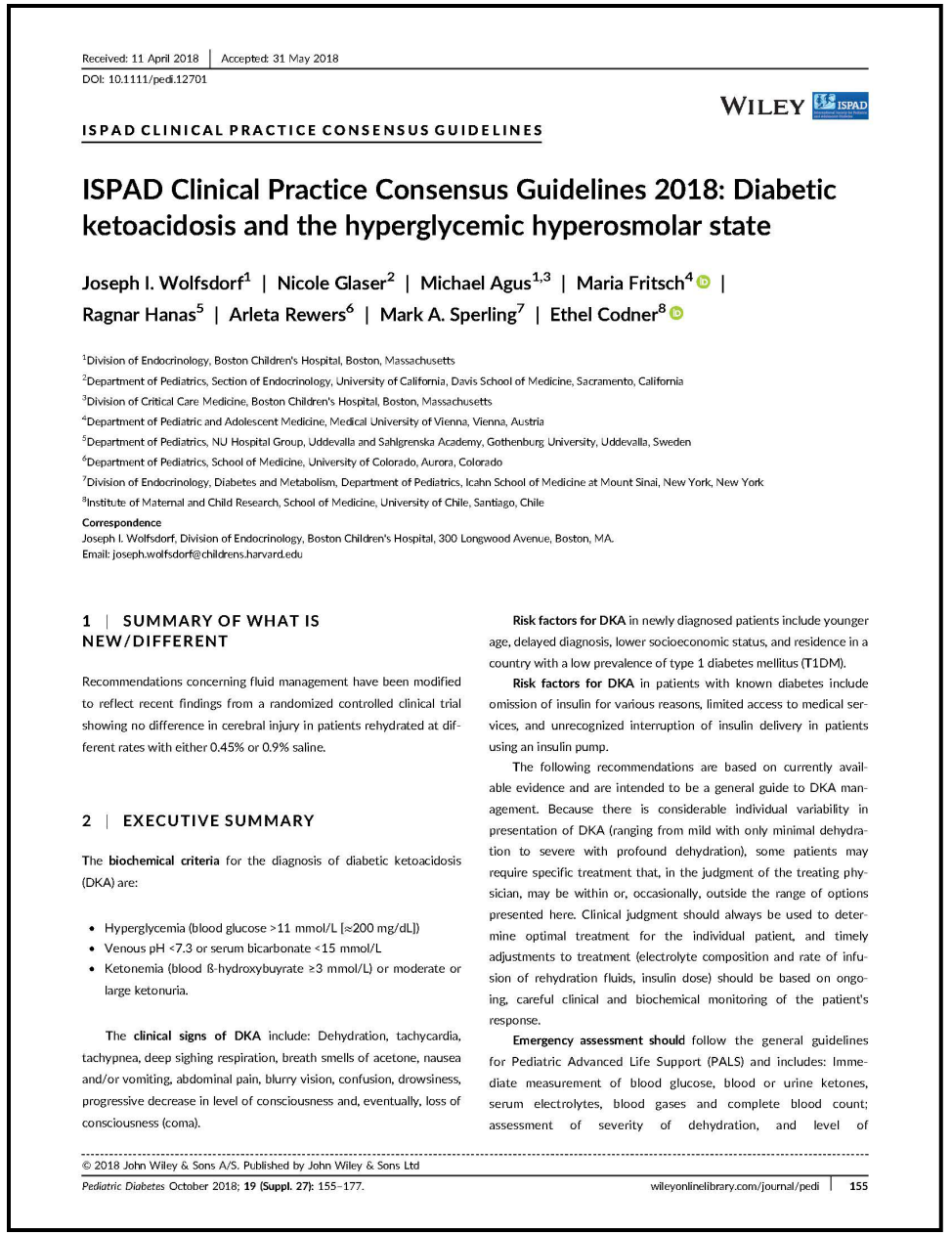
- **no** DKA protocol has been shown to eliminate the risk of cerebral injury
- current gold standard: ISPAD *Clinical Practice Consensus Guidelines 2018*
- guidelines should not replace intelligent thought and should be tailored to meet the needs of each individual patient
- involve Pediatric Endocrinology early!

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: *Pediatr Diabetes* 2019;20(1):10–14

ISPAD 2018



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WILEY ISPAD

ISPAD CLINICAL PRACTICE CONSENSUS GUIDELINES

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

2 | EXECUTIVE SUMMARY

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

- Hyperglycemia (blood glucose >11 mmol/L [≈200 mg/dL])
- Venous pH <7.3 or serum bicarbonate <15 mmol/L
- Ketonemia (blood ß-hydroxybuyrate ≥3 mmol/L) or moderate or large ketonuria.

The **clinical signs of DKA** include: Dehydration, tachycardia, tachypnea, deep sighing respiration, breath smells of acetone, nausea and/or vomiting, abdominal pain, blurry vision, confusion, drowsiness, progressive decrease in level of consciousness and, eventually, loss of consciousness (coma).

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

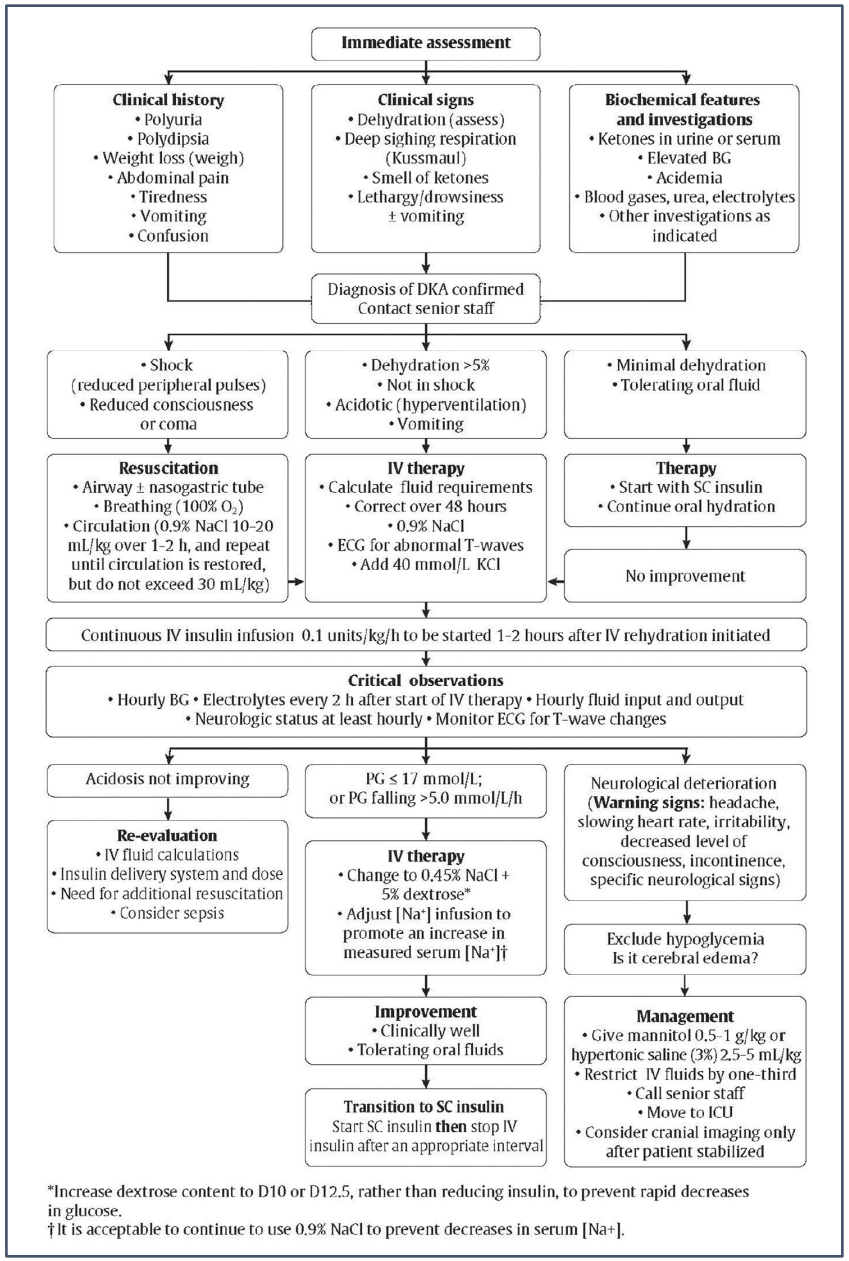
Risk factors for DKA in patients with known diabetes include omission of insulin for various reasons, limited access to medical services, and unrecognized interruption of insulin delivery in patients using an insulin pump.

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 presentation of DKA (ranging from mild with only minimal dehydration to severe with profound dehydration), some patients may require specific treatment that, in the judgment of the treating physician, may be within 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 (electrolyte composition and rate of infusion of rehydration fluids, insulin dose) should be based on ongoing, careful clinical and biochemical monitoring of the patient's response.

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, blood gases and complete blood count; assessment of severity of dehydration, and level of

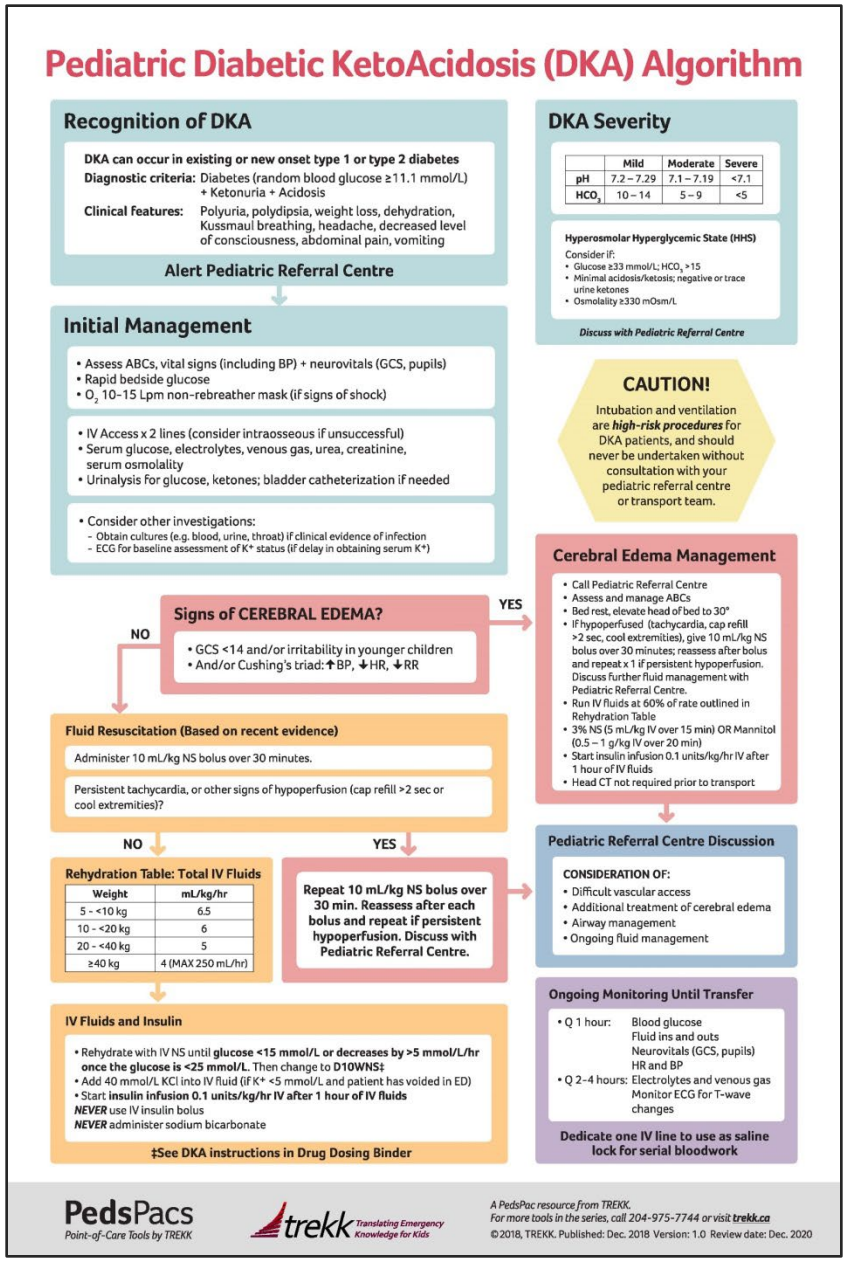
Pediatric Diabetes 2018;19(Suppl 27):155–177

DIABETES CANADA 2018



Diabetes Canada's *2018 Clinical Practice Guidelines*

TREKK



Pediatric Diabetic KetoAcidosis (DKA) Algorithm

Recognition of DKA

DKA can occur in existing or new onset type 1 or type 2 diabetes

Diagnostic criteria: Diabetes (random blood glucose ≥11.1 mmol/L) + Ketonuria + Acidosis

Clinical features: Polyuria, polydipsia, weight loss, dehydration, Kussmaul breathing, headache, decreased level of consciousness, abdominal pain, vomiting

Alert Pediatric Referral Centre

DKA Severity

	Mild	Moderate	Severe
pH	7.2 – 7.29	7.1 – 7.19	<7.1
HCO_3	10 – 14	5 – 9	<5

Hyperosmolar Hyperglycemic State (HHS)

Consider if:
- Glucose ≥33 mmol/L; HCO_3 >15
- Minimal acidosis/ketosis; negative or trace urine ketones
- Osmolality ≥330 mOsm/L

Discuss with Pediatric Referral Centre

Initial Management

- Assess ABCs, vital signs (including BP) + neurovitals (GCS, pupils)
- Rapid bedside glucose
- O_2 10-15 Lpm non-rebreather mask (if signs of shock)

- IV Access x 2 lines (consider intraosseous if unsuccessful)
- Serum glucose, electrolytes, venous gas, urea, creatinine, serum osmolality
- Urinalysis for glucose, ketones; bladder catheterization if needed

- Consider other investigations:
  - Obtain cultures (e.g. blood, urine, throat) if clinical evidence of infection
  - ECG for baseline assessment of K+ status (if delay in obtaining serum K+)

CAUTION!

Intubation and ventilation are ***high-risk procedures*** for DKA patients, and should never be undertaken without consultation with your pediatric referral centre or transport team.

Signs of CEREBRAL EDEMA?

YES

- GCS <14 and/or irritability in younger children
- And/or Cushing's triad: ↑BP, ↓HR, ↓RR

NO

Cerebral Edema Management

- Call Pediatric Referral Centre
- Assess and manage ABCs
- Bed rest, elevate head of bed to 30°
- If hypoperfused (tachycardia, cap refill >2 sec, cool extremities), give 10 mL/kg NS bolus over 30 minutes; reassess after bolus and repeat x 1 if persistent hypoperfusion. Discuss further fluid management with Pediatric Referral Centre.
- Run IV fluids at 60% of rate outlined in Rehydration Table
- 3% NS (5 mL/kg IV over 15 min) OR Mannitol (0.5 – 1 g/kg IV over 20 min)
- Start insulin infusion 0.1 units/kg/hr IV after 1 hour of IV fluids
- Head CT not required prior to transport

Fluid Resuscitation (Based on recent evidence)

Administer 10 mL/kg NS bolus over 30 minutes.

Persistent tachycardia, or other signs of hypoperfusion (cap refill >2 sec or cool extremities)?

NO

YES

Rehydration Table: Total IV Fluids

Weight	mL/kg/hr
5 - <10 kg	6.5
10 - <20 kg	6
20 - <40 kg	5
≥40 kg	4 (MAX 250 mL/hr)

Repeat 10 mL/kg NS bolus over 30 min. Reassess after each bolus and repeat if persistent hypoperfusion. Discuss with Pediatric Referral Centre.

Pediatric Referral Centre Discussion

CONSIDERATION OF:
- Difficult vascular access
- Additional treatment of cerebral edema
- Airway management
- Ongoing fluid management

IV Fluids and Insulin

- Rehydrate with IV NS until **glucose <15 mmol/L or decreases by >5 mmol/L/hr once the glucose is <25 mmol/L**. Then change to **D10WNS‡**
- Add 40 mmol/L KCl into IV fluid (if K+ <5 mmol/L and patient has voided in ED)
- Start **insulin infusion 0.1 units/kg/hr IV after 1 hour of IV fluids**

NEVER use IV insulin bolus

NEVER administer sodium bicarbonate

‡See DKA instructions in Drug Dosing Binder

Ongoing Monitoring Until Transfer

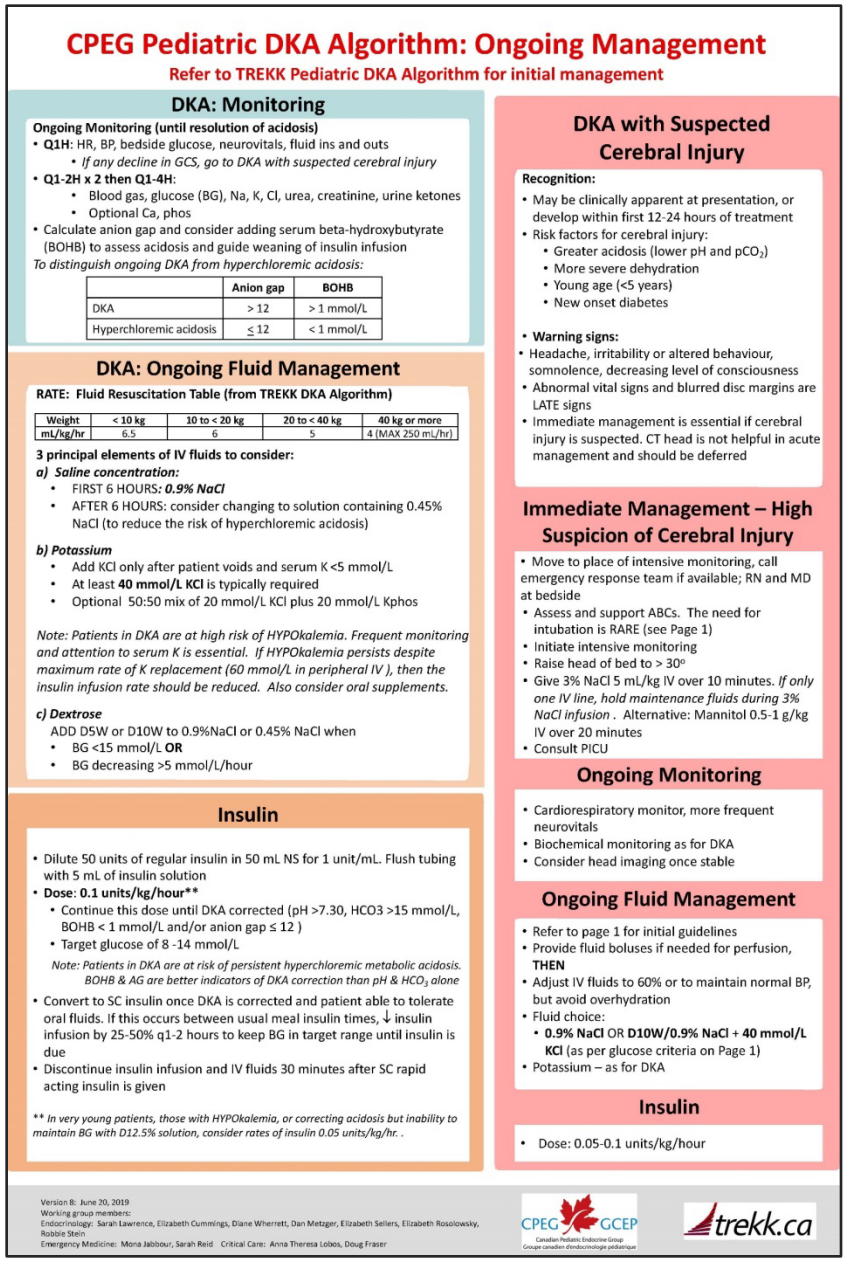
- Q 1 hour: Blood glucose, Fluid ins and outs, Neurovitals (GCS, pupils), HR and BP
- Q 2-4 hours: Electrolytes and venous gas, Monitor ECG for T-wave changes

Dedicate one IV line to use as saline lock for serial bloodwork

PedsPacs — Point-of-Care Tools by TREKK

trekk Translating Emergency Knowledge for Kids

A PedsPac resource from TREKK.
For more tools in the series, call 204-975-7744 or visit trekk.ca



CPEG Pediatric DKA Algorithm: Ongoing Management

Refer to TREKK Pediatric DKA Algorithm for initial management

DKA: Monitoring

Ongoing Monitoring (until resolution of acidosis)
- **Q1H**: HR, BP, bedside glucose, neurovitals, fluid ins and outs
  - *If any decline in GCS, go to DKA with suspected cerebral injury*
- **Q1-2H x 2 then Q1-4H**:
  - Blood gas, glucose (BG), Na, K, Cl, urea, creatinine, urine ketones
  - Optional Ca, phos
- Calculate anion gap and consider adding serum beta-hydroxybutyrate (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: Fluid Resuscitation Table (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 250 mL/hr)

3 principal elements of IV fluids to consider:

a) Saline concentration:
- FIRST 6 HOURS: ***0.9% NaCl***
- AFTER 6 HOURS: consider changing to solution containing 0.45% NaCl (to reduce the risk of hyperchloremic acidosis)

b) Potassium
- Add KCl only after patient voids and serum K <5 mmol/L
- At least **40 mmol/L KCl** is typically required
- 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 reduced. Also consider oral supplements.

c) Dextrose

ADD D5W or D10W to 0.9%NaCl or 0.45% NaCl when
- BG <15 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, HCO3 >15 mmol/L, BOHB < 1 mmol/L and/or anion gap ≤ 12)
  - 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 30 minutes after SC rapid acting insulin is given

*** In very young patients, those with 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:**
- Headache, irritability or altered behaviour, somnolence, decreasing level of consciousness
- Abnormal vital signs and blurred disc margins are LATE signs
- Immediate management is essential if cerebral injury is suspected. CT head is not helpful in acute management and should be deferred

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)
- Initiate intensive monitoring
- Raise head of bed to > 30°
- Give 3% NaCl 5 mL/kg IV over 10 minutes. *If only one IV line, hold maintenance fluids during 3% NaCl infusion* . Alternative: Mannitol 0.5-1 g/kg IV over 20 minutes
- Consult PICU

Ongoing Monitoring

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

Ongoing Fluid Management

- Refer to page 1 for initial guidelines
- Provide fluid boluses if needed for perfusion, **THEN**
- Adjust IV fluids to 60% or to maintain normal BP, but avoid overhydration
- Fluid choice:
  - **0.9% NaCl** OR **D10W/0.9% NaCl + 40 mmol/L KCl** (as per glucose criteria on Page 1)
- Potassium – as for DKA

Insulin

- Dose: 0.05-0.1 units/kg/hour

Version 8: June 20, 2019
Working group members:
Endocrinology: Sarah Lawrence, Elizabeth Cummings, Diane Wherrett, Dan Metzger, Elizabeth Sellers, Elizabeth Rosolowsky, Robbie Stein
Emergency Medicine: Mona Jabbour, Sarah Reid Critical Care: Anna Theresa Lobos, Doug Fraser

CPEG GCEP Canadian Pediatric Endocrine Group / Groupe canadien d'endocrinologie pédiatrique

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2019 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

FIRST 60 MIN

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 ≥3.0 mmol/L, and venous pH <7.3 or serum HCO_3^- <15 mmol/L. Consider possibility of an element of hyperglycemic hyperosmolar state.[B]

1. Measure body weight (BW) in kilograms ..... (1) _____ kg

2. Give 0.9% saline (normal saline, NS) resuscitation bolus[D]
   - recommended amount: 10 mL/kg BW over 30 minutes ..... (2) _____ 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 ..... (3) _____ mL

TIME = 60 MIN–36 HOURS

4. Begin rehydration, calculated for even correction over 36 hours, based on admission BW:[E]
   - 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 ..... (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 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):[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 ≥145 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 or diabetes, 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 s/he really is. The hematocrit and other clinical signs noted are more accurate.

[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%.

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.
    - dextrose[G]: aim to keep the PG ~8–12 mmol/L range
    - sodium[H]: corrected Na^+ <145 mmol/L, or falling regardless of level: continue NS
      corrected Na^+ ≥145, stable or increasing, switch to ½NS after 4–6 h
    - potassium[I,J]: patient urinating and K^+ remains <5: continue KCl 40 mmol/L
      may give 50% of K^+ as acetate or 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 (keep pCO_2 >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[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]The introduction of hypotonic fluids must be considered carefully. The corrected Na^+ should be calculated and followed closely: corrected Na^+ = [measured Na^+ + 0.36×(PG–5.6)]. 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 + 2×(Na^+ + K^+)], which should not fall >0.5 mOsm/kg/h. If the corrected sodium is 140–150 mmol/L and stable and the active osmolality has been dropping slowly, switching to ½NS 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).

[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^+ >3.0 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 or acetate, it does have the theoretical advantage of repleting 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.

[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*

BC CHILDREN'S HOSPITAL ENDOCRINOLOGY & DIABETES UNIT

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FILLABLE DKA PROTOCOL

SEVERITY OF DKA | PRINT FORM | RESET FORM

DKA vs. HHS

ESTIMATE DEHYDRATION

GLASGOW COMA SCALE

BC CHILDREN'S HOSPITAL DIABETIC KETOACIDOSIS PROTOCOL[A]

FOR CHILDREN AGES 1 MONTH TO 19 YEARS

THIS PROTOCOL IS ALSO AVAILABLE IN PLAIN PDF FORMAT

FIRST 60 MIN

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 ≥3.0 mmol/L, and venous pH <7.3 or serum HCO_3^- <15 mmol/L. Consider possibility of an element of hyperglycemic hyperosmolar state.[B]

1. Measure body weight (BW) in kilograms ..... (1) _____ kg

2. Give 0.9% saline (normal saline, NS) resuscitation bolus[D]
   - recommended amount: 10 mL/kg BW over 30 minutes ..... (2) _____ 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 ..... (3) 0 mL ☐

TIME = 60 MIN–36 HOURS

4. Begin rehydration, calculated for even correction over 36 hours, based on admission BW:[E]
   - 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 ..... (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 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):[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 ≥145 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 or diabetes, 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.

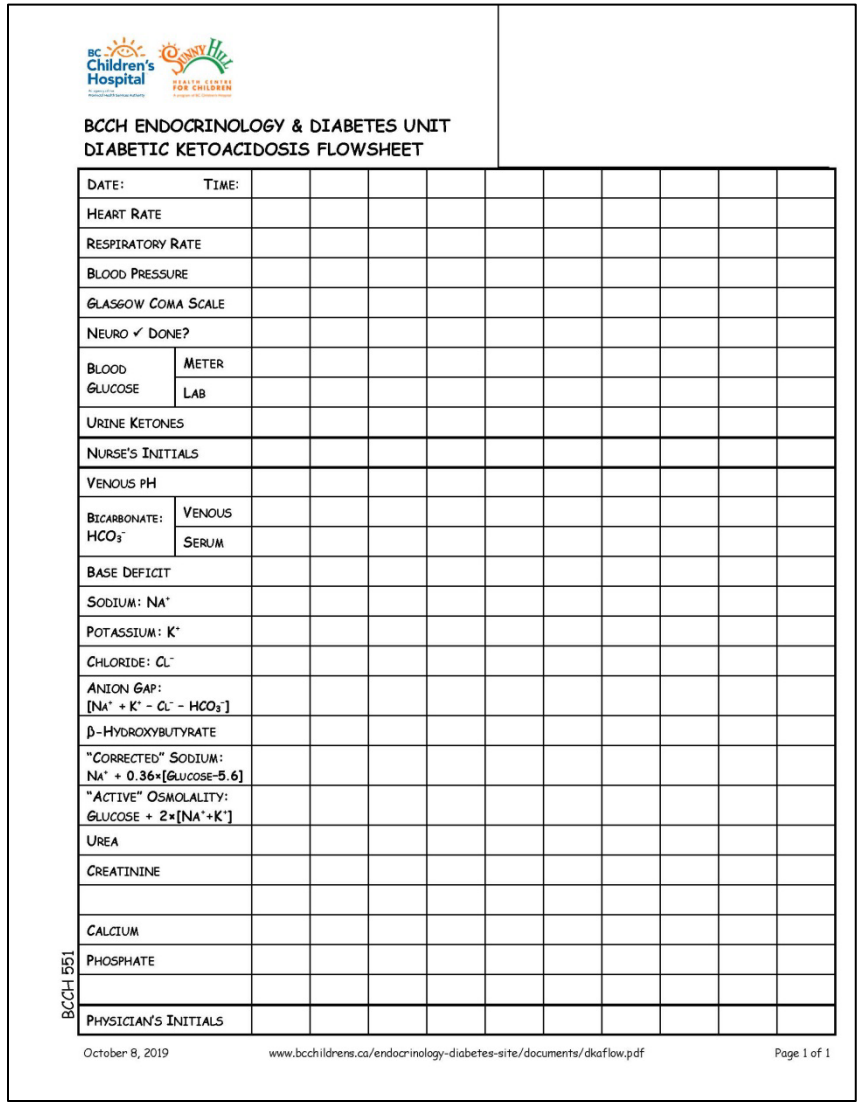
[C]Rapid, deep mouth-breathing (Kussmaul respiration) often dries out the oral mucosa, making the child appear more dehydrated than s/he really is. The hematocrit and other clinical signs noted are more accurate.

[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%.

DKA MEDICAL DOCUMENTS

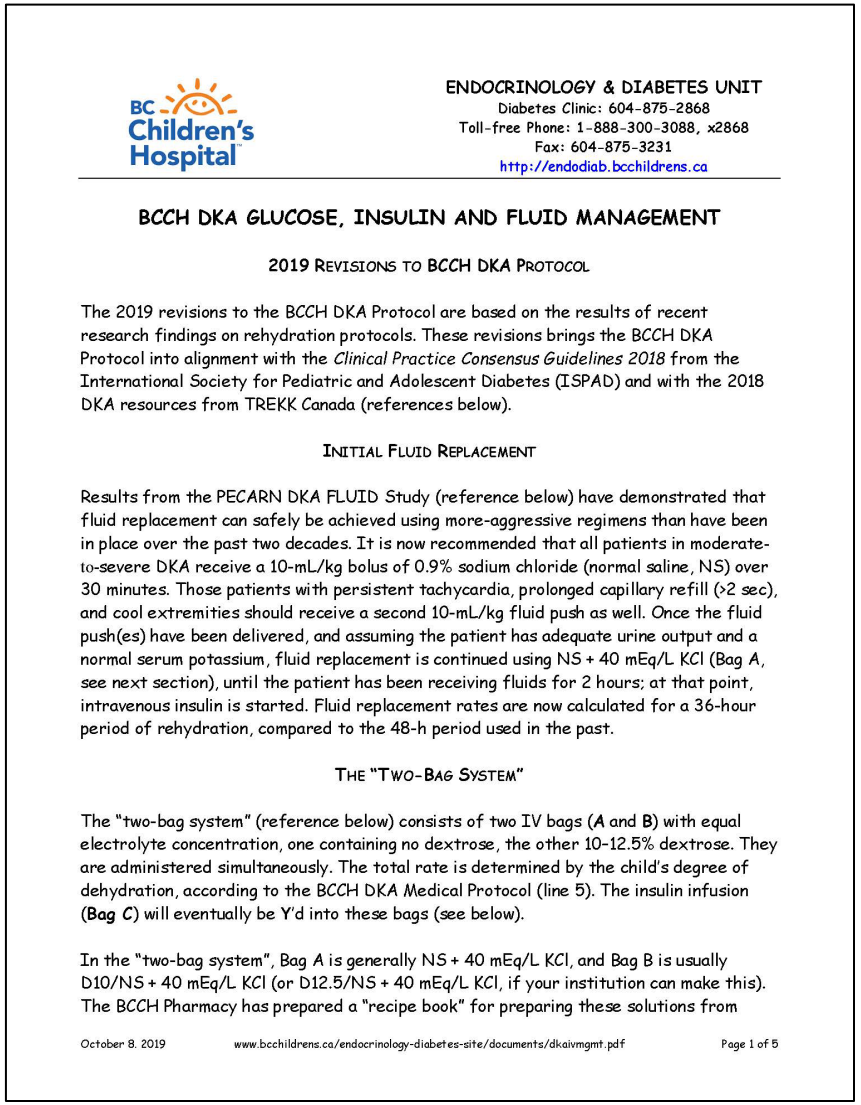


BCCH ENDOCRINOLOGY & DIABETES UNIT
DIABETIC KETOACIDOSIS FLOWSHEET

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											

BCCH 551

October 8, 2019 www.bcchildrens.ca/endocrinology-diabetes-site/documents/dkaflow.pdf Page 1 of 1



BC Children's Hospital

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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 2018* from the International Society for Pediatric and Adolescent Diabetes (ISPAD) and with the 2018 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 all patients in moderate-to-severe DKA receive a 10-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-h period used in the past.

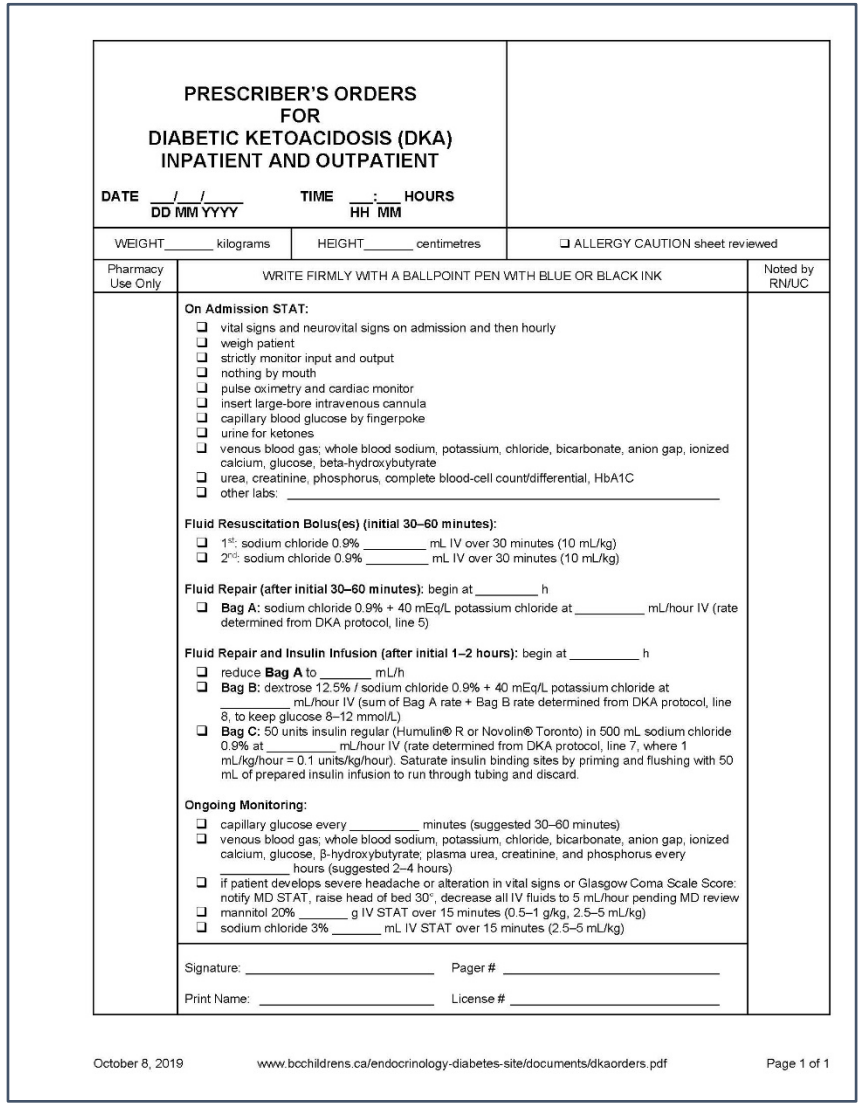
THE "TWO-BAG SYSTEM"

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 (line 5). The insulin infusion (**Bag C**) will eventually be Y'd 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

October 8, 2019 www.bcchildrens.ca/endocrinology-diabetes-site/documents/dkaivmgmt.pdf Page 1 of 5

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 (10 mL/kg)
- ❑ 2nd: sodium chloride 0.9% _____ mL IV over 30 minutes (10 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)

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

- ❑ reduce **Bag A** to _____ mL/h
- ❑ **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.

Ongoing Monitoring:

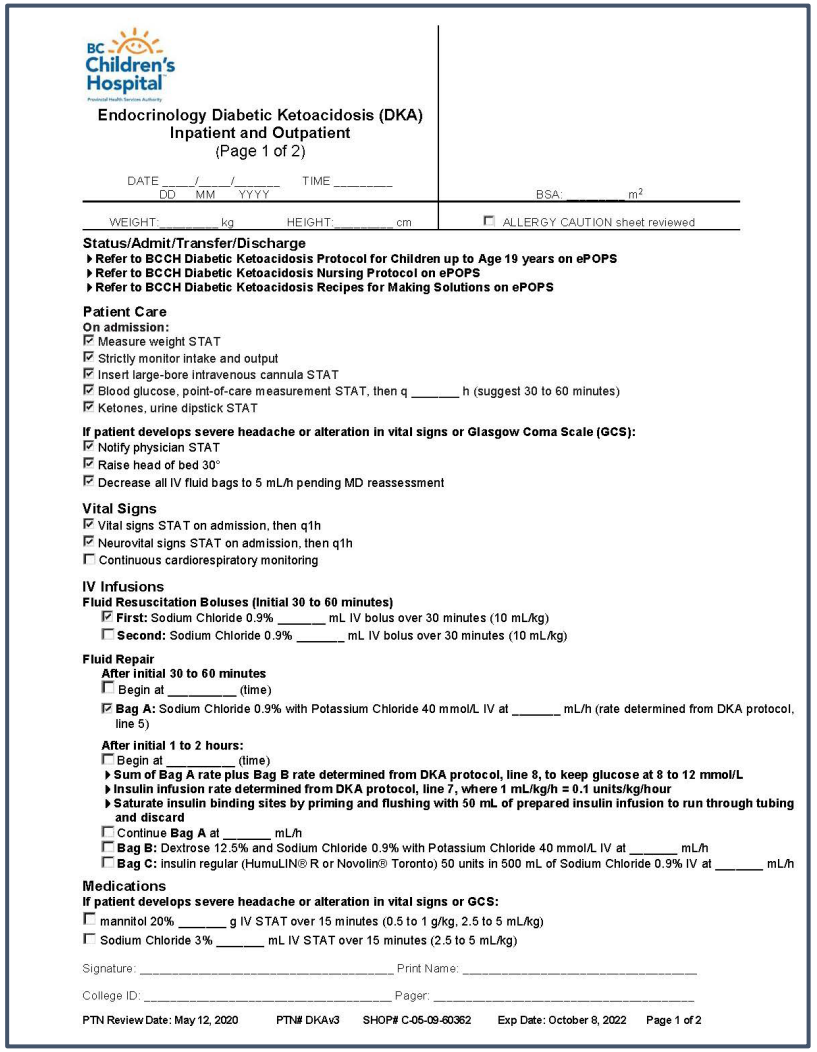
- ❑ capillary glucose every _____ minutes (suggested 30–60 minutes)
- ❑ venous blood gas; whole blood sodium, potassium, chloride, bicarbonate, anion gap, ionized calcium, glucose, β-hydroxybutyrate; plasma urea, creatinine, and phosphorus every _____ hours (suggested 2–4 hours)
- ❑ if patient develops 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 # _____

October 8, 2019 www.bcchildrens.ca/endocrinology-diabetes-site/documents/dkaorders.pdf Page 1 of 1

DKA PRESCRIBER ORDERS FROM PHSA SHOP



BC Children's Hospital

Endocrinology Diabetic Ketoacidosis (DKA)
Inpatient and Outpatient
(Page 1 of 2)

DATE ____/____/_____ TIME _____ BSA: _____ m^2
DD MM YYYY

WEIGHT: _____ kg HEIGHT: _____ cm ☐ ALLERGY CAUTION sheet reviewed

Status/Admit/Transfer/Discharge
- **Refer to BCCH Diabetic Ketoacidosis Protocol for Children up to Age 19 years on ePOPS**
- **Refer to BCCH Diabetic Ketoacidosis Nursing Protocol on ePOPS**
- **Refer to BCCH Diabetic Ketoacidosis Recipes for Making Solutions on ePOPS**

Patient Care
On admission:
- ☑ Measure weight STAT
- ☑ Strictly monitor intake and output
- ☑ Insert large-bore intravenous cannula STAT
- ☑ Blood glucose, point-of-care measurement STAT, then q _____ h (suggest 30 to 60 minutes)
- ☑ Ketones, urine dipstick STAT

If patient develops severe headache or alteration in vital signs or Glasgow Coma Scale (GCS):
- ☑ Notify physician STAT
- ☑ Raise head of bed 30°
- ☑ Decrease all IV fluid bags to 5 mL/h pending MD reassessment

Vital Signs
- ☑ Vital signs STAT on admission, then q1h
- ☑ Neurovital signs STAT on admission, then q1h
- ☐ Continuous cardiorespiratory monitoring

IV Infusions
Fluid Resuscitation Boluses (Initial 30 to 60 minutes)
- ☑ **First:** Sodium Chloride 0.9% _____ mL IV bolus over 30 minutes (10 mL/kg)
- ☐ **Second:** Sodium Chloride 0.9% _____ mL IV bolus over 30 minutes (10 mL/kg)

Fluid Repair
After initial 30 to 60 minutes
- ☐ Begin at _____ (time)
- ☑ **Bag A:** Sodium Chloride 0.9% with Potassium Chloride 40 mmol/L IV at _____ mL/h (rate determined from DKA protocol, line 5)

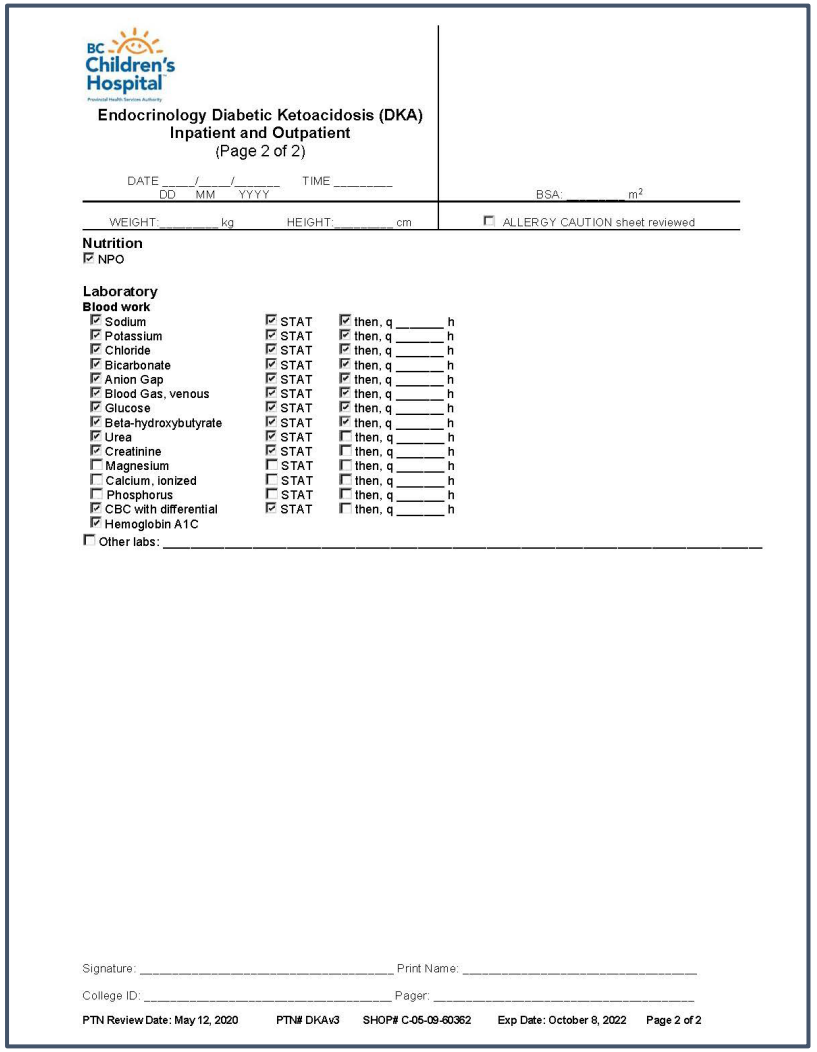
After initial 1 to 2 hours:
- ☐ Begin at _____ (time)
  - **Sum of Bag A rate plus Bag B rate determined from DKA protocol, line 8, to keep glucose at 8 to 12 mmol/L**
  - **Insulin infusion rate determined from DKA protocol, line 7, where 1 mL/kg/h = 0.1 units/kg/hour**
  - **Saturate insulin binding sites by priming and flushing with 50 mL of prepared insulin infusion to run through tubing and discard**
- ☐ Continue **Bag A** at _____ mL/h
- ☐ **Bag B:** Dextrose 12.5% and Sodium Chloride 0.9% with Potassium Chloride 40 mmol/L IV at _____ mL/h
- ☐ **Bag C:** insulin regular (HumuLIN® R or Novolin® Toronto) 50 units in 500 mL of Sodium Chloride 0.9% IV at _____ mL/h

Medications
If patient develops severe headache or alteration in vital signs or GCS:
- ☐ mannitol 20% _____ g IV STAT over 15 minutes (0.5 to 1 g/kg, 2.5 to 5 mL/kg)
- ☐ Sodium Chloride 3% _____ mL IV STAT over 15 minutes (2.5 to 5 mL/kg)

Signature: _____ Print Name: _____

College ID: _____ Pager: _____

PTN Review Date: May 12, 2020 PTN# DKAv3 SHOP# C-05-09-60362 Exp Date: October 8, 2022 Page 1 of 2



BC Children's Hospital

Endocrinology Diabetic Ketoacidosis (DKA)
Inpatient and Outpatient
(Page 2 of 2)

DATE ____/____/_____ TIME _____ BSA: _____ m^2
DD MM YYYY

WEIGHT: _____ kg HEIGHT: _____ cm ☐ ALLERGY CAUTION sheet reviewed

Nutrition
- ☑ NPO

Laboratory
Blood work

☑ Sodium	☑ STAT	☑ then, q _____ h
☑ Potassium	☑ STAT	☑ then, q _____ h
☑ Chloride	☑ STAT	☑ then, q _____ h
☑ Bicarbonate	☑ STAT	☑ then, q _____ h
☑ Anion Gap	☑ STAT	☑ then, q _____ h
☑ Blood Gas, venous	☑ STAT	☑ then, q _____ h
☑ Glucose	☑ STAT	☑ then, q _____ h
☑ Beta-hydroxybutyrate	☑ STAT	☑ then, q _____ h
☑ Urea	☑ STAT	☐ then, q _____ h
☑ Creatinine	☑ STAT	☐ then, q _____ h
☐ Magnesium	☐ STAT	☐ then, q _____ h
☐ Calcium, ionized	☐ STAT	☐ then, q _____ h
☐ Phosphorus	☐ STAT	☐ then, q _____ h
☑ CBC with differential	☑ STAT	☐ then, q _____ h
☑ Hemoglobin A1C		

☐ Other labs: _____

Signature: _____ Print Name: _____

College ID: _____ Pager: _____

PTN Review Date: May 12, 2020 PTN# DKAv3 SHOP# C-05-09-60362 Exp Date: October 8, 2022 Page 2 of 2

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DKA NURSING DOCUMENTS

ENDOCRINOLOGY & DIABETES UNIT
Diabetes Clinic: 604-875-2868
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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**					

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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 <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 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 1-2 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

- 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:
  - 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 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

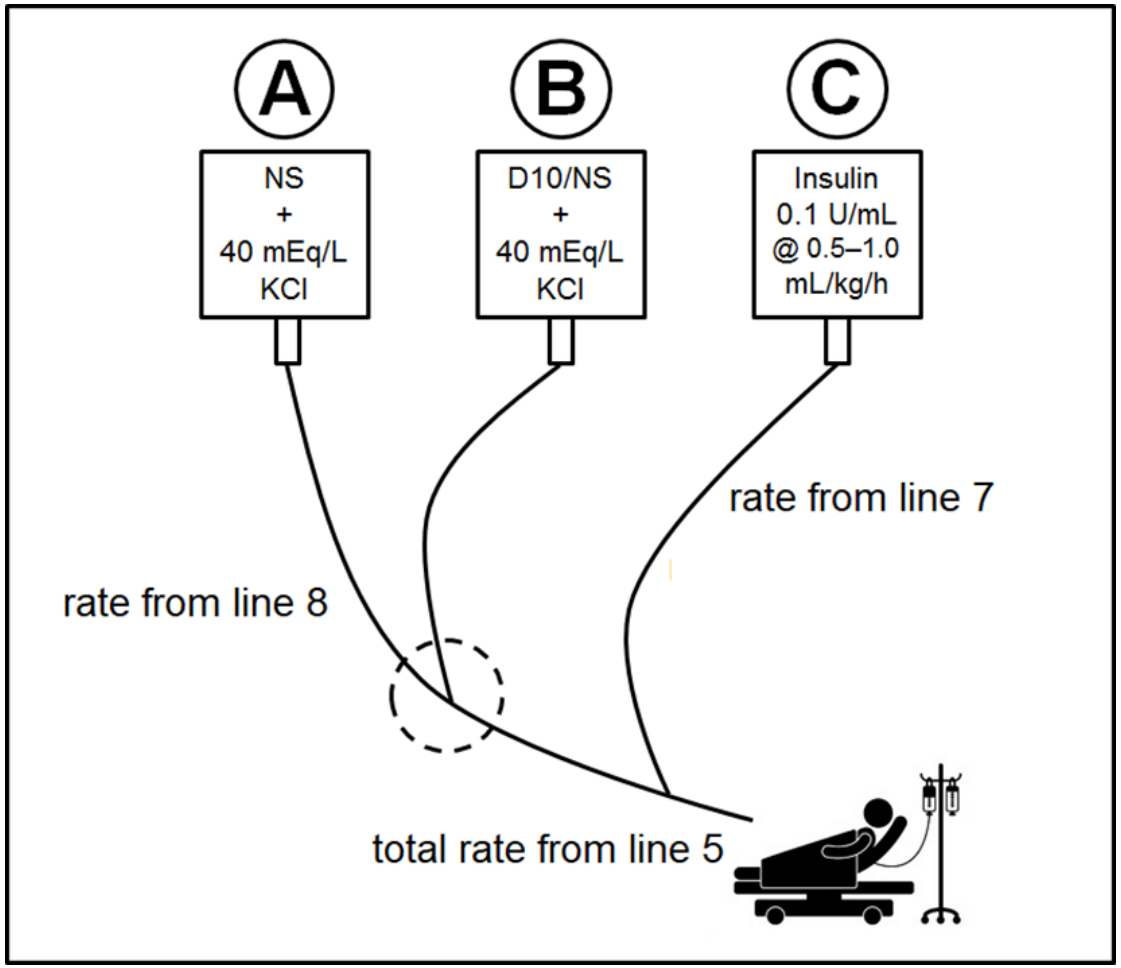
BCCH PROTOCOL: 1st 60 MINUTES

- 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:
  - 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 250 mL/h
- start with NS + 40 mEq KCl/L, assuming patient is urinating
- at 60–120 min after start of 1st fluid bolus, begin insulin infusion:
  - 0.05–0.1 Units/kg/h [= 0.5–1 mL/kg/h of 50 units/500 mL insulin solution]
- 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):
  - 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: 60 MINUTES–36 HOURS

- at 4–6 h after initial fluids and if corrected Na^+ is ≥145 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

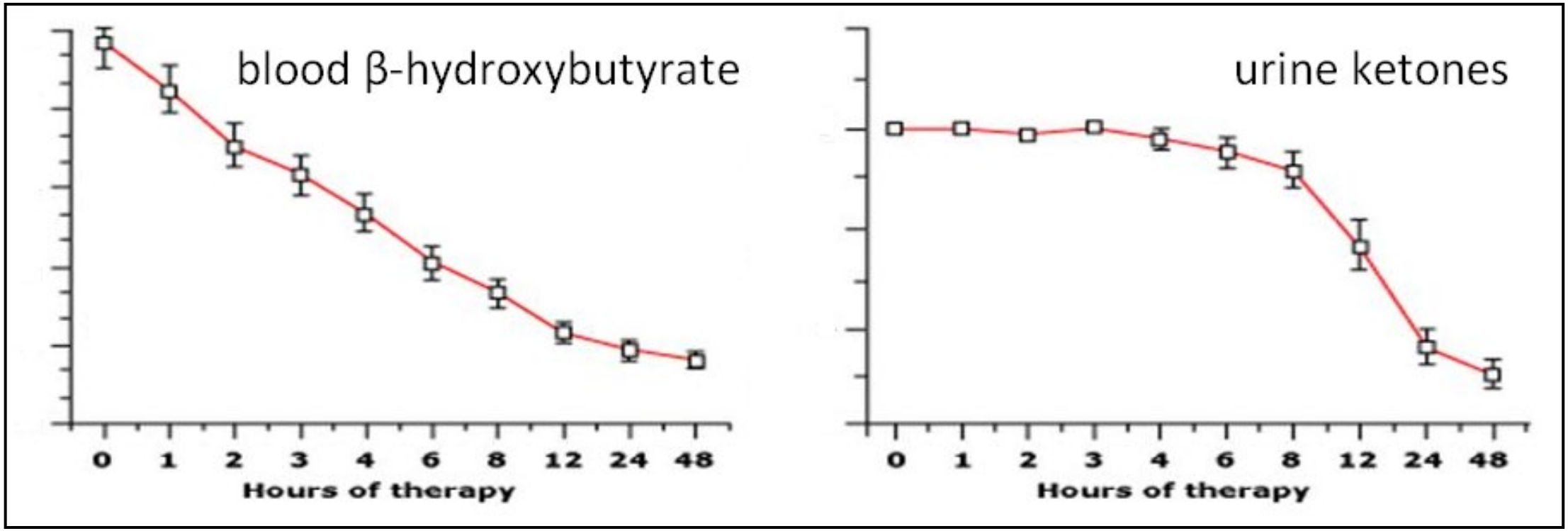
- BG by meter q30–60 min (may need lab BG if >30 mmol/L)
- Na^+, K^+, Cl^-, HCO_3^-, anion gap, urea, creatinine, venous pH q2–4 h
- Ca^{2+}, Mg^{2+}, P_i q2–4 h if giving phosphate
- β-hydroxybutyrate (preferably) or urine ketones q2–4 h
- neurovital signs/GCS q30–60 min

- 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 Pediatr 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

PECARN DKA FLUID STUDY

TABLE 1 FLUID trial treatment protocols

Protocol Components	Protocol A1	Protocol A2	Protocol B1	Protocol B2
Standard initial fluid bolus	10 cc/kg bolus of 0.9% saline	10 cc/kg bolus of 0.9% saline	10 cc/kg bolus of 0.9% saline	10 cc/kg bolus of 0.9% saline
Additional intravenous fluid bolus	Additional 10 cc/kg of 0.9% saline	Additional 10 cc/kg of 0.9% saline	No additional bolus	No additional bolus
Assumed fluid deficit	10% of body weight	10% of body weight	5% of body weight	5% of body weight
Replacement of deficit	Replace half of fluid deficit + maintenance fluids over initial 12 h, remaining deficit + maintenance fluids over subsequent 24 h	Replace half of fluid deficit + maintenance fluids over initial 12 h, remaining deficit + maintenance fluids over subsequent 24 h	Replace deficit + maintenance fluids evenly over 48 h	Replace deficit + maintenance fluids evenly over 48 h
Fluid used for deficit replacement	0.45% saline	0.9% saline	0.45% saline	0.9% saline

Abbreviation: FLUID, Fluid Therapies Under Investigation in DKA.
Modified from Glaser N. et al.[23]. Reprinted with permission.

New Engl J Med 2018;378(24):2275–2338

PECARN DKA FLUID STUDY

- fast vs slow rehydration 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

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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_aCO_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^+"
  - $Na^+ + [0.36 \times (glucose - 5.6)]$
- 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: SYMPTOMS

- severe headache
- change in sensorium: irritability, confusion, inability to arouse
- dilated pupils, papilledema, cranial nerve palsies
- posturing, incontinence
- decreased O_2 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_{art} >7.30, pH_{ven} >7.25, 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

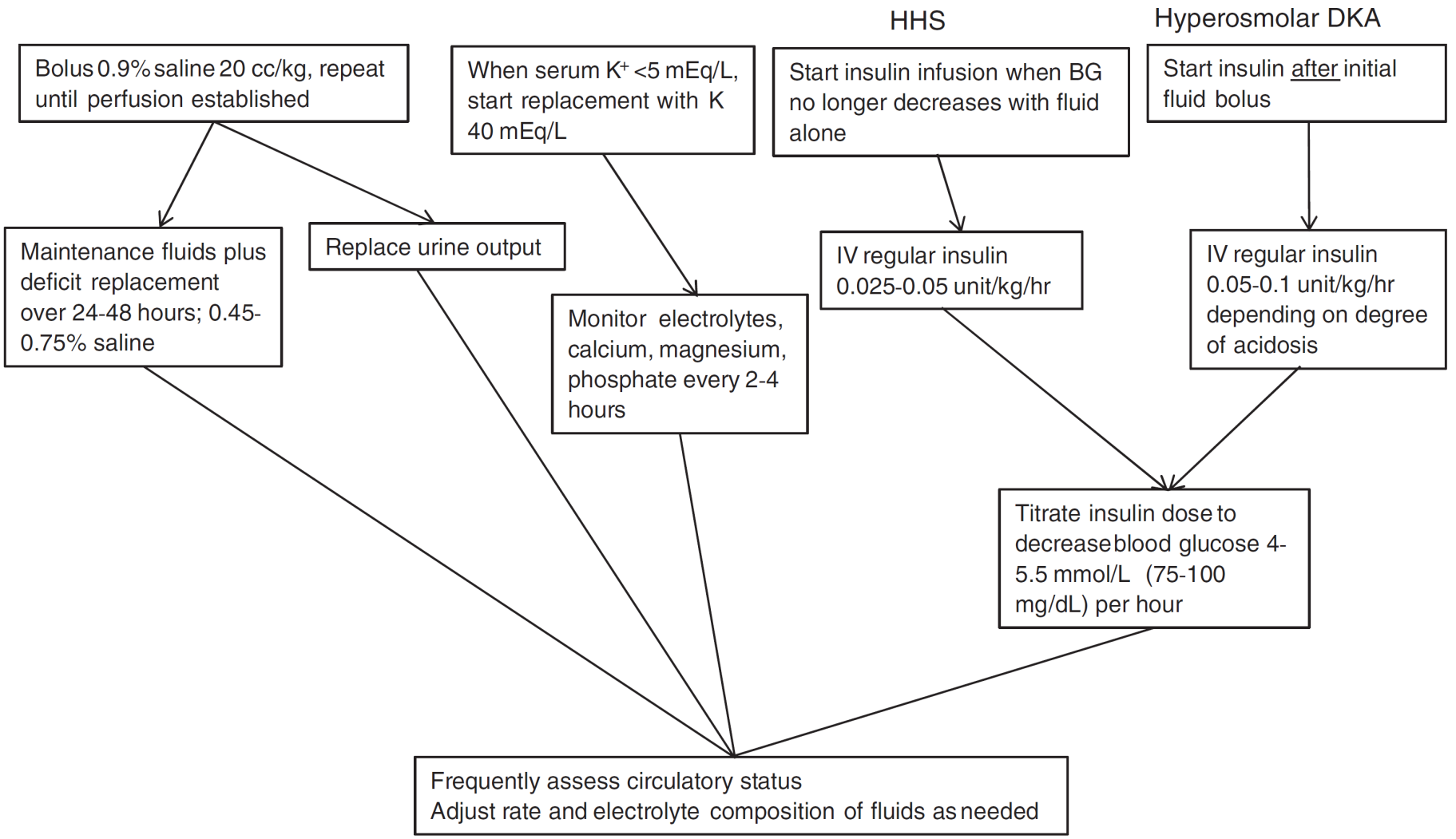
HHS vs. DKA

- ↑ 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:
  - 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



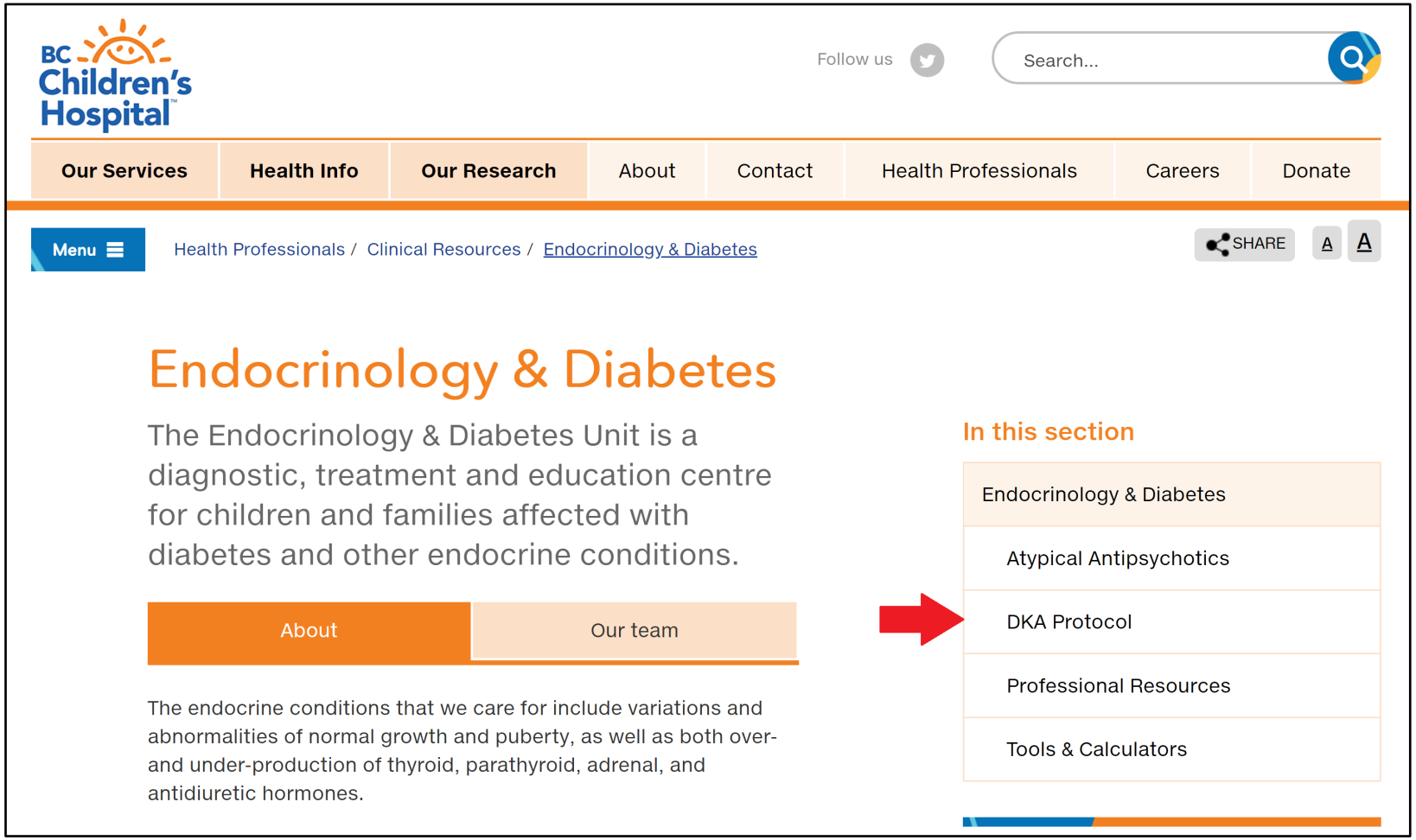
RECURRENT DKA

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

DKA PREVENTION (BC PEDIATRIC SOCIETY)

beyondtype1.org/dkacampaign

EDU WEBSITE



http://endodiab.bcchildrens.ca

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