



EM CASES SUMMARY

Episode 146 DKA Recognition & Management

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The Difficulty in Diagnosing Diabetic Ketoacidosis (DKA)

There are no definitive criteria for the diagnosis of DKA according to the 2018 Canadian DKA Guidelines. As such, it is important to have a low threshold to consider the diagnosis in any diabetic patient who presents with polyuria, polydipsia, hyperpnea, abdominal pain/nausea/vomiting and altered level of awareness. While most patients with DKA will have the triad of hyperglycemia, anion gap metabolic acidosis and ketonemia, there are exceptions:

- DKA patients can have a *normal* glucose (euglycemic DKA)
- DKA patients can have a *normal* pH and a *normal* bicarbonate (normal VBG) in the context of ketoacidosis plus metabolic alkalosis as a result of vomiting and/or the triggering illness

- Negative urine ketones should not be used to rule out diabetic ketoacidosis, as urine tests measure the presence of acetoacetate, but not β -hydroxybutyrate

A β -hydroxybutyrate level > 1.5 mmol/L has a sensitivity of 98-100% and specificity of 78.6-93.3% for the diagnosis of DKA in diabetic patients presenting to the ED with elevated serum glucose levels.

Clinical Pearl: Many patients with DKA present with some degree of abdominal pain. Severe abdominal pain with only mild ketoacidosis argues against DKA as the cause. When in doubt about need for an abdominal imaging, resuscitate the patient first, and perform serial abdominal examinations. Have a low threshold to image if the ketoacidosis improves but the patient continues to be symptomatic or clinically worsens.

Severity categorization of DKA

	Mild DKA	Moderate DKA	Severe DKA
Plasma glucose (mg/dL)	>250	>250	>250
pH	7.25–7.3	7.0–7.24	<7.0
Serum bicarbonate (mEq/L)	15–18	10–15	<10
Ketones (urine or serum)	Positive	Positive	Positive
Anion gap	>10	>12	>12
Osmolality (mOsm/kg)	Variable	Variable	Variable
Mental status	Alert	Alert/drowsy	Stupor/coma

Differentiating DKA from Hyperglycemic Hyperosmolar Syndrome (HHS)

DKA Triad	HHS Triad
Hyperglycemia	Severe hyperglycemia
Metabolic acidosis	Elevated serum osmolality
Ketonemia (elevated beta-hydroxybutyrate)	Volume depletion
Who: frequently T1DM, but can occur in T2DM	Who: T2DM, often present following longer/protracted course of illness

DKA and HHS may occur concurrently.

Evaluation for precipitating cause of DKA is paramount as it is often the cause of death in patients with DKA

DKA can be the initial manifestation of diabetes, but it often occurs in the context of known diabetes plus a trigger. Most often, it is due to medication non-adherence, incorrect dosing or infection. However, any physiologic stress can trigger DKA.

Common causes include "The 5 I's":

1. Infection (pneumonia, UTI, skin, abdominal)
2. Infraction (MI, stroke, bowel infarction)
3. Infant on board (pregnancy)
4. Indiscretion (dietary nonadherence)
5. Insulin deficiency (insulin pump failure or nonadherence)

In addition, common **drugs that can trigger DKA** include glucocorticoids, diuretics and atypical antipsychotics.

DKA lab work-up

DKA work-up should include CBC, electrolytes, extended electrolytes, creatinine, BUN, albumin, VBG, lactate, serum ketones, as well as consideration for:

- BhCG (trigger of DKA)
- ECG/Trop (only if ischemia suggested in history)
- Cultures, UA etc. for suspected infection trigger
- Beta-hydroxybutyrate if diagnosis unclear

Lactate is a potentially important prognostic factor in predicting the severity of DKA and in monitoring the progression or resolution.

Acid-base disturbances in DKA

DKA patients classically have an anion-gap metabolic acidosis due to lipolysis and an accumulation of ketoacids. However, diabetic patients with significant GI loss can have a normal pH or alkalemia because of a mixed acid-base disturbance.

In such cases, use the Simplified Stewart Approach:

Base-excess =

$[Na-Cl-35] + [1-lactate] + [0.25 \times (42-albumin)] + \text{other ions}$

Other ions =

$\text{Base excess} - [Na-Cl-35] + [1-lactate] + [0.25 \times (42-albumin)]$

If the major determinants of acid-base do not explain the base deficit, then there are unmeasured ions present.

Pitfall: Avoid ruling out DKA based on a normal or near normal VBG. They can have a normal pH due to the underlying trigger of the DKA contributing to a mixed acid-base picture.

Sorting out ketonemia: The differential diagnosis of ketoacidosis

The differential diagnosis for ketoacidosis includes:

- DKA
- Alcoholic ketoacidosis
- Starvation ketosis
- Isopropyl alcohol ingestion

In the presence of low or normal glucose levels, it is less likely that it is DKA. You can have positive serum ketones and anion gap metabolic acidosis with alcoholic ketoacidosis and starvation ketoacidosis and may be difficult to distinguish clinically.

Starvation ketosis responds quickly to glucose and the acidosis is generally less severe. The clinical history will be key in identifying the diagnosis.

Euglycemic DKA

Euglycemic DKA involves a relative carbohydrate deficiency state/normalization of serum glucose and concomitant elevation of counter-regulatory stress hormones that leads to free fatty acid catabolism and ketone production.

Maintain a high index of suspicion for DKA in the following patients who present with nausea, vomiting, shortness of breath and/or metabolic acidosis, and evaluate for DKA with serum ketones:

- T1/T2DM Patients taking SGLT-2 inhibitors (the “zins”)
- Pregnant patients – due to transplacental glucose transport, will have relative euglycemia (more common in second or third trimester)
- Chronic pancreatitis
- Bariatric surgery patients – due to absorption issues

For management of euglycemic DKA, you may need to start fluids with dextrose sooner in the treatment process, as the serum blood glucose is already low.

ED Management of DKA

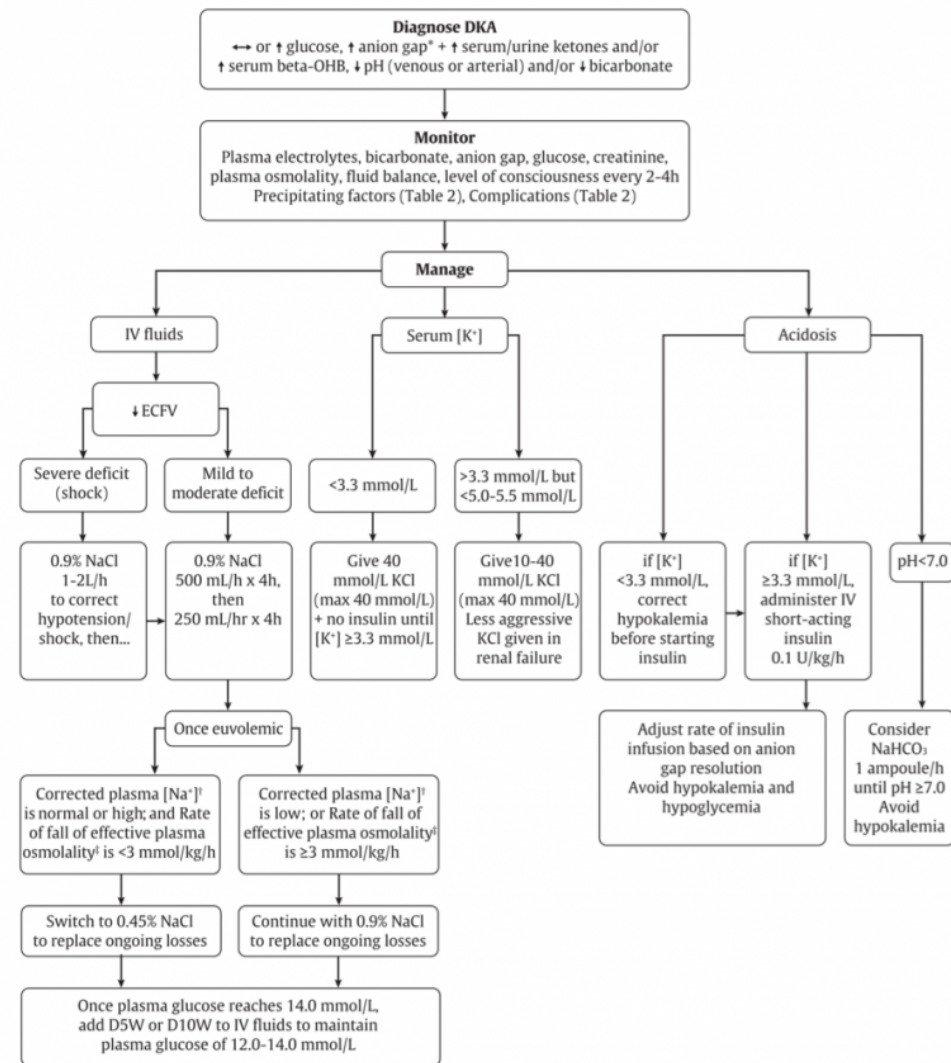
Goals of treatment in DKA

The initial goals of treatment in patients with DKA include:

- Correction of fluid deficits
- Replacement of potassium
- Stopping ketone production by closing anion gap via insulin
- Treating underlying precipitant

Essential concept in the ED management of DKA: The focus is not on lowering the glucose, but rather closing the gap
DKA is not an issue of hyperglycemia per se, but rather an excess in serum ketone production due to low circulating levels of insulin. The cornerstone of DKA treatment is the correction of metabolic homeostasis by reducing ketone production via insulin and **not** the correction of hyperglycemia.

Using **standardized DKA order sets** for the management of DKA has been shown to decrease the time to anion gap closure, reduce length of stay in hospital, and minimize complications during treatment.



2018 Canadian Diabetes Association DKA Guidelines treatment algorithm, adapted from <https://guidelines.diabetes.ca/docs/CPG-2018-full-EN.pdf>

DKA Fluid Resuscitation

Osmotic diuresis from hyperglycemia results in significant volume depletion. Fluid resuscitation will help restore intravascular volume, achieve normal tonicity, improves organ perfusion, decreases lactate formation, improves renal function.

- Use NS or RL for initial fluid replacement (ADA: 1000-1500mL NS over 1 hr) then adjust to patient's hemodynamic and electrolytes status, and maintain between 250 and 500 mL/hr
- ADA: Patients with a normal or high corrected sodium concentration can be switched to 0.45% sodium chloride after the first hour of fluid replacement
- Add dextrose (D5W) to the IV fluid if/when blood glucose approaches normal to allow continued insulin infusion at a rate sufficient to resolve DKA while avoiding hypoglycemia OR when glucose <15 (250-300mg/DL) switch to D5-1/2NS NS at an initial rate of 150 to 250 mL/h
- Our experts recommend starting with NS or RL and consider ongoing fluid resuscitation with RL to avoid the hyperchloremic acidosis associated with large volumes of NS

Key point: *Volume resuscitation must precede insulin therapy in order to adequately restore intravascular volume and tonicity. Early insulin therapy has the added risk of hypoglycemia and hypokalemia.*

The 2-bag method of fluid management in DKA

Two bags of half NS, one with and one without 10% dextrose (D10W) are adjusted on the basis of hourly blood glucose monitoring to maintain an IV fluid rate of 250 mL/h. Two retrospective studies of more than 500 patients found that the 2-bag method was associated with earlier correction of acidosis and shorter duration of intravenous insulin compared with conventional delivery of IV fluids. Use of the he 2-bag method in the ED may reduce the need for hospital admission, and it may be associated with less hypoglycemia compared with conventional treatment.

DKA Insulin Therapy

The primary problem with DKA is ketoacidosis (not hyperglycemia). Our overall goal is to titrate insulin to treat the ketoacidosis and close the gap. Glucose levels are used as a surrogate measurement of the efficacy of insulin therapy. Supplemental glucose should be provided as glucose approaches normal to allow for continued insulin therapy to resolve the ketoacidosis while avoiding hypoglycemia.

- Start short-acting insulin at a fixed weight-based dosing of 0.1U/kg/hr
- Target blood glucose of 12-14mmol/L and normalization of the anion gap
- When blood glucose <14mmol/L, add dextrose D5 infusion to prevent hypoglycemia while continuing insulin infusion

- If glucose falls < 4mmol/L, do not stop insulin infusion, but decrease by 50% (no less than 0.5U/kg/hr), provide 1 amp of D50 and switch dextrose infusion from D5 to D10

Patients should also be allowed to eat if it is deemed safe to do so. There is no evidence to support keeping the patient NPO.

***Common pitfall:** A common pitfall is stopping the insulin infusion when the glucose normalizes or falls below normal the normal limit. Do **not** stop the insulin infusion when serum glucose normalizes or is low. The patient will very quickly become ketotic again as insulin is required to shut off the underlying metabolic derangement of ketoacidosis.*

What about insulin bolus? There is *no* role for bolus dosing of insulin, except possibly in the peri-arrest situation. Bolus insulin increases the risk of hypoglycemic events, prolonged gap closure, and longer hospital stays.

Hypokalemia: A Common Complication of DKA

Patients with DKA have large total body potassium deficits. However, the initial potassium reading is commonly normal or high due to intracellular shifts secondary to volume contraction and metabolic acidosis. **Potassium must be replaced prior to initiation of insulin therapy** as insulin further promotes an intracellular shift of potassium.

Serum Potassium (mEq/L)	Repletion
>5.3	No repletion, repeat in 1 h.
4.0-5.3	Add 10 mEq/L KCl/h to IV fluids.
3.5-4.0	Add 20 mEq/L KCl/h to IV fluids.
<3.5	Hold insulin. Add 20-60 mEq/L/h to IV fluids, place on continuous cardiac monitor.

If the patient can tolerate **oral potassium replacement**, it is preferred over the IV route as it has better systemic absorption.

Starting Long-acting Insulin in the ED

Long-acting insulin should be considered early (well in advance of discontinuing the infusion) even in the ED. Early initiation of long-acting insulin facilitates transitioning off the insulin infusion, reduces the incidence of hyperglycemia, and may decrease hospital length of stay.

Patients can generally be treated with their home insulin regimen (ideally a single daily dose of glargine). For a patient naive to insulin, a starting dose of 0.25 units/kg daily of glargine (Lantus) may be given.

Role of Bicarbonate in Severe DKA

The literature does not support replacing bicarb in adult DKA patients with pH ≥ 6.9 . There is retrospective evidence of transient paradoxical worsening of ketosis and an increased need for potassium supplementation in patients who received bicarb. Our experts caution against the routine use of bicarbonate therapy in DKA. The decision to give bicarb should be tailored to the individual patient, their hemodynamics and their acid/base status.

Our experts recommend consideration for bicarbonate in the severe DKA patient just prior to endotracheal intubation, as it may help transiently buffer the pH against the rise in CO₂ that occurs during induction +/- paralysis.

Troubleshooting: Anion Gap is not Closing

If the anion gap is not closing, consider the following possibilities:

- Inadequate fluid resuscitation
- Inadequate insulin dose
- Malfunction of insulin infusion
- Underlying diagnosis contributing to anion gap that has not been addressed

Interventions if the anion gap is not closing:

- Evaluate fluid status (e.g. with ultrasonography), provide additional crystalloid if necessary
- Consider increasing the insulin infusion rate (see next section)
- Re-evaluate for a missed underlying diagnosis
- Consider checking beta-hydroxybutyrate and lactate levels, to exclude an occult/worsening *lactic* acidosis

(Avoid) Intubating the DKA Patient

Patients with DKA are physiologically challenging patients to intubate for several reasons. Their respiratory dynamics of hyperpnea to correct their underlying metabolic acidosis means

the ventilator must equally match their large tidal volume and respiratory rate. This intrinsically puts the patient at risk for ventilator induced lung injury and subsequent development of ARDS. Furthermore, these patients with profound metabolic acidosis are at risk of circulatory collapse peri-intubation as periods of apnea during intubation will cause their pCO₂ levels to rise rapidly, worsening the acidosis.

If you must intubate:

1. Resuscitate before you intubate
2. Use ketamine +/- paralytic; continue to bag if paralytic used to avoid any period of apnea
3. Consider an antiemetic
4. Consider giving bicarb, especially if serum bicarb <10
5. High tidal volume (8cc/kg) and RR (24-28) to hyperventilate
6. Consider asking for additional help from your anesthesiology colleagues

The Role of NIPPV in DKA

Oxygenation is rarely an issue in DKA, but rather work of breathing and respiratory fatigue. Our experts do not recommend the routine use of BiPAP in DKA patients given the risk of aspiration and emesis in these patients as they often concurrently have gastroparesis. Only consider NIPPV if the patient is in a highly monitored setting with one-to-one nursing care.

A non-rebreather and/or high flow nasal cannula should be considered if there is a suspected primary hypoxic issue requiring supplemental oxygen.

Avoiding Cerebral Edema in DKA

The key is to **go slow** with resuscitation.

- Avoid over-aggressive fluid administration
- Do not drop the glucose too fast; avoid reducing the glucose below <200 mg/dL (<11.1 mmol)
- Replace fluids gradually
 - Consider isotonic fluids (e.g. D5 RL can be used as a source of glucose-containing IV fluid, rather than hypotonic fluids such as D10W or D5 1/2 NS).
 - Avoid lowering the serum osmolality by more than 3 mmol/kg/hour or decreasing sodium by >10 mmol/24 hours
- Note that the sodium will often initially *increase* during resuscitation due to glucose entering the cells. This does *not* reflect an increase in serum osmolality and does *not* require treatment with free water
 - The best parameter to track is the measured or estimated serum osmolality

Criteria for resolution of DKA

Glucose <11.1 mmol (<200mg/dL) + 2 of:

1. Normalization of AG
2. Venous pH >7.3
3. Serum bicarbonate ≥ 15 mEq/L

Key take home points for ED management of DKA

1. Identify the underlying cause which is the most common cause of death in DKA and HHS patients – use the mnemonic **5 “I”s plus drugs** if that helps you remember the triggers
2. Do not rule out DKA based on a normal serum pH or a normal serum glucose – measure beta-hydroxybutyrate when in doubt
3. Main goal in DKA is to close the gap, not fix the glucose level
4. Do not stop the insulin when serum glucose becomes normal or low; instead, give glucose
5. Allow patient to eat as soon as there is no aspiration risk
6. Avoid intubation and BiPAP whenever possible in severe DKA – HFNC is your go-to if they are not doing well on a non-rebreather
7. Know how to differentiate all the causes of ketoacidosis – there are subtle clues
8. Use a protocol – there is good evidence that protocols for DKA improve patient outcomes
9. Monitor carefully for complications of DKA: hypoglycemia, hypokalemia, ARDS

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Euglycemic DKA

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