Guidelines for the Management of Diabetic Ketoacidosis (DKA) in Pediatric Patients

General Guidelines and Definitions:

Disclaimer: These are guidelines—not hard and fast rules. Some patients, such children <5 y.o. and those with HbA1c >10%, may not adhere to the usual course and guidelines may need to be modified.

DKA: A state of *insulin deficiency* and characterized by *severe depletion of water and electrolytes* (see Appendix 1). The primary goals are to treat the insulin deficiency (which will correct the acidosis and reverse the ketosis) and to replace fluids and electrolytes. Other goals include gradually achieving euglycemia, monitoring for and managing complications of DKA especially cerebral injury, and identifying and treating any precipitating event.

Clinical signs of DKA: dehydration, tachycardia, tachypnea, Kussmaul (deep sighing) respirations, acetone breath odor, nausea, vomiting, abdominal pain, blurry vision, confusion, drowsiness, progressive decrease in level of consciousness, loss of consciousness

Biochemical criteria for DKA: hyperglycemia (BG > 200mg/dl); venous PH <7.3 or serum bicarb <15 mmol/L, beta-hydroxybutyrate ≥3 mmmol/L or moderate/large ketonuria

Diabetic ketosis without significant acidosis: Urine ketones moderate/large, BOHB 1.6-3, nausea +/- vomiting, pH >7.3, Bicarb >15

- Management:
  - Oral or IV hydration, depending on vomiting, ability to tolerate PO
  - Supplemental insulin (Novolog, SQ: 0.1-0.2 units/kg every 4 hours) in addition to patient's usual long-acting insulin (ie Lantus, Tresiba)
  - Often managed as outpatient at home or in Emergency Unit
  - In established patient with good family support, sometimes managed at home by phone under guidance from on-call physician with no knowledge of laboratory results other than self-monitored blood glucose and urinary ketones

Mild DKA: pH 7.2-7.3, Bicarbonate 10-15 mmol/L, BOHB >3 mmol/L, Urine Ketones mod/large, persistent vomiting,

- Management:
  - Oral or IV hydration (usually IV)
  - Admission to Peds Floor is generally recommended
  - Supplemental insulin should be used (Novolog SQ 0.15-0.2 units/kg every 2 hours[*]) in addition to the patient's usual long-acting insulin (ie Lantus, Tresiba)
  - May require management with IV regular insulin infusion (0.05-0.1 units/kg/hr) if persistent vomiting or alterations in other organ systems

Moderate DKA: pH 7.1-7.2, Bicarbonate 5-10 mmol/L, BOHB >3 mmol/L, Urine Ketones Large

- Management:
  - May admit to Peds Floor status, but recommend admission to PICU if higher risk of cerebral edema (<5yo) or if long duration of symptoms, compromised circulation, hypokalemia, hyponatremia (after sodium corrected for glucose[†]), depressed level of consciousness or altered mental status
  - IV hydration with sips of sugar free clear liquids
  - IV regular insulin infusion (0.05-0.1 units/kg/hour)
  - Intensive monitoring

Severe DKA: pH <7.1, Bicarb <5, BOHB >3 mmol/L, Urine Ketones Large *OR* mild/moderate DKA with other organ system impairment (altered mental status, impaired renal function, respiratory distress, oxygen desaturation, compromised circulation)

- Management
  - Admit to Pediatric ICU for therapy and intensive monitoring
  - IV hydration (3 L/m^2/day)[¥]
  - IV insulin (0.1 units/kg/hour)
  - Intensive monitoring for improvement and signs of cerebral injury

Some useful formulas:

[*]Total daily insulin dose approx. = Lantus dose x 2 (In general, Lantus dose is 50% of pt's total daily insulin)

[†]Corrected sodium = [((Glucose -100)/100) x 1.6] + Pt's Na [glucose is mg/dl]

[¥]BSA (m^2)= sq root [(wt(kg) x ht(cm))/3600]; estimated BSA = (wt(kg) x 4 + 7)/(90 + wt(kg))

[‡]Anion Gap = Na – (Cl + HCO_3); normal is 12 +/- 2 mmol/L

[€]Effective osmolality = 2 x (Na + K) + glucose/18 [glucose is mg/dl]

Guidelines for the management of severe DKA

Fluid Management (2 bag system)

- Total fluids should not exceed about 3500 ml/m^2/day
- Volume expansion (fluid bolus) should be initiated prior to insulin administration, and insulin should be initiated no sooner than 1 hour after the fluid administration has begun (ie, after initial volume expansion)
    - Initial bolus of NS or LR with 10-20 ml/kg over 30-60 minutes
    - If poor peripheral perfusion, hypotension, or shock, the initial bolus should be given over 15-30 min and if symptoms persist after the initial bolus, it may be appropriate to repeat with a second 10-20 ml/kg NS bolus
    - DKA with shock, rapidly restore volume with isotonic saline in 20ml/kg boluses as quickly as possible through a large bore catheter with reassessment of circulatory status after each bolus
- Rehydration: assume 5-10% dehydration and plan to replace the deficit over 24-48 hrs along with maintenance fluids (Appendix 2)
    - This can often be accomplished by running IV fluids at 1.5 x maintenance or 3000 ml/m^2/day
    - Initial IVF with ½NS + 20meq/L K-phosphate + 20 meq/L K-acetate (or KCl if K-acetate is not available) **note, there is zero dextrose in this fluid
        - *Consider* NS instead of ½NS if measured serum Na level is low and does not rise with the fall in glucose (serum Na should rise by about 3 meq/L for each 100 mg/dl decrease in glucose)
        - If K is >5, repeat the BMP or iStat and add the K to the fluids when the K is <5; If K is low, may need up to 60 meq/L K total (typically 30 and 30 of the two types of K solution)
    - "Y-in" D10 ½NS + 20meq/L K-phosphate + 20 meq/L K-acetate (or KCl) when the serum glucose is less than 250 mg/dl or if glucose falls faster than 100mg/dl per hour
    - 2 bag method: Use 2 separate bags of IV rehydration fluid with identical electrolyte composition; 1 bag has NO dextrose and the other has 10% dextrose. Increase and decrease the rate of each bag reciprocally so that the total rate is constant at the desired rehydration rate (ie, 3 L/m^2/day) and the glucose is maintained between 100-200 mg/dl.
        - Typically, when the BG is ≤ 250, run the 2 fluids at 50/50 rates and when the BG is <200, stop running the fluid without the dextrose and run the D10 fluid at 100% of the desired rate
        - DO NOT REDUCE INSULIN INFUSION RATE BECAUSE OF FALLING BLOOD GLUCOSE UNTIL THE REDUCTION IS INDICATED BASED ON RESOLUTION OF KETOACIDOSIS; *If the patient is still acidotic, they still need the insulin*—increase the dextrose content instead (can use D12.5% fluids prn)
- **Do not administer sodium bicarbonate to correct the acidosis** (***cautious*** administration may be ***considered*** if pH <6.9 and the acidosis is so profound as to adversely affect the action of epinephrine during resuscitation, decreased cardiac contractility, impaired tissue perfusion from vasodilation, or life-threatening hyperkalemia; dose should be 1-2 mmol/kg over 60 minutes)

Insulin Therapy

- "Low-dose continuous IV insulin infusion" = 0.1 units/kg/ hour regular insulin, IV (conc. 1 unit/mL)
- Do not give intravenous insulin bolus or subcutaneous insulin bolus when starting the continuous infusion (*if a delay in starting the insulin infusion is expected to be longer than 1 hour (i.e., more than 2 hours after IVF have been started, then a SQ insulin dose may be warranted at the discretion of admitting physician)
- Continue iv insulin infusion at 0.1 units/kg/hr until DKA is resolved: pH >7.3, serum bicarbonate >15, BOHB <1 mmol/L, the anion gap <12‡, and the patient is awake and can tolerate PO fluids
    - A lower insulin rate (0.05 – 0.08 units/kg/hr) may be needed in patients with marked insulin sensitivity (ie, <5yo)
    - May need higher insulin rate if BOHB does not decrease as expected—BOHB should decrease by 0.05 mmol/L/hr
- Usually, long-acting basal insulin (ie Lantus, Tresiba) should be given at the usual time, even if the patient is on an insulin infusion (this is most frequently given at bedtime; its onset of action is approximately 1-2 hrs)
    - Administering basal insulin while on the insulin infusion allows us to d/c the insulin infusion when it is appropriate (see above) without waiting for subcutaneous insulin to be given; it also provides background insulin so that DKA does not recur after the insulin infusion is discontinued (remember: without SQ insulin, once the IV insulin infusion is stopped, the patient has no other insulin on board!)
    - In new-onset diabetes, the usual starting total daily dose of insulin is 0.5-1 units/kg/day, 50% of which should be given as basal insulin; in known diabetes, the patient's home dose of basal can be used.
    - For those patients on insulin pumps, they will not be on a long-acting basal insulin, so do not need to receive this unless there is a plan to *not* restart the patient's pump while they are hospitalized. Otherwise, they can simply be restarted on their pump when the IV insulin infusion is completed.

Guidelines for the management of severe DKA

Cerebral Injury in DKA

- The most common cause of death during DKA in children is clinically apparent cerebral injury, which occurs in about 0.5-0.9% of cases and manifests as sudden neurologic decline. It often occurs during the first 12 hours of DKA (sometimes even before treatment has been started) and when it is clinically apparent, the prognosis is usually poor; mortality rate is up to 21-24%. Additionally, 10-25% of survivors of cerebral injury have significant residual morbidity. The pathogenesis is incompletely understood, but may result from cerebral hypoperfusion and the effects of reperfusion, along with neuroinflammation. Cerebral *edema* is likely a consequence (rather than the cause) of cerebral injury, and often develops hours or days after the diagnosis of brain injury.
- Risk factors include:
    - Younger age; New-onset diabetes; Longer duration of symptoms
    - ***Sodium bicarbonate treatment for correction of acidosis***
    - Administration of insulin in the first hour of fluid treatment and greater volumes given in the first 4 hours
    - Increased BUN at presentation
    - Greater hypocapnia at presentation after adjusting for degree of acidosis
    - More severe acidosis at presentation
    - An attenuated rise in measured serum Na concentrations or early fall in corrected Na during therapy
    - Marked early decrease in serum effective osmolality
- Children with DKA are frequently sleepy, but warning signs and symptoms of cerebral injury include:
    - Worsening of Glasgow Coma Scale (GCS) Score
    - Slowing of heart rate, rising blood pressure, decreased O_2 saturation (Cushing's Triad)
    - *Change* in neurological status (restlessness, irritability, increased drowsiness, incontinence)
    - Headache, vomiting, focal neurological signs, dilated/unresponsive/sluggish/unequal pupils, papilledema
    - Decreasing urine output without clinical improvement or tapering of fluids
- Diagnosis does not require neuroimaging; diagnostic criteria include:
    - Abnormal motor or verbal response to pain, decorticate or decerebrate posture, cranial nerve palsy, abnormal neurogenic respiratory pattern (eg grunting, tachypnea, apneusis, Cheyne-Stokes respiration)
    - Major criteria: altered mentation, confusion, fluctuating level of consciousness, sustained HR deceleration (more than 20 bpm), age-inappropriate incontinence
    - Minor criteria: vomiting, headache, lethargy or not easily arousable, diastolic BP >90 mmHG, age <5yo
- Treatment should be initiated as soon as the condition is suspected:
    - Give Mannitol 0.5-1 gm/kg over 10-15 min and repeat if no initial response in 30 min to 2 hrs
        - Hypertonic saline (3% saline) 2.5-5ml/kg over 30 min may be an alternative or 2nd line therapy
    - Elevate the head of the bed to 30 deg and keep the head in a midline position
    - Adjust fluid administration as indicated to maintain normal BP and optimize cerebral perfusion; avoid hypotension that might compromise cerebral perfusion pressure
    - Administer oxygen as needed to maintain normal oxygen saturation
    - Intubation may be necessary if impending respiratory failure, but aggressive hyperventilation to hypocarbia (pCO_2 <22 mmHg) has been associated with poor outcome and is not recommended
    - Head CT scan should be obtained to rule out other possible intracerebral causes of neurologic deterioration or identify lesions requiring emergency neurosurgery *AFTER* treatment for cerebral injury has been started (DO NOT DELAY TREATMENT TO GET THE HEAD CT!); changes that will be detectable on head CT often occur late in the development of cerebral injury
- **CEREBRAL INJURY IS A LIFE-THREATENING MEDICAL EMERGENCY REQUIRING IMMEDIATE AGGRESSIVE INTERVENTION AND IMMEDIATE TRANSFER TO AN INTENSIVE CARE UNIT SETTING.**

Guidelines for the management of severe DKA

Monitoring and Other Recommendations

- Height and weight are both needed in order to calculate body surface area
- Vital Signs Q1 hour for at least first 12 hours, then Q2 hours; HR monitor and pulse oximetry
- Neuro checks/GCS score Q1 hour
- Strict monitoring of Intake and Output is essential (Strict I/O)
- Check blood sugar (bedside glucose) every hour while on insulin infusion
    - Use of a continuous glucose monitor in DKA has not been well-studied, but can be considered in mild DKA in accordance with current hospital policy for use of CGM in the hospitalized patients, once glucose is less than 600
- In severe DKA, pt should remain NPO in order to avoid excessive fluid administration, and decrease the risk of aspiration should consciousness be altered; for mild/moderate DKA, may consider sips of sugar-free CLD
- BMP, Magnesium, Phosphorus, beta-hydroxybutyrate initially and every 2-6 hours hours
- I-Stat-7 Q2 hours until pH >7.25, then Q4-6 hours
- After first 12-18 hrs of DKA treatment, check urine ketones every void until negative twice in a row
- Mannitol 1 gm/kg or 3% Saline at bedside (and ready to be given for acute change in mental status)
- Two peripheral IV catheters should be placed for fluid and insulin administration and for blood sampling
- Initial labs should include: Hemoglobin A1c, BMP, Mg, Phos, Beta-hydroxybutyrate, CBC, cultures if indicated (fever, etc; *leukocytosis is a common finding in DKA and does not alone indicate infection)
    - if new-onset diabetes, also measure: diabetes autoantibodies (islet cell antibody, insulin antibody, glutamic acid decarboxylase (GAD-65) antibody, ZnT8 antibody), celiac panel (total IgA and TTG), TSH and free T4 (if patient is very ill, the TSH and free T4 should wait until child is more stable to avoid abnormalities of "sick euthyroid syndrome"), insulin and c-peptide
- Call 907-563-2662, ask to speak with pediatric endocrinologist on call any time of the day or night

Prevention of DKA is key

- In patients with newly diagnosed diabetes, education of the patient, family, and care providers to recognize early signs of diabetes can lead to diagnosis of type 1 diabetes before DKA develops
- In patients with known diabetes, sick day reeducation with diabetes educator is important to discuss factors that led to DKA in this situation and how to avoid it in the future (ie urine ketone monitoring with illness or high blood glucose, avoiding insulin omission, appropriate use of insulin pump and trouble-shooting with pump problems)
- Appropriately manage sick days and ketones at home or in the hospital to prevent progression to DKA (see below)

Sick day management guide when a patient has ketones based on amount of ketones and the blood sugar			
Urine Ketones	Blood Glucose		
	<100	100-200	Over 200
Neg/Trace/Small	Push sugar-containing fluids	Push fluids (sugar and sugar-free)	Push sugar free fluids; continue to check ketones while ill; give correction dose if BG>250-300
Moderate	Push ~30-60g carBG to get BG over 200, consider mini-dose glucagon (see below)	Push ~30g carbs to get BG over 200 (recheck BG q 30-60min)	Give extra NovoLog (10% of total daily dose or 0.1 units/kg or double the BG correction dose); check BG and ketones in 2 hrs; repeat Novolog dose in 2 hrs if ketones do not decrease
Large, but well patient (not continuously vomiting, no difficulty breathing, awake)	Push fluids (30-60g carBG), consider mini-dose glucagon	Push ~30 g carbs to get BG over 180-200 (recheck BG q30-60min)	Give extra Novolog (20% of total daily insulin dose or double the BG correction); check BG and ket in 2 hrs ; repeat NovoLog dose in 2 hours if ketones do not decrease
Large, and sick pt (cont vomiting, difficulty breathing, lethargy)	Bring to ER, consider mini-dose glucagon on the way	Bring to ER Cont to push fluids if possible on the way	Bring to ER (can give an extra insulin dose while on their way to the ER if they live far away)

Total daily insulin dose approx. = 2 x Lantus/Tresiba dose

Double the correction: calculate what insulin dose would be based on their BG correction factor and give 2 x that dose

Appendix 1: Pathophysiology of DKA

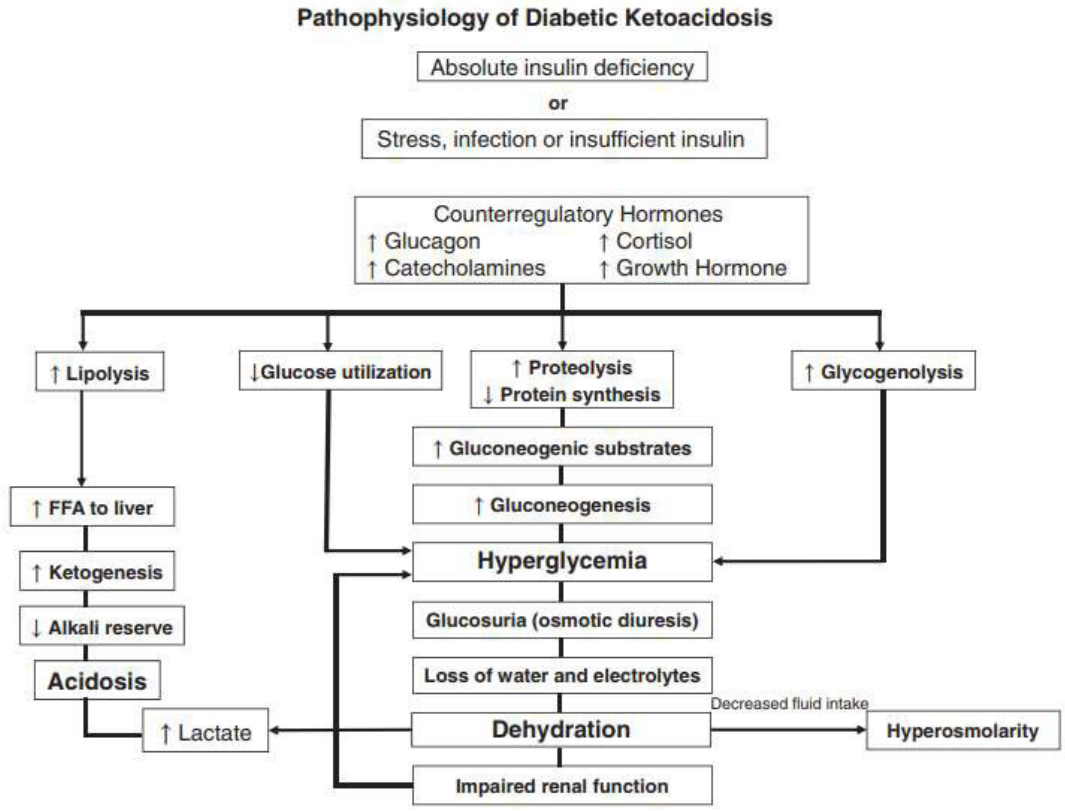

FIGURE 1 Pathophysiology of diabetic ketoacidosis. Copyright© 2006 American Diabetes Association. From diabetes care, Vol. 29, 2006:1150-1159. Reprinted with permission of *The American Diabetes Association*

Appendix 2: Fluid maintenance and replacement volumes based on body weight and an assumption of 10% dehydration

Body weight (kg)	Maintenance (mL/24 h)	DKA: give maintenance +5% of body weight/24 h	
		mL/24 h	mL/h
4	325	530	22
5	405	650	27
6	485	790	33
7	570	920	38
8	640	1040	43
9	710	1160	48
10	780	1280	53
11	840	1390	58
12	890	1490	62
13	940	1590	66
14	990	1690	70
15	1030	1780	74
16	1070	1870	78
17	1120	1970	82
18	1150	2050	85
19	1190	2140	89
20	1230	2230	93
22	1300	2400	100
24	1360	2560	107
26	1430	2730	114
28	1490	2890	120
30	1560	3060	128
32	1620	3220	134
34	1680	3360	140
36	1730	3460	144
38	1790	3580	149
40	1850	3700	154
45	1980	3960	165
50	2100	4200	175
55	2210	4420	184
60	2320	4640	193
65	2410	4820	201
70	2500	5000	208
75	2590	5180	216
80	2690	5380	224

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References:
Kuppermann et al, N Engl J Med. 2018: 378(24):2275-87
Woflsdorf et al, Ped Diab. 2018:19 (Suppl 27):155-77
Wolfsdorf et al, Diab Care. 2006:29(5):1150-59
White NH, Washington Univ in St Louis; 1989 (rev 2003)