Yukon-Kuskokwim HEALTH CORPORATION

Treatment Protocol

Pediatric Endocrine Emergency Protocols

Hypoglycemia

If low BG and cause unknown, ***GET CRITICAL SAMPLE PRIOR TO TREATMENT!***

Labs tested during hypoglycemia are critical to identifying cause and preventing recurrence.

- Serum critical sample:
  - BMP, insulin, C-peptide, Cortisol, GH
  - Free fatty acids, β-hydoxybutyrate, acetoacetate
  - Lactate, ammonia, Save serum (sulfonylureas), total and free carnitine
- At any time:
  - Acylcarnitine profile, serum amino acids
- Urine – as quickly after hypoglycemia as possible
  - Urine ketones
  - Urine organic acids
- If suspect hyperinsulinism, perform glucagon stim test (administer 0.03 mg/kg, max 1 mg) and measure lab glucose at 0, 15, and 30 minutes.

Acute Treatment: obtain critical sample and correct hypoglycemia within 10-15 minutes.

- Glucose gel per eCHAM guidelines.
- IV or IO dextrose bolus (D10% or D25%) followed by continuous infusion of dextrose IVF and frequent blood sugar checks (Q1-2h or more frequently initially)
  - D25%: 2-4 mL/kg; D10%: 5-10 mL/kg. (For neonates, give D10% 2 mL/kg.)
- If insulin-mediated, treat with glucagon 0.03 mg/kg up to 1 mg OR for patients < 20 kg give 0.5 mg IM and for patients > 20 kg give 1 mg IM.

Adrenal Insufficiency

Critical Sample before treatment: cortisol

- If suspect primary adrenal insufficiency, include ACTH, renin, aldosterone.
- If suspect CAH, include 17OH-progesterone or CAH-6b panel (send-outs).
- Also check BMP, CBC, U/A.

Treat while awaiting results.

- Normal Saline Bolus 20 mL/kg.
- Hydrocortisone 50-100 mg/m^2 IV bolus (lower end of range if less sick, higher end of range if more sick) followed by 50-65 mg/m^2/day, divided q6h
  - If no IV access, SoluCortef IM or Dexamethasone IM
  - SoluCortef 50-65 mg/m^2 IV/IM – short acting
    - At this dose, adequate mineralocorticoid activity to replace moderate doses of oral fludrocortisone (80 mg HC = 0.2 mg fludrocortisone)
  - Dexamethasone 1.5-2 mg/m^2 IV/IM—long acting
    - *No mineralocorticoid activity*
    - Does not cross react with cortisol in lab assay so can use Dex if unable to get cortisol before treatment and then do Cortrosyn stimulation test after treatment
  - SoluMedrol 10-15 mg/m^2 IV/IM–intermediate acting
    - *No mineralocorticoid activity*
- For milder presentation, ex. known diagnosis with flu symptoms, but hemodynamically stable, can skip load, use 50-65/m^2/day, divided every 6 hours.

Known adrenal insufficiency (ie CAH or hypopituitarism) and adrenal crisis

- Loading dose hydrocortisone IV or IM 50 mg/m^2 x1 then 50 mg/m^2/day divided q6h
- If BSA unknown or for more rapid dosing, can use age:

  <3 y.o.: 25 mg IM/IV bolus followed by 25-30mg/day divided q6h

  3-12 y.o.: 50 mg IM/IV bolus followed by 50-60mg/day divided q6h

  >12 y.o.: 100 mg IM/IV bolus followed by 100mg/day divided q6h
- If severely ill or unable to take PO due to continued emesis, but no IV, can give SoluCortef 30-50 mg/m^2 IM (better for CAH because has fludrocortisone activity at high doses, but only lasts about 6 hours), or Dexamethasone 1.5-2 mg/m^2 IM.
- If less ill (ie, not in crisis but needs stress doses because of fever or vomiting), can give double or triple oral dose (usually double if fever, triple if vomiting or more sick).
- Normal saline bolus 20 mL/kg/ IV then D5NS or D10NS (depending on blood sugar) at 1.5 x maintenance.
- Monitor electrolytes, BP.
- For anesthesia: begin triple dose the night before the procedure, then 30-50 mg/m^2 IV or IM on call to the OR prior to anesthesia; and continue stress doing for 24 hours after procedure.

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Hypercalcemia

Critical sample: Ca, Phos, iPTH
• Other labs: 25-OH-D, 1,25 $(OH)_2$ D, urine Ca/Cr, CBC
Treatment for severe hypercalcemia (Ca >14): same initial treatment independent of the cause
• Saline diuresis: NS bolus followed by 2.5-3 L/m^2/day
    ▫ Saline diuresis generally works rapidly, but only as long at it is continued, and usually does not normalize calcium.
• Consider calcitonin 4 units/kg IV/IM/SQ q12h
    ▫ Tachyphylaxis common (often 2nd-line therapy y
    ▫ Common side effects: nausea, vomiting, flushing
• May need bisphosphonates.
• Discontinue any medications known to cause or worsen hypercalcemia.
• Avoid immobilization.

If mild/moderate (Ca <13-14) and no contraindication to PO: 2-3 L/day water plus PO salt to promote Ca excretion.

Therapy specific for underlying disorder
• Hyperparathyroidism → parathyroidectomy
• Glucocorticoids → effective if associated with hematologic malignancy or diseases with increased 1,25 $(OH)_2$ vitamin D.

Hypocalcemia

Critical sample: Calcium, Phosphorus, Magnesium, intact PTH before treatment.
• Ca and PTH need to be simultaneous, and PTH *MUST* be obtained while Ca is low.
• Collect urine Ca/Cr while Ca low if possible.
• If there is reason to suspect low albumin, check ionized calcium or calculate corrected calcium using albumin
    ▫ Corr Ca = measured calcium + [0.8 (4-albumin)]
• Other useful labs: CMP (kidney, liver, bone function), 25-OH-D, 1,25 $(OH)_2$ D, urine Ca/Cr.

Treatment if Symptomatic - tetany, seizure, apnea, heart failure, laryngospasm.
• *Slow* (<1 ml/min) IV infusion 10% Ca gluconate 1 mL/kg
    ▫ 100 mg/ml Ca Gluconate = 9 mg/mL elemental Ca
    ▫ Cardiac monitoring (bradycardia, shortened QT_c); close attention to infusion site if not central IV (risk of tissue necrosis if peripheral IV infiltration)
• If Mg low, replace with 0.1-0.2 mL/kg 50% Mg Sulfate

If not acutely symptomatic, can do more comprehensive evaluation first to determine cause and appropriate oral treatment.

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Thyroid Storm (Thyrotoxic Crisis)

Score ≥45 → highly suggestive of thyroid storm; 25–44 →thyroid storm; and <25 → thyroid storm unlikely.

Thermoregulatory dysfunction	Score
Temperature (C)	
37-37.7	5
37.7-38.3	10
38.3-38.8	15
38.8-39.3	20
39.4-39.9	25
40	30
Central nervous system effects	
Mild - agitation	10
Moderate - delirium, psychosis, extreme lethargy	20
Severe - seizure, coma	30
Gastrointestinal-hepatic dysfunction	
Moderate - diarrhea, nausea/vomiting, abdominal pain	10
Severe - unexplained jaundice	20
Cardiovascular dysfunction	
Tachycardia (heart rate/min)	
99-109	5
110-119	10
120-129	15
130-139	20
≥ 140	25
Congestive heart failure	
Mild - pedal edema	5
Moderate - bibasilar rales	10
Severe - pulmonary edema	15
Atrial fibrillation	10
Precipitant history	
Negative	0
Positive	10

Critical Sample: **Free T4 and TSH,** run STAT
• Other labs: TBII, TSI, TPO antibodies
• Useful to measure: CMP (glucose, liver function), CBC (acute infection?), urine pregnancy test

Acute Treatment
• Oxygen
• Adrenergic blockade (if not in CHF) - goal HR<100
    ▫ Propranolol (PO 2 mg/kg/day div q6-8h or IV 0.01 mg/kg/dose (max 5mg) over 10-15 min).
    ▫ If contraindication to propranolol (ie asthma), can use atenolol (cardioselective) with caution.
• IV fluids (cooled if necessary)
• Cooling blankets
• Antipyretics should be avoided when possible.
• Sedation – phenobarbital stimulated thyroid hormone clearance.
• Hemodynamic support/treat CHF if present.

Longer term treatment:
• Block thyroid hormone synthesis and release
    ▫ Thionamides – block thyroid hormone synthesis
        ♦ PTU (propylthiouracil): black box warning in peds
        ♦ Methimazole : ~0.8 mg/kg up to 60 mg loading, then ~0.4 mg/kg up to 30 mg every 6 hours (5, 10 mg tabs)
    ▫ High Dose Iodine – blocks release of already formed thyroid hormone
        ♦ Should be delayed until 1-2 hours after thionamide, to prevent transient increase in thyroid hormone levels
        ♦ SSKI (Lugol solution) 5 drops every 6-12 hours
        ♦ Use will necessitate delay in radioactive iodine treatment if that is desired
• Block peripheral conversion of T4 to T3
    ▫ Corticosteroids (stress dose HC or equivalent)
    ▫ Propranolol
    ▫ Iodinated contrast agents

Identify and treat precipitating event causing severe decompensation.
• Infection, pregnancy, emotional stress, DKA, pulmonary embolism, CVA, trauma, hypoglycemia.

Assess for underlying cause
• Grave's disease, functioning thyroid nodule ("hot nodule").

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Treatment Protocol

Pediatric Endocrine Non-emergency Recommendations

Please remember that this is just a list of lab tests often recommend prior to seeing patients. These are not physician orders. However, they are recommended prior to specialty appointments.

Congenital Adrenal Hyperplasia (CAH): meds are often adjusted based on labs/growth/bone age
• 17-OH-P (17-OH hydroxyprogesterone) often every 3-6 months Infants/toddlers often ordered q 1-3 months. (Goal: ~300-900)
• Androstenedione: Often every 3-6 months. Infants/toddlers often ordered every 1-3 months. (Goal: w/in normal range)
• Renin Activity: Often every 3-6 months. Renin hard to obtain in villages as must be sent frozen. (Goal: w/in normal range)
• Bone age after 2-3 years of age, then annually
• Accurate height and weight measurements each visit
• F/u in endo clinic every 3 to 6 months

Newborn with + FH of CAH but no ambiguous genitalia (ie no physical s/s of CAH):
• Newborn screen after 24hrs of life (in all infants).
• Serum 17OHP around day 3-4 of life (17OHP levels are normally high during the first 2-3 days after birth but by the 3rd day, levels in healthy infants fall and levels in affected infants rise to diagnostic levels).
• Alert state newborn screening program of patient at risk of CAH.
• Measure serum electrolytes prior to hospital discharge and at 5 and 10 days of age (hyponatremia and hyperkalemia are usually not present before 7 days of age and salt-losing crisis will typically occur in the second week of life).
• After newborn is sent home, parents should be cautioned to watch for signs of salt-losing crisis including vomiting, diarrhea, lethargy, dehydration, decreased PO intake.
• If positive newborn screen or elevated 17OHP, patient should be seen immediately and consult endocrinologist on call.

Congenital Hypothyroid/Hashimoto Thyroiditis/Goiter: meds are usually adjusted based on labs
General Information
• When a med dosage change is made, labs are usually repeated in 4-6 weeks and then again before the next clinic visit.
• Under certain circumstances, a thyroid ultrasound is sometimes ordered – not routine.
• Growth records on all children with any thyroid condition should be plotted.
• Often other thyroid labs are done as part of initial workup, but depends on what the presumptive diagnosis is. (TSI, Antithyroid peroxidase AB, etc.)

Specific Labs – Goal: normal Free T4 and TSH (infants should have a free T4 at least once).

Congenital Hypothyroidism
• FT4 & TSH 2weeks after dose started.
• 0-6 Months: FT4 & TSH every month
• 6-12 Months: FT4 & TSH every 2 months
• 1-3 Years: FT4 & TSH every 3 months

Acquired Hypothyroidism
• FT4 & TSH 4-6 weeks after starting med or after dose change
• FT4 & TSH every 6 months routinely

Central Hypothyroidism (ie, hypopituitarism)
• Free T4 every 4-6 months routinely

Hypopituitarism/Septooptic dysplasia/Optic nerve hypoplasia: (any combination of deficiencies of GH, TSH, ACTH, LH/FSH, ADH)
• Labs to follow depend on deficiency
• If panhypopituitarism
    ▫ IGF-1 every 6-12 months if on GH (see below).
    ▫ Free T4 every 4-6 months (see above).
    ▫ May check BMP if concerns about inadequate adrenal hormone replacement.
    ▫ Na levels if DI depend on thirst—if intact thirst, Na level every 3-4 months; if non-intact thirst, may need Na every 2-4 weeks.
    ▫ LH/FSH pediatric, estradiol ultrasensitive or total testosterone at approximately age 12.
    ▫ Accurate height and weight plotted on growth chart.

Work-up of Short Stature
• X-ray: bone age XR left hand/wrist
• bloodwork: TSH, free T4, TTG IgA, IgA, CMP, CBC, IGF-1, IGFBP-3, ESR. Also do chromosome microarray if a girl.
• urine: urinalysis (looking for RTA)

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Pediatric Endocrine Non-emergency Recommendations

Children on Growth Hormone Injections: (GH deficiency/Turners/Noonan's/Prader-Willi Syn/SGA/Panhypopituitarism/CRF)

- Free T4 and IGF-1
  - Usually obtained q 6-12 months. Other labs including these may be done for initial diagnosis which may include GH stimulation tests.
  - GH dose will be adjusted based on IGF-1, growth pattern and weight.
- Bone age: includes left hand and wrist – please have radiology send via PACS to ANMC.
  - Initially and approximately every year.
- Accurate height and weight
  - Crucial to have correct plotting on growth record. (Lengths are done on infants and toddlers less than 2 years of age or if not able to stand well; plotted on 0-24mo WHO growth chart; heights are done when the child is over age 2 and plotted on the CDC 2-20 growth chart.)

Insulin Resistance/Obesity: goal is to prevent these children from becoming diabetic; not usually managed in endocrine clinic unless there is an endocrine condition (diabetes, prediabetes, PCOS, dyslipidemia); hypertension is managed by PCP or nephrology.

** Refer to publications in *Pediatrics*.

- Screening fasting plasma glucose, HbA1c every 2 yrs. OGTT if needed (Fasting Insulin **not** routine).
  - Fasting plasma glucose <100 is normal; 100-125 = prediabetes, >125 = diabetes.
  - OGTT-fasting plasma glucose, then drink 1.75 g/kg (max 75 g) of Glucola (within 10-15 min) and repeat plasma glucose in 2 hours.
    - Fasting 101-125 = impaired fasting glucose; over 125 = diabetes
    - 2 hour 141-199 = impaired glucose tolerance; over 199 = diabetes
  - HbA1c: 5.7% to 6.4% = prediabetes; >6.4%, likely diabetes but not necessarily diagnostic in children
- Fasting lipids initially and then per recommendation, usually every 2 years
  - If abnormal, repeat after 2 weeks but before 3 months (see below).
  - If still abnormal, dietitian referral.
- Liver function tests-AST/ALT every 2 years.
- Growth records with accurate height & weight plotted-also calculate and plot BMI.
  - Only obtain TSH & Free T4 initially if patient is showing growth deceleration.
- All patients should have initial evaluation and then monthly appointments with a dietitian whenever possible.
  - Daily activity, one hour/day with lifestyle change.
  - The more they see their primary provider and dietician, the more likely they are to comply with changes in dietary and activity levels.

Type 2 Diabetes

- At diagnosis: HgbA1C. Other labs depend on the individual case.
  - Criteria for dx of diabetes (per ADA):
    - FPG > 125 (no caloric intake for 8 hrs)
    - OR 2-hr glucose >199 during an OGTT
    - OR HbA1c >6.4% (**controversial for dx in children)
    - **the above 3 criteria require repeat testing in the absence of unequivocal hyperglycemia)
    - OR classic symptoms of hyperglycemia or hyperglycemic crisis and a random plasma glucose >199
- HbA1c every 3 months: Goal A1c <7%
- Fasting lipid panel soon after diagnosis and every 5 years if normal.
  - If abnormal, repeat after 2 weeks but before 3 months (see below).
  - If still abnormal, dietitian referral.
- Random urine microalbumin/creatinine soon after diagnosis and annually.
  - If abnormal, repeat with first morning urine MA/Cr or overnight collection; if still abnormal, referral to nephrology.
- Eye exam soon after diagnosis and annually.
- Dental exam annually.
- Dietician visit q 3-6 months.
- RN-CDE for education.

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Pediatric Endocrine Non-emergency Recommendations

Type I Diabetes Mellitus

New Diagnosis: HbA1c, BMP, c-peptide, insulin level, other labs depending on patient and presentation (for diagnostic criteria, see above; type 1 distinguished from type 2 based on presentation, physical exam, sometimes on labs such as c-peptide and diabetes antibodies)

- Hemoglobin A1C: Every 3 months (lifetime standard of care for DM)
  - This lab helps determine the overall status of blood glucose readings over a 3 month period and gives an average of all readings.
  - A1c goal is generally 7%; infants and toddlers, tolerate A1c goal of ~8%.
- Fasting Lipid Panel
  - Initial check soon after diagnosis, once blood sugars stabilized, if over 2 years old.
  - Repeat fasting lipid panel every 5 years if initial is normal (starting at 9 years old).
  - If abnormal, fasting lipid panel should be repeated at least 2 weeks later but less than 3 months later to confirm.
  - If confirmed abnormal, referral to dietician for lifestyle/diet modification.
- Thyroid and Thyroid Auto Antibodies
  - Obtain Free T4 & TSH at diagnosis and annually.
  - Antibodies not routine, but if done it includes thyroid peroxidase AB.
- Celiac screening
  - TTG IgA and total serum IgA soon after diagnosis.
  - Annually for the first 5 years, more frequent if symptoms.
- Eye exam
  - Initial eye exam soon after diagnosis to detect cataracts or major refractive errors
  - Annual eye exam should start at:
    - 9 years if 5-year duration diabetes.
    - 11 years if 2-year duration diabetes.
    - After 2 years duration if diabetes diagnosed in an adolescent.
- Urine microalbumin/creatinine screen
  - Spot urine microalbumin/creatinine annually after age 10 years.
  - If abnormal, repeat with first morning void or an overnight urine collection.
- Flu Vaccine recommended yearly.
- Dental evaluation recommended yearly.
- RN CDE referral for all aspects of Diabetes education. Work closely with CDE if patient is on Lantus + rapid acting insulin intensive regimen-ideally.
- Dietitian CDE for dietary/CHO counting/activity/insulin (learning to count carbs).
- All children should see Pediatric Endocrinologist every 3 months (may alternate depending on needs of family/primary provider).
  - Families need to know when to do Urine Ketones: if BS over 300 or if ill.

Table 8–1. Acceptable, Borderline-High, and High Plasma Lipid, Lipoprotein and Apolipoprotein Concentrations (mg/dL) For Children and Adolescents*

NOTE: Values given are in mg/dL; to convert to SI units, divide the results for TC, LDL-C, HDL-C and non-HDL-C by 38.6; for TG, divide by 88.6.

Category	Acceptable	Borderline	High+
TC	< 170	170-199	≥ 200
LDL-C	< 110	110-129	≥ 130
Non-HDL-C	< 120	120-144	≥ 145
ApoB	< 90	90-109	≥ 110
TG			
0-9 years	< 75	75-99	≥ 100
10-19 years	< 90	90-129	≥ 130

Category	Acceptable	Borderline	Low*
HDL-C	> 45	40-45	< 40
ApoA-I	>120	115-120	<115

*Values for plasma lipid and lipoprotein levels are from the National Cholesterol Education Program (NCEP) Expert Panel on Cholesterol Levels in Children. Non-HDL-C values from the Bogalusa Heart Study are equivalent to the NCEP Pediatric Panel cut points for LDL-C. Values for plasma apoB and apoA-I are from the National Health and Nutrition Examination Survey III.

†The cut points for high and borderline-high represent approximately the 95th and 75th percentiles, respectively. Low cut points for HDL-C and apoA-I represent approximately the 10th percentile.

Yukon-Kuskokwim HEALTH CORPORATION

Treatment Protocol

Pediatric Diabetic Ketoacidosis Management Protocol

General Guidelines and Definitions

Disclaimer: These are guidelines—not hard and fast rules. Some patients, such as younger children (<5 years) and poorly controlled diabetics (HbA1c >10%), may not adhere to the usual course and guidelines may need to be modified. The below categorizations of mild, moderate, and severe are not the consensus-statement published definitions, but are more "real-world" categorizations.

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 complications of DKA, and identifying and treating any precipitating event.

Clinical signs of DKA: dehydration, tachycardia, tachypnea, Kussmaul 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, beta-hydroxybutyrate ≥3 or moderate/large ketonuria

Diabetic ketosis without significant acidosis: Urine ketones moderate/large, 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 Department.
• 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-moderate DKA: Urine ketones mod/large, persistent vomiting, pH 7.2-7.3, Bicarb 10-15
Management:
• Oral or IV hydration (usually IV).
• Supplemental insulin should be used (Novolog SQ 10% of total daily insulin dose or 0.1-0.2 units/kg every 2 hours[*]) in addition to the patient's usual long-acting insulin (ie Lantus, Tresiba).
• May require admission and management with IV regular insulin infusion (0.05-0.1 units/kg/hr).

Severe DKA: Urine Ketones Large, pH <7.2, Bicarb <10 *OR* mild/moderate DKA with other organ system impairment (altered mental status, impaired renal function, respiratory distress, compromised circulation) (published definition: pH <7.1, bicarb <5)
Management:
• Admit to hospital for therapy and intensive monitoring.
• PICU status may be appropriate in some cases (altered mental status, hypokalemia, hyponatremia (after sodium corrected for glucose[†]), young age (<5 years), hypotension, per admitting physician).
• IV hydration (3 L/m^2/day)[¥]
• IV insulin (0.1 units/kg/hour).
• Intensive monitoring for improvement and signs of cerebral injury.
• Follow guidelines as given in the remainder of this protocol.

Some useful formulas:
[*]Total daily insulin dose approx. = Lantus dose x 2 (In general, Lantus dose is 50% of patient'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]

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 at least 1 hour after the fluid administration has begun.
  ▫ Initial bolus of NS or LR with 20 mL/kg over 1-2 hours.
  ▫ If poor peripheral perfusion, hypotension, or shock persist after the initial 20ml/kg, it may be appropriate to repeat with a second 10-20 mL/kg NS bolus.
• Rehydration: assume 10% dehydration and plan to replace the deficit over 24 hours. (See 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 + 20 mEq/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 if measured Na level is low and does not rise with the fall in glucose.
    ♦ If K is >6, repeat the BMP and add the K to the fluids when the K is <6; 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 + 20 mEq/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; one 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 150 and 250.
    ♦ 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).

This protocol is designed for the general use of most patients but may need to be adapted to meet the special needs of a specific patient as determined by the medical practitioner.
If comments about this protocol, please contact Jane_McClure@ykhc.org.

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Treatment Protocol

Pediatric Diabetic Ketoacidosis Management Protocol

Insulin Therapy

• "Low-dose continuous IV insulin infusion" = 0.1 units/kg/ hour regular insulin, IV (conc. 1 unit/mL).
  ▫ Start insulin 1 hour after initial fluids have been started but do not further delay in starting insulin.
• 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.)
• CONTINUE IV INSULIN INFUSION AT 0.1 UNITS/KG/HOUR UNTIL THE KETOACIDOSIS IS RESOLVED, bicarb >18, the anion gap is closed (AG <12)‡, and the patient is awake and can tolerate PO fluids.
  ▫ A lower continuous rate (0.05 – 0.08 units/kg/hr may be needed in patients with marked insulin sensitivity.
• 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 approx. 1-2 hours).
  ▫ 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.

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 early in the course 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%. 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
  ▫ 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 sodium concentrations during therapy
• 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
• **CEREBRAL INJURY IS A LIFE THREATENING MEDICAL EMERGENCY REQUIRING IMMEDIATE AGGRESSIVE INTERVENTION AND IMMEDIATE TRANSFER TO AN INTENSIVE CARE UNIT SETTING.**
• Treatment includes:
  ▫ Give Mannitol 0.5-1 gm/kg over 10-15 min and repeat if no initial response in 30 minutes to 2 hours.
    ♦ Hypertonic saline (3% saline) 2.5-5ml/kg over 30 min may be an alternative or 2nd line.
  ▫ Elevate the head of the bed to 30 degrees 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 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.

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.
• NPO until acidosis is resolved in order to strictly monitor total intake, avoid excessive fluid administration, and decrease the risk of aspiration should consciousness be altered.
• BMP, Magnesium, Phosphorus, beta-hydroxybutyrate initially and q4-6 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.
• A flow sheet with lab results and clinical response can be a useful guide to therapy.
• Initial labs should include: Hemoglobin A1c, BMP, Mg, Phos, Beta-hydroxybutyrate, 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 (do not measure insulin if patient has already been started on insulin), CBC, cultures if indicated (fever, etc; **leukocytosis is a common finding in DKA and does not alone indicate infection).
• Call 907-563-2662, ask to speak with pediatric endocrinologist on call any time of the day or night.

Yukon-Kuskokwim HEALTH CORPORATION

Treatment Protocol

Pediatric Diabetic Ketoacidosis Management Protocol

Prevention of DKA is key

• In patients with newly diagnosed diabetes, education of the public and health 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 q30-60 min)	Give extra Novolog (20% of total daily insulin dose or double the BG correction); check BG and ket in 2 hrs ; repeat Novo-Log 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

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
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Appendix 1

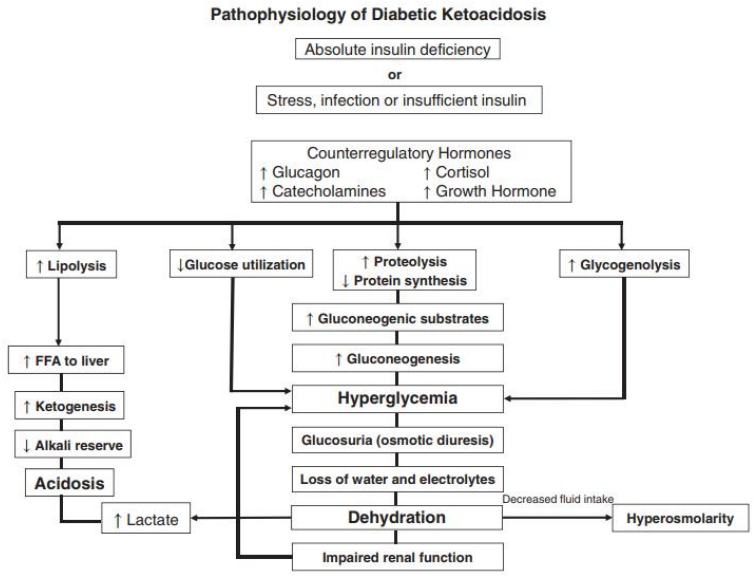

FIGURE 1 Pathophysiology of diabetic ketoacidosis. Copyright© 2006 American Diabetes Association. From diabetes care, Vol. 29, 2006:1150-1159. Reprinted with permission of *The American Diabetes Association*

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