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Diabetic Hyperglycemia and Diabetic Ketoacidosis Clinical Pathway

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Diabetic Hyperglycemia and Diabetic Ketoacidosis Clinical Pathway

Rationale:

This clinical pathway was developed by a consensus group of Johns Hopkins All Children's Hospital (JHACH) endocrinologists, hospitalists, intensivists, emergency medicine physicians, advanced practice providers, pharmacists and nurses to standardize the management of children with diabetes presenting with hyperglycemia and/or diabetic ketoacidosis (DKA). It addresses the following clinical questions or problems:

1. How to manage diabetic hyperglycemia
2. When to consider cerebral edema
3. What labs to order for new onset and established DM
4. How to use labs to guide decision making
5. When to consult Pediatric Endocrinology
6. When to give insulin
7. How to manage diabetic ketoacidosis acute phase and transition.

Background:

About 193,000 Americans ages 20 and under have diabetes (about 0.24% of the population). Nationally about 75% of new onset cases are type 1 diabetes, leaving about 25% of the population diagnosed with type 2 diabetes.

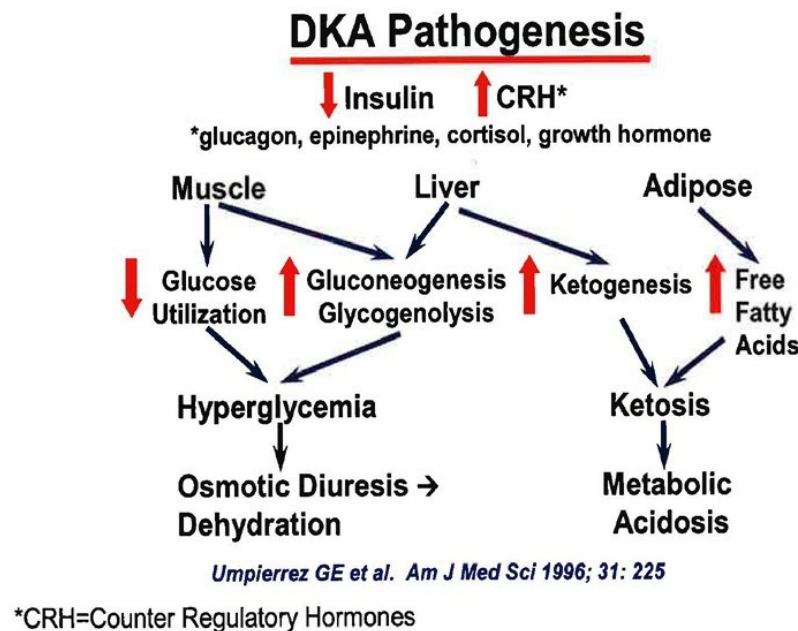
Pathogenesis of Diabetes

Diabetes Mellitus is syndrome of relative or absolute insulin deficiency that leads to disturbed metabolism of carbohydrates. This insulin insufficiency can lead to breakdown of fats as an energy source which has a byproduct of ketone production. Hyperglycemia can lead to glycosuria that can progress to dehydration. Left untreated (new onset or lack of insulin in patients with known type 1 diabetes) can progress to diabetic ketoacidosis (DKA). Patients with type 2 diabetes progress to a milder form of DKA or non-ketotic hyperosmolar coma, which is not addressed in this clinical pathway.

Diabetic Ketoacidosis (DKA)

DKA is a life-threatening acute complication of diabetes which is usually characterized by hyperglycemia, dehydration and acidosis. The cause of DKA is a deficiency of insulin, with resultant unabated gluconeogenesis and lipolysis and impaired muscle glucose utilization. This metabolic milieu generates hyperglycemia and ketosis associated with osmotic diuresis with water and electrolyte losses and metabolic acidosis. DKA is characterized by severe depletion of water and electrolytes from both the intra and extracellular fluid compartments. The magnitude of specific deficits at presentation varies depending upon the duration and

severity of illness and the amount and content of the food and fluids consumed prior to coming to medical attention.



Diagnosis of DKA:

Pediatric patients presenting with signs and symptoms of DKA such as the classic triad of polyuria, polydipsia, and polyphagia in addition to more insidious presentations such as weight loss, vomiting or abdominal pain, should be evaluated for DKA.

Laboratory Studies

Blood Glucose

Point of care blood glucose testing is an appropriate screening test for hyperglycemia and can be confirmed with serum chemistries or also when obtaining a blood gas. A blood glucose over 200 in a patient with no previous history of DKA is highly suggestive of a new diagnosis of diabetes. Patients with a history of diabetes who recently received a dose of insulin may have normal blood glucose in the setting of DKA.

Blood Gas

A venous blood gas with a pH less than 7.3 is an indicator of acidosis, suggests acute DKA. Patients with a pH ≤ 7.15 are at risk for cerebral edema.

Beta-hydroxybutyrate (BOHB)

There are two major ketone bodies that cause acidosis in DKA – Beta-hydroxybutyrate (BOHB) and acetoacetate. BOHB is the predominant ketone body in DKA, while it is detected in the blood, it is not detected with urine ketone measurements. Acetoacetate is detected in urinary ketone measurements. Acetone, which results in fruity-smelling breath, does not contribute to acidosis. Urine ketones are a poor marker of ketosis as it has a delayed clearing in the urine and may still be present when the primary markers have cleared and ketosis is actually resolved.

Beta-hydroxybutyrate levels represent the best indicator of correction of ketosis and resolution of DKA. It, unlike serum bicarb, is not affected by factors such as hyperchloremia. As the BOHB levels decrease, the pH and pCO₂ levels increase. When the BOHB levels improve, the transition to subcutaneous insulin can be planned. For those patients who were in DKA, and have resolved, once the BOHB is ≤ 1 , the patient can be transitioned to subcutaneous insulin. For those in DKA, BOHB levels should be monitored every 2 hours until ≤ 1 mmol/L.

Table 1: Comparison of Urine and Blood Ketones

Urine Ketone	Blood BOHB
Negative	<0.5 mmol/L
Trace	0.6-0.9 mmol/L
Small	1.0-1.4 mmol/L
Moderate	1.5-2.4 mmol/L
Large	2.5-2.9 mmol/L
Very Large	≥ 3.0 mmol/L

Table 2: Treatment Considerations Based on Ketones

Beta-hydroxybutyrate (BOHB)	Urine Ketone Equivalent	Likelihood of DKA	Treatment
≤ 1	(Negative/small/trace ketones)	Very low	Consider hydration, correction elevated blood glucose
> 3	(Moderate/large/very large ketones)	Very High	Evaluate for DKA

Emergency Center (EC) Initial Evaluation:

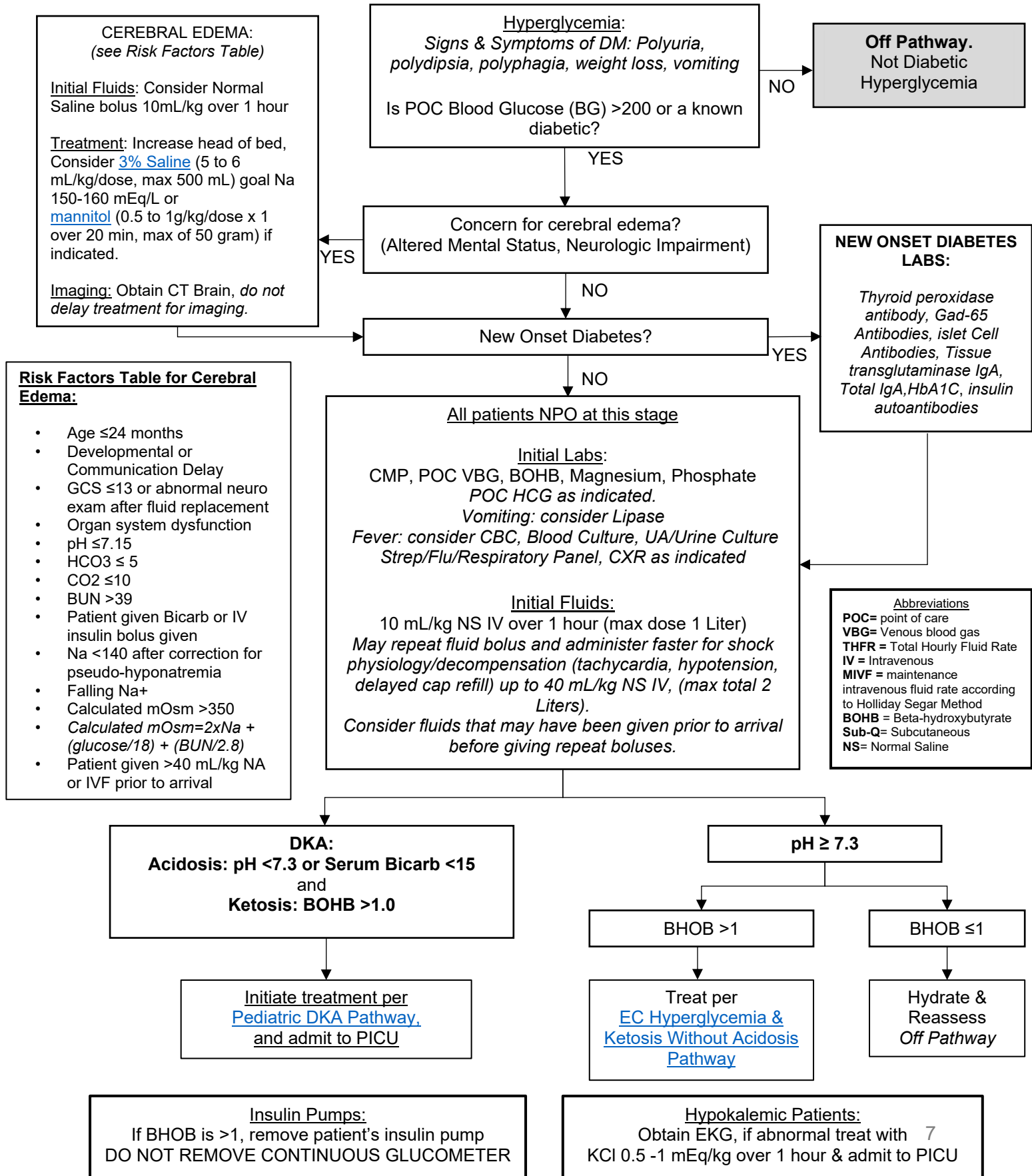
Pediatric patients commonly present to the Emergency Center with hyperglycemia. This clinical pathway only addresses those patients with an established diagnosis of diabetes or suspected new onset diabetes.

The [EC Initial Evaluation of Hyperglycemia Pathway](#) is a guide to the initial evaluation of a patient presenting to the Emergency center with a blood glucose >200mg/dl with clinical signs and symptoms of diabetes or an established diagnosis of diabetes. The pathway includes the initial laboratory studies that should be completed for screening, initial fluid hydration and a decision algorithm for guiding the provider to the appropriate algorithm for treating the patient's condition. In addition, the algorithm contains risk factors and treatment recommendations for cerebral edema, additional labs for new onset diabetes, and specific recommendations for hypokalemia.

It is important to note that hyperglycemia can be the result of stress, infection or other causes. Obtaining a thorough history and physical exam are important to make the diagnosis. Symptoms of diabetes include (but are not limited to) polyuria, polydipsia, polyphagia, weight loss, fatigue and can also include abdominal pain, vomiting, visual changes or headaches. Other presentations include slow wound healing and chronic fungal infections. Patients with obesity and skin findings such as acanthosis nigricans may have type 2 diabetes.

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**Emergency Center Diabetic Hyperglycemia - Initial Evaluation
 Clinical Pathway**

Note: Algorithm may need to be individualized depending on patient clinical condition.



EC Management of Diabetic Hyperglycemia and Ketosis without Acidosis:

Diabetic hyperglycemia is a common patient presentation in the emergency department. New onset and known patients with diabetes often present with hyperglycemia without acidosis. This algorithm is designed to guide the care of the patient who presents with hyperglycemia and ketosis with an elevated beta-hydroxybutyrate (BOHB) but is not in DKA. The pathway includes laboratory study recommendations, hydration fluids, and insulin dosing to correct the BOHB. Patients whose BOHB is not improving or are unable to tolerate PO may need further inpatient care. Patients whose ketosis (BOHB) is not corrected may need to be treated with the diabetic ketosis without acidosis algorithm.

Patients with new onset diabetes will likely be admitted for education and further management. Established patients with diabetes who cannot drink fluids may require admission, while those who are improving and stable might be appropriate for discharge from the emergency center. Discuss the disposition plan with pediatric endocrinology.

Floor Management of Diabetic Hyperglycemia:

Patients with known or new onset diabetes may present with ketosis without acidosis. Management includes hydration, laboratory studies and giving subcutaneous insulin. Typically, rapid acting insulin is given at meals (both correction dosing and carb coverage). Pediatric endocrinology should be consulted for patients with hyperglycemia and elevated BOHB whom are not in DKA as they may need correction dosing more frequently. On the floor, this can be as frequent as every four hours but may be longer between doses. Plans should be individualized with Endocrinology.

PICU Management of DKA:

Patients with known or new onset diabetes may present with moderate to severe DKA. This algorithm is designed to guide the care of the inpatient being treated in the EC and PICU. The algorithm includes a titrating hydration regimen based on the blood glucose, laboratory studies including BOHB as the primary indicator for correction of acidosis, starting long-acting insulin (basal insulin) while the insulin infusion is being run to allow for a more seamless transition, and when to contact endocrinology for guidance. The introduction of BOHB in this plan was done to provide a more accurate reflection of correction of acidosis. This is a more reliable indicator of correction than the serum bicarbonate which can sometimes correct before ketosis is fully corrected or remain low due to other causes of acidosis such as hyperchloremia even though ketosis is resolved.

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Emergency Center Hyperglycemia and Ketosis Without Acidosis Clinical Pathway

Note: Algorithm may need to be individualized depending on patient clinical condition.

Identify ketosis without acidosis:
pH $\geq$ 7.3 and BG >200 mg/dL and BOHB >1.0

Fluid Resuscitation initiated per
[EC Algorithm for Initial Evaluation of Diabetic Hyperglycemia](#)
10 mL/kg NS IV over 1 hour (max dose 1 Liter)
May repeat fluid bolus and administer faster for shock physiology/decompensation (tachycardia, hypotension, delayed cap refill) up to 40 mL/kg NS IV, (max total 2 Liters). Consider fluids that may have been given prior to arrival before giving repeat boluses.

Labs

- POC blood glucose Q2 hr
- BOHB Q2 hr

Hydration Fluids

Continue Normal Saline
Total Hourly Fluid Rate (THFR) =
1.5 x maintenance
(max 200 mL/hr) if BOHB >1.0

Patient can drink water or glucose free liquids

Consult Pediatric Endocrinology for Insulin Dosing Guidance

Patients with an insulin pump should have a new infusion site, tubing, cartridge and insulin (or new pod) at the start of the algorithm. This is to make sure patient is receiving basal insulin. All correction doses should be done by syringe injections

Rapid Acting Insulin: aspart (NovoLOG)

- Rapid acting correction insulin Sub-Q every 2 hours using correction factor dose (provided by endocrinology)
- Repeat full correction dose every 2 hours until BOHB is $\leq$ 1.0

Long-Acting Insulin: glargine (Lantus)

Per Endocrinology. Administer glargine insulin immediately if not given within last 24 hours

- Consult endocrinology for a plan to adjust glargine times to home schedule:
Usual times for most patients:
<6 years: 9am
 $\geq$ 6 years: 9pm

Abbreviations

THFR = Total Hourly Fluid Rate
IV = Intravenous
MIVF = maintenance intravenous fluid rate according to Holliday Segar Method
BOHB = Beta-hydroxybutyrate
Sub-Q = Subcutaneous
NS = Normal Saline

Disposition Plan

Patients with new onset diabetes:

- Discuss with pediatric endocrinology, likely admit using [Inpatient Hyperglycemia and Ketosis Without Acidosis Clinical Pathway](#)

Established Diabetics:

- Consider discharge home:
 - If BOHB levels drop to $\leq$ 1 and patient is tolerating PO well
 - If BOHB is improving AND patient is tolerating PO well AND is well appearing AND caregivers are comfortable with home management.
 - If patient is to be discharged, consult endocrinology for home insulin dosing recommendations and give [Managing High Blood Glucose](#) documents
- Consider admission for dehydration:
 - If patient is unable to tolerate PO or remains clinically dehydrated after the first dose of insulin
- Consider and evaluate for other etiologies for hyperglycemia
- Social Work Consult if needed (medication cost, compliance)

Inpatient Hyperglycemia and Ketosis Without Acidosis Clinical Pathway

Note: Algorithm may need to be individualized depending on patient clinical condition.

Identify ketosis without acidosis:
pH $\geq$ 7.3 and BG >200 mg/dL and BOHB >1.0

Labs

- POCT blood glucose Q3 hrs
- BOHB Q4 hrs

*Labs can be ordered using
Pediatric Subcutaneous Insulin
Order Set*

Hydration Fluids

Continue Normal Saline
Total Hourly Fluid Rate (THFR) =
1.5 x maintenance
(max 200 mL/hr) if BOHB >1.0

*Patient may eat, diet order:
Carbohydrate Controlled Diet
in Pediatric General Admission
Order Set*

Consult Pediatric Endocrinology For Insulin Dosing Guidance

*Patients with an insulin pump should have
a new infusion site, tubing, cartridge and
insulin (or new pod) at the start of the
algorithm.*

*This is to make sure patient is receiving
basal insulin. All correction doses should
be done by syringe injections*

Rapid Acting Insulin: aspart (NovoLOG)
Order using Pediatric Subcutaneous
Insulin Order Set

- Nutritional and correctional insulin
aspart (NovoLOG) for meals
 - Subcutaneous, frequency every 3
hours, using correction and carb
ratio dose provided by
endocrinology.
 - Repeat full correction dose every 3
hours until BOHB is $\leq$ 1.0

Long-Acting Insulin: glargine (Lantus)

*Per Endocrinology. Administer glargine
insulin immediately if not given within last
24 hours*

- Consult endocrinology for a plan to
adjust glargine times to home schedule:
Usual times for most patients:
 <6 years: 9am
 $\geq$ 6 years: 9pm

Abbreviations

THFR = Total Hourly Fluid Rate
IV = Intravenous
MIVF = maintenance
 intravenous fluid rate according
 to Holliday Segar Method
BOHB = Beta-hydroxybutyrate
Sub-Q = Subcutaneous
NS = Normal Saline

Continued Management & Disposition Plan

- If blood glucose is <150mg/dl and BOHB >1, consult endocrine to consider changing IVF to D5NS +20KCL
- Once BOHB is <1.0, consult endocrinology to re-establish home dosing plan

Pediatric Diabetic Ketoacidosis Clinical Pathway

Abbreviations

THFR = Total Hourly Fluid Rate
IV = Intravenous
MIVF = maintenance intravenous fluid rate according to Holliday Segar Method
BOHB = Beta-hydroxybutyrate
Sub-Q = Subcutaneous
NS = Normal Saline

Note: Algorithm may need to be individualized depending on patient clinical condition.

Does the patient meet criteria for DKA?

DKA:

1. Hyperglycemia: Blood glucose >200
2. Ketosis: BOHB >1.0
3. Acidosis: pH <7.3 or Serum Bicarb <15

HHS: pH >7.3, serum bicarbonate >15, BG >600 mg/dL, small to absent ketonemia or ketonuria, serum osmolality >320 mOsm/kg.

NO

Off Pathway, not DKA
 Discuss management strategy for HHS with Pediatric Endocrinology, **do not follow DKA algorithm**

YES

Fluid Resuscitation initiated per EC Algorithm for Initial Evaluation of Diabetic Hyperglycemia

10 mL/kg NS IV over 1 hour (max dose 1 Liter)

May repeat fluid bolus and administer faster for shock physiology/decompensation (tachycardia, hypotension, delayed cap refill) up to 40 mL/kg NS IV, (max total 2 Liters).

Consider fluids that may have been given prior to arrival before giving repeat boluses.

Labs

- POC blood glucose Q1 hr
- BOHB Q4 hr (Q2 hours if patient still in EC)

(See [Appendix A](#)) for timeline of other laboratory studies

Two Bag System

Total Hourly Fluid Rate (THFR) = **1.5 x maintenance (max 200 mL/hr)**

Order Both Non-Dextrose (Bag 1) and Dextrose Fluids (Bag 2)

1. NS + 20 mEq/L K Acetate + 20 mEq/L (14 mMol) K Phosphate
 2. D10 + ½ NS + 20 mEq/L K Acetate + 20 mEq/L (14 mMol) K Phosphate
- [Potassium amount may need adjustments based on serum levels.](#)
 - Providers must enter a calculated THFR. Nursing staff to follow Two-Bag System diagram ([below](#)) based on THFR and hourly blood glucose.

****[Click here for alternative fluids for medication shortages](#)**

Patient NPO

Continuous Insulin Infusion

Regular insulin 0.1 unit/kg/hour
 Maximum initial infusion not to exceed 10 units/hour

Long Acting Insulin: glargine (Lantus)

Lantus should be ordered and administered in the PICU unless patient transitions in the EC. Any questions consult pediatric endocrinology.

Glargine (Lantus) should be given while receiving a continuous insulin infusion. See [ordering glargine while on insulin infusion instructions](#).

- New Onset: administration of glargine to occur at the following times:
 <6 years: around 9am
 ≥ 6 years: around 9pm
- Established patients: use home schedule for dosing

Nursing to Contact Provider if:

- Patient blood glucose <100 or >450 mg/dl
- Blood glucose decreased by more than 100 mg/dL/hour
- Change in neurological status
- Critical laboratory findings
- Urine output greater than intake

Start planning for transition when BOHB <3. Place carbohydrate controlled diet ("Diet ACH") orders and insulin aspart (Novolog) orders (EC patients should have diet ordered ASAP)

Transition to Subcutaneous Insulin when Serum Bicarb ≥15 and BOHB ≤1

If patient is still in EC and DKA is corrected (BOHB ≤1) consult pediatric endocrinology for disposition

- See [DKA Transition Checklist](#)
- If glargine (Lantus) not given within last 24 hours, **GIVE ASAP PRIOR TO EATING**. Schedule can then be adjusted to patient's home schedule.
 -See [ordering glargine while on insulin infusion instructions](#)
- Confirm aspart (NovoLOG) dosing using the Provider Starting Insulin Dose Calculator. Consult Pediatric Endocrinology to review dosing and order.
- Check blood glucose **before** meal (carb controlled diet). Patient needs to consume meal within 30 minutes once they start eating.
 -**Administer aspart (NovoLOG) 15 minutes after completing meal, if no vomiting.** This Aspart (NovoLOG) dose calculation includes pre-meal blood glucose coverage AND coverage for carbohydrates consumed.
 -Immediately after subcutaneous aspart (NovoLOG) is administered OR home insulin pump is restarted* and meal insulin bolus dose given, discontinue IV regular insulin infusion and Two-Bag IV fluids
 -After initial transition dosing: at subsequent meals, for ages 6 and up, give insulin before they eat, for under age 6, give insulin after eating
- If patient appears clinically dehydrated, it is acceptable to continue Non-Dextrose Fluids or start new NS IV fluid at Maintenance IVF rate. Discontinue IV fluids when dehydration resolves.

*Patients with a home insulin pump should have a new infusion site, tubing, cartridge and insulin (or new pod) at the time of transition.

DKA Transition Checklist

Criteria for transition (**all three must be met**):

- Patient awake, hungry and ready to eat (*transition should be scheduled around a mealtime and when patient is able to be awake and drink*)
- BOHB ≤ 1
- CO₂ ≥ 15

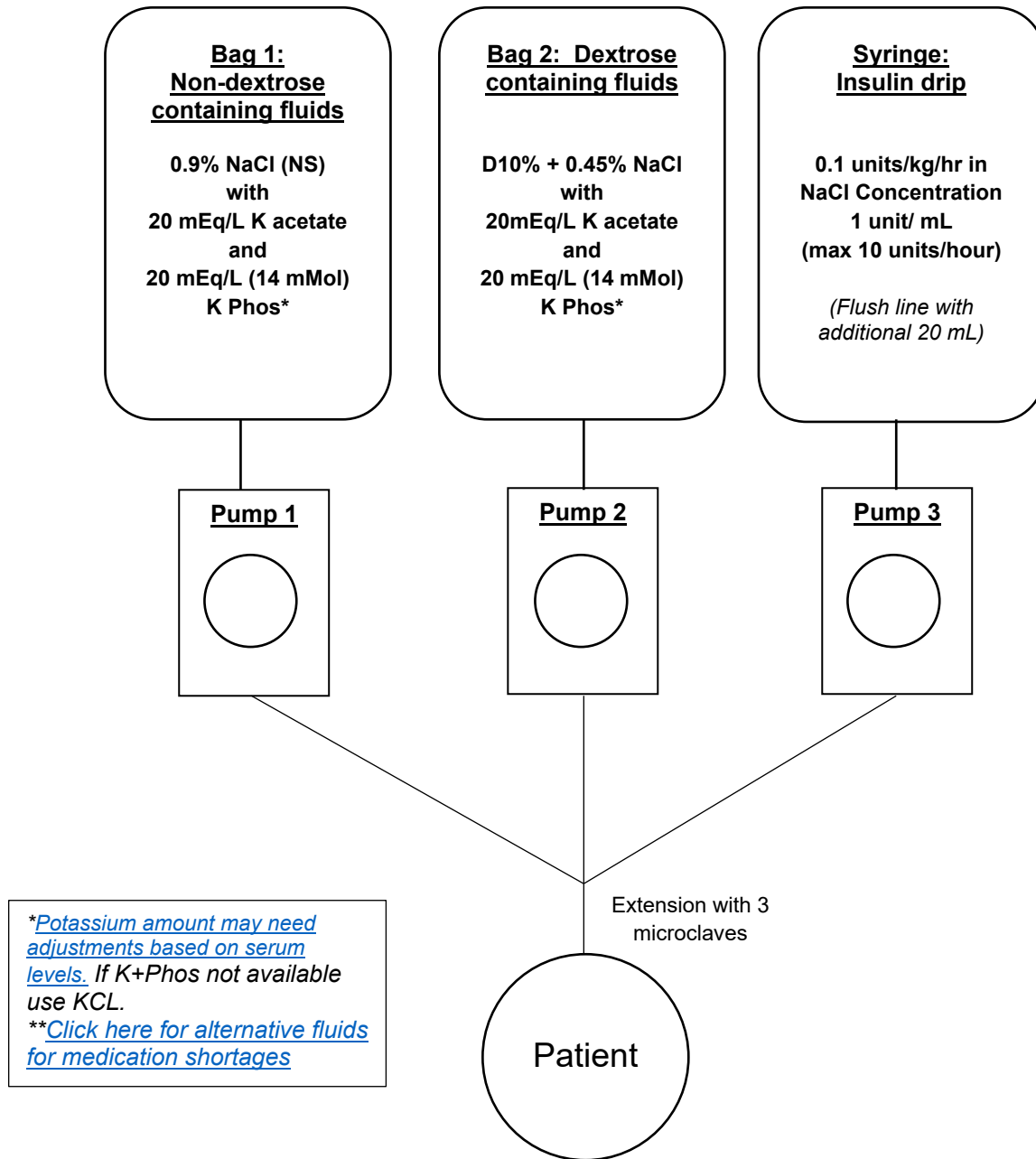
If Patient Meets All Criteria for Transition, Providers Should:

- ☐ Call Endocrinology for Rapid Acting Insulin “aspart (NovoLOG)” dosing for carbohydrates and correction.
- ☐ Place orders while on the phone with endocrinology. (*If being placed by a resident, the order should be pended and final order should be signed by Attending or APP*)
- ☐ Confirm that Long-Acting Insulin, glargine (Lantus) order is for every 24 hours. *If they have not received a dose in past 24 hours, they should get dose at the time of transition.*
- ☐ Order “ACH Diet”
- ☐ If indicated, order non-dextrose IV fluids (1/2NS or NS with 20 mEq/L K⁺ acetate + 14mMol K⁺ phos) to be continued for 12-24 hours after transition for the following patients:
 - Patient who came in with moderate to severe DKA
 - Patients who developed hypokalemia while on the DKA pathway
 - Patient who had altered mental status on arrival

Once Meal Tray Is Available, Nurses Should:

- ☐ Verify that Long-Acting Insulin, glargine (Lantus) order is to be given every 24 hours. *If they have not received a dose in the last 24 hours, they should get the dose at the time of transition.*
- ☐ Test blood glucose on point of care meter with finger stick
- ☐ Allow patient to eat meal (*meal should be consumed within 30 minutes*)
- ☐ Once patient has completed meal, Rapid Acting Insulin aspart (NovoLog) dose should be given based on the premeal blood glucose measurement and number of carbohydrates consumed.
- ☐ Stop Insulin infusion and the two bag system when patient receives Rapid Acting Insulin aspart (NovoLog)
- ☐ Provider will determine if non-dextrose IV fluids should be continued based on above criteria, refer to order

Two Bag System



Titrate according to [Two-Bag Fluid Titration Chart](#)

Monitor:

- Continuous cardiorespiratory monitor and pulse oximetry
- Hourly vital signs, glucose and neuro checks, GCS
- Labs
 - See [Appendix A](#)

Call provider for:

- Patient blood glucose <100 or >450 mg/dl
- Blood glucose decreased by more than 100 mg/dL/hour
- Change in neurological status
- Critical laboratory findings
- Urine output greater than intake

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Two-Bag Fluid Titration Chart

RN to print form and fill in to titrate the mL/hour based on the Total Hourly Fluid Rate (THFR) and percentage

Total Hourly Fluid Rate (THFR) = _____ mL/hour		
Serum Glucose (mg/dL)	Non-Dextrose Fluid % of total IVF = ____ mL/hour	Dextrose Fluid % of total IVF = ____ mL/hour
>350	100% = _____ mL/hour (1 x THFR = mL/HOUR)	0% = ____ 0 ____ mL/hour OFF
300-350	75% = _____ mL/hour (0.75 x THFR = mL/HOUR)	25% = _____ mL/hour (0.25 x THFR = mL/HOUR)
250-299	50% = _____ mL/hour (0.5 x THFR = mL/HOUR)	50% = _____ mL/hour (0.5 x THFR = mL/HOUR)
200-249	25% = _____ mL/hour (0.25 x THFR = mL/HOUR)	75% = _____ mL/hour (0.75 x THFR = mL/HOUR)
100-199	0% = ____ 0 ____ mL/hour OFF	100% = _____ mL/hour (1 x THFR = mL/HOUR)
<100	Notify provider as they will need to place an order to increase the THFR to 125% for dextrose containing fluid.	

Cerebral edema and DKA:

The mortality associated with DKA ranges from 0.15-0.3% with cerebral edema accounting for the vast majority of these fatalities. The incidence of cerebral edema among patients with DKA ranges 0.5-0.9% with an associated mortality of 21-24% and significant morbidity among survivors.

Cerebral edema may develop at any time during the treatment of DKA, although typically, it occurs 4-12 hours into treatment. There is evidence to suggest that many patients who present in DKA may have mild, subclinical cerebral edema. Because of this, it is important to be judicious with initial fluid boluses, starting with Normal Saline at a dose of 10 mL/kg (max dose of 1 Liter) unless clinical symptoms of shock or hypovolemia are present. Demographic factors associated with an increased risk of cerebral edema (all of which are likely to reflect DKA severity at presentation) include:

- Young age
- New onset diabetes mellitus

All healthcare providers should be aware of signs and symptoms of cerebral edema:

- Headache in conjunction with other neurological signs
- Alterations in neurological status (restlessness, irritability, increased drowsiness, incontinence, deterioration of GCS)
- Specific neurological signs can include cranial nerve palsies, anisocoria, asymmetric facies, or posturing, double vision
- Progressive heart rate slowing, rising blood pressure, and irregular respirations (Cushing's triad)

Management of DKA-associated cerebral edema should occur as soon as the condition is suspected. **Do NOT delay treatment to obtain imaging.**

Management of Cerebral Edema:

- Provide a bolus of 3% saline, 5 to 6 mL/kg (max 500 mL) over 30 minutes, however can be administered over 10-15 minutes at the provider's discretion for acute decompensation. Targeting a serum sodium (Na) of 150-160 mEq/L.
- If there is no response to 3% saline, or if 3% saline is not immediately available, administer mannitol 0.5 to 1 g/kg IV over 20 minutes (max 50 grams) and repeat in 30 minutes if there is no improvement in neurological status.
- Obtain a CT scan of the head to assess for cerebral edema, thrombosis, and intracranial hemorrhage if the patient is stable to travel to radiology.
- In general, avoid endotracheal intubation and mechanical ventilation unless the patient is exhausted, hypoventilating for any reason or if airway protective reflexes are lost. If endotracheal intubation and ventilation are undertaken for patients with DKA, target a PaCO₂ appropriate for estimated HCO₃, and treat with great caution those presenting with arterial pH < 7.

IV Fluids:

Fluid and electrolyte losses for patients presenting in DKA are common, and secondary to both glycosuria and osmotic diuresis, which are a result of prolonged or significant hyperglycemia. The acute sodium losses associated with diuresis can contribute to intravascular dehydration while more prolonged losses can contribute to intracellular dehydration. This volume depletion can also trigger counter-regulatory hormones, which will continue to contribute to insulin resistance². As a result, patients will have fluctuating shifts in their fluid and electrolyte deficiencies, which should be considered carefully in the management of patients presenting in DKA.

During [acute DKA management](#), maintenance rates are calculated using the Holliday Segar Method and are based on the measured weight at the time of admission and are NOT to be based on Ideal Body Weight (IBW). The Total Hourly Fluid Rate (THFR) is 1.5 times the maintenance rate, with the maximum initial rate at 200 mL/hour. This rate can be adjusted based on patient response to hydration based on clinical judgement.

Caution is advised when patients present with [symptoms of cerebral edema](#), and fluid hydration should be more judicious.

Insulin:

Clinical providers and prescribers should be comfortable with the various insulin types, their onset, peak and duration. Though there are many preparations, the following chart includes the commonly used insulin types at JHACH. This includes a rapid acting insulin, which is given subcutaneously for glycemic correction and/or carbohydrate coverage. Long-acting insulin is given once daily for better overall glycemic control in-between meals and overnight.

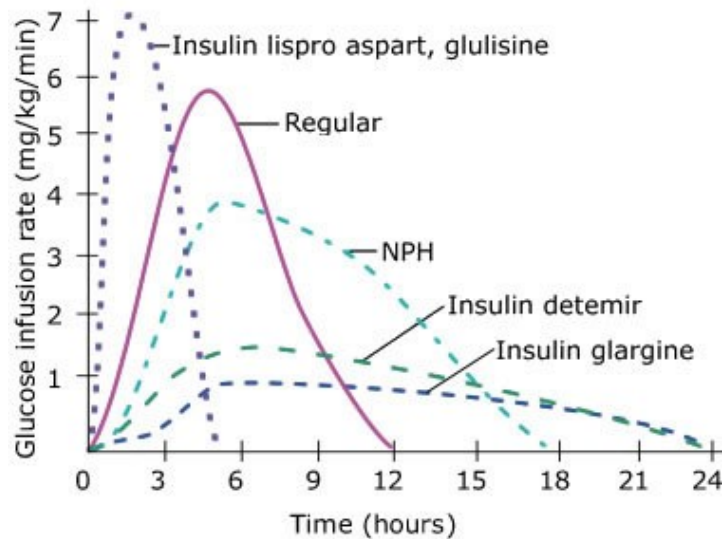
Infants under 1 year of age are given diluted insulin to ensure accurate dosing.

Commonly Used Insulins at JHACH

This chart is not all inclusive. Please refer to [Appendix B](#) for a more list of several types of insulin available in the United States

Insulin Type (Trade name)	Onset	Peak	Duration
Rapid Acting			
insulin aspart (NovoLOG)	10-20 min	30-90min	3-5 hours
Long Acting			
insulin glargine (Lantus)	1 hour	No peak	20-26 hours

Activity Profiles of Different Types of Insulin



Insulin Drips

Patients in DKA should be started on an insulin drip per the [Pediatric Diabetic Ketoacidosis Clinical Pathway](#). IV insulin dosing should be based on the measured weight at the time of admission and are NOT to be based on Ideal Body Weight (IBW). Per national recommendations, pediatric patients should not receive intravenous (IV) insulin boluses, as it has been shown to increase their risk of complications such as cerebral edema.

Potassium amount in IV fluids may need adjustments based on serum levels.

	Non-Dextrose Fluid	Dextrose Fluid
Potassium level <3.0	NS + 30 mEq/L K Acetate plus 30 mEq/L (21 mMol) K Phosphate	D10 + ½ NS + 30 mEq/L K Acetate + 30 mEq/L (21 mM) K Phosphate
Potassium level 3.1-5.5	NS plus 20 mEq/L K Acetate plus 20 mEq/L (14 mMol) K Phosphate	D10 + ½ NS + 20 mEq/L K Acetate + 20 mEq/L (14 mMol) K Phosphate
Potassium level >5.5	(Normal Saline) NS	D10 + ½ NS

Medication Shortages

There have been national drug shortages of potassium containing fluids such as K Acetate and K Phosphate.

- If K Acetate is not available then use an equal dose of K Phosphate to replace
- If K Phosphate is not available, then use an equal dose of K Acetate to replace
- If neither are available, the next best option would be K Chloride however patients will have an increased risk of becoming hyperchloremic, and the serum CO₂ may not fully correct as a result. If the BOHB is ≤ 1 then consult endocrinology for early transition.

Transition and Subcutaneous Insulin

Patients who are no longer in DKA will transition from an IV insulin drip to getting rapid acting subcutaneous insulin. The details of how to transition can be found in the "[Transition box](#)" of the [Pediatric DKA Clinical Pathway](#) or providers can follow the [DKA Transition Checklist](#)

There are two common reasons patients are given subcutaneous insulin. The first reason is to correct hyperglycemia (correction coverage), and the second is to account for ingested carbohydrates (carbohydrate coverage). Patients can be given insulin for correction coverage only or carbohydrate coverage only, OR both doses at the same time, depending on the clinical scenario. The dose of insulin will vary, depending on the patient's blood glucose and/or the amount of carbohydrates ingested.

Table 3: When To Cover for Carbohydrates and Correct for High Blood Glucose

	<i>Blood Glucose Testing</i>	<i>Correction Coverage</i>	<i>Carbohydrate Correction</i>
New Onset Patients	Before meals, bedtime and 2am, the bedtime and 2 am blood glucose should not be covered as a routine.	At meals (Breakfast, Lunch, Dinner) Bedtime coverage may be added for older patients at the discretion of pediatric endocrinology	At meals (Breakfast, Lunch, and Dinner)
Patient with known diabetes	Before meals, bedtime and 2am, the bedtime and 2 am blood glucose should not be covered as a routine.	At meals (Breakfast, Lunch, Dinner) Bedtime coverage may be added for patients on higher insulin dosing.	At meals (Breakfast, Lunch, and Dinner). Snack coverage may be added for patients on higher insulin dosing.

Correction Coverage Using Correction Factor:

JHACH is transitioning patients from sliding scale to correction factor. The correction factor is a much more sensitive way to dose insulin. With the correction factor formula, we have the ability to adjust how many points the blood glucose will come down with each unit of insulin. We also can adjust the target based on the age of the patient. The nursing insulin dose calculator allows the doses to be calculated for carbs and correction, then added together and rounded for more accurate dosing.

A Correction Factor (sometimes called insulin sensitivity) is how much 1 unit of rapid acting insulin will generally lower blood glucose over 2 to 4 hours when patients are in a fasting or pre-meal state. This is an estimate and may need to change as the baseline dose changes. Expect variations, since sensitivity to insulin varies from one person to the next, sometimes 1 unit will lower blood glucose by more, and other times 1 unit will lower it by less.

The patient also has a target that can be changed based on the patient's age and allow much tighter control of the blood glucose. When patients are hyperglycemic, a correction dose of insulin should be given. This is often referred to as "correction coverage". Established diabetic patients will have a correction factor assigned to them, which is calculated by endocrinology, however new onset diabetics will need a correction factor calculated in order to determine the right insulin dosing.

When determining insulin doses for patients with known diabetes, review dosing with the patient and compare it with the last outpatient clinic note in Endocrinology. The ordering provider should consult with endocrinology to verify the dosing at the time of ordering. Pharmacy will use the last outpatient note when verifying dosing. **The Provider Starting Insulin Dose Calculator is only for patients with new onset, it is NOT to be used for known patients.**

How to Calculate a Patient's Correction Factor:

Patients with New Onset Diabetes, Not in DKA

- All patients not in DKA start at 0.5-0.7units/kg/day
 - *Total daily dose calculation*
 - $\text{Total daily dose (TDD)} = \text{body weight (KG)} \times \text{factor based on age below}$
 - Age ≤ 5 years = 0.5 units/kg/day
 - Age 6 years = 0.6 units/kg/day
 - Age ≥ 7 years = 0.7units/kg/day
- *Basal Insulin calculation*
 - Take half of TDD as basal insulin glargine (Lantus)
- *Carb coverage and correction for high blood glucose dose calculations*
 - *Calculate carb ratio*
 - Carb ratio = 500/TDD
 - *Calculate Correction Factor*
 - Correction factor = 1800/TDD
- *Target Blood glucose*
 - <1 year old target = 200
 - 1 to < 5 years old target = 150
 - 5 years and up target = 100

Patients with New Onset Diabetes, Presented in DKA

- All patients in DKA have doses based on age:
 - *Total daily dose calculation*
 - $\text{Total daily dose (TDD)} = \text{body weight (KG)} \times \text{factor based on age below}$
 - *TDD for patients presenting in DKA:*
 - $\leq$ Age 5 years = 0.5 units/kg/day
 - Age 6 years = 0.6 units/kg/day
 - Age 7 years = 0.7 units/kg/day
 - Age 8 = 0.8 units/kg/day
 - Age 9 = 0.9 units/kg/day
 - Age ≥ 10 =1.0 units/kg/day
- *Basal Insulin calculation*
 - Take half of TDD as basal insulin glargine (Lantus)
- *Carb coverage and correction for high blood glucose dose calculations*
 - *Calculate carb ratio*
 - Carb ratio = 500/TDD
 - *Calculate Correction Factor*
 - Correction factor = 1800/TDD
- *Target Blood glucose*
 - <1 year old target = 200
 - 1 to < 5 years old target = 150
 - 5 years and up target = 100

How to use the patient's Correction factor to calculate the insulin dose:

- Take the current blood glucose minus the target blood glucose and divide by the calculated correction factor

Example:

Correction factor = 1 unit for every 35 points

Target = 100

Blood glucose is 205

Correction dose = $(205-100)/35 = 3$ units

See [Appendix C](#) for calculation examples for patients with new onset diabetes not in DKA and [Appendix D](#) for patients with new onset diabetes who present in DKA.

Carbohydrate Ratios and Insulin Carbohydrate Coverage:

When patients ingest carbohydrates, they will need to account for it by taking an appropriate dose of insulin. The carbohydrate ratio helps patients know how much insulin to take for a certain number of carbohydrates. This varies for each patient and is usually assigned by the pediatric endocrinologist.

How to calculate the insulin dose using a patient's carbohydrate ratio:

- Add up the total amount of carbohydrates to be eaten with a meal (dietary should provide).
- Divide that number by the calculated carbohydrate ratio from [Appendix E](#).

Example:

Patient's Carbohydrate ratio = 1 unit for every 12 grams of carbs

Patient eats 60 grams of carbohydrates

Dose of Insulin for carbohydrate = 60 grams/12 (ratio)= 5 units

Infants under 1 year of age may only need correction coverage using diluted aspart (NovoLog) in combination with long-acting insulin. For those that correction alone is not enough, then carbohydrate counting for infants <1 year of age and on tube feeding/ formula or breastmilk will be calculated differently than for those who are able to eat solids. For those not eating solids, the dietitian will have a dietitian consult to help with the carb counting plan.

Breastmilk and formula have a specific carb count of 6-8 grams per 100 mL. If the formula is fortified, the carb count will change. Consultation of the dietician and endocrinology is required to assure clarity in management of patients requiring formula or breastmilk carb counting. The dietitian will enter carb amount per 100 mL into the diet order.

When to give insulin for Carbohydrate Coverage

Patients $\leq$ 5 years-old or picky eaters	• Test the blood glucose before the meal • Allow the child to eat • Calculate the insulin dose with the pre-meal blood glucose and total carbohydrates eaten. • Give the total dose of insulin immediately <u>after</u> the meal.
Patients 6 years and older and reliable eaters	• Test the blood glucose before the meal • Have the patient/family plan the meal (carbohydrate amount to be eaten). • Calculate the insulin dose with the pre-meal blood glucose and total carbohydrates planned to be eaten. • Give the total dose of insulin <u>before</u> the meal.

Giving Glargine (Lantus) While Patients Are On An Insulin Infusion

For known patients:

- Glargine (Lantus) should be given at their regularly scheduled time with the same dose.
 - Consult pediatric endocrinology if there are concerns about timing of scheduling the dose or if patient is on an insulin pump.
 - **If the home dose of glargine (Lantus) is >0.6 units/kg, please consult pediatric endocrinology to verify dosing before ordering.**
- If patient is ready to transition off of the insulin drip before their dose of glargine (Lantus) was scheduled to be given, it should be given at the time of transition per the [transition plan](#).

For patients with new onset diabetes:

Glargine should be scheduled based on the following times.

- <6 years: 9am
- ≥ 6 years: 9pm
- Consult pediatric endocrinology if there are concerns about timing of scheduling the dose.

New onset dosing of glargine (Lantus) is based on the following:

Age	Dose
≤ 5 years	= 0.25 units/kg
6 years	= 0.3 units/kg
7 years	= 0.35 units/kg
8 years	= 0.4 units/kg
9 years	= 0.45 units/kg
≥10 years	= 0.5 units/kg

If calculated dose of glargine (Lantus) is greater than 80 units, consult pediatric endocrinology for dosing plan.

Documentation Reminders:*Patient Status:*

For all patients admitted for acute management of DKA treated on the above protocol, select inpatient status

Documentation Recommendations:

It is important to document

- the type of diabetes and whether neurologic complications are present:
 - E10.10 Type 1 DM with DKA without coma
 - E10.11 Type 1 DM with DKA with coma
 - E11.01 Type 2 DM with hyperosmolar coma
- weight loss and any malnutrition present
- abnormal vital signs (tachycardia, etc.)
- abnormal lab values (hypokalemia, hyponatremia, etc.)
- if acute kidney injury or acute kidney failure is present

References:

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3. Inward CD, Chambers TL. Fluid management in diabetic ketoacidosis. *Archives of Disease in Childhood* 2002;86:443-444.
4. Johns Hopkins Children's Center DKA Pathway
5. Seattle Pathway
<https://www.seattlechildrens.org/healthcare-professionals/gateway/clinical-resources/pathways/>
6. Wolfsdorf, J. I., Glaser, N., Agus, M., Fritsch, M., Hanas, R., Rewers, A., ... & Codner, E. (2018). ISPAD Clinical Practice Consensus Guidelines 2018: Diabetic ketoacidosis and the hyperglycemic hyperosmolar state. *Pediatric diabetes*, 19, 155-177.

Outcome Measures:

- Number of insulin-related safety events- Kevin Lewis
- Length of stay in the EC
- Time to therapeutics
 - Time to Long-acting insulin eg glargine (Lantus)
 - Time to Short acting insulin eg aspart (NovoLOG)
 - Time to NS Bolus
- Length of stay in hospital
- Length of stay in PICU
- Errors in transition (by chart review)- Kevin Lewis

Diabetic Hyperglycemia and Diabetic Ketoacidosis Clinical Pathway
Johns Hopkins All Children's Hospital

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Electrolyte frequency changed to match order sets.

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Disclaimer:

Clinical Pathways are intended to assist physicians, physician assistants, nurse *practitioners* and other health care providers in clinical decision-making by describing a range of generally acceptable approaches for the diagnosis, management, or prevention of specific diseases or conditions. The ultimate judgment regarding care of a particular patient must be made by the physician in light of the individual circumstances presented by the patient.

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Appendix A- Hourly Lab Plan for a Patient in DKA (PICU)

DKA Algorithm	Confirmed DKA: NS Begins Hour 0	Hour 1	Hour 2	Hour 3	Hour 4	Hour 5	Hour 6	Hour 7	Hour 8	Hour 9	Hour 10	Hour 11	Hour 12
Time													
POC Glucose	X	X	X	X	X	X	X	X	X	X	X	X	X
RFP	X				X				X				X
VBG	X												
BOHB	X		X (EC)		X		X (EC)		X		X (EC)		X
IVF	NS 10 mL/kg over 1 hour	Start 2 bag system, Titrate per algorithm (max 200 mL/hour)											
Insulin	Order Insulin infusion	Start insulin infusion at 0.1 units/kg/hour, Do not titrate (max 10 units/hour)											
Neurological Exams	X	X											
I/O's	X	X											

Appendix B- Insulin Types in the United States

Insulins Available in the United States

Generic Name (U-100, except where noted)	Brand Name	Manufacturer	Form	Delivery	Cloudy or Clear	Onset	Peak	Duration
Rapid Acting								
Insulin aspart	NovoLog	Novo Nordisk	analog	syringe; prefilled, 300-unit disposable pen; reusable pen with 300-unit cartridges; pump	clear	10 to 20 min.	30 to 90 min.	3 to 5 hours
Insulin human	Afrezza	Sanofi	human	Inhaler with 4- and 8-unit cartridges	N/A (inhaled powder)	10 to 20 min.	12 to 15 min.	3 hours
Insulin glulisine	Apidra	Sanofi	analog	syringe; prefilled, 300-unit disposable pen; pump	clear	10 to 20 min.	30 to 90 min.	3 to 5 hours
Insulin lispro	Humalog*	Eli Lilly	analog	syringe; prefilled disposable pen; reusable pen with cartridges; pump	clear	10 to 20 min.	30 to 90 min.	3 to 5 hours
Regular								
Regular	Humulin R*	Eli Lilly	human	syringe	clear	30 to 60 min.	2 to 4 hours	5 to 8 hours
Regular	Novolin R	Novo Nordisk	human	syringe	clear	30 to 60 min.	2 to 4 hours	5 to 8 hours
Intermediate Acting								
NPH	Humulin N	Eli Lilly	human	syringe; prefilled, 300-unit disposable pen	cloudy	1 to 3 hours	8 hours	12 to 16 hours
NPH	Novolin N, ReliOn (Walmart)	Novo Nordisk	human	syringe	cloudy	1 to 3 hours	8 hours	12 to 16 hours
Long Acting								
Insulin detemir	Levemir	Novo Nordisk	analog	syringe; prefilled, 300-unit disposable pen	clear	1 hour	No peak	20 to 26 hours
Insulin glargine	Lantus	Sanofi	analog	syringe; prefilled, 300-unit disposable pen	clear	1 hour	No peak	20 to 26 hours
Ultra Long Acting								
Insulin glargine U-300	Toujeo	Sanofi	analog	prefilled, 300-unit disposable pen	clear	6 hours	No peak	36 hours
Mixtures								
50% lispro prota- mine/50% insulin lispro	Humalog Mix 50/50	Eli Lilly	analog	syringe; prefilled, 300-unit disposable pen	cloudy	10 to 15 min.	Varies	10 to 16 hours
75% lispro protamine (NPL)/25% insulin lispro	Humalog Mix 75/25	Eli Lilly	analog	syringe; prefilled, 300-unit disposable pen	cloudy	10 to 15 min.	Varies	10 to 16 hours
70% aspart prota- mine/30% insulin aspart	NovoLog Mix 70/30±	Novo Nordisk	analog	syringe; prefilled, 300-unit disposable pen	cloudy	5 to 15 min.	Varies	10 to 16 hours
70% NPH/30% Regular	Humulin 70/30	Eli Lilly	human	syringe; prefilled, 300-unit disposable pen	cloudy	30 to 60 min.	Varies	10 to 16 hours
70% NPH/30% Regular	Novolin 70/30±, ReliOn (Walmart)	Novo Nordisk	human	syringe	cloudy	30 to 60 min.	Varies	10 to 16 hours
Less Commonly Used Insulins								
regular U-500	Humulin R U-500 +A	Eli Lilly	human	syringe	clear	30 min.	8 hours	Up to 24 hours
Insulin lispro U-200	Humalog U-200*	Eli Lilly	analog	prefilled, 600-unit disposable pen	clear	15	30 to 90 min.	3 to 5 hours
Key								

* Note difference between Humalog and Humalog U-200, + Note difference between Humulin R and Humulin R U-500, ± Note difference between Novolin 70/30 (70% NPH/30% Regular) and Novolog Mix 70/30 (70% aspart protamine/30% aspart), A U-100, U-200, U-300, and U-500 are different concentrations of insulin. Higher concentrations are typically used in very insulin-resistant people.

Appendix C - Insulin Dosing Calculations for Patients with New Onset Diabetes NOT in DKA

This is a guide to help determine starting doses of insulin for patients with new onset diabetes.

- Starting insulin doses are based on the patient's weight, age, and whether they present with DKA or not in DKA.
- Insulin dosing for patients ranges from 0.5 units/kg/day up to 1.0 units/kg/day depending on whether they present in DKA or not

Calculating Starting Insulin Doses for New Onset Diabetes: Not in DKA

- Patients not presenting in DKA start at 0.5-0.7units/kg/day
 - *Total daily dose calculation*
 - Total daily dose (TDD) = body weight (kg) x factor based on age below
 - Age $\leq$ 5 years = 0.5 units/kg/day
 - Age 6 years = 0.6 units/kg/day
 - Age $\geq$ 7 years = 0.7 units/kg/day
- *Basal Insulin calculation*
 - Take half of TDD as basal insulin i.e. glargine (Lantus)
- *Carb coverage and correction for high blood glucose dose calculations*
 - *Calculate Carb Ratio*
 - Carb ratio = 500/TDD
 - *Calculate Correction Factor*
 - Correction factor = 1800/TDD
- *Target Blood glucose*
 - <1 year old target = 200
 - 1 to <5 years old target = 150
 - 5 years and up target = 100

Example calculation : 10 year old not in DKA with new onset diabetes

Weight = 40 kg

1. TDD = 40 x 0.7
2. TDD = 28 units
3. Glargine (Lantus) dose = 0.5 x 28 units = 14 units
4. Carb ratio = 500/28 = 17.8 (round UP to 20)
5. Correction = 1800/28 = 64.3 (round UP to 65)
6. Target = 100
7. Correction dose = (blood glucose – 100)/65

Appendix D - Insulin Dosing Calculations for Patients with New Onset Diabetes in DKA

Calculating Starting insulin doses for new onset diabetes: Patient Presented in DKA

- All patients in DKA have doses based on age:
 - *Total daily dose calculation*
 - Total daily dose (TDD) = body weight (kg) x factor based on age below
 - *TDD for patients presenting in DKA:*
 - Age $\leq$ 5 years = 0.5 units/kg/day
 - Age 6 years = 0.6 units/kg/day
 - Age 7 years = 0.7 units/kg/day
 - Age 8 years = 0.8 units/kg/day
 - Age 9 years = 0.9 units/kg/day
 - Age $\geq$ 10 years = 1.0 units/kg/day
- *Basal Insulin calculation*
 - Take half of TDD as basal insulin glargine (Lantus)
- *Carb coverage and correction for high blood glucose dose calculations*
 - *Calculate Carb Ratio*
 - Carb ratio = 500/TDD
 - *Calculate Correction Factor*
 - Correction factor = 1800/TDD
- *Target Blood glucose*
 - <1 year old target = 200
 - 1 to <5 years old target = 150
 - 5 years and up target = 100

Example calculation: 10-year-old presented in DKA with new onset diabetes

Weight = 40 kg

1. TDD = 40 x 1.0
2. TDD = 40 units
3. Glargine (Lantus) dose = 0.5 x 40 units = 20 units
4. Carb ratio = 500/40 = 12.5 (round UP to 15)
5. Correction = 1800/40 = 45 (round UP when necessary)
6. Target = 100
7. Correction dose = (blood glucose – 100)/45

Appendix E: Common Correction Factors & Common Carbohydrate Ratios

Common Carb Ratios

(Expressed as 1:4, 1:8, 1:15 etc)

1 unit for every 4 grams of carbs
1 unit for every 5 grams of carbs
1 unit for every 6 grams of carbs
1 unit for every 7 grams of carbs
1 unit for every 8 grams of carbs
1 unit for every 10 grams of carbs
1 unit for every 12 grams of carbs
1 unit for every 15 grams of carbs
1 unit for every 18 grams of carbs
1 unit for every 20 grams of carbs
1 unit for every 22 grams of carbs
1 unit for every 25 grams of carbs
1 unit for every 30 grams of carbs
1 unit for every 40 grams of carbs
1 unit for every 60 grams of carbs

Common Correction Factors

20
25
30
35
40
45
50
55
60
65
70
75
80
100
120
150
200
250
300

When calculating the carb ratio and correction factor, if the value does not fall on the exact number, the higher number is used. Example calculated carb ratio 1:10.8 would be rounded up to 1:12.

Target Blood glucose

- *<1 year old target = 200*
- *1 to < 5 years old target = 150*
- *5 years and older target = 100*