Primary Objective
To create and implement an evidenced based pathway that guides treatment of diabetic ketoacidosis (DKA) from initial evaluation through transition to subcutaneous insulin.

Definitions
• DKA is defined as the triad of blood glucose greater than 200 mg/dL, metabolic acidosis (defined as pH less than 7.3 or serum bicarbonate less than 15), and ketosis in the blood or urine.\(^1\)
  • Mild DKA is defined as pH of 7.2-7.3 or serum bicarbonate of 10-15.
  • Moderate DKA is defined as pH of 7.1-7.2 or serum bicarbonate of 5-10.
  • Severe DKA is defined as pH of less than 7.1 or serum bicarbonate less than 5.
  • DKA at any pH which is associated with mental status changes, such as focal neurologic deficits, GCS less than 14, severe headache or hypotension is also automatically classified as severe.
• Successful treatment of DKA includes volume resuscitation and correction of ketoacidosis, while also managing co-morbid diagnoses.
• Cerebral edema is a rare, but potentially catastrophic consequence of DKA, accounting for 60-90% of all DKA deaths.\(^2,3\)
  It occurs in 0.39-1% of episodes of DKA with a mortality rate of 20-30% and similar rates of morbidity in survivors.\(^1,2,3,4\)

DKA Pathophysiology
Diabetic ketoacidosis results from a complete or relative deficiency of insulin in comparison to counter-regulatory hormones, including glucagon, epinephrine, growth hormone and cortisol. Complete deficiency or circulating insulin occurs in new-onset type 1 diabetes mellitus, as well as those who did not take insulin. Alternately, during times of stress, such as illness or trauma, a relative insulin deficiency can occur due to elevations in counter-regulatory hormones. In this pathophysiologic state, the body rapidly undergoes glycogenolysis and gluconeogenesis in the liver, while simultaneously having impaired peripheral glucose uptake and increasing peripheral lipolysis. This results in severe hyperglycemia, hyperosmolality and ketone production, causing osmotic diuresis, dehydration, ketoacidosis, and electrolyte derangements. Clinical signs and symptoms include nausea, vomiting, abdominal pain, tachypnea and/or deep breathing (Kussmaul respirations), changes in mental status from confusion to coma.\(^1\)

Recommendations/Goals
1. Develop a standard initial evaluation and treatment plan to provide evidence-based care while improving time to initiation of insulin infusion, as well as initial patient disposition.
2. Standardize laboratory monitoring during insulin infusion with the addition of serum beta-hydroxybutyrate in an attempt to shorten the time patients require an insulin infusion.
3. Implement transition to subcutaneous insulin guidelines and decrease delays in transition to SQ insulin through standardized transfer from the pediatric ICU to the floor and development of a transition order set.

Rationale (safety, quality, cost, delivery, engagement and satisfaction)
Safety: Will be improved by limiting practice variation and reducing gaps in management, which increase the risk for harm.
Quality: Will be enhanced by reducing unnecessary patient transfers, shortening the duration of therapy on an insulin drip, and standardizing the transition to subcutaneous insulin.
Cost: Will be reduced by limiting redundant laboratory tests and total laboratory tests, as well as decreasing the duration of therapy on an insulin drip.
Engagement: The pathway is created and implemented with support of providers and staff across the institution who care for patients with DKA.
Satisfaction: We will improve satisfaction by providing high quality, evidence-based care, as well as limiting frequency of new needle sticks for lab draws.

Disclaimer: Pathways are intended as a guide for practitioners and do not indicate an exclusive course of treatment nor serve as a standard of medical care. These pathways should be adapted by medical providers, when indicated, based on their professional judgement and taking into account individual patient and family circumstances.
Implementation items
- Diabetic Ketoacidosis Initial Evaluation Algorithm
- Revised ED Epic DKA Order Set
- Diabetic Ketoacidosis Inpatient Algorithm
- Revised Inpatient Epic DKA Order Set
- Creation of a DKA Transition Order Set

Metric Plans
1. Utilization of the DKA pathway during the initial evaluation and medical management. Will measure based on use of diabetic ketoacidosis order set, goal >60%.
2. Decrease time from arrival to the Emergency Department to initiation of insulin drip by 20% in 2019.
3. Decrease rate of patient transfers (PICU->floor or floor ->PICU) in the first 6 hours to less than 2% in 2019.
4. Decrease length of time on an insulin drip measured as time of insulin drip initiation to discontinuation by 5% in 2019.
5. Decrease cost per case day of DKA care by 5% in 2019.

DKA Pathway Committee Follow-up Plan
1. Meet quarterly for 6 months, then yearly.
2. Review data for adherence to pathway, patient transfers, length of insulin drip, length of stay and transitioning to SQ insulin.

THE DIABETIC KETOACIDOSIS CLINICAL CARE PATHWAY

Clinical care guidelines:
Intended for patients:
- Known diabetes or new onset diabetes with clinical concerns for diabetic ketoacidosis

Excludes:
- Patients with corrected serum sodium > 160
- Patients with an initial serum glucose >1000
  - Consult Endocrinology for recommendations, as these are concerning for possible hyperglycemic hyperosmolar syndrome
- Patients with hemodynamic instability
- Patients with concern for cerebral edema

Emergency Department
All patients with suspected or potential DKA should first be assessed in the Emergency Department. Direct admissions to the floor are discouraged, unless patient is being transported via CHMC critical care transport team and meets the Med Surg floor admission criteria (see below).

Clinical Assessment
1. Triage as minimum of level 2 and notify provider immediately
2. Vital signs and neurologic checks q1H
3. If patient uses an insulin pump, discontinue and remove the device.
Emergency Department (cont.)

Initial Management and Laboratory Studies
1. Manage airway, breathing, circulation (ABC’s) or comorbid problems as appropriate. Evaluate mental status by Glasgow Coma Scale (GCS).
   a. If patient has hemodynamic instability or acute respiratory failure, manage off this pathway.
2. Obtain STAT EPOC on arrival to ED room
3. If EPOC is consistent with DKA (pH < 7.3 and/or HCO3 < 15) - obtain stat BMP, VBG and serum beta-hydroxybutyrate with placement of two PIVs.
4. Evaluate for co-morbid diagnoses
   a. Consider additional studies such as lipase, CBC, blood culture, etc. based on clinical assessment
5. Order and infuse 10ml/kg (up to 1L) normal saline bolus over 1 hour.
   a. If patient is hypotensive or demonstrates signs of shock, additional fluid should be given to stabilize the patient’s cardiovascular status, as appropriate, and the patient should be managed off pathway.
6. Also order (for pharmacy to prepare) from the ED DKA order set
   a. Insulin infusion at 0.1 units/kg/hr to start after completion of normal saline bolus
   b. If initial serum potassium 3.5-5.9 mEq/L
      i. “S” fluid bag: 0.9% sodium chloride with 20mEq/L potassium acetate and 20mEq/L potassium phosphate
      ii. “D” fluid bag: 10% dextrose with 0.9% sodium chloride and 20mEq/L potassium acetate and 20mEq/L potassium phosphate.
   c. If initial serum potassium ≥ 6.0 mEq/L
      i. “S” fluid bag: 0.9% sodium chloride
      ii. “D” fluid bag: 10% dextrose with 0.9% sodium chloride
      iii. Addition of potassium should occur when patient demonstrates adequate urine output for age
   d. If initial serum potassium is < 3.5 mEq/L
      i. Begin potassium repletion during the first hour of fluid resuscitation and prior to starting the insulin infusion.
      ii. “S” fluid bag: 0.9% sodium chloride with 30mEq/L potassium acetate and 30mEq/L potassium phosphate
      iii. “D” fluid bag: 10% dextrose with 0.9% sodium chloride and 30mEq/L potassium acetate and 30mEq/L potassium phosphate.
   e. Order total fluid rate as 1.5x maintenance with sliding scale based on serum glucose values

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7. Repeat blood glucose hourly.
   a. Goal is decrease blood glucose by less than 100 mg/dL per hour.
8. Confirm DKA and determine severity based on initial BMP and VBG results, as well as a positive serum beta-hydroxybutyrate.
   a. Calculate corrected sodium [serum sodium + (serum glucose - 100) / 100 x 1.6]. If corrected sodium is greater than 160, strongly consider discussing plan of care with Endocrinology. Patients should not be managed on this pathway if corrected serum sodium is greater than 160.
9. After completion of fluid bolus, start insulin infusion and fluid infusion with combination of “S” and “D” fluids based on orders.
10. Page Pediatric Hospitalist or Intensivist for admission based on placement criteria below.
11. Repeat BMP +/- VBG every 2 hours while in the Emergency Department.
Patient Placement
Criteria for PICU admission – based on initial BMP and VBG lab value and current neurologic status
1. Mild or Moderate DKA (pH < 7.3 or bicarbonate < 15) and any of the following:
   • Significant headache
   • Mental status abnormalities or GCS < 14
   • Hemodynamic instability
   • Age < 24 months
2. Severe DKA (pH < 7.1 or bicarbonate < 5)
   i. Patients who are clinically stable with biochemically severe DKA should receive care in the ICU and monitoring for 12 hours or more before transfer to the floor.
      1. Note: ICU-level care is the combined time patient is receiving DKA management including transport, ED and PICU.
      2. If patient remains stable for 12 hours of ICU care with improving biochemical markers, transfer to the floor is encouraged to avoid delays in the transition to SQ insulin.
*Strongly consider PICU admission for any patient less than 5 years of age or with corrected serum sodium > 160.

Transport Team
Initial assessment and continued management - Per transport team policy.
1. Confirm the diagnosis by reviewing the outside hospital’s labs and repeat EPOC lab on arrival.
2. Review management including volume of fluid resuscitation given by the outside hospital.
3. Notify Medical Control provider (MCP) for management during transport.

Disposition - Med/Surg vs PICU
1. Per patient placement definition listed above as well as discussion with MCP and pediatric hospitalist on call.

Inpatient Med/Surg
Clinical Assessments
1. Perform admission evaluation, including ABC’s and neurologic assessment (GCS)
2. Repeat vital signs every 2 hours and neurologic checks with vitals while on an insulin drip
3. If patient develops any of the following, escalate care based on clinical appropriateness, and follow recommendations for treatment outlined in the cerebral edema section below until intensivist or transfer to the PICU is available.
   a. Significant headache
   b. Mental status abnormalities or GCS < 14
   c. Focal neurologic deficits
   d. Elevated blood pressure and bradycardia

Initial Management and Laboratory Studies
1. Review workup and treatment from Emergency Department or referring facility. Verify isotonic fluid bolus has been completed - 10ml/kg (up to 1L) normal saline bolus over 1 hour.
   a. If patient is directly admitted via CHMC transport team, it is strongly encouraged that a licensed provider be present for bedside handoff when the patient arrives.
2. Continue or initiate insulin infusion and two-bag system for rehydration
   a. Insulin infusion at 0.1 units/kg/hr
   b. If most recent serum potassium is 3.5-5.9 mEq/L
      1. “S” fluid bag: 0.9% sodium chloride with 20mEq/L potassium acetate and 20mEq/L potassium phosphate
      2. “D” fluid bag: 10% dextrose with 0.9% sodium chloride and 20mEq/L potassium acetate and 20mEq/L potassium phosphate.
   c. If most recent serum potassium ≥ 6.0 mEq/L
      1. “S” fluid bag: 0.9% sodium chloride
      2. “D” fluid bag: 10% dextrose with 0.9% sodium chloride
      3. Addition of potassium to “D” and “S” bags should occur when patient demonstrates adequate urine output for age
   d. If initial serum potassium is < 3.5 mEq/L
      1. Begin potassium repletion during the first hour of fluid resuscitation and prior to starting the insulin infusion.

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Inpatient Med/Surg (cont.)

3. Repeat blood glucose hourly and adjust fluids based on table – goal is decrease blood glucose by less than 100 mg/dL per hour.
   a. If blood glucose is falling >100 mg/dL per hour, increase “D” bag rate by one additional step from what the table indicates.
   b. If blood glucose < 100, increase “D” bag dextrose concentration to D12.5%. Pause the insulin drip and repeat blood glucose every 15 minutes until blood glucose is > 120 mg/dL, then resume the insulin drip.
   c. Do not decrease the insulin infusion rate unless unable to maintain blood glucose > 100 mg/dL on D12.5% fluids or serum glucose is falling > 100mg/dL despite dextrose infusion.

1. **Note:** an insulin rate less than 0.05 U/kg/hr will fail to correct diabetic ketoacidosis

4. Repeat BMP every 2 hours for two checks then, if improving, every 4 hours with serum beta-hydroxybutyrate until discontinuation of the insulin drip.
   a. Calculate corrected sodium [serum sodium + (serum glucose - 100) / 100 x 1.6].
   b. If serum potassium falls to < 3.5, consider:
      1. Increasing “D” and “S” bag fluids to include 30 mEq/L potassium phosphorus and 30 mEq/L potassium acetate
      2. If failing to improve, further treatment can include decreasing the insulin infusion rate and/or giving a potassium repletion (oral vs IV depending on the patients ability to tolerate).

5. Recommend obtaining serum magnesium and phosphorus levels every 8 hours if initial values are normal. If initial values are abnormal or the patient has more severe illness, consider obtaining every 4 hours with routine labs.
   a. Treatment of hypophosphatemia is not indicated unless severe and/or chronic
   b. Treatment of hypomagnesemia is deferred to the licensed provider

**Transition to subcutaneous insulin**

1. Patient is ready to transition when one of the following has been met:
   a. Serum HCO3 > 15 and serum beta-hydroxybutyrate ≤ 1 mmol/L AND able to tolerate oral intake OR
   b. Serum HCO3 > 17 with normal anion gap AND able to tolerate oral intake

2. Utilize the DKA transition order set to standardize insulin drip transition
   a. Place order “Discontinue insulin drip”
   b. Allow patient to order meal and calculate carbohydrates.
   c. Once food has arrived and immediately prior to eating:
      1. Check blood glucose.
      2. Give long-acting and short acting insulin **OR** if patient has insulin pump, family to insert new pump site and restart insulin pump, including basal rate and giving a bolus for food and/or blood sugar.
         1. If patient < 5 years old or concerns about nausea, consider post-meal dosing of short-acting insulin.
   3. Allow patient to eat meal

4. Turn off the insulin drip and IV fluids 30 minutes after subcutaneous insulin given or restarting the insulin pump.
   1. If blood glucose < 100, consider continuing “D” bag for 15 minutes after discontinuation of insulin infusion.

5. If patient is able to tolerate oral intake, we suggest setting an oral fluid goal over continuation of IV fluids for rehydration.
   1. Continue IV fluids based on patient hydration status and toleration of oral intake.
Cerebral Edema

Cerebral edema accounts for the majority of morbidity and mortality associated with pediatric type 1 diabetes mellitus. It typically develops within the first 12 hours of treatment, although it can be present at presentation to the hospital or develop greater than 12 hours into treatment. The exact mechanism is not understood, but may include cytotoxic edema, vasogenic edema, and/or osmotic edema from fluid therapy. Risk factors for cerebral edema include age less than 5, new onset diabetes, and severe acidosis. **Modifiable risks** include rapid drop in blood sugar caused by insulin bolus, initiation of insulin drip before the one hour fluid resuscitation is completed, rapid or aggressive fluid bolus(es) or bicarbonate bolus. 1,2,3,4

**Clinical Findings Concerning for Cerebral Edema**

1. Headache and/or vomiting
   - Specifically if these first occur or worsen during the treatment of DKA.
2. Irritability, lethargy, or change in mental status
3. Elevated blood pressure and decreased heart rate
4. Incontinence
5. Pupillary reflex changes or cranial nerve palsy
6. Abnormal respiratory pattern or decreased oxygen desaturation
7. Decorticate or decerebrate posturing

**Treatment of Cerebral Edema in DKA**

1. Activate Code
2. Evaluate and manage airway, breathing and circulation
3. Elevated head of bed to 30 degrees
4. Decrease IV fluid rate by one-third while maintaining adequate circulation
5. Obtain rapid bedside blood glucose
6. Give Mannitol 0.5-1.0 g/kg IV over 20 minutes by PIV or 3% hypertonic saline 5mL/kg (preferably by central line), followed by continuous 3% saline infusion.5
7. After patient has been stabilized, obtain CT head to assess for cerebral edema vs alternate diagnoses, such as venous sinus thrombosis or intracranial hemorrhage.
8. Neurosurgery consult for possible placement of ICP monitoring device

**Discharge Criteria**

1. Reason for DKA identified and addressed as well as successfully transitioned to sub-cutaneous insulin regimen
2. Patient and/or caregiver has demonstrated ability to complete diabetes education, perform self-monitoring of blood glucose, independently calculate insulin doses, administer insulin, identify and treat hypoglycemia and ketonuria
3. Appointments with Endocrine and PCP (if needed) scheduled
4. All diabetes supplies and prescriptions filled as needed

**Pathway Development Team**

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**Literature**