Diabetic Ketoacidosis (DKA)

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DKA definition: Elevated glucose, presence of ketones, metabolic acidosis (triad) + dehydration, with absolute or relative insulin deficiency → increase counter regulator hormones → breakdown of fat and muscle. Not a hyperosmolar state like Hyperglycemic Hyperosmolar State (HHS).

Epidemiology:

- Most common at onset Type 1 DM, recurrent episodes common
- Can occur in Type 2 DM. More often affects young
- Death can be related to cerebral edema or the precipitating trigger/illness for the DKA.
- Mortality < 1%, significantly lower than mortality of HHS

Triggers (The "I's"):

- ***I***nitial (new onset) disease
- ***I***nsulin omission (adherence, access, absorption)
- ***I***nfection
- ***I***schemia (ACS, stroke)
- ***I***ntra-abdominal (pancreatitis, cholecystitis, ischemic bowel, pregnancy)
- ***I***ngestions (ETOH, substance abuse, meds-steroids, antipsychotics, thiazides, pentamidine),

Pathophysiology:

- 3 causes of increased glucose: Gluconeogenesis, Glycogenolysis, Impaired glucose utilization
- Increase glucose + deficiency of insulin + stress (trigger) → increases the secretion of glucagon, catecholamines, cortisol, and growth hormone (counter-regulatory hormones) → promotion of lipolysis → increases FFA delivery to the liver → FFA converted by free fatty acyl CoA into ketones

Clinical presentation:

- Develops over hours to days; not days to weeks, like HHS.
- Polyuria, Polydipsia, Polyphagia, Fatigue, Muscle cramps (from Acidosis), Flushed facial appearance, Kussmaul's respirations and dyspnea (from acidosis) → Nausea and vomiting → Abdominal pain, Dehydration → Hypotension, Shock, Altered consciousness/Coma

Workup:

- Basic metabolic panel (Mg, phos, calcium), urinary glucose, serum & urine ketones, ABG.
- Consider: Infectious workup, CBC, cultures, CXR, urine culture, telemetry, UDS, amylase (can be increased even without pancreatitis), lipase, troponin, EKG, pregnancy test, CT head

Results:

- Elevated anion gap > 12+ moderate, severe; pH< 7.3
- Sodium can be low or high depending on degree of water loss
- Correction of initial low → Sodium 1.6 increase in Na for every 100 increments of glucose over initial 200 mg/dL
- Presence of urinary ketones (Beta-hydroxybutyrate may not be detected on urine dipsticks)

- Glucose elevated but usually much lower than HHS
- Potassium can be high or low. If presenting K is high, patients are usually still total body K depleted and K rapidly falls as acidosis is corrected.

Treatment:

- **Volume resuscitation:** initially IV NS, rate depends on clinical scenario; change fluids to D5 1/2 NS, when glucose less than 200mg/dL (Fluid deficits usually 5-7 L in DKA compared to HHS 8-10 L)
- **Monitor:** glucose hourly, basic chemistry profile (anion gap), plasma osmolality, and venous pH every two to four hours. Monitor BP, urine output.
- **Replace electrolytes**: Potassium replacement when Potassium < 5.3
    - No routine phosphate replace, unless Phos < 1.0
    - No clear role for HCO3 replace (unless pH<6.9, potassium life threateningly high)
- **Insulin**
    - Insulin lowers blood glucose by decreasing hepatic gluconeogenesis and lowers ketones by reducing lipolysis and glucagon release.
    - IV regular insulin: 0.14 units/kg/hour without bolus after fluid resuscitation (or 0.1 units/kg/hour with bolus of 0.1 units/kg), only use SQ if ***mild DKA***.
    - ***Do not start insulin unless K+ > 3.3-*** concerns for arrhythmia. When glucose reaches 200 mg/dL, consider decreasing the insulin infusion rate to 0.02 to 0.05 U/kg per hour
    - When starting SQ insulin, make sure there is clinical improvement and the ability to tolerate oral intake. There should be a 2 hour overlap of IV drip and SQ insulin.

End point of treatment:

- Closed gap < 12, BS <200, and subcutaneous insulin already begun
- Most patients will develop a non-gap acidosis (unless CKD V, ESRD) due to resolving ketoacidosis after gap is closed.
- Ketonuria may persist for more than 36 hours due to the slower removal of acetone.

DKA in atypical patients (AKA: DM 1.5, atypical DM)

- DKA presenting in patients who are not completely insulin deficient
- Features similar to Type 2: more common in obese, Hispanic or African-American, Native-American, associated with + Fam Hx, low prevalence of auto-antibodies, possible to eventually be treated without insulin
- Features similar to Type 1: often with short onset, ketosis formation,
- Quick correction, initially insulin is required but may not be needed long-term.
- May be helpful to obtain C-peptide

Clinical Pearls:

1) DKA and Hyperosmolar state (HHS) are disease on the same spectrum, but their clinical presentation and pathophysiology, and thus, their treatment differ.

2) DKA is an acidosis from a deficiency or relative deficiency of insulin which leads to a metabolic acidosis. The fluid deficits are not as severe as those seen in hyperosmolar state and DKA can occur at much lower glucose levels than seen in HHS.
3) The initial evaluation of DKA must include a careful search for an underlying trigger (infection, cardiac disease) and timely replacement of intravascular volume, correction of electrolytes and administration insulin.

References: Kitabchi AE, Umpierrez GE, et al. **Hyperglycemic Crises in Adult Patients With Diabetes. A consensus statement from the American Diabetes Association** *Diabetes Care July 2009 vol. 32 no. 7 1335-1343*