What is the clinical spectrum of DKA and HONKC?

- Diabetic ketoacidosis and hyperosmolar coma represent the extremes of a clinical spectrum of uncontrolled DM with hyperglycemia with variable levels of ketoacid accumulation (DKA) and hyperosmolality (NKH). This is due to lack of insulin (deficiency or resistance) and excess glucagon.
  - Hyperglycemia is a result of impaired peripheral glucose utilization due to insulin deficiency and increased hepatic gluconeogenesis due to excess glucagon and to a lesser extent insulin deficiency.
  - Ketoacid production is a result of increased free fatty acid production due to enhanced lipolysis from insulin deficiency and altered hepatic metabolism of FFA due to excess glucagon facilitating FFA entry into the mitochondria where converted to ketoacids. These ketoacids are β-hydroxybutyrate (main ketone, especially in early DKA, NOT picked up with nitroprusside test) and acetoacetate (rising pH favors the formation of this acid, should be strongly positive in late DKA, picked up by nitroprusside test.)

- Clinical variability is common, patients with type 2 DM can get DKA, while those with type 1 DM can be hyperosmolar. It is known that much lower levels of insulin are needed to suppress lipolysis than to promote glucose utilization. It is postulated that fat and muscle cells may have different sensitivities insulin effects. A combination of the above leads to the clinical spectrum.

Clinical pearls:
- ALWAYS look for precipitating factor-infection, ischemia, insufficient insulin, stress, meds
- Kussmaul breathing (think pH <7.2), abdominal pain 30 %, vomiting 80%, if febrile look for ID
- Prognosis determined by osmolality

What about the serum osmolality and its complications?

- Plasma osmolality is determined by solutes that are restricted to ECF = 2Na + Glu/18 + Bun/2.8, the normal difference between the calculated and measured should be 10-15.
- If the osmolar gap is elevated, evaluate for the presence of other osmolytes such as mannitol, isopropyl alcohol, ethylene glycol, ethanol, methanol, and in DKA acetone.
- Hyperosmolality leads to the osmotic shift of water out of cells causing intracellular dehydration and shrinkage, in the brain this leads to neurological deficits and coma, seen with calculated osmolality above 340.
- Remember, when replacing fluids, do not use hypertonic solutions because will worsen osmolality.

Why do you develop the non-gap acidosis in the recovery phase of DKA?

- Anion gap is determined by the negative charges on plasma proteins (usually albumin) using the following equation, Na- (Cl + HCO3), normal 7-13. Delta-delta gap determined by the presence of a concomitant non-gap acidosis or metabolic alkalosis, (AG-12) + HCO3; if >24 alkalosis, <22 acidosis.
- AG becomes elevated when excess anions (MUDPILES) accumulate and are buffered by extracellular HCO3 (creating the anion gap). Excess acids are also buffered by non-bicarbonate intracellular and bone buffers (does not raise AG). Of note, ketoacid anions are also excreted in urine as Na and K salt (in exchange for chloride retention) which lowers the AG (especially in normal functioning kidneys), balancing the effect of intracellular buffering.
- To restore normal acid base balance, sufficient alkali needs to be present. In DKA, there is a net deficit of bicarbonate because it’s precursor (ketone anions) have been excreted and the remaining anions once converted back to bicarbonate are drawn into cells and bones to replenish buffer stores. Thus, with initial treatment, a hyperchloremic non-gap acidosis always observed.

Why such crazy electrolyte abnormalities?

- Sodium, MUST correct for hyperglycemia. For every 100 mg/dl of serum glucose above 100, add 1.6 to the sodium. This is due to osmotic movement of water out of cells creating a pseudohyponatremia. However, hyperglycemia induced osmotic diuresis promotes both water and sodium loss. Water loss is in excess of Na and in normal kidneys, this will result in hypernatremia and severe hyperosmolality.
Potassium, net deficit of 3-5mg/kg due to multiple factors: urinary loss with osmotic diuresis, maintenance of electroneutrality with ketonuria, and GI losses. However, usually falsely normal or elevated because of cellular shifts seen with buffering of protons inside cells (K leaves for neutrality), osmotic movement of water out of cells promotes passive potassium exit out of cells and insulin deficiency (promotes uptake of potassium into cells).

Begin to replace potassium when K < 4.5, add 20-40 MEQ to ½ NS.

Why is important to use normal saline aggressive fluid rehydration in the initial treatment of DKA?
- Average water deficit is 10% TBW or between 5-10 liters. This marked fluid deficit is due to the glucose induced osmotic diuresis and possibly GI losses with vomiting.
- Fluid repletion corrects intravascular fluid deficits, lowers plasma osmolality, reduces plasma glucose via increasing urinary glucosuria, and decreases glucagon and insulin resistance.
  - NS initial fluid of choice: 1 liter/hr x 3-4 hrs, then 250-500 cc/hr 2-4 hrs, then 100-250cc/hr.
  - Change to ½ normal saline if Na >150 or if adding KCL to bag. (Do NOT add KCL to NS because will create hyperosmolar fluid that will increase osmolality).
  - Start D5 ½ NS when blood glucose <250.
  - Stop fluids when patient is eating and drinking.

How do you administer insulin?
- Insulin without fluids is dangerous, will trigger movement of glucose and water into cells thus worsening intravascular hypovolemia and hypernatremia.
- Initial: insulin IV bolus, dose 0.1 unit/kg or 10 units is reasonable. Goal to saturate receptors.
- Maintenance: insulin drip at 5 units/hour, check sugar every hour, goal is to decrease serum glucose by 50-200 mg/dl/hour. If not at goal, adjust rate as needed to achieve this goal.
- Once serum glucose <250 mg/dl and D5 ½ NS is initiated, decrease drip, approximate 1 unit/hr is needed for 100 cc/hr saline infusion.
- Start SQ insulin when AG is closed, give ½ of maintenance dose, about 1 hr prior to d/c infusion.
- Note, the only difference is SQ vs. IV is the rapidity that serum glucose and ketones fall in the first two hours, however after this time, no difference is DKA resolution.

Why NOT HCO3 therapy?
- May dampen the acidemic stimulus to hyperventilate, increase serum PCO2, which then crosses the blood brain barrier and neurologic deterioration.
- May slow the rate of recovery of ketoacidosis, in dogs increased hepatic ketogenesis.

References:
Up to date, 2002.