Pathophysiology of Ketoacidosis

- Hyperglycemia and accelerated ketogenesis occur when there is an absolute or relative deficiency of insulin, and relative excess of glucagon, cortisol, growth hormone, epinephrine
- Nitroprusside reaction:
  - Used for detection and semiquantification of plasma, serum and urinary ketones
  - Detects acetone and acetoacetate
  - (when measuring serum ketones, an additive metabolizes B-OHB to acetoacetate in a known/1:1 manner, and this value is reported)
- When insulin therapy is instituted, B-OHB is metabolized to acetoacetate
  - Subjective urine ketone tests may ‘worsen’ in the initial 2-3 days
  - Ketosis may persist 3-4 days after instituting treatment due to decreased clearance of acetone
    - Never base insulin doses on presence or degree of ketosis (use blood glucose concentration)

Diagnosis

- Usually indicate anorexia, depression, weakness, vomiting: 1-3d
- Complete workup usually for a ‘sick’ diabetic dog or cat
  - TxR, AxR, AUS, CBC, chem, UA
- Extreme levels of hyperglycemia tend to occur only when extracellular fluid volume and blood pressure have decreased to the point of causing impaired urine flow
- Metabolic acidosis: due to ketone bodies and possible concurrent disease
- Anion gap: increased
- Hyponatremia
  - ‘real’: renal or gastric losses
  - ‘fictitious’: dilution from osmotic draw of intravascular hyperglycemia
- Hyperkalemia
  - Acidemia, insulin deficiency and plasma hyperosmolarity cause a shift of K from intracellular to extracellular
- Hypokalemia
  - Usually due to depletion of whole-body potassium stores
  - Losses occur with vomiting and osmotic diuresis
  - May be unmasked by rehydration, continued urinary losses, correction of acidosis, and increased cellular uptake
- Hypophosphatemia
  - Increased urinary phosphorus wasting
- Increased ALT/ALP
  - Commonly increased due to hepatic lipidosis
Hypovolemia or coexisting pancreatitis can also cause (reversible) increases

- Azotemia
  - Renal or prerenal
- Neutrophilia
  - Mature: common due to the stress of the primary disorders
  - Bands and toxic changes: search for an inflammatory focus

**Treatment**
- **IVF**
- Dextrose supplementation, as dictated by patient blood glucose
- Potassium supplementation
  - If concurrent hypophosphatemia, supplement 1/3 of the potassium in the form of KPhos
  - If severe hypokalemia, 1.0mEq/kg/hr potassium can be ‘safely’ supplemented (author’s experience): recommended to perform ECG and urine output monitoring
- At least q12h electrolyte monitoring
- IVF discontinued when chem and hydration are normal, and when the dog/cat is able to drink/eat without vomiting
- Phos dose: 0.01-0.03mmol/kg/hr, repeat serum phos assessment q6h and d/c supplementation when serum phos is 2.5mg/dL
- NaHCO3 supplementation: controversial! Use when:
  - pH <7.1
  - HCO3 <10-12 mEq/L
  - NaCO3 (mEq) = base deficit (mEq) x 0.3 x kg
    - D/c treatment when pH >7.2, HCO3 > 10-12 mEq/L
- Insulin therapy: cornerstone of management for ‘sick’ DKA/HHS patients
  - Regular crystalline (IV, IM, SC) when patient is depressed, dehydrated, anorexic or vomiting
  - Correct hypovolemia prior to use
  - Do not exceed 75-100mg/dL/hr decrease in blood glucose
  - Transition to long acting insulin when:
    - Euhydrated
    - BG <250mg/dL
    - Serum and urine ketones are minimal to absent
    - Patient eating

**Complications**
- Hypoglycemia
- Hypokalemia
- Cerebral edema
- Metabolic alkalosis
- Paradoxical cerebrospinal fluid acidosis
Questions
1. Of the three ketone bodies, which is/are measured by the nitroprusside reaction?
2. NaHCO3 use is controversial, though use typically is recommended at pH____. Discontinuation of therapy is recommended when the pH is____.
3. What are the criteria for transition from regular to long acting insulin?

Answers
1. Of the three ketone bodies, which is/are measured by the nitroprusside reaction?
   a. Acetone
   b. Acetoacetate
2. NaHCO3 use is controversial, though use typically is recommended at pH <7.1. Discontinuation of therapy is recommended when the pH is >7.2.
3. What are the criteria for transition from regular to long acting insulin?
   a. Eufhydrated
   b. BG <250mg/dL
   c. Serum and urine ketones are minimal to absent
   d. Patient eating