Diabetic Ketoacidosis
and
Hyperosmolar Hyperglycemic State

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The Endocrine Group

Figure 1. The “Ominous Octet” of Defects in Diabetes

8 Defects
1: Beta Cell
2: Alpha Cell
3: Brain
4: Kidney
5: Muscle
6: Adipocyte
7: Liver
8: GI Tract
Diabetes Complications

- **Acute**
  - Hypoglycemia
  - DKA/HHS

- **Chronic**
  - Microvascular
  - Macrovascular
  - Neurologic

Diabetic Ketoacidosis

- An acute, life threatening metabolic acidosis complicating type 1 and some cases of type 2 DM (usually with intercurrent illness: infection or surgery)

- Usually coupled with an increase in glucagon concentration with two metabolic consequences:
  - 1) Maximal gluconeogenesis with impaired peripheral utilization of glucose
  - 2) Activation of the ketogenic process and development of metabolic acidosis
DKA Biochemistry

Fed State
- Increased Insulin
- Decreased Glucagon
Results in liver converting FFAs to TGs and stored as fat, inhibition of gluconeogenesis and storage of glycogen

Fasting State
- Decreased Insulin
- Increased Glucagon
Results in breakdown of FFAs to ketones

Insulin and Glucagon Regulate Normal Glucose Homeostasis

Glucose output
- Glucagon (alpha cell)
- Insulin (beta cell)

Blood glucose
- Liver
- Muscle

Blood glucose

Insulin and Glucagon Regulate Normal Glucose Homeostasis

Pancreas

Glucose output

Glucose uptake

Liver

Muscle

Adipose tissue

Fasting state

Glucagon (alpha cell)

Insulin (beta cell)

Ketogenesis

- **KETOGENESIS** occurs as a result of high glucagon/insulin ratio:
  - 1) increased liberation of free fatty acids due to the loss of the inhibitory action of insulin on the hormone sensitive lipase.
  - 2) activation of the transport system (or reestrafication to VLDL will occur and nothing will happen)

- this results in high levels of acetone, acetoacetate and β-hydroxybutyrate

[Diagram showing the metabolic pathways of ketogenesis]

The initial step in diagnostic approach is testing urine for glucose and ketones.

**Diagnostic criteria for DKA:**
- hyperglycemia (>250 mg/dl)
- ketosis (ketonemia and ketonuria)
- acidosis (pH<7.3, HCO₃<15mEq/L)

**Supporting features are volume depletion and Kussmaul’s breathing.**

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**Case Presentation**

- 21 yo ACP student
- Presents with complaints of N/V x 2 days
- ROS: dry mouth, nocturia
- Physical Examination:
  - Vitals: BP 90/60; Pulse 110 (140 standing); RR 16; Temp 101°
  - Abdomen: Tender       LE: No edema
- Labs: 13.5
  - L shift 22>455
  - 46
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Case Presentation

- Profile
  
<p>| | | |</p>
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>132</td>
<td>92</td>
<td>41</td>
</tr>
<tr>
<td>5.8</td>
<td>8</td>
<td>1.5</td>
</tr>
<tr>
<td>512</td>
<td></td>
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</tr>
</tbody>
</table>

- Anion Gap
  - Na – (Cl and CO2)
  - Normal: 8-10
  - This Patient:

- Causes of an Anion Gap metabolic acidosis
  - MUDPILES
Case Presentation

- Profile
  - 132  | 92  | 41
  - 5.8  | 8   | 1.5  | 512

- Anion Gap
  - Na – (Cl and CO2)
  - Normal: 8-10
  - This Patient: 132 - (92 + 8) = 32

- Causes of an Anion Gap metabolic acidosis
  - MUDPILES
Anion Gap Metabolic Acidosis

- Methanol
- Uremia
- DKA
- Paraldehyde
- Ischemia/Infection
- Lactic Acidosis
- Ethylene Glycol
- Salicylates

Case Presentation

- Kussmaul breathing with fruity odor
- Signs of dehydration (↑ HR, postural BP, tenting of skin, sunken eye balls)
Case Presentation

- **Osmolality**
  \[ \text{osmolality} = 2[\text{Na}] + \frac{\text{Glu}}{18} + \frac{\text{BUN}}{2.8} \]
  This patient: 2(132) + 512/18 + 41/2.8 = 307

- **Urine analysis**
  pH 4.3; 4+ glucose; 2+ ketones; no WBCs; no bacteria

- **Arterial Blood Gas**
  pH 7.12; pCO2 20; pO2 100; HCO3 8
Case Presentation

- **Osmolality**

  \[
  \text{osmolality} = 2[\text{Na}] + \frac{\text{Glu}}{18} + \frac{\text{BUN}}{2.8}
  \]

  This patient: \(2(132) + \frac{512}{18} + \frac{41}{2.8} = 307\)

- **Urine analysis**

  pH 4.3; 4+ glucose; 2+ ketones; no WBCs; no bacteria

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  pH 7.12; pCO2 20; pO2 100; HCO3 8

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<table>
<thead>
<tr>
<th>Clinical Signs and Symptoms</th>
<th>Laboratory Values</th>
</tr>
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<tbody>
<tr>
<td>Dehydration</td>
<td>Hyperglycemia</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>(usually 350–700 mg/dL)</td>
</tr>
<tr>
<td>Abnormal skin turgor</td>
<td>Bun, Cr increased*</td>
</tr>
<tr>
<td>Dry mucous membranes</td>
<td>Hyperosmolar</td>
</tr>
<tr>
<td>Hypotension</td>
<td>Hypokalemia†</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>Hypophosphatemia</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>Anion gap acidosis</td>
</tr>
<tr>
<td>Ileus</td>
<td>Low bicarbonate</td>
</tr>
<tr>
<td>Kussmaul respiration</td>
<td>(&lt;15 meq/l)</td>
</tr>
<tr>
<td>Ketotic (fruity) breath</td>
<td>Serum and urine ketones</td>
</tr>
<tr>
<td>Altered mental status</td>
<td>Arterial pH &lt;7.3</td>
</tr>
<tr>
<td>Somnolence to coma (coma unusual)</td>
<td>Leukocytosis</td>
</tr>
</tbody>
</table>

*Creatinine increased secondary to dehydration and because of interference by ketones with standard creatinine assay.
†Serum levels may initially be high or normal in setting of acidosis; however, total K+ deficit is usually profound.

### Etiology of DKA / HHS

- Omission of insulin
- Insulin under-dose during sick days
- Newly diagnosed type 1 diabetes
- Infection
- MI
- Pancreatitis
Treatment of DKA / HHS

- Fluid Consideration
  - NS
  - D5 1/2NS
- Insulin Therapy
  - Insulin Drip
- Potassium
  - Minibags
- Phosphate
  - As potassium salt
- Bicarbonate (consideration for pH<7.0)
- Identify and treat underlying cause of event


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**Table 2—Typical total body deficits of water and electrolytes in DKA and HHS**

<table>
<thead>
<tr>
<th></th>
<th>6</th>
<th>9</th>
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<tbody>
<tr>
<td>Total water (l)</td>
<td>100</td>
<td>100–200</td>
</tr>
<tr>
<td>Water (ml/kg)†</td>
<td>7–10</td>
<td>5–13</td>
</tr>
<tr>
<td>Na⁺ (mEq/kg)</td>
<td>3–5</td>
<td>5–15</td>
</tr>
<tr>
<td>Cl⁻ (mEq/kg)</td>
<td>3–5</td>
<td>4–6</td>
</tr>
<tr>
<td>K⁺ (mEq/kg)</td>
<td>5–7</td>
<td>3–7</td>
</tr>
<tr>
<td>PO₄ (mmol/kg)</td>
<td>1–2</td>
<td>1–2</td>
</tr>
<tr>
<td>Mg²⁺ (mEq/kg)</td>
<td>1–2</td>
<td>1–2</td>
</tr>
<tr>
<td>Ca²⁺ (mEq/kg)</td>
<td></td>
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</tr>
</tbody>
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*Data are from Ennis et al. (15) and Kreisberg (8);† Per kilogram of body weight.
Treatment of DKA / HHS

- Fluid Consideration
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  - D5 1/2NS
- Insulin Therapy
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Correction of dehydration, hyperglycemia, and electrolyte imbalances

- **IVF:** the usual fluid deficit is 5-7L
  - on arrival the patient is given 1-2L of isotonic saline or ringer’s lactate followed by infusion rates dependent on fluid status and urine output.
  - when glucose reaches 250mg/dl add 5% glucose solution (hypoglycemia, cerebral Edema)
- **Insulin:** is a prerequisite for recovery
  - initial IV bolus (or IM) of 0.1 unit/kg followed by infusion of 0.1-0.2 units/kg /hour till ketosis is reversed; goal of glucose decrease of 100 mg/dL per hour
**Potassium**: replacement is always necessary
- if value on arrival is high: delay replacement
- if values are low: give K early
- if values are very low (K > 3.3): hold insulin for 60-90 min. until 40-50 mEq of K are given

**Bicarbonate**: consider need
- indicated in severe acidosis (pH<7.0) or with hypotension (that can be caused by acidosis alone)
- stop the infusion at pH 7.2 to avoid alkalosis upon reversal of ketosis
ALL patients should be followed with a flow sheet outlining amounts and timing of insulin and fluids together with record of vital signs, urine volume, and blood chemistries. Without such a record therapy tends to be chaotic.

Each patient should receive intensive detailed instructions about how to avoid future episodes of this potentially disastrous complication of diabetes.

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**SUGGESTED DIABETES FLOW SHEET**

<table>
<thead>
<tr>
<th>Date</th>
<th>Hour</th>
<th>B/P</th>
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</table>

- **Temperature**
- **Pulse**
- **Respiration (R)**
- **Blood Pressure**
- **Serum Glucose (mg/dL)**
- **Serum Ketones**
- **Urinalysis**

**ELECTROLYTES**

- **Sodium (Na+)**
- **Potassium (K+)**
- **Chloride (Cl-)**
- **Calcium (Ca++)**
- **Magnesium (Mg++)**

- **Effective Osmolality**
- **Glucose (mg/dL)**

**PIMC**

- **Hgb**
- **Hct**
- **WBC**
- **Platelet**
- **Albumin**

**INSULIN**

- **Units Per Hour**

**FLUIDS**

- **Intake**
- **Output**

**METABOLITES**

- **Na+**
- **K+**
- **Cl-**
- **Ca++**
- **Mg++**
- **Osmolality**
- **Other**

<table>
<thead>
<tr>
<th>A.B.O.</th>
<th>pH</th>
<th>1.25H</th>
<th>0.67H</th>
<th>0.43H</th>
<th>0.21H</th>
<th>0.11H</th>
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Sick Day Rules (Prevent DKA/HHS)

- DO NOT STOP INSULIN!
- Keep usual basal insulin
- Cover with quick-acting insulin
- Frequent finger stick monitoring (q 1-2 hrs)
- Check urine ketones
- Use sport drinks to maintain hydration
- Supplement calories to support insulin coverage (glucose affected prior to ketones)
- If vomit, go to ER
Pitfalls of DKA Management

- Not giving enough fluid (continued dehydration)
- Delay in initiating insulin drip (hyperglycemia)
- Failure to adequately keep up with K+ (hypokalemia and potential arrhythmias)
- Too fast a rate of glucose decrease (cerebral edema)
- Failure to include glucose in IV fluids when blood sugar falls below 250 mg/dL (hypoglycemia)
- Early DC of insulin drip (hyperglycemia, ketonemia; wait until urine ketones clear and anion gap is closed)

You’re fired!
Your Turn - You manage the patient!

12/28/06: Admission to St. Peter's Hospital

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<tr>
<td></td>
<td>pH 7.03</td>
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<tr>
<td></td>
<td>51</td>
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Anion Gap = ?

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<tr>
<td></td>
<td>884</td>
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<tr>
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<td>21.6</td>
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<tr>
<td></td>
<td>47.4</td>
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<tr>
<td>Time</td>
<td>Heart Rate</td>
</tr>
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<td>-------</td>
<td>------------</td>
</tr>
<tr>
<td>1200</td>
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<td>6 2.5 950</td>
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<td>1900</td>
<td>137</td>
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<td>14 1.7 250</td>
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Your Turn - You manage the patient!
Questions