Hyperglycemic Crisis: 
Diabetic Ketoacidosis and Hyperosmolar Hyperglycemic Syndrome

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DKA and HHS: Definitions and Differentiation

• Diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic syndrome (HHS)* are potentially fatal hyperglycemic crises that occur as acute complications of diabetes.

• They are found to occur simultaneously in up to 1/3 of cases (“overlap syndrome” of hyperosmolar ketoacidosis).

* Previous terminology for HHS: hyperglycemic hyperosmolar nonketotic coma or hyperglycemic hyperosmolar nonketotic state

DKA and HHS: Definitions and Differentiation

DKA characterized by:
- Uncontrolled hyperglycemia
- Metabolic acidosis
- Increased ketone concentration

HHS characterized by:
- Severe hyperglycemia
- Dehydration
- Hyperosmolality
- Absence of significant ketoacidosis (residual β-cell function prevents lipolysis)

## DKA and HHS: Definitions and Differentiation

*Up to 1/3\(^{rd}\) of cases in type 2 diabetes*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>DKA</th>
<th>HHS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Age</td>
<td>Younger</td>
<td>Elderly</td>
</tr>
<tr>
<td>Diabetes Type</td>
<td>Primarily type 1 DM*</td>
<td>Primarily type 2 DM</td>
</tr>
<tr>
<td>Acidosis</td>
<td>Yes (pH &lt;7.3)</td>
<td>Typically no (pH &gt;7.3)</td>
</tr>
<tr>
<td>Ketonemia/Ketonuria</td>
<td>Present</td>
<td>Typically no (or mild)</td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>Elevated (&gt;250 mg/dL)</td>
<td>Sig. elevated (&gt;600 mg/dL)</td>
</tr>
<tr>
<td>Osmolality</td>
<td>Typically normal</td>
<td>Elevated (&gt;320 mOsm/kg)</td>
</tr>
</tbody>
</table>

Epidemiology of DKA and HHS

• Annual U.S. incidence of DKA in all age groups is 4-8 per 1,000 type 1 diabetic patients

• ~140,000 hospitalizations for DKA in 2009 in U.S.

• 56% of patients between 18-44 yo, 24% between 45-65 yo, and 18% <20 yo

• 50% female and 45% non-white

• 1/3rd of DKA cases in patients with type 2 diabetes

• HHS has been estimated to account for approximately 1% of all diabetes admissions (likely an underestimate)

DKA Hospital Discharges

• The number of hospital discharges with DKA as the first-listed diagnosis increased from about 80,000 discharges in 1988 to about 140,000 in 2009.

• In 2011, approximately 175,000 emergency room visits had hyperglycemic crisis as the first-listed diagnosis.


DKA Average Length of Stay

• From 1988 to 2009, the average length of stay of hospital discharges with DKA as the first-listed diagnosis decreased by 2.3 days (from 5.7 to 3.4 days).

• ~$2.5 billion per year (direct and indirect medical costs)

Kim S. Diabetes Care 2007;30:1281-1282
Mortality of Hyperglycemic Crisis

• DKA is the most common cause of death in children and adolescents with type 1 diabetes.

• In 2010, among adults aged 20 years or older, hyperglycemic crisis caused 2,361 deaths in the U.S.

• The mortality rate from HHS is significantly higher than for DKA (reported as high as 20% in adults vs. <1% for adults with DKA).

• Mortality is higher at age extremes and in the presence of coma, hypotension, and severe comorbidities.

• Overall hyperglycemic crisis death rate has declined by over 15% in the past 20 years in the U.S.


Pathogenesis of DKA and HHS

- Insulin deficiency (absolute and/or relative) and increased counter-regulatory hormones lead to:

1. Hyperglycemia
   - Osmotic diuresis
   - Dehydration
   - Hyperosmolarity
   - Electrolyte loss
   - Decreased renal function

2. Exaggerated lipolysis
   - Elevated free fatty acids
   - Ketone body formation
   - Acidosis
   - Vomiting (dehydration)
   - Decreased renal function

- In HHS, generally enough insulin secretion to prevent exaggerated lipolysis and ketogenesis

Pathogenesis of DKA and HHS

• Both disorders are associated with severe inflammatory state (even in the absence of infection).

• Elevation of pro-inflammatory cytokines (e.g., TNF-α, IL-6), CRP, reactive oxygen species, and CV markers such as PAI-1.

• These parameters return to normal with appropriate therapy (hydration and insulin therapy).

Polling Question 1

True or False, the most common precipitating factor of DKA and HHS is concurrent infection?

- True
- False
Key Precipitating Factors and Patient Characteristics

- Infection (e.g., pneumonia, UTI) or other concurrent illness
- Omission of insulin or poor adherence to insulin therapy
- Psychological or behavioral issues (e.g., eating disorders, depression, fear of weight gain)
- Drugs that affect CHO metabolism (e.g., atypical antipsychotics, corticosteroids)
- Restricted water intake (e.g., elderly nursing home residents)
- Drug or ETOH abuse
- Poor baseline glycemic control
- Past history of DKA

Clinical Presentation

• Important to differentiate between DKA and HHS (not always straightforward based on history and exam)

• Classic symptoms of hyperglycemia: Thirst, polydipsia, polyuria, and weight loss

• Non-specific complaints and/or complaints of a precipitating condition

• Tachycardia, hypotension, Kussmaul respirations and ketones on breath (DKA), dry mucous membranes, poor skin turgor

Clinical Presentation

• **DKA**: Abdominal pain, nausea and vomiting (secondary to ketosis), may present with altered mental status

• **HHS**: Neurologic deficit due to profound dehydration and hyperosmolarity

• Patients “look sick” and most require hospitalization

Polling Question 2

Is the laboratory panel below most consistent with DKA or HHS?

<table>
<thead>
<tr>
<th>Glucose (mg/dL)</th>
<th>275 mg/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.14</td>
</tr>
<tr>
<td>Urine ketones</td>
<td>Large</td>
</tr>
<tr>
<td>Osmolality (mOsm/kg)</td>
<td>290</td>
</tr>
<tr>
<td>WBC</td>
<td>24,000</td>
</tr>
<tr>
<td>Mental Status</td>
<td>Drowsy, but alert and oriented</td>
</tr>
</tbody>
</table>

- DKA
- HHS
# Clinical Presentation (laboratory)

<table>
<thead>
<tr>
<th></th>
<th>Mild DKA</th>
<th>Moderate DKA</th>
<th>Severe DKA</th>
<th>HHS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma glucose (mg/dL)</td>
<td>&gt;250</td>
<td>&gt;250</td>
<td>&gt;250</td>
<td>&gt;600</td>
</tr>
<tr>
<td>pH</td>
<td>7.25-7.3</td>
<td>7.0-7.24</td>
<td>&lt;7.0</td>
<td>&gt;7.3</td>
</tr>
<tr>
<td>Serum bicarbonate (mEq/L)</td>
<td>15-18</td>
<td>10-15</td>
<td>&lt;10</td>
<td>&gt;18</td>
</tr>
<tr>
<td>Ketones (urine or serum)</td>
<td>Positive</td>
<td>Positive</td>
<td>Positive</td>
<td>Min. to Neg.</td>
</tr>
<tr>
<td>Anion gap</td>
<td>&gt;10</td>
<td>&gt;12</td>
<td>&gt;12</td>
<td>Variable</td>
</tr>
<tr>
<td>Osmolality (mOsm/kg)</td>
<td>Variable</td>
<td>Variable</td>
<td>Variable</td>
<td>&gt;320</td>
</tr>
<tr>
<td>Mental status</td>
<td>Alert</td>
<td>Alert/Drowsy</td>
<td>Stupor/Coma</td>
<td>Stupor/Coma</td>
</tr>
</tbody>
</table>

Overview of Treatment

• Therapy to correct:
  – Hypovolemic
  – Hyperglycemia and ketonemia
  – Electrolyte abnormalities
  – Identify and treat precipitating factors (e.g., infection, MI)

• Fluid resuscitation

• Insulin administration

• Potassium administration

• **Complications of therapy** include cerebral edema (most commonly in pediatric patients), rhabdomyolysis and pulmonary edema

Overview of DKA Treatment in Adults

Figure 1 Workflow of management of adult DKA.
Abbreviations: BG, blood glucose; DKA, diabetic ketoacidosis; h, hour; IV, intravenous; SC, subcutaneous.
# DKA Management Checklist

<table>
<thead>
<tr>
<th>Phase I (0–6 h)</th>
<th>Phase II (6–12 h)</th>
<th>Phase III (12–24 h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perform history and physical exam and order initial laboratory studies</td>
<td>Continue biochemical and clinical monitoring</td>
<td>Continue biochemical and clinical monitoring</td>
</tr>
<tr>
<td>Implement monitoring plan (biochemical and clinical)</td>
<td>Change isotonic fluids to hypotonic fluids if corrected Na normal/high</td>
<td>Adjust therapy to avoid complications</td>
</tr>
<tr>
<td>Give intravenous bolus of isotonic fluids</td>
<td>If glucose is &lt;200–250 mg/dL, add dextrose to intravenous fluids</td>
<td>Address precipitating factors</td>
</tr>
<tr>
<td>Start insulin therapy (after fluids started and only if K &gt; 3.3 mmol/L)</td>
<td>Adjust insulin infusion rate as needed</td>
<td>If DKA resolved, stop intravenous insulin and start subcutaneous insulin</td>
</tr>
<tr>
<td>Consult diabetes team</td>
<td>Maintain K at 3.3–5.3 mmol/L range</td>
<td>Consult diabetes educator</td>
</tr>
</tbody>
</table>

**Abbreviations:** DKA, diabetic ketoacidosis; h, hours.
Prevention

“Because repeated admission for DKA are estimated to drain approximately one of every two health care dollars spent on adult patients with type 1 diabetes, resources need to be redirected toward prevention by funding better access to care and educational programs tailored to individual needs, including ethnic and personal health care beliefs.”

Polling Question 3

Which of the following are important in the prevention of DKA?

- Education about diabetes management when sick with another illness ("sick day management")
- Access to healthcare (e.g., insulin)
- Appropriate monitoring of blood glucose (SMBG)
- Calling healthcare team early if glucose not controlled and positive ketones
- Not missing insulin doses
- All of the above
Prevention

• Access to healthcare and to therapy (insulin, SMBG)
• EDUCATION (patient and family members/caregivers)
• Importance of taking insulin as prescribed (and not discontinuing)
• Sick day management (review ‘rules’ periodically)
  – Early contact with HCP (after hours procedures)
  – Appropriate insulin dose modification (NEVER discontinue insulin)
  – Monitoring and record glucose and ketones
  – Oral fluids (appropriate liquid diet)
• If needed, mental health support or drug rehabilitation

“the person with diabetes who knows the most, lives the longest”

- Elliot Joslin -
# Applying Self-Care Behaviors for Prevention of DKA

<table>
<thead>
<tr>
<th>AADE 7 Self-Care Behaviors™</th>
<th>Concept</th>
<th>Application</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Taking Medication</strong></td>
<td>Exogenous insulin essential for people with type 1 diabetes. Taking the right insulin in the right amount at the right time helps prevent very high BG. Other drugs may help improve/stabilize glucose.</td>
<td>Inadequate insulin increases the risk for DKA. Omitting insulin almost guarantees it. To reduce risks for acute hyperglycemia, understand how insulin works and maintain the skills needed to take it appropriately.</td>
</tr>
<tr>
<td><strong>Monitoring</strong></td>
<td>Monitoring BG and ketone levels provides feedback about the treatment plan and early warning of impending DKA.</td>
<td>Monitor regularly to identify hyperglycemia early. Increase monitoring frequency when not eating or ill. Relying on “how you feel” may be an inaccurate measure of BG. Access to monitoring supplies may be a barrier to self-monitoring of BG. Assess problems with monitoring. Resistance to monitoring may have multiple causes.</td>
</tr>
</tbody>
</table>
### Applying Self-Care Behaviors for Prevention of DKA

<table>
<thead>
<tr>
<th>Problem Solving</th>
<th>Applying information to individual situations so information already learned helps solve problems—avoiding initial events as well as recurrence.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Review the circumstances preceding a DKA episode. Identify precipitating factors Questions to reduce risk may relate to delaying exercise, limiting carbohydrate intake, monitoring blood glucose, or adjusting medication. Review factors contributing to DKA and learn to recognize signs and symptoms to prevent recurrence.</td>
</tr>
<tr>
<td>Reducing Risks</td>
<td>Reducing the risk as well as the impact of DKA is possible. Unlike most diabetes management decisions, reducing complications from DKA treatment is primarily a provider responsibility.</td>
</tr>
<tr>
<td></td>
<td>Delayed treatment, excessive insulin, and inadequate insulin are common complications of treating DKA. Reduce complications with prompt diagnosis, adjusting insulin to glucose response, and beginning injected insulin before stopping IV. Discuss sick days—interventions for nausea, fever, loss of appetite; correction factors for hyperglycemia and further corrections for ketones; when to seek medical care and after-hours procedures.</td>
</tr>
</tbody>
</table>

Accessed online December 12, 2014
http://www.diabeteseducator.org/export/sites/aade/_resources/pdf/core_concepts/Supplementary_Course_Materials.pdf
## Applying Self-Care Behaviors for Prevention of DKA

<table>
<thead>
<tr>
<th>Healthy Coping</th>
<th>Eating well, taking medications, testing BG, and using results to problem-solve are difficult, never-ending aspects of self-management.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Use information, support, and encouragement to help lower the barriers that interfere with optimal prevention of DKA. Acknowledge the inevitable struggle that is part of living with diabetes to lighten the load. Discuss growth and hormonal spurts. Discuss inattention to signs and distractions of life. Identify resources and situations in which to seek medical attention.</td>
</tr>
</tbody>
</table>

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## Applying Self-Care Behaviors for Prevention of HHS

<table>
<thead>
<tr>
<th>AADE 7</th>
<th>Concept</th>
<th>Application</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Being Active</strong></td>
<td>Activity continues to lower insulin resistance and improve blood glucose (BG) levels. Be safely active at all ages. Maintain adequate hydration.</td>
<td>To compensate for fluids lost during physical activity, drink adequately before, during, and after, especially on hot days.</td>
</tr>
<tr>
<td><strong>Healthy Eating</strong></td>
<td>Matching timing of food with medication activity. Having sick day plan and supplies (food and fluids).</td>
<td>To avoid high BG, do not consume extra carbohydrate without taking extra insulin. It is easy to consume extra carbohydrate with liquids. A large soft drink at a fast-food restaurant offers as much carbohydrate as 5 slices of bread.</td>
</tr>
<tr>
<td><strong>Taking Medications</strong></td>
<td>If glucose goals are not met with activity and meal planning, medication is necessary.</td>
<td>Inadequate levels of diabetes medication, especially reluctance to initiate insulin when needed, significantly contributes to high glucose levels.</td>
</tr>
</tbody>
</table>
### Applying Self-Care Behaviors for Prevention of HHS

<table>
<thead>
<tr>
<th>Monitoring Blood Glucose</th>
<th>Monitoring provides feedback about the treatment plan and warning of impending hyperosmolar hyperglycemic state.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Monitor regularly to help identify hyperglycemia early. True even for those not treated with medication, especially during illness or other stress. Discuss usual monitoring routine and what to do when not eating or ill. Relying on “how you feel” may be an inaccurate measure of BG values. Access to monitoring supplies may present a barrier to self-monitoring of BG. Address issues of concern. Assess problems with monitoring. Resistance to monitoring may have multiple causes.</td>
</tr>
<tr>
<td>Problem Solving</td>
<td>Applying information already learned to individual situations helps solve problems.</td>
</tr>
<tr>
<td></td>
<td>Review the circumstances preceding the HHS episode to look for clues to prevent another. Would a system for drinking fluids, monitoring blood glucose, or a change in medication have reduced the risk? To prevent recurrence, review signs, symptoms, and treatment.</td>
</tr>
</tbody>
</table>

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## Applying Self-Care Behaviors for Prevention of HHS

<table>
<thead>
<tr>
<th>Reducing Risks</th>
<th>Reducing the risk as well as the impact of HHS is possible. HHS also increases risks for many concomitant conditions.</th>
<th>As HHS usually occurs in an older, more vulnerable population, individualize and carefully monitor therapy for these persons to help prevent complications. Discuss sick days—interventions for nausea, fever, loss of appetite; correction factors for hyperglycemia; when to seek medical care and after-hours procedures.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy Coping</td>
<td>Eating well, taking medications, testing blood glucose, and using the results to problem solve are difficult, never-ending aspects of self-management.</td>
<td>Use information, support, and encouragement for caregivers as well as patients to help prevent HHS. Identify resources and situations in which to seek medical attention.</td>
</tr>
</tbody>
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Summary

• DKA and HHS are two of the most serious acute complications of diabetes.

• They are both associated with significant morbidity and mortality and cost to the healthcare system.

• Concurrent infection and omission of insulin are the most common precipitating factors.

• Key principles of treatment are hydration, insulin, management of electrolyte disturbances, and identification of precipitating factors.

• Many cases can be prevented. Patient and/or caregiver education is the cornerstone of prevention.
Thank you very much!

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