Diabetic Emergencies

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Case 1

- 32 y/o F: N/V and diffuse abd pain for 24 hr
  - PHx: type 1 DM for 7 yr
  - Meds: Insulin 70/30 28UqAM, 16UqPM

What do you like to know?

Case 1

- Case Presentation
  - No fever/chills, URI s/s
  - Urinary frequency
  - Stop insulin for 24 hr because of poor appetite
  - F/S = High*

F/S device only accurate to 500 mg/dL

Case 1

- PE:
  - Gen: Mild distress but A&O x 3
  - 36.8, 120, 34, 132/88
  - HEENT: WNL
  - Heart: RHB, Lungs: OK
  - Abd: (+) BS, diffuse tenderness, no rebound
  - Ext: WNL, Neuro: WNL

What Lab Data would you like to obtain?

Case 1

- Lab Data
  - WBC 15.7, H/H 15/45, Plt 229
  - Na 132, K 5.2, Cl 96, BUN 10, Cr 1.0 Gluc 612
  - ABGs: pH 7.27, $PaCO_2$ 22, PaO_2 97%, HCO_3 11

What is the anion gap?

Anion Gap

- AG = Na - (Cl + HCO3)
- AG = 132 – (96 + 11) = 25
- Normal range: 12 +/- 4 meq/L

What is the DDx for wide AG metabolic acidosis?

Wide AG met. acidosis

- C
- A
- T

- M
- U
- D

- P
- I
- L
- E
- S

Wide AG met. acidosis

- C: Carbon monoxide, Cyanide
- A: Alcoholic ketoacidosis
- T: Toluene

- M: Methanol
- U: Uremia
- D: Diabetic ketoacidosis

- P: Paraldehyde, Phenformin
- I: Iron, Isoniazid
- L: Lactic acidosis
- E: Ethylene glycol
- S: Salicylates

Case 1

- Lab Data
  - WBC 15.7, H/H 15/45, Plt 229
  - Na 132, K 5.2, CL 96, BUN 10, Cr 1.0 Gluc 612
  - ABGs: pH 7.27, $PaCO_2$ 22, PaO_2 97%, HCO_3 11

What is the actual serum sodium?

Pseudohyponatremia

- Lab Data
  - WBC 15.7, H/H 15/45, Plt 229
  - Na 132, K 5.2, CL 96, BUN 10, Cr 1.0 Gluc 612
  - ABGs: pH 7.27, $PaCO_2$ 22, PaO_2 97%, HCO_3 11
- Na = Na + 1.6 x (Gluc - 100)/100
  - Use 2.4 instead of 1.6 if BG > 400
  - Na = 132 + 1.6 (612-100)/100 = 140.2
  - Na = 132 + 2.4 (612-100)/100 = 144.3

Case 1

- Lab Data
  - WBC 15.7, H/H 15/45, Plt 229
  - Na 132, K 5.2, CL 96, BUN 10, Cr 1.0 Gluc 612
  - ABGs: pH 7.27, $PaCO_2$ 22, PaO_2 97%, HCO_3 11

What additional data do you need?

Case 1

- Lab Data (Continued)
  - Urine:
    Protein 3+
    ketones 3+
  - Serum:
    ketones +ve
    osmolarity = 323mOsm/kg

Diabetic Ketoacidosis

- Life-threatening emergency
- American Diabetic Association: biochemical criteria of DKA
  - Hyperglycemia > 250 mg/dL
  - Ketonuria / ketonemia
  - Met. Acidosis
    - ABGs – pH <7.35
    - VBGs – pH <7.30
    - HCO_3 <15 meq/L

Diabetic Ketoacidosis

- Cause: relative/absolute insulin deficiency
  - Most common in type 1 DM
  - Also in type 2 DM due to progressive loss of β-cell reserve
- Mortality is ~5%

DKA: Ppt factors

- DC insulin / noncompliance
- Infection - UTI, pneumonia, cellulitis, foot gangrene
- MI
- Trauma
- GI bleeding
- Pregnancy
- Stress

DKA: Pathophysiology

- Insulin deficiency:
  - Decreased glucose utilization
- Elevations in counterregulatory hormones:
  - Increased *lipolysis* in adipose tissue with increased hepatic *ketogenesis*
  - Increased proteolysis in muscle
  - Increased glycogenolysis
  - Increased gluconeogenesis
- Results:
  - *Hyperglycemia* → osmotic diuresis → *dehydration*
  - *Ketoacidosis* → N/V → dehydration / *e- imbalance*

Counterregulatory hormones

- Catecholamines
- Glucagon
- Growth hormone
- Cortisol

DKA: Hx taking

- *Have you had increased thirst or urinary frequency? Any weight loss? (三多)*
- *Have you had nausea, vomiting, or abdominal pain?*
- *Have you been following your usual insulin schedule recently?*
- *Have you missed insulin doses or changed your diet?*
- *Have you had a fever, painful urination, cough, or shortness of breath?*
- *Have you had any chest pain or dark stool?*

DKA: Symptoms & signs

- Blurred vision
- Increased thirst
- Increased urination
- Nausea/vomiting
- Confusion
- Loss of consciousness
- Acute abd pain
- Tachycardia (最常見)
- Deep respirations (Kussmaul)
- Fruity breath
- Dehydration (dry skin)
- Hyperglycemia
- Ketosis
- Acidosis
- Abd tenderness, *peritoneal signs*

Fever

- DKA 本身原則上不會 fever
- Fever → infection → septic work-up:
  - Blood routines
  - B/C x 2
  - CXR
  - U/A, U/C
  - Abd echo - liver abscess
  - Feet - gangrene
  - Rectal – perianal abscess

ECG

- Mandatory
- Look for
  - AMI / ischemia
  - Hyperkalemia
  - Hypokalemia

Other expected labs

- Hyponatermia unless dehydrated
- Hyperkalemia due to cellular shift
- Leukocytosis in the absence of infection
- Elevation of amylase and lipase in the absence of pancreatitis

Ketones

- Ketones are the end-product of rapid or excessive fatty-acid breakdown:
  - **Acetoacetic acid**
  - **Acetone**
  - **Beta-hydroxybutyric acid** - not detected by nitroprusside reaction

Urine ketone – false negative

- Active reagent: nitroprusside (7.5%)
- Nitroprusside reacts with acetoacetic acid but does not react with acetone or B-hydroxybutyrate

Urine ketone – false positive

- Insulin overdose
- Insufficient food intake
- Nausea and vomiting
- Starvation
- Strict dieting
- Severe stress
- Severe fever due to infection

Ketone Negative DKA

- Alcoholic ketoacidosis
- Hypoxia
- Beta hydroxybutirate is the dominant ketone - not detected by nitroprusside reaction

Simple DKA 治療有三大禁忌

- Simple DKA 治療有三大禁忌 (尤其是<20y者)
  - 不能開始就用 hypotonic solution 來 challenge (即使有 hypernatremia)！
  - 不能用 Jusomine (即使 pH小於7.2)！
  - 不能使 blood sugar 降太快 (每小時下降不可大於100mg/dL)！
- 另外，記得不要只 f/u K and VBG，還要 f/u Na 及 Cl，因為治療的最佳 end-point 是 AG (anion gap)！
- And, sugar 小於250 就要馬上換上糖水 + insulin

Hyperosmolar Hyperglycemic State

- HHS = HHNKS = HNKC = HHNK
- Life-threatening emergency, mortality (~15%) higher than DKA (~5%)
  - Elderly – type-2 DM, inadequate access to fluids
  - Underlying diseases
- Criteria
  - Hyperglycemia,
  - Hyperosmolality
  - Dehydration from osmotic diuresis (volume depletion often >20%BW)
  - No / minimal ketoacidosis

HHS Hx: Symptoms

- Elderly with non-specific complaints
  - Fatigue, weakness
  - Polyuria
  - Polydipsia
- Ask for hints of
  - Infection – UTI, pneumonia, cellulitis, foot gangrene
  - MI
  - Stroke
  - GI bleed

HHS PE: Signs

- Altered mental status (AMS, ALOC)
  - Degree of lethargy/coma correlates well with serum osmolality
  - If coma, osm usually >340 mOsm/L
- Dehydration
  - Poor skin turgor, dry mucosa, tachycardia, orthostatic hypotension
- Look for
  - Pyuria, cellulitis, melena...

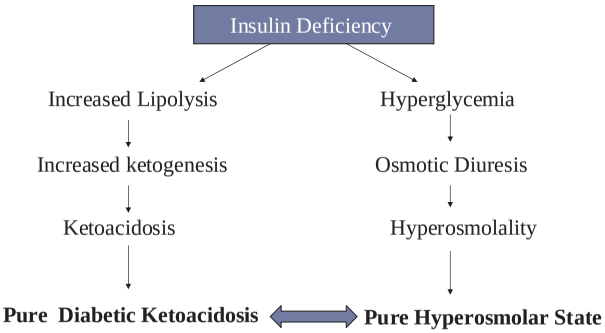
HHS Lab

- Similar to DKA
- Add serum osmolality
- Dx criteria
  - BG >600 mg/dL (typically 600-1,200)
  - Serum Osm >320 mg/dL (up to 380)
  - No / minimal ketoacidosis
  - Neurologic sequelae common – ALOC, seizures, hemiparesis...

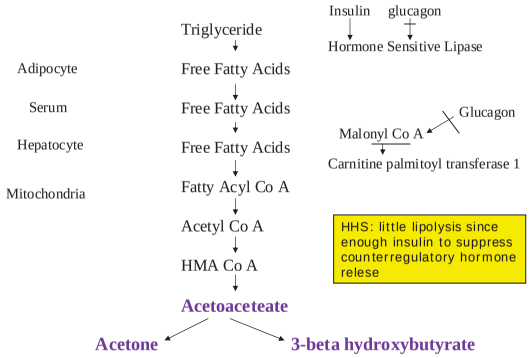
DKA / HHS

- Not mutually exclusive !

Pathophysiology of DKA/HHS



Physiology of DKA



Comparison

	DKA	HHS
History	Known type I / new DM	Mild / new type II DM
Age	Young	Old
Onset	Days	Days to weeks
ALOC	o/+	++
Acidosis	+++	o/+
Fluid Loss	++	+++
Blood Sugar	++	+++

Management of DKA/HHS

- Start with the 4 triads
  - A-B-C
  - O2-IV-Monitors
  - Vital signs (BP-HR-RR-BT-SpO2)
  - Hx-PE-Lab (F/S)
- Fluid → fluid → e- → insulin
  - Hydration – esp. important if BG > 300 mg/dL
  - Correct potassium level
  - Give insulin

Fluids in DKA/HHS

- Fluid resuscitation
  - Mandatory
  - Vigorous
  - Before lab results
- Initially - NS
  - 2L over 2h
  - 4L over next 4h
  - Thereafter: 250-500 ml/hr
- Estimated fluid deficits
  - DKA: 6-8 L
  - HHS: 8-10 L

Fluids in DKA/HHS

- NS to maintain hemodynamic:
  - NS (4L) for first 4 hours
  - Ok to repeat CXR after 4 L fluids
  - Consider HS(1/2NS) thereafter
  - Change to D5S when BG < 250 mg/dl
  - Adjust type and rate of fluid administration in
    - Elderly
    - CHF and
    - CRF

Insulin in DKA/HHS

- Start insulin once lab data shows no hypokalemia
  - Bolus = 0.1 U/kg
  - Continuous = 0.1 U/kg/h (max 10 U/h) in DKA; 0.05 U/kg in HHS
    - RI 50U in NS 500 cc run 50 cc/h = 5 U/h
    - Increase 50%/h if BG decrease <50
    - Decrease 50%/h if BG decrease >100
    - Do not decrease insulin infusion to <1 U/h, shift to D5S if BG <250

Insulin in DKA/HHS

- Monitor
  - F/S q1h x 3 (lowering rate ok), then q2h
  - ABGs and e- q2h x 2, then q4h
  - OK to check VBG pH (0.03 unit < ABG pH)
- End-point of continuous drip:
  - DKA → AG < 12; pH >7.35; HCO_3 >15
  - HHS → BG 250-300, GCS ok
- Failure to give SC insulin when IV insulin stopped
  - → rebound hyperglycemia
  - → worsening mental status in HHS
  - → worsening acidosis in DKA

Potassium

- Generally, DKA → K depletion
  - Insulin deficiency, acidosis, vomiting, osmotic diuresis
- K replacement for all DKA, except:
  - K >5.5 meq/dL
  - Anuric
- Give K prior to insulin if K <3.5 meq/dL

Potassium

Serum K (mEq/L)	Additional K required
<3.5	40 mEq/L
3.5 - 4.5	20 mEq/L
4.5 - 5.5	10 mEq/L
> 5.5	Stop K infusion

Na and K

- In both DKA and HHS
  - Though initial Na or K can be variable
  - Total body Na and K are depleted since diuresis → loss of Na and K

Bicarbonate

- Controversial
  - Should not be routine!
  - Increased risk of cerebral edema (esp. pediatric group)
- Considered only if
  - pH <7.0
  - Cardiovascular instability

Bicarbonate in DKA

PRO:

- Severe acidosis is associated with adverese effects: hypotension, decreased cardiac output decreased peripheral vascular resistance, increased pulmonary arterterial resistance , bardycardia, arrhytimas , renal and mesenteric ischemia, cerebral vasodilatation

CONS:

- No studies have shown any benefit of HCO3 if pH is 6.9-7.1
- SIDE EFF : Overshoot alkalosis, paradoxical CSF acidosis , hypokalemia, volume overload, overproduction of ketoacids

Phosphate

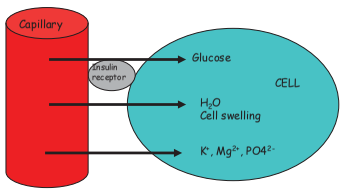
- Controversial
  - Should not be routine!
  - Only theoretical benefits

Phosphate Replacement

- Phosphate depletion is common:
  - Renal loss, intracellular uptake during insulin Rx
- Problem (rare):
  - Low cardiac output, respiratory muscle weakness, rhabdomyolisis , CNS depression , seizures , coma, renal failure
- No benefit in routine replacement
  - Replacement if phosphate < 1.5 mg/dl AND Ca is normal
  - Oral replacement preferred ; iv Phosphate leads to hypocalcemia

Complications of RX

- Hypoglycemia
- Hypokalemia
- Hyperchloremia; Hyperchloremic acidosis
- Cerebral edema - children



Special patients

- Pediatric → cerebral edema
  - Cause unknown, risks:
    - Tx with NaHCO3
    - Low initial PaCO2
    - High initial BUN
- Pregnancy → fetal demise
- CHF → fluid overload
- CRF → fluid overload / hyper-K

Complications

- Cerebral edema
  - More in pediatric, high mortality
  - No warning signs – *sudden deterioration in mental status after initial improvement*
  - Tx: mannitol, dexamethasone, hyperventilation
- ARDS
  - Rare but high mortality
- Iatrogenic
  - Pulmonary edema - fluid overloading
  - Hypoglycemia – inadequate monitoring, not adding glucose solution when BG <250 mg/dL

Hypoglycemia

- Whipple Triad
  - Consistent signs and symptoms
  - Low blood glucose
  - Relief with supplemental glucose
- Two categories of hypoglycemia
  - Reactive
  - Nonreactive

Hypoglycemia

- Reactive Hypoglycemia
  - In response to a nutrient challenge
  - Etiology
    - Some pts with type 2 DM
    - Some post GI surgery pts
    - Idiopathic
- Nonreactive Hypoglycemia
  - Iatrogenic
  - Fasting/Factious

Causes of Hypoglycemia

Fasting - ***Underproduction of glucose***
- Hormone deficiencies: Hypopituitarism, adrenal insufficiency, catecholamine deficiency, glucagon deficiency
- Enzyme defects
- Substrate deficiency (malnutrition, late pregnancy)
- Liver disease
- Drugs

Fasting - ***Overuse of glucose***
- Hyperinsulinism: Insulinoma, exogenous insulin, sulfonylureas, drugs, shock
- Tumors

Postprandial
- Alimentary hyperinsulinism
- Fructose intolerance
- Galactemia
- Leucine sensitivity

Fasting/Factious Hypoglycemia

- 3 main causes
  - Factitious taking of oral hypoglycemics/insulin
  - Autoimmune etiology
  - Insulinoma from an islet cell tumor
- Heavy EtOH can also cause hypoglycemia
- 3 tests for nonreactive hypoglycemia workup
  - Serum insulin
  - C-peptide
  - Urinary sulfonylurea test

Hypoglycemia

- C-peptide
  - Low → factitious insulin injection
  - High → autoimmune hypoglycemia, insulinoma, and sulfonylurea ingestion
- Urinary sulfonylurea test
  - To rule in or out oral hypoglycemic use
- Insulin levels
  - < 100 suggest insulinoma
  - > 100 suggest autoimmune

Treatment of hypoglycemia

- Start with the 4 triads
  - A-B-C
  - O2-IV-Monitors
  - Vital signs (BP-HR-RR-BT-SpO2)
  - Hx-PE-Lab (F/S)
- If F/S < 60 mg/dL and symptomatic
  - Oral glucose if alert and able to swallow
  - IV dextrose 25g (50cc of D50W)
    - Pd: 0.5-1 g/kg as D25W IV (2-4 ml/kg);
    - NB: 0.5-1 g/kg (1-2 ml/kg) as D10W
  - IM Glucagon 1 mg q20min if unable no IV
    - Pd: 0.025-0.1 mg/kg SC or IM q20min

TABLE 28.1 **Initial Laboratory Values in Diabetic Ketoacidosis and Hyperosmolar Hyperglycemic State**

	DKA			
Value	**Mild**	**Moderate**	**Severe**	**HHS**
Plasma glucose (mg/dL)	>250	>250	>250	>600
Arterial pH	7.25–7.30	7–7.24	<7	>7.30
Serum bicarbonate (meq/L)	15–18	10–14	<10	>15
Urine and serum ketones	Positive	Positive	Positive	Trace/small
Serum osmolarity (mOsm/L)	<320	<320	<320	330–380
Anion gap	>10	>12	>12	<12
Mental status	Alert	Alert/drowsy	Stupor/coma	Stupor/coma
Sodium (mmol/L)	125–135	125–135	125–135	135–145
Potassium (mmol/L)	Normal to ↑	Normal to ↑	Normal to ↑	Normal
Creatinine (mg/dL)	Slight ↑	Slight ↑	Slight ↑	Moderate ↑

DKA, diabetic ketoacidosis; HHS, hyperosmolar hyperglycemic state.

INSULIN TREATMENT

1) Bolus 0.1–0.15 U/kg regular insulin intravenously (IV) (subcutaneous [SC]/intramuscular [IM] can be given if no IV access)
2) Start continuous IV insulin infusion via an infusion pump
   Standard infusion is 100 U **regular human insulin** (IV $t_{1/2}$ 5–9 minutes) in 100 mL 0.9% NaCl.
   For **DKA** start at 0.1 U/kg/hr
   For **HHS** start at 0.05 U/kg/hr

BLOOD GLUCOSE MONITORING

1) Check initial blood glucose (BG) q1h. **Goal decrease in BG is 50–75 mg/dL/hr.**
2) Once stable (3 consecutive values decreased in target range), change BG monitoring to q2h. Resume q1h BG monitoring for each change in the insulin infusion rate (see below).
3) Add dextrose 5% to IV fluids when BG <250 mg/dL
   For **DKA goal BG 150–200 mg/dL until anion gap closed.**
   For **HHS goal BG is 250–300 mg/dL until mental status improves.**

CHANGING THE INSULIN INFUSION RATE

1) ↓ IV insulin by 50%/hr if BG decreases by >100 mg/dL/hr in any 1 hour period.*
2) ↑ insulin drip by 50%/hr if change in BG is <50 mg/dL/hr.
3) For **DKA and HSS**, when BG decreases to 250 mg/dL, insulin infusion may need to be decreased 50% to maintain glucose at target levels (see Blood Glucose Monitoring above).

Start SC insulin when:

1) Anion gap closed (DKA)
2) Serum bicarbonate increases to >15 meq/L (DKA)
3) Patient able to eat
4) Mental status improves (HHS)

Stop the insulin drip after all of the following are done**

1) Give short acting insulin (aspart or lispro) SC at twice the hourly IV rate (e.g., if IV rate is 5 U/hr, give 10U short acting insulin SC).
2) Give long acting insulin (regular, NPH or glargine) SC at 0.2–0.3 U/kg, or home insulin dose.
3) Ensure patient has a meal and is eating.

FLUID MANAGEMENT*

Fluid replacement varies based on age, weight, hemodynamics, and comorbidities. A reasonable approach follows:

1) **Replace intravascular volume**
   Give 1 L 0.9% NaCl over 30–60 min. Give an additional 1–2 L q30–60 min until hemodynamically stable and urine output increased.
2) **Replace total body water deficit**
   Change to 0.45% NaCl and infuse at 150–500 mL/hr.
   When BG <250 mg/dL add dextrose 5% and decrease to 100–200 mL/hr.

*Fluid is replaced over 12–24 hr and patients are generally depleted 3–6 L in DKA and 8–12 L in HHS.

*Monitor urine output, heart rate, blood pressure, and respiratory status. Care must be taken in patients with congestive heart failure and kidney disease.

ELECTROLYTE MANAGEMENT

1) Check basic metabolic panel (BMP), arterial blood gas, magnesium (Mg^{2+}), and phosphorous (PO_4^{3-}).
2) Repeat BMP, Mg, PO_4^{3-} q2–4h depending on degree of electrolyte imbalance.

Potassium (K^+)

K^+ >_5.5 meq/L: leave potassium supplement out of IVF
K^+ 4–5.4 meq/L: add 20 mEq KCl/L to IVF
K^+ 3–3.9 meq/L: add 40 mEq KCl/L to IVF
K^+ <3 meq/L: add 60 mEq KCl/L to IVF
In DKA, if initial K^+ is <3.3 meq/L, **DO NOT** give IV insulin until the serum K^+ is supplemented to >3.3 mmol/L due to the risk of severe hypokalemia.

Sodium (Na^+)

Hypoglycemia causes an artifactually low serum sodium, and the correct value must be calculated. Corrected Na^+ = Measured Na^+ [mmol/L] + (1.6 (Measured BG [mg/dL] – 100)/100)

Na^+ replaced with IV fluids initially as 0.9% NaCl for first 1–3 L and then as 0.45% NaCl (see Fluid Management).

Bicarbonate (HCO_3^-)

Usually in DKA only.

Replacement generally not necessary as insulin will reverse the HCO_3^- deficit with its inhibition of lipolysis.

Consider HCO_3^- in the following situations (see Chapter 24; metabolic acidosis):

1) Severe acidosis with pH <7 (the HCO_3^- should be stopped once the pH is >7.1)
2) Severe loss of buffering capacity when serum HCO_3^- <5–10 meq/L
3) Acidosis induced cardiac or respiratory distress
4) Severe hyperkalemia

Magnesium and Phosphorus

Severe hypomagnesemia and hypophosphatemia are not common complications of DKA and HHS (see Chapter 23 if they occur) and supplementation is usually not necessary.

Thank You