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Diabetic Ketoacidosis and Hyperosmolar Hyperglycemic State

Jennifer N. Thompson, MD
Project Hope

Objectives

DKA: Diabetic Ketoacidosis

HHS: Hyperosmolar Hyperglycemic State

(HONKC – hyperosmolar nonketotic coma)

- What is the difference between DKA and HHS?
- How do I manage DKA and HHS?
- What complications should I look out for?
- What does the data say about cerebral edema?

	Diabetic Ketoacidosis	HHS - Hyperosmolar hyperglycemic state
Blood glucose	Glucose >250 (13.9)	Glucose >600 (33.3)
Arterial pH	pH <7.3	pH >7.3
Serum Bicarbonate	<15	>15
Serum osmolality	varies	>320 mOsm
Urine ketones	+++	Small or none
Anion gap	>12	
Demographics	Mostly type I DM Children, young people	Mostly type II DM Elderly, mentally or physically impaired
Insulin activity	**Absolute** functional insulin deficiency	**Relative** insulin deficiency
Mortality in admitted patients	1-4%	10% or more

Classic presentation of DKA

Age

- Young people, Type I DM

History

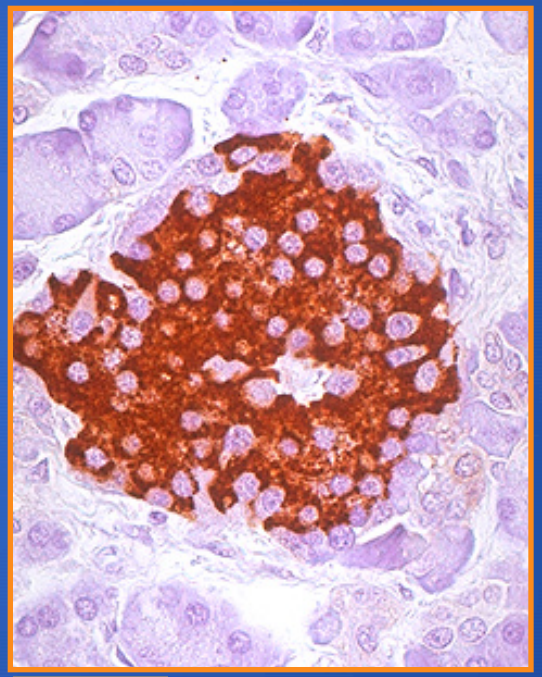
- Polydipsia, Polyuria, Fatigue
- Nausea/vomiting, diffuse abdominal pain.
- In severe cases – lethargy, confusion

Physical

- Ill appearance
- Signs of dehydration: Dry skin, dry mucous membranes, decreased skin turgor (skin tenting)
- Signs of acidosis:
  - Tachypnea → Kussmaul respirations
  - Characteristic acetone (ketotic) breath odor

Role of Insulin

- Required for transport of glucose into cells for use in making ATP
  - Muscle
  - Adipose
  - Liver
- Inhibits lipolysis
- Type I DM = inadequate insulin



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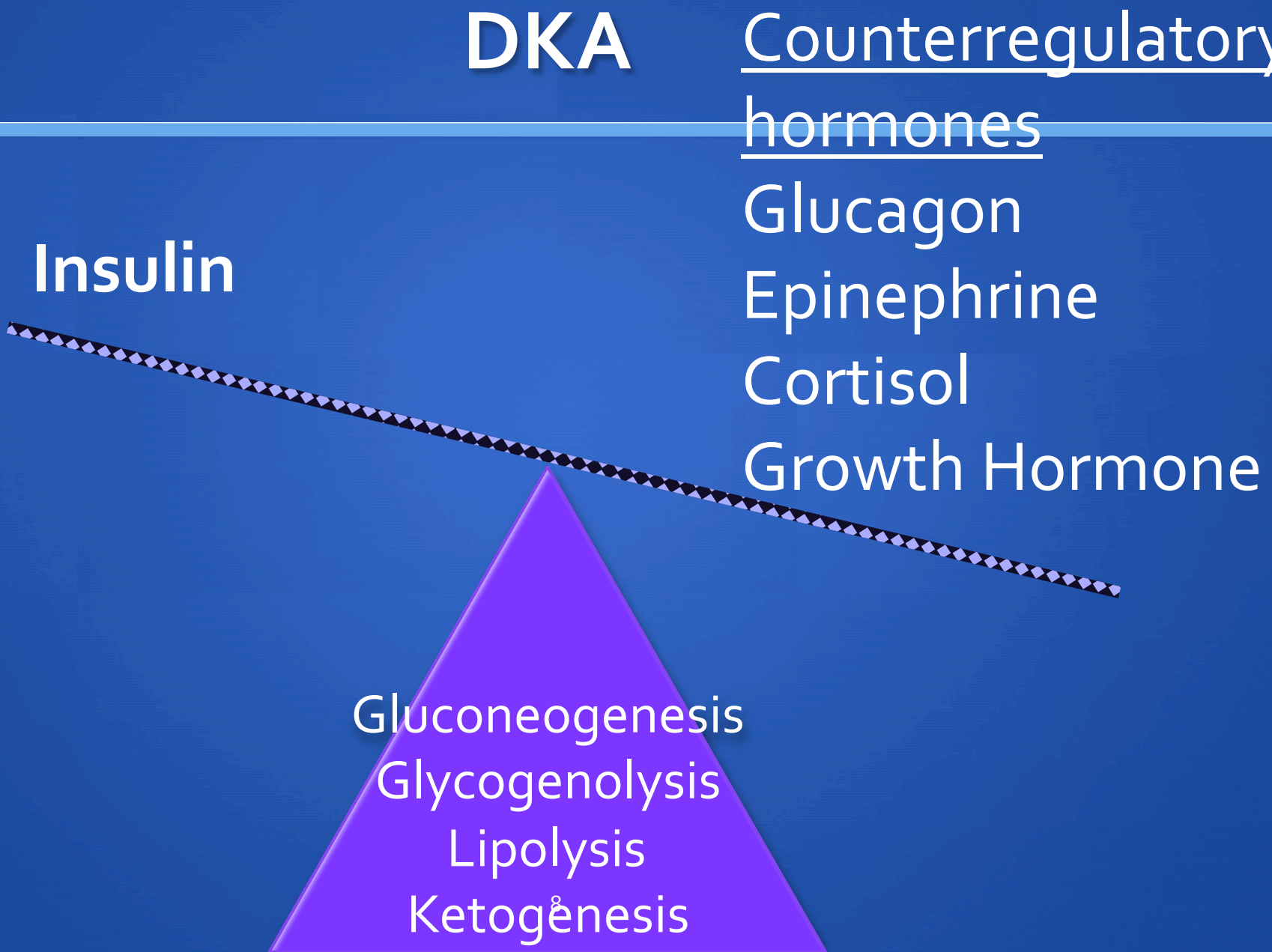
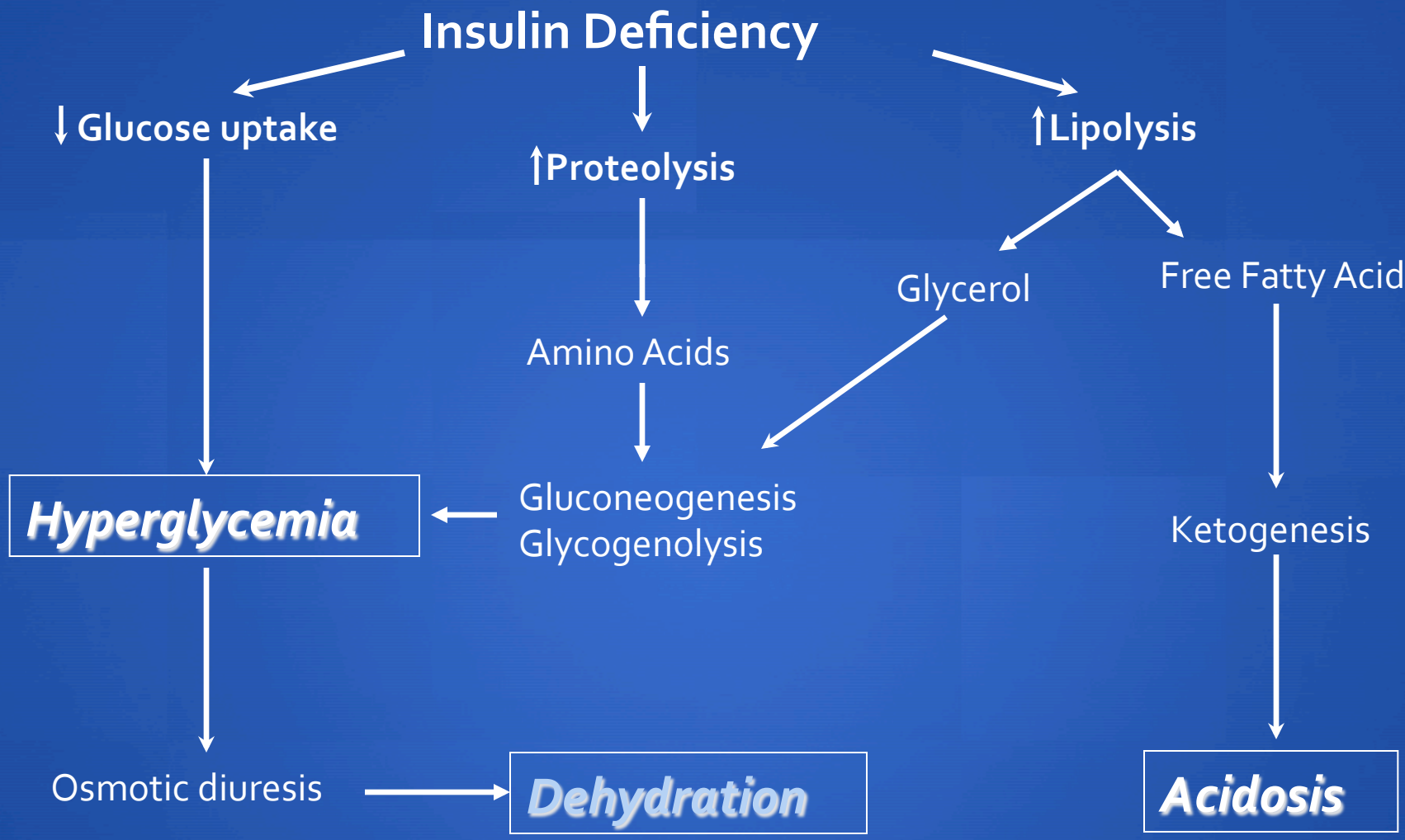
Pathophysiology in DKA



Counterregulatory Hormones - DKA

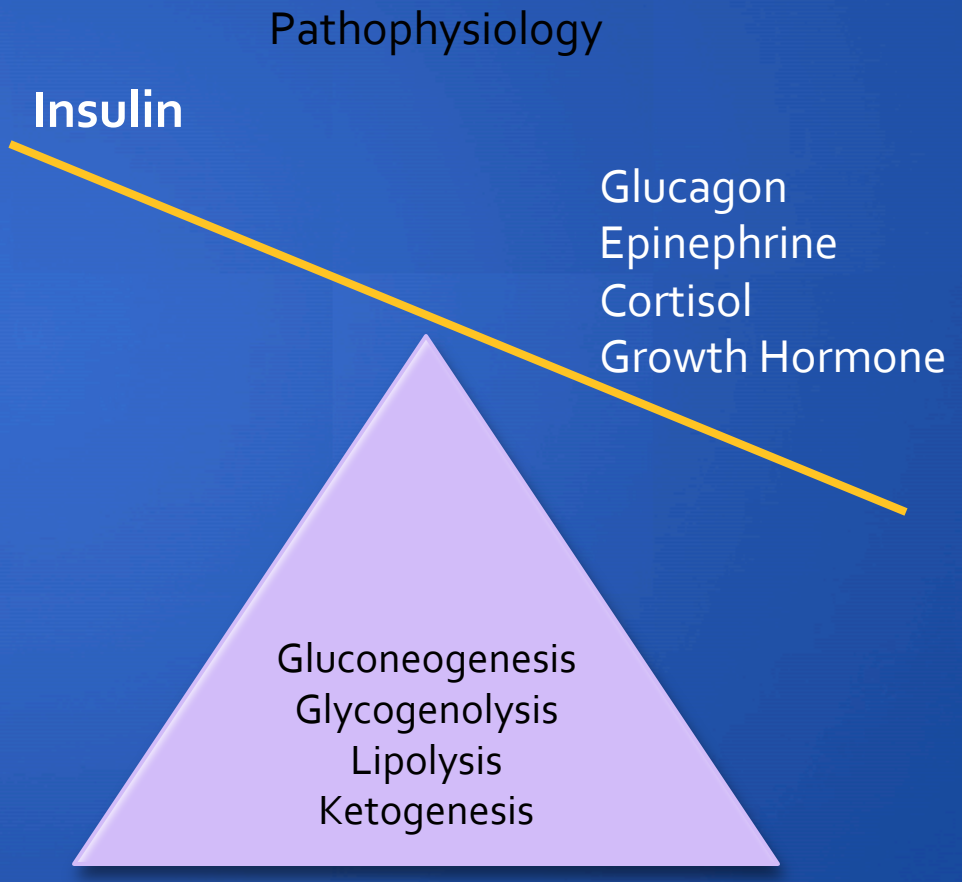
	Increases insulin resistance	Activates glycogenolysis and gluconeogenesis	Activates lipolysis	Inhibits insulin secretion
Epinephrine	X	X	X	X
Glucagon		X		
Cortisol	X	X		
Growth Hormone	X		X	X



- No Liploysis = No Ketoacidosis
- Only a small amount of functional insulin required to suppress lipolysis

Underling stressors that tip the balance

- Newly diagnosed diabetics
- Missed insulin treatments
- Dehydration
- Underlying infection
- Other physiologic stressors:
  - Ex) Pulmonary embolism, Illicit drug use (sympathomimetics), Stroke, Acute Myocardial Infarction,
- Young type II diabetics with stressors



Workup

Most important labs to diagnose DKA:

- Basic metabolic panel (glucose, anion gap, potassium)
- Arterial or venous blood gas to follow pH
- Urine dipstick for glucose and ketones (high sensitivity, high negative predictive value)

- Additional tests:
- Serum ketones
- Magnesium, phosphorus
- EKG – if you suspect hyperkalemia, hypokalemia, arrhythmias

**Determine the underlying cause!

Management

- Fluids
- Insulin
- Electrolyte repletion
- Find and treat any underlying cause!

Fluids

- Increases intravascular volume
  - Reverses dehydration
  - Restores perfusion to kidneys → ⇧ GFR → urinate out excess glucose
  - Restores perfusion to periphery → ⇧ uptake and use of glucose (when insulin present)

Take home message: Fluids hydrate patient AND reverse hyperglycemia

Fluids

Pediatrics

- Hypotension: treat with 20cc/kg NS boluses
- If no hypotension:
  - 10-20cc/kg NS bolus then 1.5 – 2x maintenance

    OR
  - Assume 10% dehydration and calculate fluid deficit plus maintenance
  - Replete deficit (plus maintenance) over 48-72hrs.

Insulin

- Allows glucose to enter and be used by cells
- Stops proteolysis and lipolysis
  - Stops Ketogenesis → Stops Acidosis
- Allows potassium to enter cells

Insulin goal: Treat the anion gap acidosis
(not the hyperglycemia)

- Never stop the insulin before the anion gap is closed.

Insulin

- Dosing: 0.05 units/kg bolus then .05 units/kg/hr insulin drip. (Previously 0.1 units/kg/hr)
- Goal: Decrease glucose by <100 (5.5) per hour
  - Avoids sudden fluid shifts that may lead to cerebral edema
- Reason for IV insulin
  - Not affected by decreased peripheral circulation as with subcutaneous insulin
  - Smooth decline of glucose
  - Short half-life allows for more precise control of serum insulin concentration

Insulin

- If pt has an anion gap and your glucose is <250 (14), do you stop the insulin drip?
- NO!
  - Add D5 when glucose <250 (14).
    If glucose <150 (8.3), consider D10.

TAKE HOME POINT:

- Do not stop insulin until anion gap is closed.
- Main goal of insulin therapy is to fix the acidosis.

Transitioning to Subcutaneous Insulin

- ONLY after the Anion Gap is closed!
- OVERLAP IV and subcutaneous insulin administration
  - Give long-acting insulin dose (ex. lantus) at least 30 to 60 minutes prior to stopping insulin drip.
- Feed patient

Managing electrolytes

- Potassium
- Sodium
- Phosphorus
- Glucose

Electrolyte management
Potassium

Total Body Potassium depletion

- Acidosis → K^+ exits cells as H^+ enters to buffer
- Dehydration and volume depletion
  - Osmotic diuresis + ⇧ aldosterone → loss of K+

➡ Although serum K^+ is usually normal or high, total body K^+ is low.

Electrolyte Management
Potassium

- With insulin therapy
  - K^+ moves into cells
- To avoid hypokalemia
  - Give oral and/or IV potassium to avoid hypokalemia when K < 4.5
  - Monitor K^+ levels and EKG
    - Low K – Biphasic T, U-wave
    - High K - tall peaked T, flat P waves, wide QRS
    - Cardiac dysrhythmia

Electrolyte Management
Sodium

Pseudohyponatremia:

- For each 100mg/dl increase of glucose above 100, Na^+ decreases by 1.6 mEq/L

- Corrected Na^+ = measured Na +

  1.6 meq/L x (glucose-100)/100))

- Example:

  Na^+ = 125 meq/L and Glucose = 500 mg/dl

  500 – 100 = 400

  400/100 = 4

  4 x 1.6 = 6.4 meq/L

  Corrected Na^+ = 125 + 6.4 = 131.4 meq/L

**Electrolyte Management Phosphorus

Hypophosphatemia

- Occurs after aggressive hydration/treatment
- Monitor phosphorus and replete as needed to keep > 1
  - Total body phosphorus depleted
  - Mostly a theoretical problem
    - Potential complications: muscle weakness, myocardial dysfunction, CNS depression

Management review

- Rehydrate patient with IV fluids
- Continue insulin drip until anion gap is closed
- Until insulin drip is off:
  - Check glucose every hour. Avoid hypoglycemia.
  - Check electrolytes every 1-2hrs. Avoid hypokalemia.
- Replete potassium when K < 4.5 and patient making urine

ICU Monitoring

Careful nursing monitoring of the following:

- I/Os (input and urine output.)
- Urine dipstick with every void
  - resolution of ketonuria may lag behind clinical improvement
- Monitor for any signs of cerebral edema:
  - Change in mental status, severe headache
  - Sudden drop in heart rate
  - Neurologic deficits

DKA Complications

- Dehydration, shock, hypotension
- Hypokalemia/ hyperkalemia
- Hypoglycemia
- Aspiration pneumonia
- Sepsis
- Acute tubular necrosis
- Myocardial infarction
- Stroke
- Cerebral edema

* Death rate in U.S when managed in hospital setting = 1-4%

DKA Complications Cerebral edema

- Clinical manifestations:
  - Altered mental status
  - Headache
  - Persistent vomiting
  - Sudden and persistent drop in heart rate
  - Seizure
  - Unequal or fixed, dilated pupils
- Mostly children
- High mortality rate
  - 1% of DKA pts, > 25% mortality rate
- High morbidity rate
  - High rate of neurologic complications

DKA Complications Cerebral edema

- Risk Factors
  - Age < 5 years
  - More often seen in your sickest patients
    - (high BUN, low bicarb <15)
    - Fall in serum Na or lack of increase during treatment
  - Rapid correction of hyperglycemia
    - Goal: decrease glucose <100 mg/dl (5.5) per hour
  - Sodium bicarbonate administration
  - Excessive fluids

DKA Complications
Cerebral Edema - treatment

- Mannitol 1mg/kg IV
- Reduce IV fluid rate (ex. 70% maintenance)
- Consider intubation
  - set the ventilator close to rate that patient was breathing beforehand
  - be cautious of over hyperventilation
    - Temporary measure
    - Keep pCO_2 > 22mmHg
- May consider 3% hypertonic saline
  - but not enough data to truly recommend

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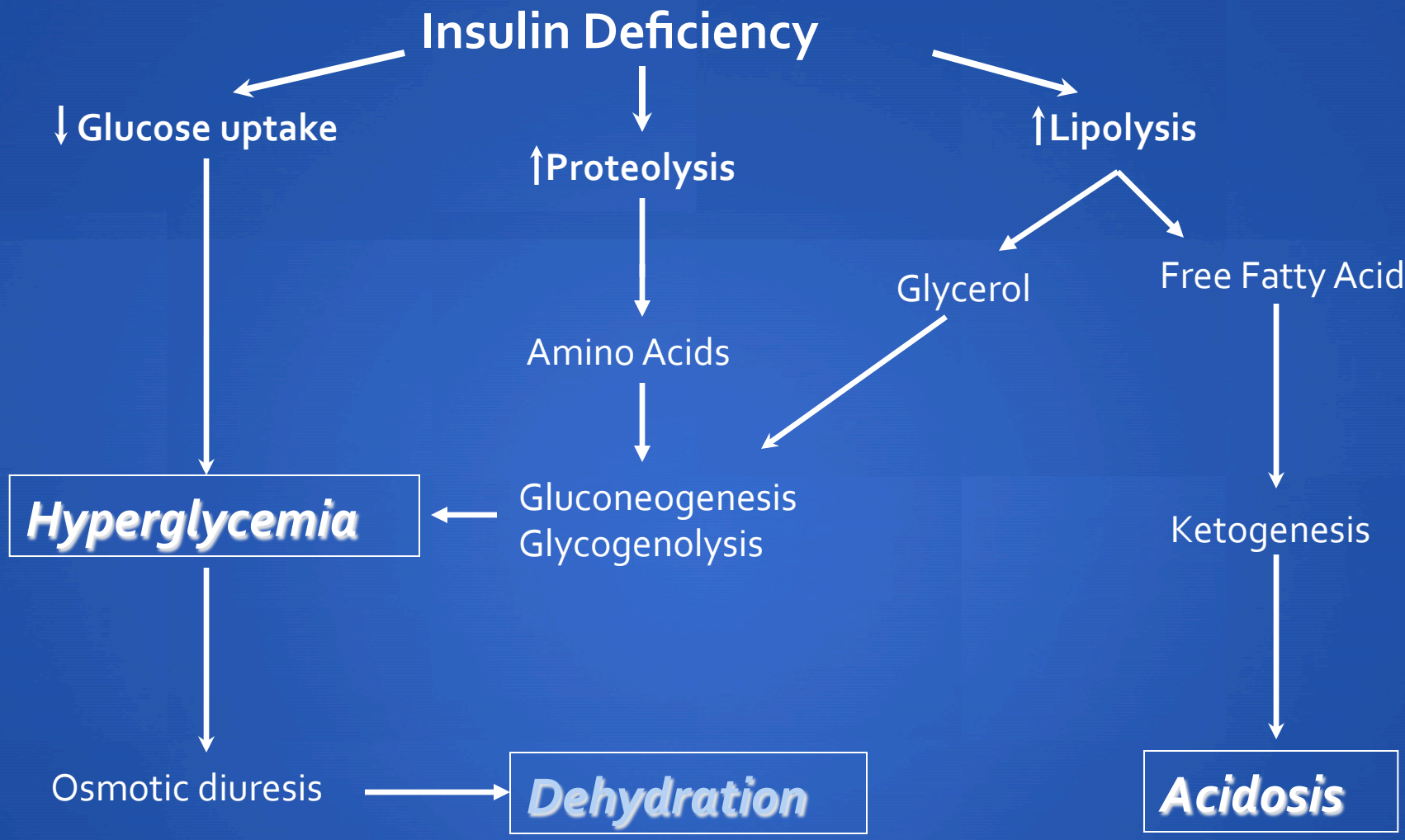
Demographics	Mostly type I DM Children, young people	Mostly type II DM Elderly
Insulin activity	Absolute functional insulin deficiency	Relative insulin deficiency
Mortality in admitted patients	1-4%	10% or more

HHS
(Hyperosmolar Hyperglycemic State)

- Elderly and mentally or physically impaired patients
- Usually associated with underlying physiologic stressors
  - Ex. Infection, myocardial infarction, stroke.
- Slower onset (ex. 1 week vs. 1-2 days in DKA)
- Higher Mortality rate than DKA (>10%)
  - Older patients, more comorbidities

<u>Presentation</u>:

- Altered mental status (confusion, neurologic deficits)
- Signs of severe dehydration (tachycardia, hypotension, dry mucous membranes, skin tenting)



- No Liploysis = No Ketoacidosis
- Only a small amount of functional insulin required to suppress lipolysis
- Low catecholamine levels in elderly patients → less insulin resistance

HHS
- State of severe dehydration

Therapy:

- Fluid repletion
  - Total fluid deficit ≈ 10 liters in adults
  - Normal saline 2-3 liters rapidly
  - Replete ½ in first 6 hours
- Insulin drip 0.05 units/kg/hr
  - Decrease glucose by approximately 50 mEQ/hr
- Check electrolytes q1-2hrs. Check glucose q1hr
  - Monitor potassium for hypokalemia/hyperkalemia
- Treat underlying precipitating illness

- Potential complications are the same as DKA

Summary

- Pathophysiologic difference between DKA and HHS
  - DKA is a state of absolute functional insulin deficiency
  - Only in DKA : Lipolysis →ketogenesis →acidosis

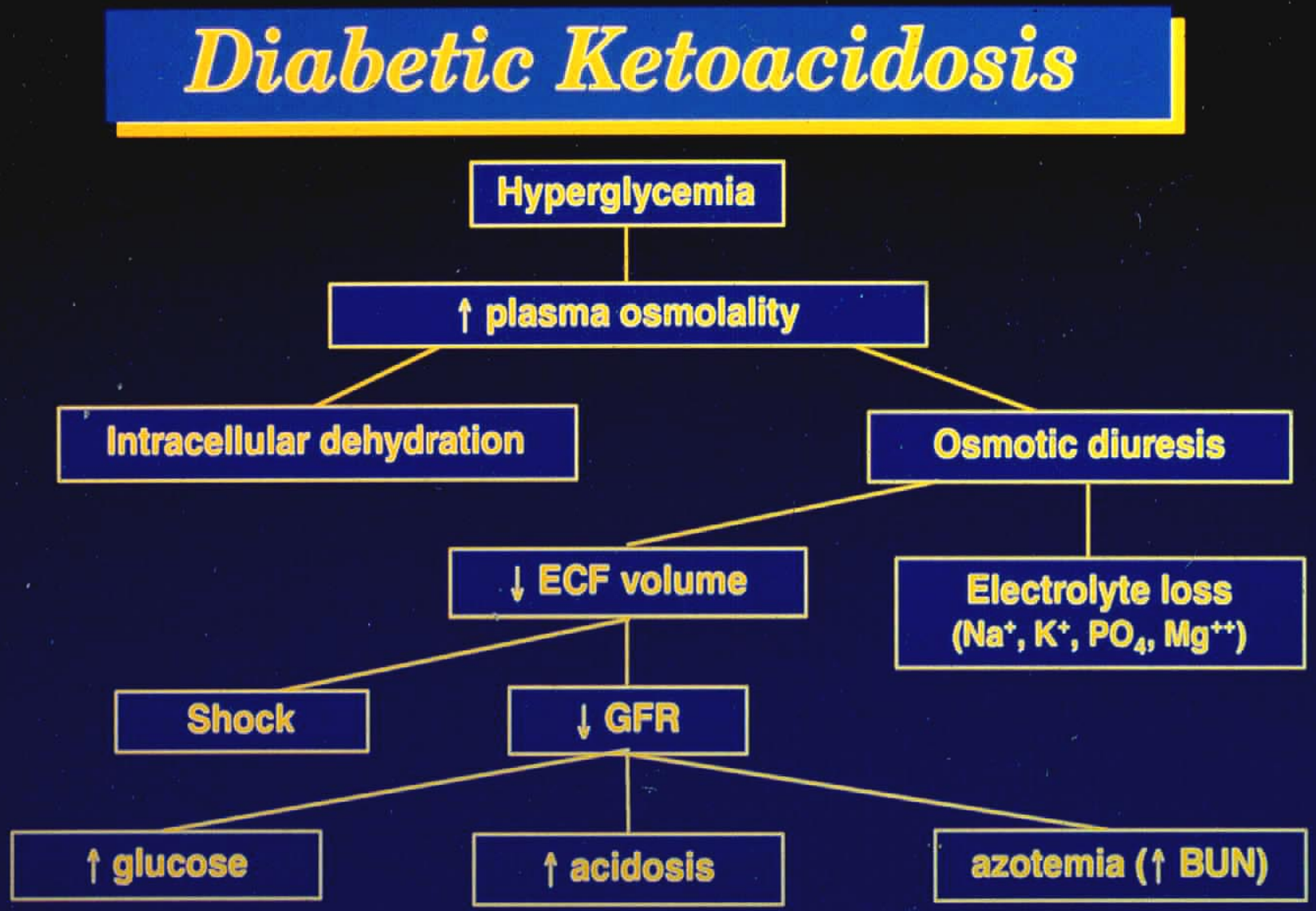
- You are never specifically treating the glucose
  - In DKA – you are treating the underlying acidosis/ ketogenesis (reflected by the anion gap)
  - In HHS – you are treating the underlying shock caused by poor tissue perfusion/severe dehydration

Summary (continued)

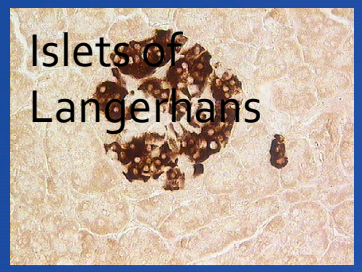
- Being too aggressive in management may cause more harm than good
- If you don't pay attention to details, you will cause an iatrogenic death
  - Monitor electrolytes (especially potassium)
- Beware cerebral edema.
- Therapy for DKA and HHS is similar.

Thank you

diabetees.spreadshirt.com



Pathophysiology of diabetic ketoacidosis



β-cell destruction

Insulin Deficiency

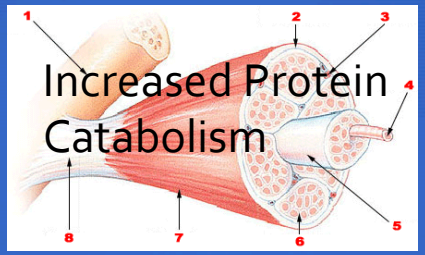
Stress

Epi, Cortisol
GH

Decreased Glucose Utilization &
Increased Production

Muscle

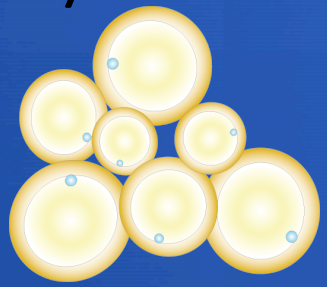
Amino
Acids



Glucagon

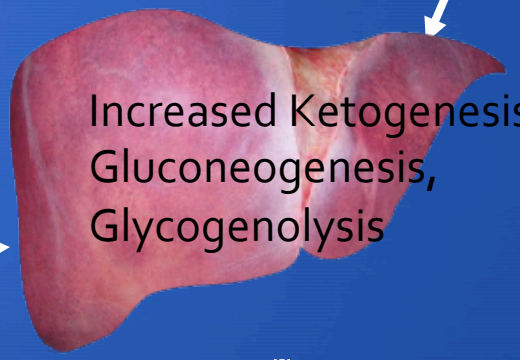
Liver

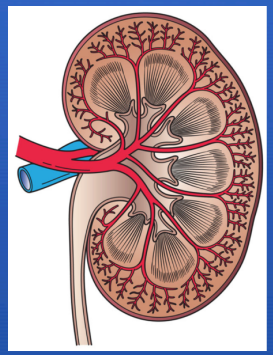
Adipocytes



Increased Lipolysis

FattyAcids





Threshold
180 mg/dl

Polyuria
Volume Depletion
Ketonuria

Hyperglycemia
Ketoacidosis
HyperTG

Additional Information

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