

Acute Metabolic Complications of Diabetes

Diabetic ketoacidosis · Hyperosmolar hyperglycemic state · Hypoglycemia

Mechanistic pathology and clinicopathologic interpretation

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Learning objectives

- Connect insulin deficiency and counterregulation to acute metabolic derangements.
- Trace the distinct mechanisms leading to ketoacidosis and hyperosmolar dehydration.
- Recognize clinically important symptom patterns and precipitating conditions.
- Differentiate the three emergencies and explain the therapeutic principles stated.

Mechanism → manifestation → clinical recognition

Three emergencies, three dominant metabolic problems

Complication	Dominant disturbance	Characteristic consequence
Diabetic ketoacidosis	Insulin deficiency; excessive ketone-body production	Metabolic acidosis + dehydration
Hyperosmolar hyperglycemic state	Sustained severe hyperglycemia; water losses	Profound dehydration + altered mental status
Treatment-associated hypoglycemia	Glucose availability becomes inadequate	Autonomic and neurologic manifestations

Each has a distinct proximate mechanism; All warrant prompt recognition.

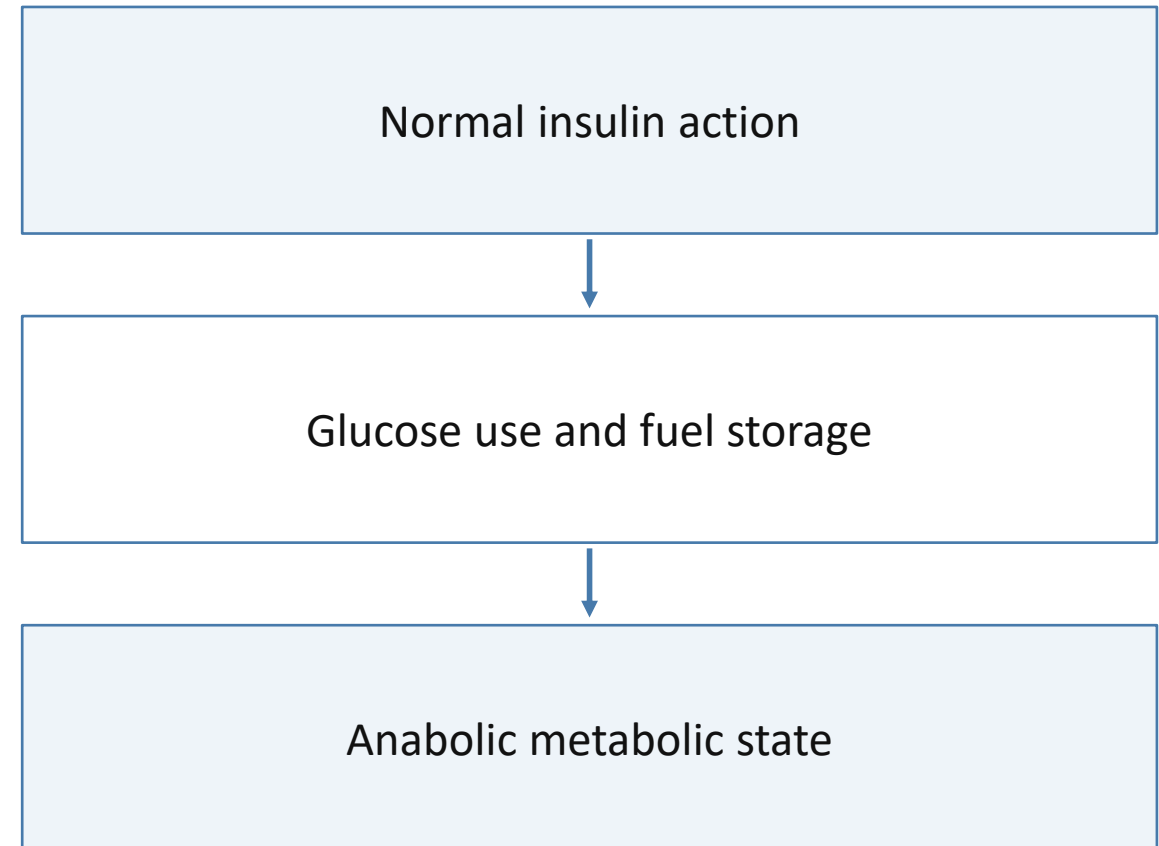
Acute and chronic complications require different lenses

- Acute metabolic complications reflect an immediate disruption of metabolic homeostasis.
- Hyperglycemic crises can rapidly produce fluid loss and neurologic deterioration.
- Treatment-associated hypoglycemia is an acute consequence of glucose-lowering therapy.
- Chronic diabetic vascular injury is a separate topic, not the principal focus here.

The acute clinical question is what metabolic process is failing now.

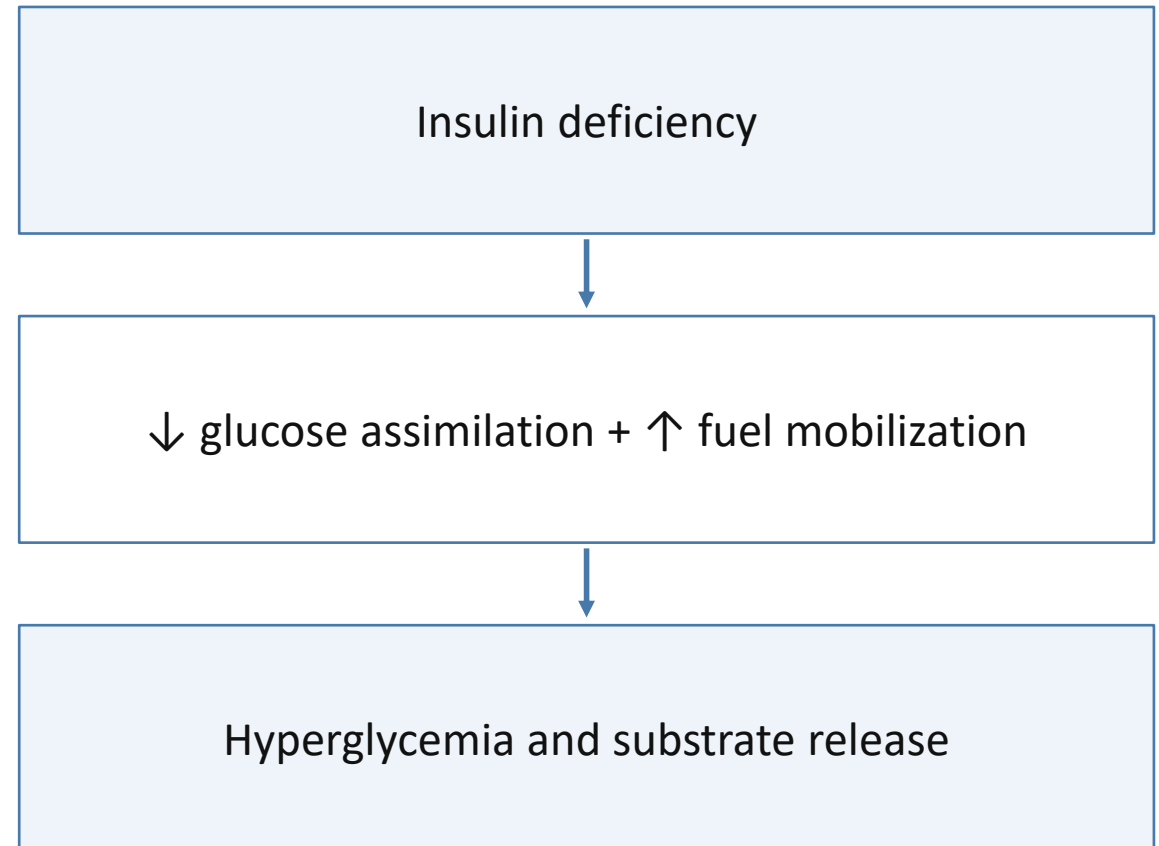
Insulin normally favors nutrient storage

- Insulin is a major anabolic hormone regulating glucose, lipid, and protein metabolism.
- Its action supports glucose assimilation by muscle and adipose tissue.
- Insulin deficiency shifts metabolism toward mobilization of stored fuels.



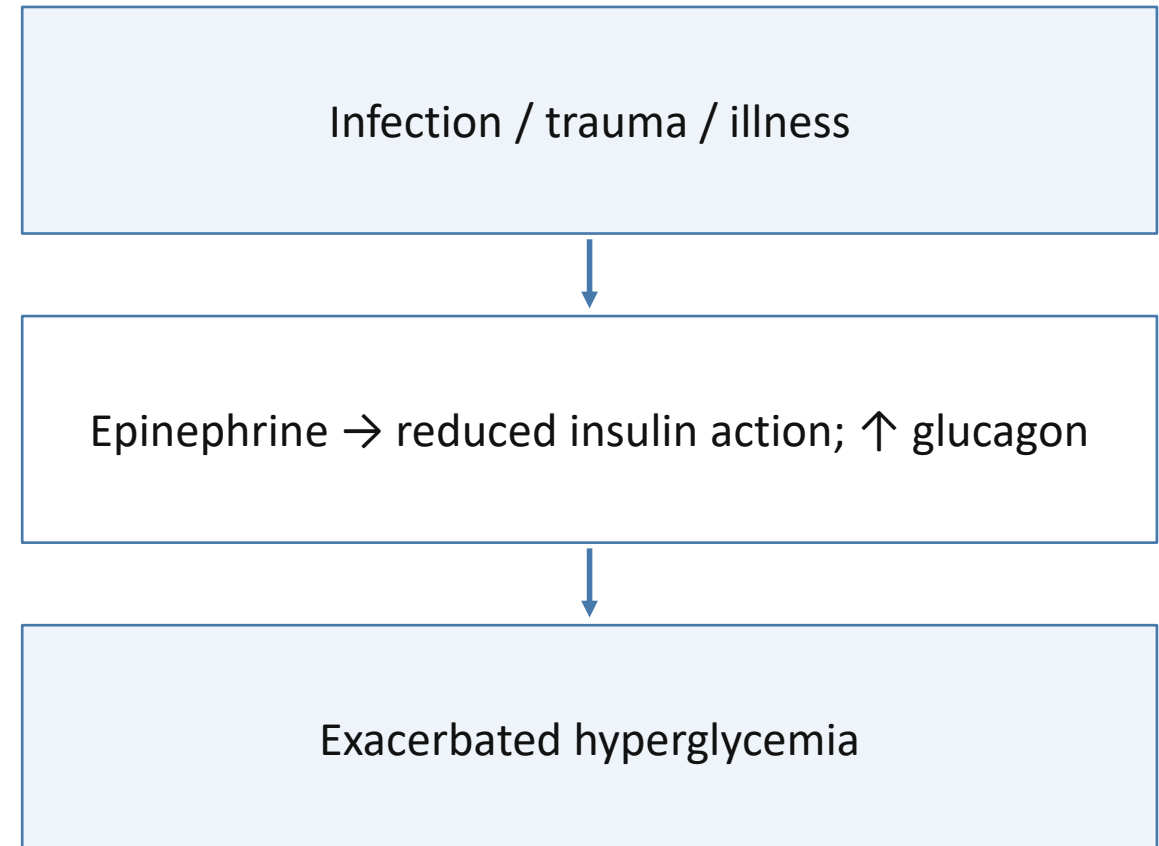
Loss of insulin produces a catabolic shift

- Peripheral glucose uptake falls when insulin action is markedly deficient.
- Glycogen reserves become mobilized rather than replenished.
- Fat and protein breakdown supply alternate circulating substrates.
- The same hormonal disturbance can drive both hyperglycemia and ketogenesis.



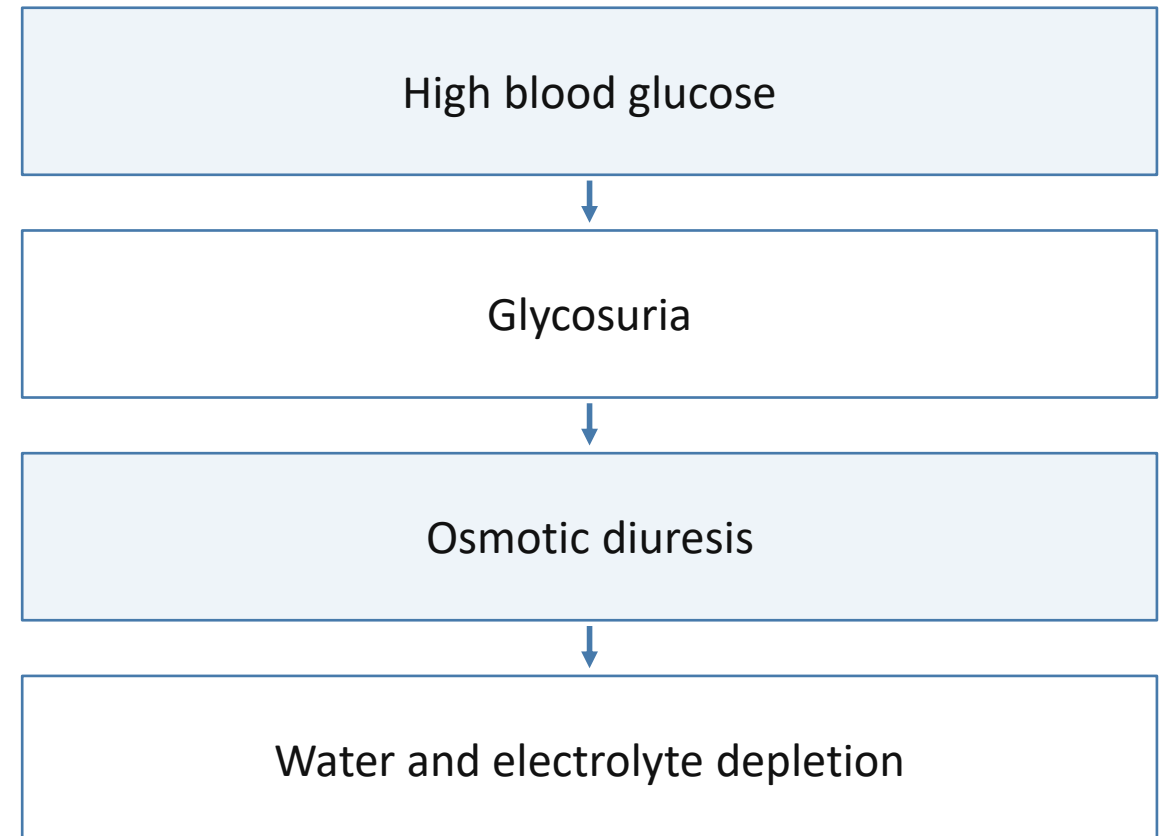
Counterregulatory signals intensify metabolic failure

- Glucagon acts in opposition to insulin in the ketoacidotic state.
- Stress-related epinephrine reduces residual insulin action and stimulates glucagon secretion.
- These effects intensify the loss of metabolic restraint on glucose production.



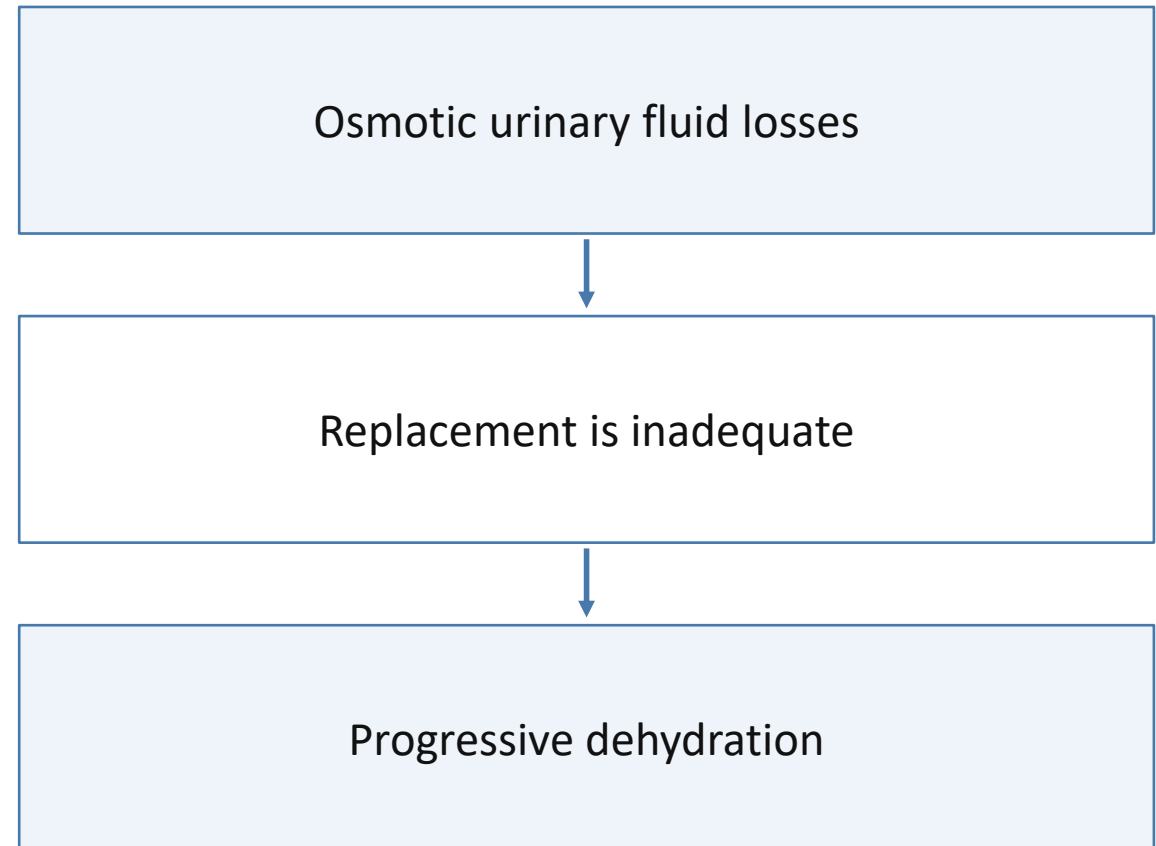
Hyperglycemia begins a renal water-loss cascade

- As plasma glucose rises, filtered glucose can exceed tubular reabsorption capacity.
- Glucose then appears in urine (glycosuria).
- Urinary glucose increases osmotic water loss, generating polyuria.
- Continued diuresis progressively depletes water and electrolytes.



Why dehydration amplifies the clinical problem

- Prolonged polyuria creates a continuing deficit unless fluid intake replaces losses.
- Dehydration compromises urinary clearance of circulating ketones in DKA.
- In HHS, inability to compensate for water loss is especially important.
- The resulting volume depletion is itself clinically consequential.



Two hyperglycemic pathways diverge at ketogenesis

Marked insulin deficiency

- Unrestrained lipolysis
- Ketone acids accumulate
- DKA phenotype

Residual portal insulin

- Ketogenesis relatively restrained
- Prolonged osmotic diuresis
- HHS phenotype

Precipitating context directs the initial reasoning

Hyperglycemic deterioration

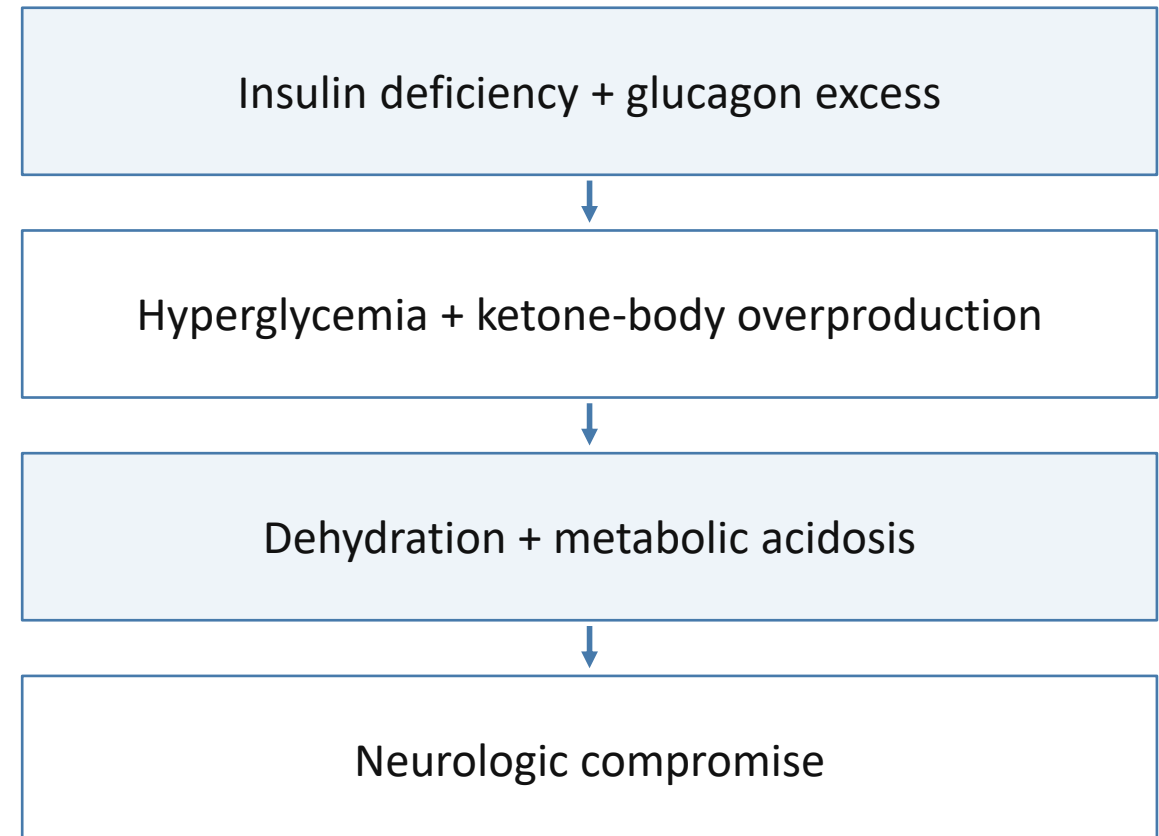
- Missed insulin
- Infection or severe stress
- Insufficient water intake

Glucose-lowering therapy

- Insulin or sulfonylurea
- Missed meal or exertion
- Excess dosing / misdosing

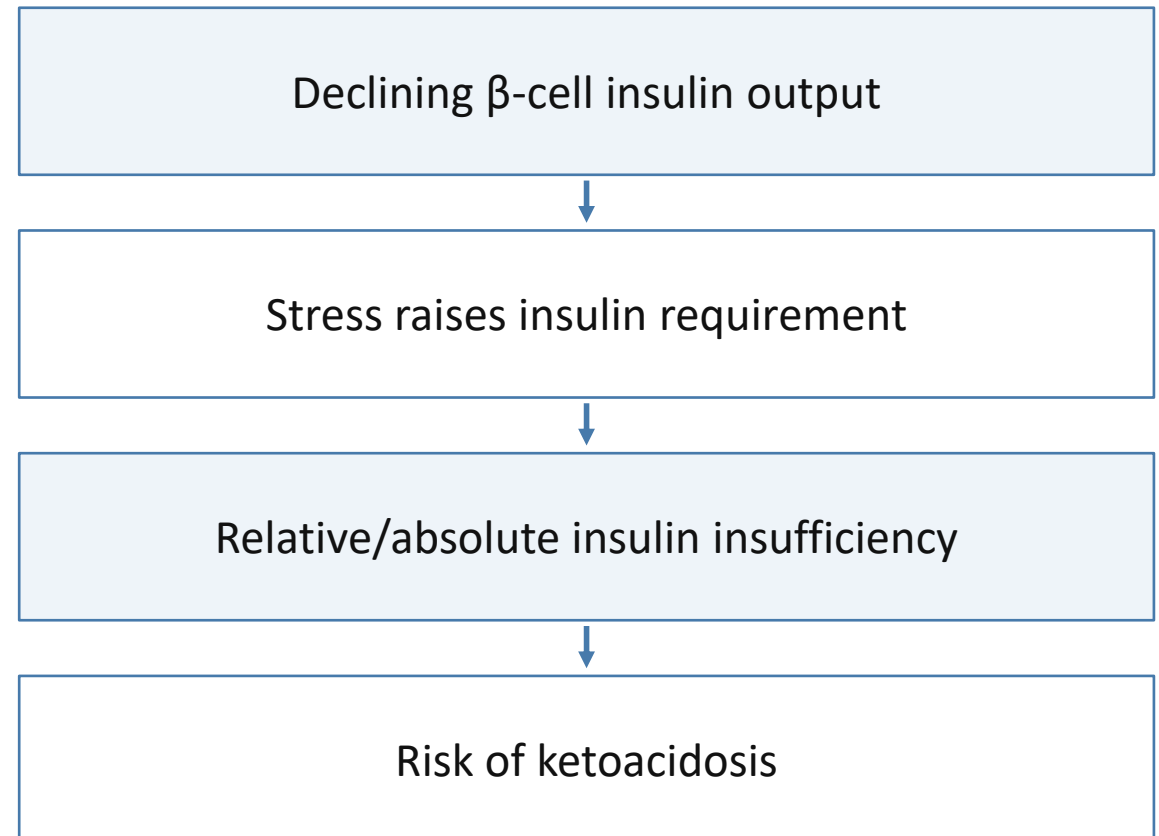
Diabetic ketoacidosis: Linked hyperglycemia and acid production

- DKA is a severe acute metabolic complication, encountered mainly in type 1 diabetes.
- Insulin deficiency plus glucagon excess increase blood glucose and ketone production.
- Osmotic diuresis and ketoacidosis jointly account for systemic illness.
- Depressed consciousness and coma may follow persistent derangement.



Why type 1 diabetes is especially vulnerable

- Progressive β -cell loss ultimately produces major insulin deficiency.
- An intercurrent stress can abruptly increase insulin requirements.
- When endogenous or administered insulin is insufficient, catabolism becomes unrestrained.
- DKA may be a severe manifestation of this metabolic transition.



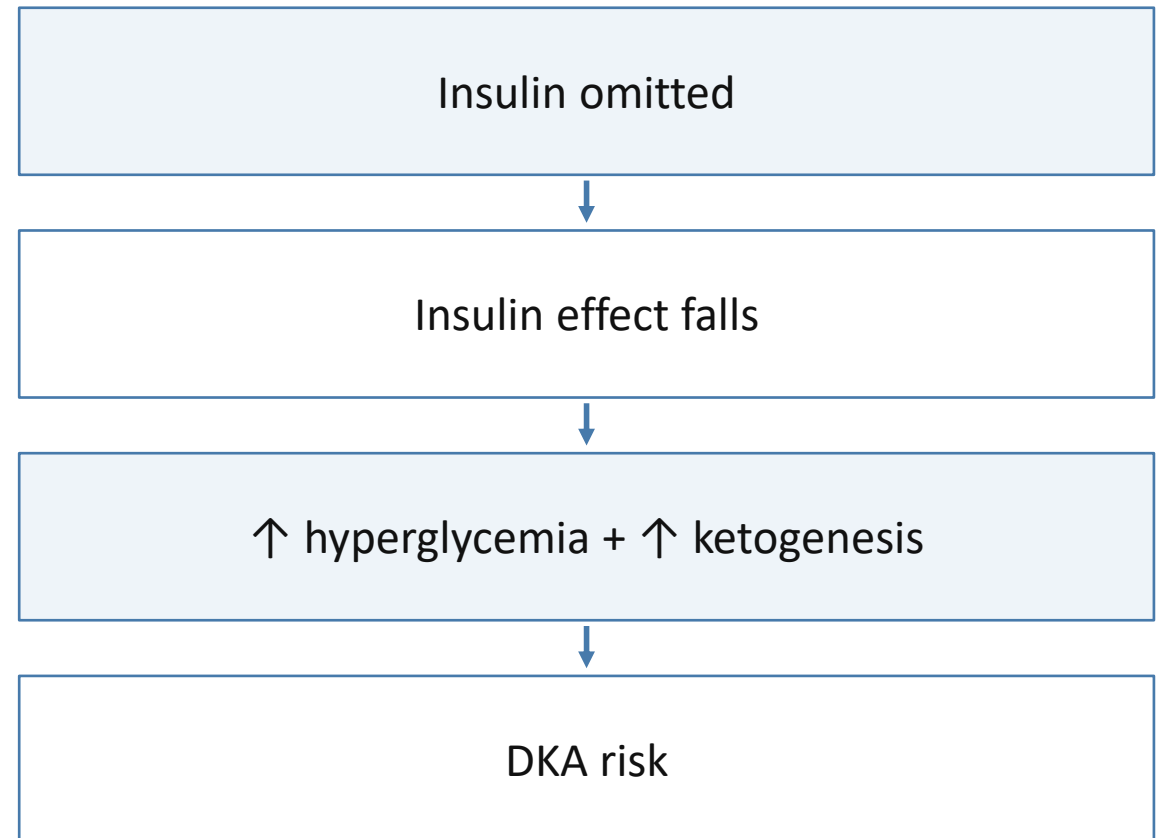
DKA can also occur in type 2 diabetes

- Type 2 diabetes usually retains more portal-vein insulin than type 1 disease.
- This residual insulin can restrain hepatic fatty-acid oxidation and ketone formation.
- Under especially severe stress, DKA nevertheless may develop in type 2 diabetes.
- Diabetes subtype is therefore informative but not an absolute exclusion.

“Mainly type 1” does not mean “type 1 exclusively.”

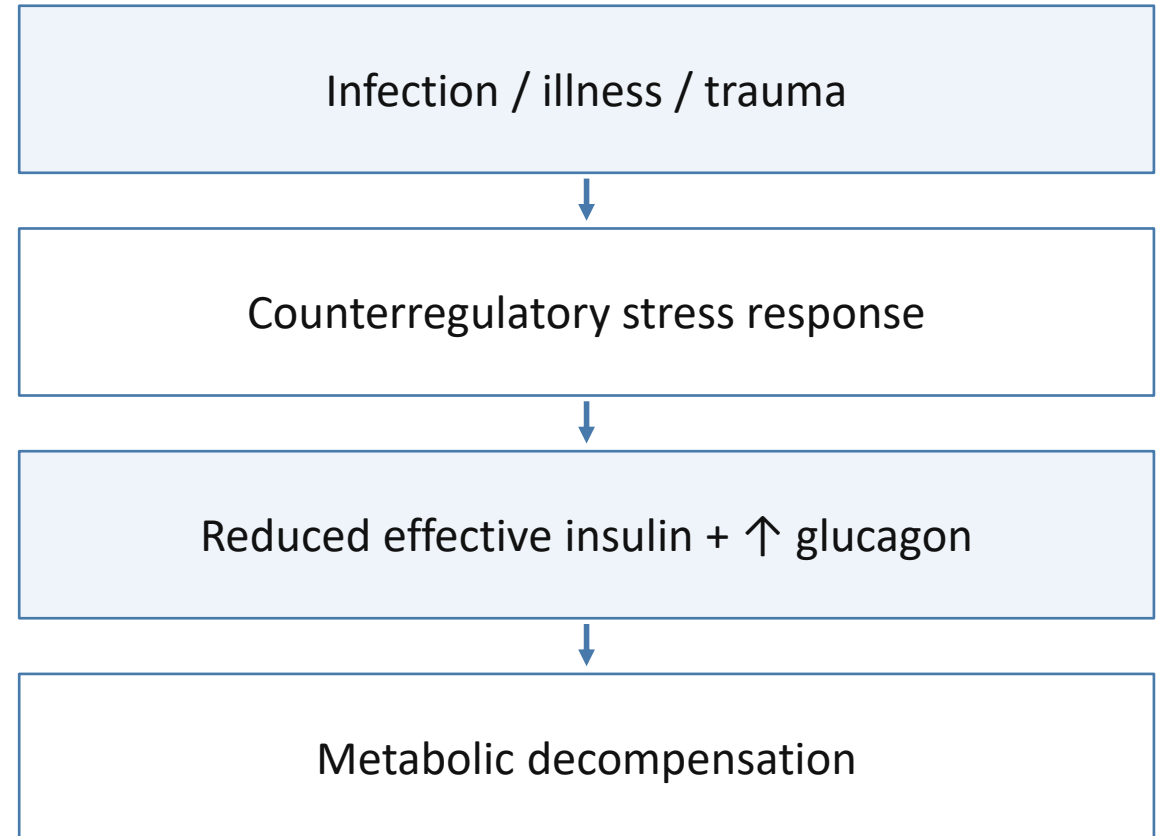
Insulin omission is an important DKA trigger

- Failure to take insulin is described as a frequent precipitating event.
- Reduced insulin signaling removes restraint on glucose production and lipolysis.
- Clinical assessment must connect drug exposure with the metabolic process.
- Addressing the trigger is necessary in addition to reversing the crisis.



Infection and tissue stress can precipitate DKA

- Infection, other illness, trauma, and certain drugs are recognized precipitants.
- Stress responses can increase secretion of epinephrine.
- Epinephrine opposes residual insulin action and promotes glucagon release.
- Metabolic demand may then exceed available insulin.



The insulin–glucagon imbalance has two glucose effects

Peripheral tissues

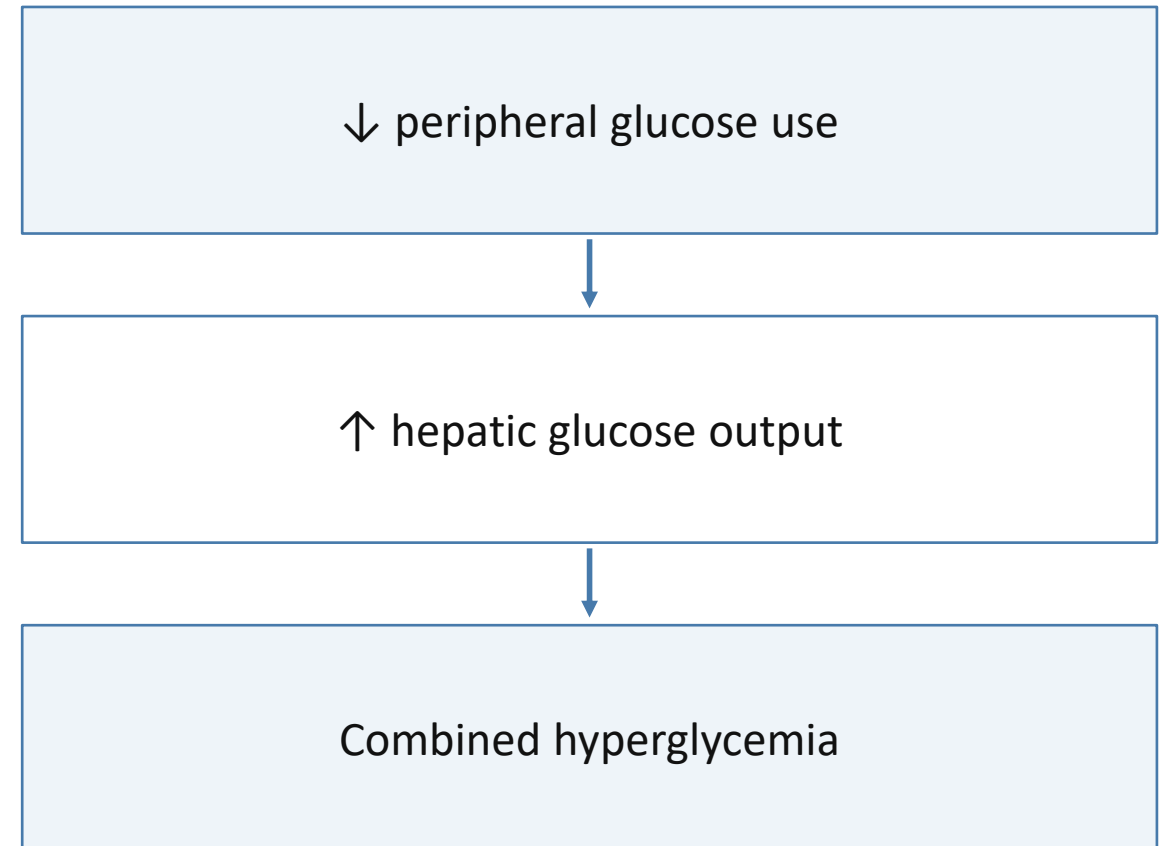
- Less glucose assimilation
- Circulating glucose remains elevated

Liver

- Increased gluconeogenesis
- Additional glucose enters blood

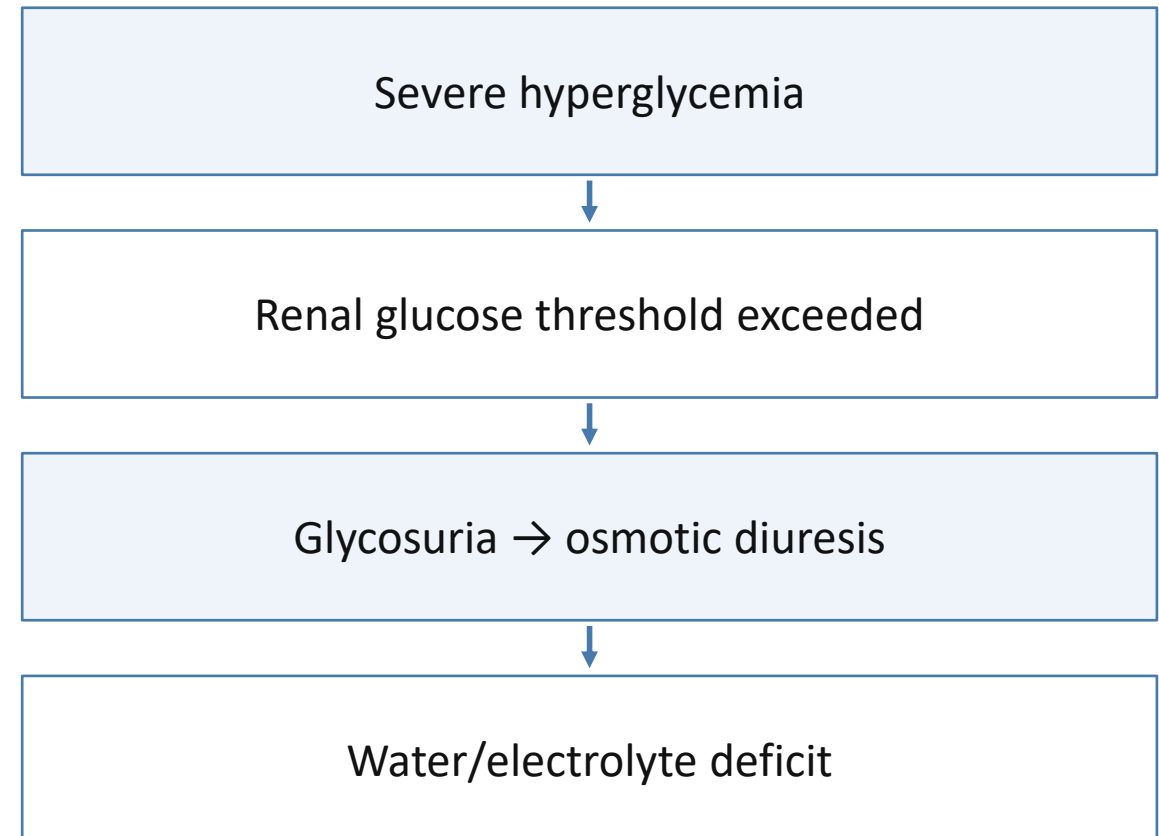
Reduced glucose utilization is not the whole story

- Hyperglycemia is not explained solely by failure of tissue glucose uptake.
- Concurrent hepatic glucose production further increases plasma glucose.
- The two processes operate simultaneously during severe insulin insufficiency.
- This helps explain why DKA can evolve rapidly under superimposed stress.



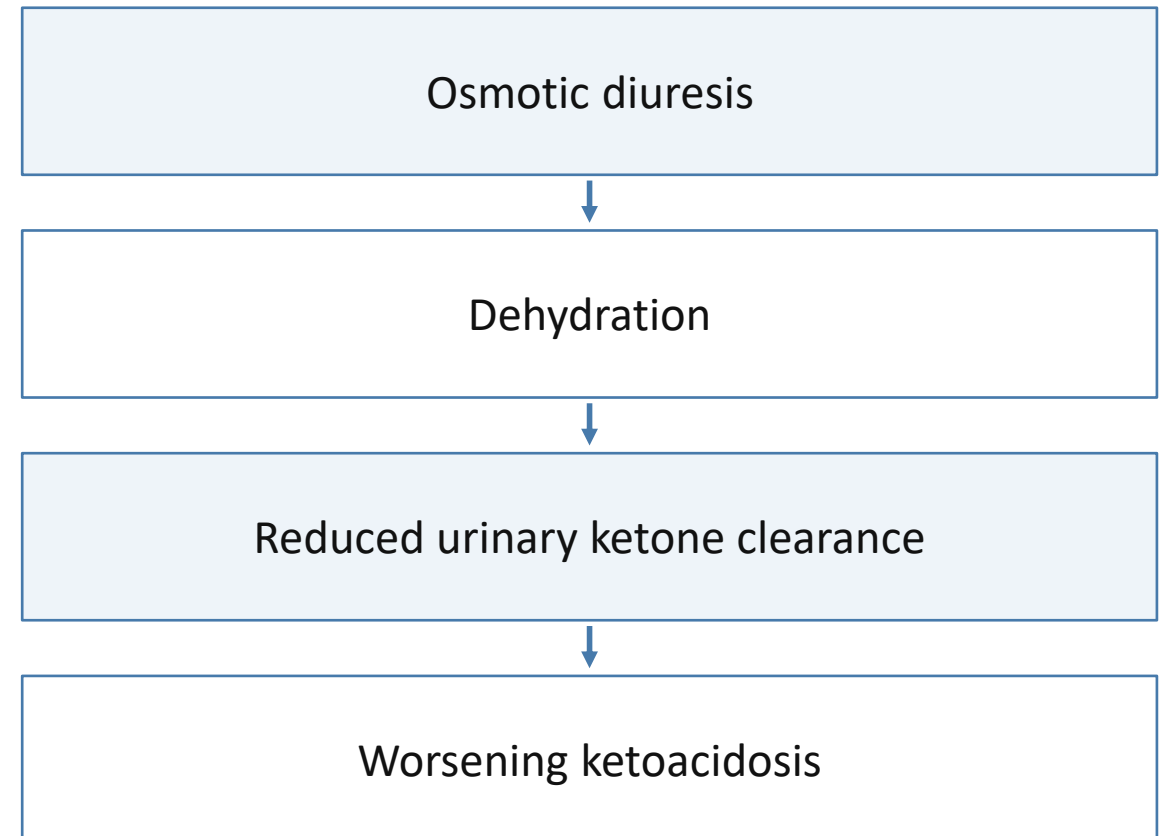
Urinary glucose drives osmotic diuresis in DKA

- Excess filtered glucose is not completely reclaimed by renal tubules.
- Glycosuria retains osmotic solute within tubular fluid.
- Increased urinary water loss produces polyuria and dehydration.
- Loss of electrolytes accompanies this water loss.



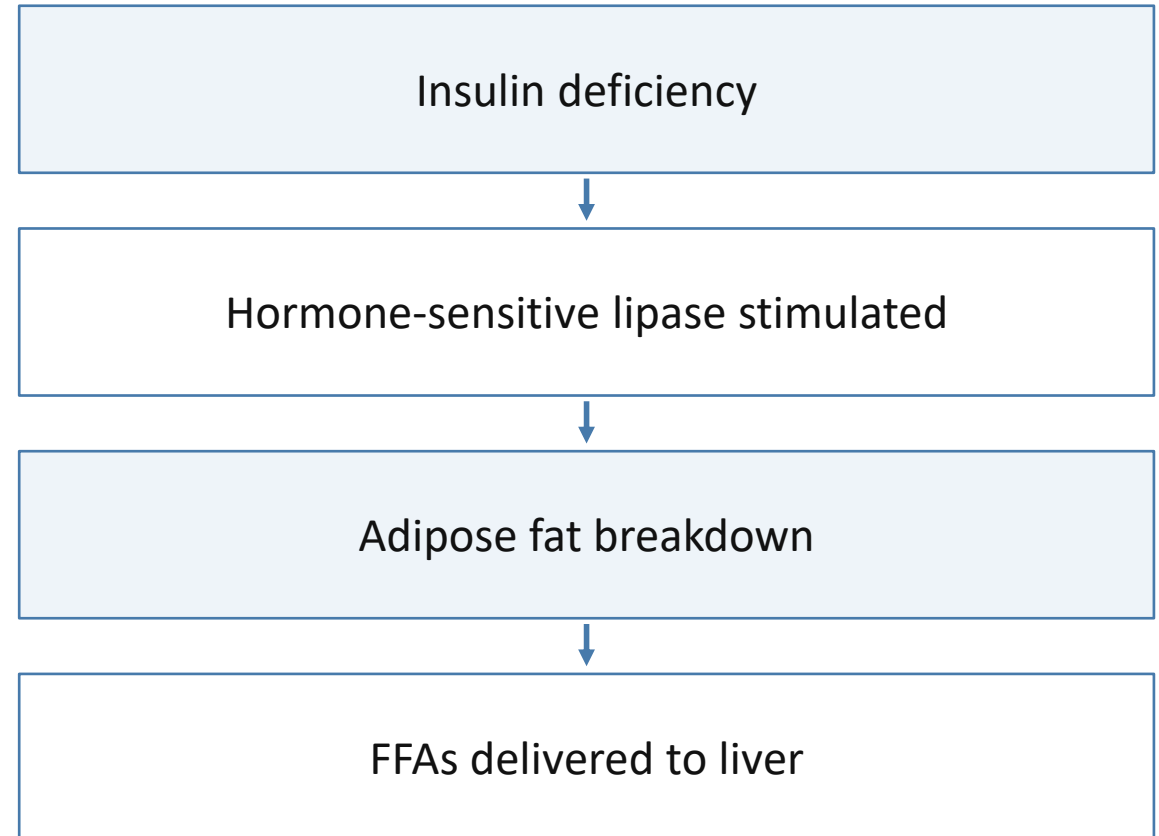
DKA dehydration impairs ketone elimination

- The kidney normally contributes to urinary excretion of ketones.
- Dehydration can compromise that elimination pathway.
- Continued ketone-body production then outstrips utilization and excretion.
- The systemic acid burden becomes progressively greater.



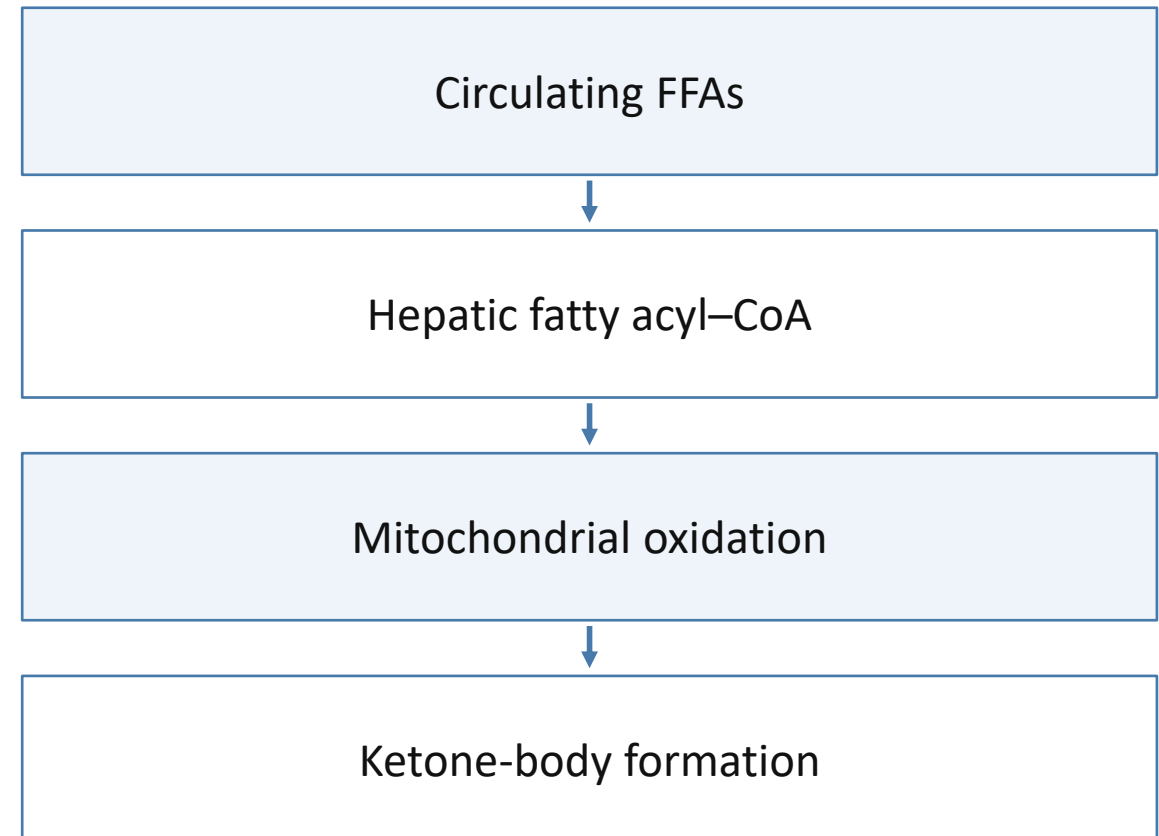
Insulin deficiency activates adipose lipid mobilization

- In the deficient-insulin state, hormone-sensitive lipase activity increases.
- Adipose triglyceride stores are broken down.
- Circulating free fatty acids (FFAs) rise and reach the liver.
- This supplies the substrate for hepatic ketone-body production.



Free fatty acids enter a hepatic mitochondrial pathway

- FFAs arriving at the liver are esterified to fatty acyl-coenzyme A.
- Fatty acyl-CoA molecules are oxidized within hepatic mitochondria.
- The pathway generates ketone bodies that enter the circulation.
- Ketone-body output increases when the hormonal brake is lost.



Two principal ketone acids are named

Acetoacetic acid

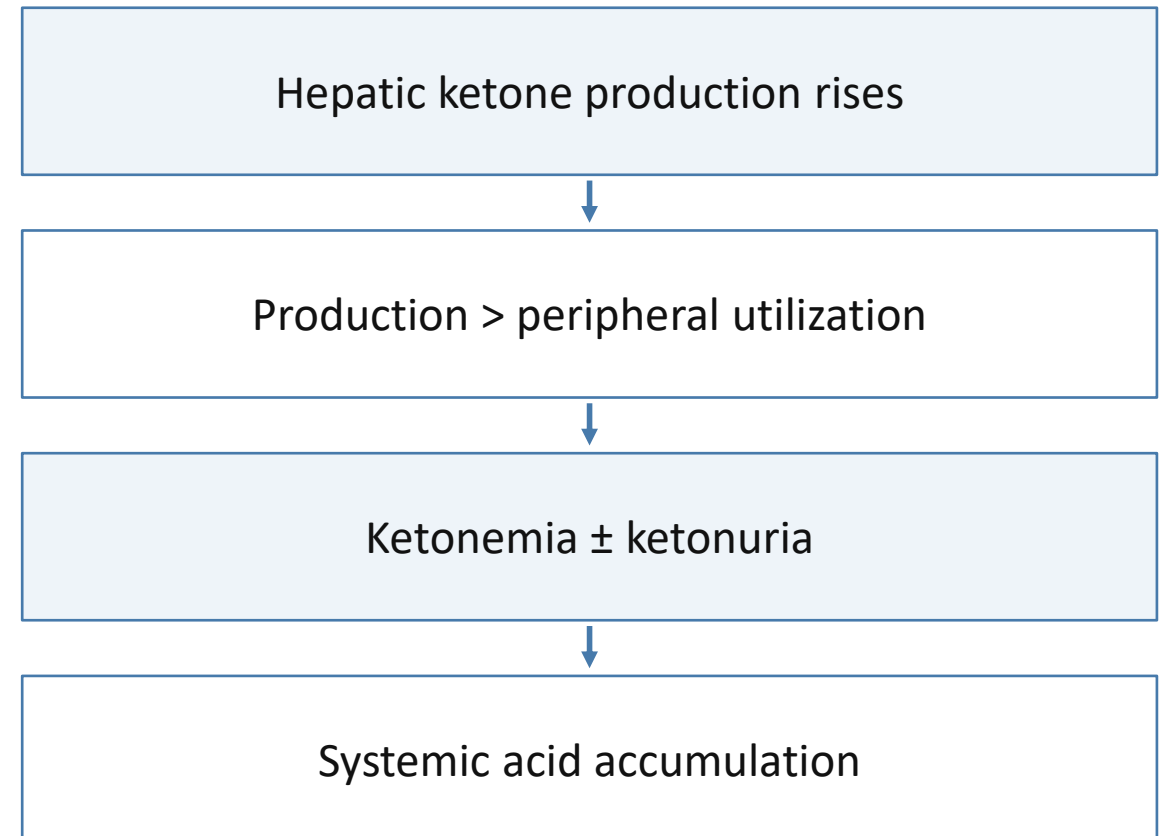
- Produced during hepatic fatty-acid oxidation
- Contributes to circulating ketone burden

β -Hydroxybutyric acid

- Major accompanying ketone-body product
- Contributes to metabolic acidosis

Ketone production can exceed peripheral utilization

- Tissues can utilize circulating ketone bodies as fuels.
- When the liver synthesizes them faster than they are consumed, ketonemia develops.
- Excess ketone bodies may also appear in urine (ketonuria).
- Excess production is the central driver of the ketoacidotic state.



Ketonemia and ketonuria are related, not identical

In circulation

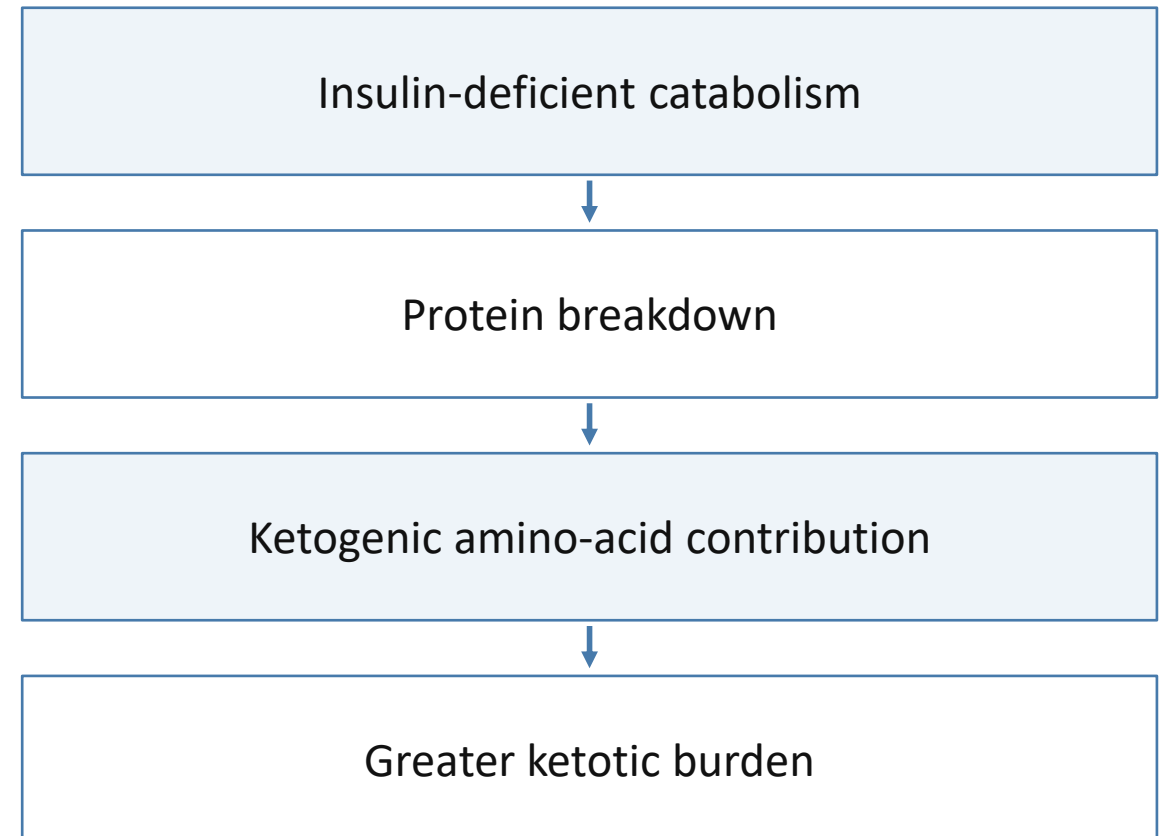
- Hepatic output exceeds utilization
- Ketones accumulate in blood

In urine

- Ketones are eliminated renally
- Dehydration may compromise clearance

Protein catabolism can further aggravate ketosis

- Insulin deficiency also favors breakdown of body proteins.
- Catabolism releases amino acids that can supply metabolic pathways.
- Ketogenic amino acids aggravate the ketotic state.
- The dysregulation affects carbohydrate, fat, and protein metabolism together.



Two disturbances converge to produce serious DKA

Glucose pathway

- Hyperglycemia
- Glycosuria
- Dehydration

Lipid pathway

- Lipolysis
- Ketone-body production
- Metabolic ketoacidosis

Fatigue in DKA reflects systemic metabolic derangement

- Fatigue is a recognized presenting manifestation.
- Hyperglycemia, dehydration, and the catabolic state evolve concurrently.
- Fatigue is nonspecific and needs interpretation alongside other DKA features.
- It should not be used in isolation to identify a hyperglycemic emergency.

Use constellations of findings, not a single symptom.

Nausea and vomiting are DKA warning manifestations

- Nausea and vomiting occur in the ketoacidotic syndrome.
- They may complicate the ability to replace ongoing fluid losses.
- Their presence can reinforce a dehydrating process already driven by glycosuria.
- These symptoms with their relative absence in HHS.

Gastrointestinal symptoms belong to the DKA phenotype.

Severe abdominal pain can accompany DKA

- Severe abdominal pain is a characteristic potential manifestation.
- It occurs with a systemic metabolic disturbance rather than requiring a separate named lesion.
- The symptom is clinically important when paired with polyuria, dehydration, or deep breathing.
- Differential evaluation still requires consideration of concurrent illnesses.

Abdominal pain does not exclude a primary metabolic emergency.

Fruity breath odor is a bedside clue in DKA

- A characteristic fruity odor among DKA manifestations.
- It appears within the broader clinical pattern of exaggerated ketone metabolism.
- It is a supportive clue rather than a standalone test.
- The core diagnosis still concerns the underlying metabolic state.

A clue supports a mechanism; It does not substitute for assessment.

Kussmaul breathing signals a severe metabolic pattern

DKA

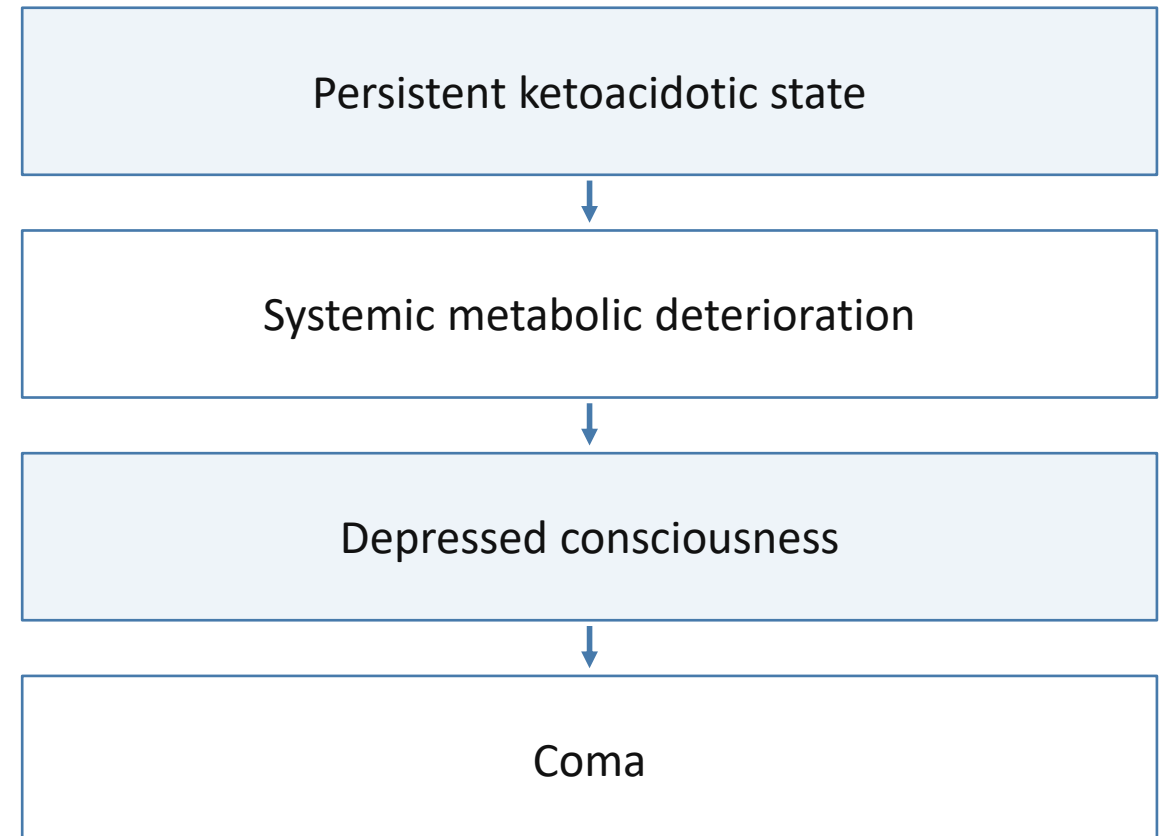
- Systemic metabolic ketoacidosis
- Deep, labored breathing may be present

HHS

- Ketoacidosis usually absent
- Kussmaul breathing may therefore be absent

Prolonged DKA can impair consciousness

- Sustained ketoacidosis can lead to depressed consciousness.
- Progression to coma is possible without reversal of the metabolic crisis.
- The neurologic finding occurs in the context of systemic derangement.
- It marks escalation beyond early symptoms such as fatigue or nausea.



Mechanistic reading of a DKA presentation

Fluid-loss signals

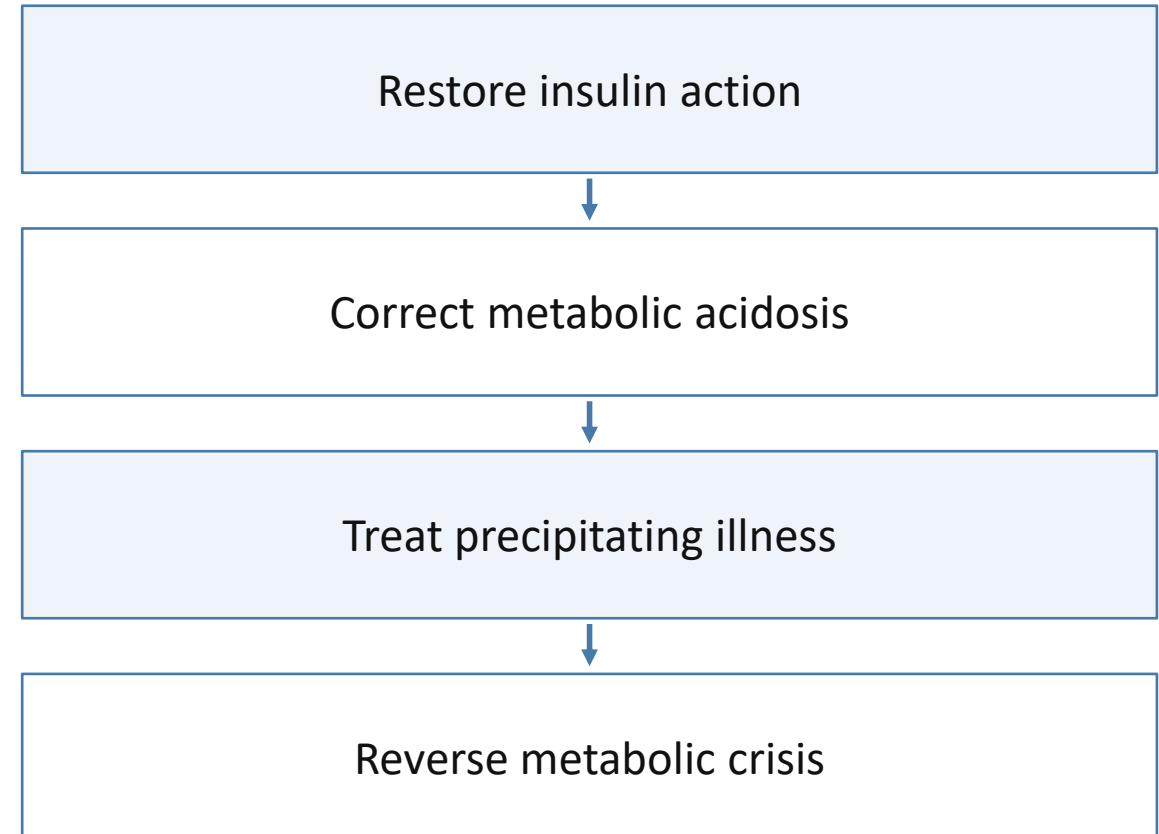
- Polyuria / thirst
- Dehydration
- Possible mental-status decline

Ketone-acid signals

- GI symptoms / fruity odor
- Deep, labored breathing
- Progressive ketoacidosis

DKA reversal requires addressing several mechanisms

- Insulin administration as necessary for reversal.
- Metabolic acidosis must be corrected as part of treatment.
- Precipitating conditions such as infection also require treatment.
- Addressing only one factor risks leaving a driver of the syndrome unresolved.



Teaching case: Missed insulin and acute deterioration

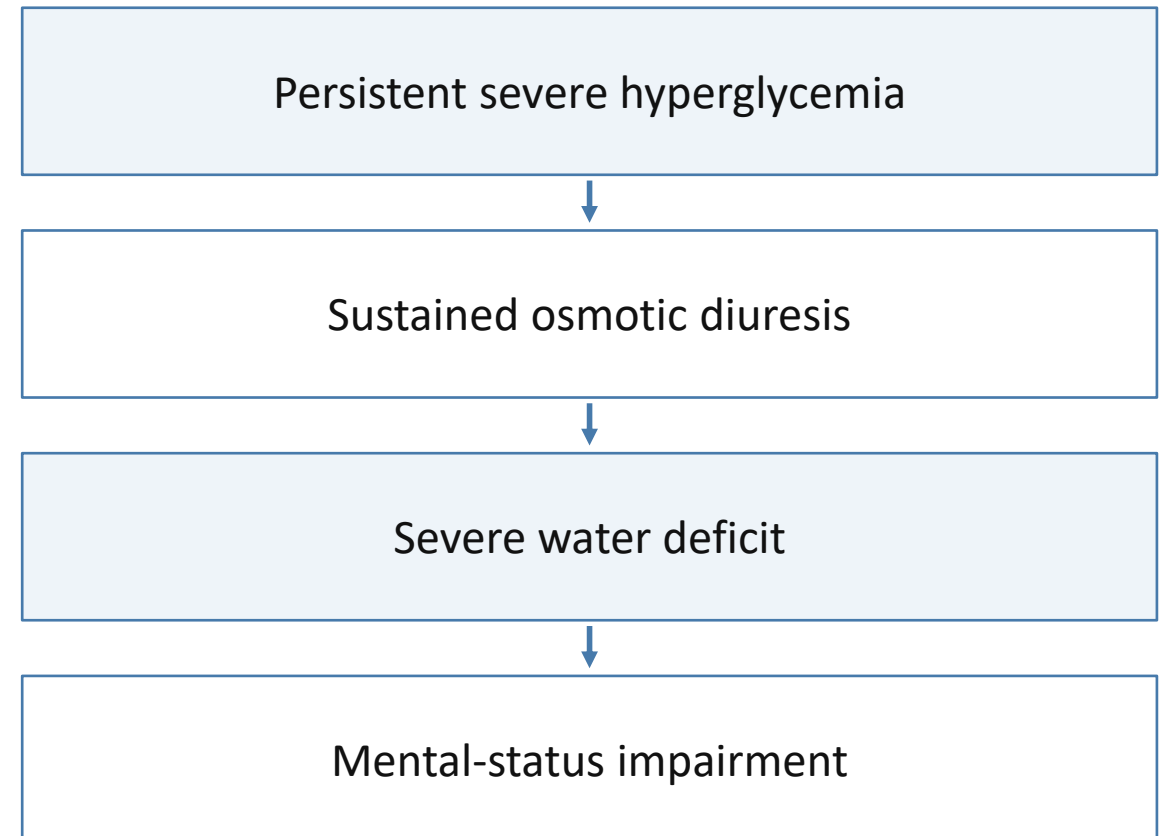
HYPOTHETICAL TEACHING SCENARIO

- A person with established insulin-treated diabetes misses insulin doses.
- An intercurrent infection is followed by polyuria, vomiting, and deep breathing.
- Identify the common hormonal disturbance linking these findings.
- Explain how the renal and hepatic pathways contribute differently.

Teaching interpretation (presenter notes): See discussion key

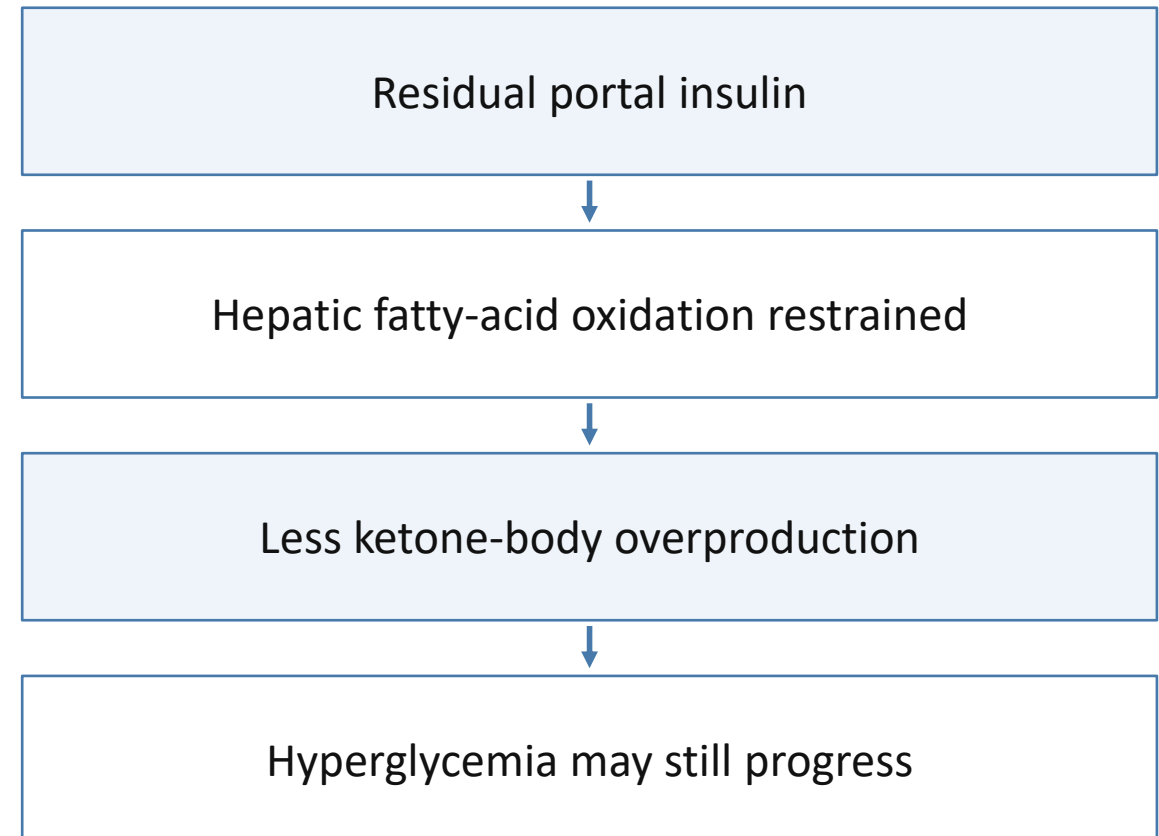
Hyperosmolar hyperglycemic state: A dehydration-dominant crisis

- HHS is described particularly in type 2 diabetes.
- Sustained hyperglycemia causes continued osmotic diuresis.
- Inadequate replacement of urinary water losses leads to severe dehydration.
- Impaired mental status may be the presenting consequence.



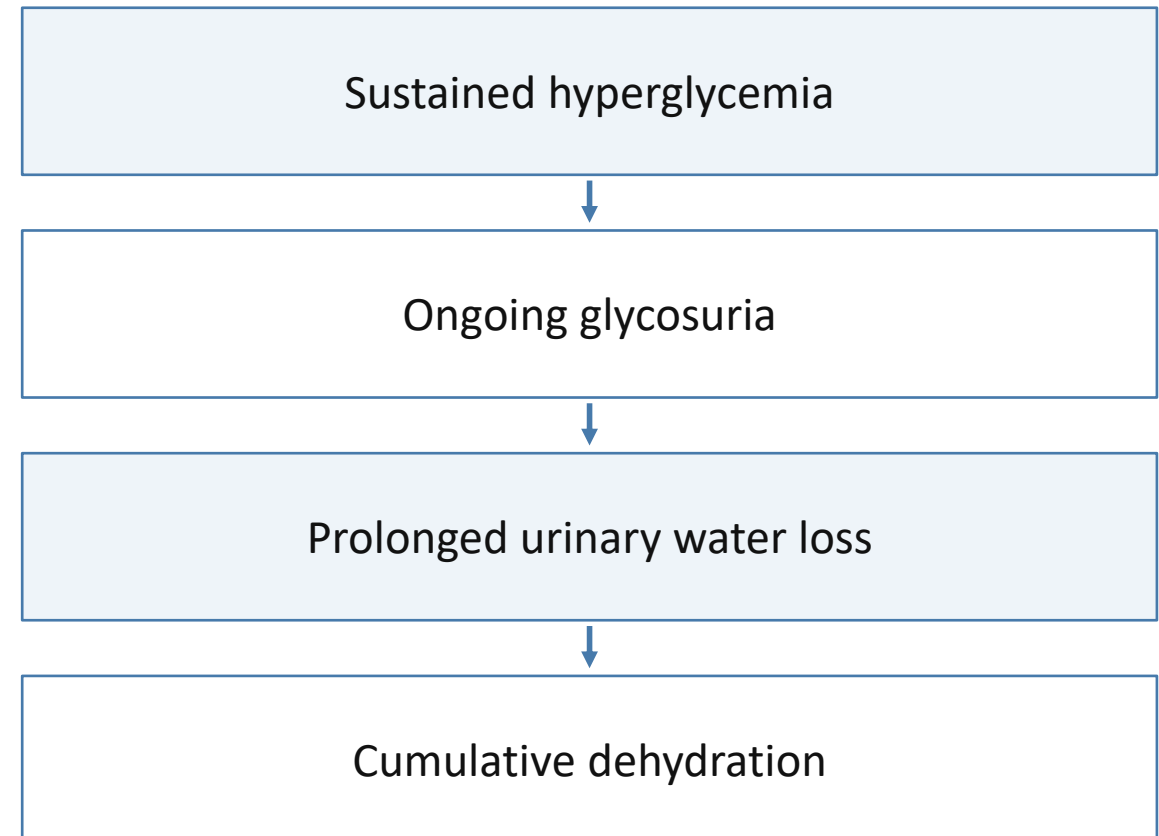
Residual portal insulin helps explain absent ketoacidosis

- Patients with type 2 diabetes may retain higher portal-vein insulin levels.
- This insulin restrains unrestricted hepatic fatty-acid oxidation.
- Ketone-body formation is therefore more effectively limited.
- Hyperglycemia can nonetheless become extremely severe.



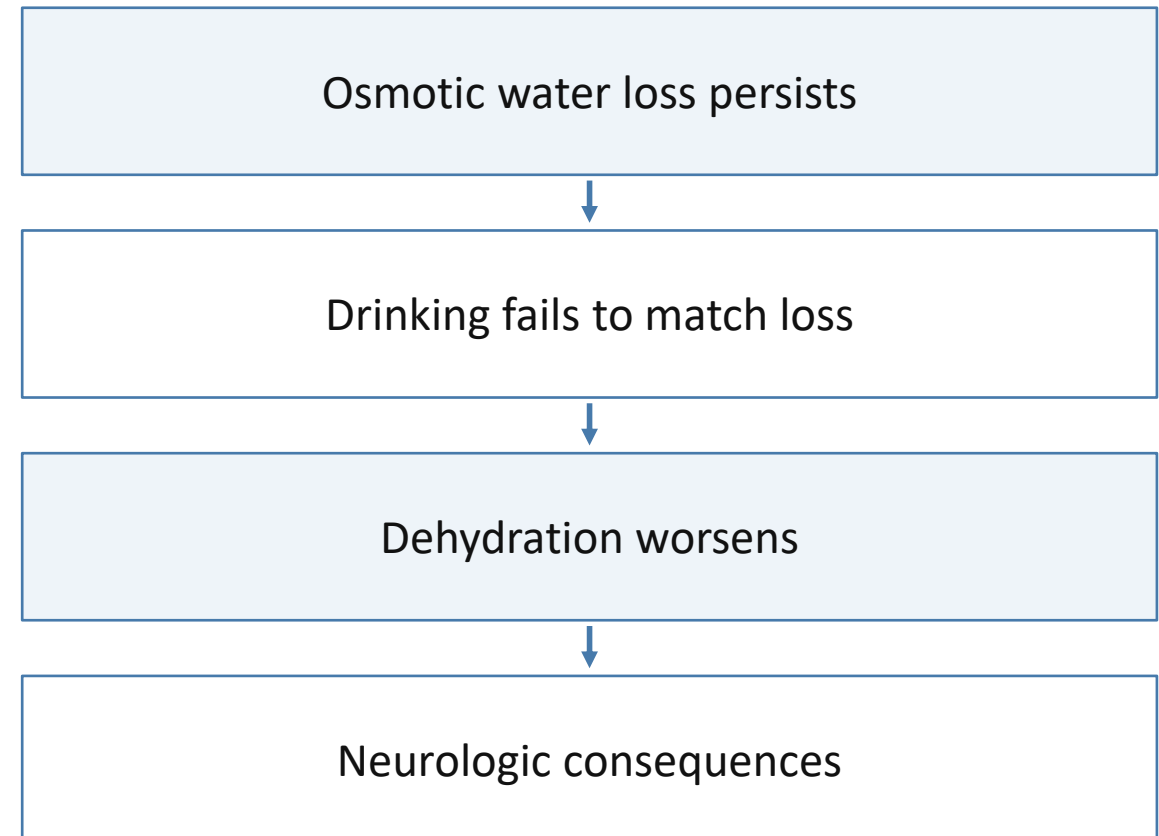
Osmotic diuresis is sustained over time in HHS

- Chronic or sustained hyperglycemia continuously exposes renal tubules to excess glucose.
- Glycosuria drives ongoing loss of water in urine.
- If oral water intake is inadequate, the deficit accumulates.
- This explains why profound dehydration dominates HHS.



Failure to replace water loss is a central vulnerability

- HHS is particularly associated with an inability to drink enough water.
- Water replacement may be restricted by acute disability or intercurrent illness.
- Physiologic urinary losses then exceed intake.
- Clinical severity reflects the resulting progressive fluid deficit.



HHS with an older, disabled patient

- An older patient with diabetes and stroke or infection.
- Neurologic disability or illness can prevent adequate access to drinking water.
- This circumstance permits continuing glycosuric fluid depletion.
- Age alone is not the mechanism: Inadequate water replacement is.

Interpret patient vulnerability through the water-balance mechanism.

HHS may lack the early symptoms of ketoacidosis

- In HHS, ketoacidosis is absent or much less prominent description.
- Nausea, vomiting, and Kussmaul breathing may therefore be absent.
- Without these alerts, medical attention may be delayed.
- Late presentation is associated with severe dehydration and altered mental status.

Ketoacidosis-associated symptoms absent



Warning features less conspicuous



Delayed clinical presentation



Severe dehydration / mental impairment

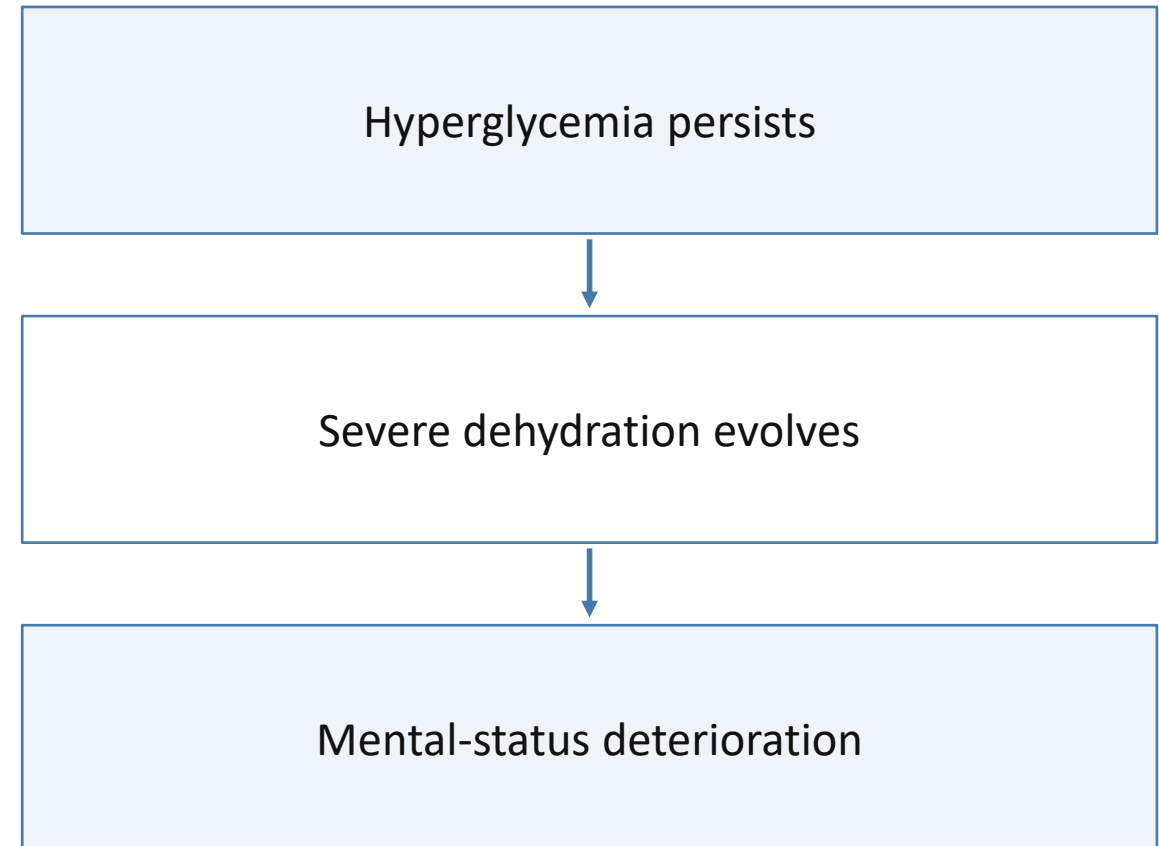
Hyperglycemia in HHS is usually more extreme

Textbook pattern	DKA	HHS
Typical glucose description	250–600 mg/dL	600–1200 mg/dL
Key accompanying disturbance	Ketoacidosis + dehydration	Profound dehydration; little/no ketoacidosis
Interpretation	Ranges may overlap	Do not classify by glucose alone

These are Robbins descriptive ranges, not formal diagnostic criteria.

Neurologic impairment in HHS reflects crisis severity

- Mental-status change is a defining clinical concern account.
- It develops against a background of marked hyperglycemia and dehydration.
- The absence of prominent ketoacidotic symptoms may conceal progression.
- Altered consciousness is a warning of advanced hyperglycemic decompensation.



DKA and HHS share a renal mechanism but differ in ketogenesis

Feature	DKA	HHS
Major substrate problem	Glucose + ketone acids	Glucose-driven fluid loss
Common diabetes association	Mainly type 1; sometimes type 2	Typically type 2
Ketogenesis	Unrestrained in severe insulin deficiency	Relatively restrained by portal insulin
Prominent manifestations	GI symptoms, fruity breath, Kussmaul	Dehydration, impaired mental status

Both involve glycosuric diuresis; Ketone-acid generation distinguishes them.

Teaching case: Dehydration without classic acidotic symptoms

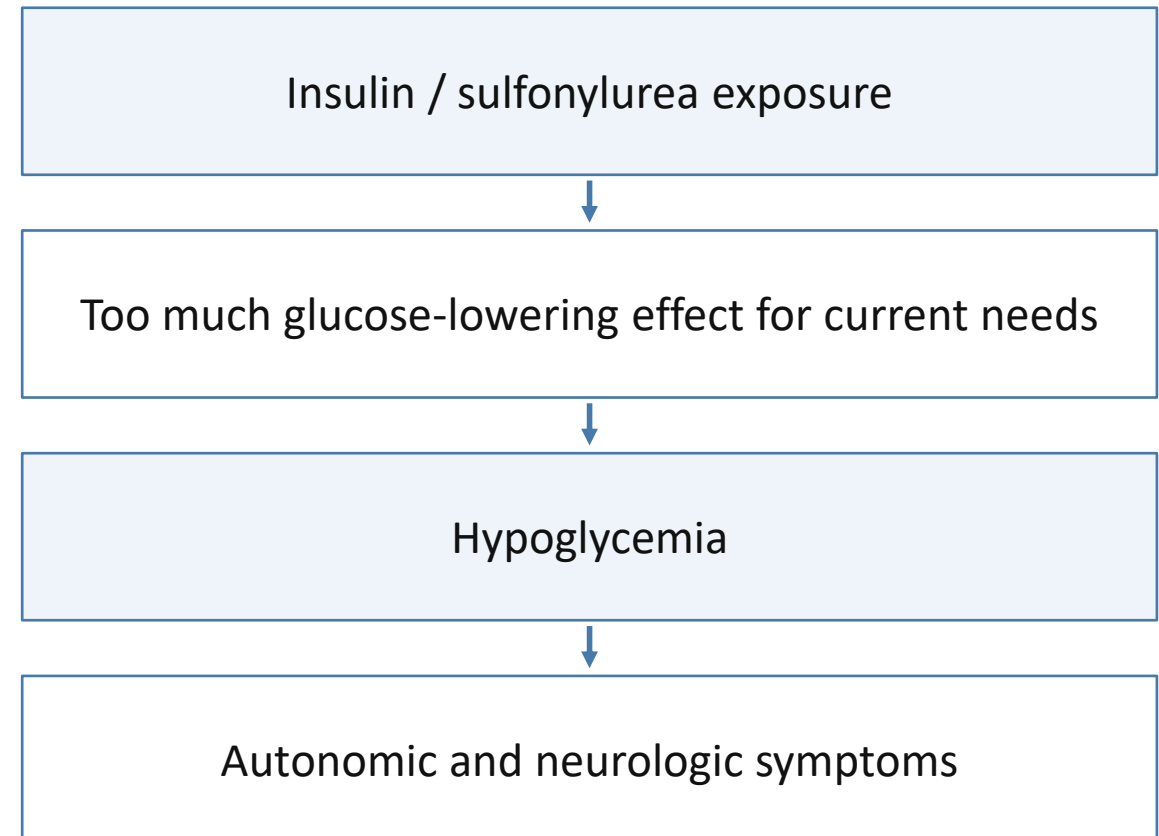
HYPOTHETICAL TEACHING SCENARIO

- An older person with type 2 diabetes becomes ill and cannot maintain water intake.
- Polyuria continues; Consciousness progressively deteriorates.
- Prominent vomiting and deep labored breathing are not reported.
- Explain why an HHS-type presentation is more plausible than classic DKA.

Teaching interpretation (presenter notes): See discussion key

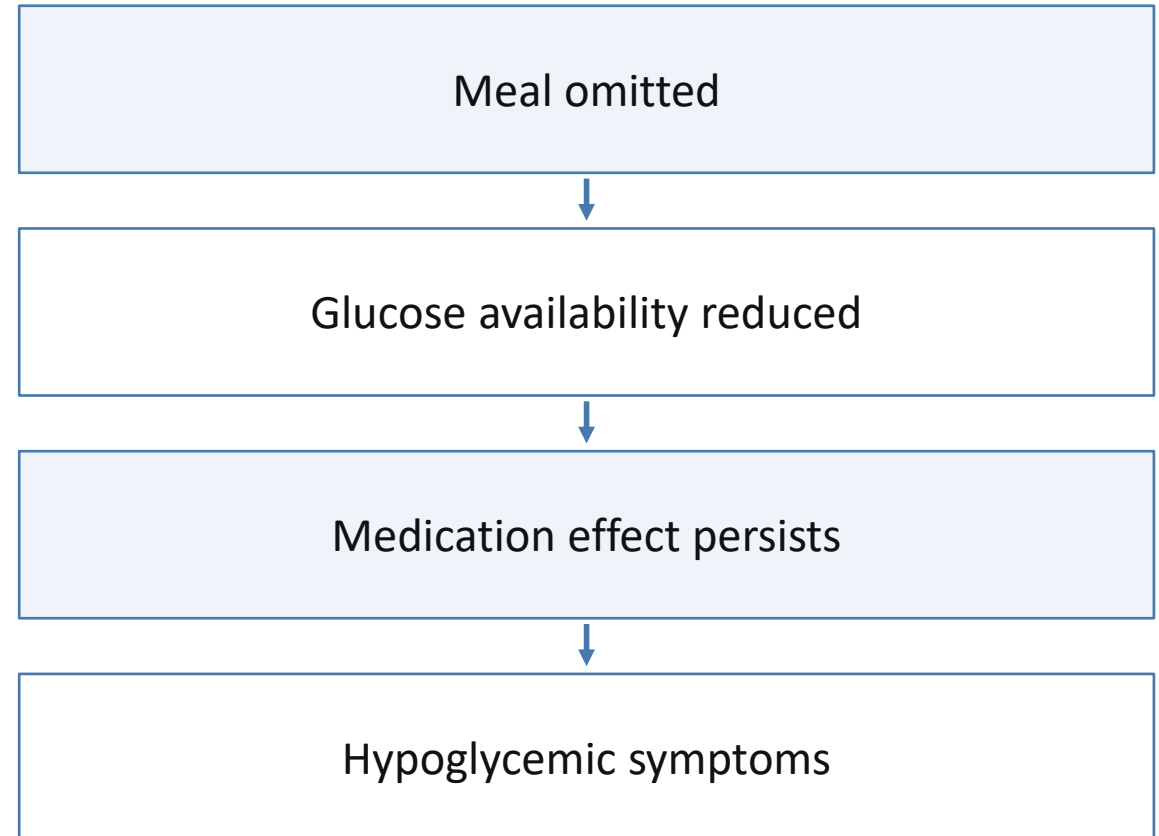
Hypoglycemia is a treatment-associated acute danger

- Insulin therapy as a common context in both diabetes types.
- Sulfonylurea therapy is another important context in type 2 diabetes.
- The emergency is inadequate circulating glucose during glucose-lowering therapy.
- Rapid correction is important to avoid neurologic injury.



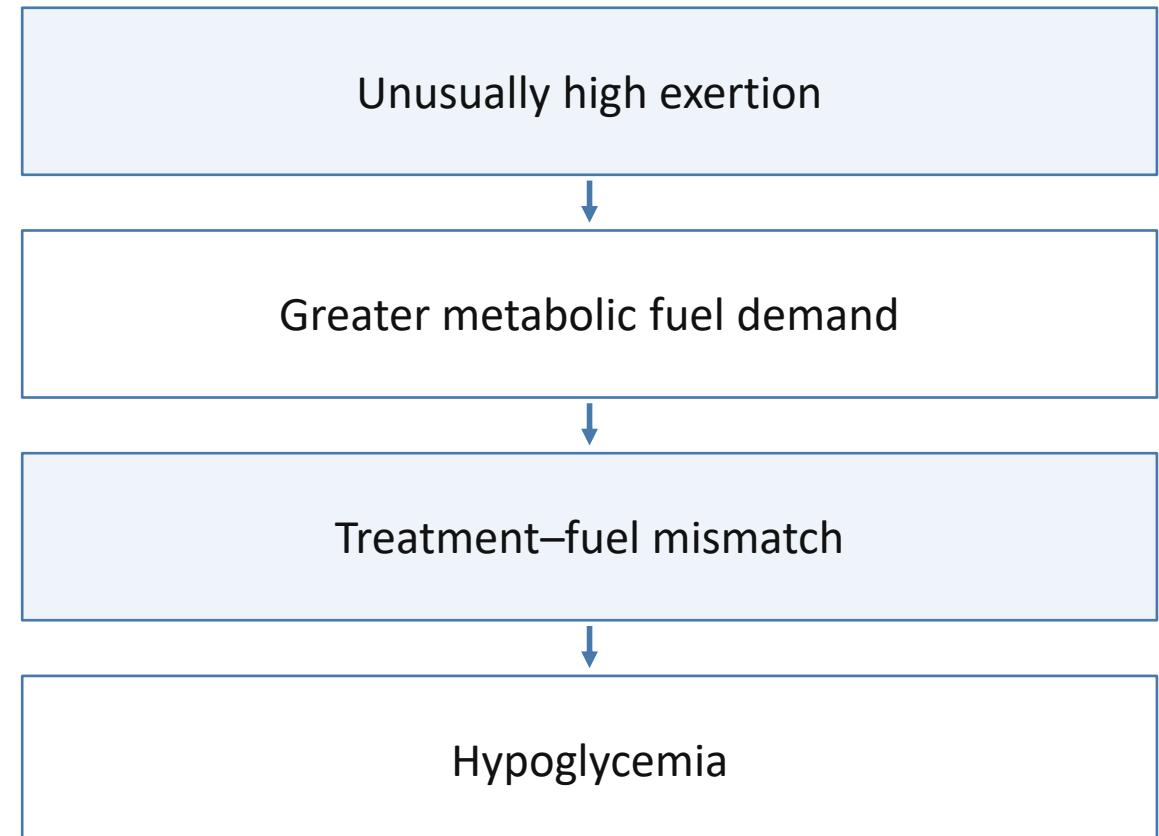
A missed meal can precipitate hypoglycemia

- Food intake may be lower than anticipated while medication action persists.
- Missing a meal as a precipitating circumstance.
- The relevant clue is a mismatch between glucose supply and glucose-lowering treatment.
- History-taking should identify recent meals and drug use.



Excessive physical exertion is a recognized trigger

- Physical activity changes the balance between available fuel and its use.
- Excessive exertion among causes of treatment-associated hypoglycemia.
- The circumstances should be interpreted alongside insulin or sulfonylurea exposure.
- The exercise history may explain an otherwise unexpected episode.



Insulin overadministration or misdosing can be causal

Drug exposure

- Insulin dose too high
- Administration error / misdosing

Context

- Meal not taken
- Exertion greater than expected

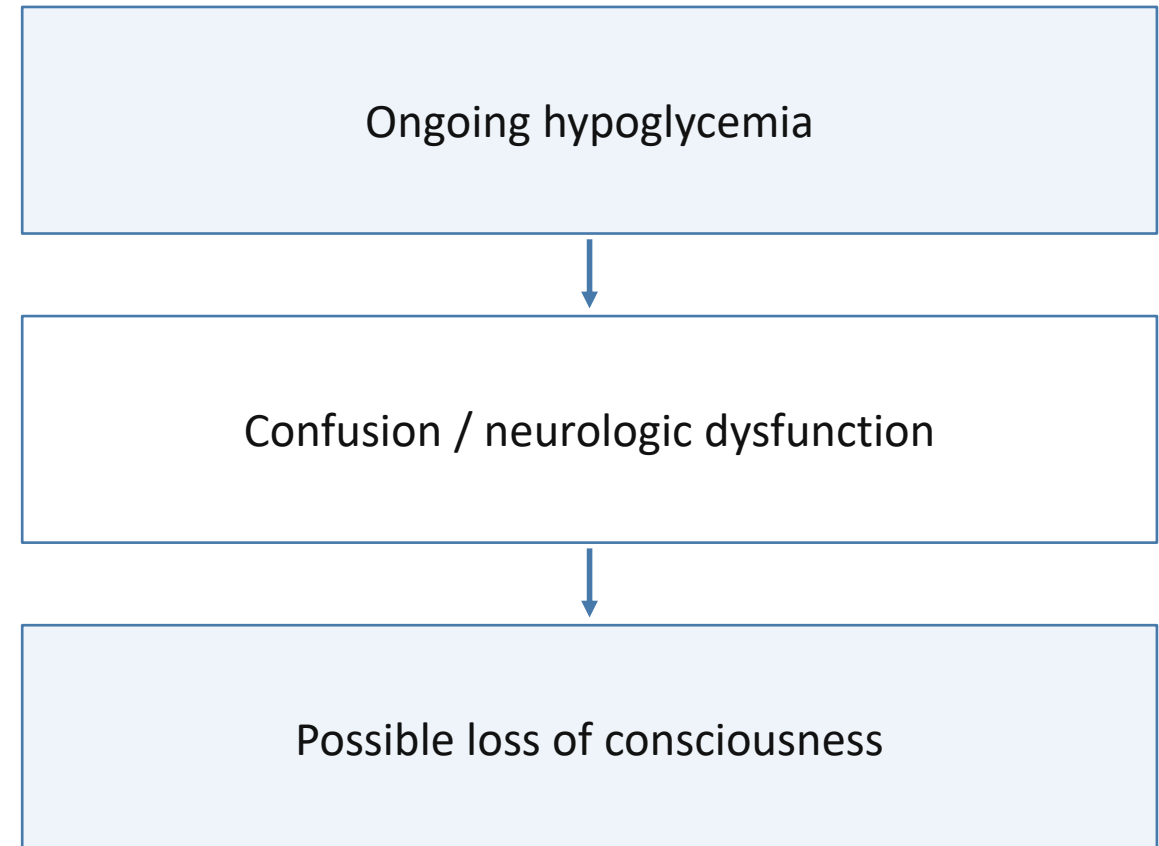
Autonomic symptoms can be early hypoglycemic clues

- Sweating is among the warning symptoms in the Robbins account.
- Palpitations and tachycardia are also characteristic findings.
- Dizziness may accompany these symptoms.
- Look for the medication and meal/activity context rather than treating each symptom alone.

Sweating + palpitations during glucose-lowering therapy require urgent consideration of hypoglycemia.

Confusion identifies neurologic compromise

- Confusion is among the listed hypoglycemic manifestations.
- If low glucose persists, loss of consciousness may develop.
- Neurologic deterioration is a central reason immediate reversal is necessary.
- Presentation can vary among individuals and episodes.



Repeated episodes may obscure warning symptoms

Usual symptom pattern

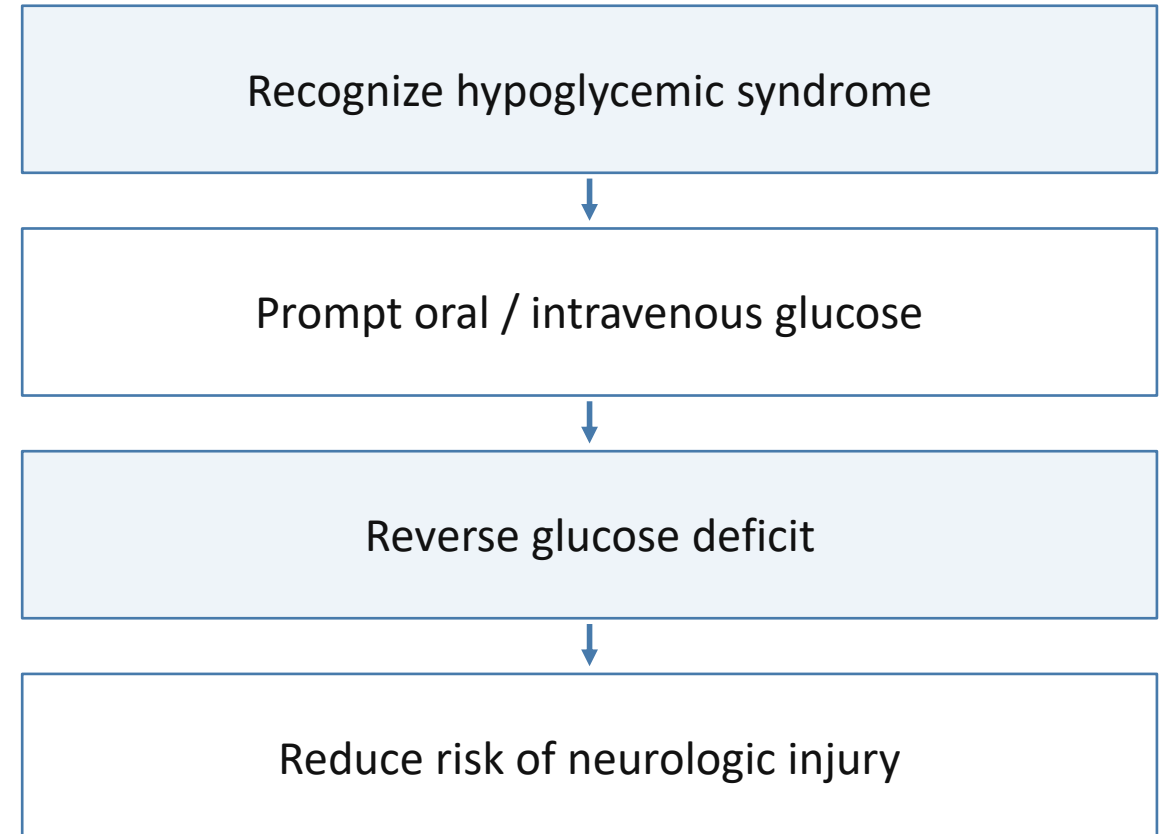
- Sweating / palpitations
- Dizziness, then possible confusion

Hypoglycemia unawareness

- Warning symptoms may be blunted
- Neurologic impairment may appear first

Rapid glucose delivery reverses the immediate problem

- Urgent restoration of glucose availability.
- Oral glucose and intravenous glucose are named means of reversal.
- Prolonged untreated hypoglycemia can produce permanent neurologic damage.
- Correction of the episode must be paired with recognition of the precipitating circumstance.



Teaching case: Altered mental status after a missed meal

HYPOTHETICAL TEACHING SCENARIO

- A person receiving insulin has skipped a meal.
- Sweating and palpitations are followed by confusion.
- Identify the acute disturbance and the most relevant precipitating clue.
- Explain why prompt correction matters to neurologic outcome.

Teaching interpretation (presenter notes): See discussion key

Three syndromes differ by clinical clues and mechanism

Clinical dimension	DKA	HHS	Hypoglycemia
Underlying disturbance	Insulin deficiency + ketone acids	Prolonged hyperglycemic diuresis	Excess glucose-lowering effect
Key context	Missed insulin / stress	Impaired water intake	Insulin / sulfonylurea + mismatch
Illustrative clues	Vomiting, abdominal pain, Kussmaul	Marked dehydration, mental decline	Sweating, palpitations, confusion
Major immediate risk	Acidosis / dehydration / coma	Severe dehydration / mental decline	Neurologic injury / unconsciousness

Interpret treatment history, water balance, and ketotic features together.

Clinical reasoning: Choose the dominant mechanism

Hyperglycemic crises

- DKA: Ketone-acid clues
- HHS: Prolonged water-loss clues

Glucose deficit

- Treatment or meal mismatch
- Autonomic $\pm$ neurologic clues

Three questions organize the emergency history

- Has insulin been omitted, or has major illness increased insulin needs?
- Has urine output remained high while access to water has been inadequate?
- Has an insulin/sulfonylurea dose coincided with a missed meal or unusual exertion?
- Which symptom cluster best matches the predicted metabolic mechanism?

History is most useful when it explains the causal sequence.

Integrated mechanism summary

Initiating imbalance	Metabolic pathway	Clinical syndrome
Marked insulin deficiency + glucagon excess	↑ glucose production + ↑ lipolysis/ketones	DKA: dehydration and ketoacidosis
Sustained hyperglycemia; inadequate drinking	Persistent glycosuria → urinary water depletion	HHS: profound dehydration
Insulin or sulfonylurea action exceeds fuel supply	Circulating glucose falls	Hypoglycemia: autonomic/neurologic effects

Different biochemical pathways lead to distinct bedside patterns.

Applied comparison: Three hypothetical presentations

HYPOTHETICAL TEACHING SCENARIO

- Presentation A: Insulin omitted, infection, vomiting, and Kussmaul breathing.
- Presentation B: Type 2 diabetes, restricted access to water, progressive mental decline.
- Presentation C: Insulin-treated diabetes, missed meal, sweating, and confusion.
- Name the dominant emergency in each and trace one key causal step.

Teaching interpretation (presenter notes): See discussion key

High-yield synthesis

- DKA: Insulin deficiency with glucagon excess promotes both hyperglycemia and ketone-acid formation.
- HHS: Residual insulin restrains ketogenesis, but sustained glycosuria can cause severe dehydration.
- Hypoglycemia: Insulin or sulfonylurea treatment becomes hazardous when exposure and available fuel are mismatched.
- All three may impair consciousness; The preceding mechanism determines the appropriate interpretation.

Recognize the physiology—not just the label.

Core source and scope

- Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th ed. (2026).
- Main coverage: ketoacidosis, hyperosmolar hyperglycemic state, and treatment-associated hypoglycemia.
- Physiologic context: insulin deficiency, glycosuria, and the classic type 1 diabetes symptom triad.
- This lecture emphasizes the textbook account; numeric glucose ranges are descriptions rather than formal diagnostic cutoffs.

Chapter/page mapping and content origin are recorded in speaker notes.