

# Clinical Features of Diabetes

Patterns of presentation, metabolic emergencies, and long-term clinical consequences

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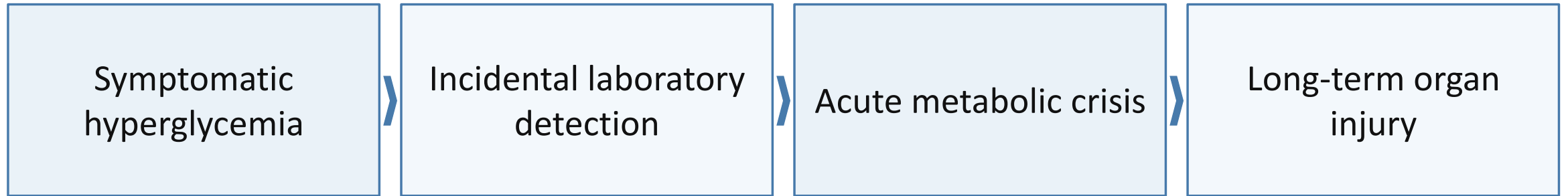
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# Learning objectives

- Contrast common initial presentations of type 1 and type 2 diabetes.
- Derive polyuria, polydipsia, polyphagia, and weight loss from insulin deficiency.
- Recognize clinical patterns of ketoacidosis, hyperosmolar hyperglycemia, and hypoglycemia.
- Connect chronic vascular injury with characteristic organ manifestations.

# Clinical diabetes has several entry points



Clinical phenotype reflects metabolic severity, pace of onset, and accumulated tissue damage.

## Two major subtypes—different first encounters

### Type 1 diabetes

- Autoimmune  $\beta$ -cell loss
- Often symptomatic near overt onset
- Can present with ketoacidosis

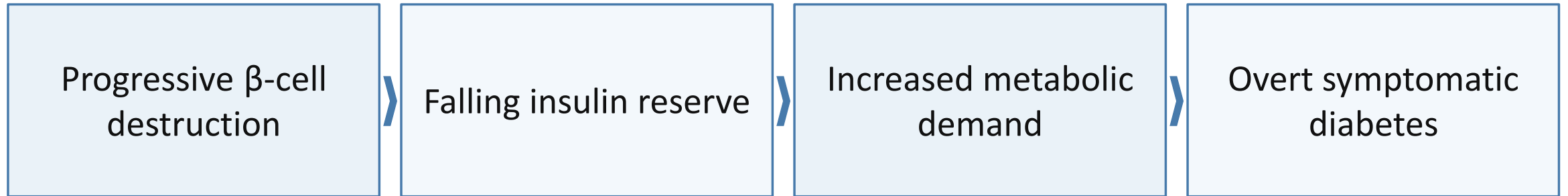
### Type 2 diabetes

- Insulin resistance plus  $\beta$ -cell dysfunction
- Often detected while asymptomatic
- Chronic effects may precede recognition

## Type 1 diabetes can present at any age

- The label “juvenile-onset diabetes” is misleading.
- Autoimmune  $\beta$ -cell destruction can occur in childhood or adulthood.
- The rate of residual insulin loss determines clinical tempo.
- Age alone does not establish diabetes subtype.

# Type 1 diabetes: Silent loss, then overt disease

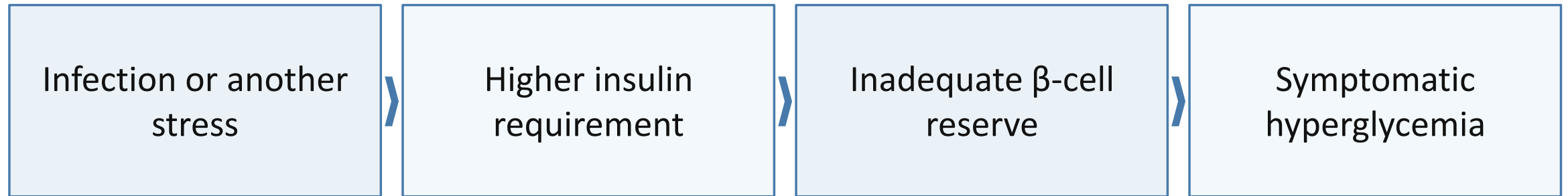


Biologic decline is gradual; Clinical transition may appear abrupt.

## Why a gradual disease may seem sudden

- Residual  $\beta$ -cell secretion compensates until a functional threshold is crossed.
- The final transition from dysglycemia to overt diabetes may be rapid.
- Clinical onset therefore does not identify the beginning of autoimmunity.
- New symptoms should prompt assessment of metabolic decompensation.

## Intercurrent infection can expose insulin deficiency



A precipitating illness may reveal previously unrecognized type 1 diabetes.

## The type 1 “honeymoon period”

- Shortly after diagnosis, some endogenous insulin secretion persists.
- Insulin requirement may be low during the first 1–2 years.
- The period is temporary: Residual  $\beta$ -cell function continues to decline.
- Reduced insulin dose does not mean that autoimmune diabetes has resolved.

# Early remission is not reversal of disease

## Observed during honeymoon

- Lower exogenous insulin requirement
- Residual endogenous insulin output
- Improved early metabolic stability

## Underlying trajectory

- Progressive  $\beta$ -cell loss persists
- Absolute deficiency eventually dominates
- Insulin requirement often rises substantially

# The classic triad of type 1 diabetes

**Marked insulin deficiency**

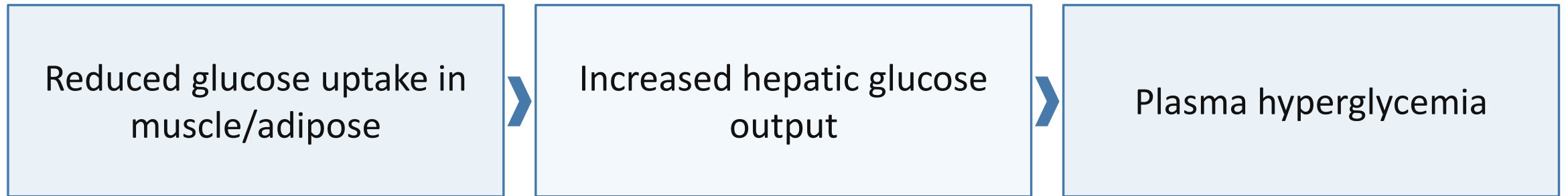
Polyuria

Polydipsia

Polyphagia

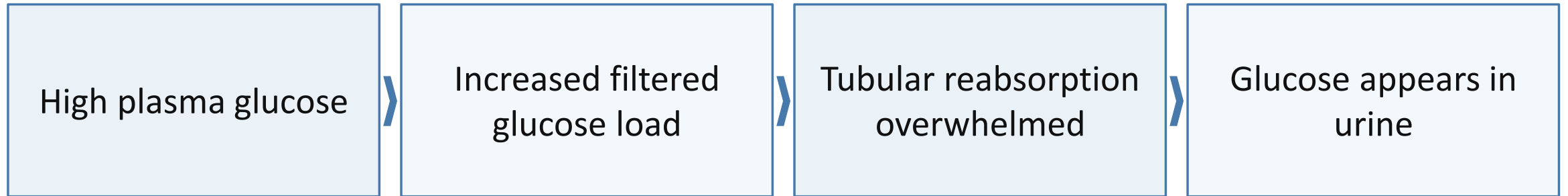
Catabolism commonly produces weight loss and weakness despite increased appetite.

# How insulin deficiency produces hyperglycemia



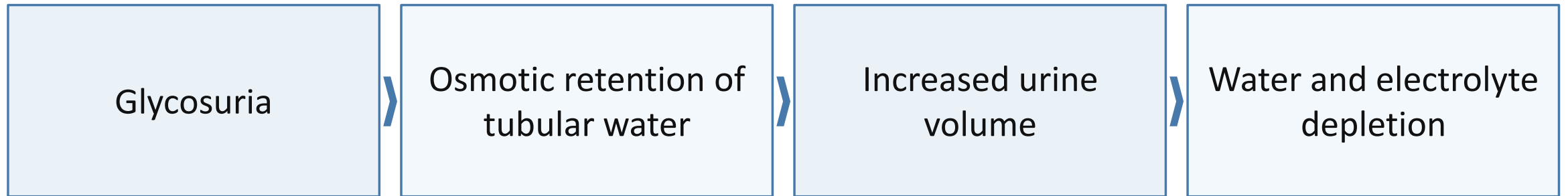
Counterregulatory hormones, particularly glucagon, aggravate the imbalance.

# Glycosuria occurs when reabsorption is exceeded



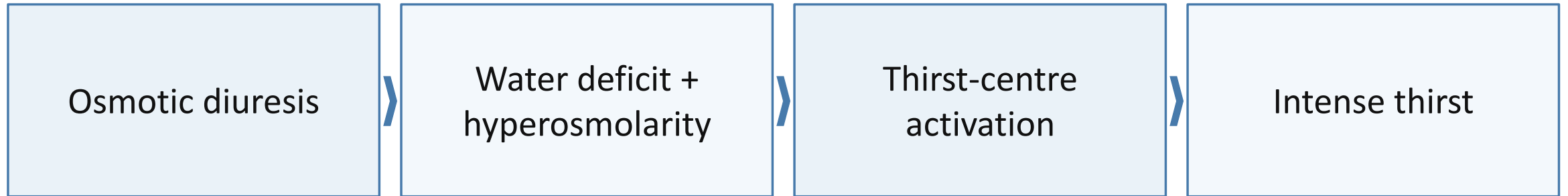
This renal event initiates osmotic water loss.

## Polyuria: The osmotic-diuresis mechanism



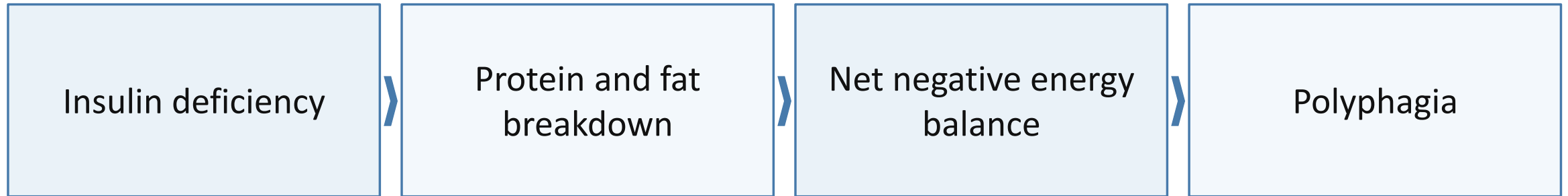
Polyuria is a mechanistic consequence of sustained marked hyperglycemia.

## Polydipsia is the response to fluid depletion



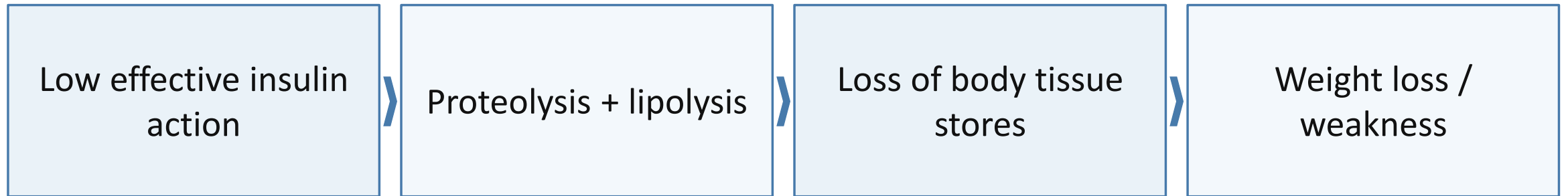
Hyperosmolarity also draws water from intracellular compartments.

# Why appetite rises despite hyperglycemia



Circulating glucose is abundant, but insulin-dependent anabolic use is impaired.

# Why diabetes may cause weight loss



The coexistence of increased appetite and weight loss is diagnostically important.

# Polyphagia with weight loss is a warning pattern

## History

- Increased appetite
- Unintentional weight loss
- Thirst and frequent urination

## Pathophysiologic interpretation

- Anabolic signaling inadequate
- Catabolism predominates
- Hyperglycemia with osmotic diuresis

## A targeted history for symptomatic diabetes

- Ask specifically about increased urine output and thirst.
- Establish appetite change and unintended weight loss.
- Ask about fatigue, muscle weakness, and blurred vision.
- Assess recent infection or other stress before acute deterioration.

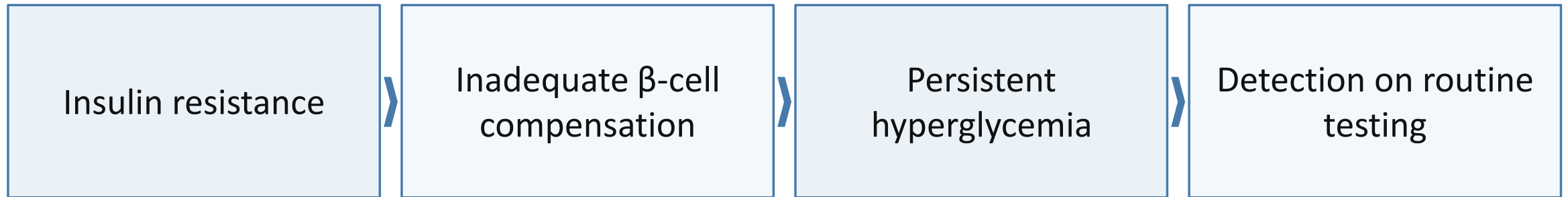
## Type 1 severity is not captured by glucose alone

- Water loss can cause clinically important volume depletion.
- Catabolism explains muscle weakness and ongoing weight loss.
- Insulin absence creates the metabolic setting for ketogenesis.
- Nausea, vomiting, labored breathing, or mental-status change suggest crisis.

## Type 2 diabetes: A common clinical setting

- Classically recognized in adults over 40 years with obesity.
- Type 2 diabetes is also increasingly diagnosed in younger people.
- Increasing childhood obesity and sedentary behavior contribute.
- Age and body habitus suggest risk but are not definitive classification tests.

## Type 2 diabetes may develop with few symptoms



The most frequent diagnosis pathway is incidental blood testing.

## Type 2 diabetes: Symptoms when present

- Unexplained fatigue can prompt a clinical visit.
- Dizziness is a possible nonspecific complaint.
- Blurred vision can accompany hyperglycemia.
- Absence of classic symptoms does not exclude diabetes.

# Overt symptoms versus incidental diagnosis

## Symptom-driven evaluation

- Thirst, urination, appetite changes
- Weight loss or fatigue
- Possible acute decompensation

## Laboratory-driven diagnosis

- No volunteered symptoms
- Unexpected elevated glucose/HbA1c
- Requires deliberate clinical follow-up

## Risk clues for recognizing silent type 2 diabetes

- Obesity or an adverse metabolic phenotype.
- A family history of diabetes.
- Metabolic syndrome or associated cardiometabolic risk.
- Older age is relevant, but type 2 diabetes also occurs in youth.

# Diabetes may be clinically silent

## Unrecognized hyperglycemia

```
graph TD; A[Unrecognized hyperglycemia] --> B[No classic symptoms]; A --> C[Routine testing detects disease]; A --> D[Long-term injury may accumulate];
```

No classic symptoms

Routine testing detects  
disease

Long-term injury may  
accumulate

Symptoms are an unreliable gatekeeper for identifying type 2 diabetes.

## Compare typical type 1 and type 2 presentations

| Feature          | Type 1 diabetes           | Type 2 diabetes                   |
|------------------|---------------------------|-----------------------------------|
| Onset            | Often conspicuous         | Frequently clinically silent      |
| Age              | Any age                   | Often adult; Also youth           |
| Core defect      | $\beta$ -cell destruction | Resistance + secretory failure    |
| Ketosis          | Higher risk               | Less common; Possible with stress |
| Diagnostic route | Symptoms / crisis         | Often routine testing             |

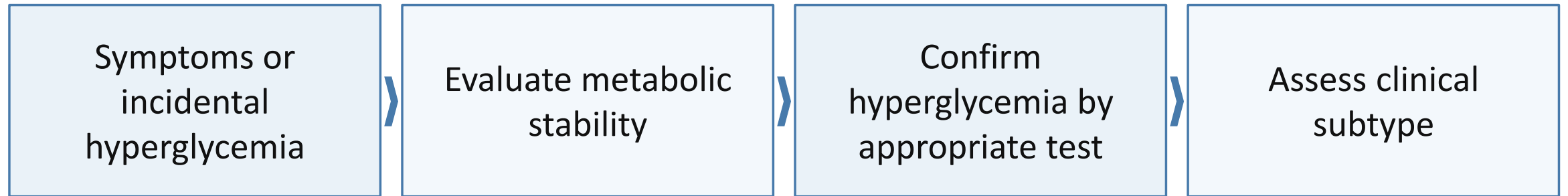
# Clinical phenotype is not a substitute for classification

- Older age does not rule out autoimmune type 1 diabetes.
- Obesity does not by itself prove type 2 diabetes.
- Other forms of diabetes can require insulin.
- Clinical context should be interpreted alongside etiologic assessment.

## Slowly progressive autoimmune diabetes in adults

- Latent autoimmune diabetes in adults (LADA) occurs in adulthood.
- Its course may initially resemble type 2 diabetes.
- Diabetes-associated autoantibodies support autoimmune etiology.
- Many patients ultimately require insulin, even if not initially.

# Clinical assessment of a possible new diagnosis



Acute deterioration and marked dehydration require priority assessment.

# Laboratory routes to diagnosing diabetes

| Test                                     | Textbook diagnostic threshold |
|------------------------------------------|-------------------------------|
| Fasting plasma glucose                   | ≥126 mg/dL                    |
| Random plasma glucose + classic symptoms | ≥200 mg/dL                    |
| 2-h plasma glucose after 75-g OGTT       | ≥200 mg/dL                    |
| HbA1c                                    | ≥6.5%                         |

## When confirmation of hyperglycemia matters

- The text recommends repeat confirmation for most diagnostic tests.
- Exception: Classic hyperglycemic symptoms with qualifying random glucose.
- Serious illness may cause transient stress hyperglycemia.
- Reassess persistence after the acute illness has resolved.

# HbA1c and plasma glucose answer different questions

## Plasma glucose

- Measurement at the testing time
- Sensitive to recent metabolic fluctuations
- Especially useful in overt symptomatic hyperglycemia

## HbA1c

- Glycation reflects preceding weeks–months
- Less influenced by day-to-day fluctuation
- Supports diagnosis and longer-term control assessment

# Three acute clinical patterns to recognize

## Altered glucose homeostasis

```
graph TD; A[Altered glucose homeostasis] --> B[Diabetic ketoacidosis]; A --> C[Hyperosmolar hyperglycemic state]; A --> D[Treatment-associated hypoglycemia];
```

Diabetic ketoacidosis

Hyperosmolar  
hyperglycemic state

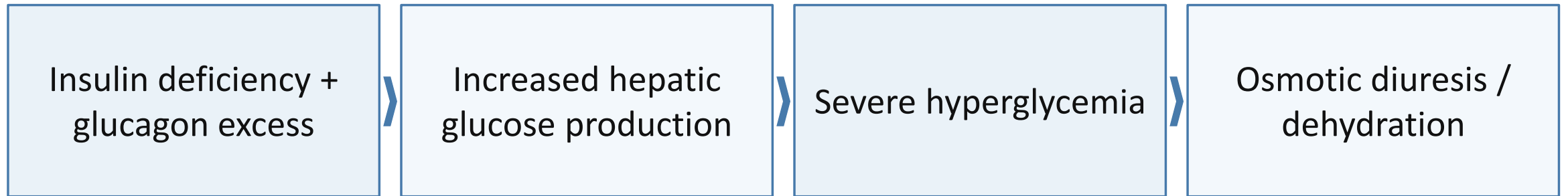
Treatment-associated  
hypoglycemia

These syndromes differ in mechanism, but each can impair consciousness.

## Diabetic ketoacidosis: Common triggers

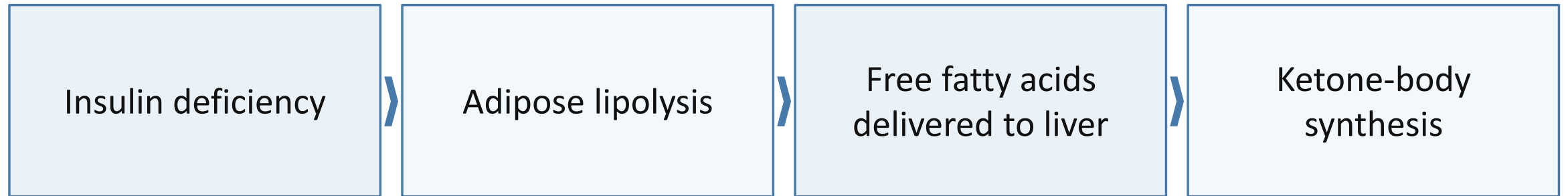
- An omitted or inadequate insulin dose is a frequent precipitant.
- Infection and intercurrent illness increase insulin needs.
- Trauma and certain medications can be additional stressors.
- DKA is typical of type 1 diabetes but possible in type 2 diabetes.

# DKA reflects combined insulin lack and glucagon excess



Impaired peripheral glucose utilization further intensifies hyperglycemia.

# Ketone production in diabetic ketoacidosis



Major ketone bodies include acetoacetate and  $\beta$ -hydroxybutyrate.

# Why ketosis becomes ketoacidosis

Accelerated hepatic  
ketogenesis



Ketone production  
exceeds utilization



Ketone accumulation



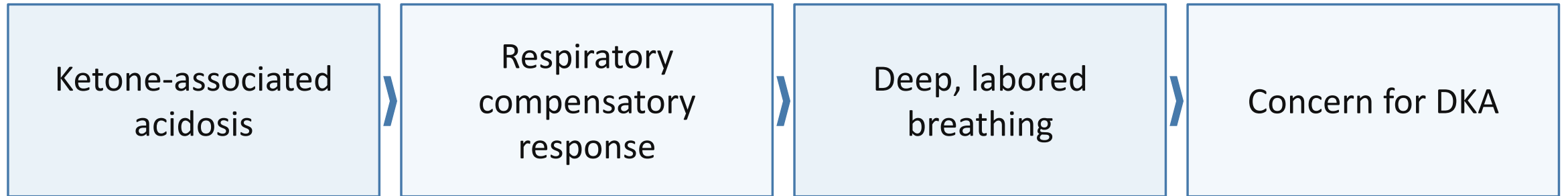
Metabolic acidosis

Dehydration may compromise urinary ketone excretion and aggravate the disturbance.

## Clinical clues to diabetic ketoacidosis

- Fatigue with nausea and vomiting.
- Abdominal pain may be severe.
- Fruity breath odor and deep, labored respiration.
- Mental status may deteriorate as the crisis persists.

# Kussmaul breathing is a metabolic clue



Do not interpret the breathing pattern as an isolated respiratory diagnosis.

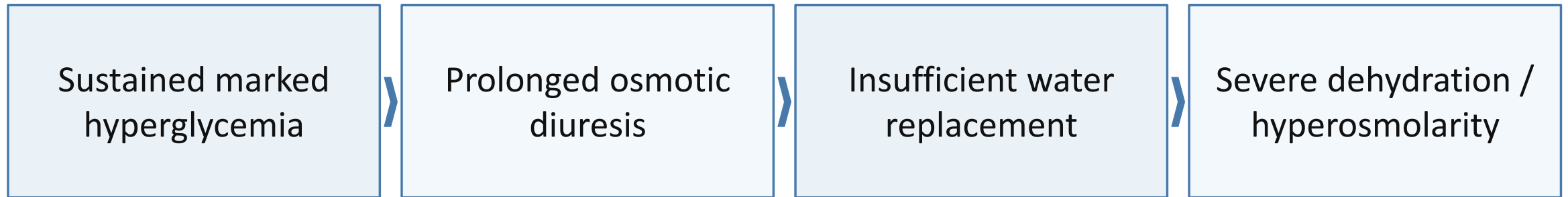
# Neurologic deterioration in ketoacidosis

- Persisting dehydration and metabolic disturbance can impair consciousness.
- Depressed alertness may progress to coma.
- Severe DKA is a medical emergency requiring urgent evaluation.
- The precipitating illness remains clinically important.

## DKA is not exclusive to type 1 diabetes

- Severe stress may provoke ketoacidosis in type 2 diabetes.
- Serious infections and trauma are examples in the source.
- The clinical syndrome should be recognized before assuming subtype.
- Risk depends on effective insulin availability in the stress state.

# Hyperosmolar hyperglycemic state: Water deficit dominates



Residual insulin often restrains unrestricted ketogenesis.

## Hyperosmolar state: Clinical setting

- Often described in an older person with type 2 diabetes.
- Stroke, infection, or disability may prevent adequate fluid intake.
- Severe dehydration develops as urinary water loss continues.
- Altered mental status can be the presenting feature.

# Why hyperosmolar presentation can be delayed

## Often absent or less prominent

- Marked ketoacidosis
- Kussmaul breathing
- Ketotic nausea and vomiting

## May become prominent late

- Prolonged water deficit
- Severe hyperglycemia
- Depressed mental status

## Clinical contrast: Ketoacidosis versus hyperosmolar state

| Pattern                       | DKA                     | HHS                                    |
|-------------------------------|-------------------------|----------------------------------------|
| Predominant metabolic problem | Ketosis + acidosis      | Hyperosmolar water depletion           |
| Typical association           | Type 1 diabetes         | Type 2 diabetes                        |
| Respiratory clue              | Kussmaul breathing      | Usually no ketotic breathing           |
| GI symptoms                   | Nausea / pain may occur | May be absent                          |
| Consciousness                 | May be impaired         | Often impaired with severe dehydration |

## Treatment-associated hypoglycemia

- Most relevant during insulin therapy in either major subtype.
- Sulfonylurea therapy in type 2 diabetes is another cause.
- The problem reflects excessive glucose-lowering action relative to need.
- Prompt recognition is essential because brain function can deteriorate.

# Common precipitants of hypoglycemia

**Glucose availability < treatment effect**

Missed meal

Excessive exertion

Excessive or incorrect dose

Evaluate the relationship among medication, nutritional intake, and activity.

# Hypoglycemia: Autonomic and neurologic features

## Warning / adrenergic features

- Sweating
- Palpitations
- Tachycardia

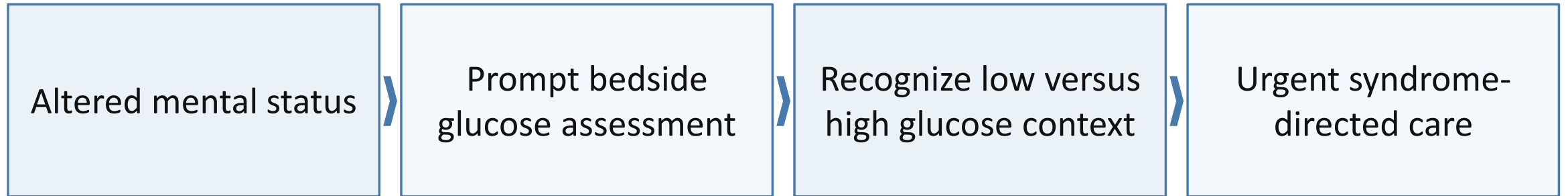
## Neuroglycopenic features

- Dizziness or confusion
- Reduced consciousness
- Possible loss of consciousness

# Hypoglycemia unawareness

- Repeated episodes may blunt recognizable early warning features.
- Neurologic impairment can become the first evident symptom.
- The patient may have little opportunity for self-correction.
- Repeated severe episodes require urgent review of therapy and risk.

# Approach to acute altered consciousness in diabetes



Hypoglycemia, DKA, and HHS must not be clinically conflated.

# Chronic complications: Two vascular compartments

## Macrovascular disease

- Large and medium arteries
- Accelerated atherosclerosis
- Coronary, cerebral, peripheral ischemia

## Microvascular disease

- Small-vessel dysfunction / injury
- Retinal, renal, neural involvement
- Progressive end-organ impairment

# Clinical consequences of macrovascular diabetes

Chronic vascular risk



Accelerated atherosclerosis



Cardiac / cerebral / limb  
ischemia

Common clinical events include myocardial infarction, stroke, and lower-extremity ischemia.

# Three major microvascular targets

## Diabetic microvascular injury

```
graph TD; A[Diabetic microvascular injury] --> B[Retina → visual disease]; A --> C[Kidney → nephropathy]; A --> D[Peripheral nerve → neuropathy];
```

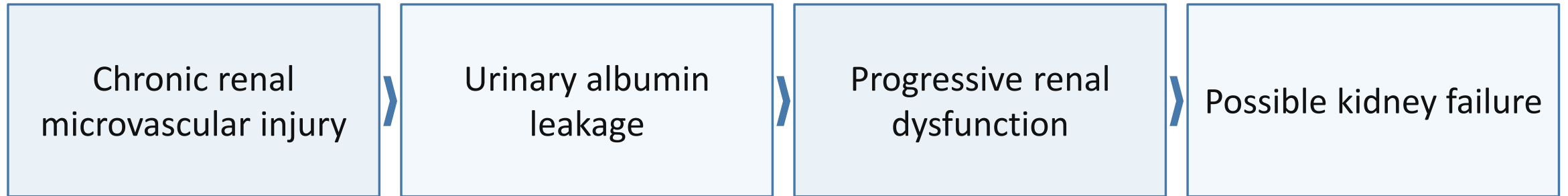
Retina → visual disease

Kidney → nephropathy

Peripheral nerve →  
neuropathy

Organ-specific manifestations can arise after prolonged hyperglycemia.

## Nephropathy may begin without symptoms

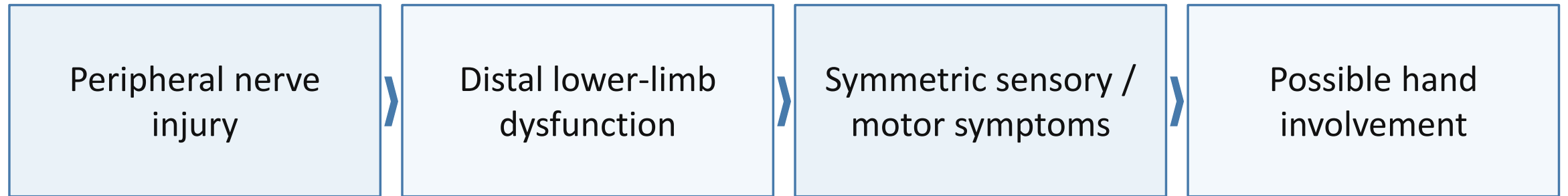


Urinary albumin excretion may reveal renal injury before overt symptoms.

## What brings ocular diabetes to attention?

- Blurred vision can occur with hyperglycemia early in diabetes.
- Long-standing diabetes may produce retinopathy.
- The source links retinal neovascularization to VEGF expression during hypoxia.
- Cataract and glaucoma also contribute to visual impairment.

# Distal symmetric diabetic polyneuropathy



Advanced distribution may resemble a stocking-and-glove pattern.

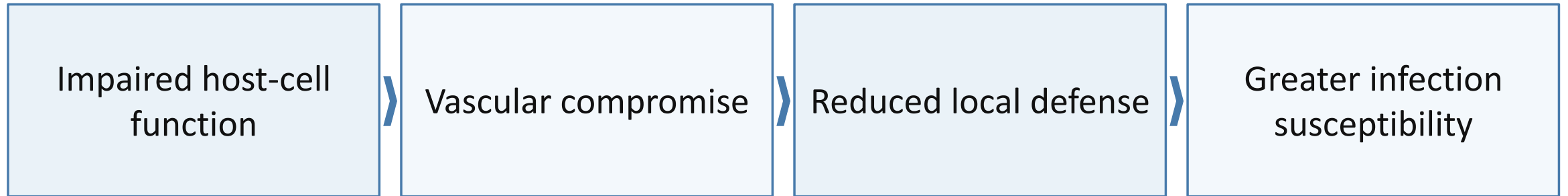
# Autonomic neuropathy: Clinical manifestations

- Disorders of bowel function.
- Bladder dysfunction.
- Erectile dysfunction may occur.
- Symptoms reflect autonomic—not only sensory—nerve involvement.

## Focal diabetic neuropathy can appear abruptly

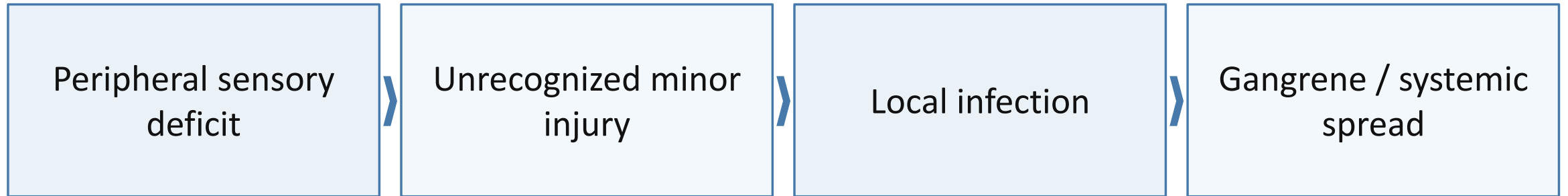
- A mononeuropathy may produce footdrop.
- Wrist-drop is another recognized presentation.
- Isolated cranial nerve palsies may occur.
- A focal neurological presentation requires appropriate differential assessment.

# Why infections may be more consequential



Altered neutrophil function and impaired macrophage responses.

# Neuropathy and foot infection can amplify each other



A small toe lesion can initiate a clinically serious sequence in high-risk patients.

## Long duration increases cumulative injury

- Severity and duration of hyperglycemia correlate with chronic complications.
- End-organ disease often evolves over many years.
- Glycemic control reduces risk but does not remove all risk.
- Obesity, insulin resistance, and cardiovascular comorbidities matter as well.

# Glucose measures: Symptoms versus cumulative exposure

## Single glucose observation

- Useful for current metabolic state
- Essential in acute symptomatic evaluation
- May vary across hours and days

## Longitudinal glycemic burden

- HbA1c reflects longer exposure
- Sustained dysglycemia drives tissue injury
- Time in range adds temporal information

# Case 1: Abrupt symptomatic presentation

## Clinical vignette (hypothetical)

An adolescent reports excessive urination, intense thirst, increased appetite, and unintentional weight loss after a febrile illness.

**Which pathophysiologic sequence best unifies these findings?**

## Case 1: Mechanism-based interpretation

**Progressive insulin deficiency can become clinically apparent under stress.**

- Hyperglycemia leads to glycosuria and osmotic diuresis.
- Fluid depletion and hyperosmolarity stimulate thirst.
- Protein and fat catabolism produce weight loss despite hunger.

## Case 2: Asymptomatic detection

### Clinical vignette (hypothetical)

A middle-aged adult with obesity and a family history of diabetes feels generally well; An elevated plasma glucose is found at a routine visit.

**What is the most appropriate clinical interpretation of the presentation?**

## Case 2: Interpretation and next step

**Type 2 diabetes is frequently detected by laboratory testing before classic symptoms emerge.**

- Clinical silence does not exclude persistent hyperglycemia.
- Confirm the abnormality with an appropriate diagnostic strategy.
- Consider metabolic context without using obesity as a definitive subtype test.

## Case 3: Acute abdominal and respiratory symptoms

### Clinical vignette (hypothetical)

A person with diabetes misses insulin during an infection and develops nausea, abdominal pain, fruity breath, and deep labored respirations.

**Which acute complication should be suspected immediately?**

## Case 3: Recognize diabetic ketoacidosis

**Insulin deficiency during stress favors simultaneous hyperglycemia and ketogenesis.**

- Lipolysis supplies free fatty acids for hepatic ketone production.
- Ketone accumulation produces metabolic acidosis.
- Kussmaul breathing and abdominal symptoms are red flags.

## Case 4: Sudden confusion during glucose-lowering therapy

### Clinical vignette (hypothetical)

A treated patient becomes sweaty, tachycardic, and confused after missing a meal.

**Which reversible complication must be checked first?**

## Case 4: Recognize hypoglycemia

**The symptom combination is consistent with treatment-associated hypoglycemia.**

- Missing food can increase the glucose-lowering effect of medication.
- Sweating and palpitations may precede neuroglycopenia.
- Immediate glucose assessment and prompt correction are critical.

# Clinical synthesis: Match the pattern to the mechanism

## Clinical presentation

```
graph TD; A[Clinical presentation] --> B[Triad + weight loss → catabolism]; A --> C[Silent hyperglycemia → screening]; A --> D[Acidosis / dehydration → crisis]; A --> E[Organ injury → chronic disease];
```

Triad + weight loss →  
catabolism

Silent hyperglycemia →  
screening

Acidosis / dehydration  
→ crisis

Organ injury → chronic  
disease

Clinical findings make sense when traced back to insulin availability, glycemic burden, and vascular injury.

## Core clinical conclusions

- Type 1 diabetes may be abrupt clinically despite gradual  $\beta$ -cell loss.
- Type 2 diabetes is often silent and found incidentally.
- Polyuria, thirst, increased appetite, and weight loss have distinct metabolic mechanisms.
- Acute crises and long-term complications must be recognized as different clinical pathways.

## Suggested source reading

Robbins, Cotran & Kumar: Pathologic Basis of Disease. 11th ed. Chapter 24, The Endocrine System.

### **Sections used for this clinical lecture**

- Clinical Features of Diabetes
- The Classic Triad of Type 1 Diabetes
- Acute Metabolic Complications of Diabetes
- Chronic Complications of Diabetes
- Clinical Manifestations of Chronic Diabetes