

Malabsorption and Diarrhea

Mechanisms, nutrient deficits, clinicopathologic patterns, and
diagnostic reasoning

Mechanism-based pathology lecture

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Teaching objectives

- Explain the four successive phases of intestinal nutrient absorption.
- Relate defects in digestion, mucosa, epithelial transport, and lipid traffic to malabsorption.
- Recognize steatorrhea and major consequences of micronutrient loss.
- Distinguish secretory, osmotic, malabsorptive, and exudative diarrhea.
- Apply mechanism-based reasoning to common intestinal disorders.

Malabsorption is a failure of nutrient assimilation

A failure to absorb one or more essential dietary components.

- Fat and fat-soluble vitamins
- Protein and carbohydrate
- Water-soluble vitamins

- Electrolytes and minerals
- Water
- Single defects may disrupt several nutrients simultaneously.

Diarrhea and malabsorption are not synonyms

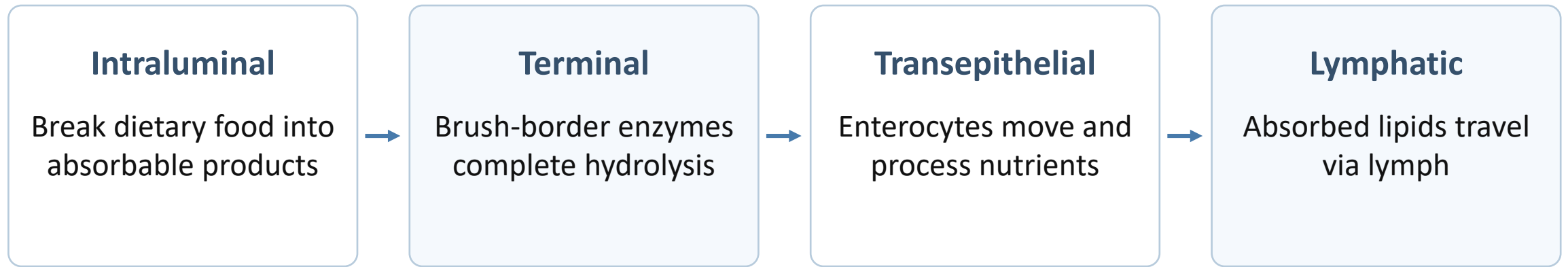
Malabsorption

- Failure of digestion, uptake, or nutrient delivery
- May produce steatorrhea and nutritional depletion
- Frequently causes diarrhea, but consequences extend beyond stool change

Diarrhea

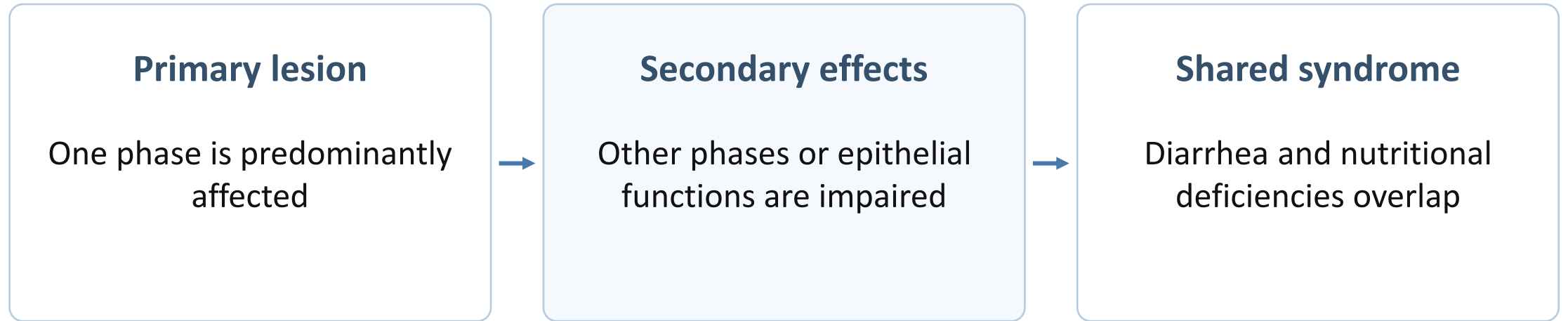
- Increase in stool mass, frequency, or fluidity
- Can arise from secretion, unabsorbed solutes, malabsorption, or inflammation
- May occur without generalized nutrient malabsorption

Four phases make intestinal absorption possible



An abnormality at any phase can cause a malabsorptive syndrome.

One predominant defect rarely tells the whole story

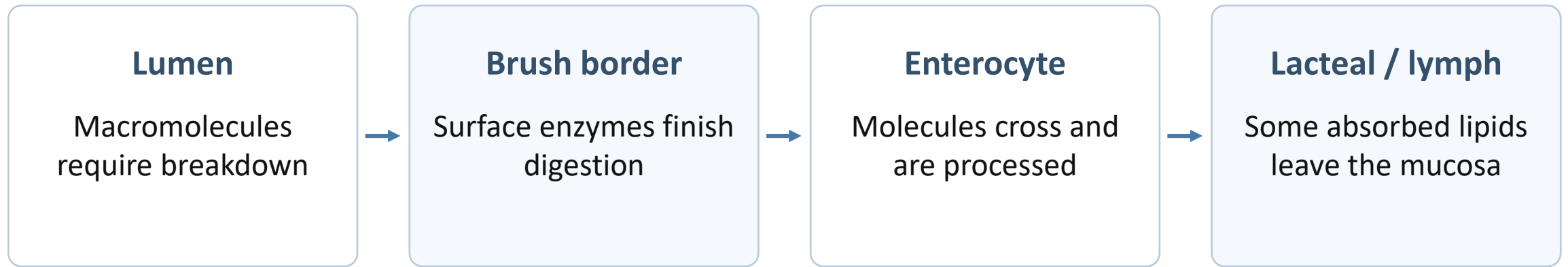


Clinical presentations often resemble each other even when initiating mechanisms differ.

Important causes in the Robbins framework

Clinical context	Representative disorder	Dominant teaching emphasis
Commonly encountered	Pancreatic insufficiency	Intraluminal digestion
Commonly encountered	Celiac disease	Mucosal surface and brush border
Commonly encountered	Crohn disease	Inflammatory intestinal injury
After allogeneic transplant	Intestinal graft-versus-host disease	Enteric injury and diarrhea

Think anatomically: Lumen to lymph

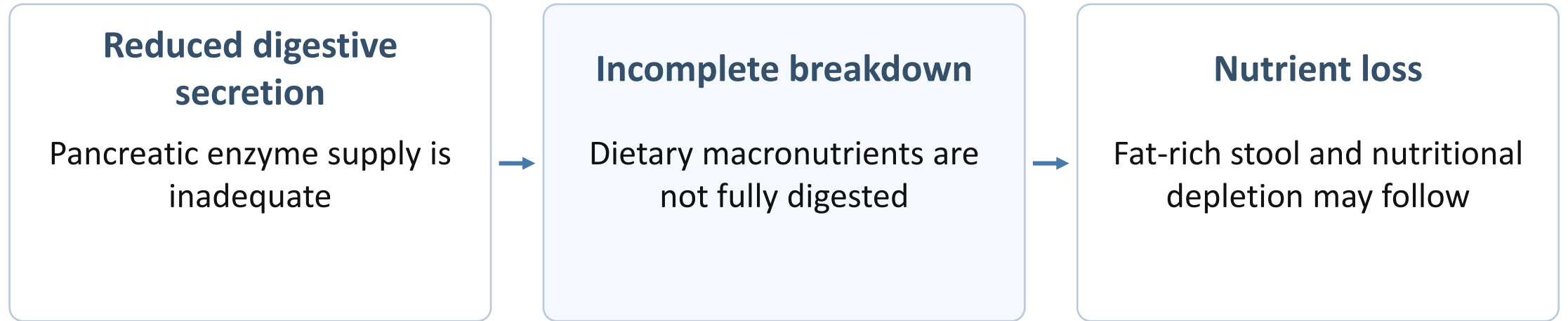


Use the site of physiological failure to organize the differential.

Intraluminal digestion: The first checkpoint

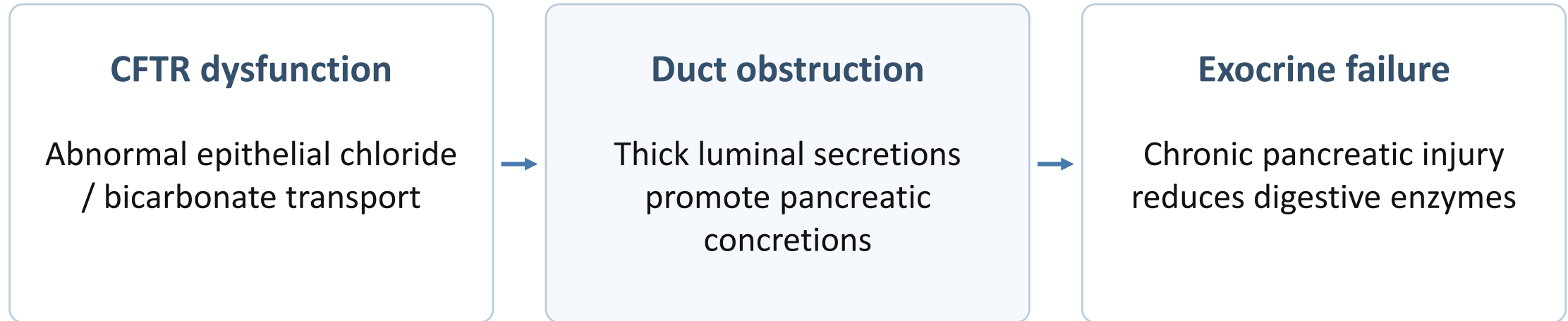
- Proteins, carbohydrates, and fats must be reduced to forms suitable for epithelial absorption.
- The phase occurs before final enzymatic processing at the brush border.
- Defective luminal digestion leaves nutrients unavailable for later uptake.
- Pancreatic insufficiency is a central example of impaired intraluminal digestion.

Pancreatic exocrine failure compromises assimilation



The principal problem is upstream of otherwise potentially intact epithelial uptake.

Cystic fibrosis: Epithelial transport to pancreatic injury



The resulting intestinal malabsorption is predominantly an intraluminal digestion defect.

Cystic fibrosis illustrates an indirect intestinal defect

Initiating abnormality

- Inherited defect of epithelial CFTR function
- Decreased hydration of secretions
- Pancreatic ducts become obstructed

Intestinal consequence

- Reduced exocrine pancreatic output
- Impaired luminal nutrient breakdown
- Enzyme replacement can address the digestive deficit

Fat malabsorption produces a recognizable stool phenotype

Poor fat assimilation

Lipids remain within
intestinal contents



Fecal fat increases

More fat is excreted in stool



Steatorrhea

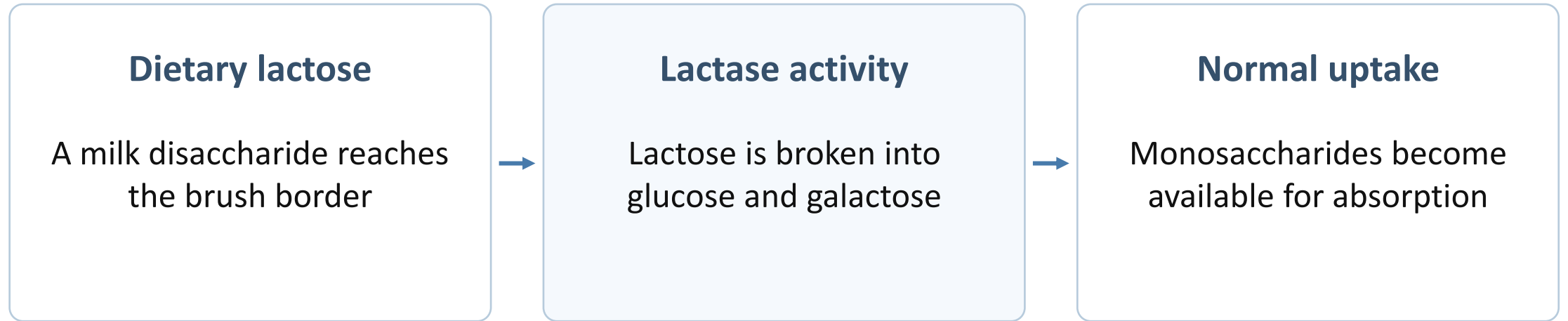
Bulky, greasy, often frothy
and pale stool

Steatorrhea is a hallmark phenotype, not a disease-specific diagnosis.

Terminal digestion occurs at the brush border

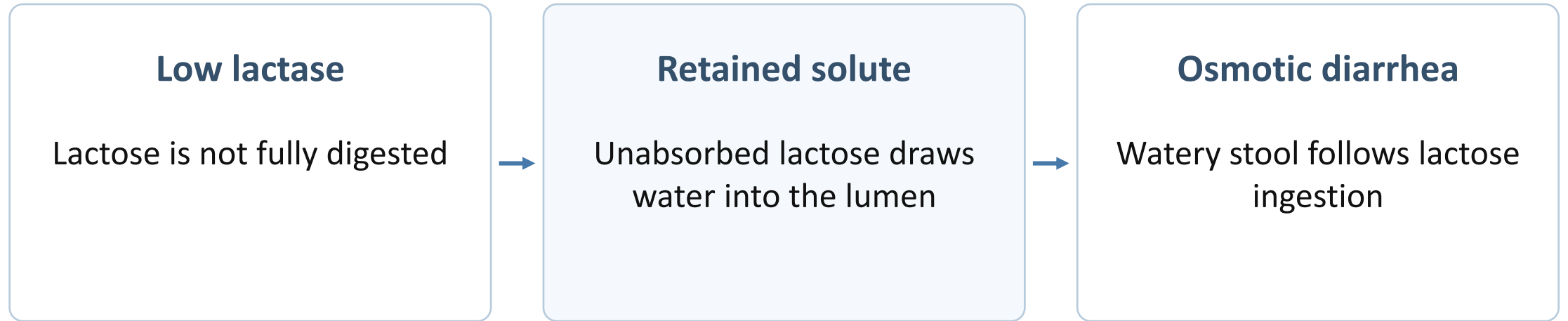
- Disaccharidases hydrolyze carbohydrates to absorbable units.
- Peptidases contribute to final peptide breakdown.
- Enzymes operate at the small-intestinal epithelial surface.
- Loss of functional brush border can impair terminal digestion even when luminal digestion is preserved.

Lactase converts lactose to absorbable sugars



Without lactase, lactose remains in the lumen and exerts an osmotic effect.

Lactase deficiency creates an osmotic load



Removing the dietary trigger or fasting reduces the osmotic burden.

Lactase deficiency may be inherited or acquired

Form	Underlying basis	Characteristic presentation
Congenital	Rare inherited enzyme defect	Severe diarrhea following milk ingestion
Acquired with age	Declining lactase expression	Dose-dependent bloating, gas, diarrhea
Postinfectious	Transient mucosal injury and enterocyte turnover	Temporary lactose intolerance after enteritis

A biochemical enzyme defect need not alter histology

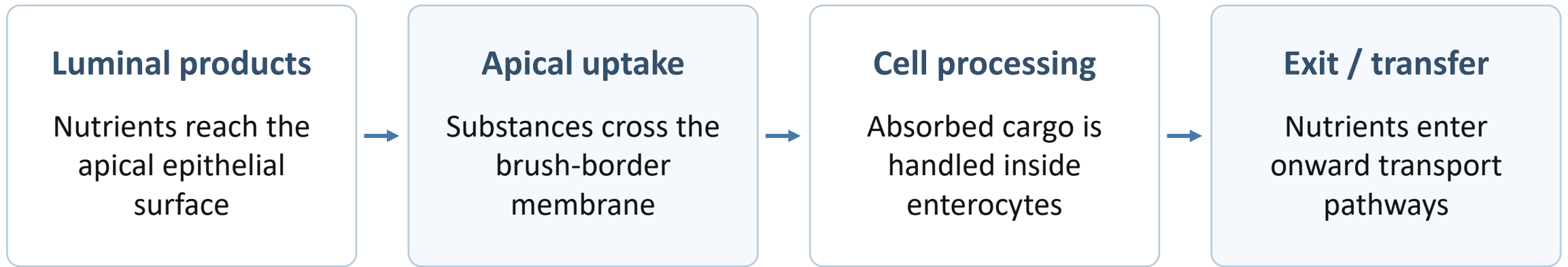
Lactase deficiency

- Primary defect is enzyme activity
- Routine intestinal histology may be unremarkable
- Symptoms are linked to lactose exposure

Mucosal destructive disorder

- Enterocyte and villus integrity may be altered
- Histological architectural changes may be present
- Several nutrients or transport functions may be impaired

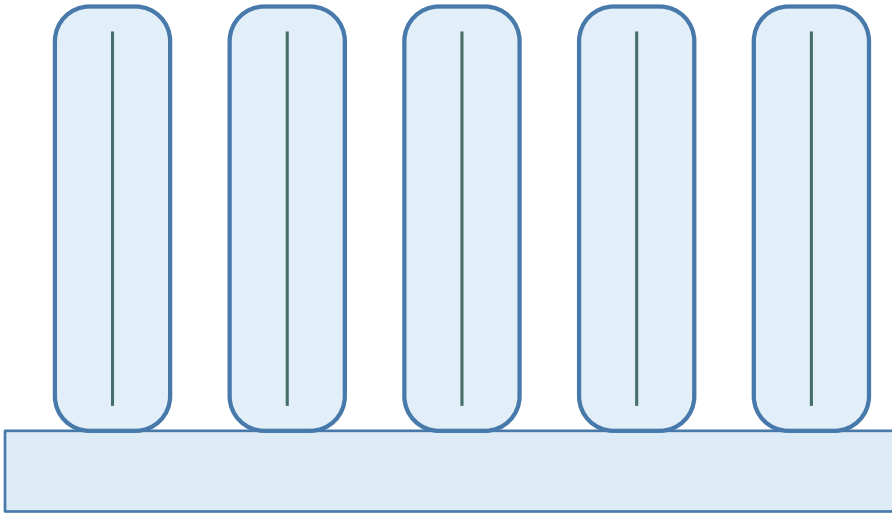
Transepithelial transport is more than entry



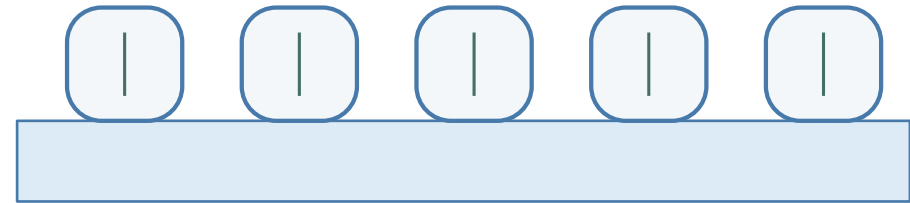
Epithelial damage and intracellular defects can both disrupt assimilation.

Mucosal surface area supports effective uptake

Preserved villous surface



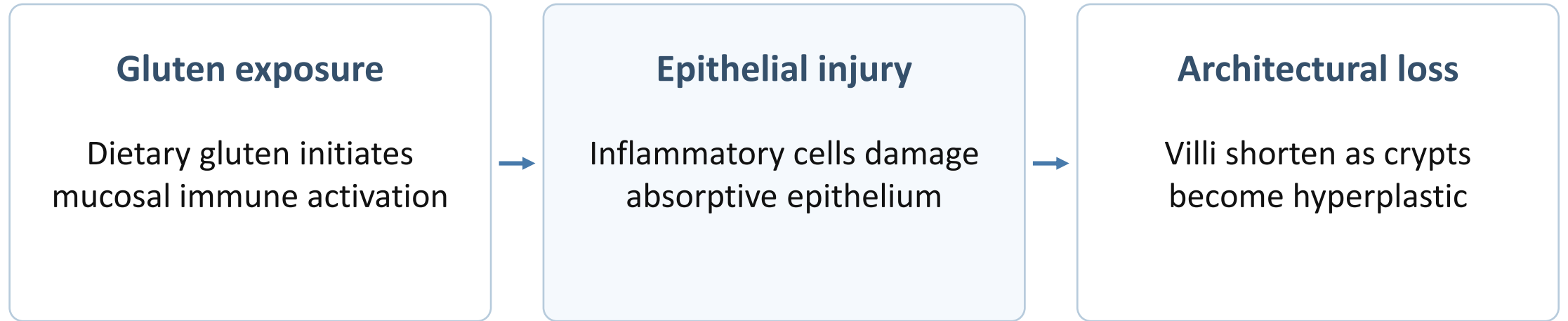
Reduced villous surface



Schematic — not a histologic specimen

A healthy villous surface offers greater contact area for digestion and absorption; Villous shortening reduces that capacity.

Celiac disease is an example of immune-mediated injury



Reduced brush-border area impairs terminal digestion and transepithelial absorption.

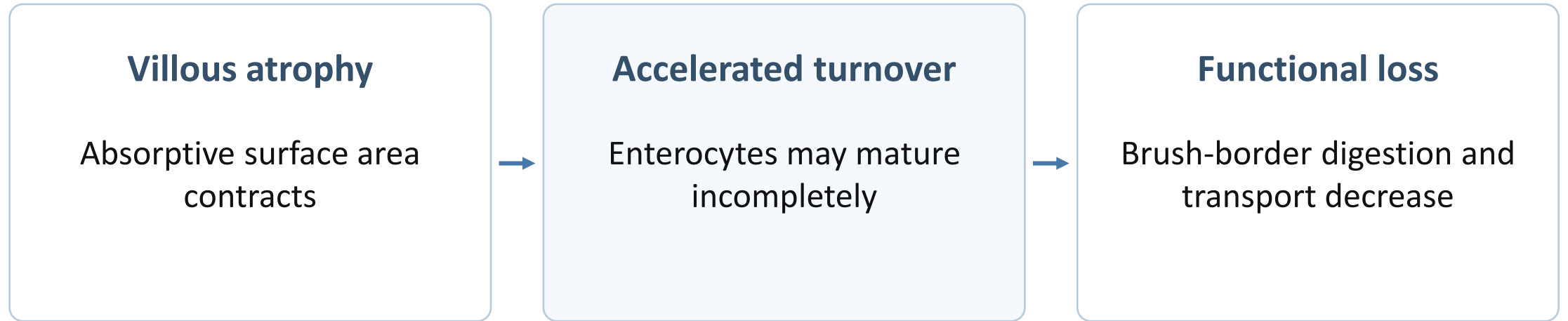
Celiac mucosal injury has three characteristic features

The characteristic biopsy pattern couples structural change to epithelial immune injury.

- Villous atrophy reduces the surface available for nutrient absorption.
- Crypt hyperplasia reflects accelerated epithelial renewal.

- Intraepithelial lymphocytosis reflects mucosal T-cell infiltration.
- None of these features is individually specific for celiac disease.

Why does shortened villous architecture matter?



Morphology and epithelial function reinforce each other in mucosal malabsorption.

Mucosal histology is informative but not specific

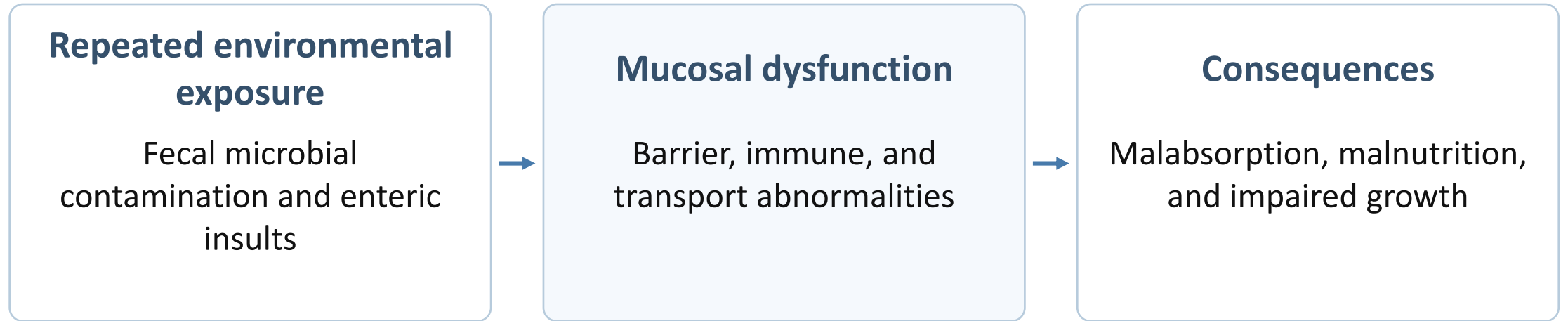
Suggestive finding

- Intraepithelial lymphocyte increase
- Villous blunting or atrophy
- Crypt architectural change

Interpretation limit

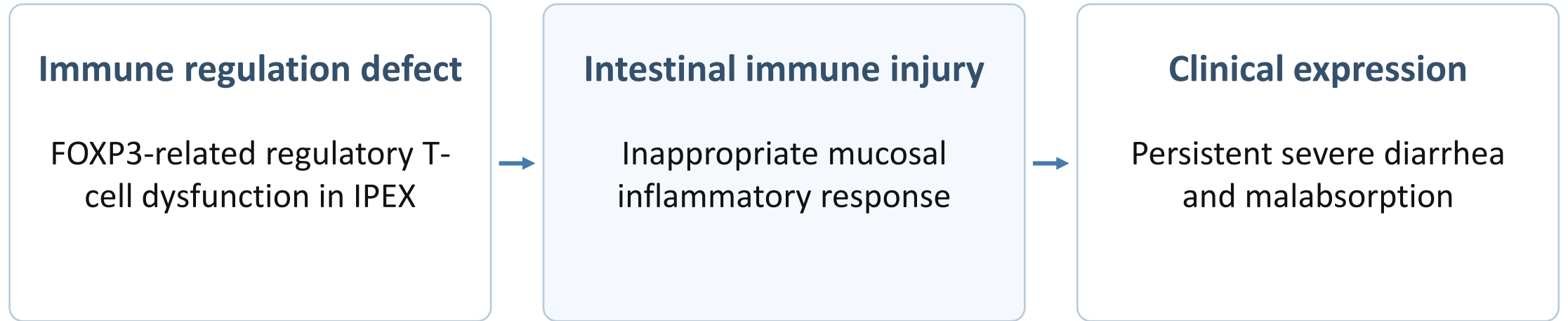
- Can occur in diseases other than celiac
- Must be interpreted with clinical context
- Celiac assessment combines compatible histology with serology

Environmental enteric dysfunction impairs mucosal function



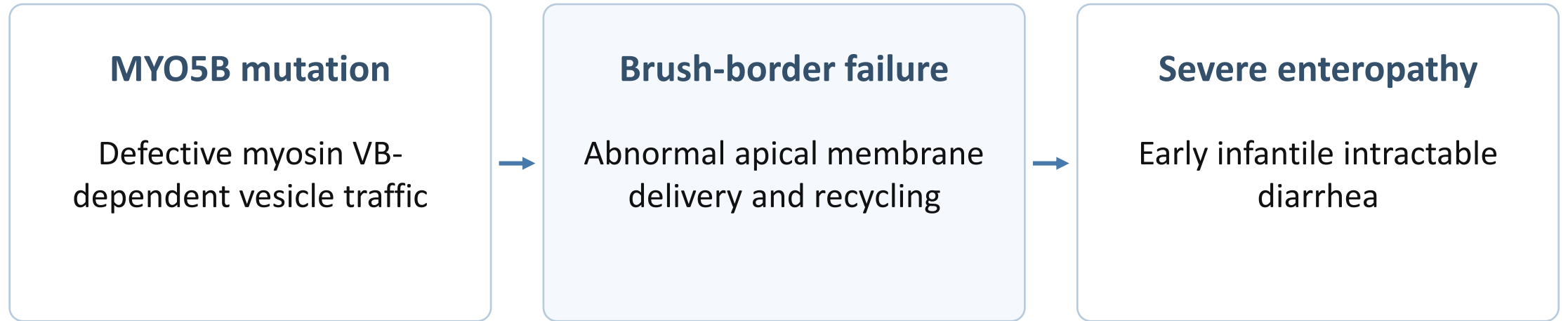
Uncertain causation and absence of accepted diagnostic criteria.

Autoimmune enteropathy disrupts epithelial integrity



Autoimmune enteropathy exemplifies intestinal dysfunction initiated by immune dysregulation.

Microvillus inclusion disease disrupts apical assembly



Terminal digestion and transepithelial transport are both compromised.

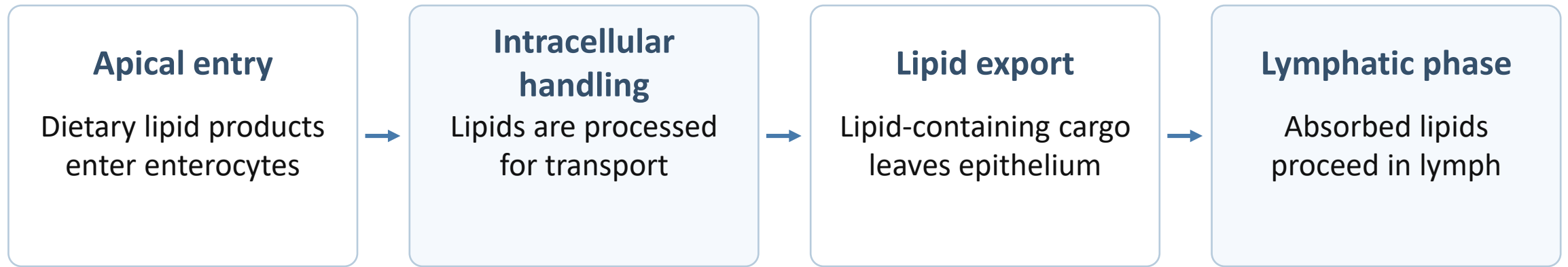
Microvillus inclusion disease has a structural clue

Cellular trafficking failure can become a recognizable microscopic feature.

- Abnormal apical vesicles contain microvillus components.
- The inclusions may be identified by electron microscopy.

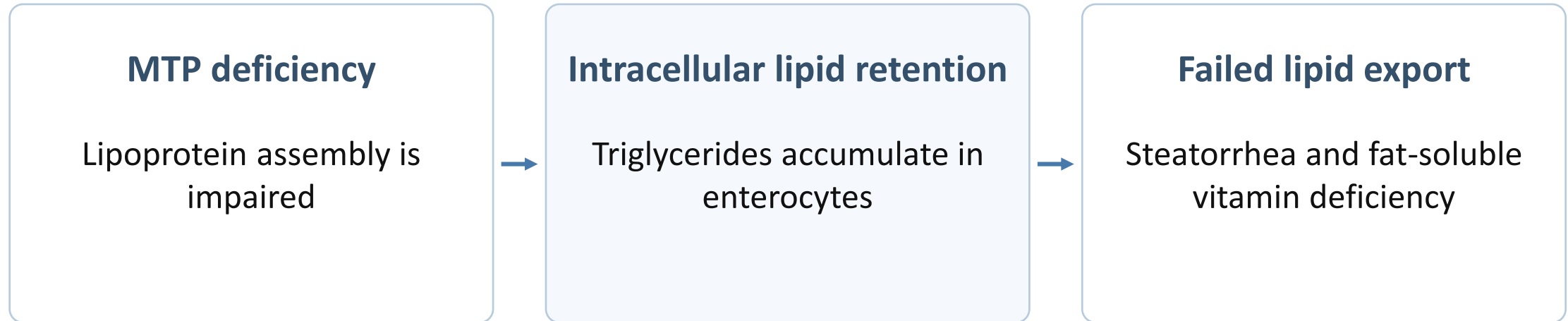
- Villin immunostaining can support identification.
- CD10 immunostaining can label inclusions and additional structures.

Post-epithelial lipid handling is a separate step



A failure after luminal digestion can still cause steatorrhea.

Abetalipoproteinemia: A lipid assembly problem



The mucosa may show lipid vacuolization rather than destructive villous inflammation.

The four-phase model localizes representative disorders

Predominant functional site	Exemplar	Functional deficit
Intraluminal digestion	Pancreatic insufficiency / cystic fibrosis	Insufficient digestive enzyme action
Terminal digestion	Lactase deficiency	Inability to hydrolyze lactose
Transepithelial function	Celiac disease / microvillus inclusion disease	Surface or membrane transport impairment
Postabsorptive lipid handling	Abetalipoproteinemia	Impaired lipid assembly and export

Steatorrhea signals fat loss, not its precise location

Characteristic stool does not identify whether the lesion is luminal or epithelial.

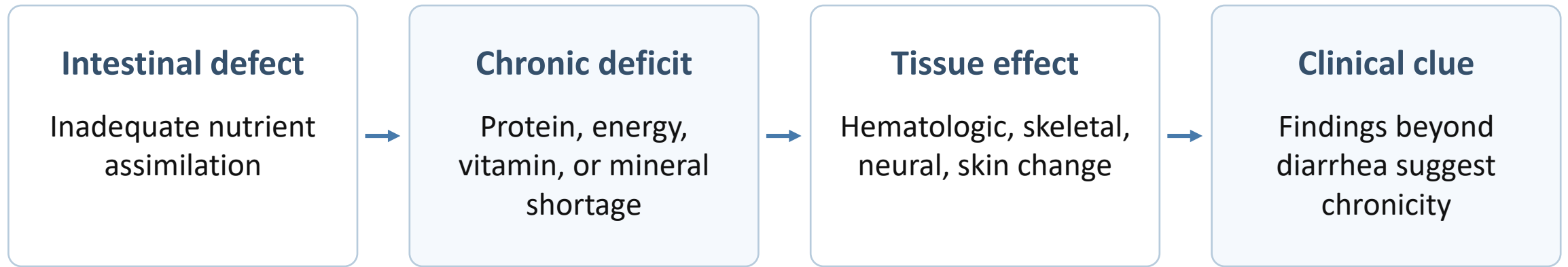
- Bulky stool with excessive fecal fat
- Greasy or frothy consistency
- Yellowish or pale appearance

- Pancreatic enzyme defects
- Mucosal absorptive surface loss
- Cellular lipid transport defects

Malabsorption frequently produces a symptom cluster

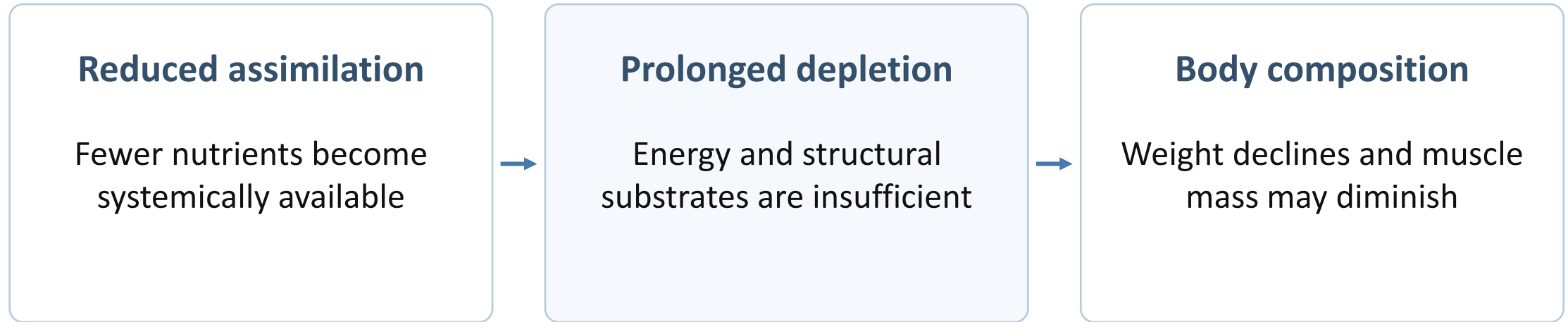
- Diarrhea, abdominal pain, and excess flatus are common.
- Abdominal distention and audible bowel sounds (borborygmi) may occur.
- Weight loss and reduced muscle mass reflect chronic nutrient loss.
- Anorexia may coexist and compound nutritional depletion.

Nutrient loss links the gut to systemic findings



Assess the systemic consequences rather than treating stool frequency as the sole manifestation.

Weight loss and muscle wasting reflect chronic deficit

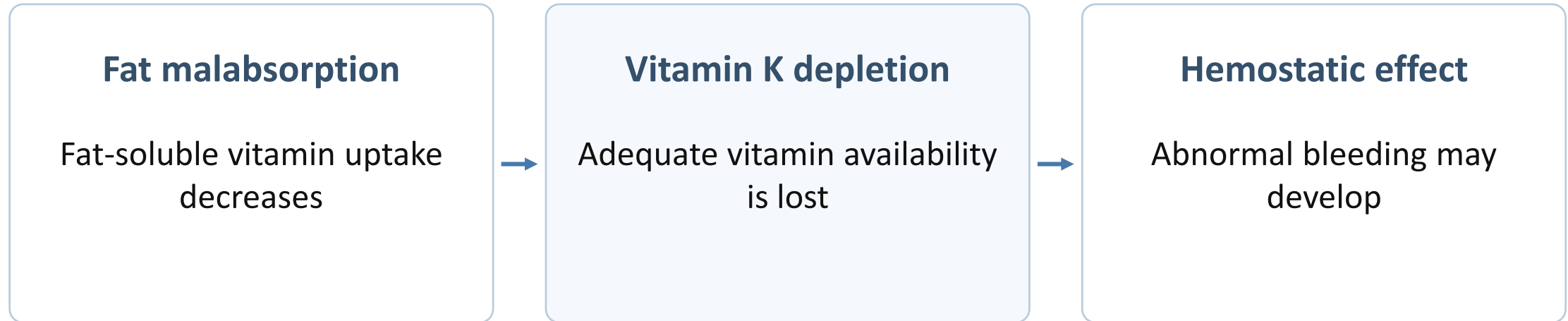


Failure to thrive may be the prominent pediatric expression of sustained malabsorption.

Anemia and mucositis reveal hematinic deficits

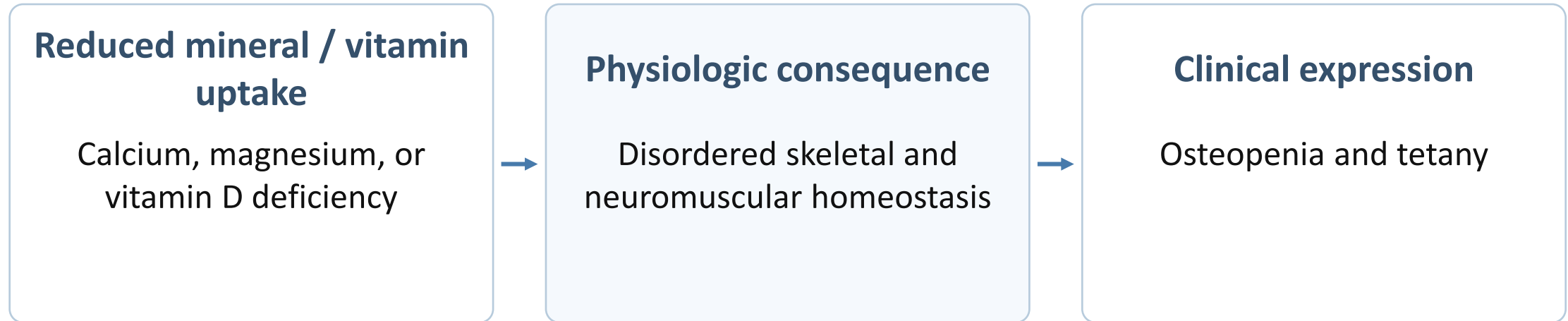
Deficient nutrient	Potential clinical expression	Mechanistic teaching point
Folate	Anemia and mucosal injury	Rapidly proliferating tissues are vulnerable
Vitamin B12	Anemia; neurologic dysfunction	Absorption defect has multisystem effects
Pyridoxine (B6)	Anemia and mucositis	Micronutrient depletion broadens the phenotype

Vitamin K deficiency creates a bleeding tendency



Bleeding in a chronic diarrhea syndrome should prompt attention to nutrition, not just mucosal blood loss.

Calcium, magnesium, and vitamin D affect bone and muscle



A single malabsorptive process may manifest through both stool change and metabolic complications.

Peripheral neuropathy may accompany malabsorption

- Neurologic symptoms can reflect specific vitamin depletion rather than direct bowel injury.
- Vitamin B12 deficiency among the causes of neuropathy.
- Nutrient assessment helps interpret neurologic features alongside chronic diarrhea.

Skin and endocrine abnormalities expand the differential

- Sustained nutritional deficits may affect multiple organ systems.
- The Robbins overview includes skin and endocrine associations such as vitiligo and goiter.
- These associations are nonspecific; Correlate them with the intestinal and nutritional phenotype.

Clinical burden is not proportional to stool frequency

Stool-based view

- Stool volume, frequency, appearance
- Blood or purulence in stool
- Relationship to meals and fasting

Whole-patient view

- Weight and muscle mass
- Anemia, bleeding, bone or neurologic signs
- Timing, transplant history, and associated immune illness

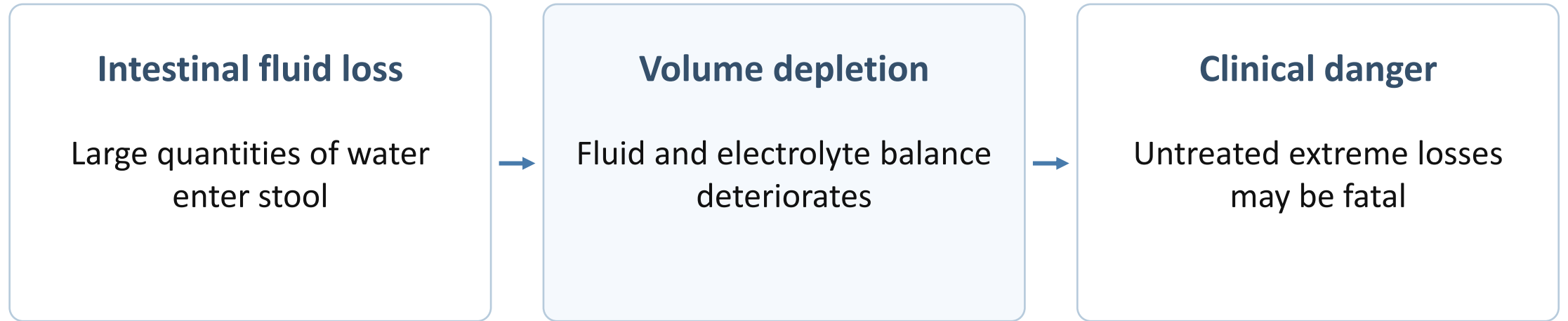
Diarrhea has three defining dimensions

The Robbins definition concerns increased stool mass, frequency, or fluidity.

- A typical quantitative reference is more than 200 g stool per day.
- Patients may report fluidity without measuring stool mass.

- Frequency alone does not identify mechanism.
- Stool composition, fasting response, and inflammation help classify diarrhea.

Severe diarrhea is fundamentally a fluid-loss emergency



The pathophysiologic category informs etiology; Immediate volume loss determines urgency.

Four major pathophysiologic patterns of diarrhea

Secretory

Fluid secretion; Continues while fasting

Osmotic

Unabsorbed solutes; Improves during fasting

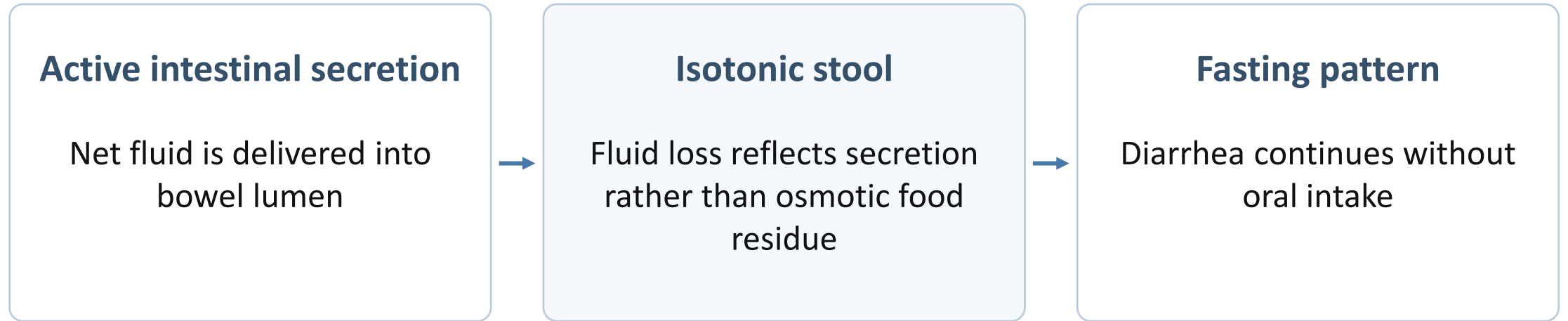
Malabsorptive

Generalized nutrient loss; Often steatorrhea

Exudative

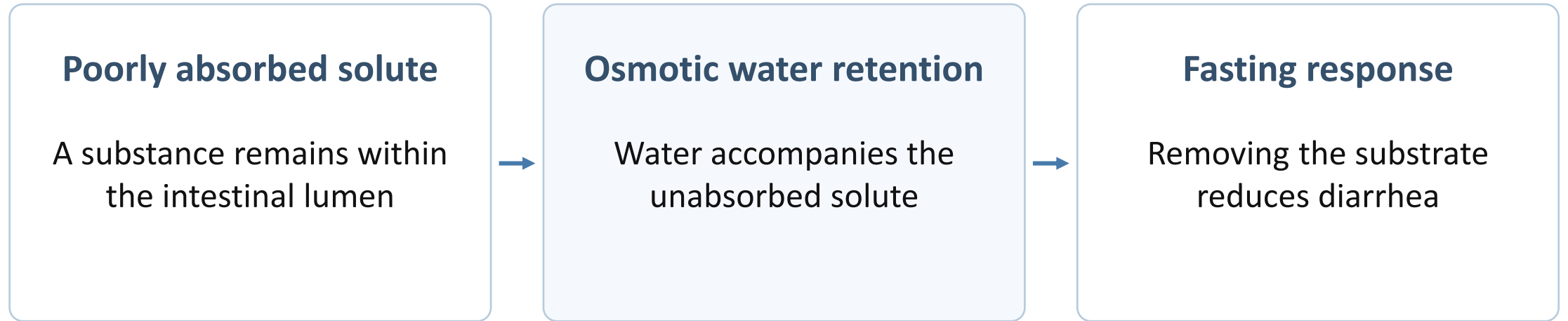
Inflammation; Purulent or bloody stool

Secretory diarrhea persists during fasting



Persistence despite fasting is an important functional discriminator.

Osmotic diarrhea depends on retained luminal solutes



Lactose intolerance is the Robbins example of the osmotic pattern.

Lactose intolerance connects symptom to mechanism

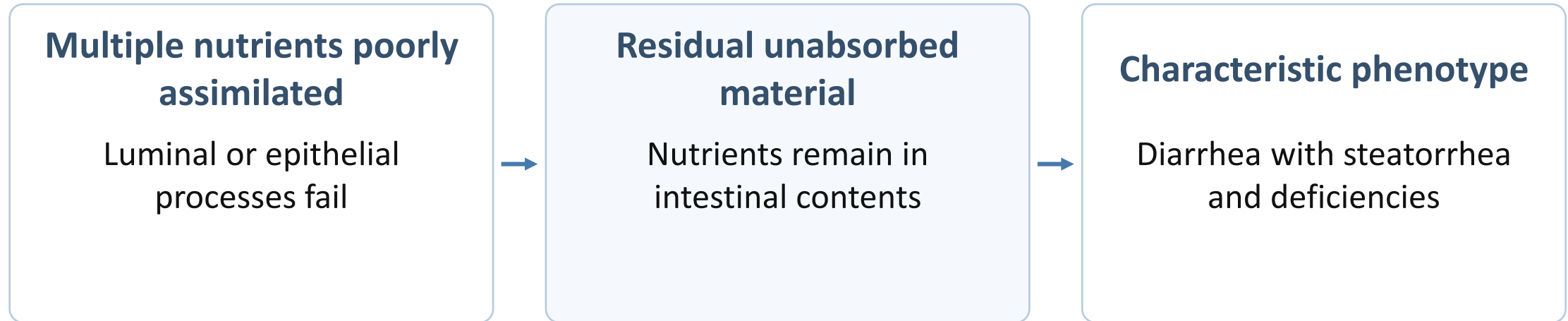
After lactose exposure

- Undigested sugar remains in lumen
- Water accumulation increases
- Abdominal fullness, flatulence, loose stool

After lactose withdrawal

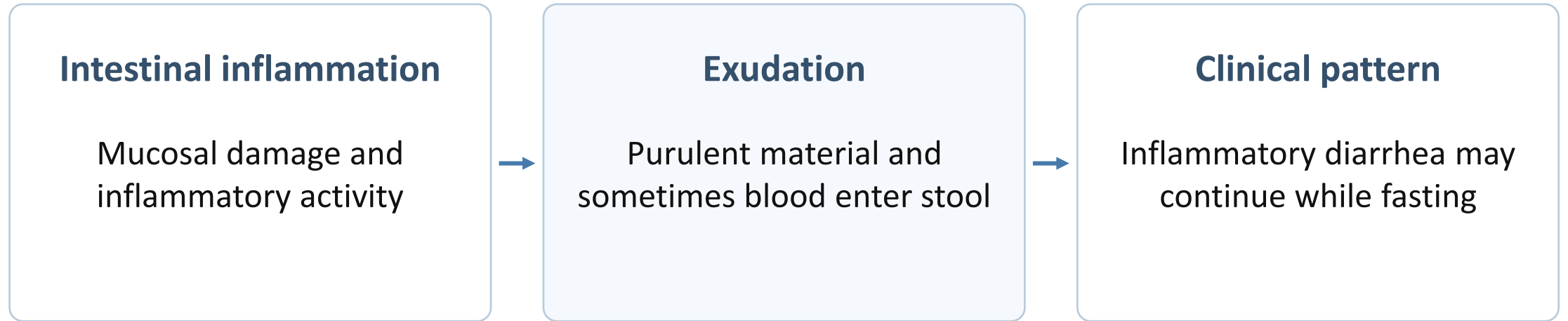
- Less unabsorbed substrate reaches the bowel
- Osmotic load declines
- Symptoms usually diminish

Malabsorptive diarrhea reflects global assimilation failure



Fasting can lessen this diarrhea, although underlying nutrient-handling disease remains.

Exudative diarrhea originates in inflammatory injury



The presence of blood or pus distinguishes this pattern from uncomplicated lipid malabsorption.

Dysentery is a clinically distinct stool phenotype

Dysentery

- Painful, small-volume stools
- Blood is a defining feature
- Suggests an inflammatory intestinal process

Steatorrhea

- Bulky, fatty stools
- Greasy or frothy character
- Suggests defective fat absorption

Fasting response separates two broad groups

Diarrheal mechanism	Usually persists fasting?	Recognizable clue
Secretory	Yes	Ongoing isotonic fluid loss
Osmotic	No	Unabsorbed dietary or luminal solute
Malabsorptive	Usually diminishes	Steatorrhea and nutritional depletion
Exudative	Yes	Inflammatory, bloody or purulent stool

Secretory and osmotic are physiologically different

Secretory

- Dominant process: Fluid secretion
- Stool described as isotonic
- Persists during fasting

Osmotic

- Dominant process: Retained osmotically active solutes
- Example: Undigested lactose
- Typically improves with fasting

Malabsorptive and exudative differ in stool content

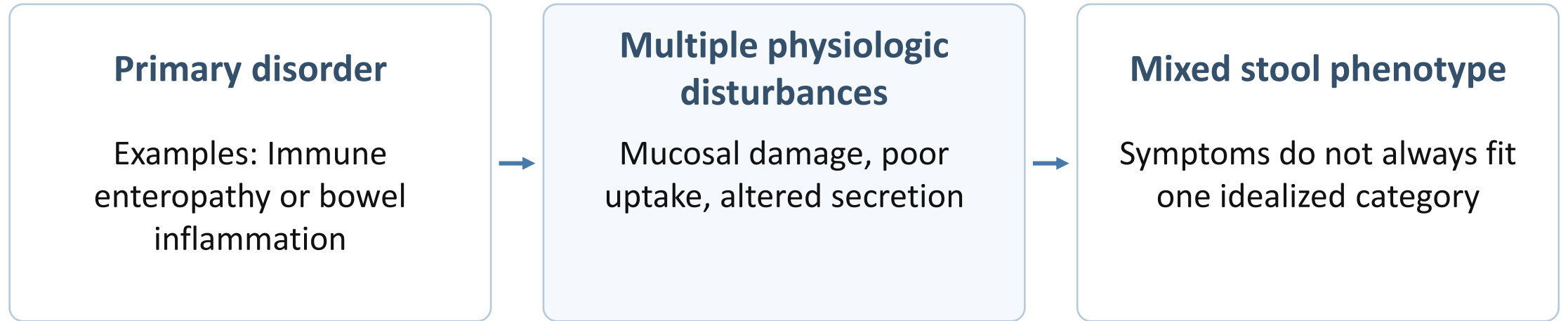
Malabsorptive

- Dominant problem: Failure of nutrient assimilation
- Fatty stool and nutritional deficits
- Generally relieved by fasting

Exudative

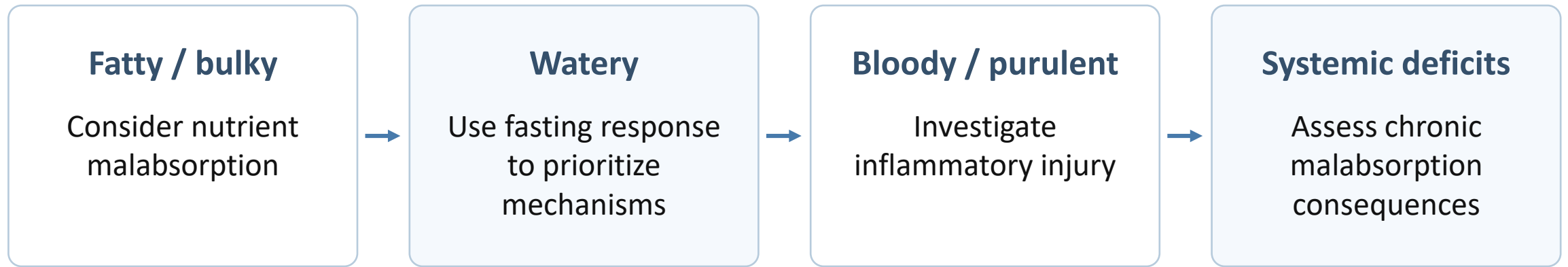
- Dominant problem: Intestinal inflammatory injury
- Blood and purulent material may appear
- Continues during fasting

Diarrhea mechanisms may coexist in the same patient



The four categories are a mechanistic framework rather than mutually exclusive diagnoses.

Clinical reasoning starts with stool phenotype



A descriptive category guides targeted evaluation; It does not by itself establish etiology.

Case: Greasy stool with pancreatic disease

An adult with known chronic pancreatic damage develops bulky, greasy stools and progressive weight loss.

Which stage of nutrient absorption is most likely impaired?

Intraluminal digestion

- Pancreatic exocrine output is required for digestion before epithelial uptake.
- Fat maldigestion links the pancreatic disease to steatorrhea.

Case: Loose stools after consuming milk

An individual experiences abdominal fullness, flatus, and watery stool following dairy intake; Symptoms improve when dairy is avoided.

What mechanism best explains the watery diarrhea?

Osmotic diarrhea from lactase deficiency

- Lactose is not completely hydrolyzed at the brush border.
- Retained lactose creates a luminal osmotic load.

Case: Villous injury and nutritional depletion

A patient has chronic diarrhea, weight loss, and evidence of small-intestinal villous shortening with increased intraepithelial lymphocytes.

What absorptive functions could be disrupted?

Terminal digestion and transepithelial transport

- Loss of absorptive surface reduces nutrient uptake.
- Immature enterocytes may express fewer differentiated brush-border functions.

Case: Infant with severe early-onset diarrhea

A neonate develops persistent severe diarrhea shortly after birth; Investigation raises concern for abnormal enterocyte microvillus trafficking.

Which molecular disease mechanism fits the pattern?

MYO5B-related microvillus inclusion disease

- Defective apical membrane trafficking disrupts brush-border assembly.
- Both terminal digestion and epithelial transport become impaired.

Case: Bloody, painful, low-volume stools

A patient develops frequent painful passage of small quantities of bloody stool during an inflammatory enteric illness.

Which pattern is illustrated?

Dysentery with exudative diarrhea

- Blood and pain support inflammatory mucosal injury.
- This phenotype differs from bulky fatty steatorrhea.

Case: Diarrhea continues with no oral intake

A patient has abundant watery stool that continues despite a period of fasting.

Which mechanisms remain most compatible?

Secretory or exudative diarrhea

- Secretory fluid losses persist during fasting.
- Exudative diarrhea may also persist, but blood or pus would suggest inflammation.

Diagnostic reasoning should account for chronology

Mechanistic clues are strongest when combined with the clinical setting.

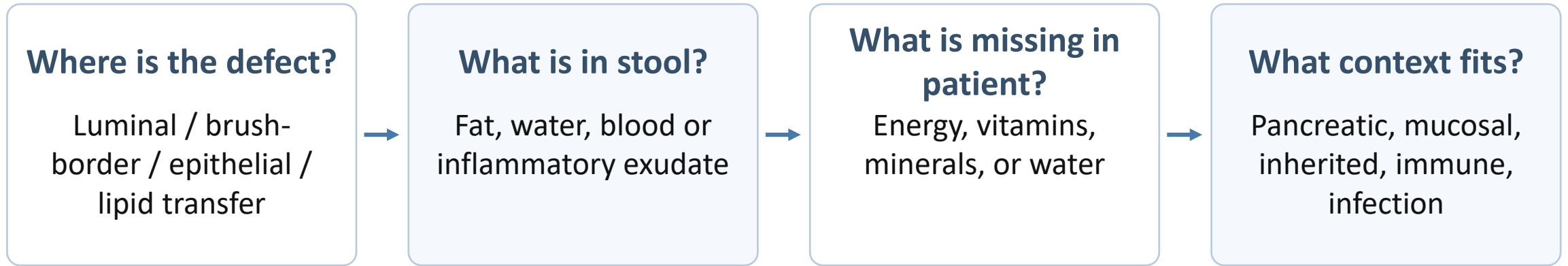
- Diarrhea since early infancy: Consider inherited epithelial or enzyme disorders.
- After milk exposure: Prioritize disaccharidase deficiency.
- After intestinal infection: Transient brush-border dysfunction may occur.

- After allogeneic stem-cell transplantation: Consider intestinal graft-versus-host disease.
- With immune-mediated intestinal injury: Evaluate the villous and epithelial phenotype.
- With pancreatic injury: Prioritize intraluminal maldigestion.

Key distinctions at a glance

Clinical clue	Physiologic implication	Exemplar
Greasy and bulky stool	Fat malabsorption	Pancreatic insufficiency
Watery after milk; improves fasting	Osmotic load from carbohydrate	Lactase deficiency
Villous atrophy + nutrient loss	Mucosal absorption defect	Celiac disease
Bloody or purulent stool	Inflammatory exudation	Exudative diarrhea

Integrative model: Site, stool, and system



A defensible clinicopathologic explanation connects lesion, function, stool phenotype, and clinical consequence.

Five principles to retain

- Malabsorption may arise in any of four distinct but interdependent phases.
- Steatorrhea is a hallmark of fat malabsorption, not a unique diagnosis.
- Micronutrient deficiency can dominate presentation outside the intestine.
- Fasting response and stool content distinguish major diarrhea mechanisms.
- Real disorders may combine malabsorptive, inflammatory, and secretory components.

Reference and source boundaries

- Robbins, Cotran & Kumar: Pathologic Basis of Disease. 11th edition (2026).
- Primary basis: “Malabsorption and Diarrhea” section.
- Disease-specific mechanistic examples are limited to adjacent textbook sections on cystic fibrosis, celiac disease, environmental enteric dysfunction, autoimmune enteropathy, lactase deficiency, microvillus inclusion disease, and abetalipoproteinemia.
- All villous figures and mechanistic sequences are original editable teaching schematics; they are not clinical specimens.