

Abetalipoproteinemia

Defective assembly of triglyceride-rich lipoproteins

Molecular mechanism, intestinal morphology, and clinicopathologic diagnosis

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Learning objectives

Locate the molecular defect within normal intestinal lipid transport.

Link enterocyte vacuolization to the systemic lipoprotein phenotype.

Interpret steatorrhea, acanthocytes, and malabsorption differentials.

Core definition: A lipoprotein assembly disorder

A rare, inherited disorder with inability to assemble triglyceride-rich lipoproteins.

The abnormality involves microsomal triglyceride transfer protein (MTP).

Enterocyte lipid handling is impaired despite the presence of ingested fat.

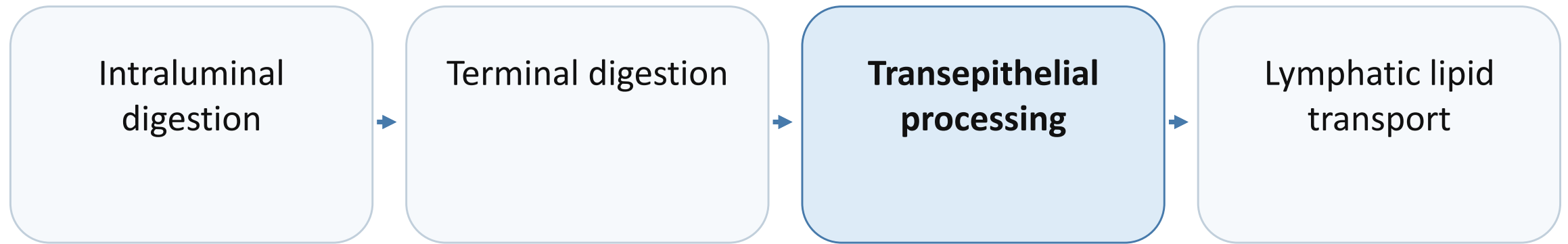
Why this condition belongs in intestinal pathology

The gastrointestinal presentation is a disorder of nutrient absorption.

Lipid processing within the intestinal epithelial cell is central.

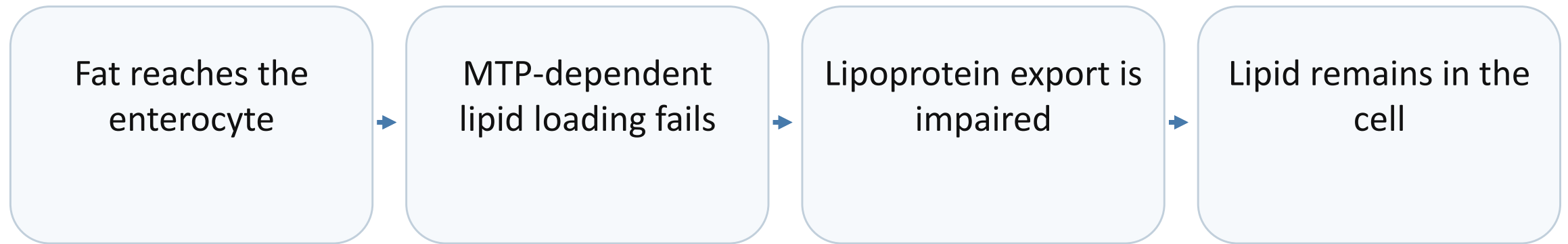
A cellular transport defect explains both mucosal changes and systemic findings.

Four phases of nutrient absorption



Normal sequence from the intestinal lumen toward the circulation.

Localize the abetalipoproteinemia lesion



The lesion is in intracellular packaging/transport, not described as an enzyme deficiency in the intestinal lumen.

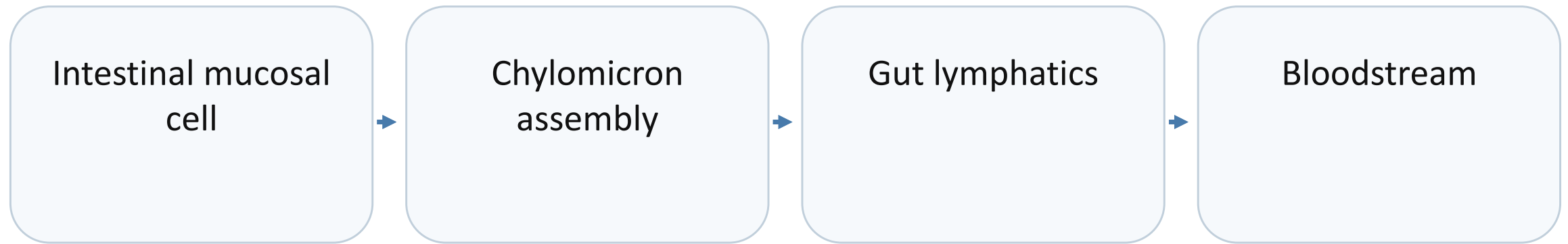
Dietary lipid requires a transport vehicle

In the normal intestine, dietary triglycerides and cholesterol enter chylomicrons.

Chylomicrons subsequently move through intestinal lymphatics to the bloodstream.

Thus, processing lipid within the mucosa is distinct from simply taking it up.

Chylomicrons connect gut and circulation



Source-grounded normal transport sequence.

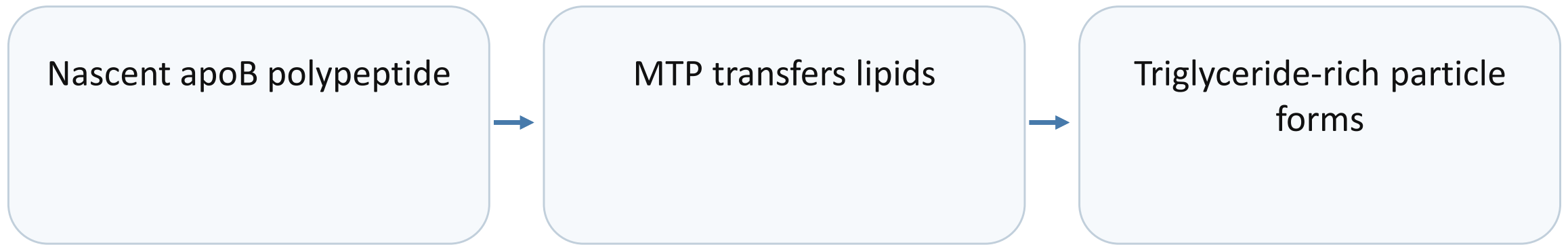
Apolipoprotein B is an assembly partner

Nascent apolipoprotein B is the protein scaffold receiving lipid in the ER.

The supplied Robbins text identifies MTP as the required transfer machinery.

Without this step, triglyceride-rich lipoprotein formation is disrupted.

MTP acts in the endoplasmic reticulum



Mechanistic diagram: Normal lipid transfer to nascent apoB in the ER.

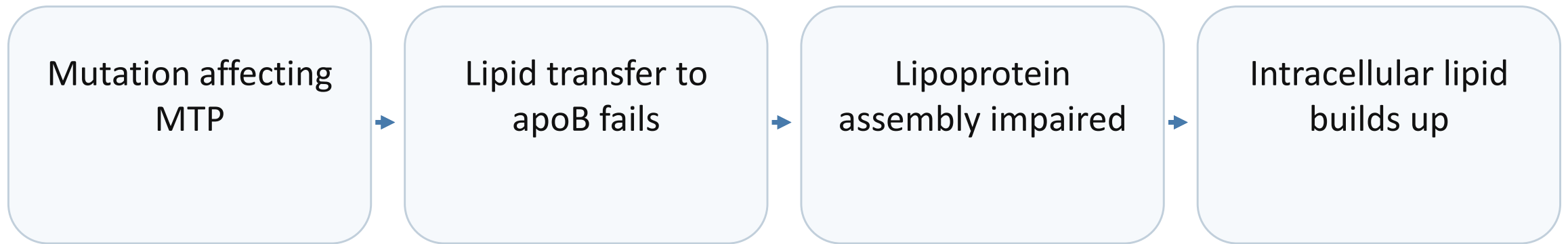
Inherited mechanism: Autosomal recessive

The disease is characterized as autosomal recessive.

Its fundamental genetic effect is defective MTP function.

Inheritance explains why the defect is constitutional rather than acquired.

A protein defect has a subcellular consequence



Unassembled lipid is retained in enterocytes

MTP deficiency blocks normal handling of lipids destined for apoB particles.

Intracellular triglycerides therefore accumulate.

The retention is visible morphologically as cytoplasmic epithelial vacuolization.

The same defect operates at two scales

Microscopic scale

Lipid retained inside epithelial cells

Vacuolated enterocyte cytoplasm

Triglyceride content can be highlighted

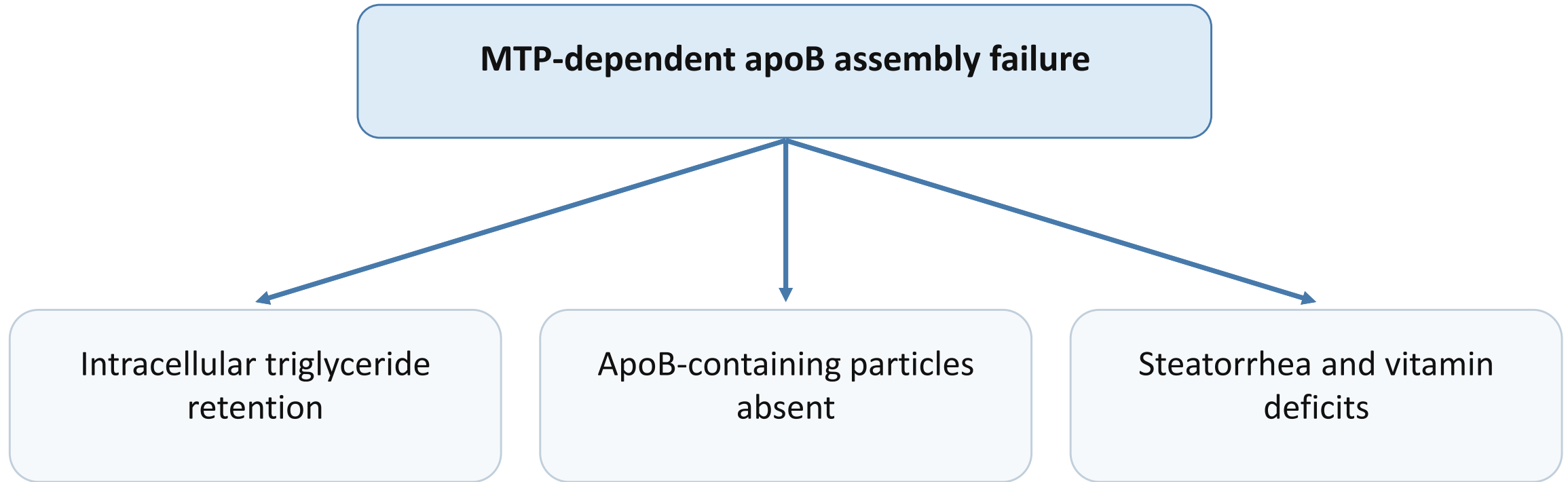
Systemic scale

Loss of circulating apoB-containing particles

Impaired lipid delivery from intestine

Consequences of fat malabsorption

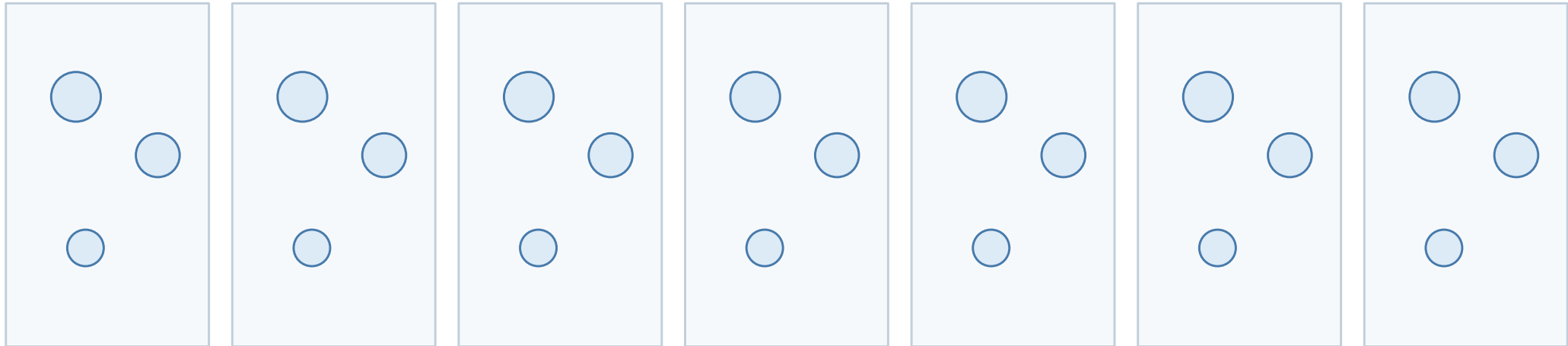
Causal map from MTP defect to disease



Parallel consequences of defective assembly; Schematic causal relationships.

The enterocyte is the site of lipid retention

Intestinal lumen



Enterocyte cytoplasm: Retained lipid droplets

Schematic: Intracellular neutral-lipid droplets can appear as epithelial vacuoles.

Epithelial vacuolization is a morphologic clue

The characteristic microscopic finding is vacuolization of intestinal epithelium.

Vacuoles reflect accumulated triglycerides rather than a specific inflammatory infiltrate.

Interpret this finding together with the clinical and plasma phenotype.

Why an epithelial vacuole appears

Dietary triglyceride
is handled



ApoB lipidation is
defective



Triglyceride
accumulates



Cytoplasmic vacuoles
become evident

Oil red O highlights accumulated lipid

Oil red O as a special stain that can highlight triglyceride accumulation.

A positive lipid stain supports the interpretation of fat-filled epithelial vacuoles.

Staining supports the mechanism; It does not independently establish the inherited defect.

The fatty meal changes morphologic visibility

Epithelial lipid accumulation can be particularly evident after a fatty meal.

Postprandial lipid load accentuates the consequence of impaired packaging.

The temporal context matters when interpreting biopsy appearances.

Histologic observation versus etiologic inference

Direct observation

Vacuolated epithelial cytoplasm

Lipid can be shown by oil red O

Appearance depends in part on fat exposure

Disease interpretation

Transport defect involving MTP

Failure of apoB-lipoprotein assembly

Explains epithelial lipid retention

Morphology can localize the metabolic bottleneck

Defective intracellular packaging

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graph TD; A[Defective intracellular packaging] --> B[Enterocyte triglyceride retention]; A --> C[Absent apoB-containing particles]
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Enterocyte triglyceride retention

Absent apoB-containing particles

Both findings arise from the same cellular assembly defect.

Which lipoproteins are absent?

The plasma is completely devoid of lipoproteins containing apolipoprotein B.

The finding follows defective assembly of apoB-dependent particles.

Do not misstate this as absence of every circulating lipoprotein.

The plasma signature is molecularly specific

Root cause

MTP-dependent lipid transfer to nascent apoB fails

Triglyceride-rich lipoprotein assembly is impossible

Measurable consequence

ApoB-containing lipoproteins are absent

Provides a strong systemic clue to the intestinal defect

Enterocyte and plasma findings reinforce each other

Defective MTP

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graph TD; A[Defective MTP] --> B[Lipid trapped within mucosa]; A --> C[No apoB-containing plasma particles];
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Lipid trapped within mucosa

No apoB-containing plasma particles

A single protein defect produces two parallel observations.

Malabsorption affects more than stool fat

Lipid handling failure is associated with impaired absorption of essential fatty acids.

Fat-soluble vitamin deficiency accompanies the disorder.

Systemic lipid membrane alterations may become visible in red cells.

Fat-soluble vitamin deficiency: A general consequence

Abetalipoproteinemia with fat-soluble vitamin deficiencies.

Its parent malabsorption discussion explains broader consequences of vitamin depletion.

The excerpt provides no disease-specific frequencies or laboratory thresholds.

Vitamin K deficiency and bleeding risk

The general malabsorption section identifies bleeding as a consequence of vitamin K deficiency.

This illustrates why lipid-absorption disorders can have extraintestinal manifestations.

A patient's bleeding history requires clinical evaluation; No frequency is supplied.

Vitamin D deficiency and bone effects

Osteopenia and tetany among manifestations of calcium, magnesium, or vitamin D deficiency.

These are broader consequences of malabsorption rather than defining criteria for this disease.

The clinical phenotype extends beyond diarrhea and weight change.

The membrane phenotype can be seen in blood

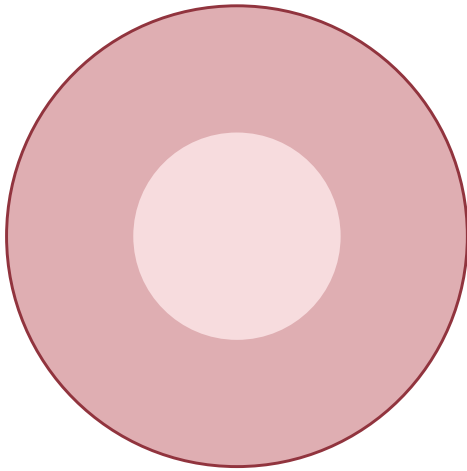
Lipid membrane defects can alter the appearance of red blood cells.

The peripheral smear can contain acanthocytes.

This connects disordered lipid handling to a distinctive extraintestinal morphologic sign.

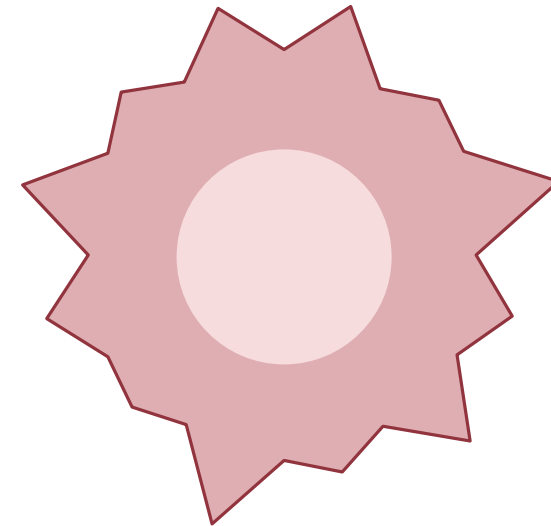
Acanthocytes: Recognize the described feature

Normal red cell



Smooth perimeter

Acanthocyte



Spiky membrane protrusions

Schematic comparison: Acanthocytes have spiky membrane protrusions; Not a patient smear.

Acanthocytosis is a clinicopathologic clue

Acanthocytes are red cells with spiky surface projections.

The excerpt directly links the phenotype to lipid membrane abnormalities.

Use the smear finding with steatorrhea and the plasma lipoprotein pattern, not in isolation.

Infantile presentation is characteristic

The disease presents in infancy.

Failure to thrive, diarrhea, and steatorrhea are emphasized.

The combination points toward an early-onset nutrient absorption disorder.

Failure to thrive: Pathophysiologic interpretation

The hallmark infant finding is inadequate growth or weight gain.

Impaired absorption of dietary lipid contributes to nutrient loss.

The association is mechanistically coherent with the observed steatorrhea.

Diarrhea is part of the presenting syndrome

Diarrhea is explicitly part of the textbook phenotype.

It occurs within a malabsorption syndrome rather than a named infectious enterocolitis.

Stool characterization helps determine the likely diarrhea mechanism.

Steatorrhea is a defining clinical clue

Steatorrhea denotes increased fecal fat.

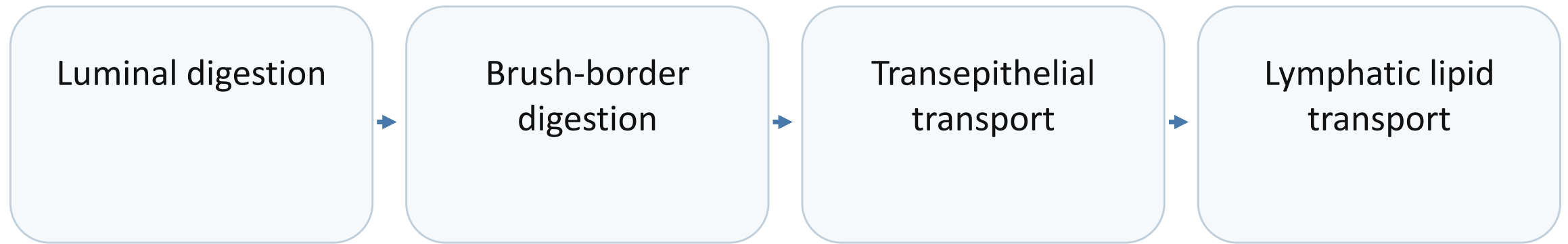
The parent section describes bulky, frothy, greasy stools that may be yellow or clay colored.

This pattern signals defective handling or absorption of dietary lipid.

Distinguishing malabsorptive diarrhea

Mechanism	Illustrative pattern	Relationship to fat
Malabsorptive	Steatorrhea; Relieved by fasting	Central clue
Osmotic	Unabsorbed luminal solute; Relieved by fasting	Not necessarily fatty
Secretory	Persists during fasting	Fat not defining
Exudative	Purulent or bloody; Persists during fasting	Inflammatory pattern

Where can the malabsorption process fail?



Robbins' four-part classification of absorption defects.

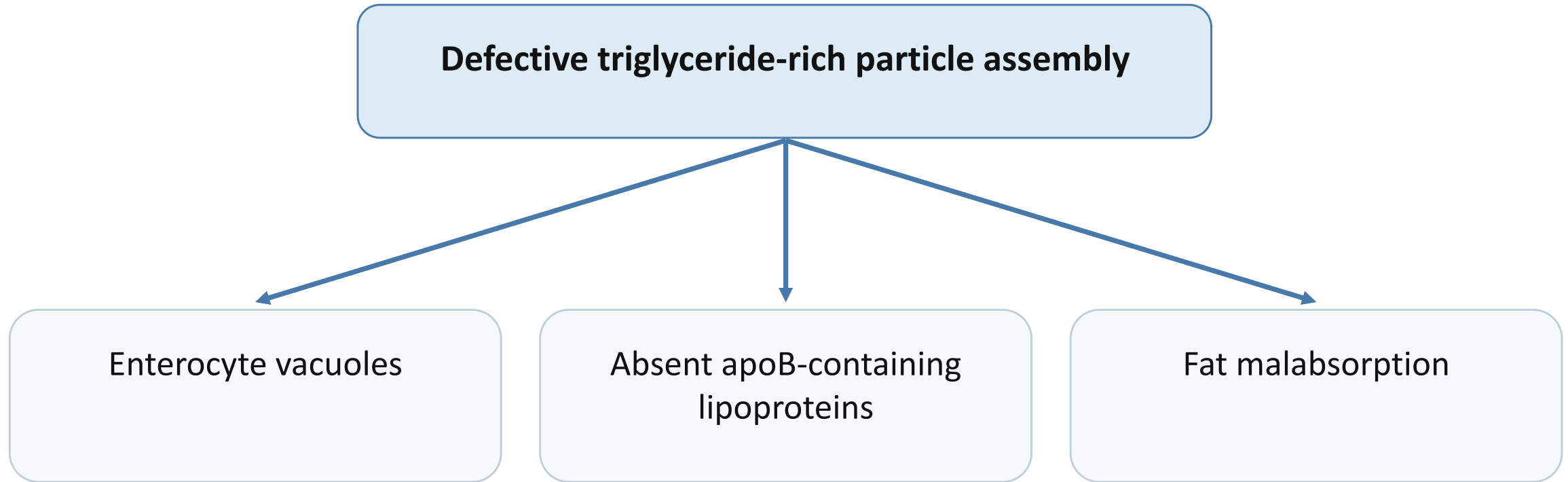
The bottleneck is cellular packaging

The lesion is downstream of luminal exposure to dietary lipid.

Lipid is retained in epithelial cytoplasm because apoB-particle formation fails.

The defect relates to epithelial processing/transport and ultimately lipid export.

One disease, four interconnected findings



These downstream findings are not a linear sequence of causes.

A feature-to-mechanism interpretation table

Finding	Underlying process
Steatorrhea	Defective lipid absorption/transport
Vacuolated enterocytes	Intracellular triglyceride accumulation
Absent apoB particles	Failure of apoB-dependent assembly
Acanthocytes	Altered red-cell membrane lipids
Fat-soluble vitamin deficiency	Disordered lipid-related nutrient absorption

The source does not define a gross lesion

The abetalipoproteinemia passage emphasizes an intracellular microscopic feature.

It does not describe a characteristic gross intestinal mass or ulcer.

Avoid inventing a gross appearance when teaching this disorder.

Differential diagnosis starts with the impaired step

Different disorders produce malabsorption through distinct phases of digestion or transport.

Lipid-rich enterocyte vacuoles and absent apoB particles favor an intracellular assembly defect.

The same nonspecific complaint—diarrhea—can arise from unrelated mechanisms.

Compare pancreatic insufficiency in cystic fibrosis

Abetalipoproteinemia

MTP-dependent particle assembly fails

Enterocyte lipid retention

ApoB-containing particles absent

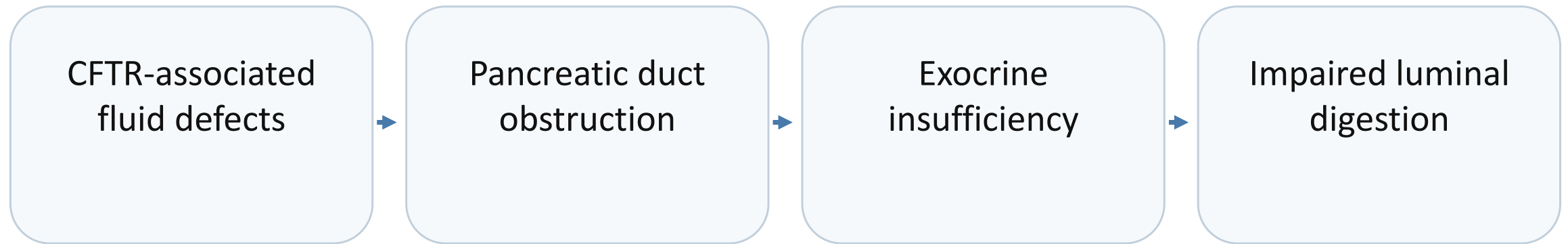
Cystic fibrosis

Pancreatic duct obstruction may produce
exocrine insufficiency

Insufficient luminal pancreatic enzymes

Impaired intraluminal digestion

Why the cystic fibrosis mechanism differs



In cystic fibrosis, Robbins localizes malabsorption upstream of enterocyte packaging.

Compare immune-mediated celiac disease

Abetalipoproteinemia

MTP deficiency disrupts lipid packaging

Epithelial lipid vacuolization

ApoB lipoproteins absent

Celiac disease

Immune-mediated gluten response

Villous atrophy and intraepithelial
lymphocytes

Loss of absorptive surface area

Celiac morphology has a different explanation

Villous atrophy, crypt hyperplasia, and intraepithelial lymphocytosis in celiac disease.

These reflect immune-mediated epithelial injury and turnover.

In abetalipoproteinemia, the highlighted lesion is triglyceride accumulation in epithelium.

Compare lactase deficiency

Abetalipoproteinemia

Defect in lipid particle assembly

Steatorrhea, lipid vacuoles

Fat-soluble vitamin deficiency

Lactase deficiency

Defect in brush-border lactose digestion

Osmotic diarrhea after lactose intake

Histology generally unremarkable

Contrast with microvillus inclusion disease

Abetalipoproteinemia

MTP-related lipid assembly failure

Triglyceride accumulation in enterocytes

Steatorrhea and absent apoB particles

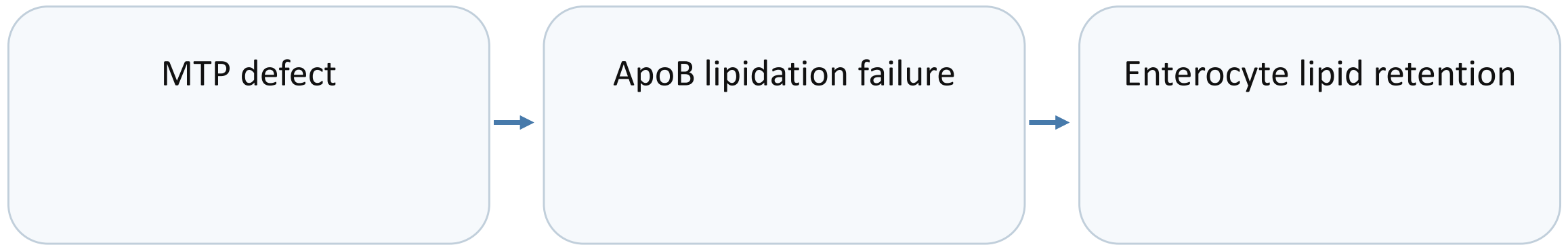
Microvillus inclusion disease

MYO5B-mediated vesicular transport defect

Defective brush-border assembly

Severe early diarrhea; Inclusions detectable
by EM/villin/CD10

Two rare infant enteropathies, two cell defects



Compare with the MYO5B pathway: Vesicle trafficking → abnormal brush border → diarrhea.

Pattern-based comparison across four diseases

Disease	Principal defect	Useful contrast
Abetalipoproteinemia	Lipoprotein assembly	Lipid vacuoles; Absent apoB particles
Cystic fibrosis	Pancreatic intraluminal digestion	Exocrine enzyme deficiency
Lactase deficiency	Brush-border carbohydrate digestion	Lactose-associated osmotic diarrhea
Celiac disease	Immune epithelial injury	Villous atrophy; Immune changes

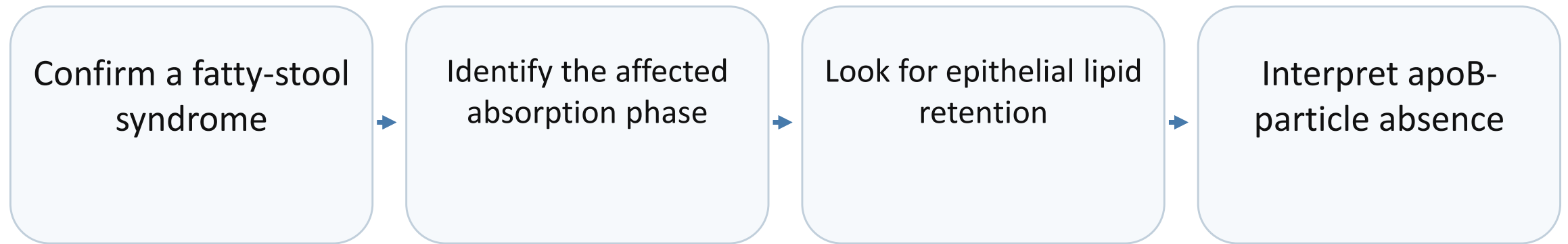
Avoid relying on diarrhea alone

Diarrhea is shared across inherited, inflammatory, enzymatic, and infectious processes.

The stool-fat phenotype improves physiologic localization.

The apoB lipoprotein phenotype provides more specific mechanistic information.

Stepwise localization in an infant with steatorrhea



Educational reasoning sequence—not a validated clinical decision rule.

Morphology is supportive, not self-sufficient

A vacuolated enterocyte should prompt identification of retained material.

Oil red O links the vacuoles to intracellular lipid.

The characteristic biochemical and clinical context is needed before assigning the disease.

Diagnostically useful conjunction of findings

Domain	Feature
Clinical	Infancy; Failure to thrive; Diarrhea; Steatorrhea
Plasma	Absence of apoB-containing lipoproteins
Intestinal tissue	Cytoplasmic epithelial lipid vacuoles
Special stain	Oil red O highlights triglyceride accumulation
Peripheral blood	Acanthocytes

Case exercise: Infant with fatty stools

Clinical / laboratory observation

An infant has impaired weight gain, diarrhea, and bulky greasy stools.

Which physiological category of diarrhea best accounts for the stool description?

Interpretation: Malabsorptive diarrhea: The fatty stools indicate steatorrhea.

Case exercise: Identify the failed molecular event

Clinical / laboratory observation

Intestinal epithelial cells show abundant lipid vacuoles. Plasma lacks apoB-containing lipoproteins.

Which cellular function is most likely defective?

Interpretation: MTP-mediated transfer of lipid to nascent apoB during lipoprotein assembly.

Case exercise: Read an oil red O preparation

Clinical / laboratory observation

Epithelial vacuoles are accentuated after dietary fat and are highlighted by oil red O.

What substance best explains this staining pattern?

Interpretation: Intracellularly retained triglyceride, as.

Case exercise: Interpret the peripheral smear

Clinical / laboratory observation

A child with steatorrhea has erythrocytes with spiky membrane projections.

What is the cell name and its connection to the disorder?

Interpretation: Acanthocytes; Membrane lipid defects accompany abnormal lipid handling.

Case exercise: Avoid a false inference

Clinical / laboratory observation

A report states that plasma has no apoB-containing lipoproteins.

Does this establish that all classes of plasma lipoproteins are absent?

Interpretation: No. The supplied source specifically refers to apoB-containing particles.

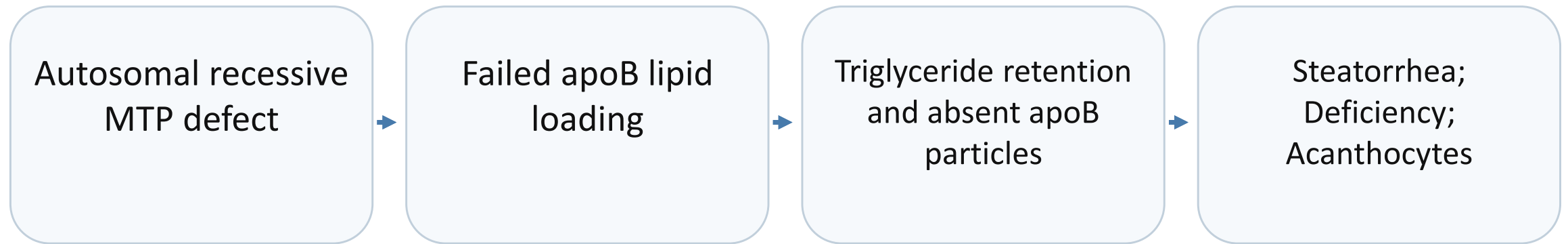
Common teaching pitfalls

Do not equate abnormal enterocyte lipid packaging with failure of brush-border digestion.

Do not interpret lipid vacuolization alone as a genetically specific diagnosis.

Do not claim a gross lesion, diagnostic cutoff, or treatment protocol absent from the source.

Integrated disease mechanism



Conceptual synthesis of the core Robbins account.

Four facts to retain

A rare autosomal recessive disorder prevents triglyceride-rich lipoprotein assembly.

MTP normally transfers lipids to nascent apoB within the ER.

Enterocytes become lipid vacuolated; Oil red O can highlight the retained fat.

ApoB-containing plasma particles are absent, with infantile steatorrhea and acanthocytes.

References and scope

Robbins, Cotran & Kumar: Pathologic Basis of Disease. 11th ed. (2026).

“Abetalipoproteinemia,” in The Gastrointestinal Tract.

Supporting textbook context: “Malabsorption and Diarrhea” and “Normal Cholesterol Metabolism and Transport.”

Conceptual diagrams are original, editable teaching schematics; no textbook figures or clinical specimens have been reproduced.