

Gastrointestinal Pathology

Small Bowel

I. Duodenal Atresia

Definition

- Congenital failure of the duodenum to canalize
-

Association

- Strongly associated with Down syndrome
-

Embryologic Pathogenesis (Flowchart)

During development:

Duodenal lumen temporarily becomes obliterated →

Normally recanalizes later


Failure of recanalization → Complete duodenal

obstruction → Duodenal atresia

Clinical Features

1.  Polyhydramnios

Fetus cannot swallow amniotic fluid properly.

2.  "Double Bubble" Sign

Air accumulates in:

- Stomach
- Proximal duodenum

→ Two air-filled bubbles on imaging 


3. 🤢 Bilioous Vomiting

Obstruction occurs:

- Distal to ampulla of Vater

👉 Therefore bile is present in vomitus.

⚙️ Mechanism of Bilioous Vomiting

Duodenal obstruction below ampulla → Bile enters proximal bowel → Vomiting contains bile 

🎯 Exam Focus

- Double bubble sign = classic clue 

- Biliious vomiting is highly tested
 - Association with Down syndrome
-

II. Meckel Diverticulum

Definition

- True diverticulum containing:
 - Mucosa
 - Submucosa
 - Muscularis propria
-

Embryologic Pathogenesis

Failure of vitelline duct involution → Persistent outpouching of ileum → Meckel diverticulum



"Rule of 2s" ★

Feature	Detail
Frequency	2% of population
Length	2 inches
Distance from ileocecal valve	Within 2 feet
Age of presentation	First 2 years
Common ectopic tissue	Gastric mucosa



Concept Insight

Why does bleeding occur?

Ectopic gastric mucosa secretes acid:


Heterotopic gastric tissue → Acid secretion → Ulceration
of adjacent ileum → Bleeding 🩸


Clinical Presentations

Presentation	Mechanism
Bleeding	Acid-induced ulceration
Obstruction	Mass effect
Volvulus	Twisting around diverticulum
Intussusception	Acts as leading point
Appendicitis mimic	RLQ pain


 Concept Insight

True vs False Diverticulum

Type	Layers Included
True diverticulum	All layers 
False diverticulum	Mucosa/submucosa only

 Meckel diverticulum is a true diverticulum

 Exam Focus


- Most common congenital GI anomaly 
- Ectopic gastric mucosa causes bleeding

III. Volvulus

Definition

- Twisting of bowel around its mesentery
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Pathogenesis (Flowchart)

Bowel twists around mesentery → Luminal obstruction
→ Compression of blood vessels → Ischemia/infarction
→ Necrosis if untreated 

Common Sites

Age Group	Common Site
Elderly	Sigmoid colon

Young adults	Cecum
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Clinical Features

- Severe abdominal pain
 - Distension
 - Obstruction
 - Possible bowel necrosis
-

Concept Insight

Volvulus causes:

1. Mechanical obstruction
2. Vascular compromise

 This makes it a surgical emergency

Exam Focus

- Sigmoid volvulus in elderly = classic association
 - Risk of infarction
-

IV. Intussusception

Definition

- Telescoping of one bowel segment into another
-


Pathogenesis (Flowchart)

Leading point develops → Peristalsis pulls proximal bowel forward → Bowel telescopes into distal segment →

Obstruction + vascular compression →

Ischemia/infarction

 Leading Point

 In Children

Most common cause:

- Lymphoid hyperplasia

Often due to:

- Viral infections (e.g., rotavirus)
-

 Childhood Mechanism

Rotavirus infection → Peyer patch hyperplasia → Leading edge forms → Terminal ileum telescopes into cecum

In Adults

Most common cause:

- Tumor 

Clinical Features

- Colicky abdominal pain
- Obstruction
- Ischemia

(Classically may cause "currant jelly stool")


Concept Insight

Why does ischemia occur?

Mesenteric vessels are compressed during telescoping:

- Reduced blood flow
 - Infarction risk
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Exam Focus

- Children → lymphoid hyperplasia
 - Adults → tumor until proven otherwise 
 - Terminal ileum into cecum is classic
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V. Small Bowel Infarction

Definition

- Ischemic necrosis of small bowel
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! Why is the Small Bowel Vulnerable?

- High metabolic demand
 - Requires constant blood supply
-

Types of Infarction

Type	Cause
Transmural infarction	Arterial/venous occlusion
Mucosal infarction	Severe hypotension

A. Transmural Infarction

Pathogenesis

Superior mesenteric artery embolus/thrombosis OR
Mesenteric vein thrombosis → Complete vascular
obstruction → Full-thickness ischemia → Transmural
infarction

Concept Insight

Superior Mesenteric Artery (SMA)

The SMA supplies:

- Most of small bowel


 Occlusion causes catastrophic ischemia.

B.  Mucosal Infarction

 Pathogenesis

Severe hypotension/shock → Reduced perfusion →
Superficial mucosal ischemia → Mucosal infarction

Clinical Features

Feature	Explanation
Severe abdominal pain	Ischemia
Bloody diarrhea 	Mucosal necrosis
Decreased bowel sounds	Loss of bowel activity

Exam Focus

- SMA occlusion = transmural infarction
- Shock/hypotension = mucosal infarction

- Severe pain with bloody diarrhea is classic
-

Volvulus vs Intussusception

Feature	Volvulus	Intussusception
Mechanism	Twisting	Telescoping
Blood supply compromise	Yes	Yes
Common in elderly?	Sigmoid volvulus	Less common
Childhood association	Rare	Very common

VI. Lactose Intolerance

Definition

- Decreased activity of the lactase enzyme
 - Lactase is located in the brush border of enterocytes
-

Normal Function of Lactase

Lactose → Broken down by lactase → Glucose + galactose → Absorption in small intestine


Pathogenesis of Lactose Intolerance (Flowchart)

↓ Lactase activity → Lactose remains undigested in intestinal lumen → Lactose retains water osmotically → Bacterial fermentation of lactose → Gas production + diarrhea → Abdominal distension and osmotic diarrhea


Concept Insight

Why does bloating occur?

Colonic bacteria ferment undigested lactose:

- Produce hydrogen and gas
 - Cause abdominal distension and flatulence 
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Clinical Features

Feature	Mechanism
Diarrhea 	Osmotic effect of lactose
Abdominal distension	Gas formation
Bloating	Fermentation

Symptoms after milk products 🥛	Lactose ingestion
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Types of Lactase Deficiency

Type	Description
Congenital	Rare autosomal recessive disorder
Acquired	Common; develops later in childhood/adulthood
Temporary	After small bowel infection

Concept Insight

Why is lactase easily damaged?

Lactase is located on:

- Tip of intestinal villi

These cells are highly susceptible to injury ⚠️

👉 Temporary deficiency often follows gastroenteritis.

🎯 Exam Focus

- Osmotic diarrhea after milk intake = classic clue
 - Brush border enzyme deficiency
 - Lactase deficiency is often acquired
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VII. 🌾 Celiac Disease

📌 Definition

- Immune-mediated destruction of small bowel villi triggered by gluten exposure

Genetic Associations

- HLA-DQ2
- HLA-DQ8

Role of Gluten

Gluten Sources

Present in:

- Wheat
- Barley
- Rye

 Most Pathogenic Component

- Gliadin
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Pathogenesis (Flowchart)

Gluten ingestion → Gliadin reaches small intestine →
Tissue transglutaminase (tTG) deamidates gliadin →
Deamidated gliadin presented via MHC II → Activation of
helper T cells → Immune-mediated villous destruction →
Malabsorption

Concept Insight

Why is tTG important?

Tissue transglutaminase:

- Modifies gliadin
- Makes it more immunogenic

👉 Also becomes a target of antibodies.

🔍 Clinical Presentation

👶 Children

Classic features:

Feature	Explanation
Abdominal distension	Malabsorption + gas
Diarrhea 💧	Fat/carbohydrate malabsorption
Failure to thrive	Nutritional deficiency

Adults

- Chronic diarrhea
 - Bloating
 - Weight loss
-

Dermatitis Herpetiformis

Definition

- Pruritic vesicular skin rash associated with celiac disease
-

Pathogenesis

IgA deposition at dermal papillae → Inflammatory reaction → Vesicle formation

Appearance

- Small grouped vesicles
- "Herpes-like" appearance

 Not caused by herpes virus.

Concept Insight

Why does rash improve with gluten-free diet?

Removing gluten:

- Stops immune activation
 - Reduces IgA deposition
-

Laboratory Findings



Important Antibodies

Antibody	Importance
Anti-endomysial IgA	Highly specific
Anti-tTG IgA	Most commonly tested ★
Anti-gliadin antibodies	Supportive

! Important Exception

Celiac disease has increased association with:

- IgA deficiency

👉 In such cases:

- Use IgG-based tests

Duodenal Biopsy Findings

Classic Histology

Finding	Explanation
Villous atrophy	Flattened villi
Crypt hyperplasia	Regenerative response
Intraepithelial lymphocytes	Immune activation

Histologic Progression

Gluten exposure → Immune-mediated epithelial injury →
Villous flattening → ↓ Surface area for absorption →
Malabsorption

 Most Affected Area

- Duodenum

Less involvement:

- Jejunum
- Ileum

 Treatment


Gluten-free diet

Results in:

- Symptom resolution
- Histologic improvement

Complications

Persistent inflammation despite treatment → Refractory disease → Increased risk of:

- Small bowel carcinoma
 - T-cell lymphoma 
-

Concept Insight

Why lymphoma risk increases?

Chronic T-cell stimulation:

- Promotes malignant transformation
-

Lactose Intolerance vs Celiac Disease

Feature	Lactose Intolerance	Celiac Disease
Mechanism	Enzyme deficiency	Immune-mediated
Trigger	Milk products 🥛	Gluten 🌾
Villous atrophy	No	Yes
Antibodies	Absent	Present
Diarrhea type	Osmotic	Malabsorptive
Treatment	Avoid lactose	Gluten-free diet

🎯 Exam Focus

- Lactase is a brush border enzyme
- Undigested lactose causes osmotic diarrhea

- Celiac disease associated with HLA-DQ2/DQ8
 - Anti-tTG antibodies are highly tested
 - Villous atrophy + crypt hyperplasia = classic biopsy finding
 - Dermatitis herpetiformis = IgA deposition
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VIII. 🌴 Tropical Sprue

📌 Definition

- Malabsorption syndrome due to damage of small bowel villi by an unknown infectious organism
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⚙️ Pathogenesis (Flowchart)

Infectious diarrhea → Persistent mucosal injury → Villous damage → Malabsorption → Nutritional deficiencies

Concept Insight

Tropical sprue resembles celiac disease because both cause:

- Villous injury
- Malabsorption
- Chronic diarrhea

 But the underlying mechanism differs.

Tropical Sprue vs Celiac Disease

Feature	Tropical Sprue	Celiac Disease
Cause	Likely infectious	Immune-mediated
Geographic association	Tropical regions 🌴	Worldwide
Trigger	Post-infectious	Gluten
Response to antibiotics	✅ Yes	❌ No
Most affected bowel	Jejunum + ileum	Duodenum

Geographic Association

Common in:

- Caribbean
- Tropical regions

Clinical Features

- Chronic diarrhea
- Malabsorption
- Weight loss
- Nutritional deficiencies

Vitamin Deficiencies

Jejunal/ileal involvement → Impaired absorption →
Vitamin B12 or folate deficiency

Concept Insight

Why B12 deficiency occurs?

Vitamin B12 is absorbed in:

- Terminal ileum

👉 Ileal damage leads to deficiency.

🎯 Exam Focus

- Tropical region + responds to antibiotics = classic clue ★
 - Jejunum/ileum involvement distinguishes it from celiac disease
-

IX. 🦠 Whipple Disease

📌 Definition

- Systemic disease caused by *Tropheryma whipplei*

Characterized by:

- PAS-positive macrophages loaded with organisms
-

Pathogenesis (Flowchart)

T. whipplei infection → Macrophages ingest bacteria →
Incomplete bacterial destruction → PAS-positive
macrophage accumulation → Tissue infiltration and
dysfunction

Classic Site

- Small bowel lamina propria
-

Mechanism of Malabsorption

Macrophage accumulation in lamina propria →
Compression of lacteals → Impaired chylomicron
transport → Fat malabsorption → Steatorrhea 🍌

🧠 Concept Insight

Why are macrophages PAS-positive?

Partially degraded bacterial glycoproteins accumulate
inside lysosomes:

- Stain positive with PAS stain
-

🔍 Clinical Features

Feature	Mechanism
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Steatorrhea 🍌	Fat malabsorption
Weight loss	Malabsorption
Diarrhea	Intestinal involvement
Arthritis 🦴	Synovial involvement

📌 Extraintestinal Involvement

Organ	Manifestation
Joints	Arthritis
Heart valves	Endocardial involvement
CNS	Neurologic symptoms

Lymph nodes	Lymphadenopathy
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Exam Focus

- PAS-positive macrophages = hallmark 
 - Steatorrhea due to lacteal compression
 - Multisystem involvement is important
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X. Abetalipoproteinemia

Definition

- Autosomal recessive deficiency of:
 - Apolipoprotein B-48
 - Apolipoprotein B-100
-

Normal Functions

Apolipoprotein	Function
Apo B-48	Chylomicron formation
Apo B-100	VLDL and LDL formation

Pathogenesis (Flowchart)

Apo B deficiency → Failure of chylomicron formation →
Fat cannot be transported → Fat malabsorption

AND

↓ VLDL + LDL production → Extremely low plasma
lipoproteins

Clinical Features

Feature	Mechanism
Fat malabsorption	Defective chylomicrons
Steatorrhea 🍌	Fat remains unabsorbed
Absent LDL/VLDL	Lack of Apo B-100

Concept Insight

Why is fat absorption impaired?

Dietary lipids require:

- Chylomicron packaging

Without Apo B-48:

- Chylomicrons cannot form

👉 Lipids accumulate inside enterocytes.

🎯 Exam Focus

- Apo B-48 → chylomicrons
 - Apo B-100 → LDL/VLDL
 - Fat malabsorption is key
-

XI. 🤗👹 Carcinoid Tumor


📌 Definition

- Low-grade malignant neuroendocrine tumor
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🔬 Histologic Feature

Tumor cells contain:

- Neurosecretory granules
 - Positive for chromogranin ★
-

 Common Site

- Small bowel (most common)
-

 Gross Appearance

- Submucosal polyp-like nodule
-

 Serotonin Production

Carcinoid tumor → Serotonin secretion → Portal circulation → Liver metabolism by monoamine oxidase (MAO) → Conversion into 5-HIAA → Urinary excretion

 Important Marker

↑ Urinary 5-HIAA

Used for diagnosis.

 Concept Insight

Why is carcinoid syndrome uncommon initially?

Normally:

- Liver metabolizes serotonin before it reaches systemic circulation

👉 Symptoms usually appear only after liver metastasis.

⚠️ Liver Metastasis & Carcinoid Syndrome

⚙️ Pathogenesis (Flowchart)

Liver metastasis develops → Serotonin bypasses liver metabolism → Serotonin enters systemic circulation → Carcinoid syndrome

🤖 Carcinoid Syndrome

📊 Classic Features

Feature	Mechanism
Flushing 🔥	Vasodilation

Diarrhea 💧	Increased GI motility
Bronchospasm 😷	Smooth muscle constriction

⚠️ Triggers

- Alcohol 🍺
- Emotional stress 😞

These stimulate serotonin release.

❤️ Carcinoid Heart Disease

⚙️ Pathogenesis

Excess serotonin → Endocardial fibrosis → Right-sided valvular thickening → Valve dysfunction



Valvular Lesions

Valve	Lesion
Tricuspid valve	Regurgitation
Pulmonary valve	Stenosis



Concept Insight

Why is the left heart spared?

Lungs contain monoamine oxidase:

- Metabolizes serotonin before it reaches left heart



Therefore:

- Right-sided lesions predominate

Whipple Disease vs Celiac Disease

Feature	Whipple Disease	Celiac Disease
Cause	Bacterial infection	Autoimmune
Histology	PAS+ macrophages	Villous atrophy
Extraintestinal findings	Arthritis, CNS	Dermatitis herpetiformis
Treatment	Antibiotics	Gluten-free diet

Exam Focus

- Tropical sprue responds to antibiotics
- Whipple disease = PAS-positive macrophages

- Abetalipoproteinemia = Apo B deficiency
 - Carcinoid tumor secretes serotonin
 - ↑ Urinary 5-HIAA is diagnostic
 - Carcinoid heart disease affects right side only
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Revision Summary

- Duodenal atresia → double bubble sign + bilious vomiting
- Meckel diverticulum → true diverticulum + Rule of 2s
- Volvulus → twisting causing obstruction + infarction
- Intussusception → telescoping bowel
- Intussusception → Children: lymphoid hyperplasia and Adults: tumor
- SMA occlusion → transmural infarction
- Lactose intolerance → osmotic diarrhea after milk

- Lactase located in brush border
- Celiac disease → immune reaction to gliadin
- tTG deamidates gliadin
- Villous atrophy causes malabsorption
- Anti-tTG IgA = important diagnostic test
- Gluten-free diet improves symptoms
- Late complication → T-cell lymphoma
- Tropical sprue resembles celiac disease but is infectious
- Whipple disease → PAS-positive macrophages + steatorrhea
- Abetalipoproteinemia → defective chylomicrons
- Carcinoid tumors are neuroendocrine tumors
- Liver metastasis causes carcinoid syndrome
- Right-sided valvular fibrosis is classic

-> The End <-