MICRO-MECHANISM MCQ BANK

Gastroenterology Chapters 1–7

For the Egyptian Board of Gastroenterology and Hepatology

175 Micro-Trap Questions

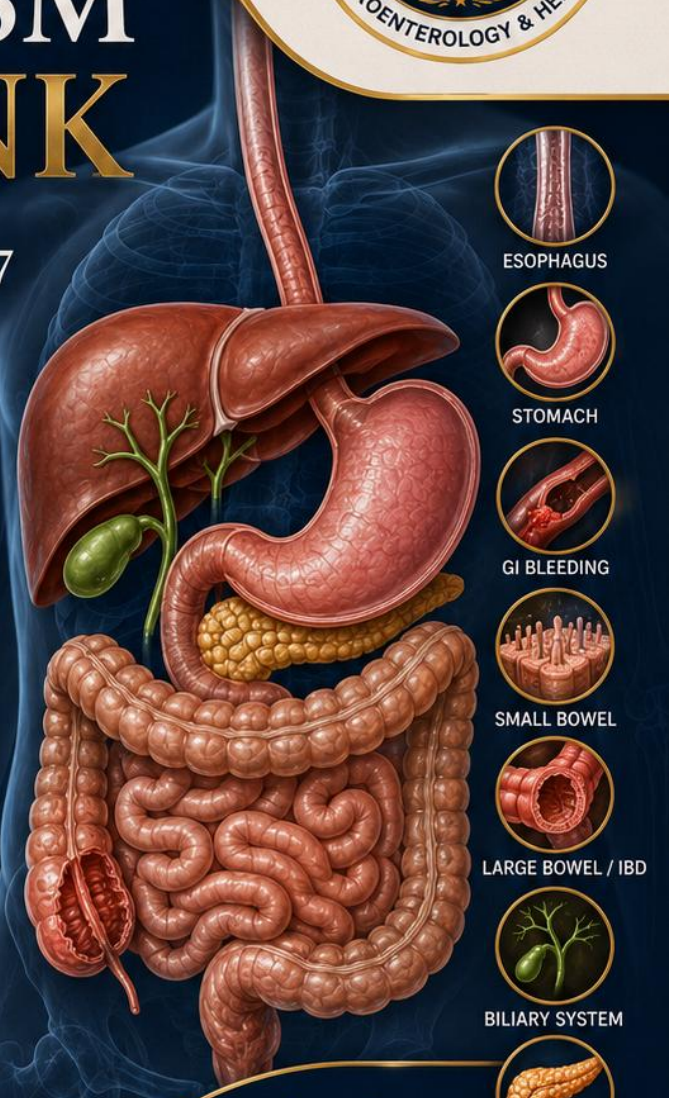
+

100 Integrated Case Scenarios

EXAM-FOCUSED MCQS
Target High-Yield Concepts

INTEGRATED CLINICAL REASONING
Link Mechanisms to Real Cases

HIGH-YIELD REVISION
Recall Faster. Score Higher.



KNOWLEDGE TODAY
EXCELLENCE TOMORROW

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Dedication

In loving memory of my mother,

who recently returned to the mercy of Allah.

Her love, prayers, patience, and sacrifices were among the greatest blessings of my life. Whatever good I achieve carries something of her guidance and support.

May Allah forgive her, have mercy upon her, illuminate her grave, and grant her the highest place in **Jannat al-Firdaws**.

This work is dedicated to her memory.

أسأل الله أن يرحم أمي رحمة واسعه وأن يدخلها الفردوس الأعلى من الجنة، ورجاءً أسألكم لها خالص الدعاء..

Micro-Mechanism MCQ Bank

Gastroenterology Chapters 1-7: 175 Micro-Trap Questions + 100 Integrated Case Scenarios

Purpose: This version deliberately uses close distractors within the same disease **pathway**. The correct answer depends on the precise **receptor**, **intracellular** signal, **immune pathway**, **biomarker** logic, or upstream-to-downstream **micro-mechanism** requested in the final line of the stem.

Source rule: Built as original questions from the uploaded GI/hepatology reference pool only. Questions are not reproduced from existing banks. Correct-answer positions are randomized.

Disease/phenotype keywords	Drug/receptor keywords	Biomarkers/genes	Pathway/mechanism terms

Structure and table of contents

Chapter 1 - Esophagus

Q1. PPI meal timing

A man with LA grade C reflux is told to take omeprazole before breakfast. Symptoms improve when he follows meal timing, but not when he takes it randomly at night.

Which **micro-mechanism** best explains the timing effect?

A. Meal-stimulated recruitment of active canalicular **H+/K+-ATPase** pumps permits irreversible **PPI** binding

B. **Gastrin receptor** blockade peaks only after fasting

C. **Histamine** H2 **receptor** blockade prevents nocturnal acid escape

D. Direct intragastric acid neutralization requires food buffering

E. **GABA-B receptor** activation suppresses transient **LES** relaxations

Answer: A. Meal-stimulated recruitment of active canalicular **H+/K+-ATPase** pumps permits irreversible **PPI** binding

Micro-pearl: PPI efficacy depends on active proton pumps exposed after meal stimulation.

Q2. PCAB pharmacology

A patient with severe nocturnal reflux is switched from a **PPI** to **vonoprazan**-like therapy and develops faster, more sustained acid suppression.

Which pharmacologic distinction is most precise?

A. Muscarinic M3 blockade reducing vagal **acetylcholine** signaling

B. Irreversible sulfhydryl binding after acid-canaliculus activation

C. **GABA-B** agonism reducing transient **LES** relaxations

D. Potassium-competitive inhibition of **H+/K+-ATPase** without obligatory acid activation

E. Competitive H2 **receptor** blockade with parietal-cell **cAMP** suppression

Answer: D. Potassium-competitive inhibition of **H+/K+-ATPase** without obligatory acid activation

Micro-pearl: PCABs inhibit the proton pump by potassium-competitive binding, distinct from acid-activated **PPI**s.

Q3. H2 blocker tachyphylaxis

A woman takes **famotidine** nightly for reflux. It works for 10 days, then loses effect despite adherence.

Which mechanism best explains the escape?

A. Irreversible proton pump inhibition requires de novo pump synthesis

B. **Somatostatin** D-cell activation suppresses antral **gastrin**

C. Loss of **LES** nitrergic neurons causes secondary acid secretion

D. Permanent destruction of **ECL** cells prevents **histamine** release

E. Compensatory **gastrin** and **acetylcholine** acid-secretory signaling bypass **histamine** blockade

Answer: E. Compensatory **gastrin** and **acetylcholine** acid-secretory signaling bypass **histamine** blockade

Micro-pearl: H2 blockers target one acid **pathway**; **gastrin** and **acetylcholine** can maintain secretion.

Q4. Baclofen and TLESR

A patient on adequate **PPI** has persistent regurgitation. Impedance shows weakly acidic reflux temporally related to transient **LES** relaxations.

Which add-on mechanism best targets this phenotype?

A. Irreversible **H+/K+-ATPase** inhibition of active pumps

B. Topical steroid suppression of epithelial **IL-13** signaling

C. **5-HT4** agonism increasing gastric accommodation

D. Alpha-1 blockade of the crural diaphragm

E. **GABA-B** agonism reduces transient lower esophageal sphincter relaxations

Answer: E. GABA-B agonism reduces transient lower esophageal sphincter relaxations

Micro-pearl: Baclofen is a **TLESR**-targeting strategy for regurgitation/non-acid reflux.

Q5. Alginate

Postprandial regurgitation persists despite normal acid suppression. An **alginate** preparation helps more than increasing the **PPI** dose.

What is the relevant mechanism?

A. Restoration of **LES** nitrergic inhibitory neurons

B. Formation of a floating mechanical raft that limits proximal migration of refluxate

C. Direct neutralization of pepsinogen gene transcription

D. Covalent inhibition of newly synthesized proton pumps

E. Reduction of esophageal eosinophil trafficking through **eotaxin** blockade

Answer: B. Formation of a floating mechanical raft that limits proximal migration of refluxate

Micro-pearl: **Alginate**s are barrier therapy, not **receptor** pharmacology.

Q6. Hiatal hernia barrier

An obese man has severe erosive reflux and a large sliding hiatal hernia. HRM shows a weak **EGJ** barrier.

Which mechanism best explains severe reflux?

A. Acid-induced conversion of columnar to squamous mucosa

B. Gastric **somatostatin** excess increases intragastric pressure

C. **IL-13**-mediated basal-zone hyperplasia causes reflux

D. Separation of **LES** and crural diaphragm disrupts the composite anti-reflux barrier

E. Excessive nitrergic inhibition prevents esophageal clearance

Answer: D. Separation of **LES** and crural diaphragm disrupts the composite anti-reflux barrier

Micro-pearl: A sliding hernia weakens the **EGJ** barrier by separating **LES** from crural diaphragm.

Q7. Scleroderma esophagus

A woman with systemic sclerosis has severe reflux, absent smooth-muscle peristalsis, and a hypotensive **LES**.

Which mechanism links her motility disorder to **GERD**?

A. Poor reflux clearance plus weak **LES** from smooth-muscle atrophy and fibrosis

B. Spastic distal contractions from impaired deglutitive inhibition

C. Cricopharyngeal dysfunction causing Killian dehiscence

D. Food antigen-driven eosinophil recruitment causing rings

E. Excess **ECL histamine** release causing isolated acid hypersecretion

Answer: A. Poor reflux clearance plus weak **LES** from smooth-muscle atrophy and fibrosis

Micro-pearl: Scleroderma creates a low-pressure barrier and ineffective clearance.

Q8. Reflux hypersensitivity

A woman has normal endoscopy and normal **acid exposure**, but impedance shows strong **symptom association** with physiologic weakly acidic reflux.

Which mechanism best explains symptoms?

A. Peripheral and central sensitization makes physiologic reflux events painful

B. **Candida** plaque adherence causing chemical nociception

C. Loss of myenteric **NO/VIP** neurons causing **EGJ** obstruction

D. **PPI** failure producing persistent pathological **acid exposure**

E. **EoE**-related **IL-13**/**eotaxin** eosinophil recruitment

Answer: A. Peripheral and central sensitization makes physiologic reflux events painful

Micro-pearl: Normal AET with positive **symptom association** = reflux hypersensitivity.

Q9. Functional heartburn

A patient with burning chest discomfort has normal endoscopy, normal HRM, normal **acid exposure**, and negative **symptom association** on impedance.

Which therapeutic logic is most mechanism-based?

A. **Dupilumab** because type 2 inflammation is dominant

B. POEM because **IRP** is usually elevated

C. Neuromodulation of visceral pain processing rather than escalation of anti-reflux therapy

D. **Baclofen** because **symptom association** is strongly positive

E. Higher-dose **PPI** because **acid exposure** is underestimated

Answer: C. Neuromodulation of visceral pain processing rather than escalation of anti-reflux therapy

Micro-pearl: Functional heartburn is pain processing without reflux-symptom coupling.

Q10. Barrett metaplasia

An obese man with long-standing **GERD** has intestinal metaplasia in documented columnar-lined distal esophagus.

Which **micro-mechanism** best explains **Barrett** development?

A. Chronic acid-bile injury reprograms epithelial progenitor differentiation toward intestinal columnar phenotype

B. **Candida** invasion converts squamous cells into columnar epithelium

C. IgE-mediated food allergy creates metaplastic glands

D. Gastrin excess from antral G cells causes squamous intestinalization

E. Loss of LES nitrergic neurons directly induces goblet cells

Answer: A. Chronic acid-bile injury reprograms epithelial progenitor differentiation toward intestinal columnar phenotype

Micro-pearl: Barrett is metaplastic adaptation to chronic reflux injury.

Q11. Barrett p53/p16

A Barrett surveillance biopsy shows low-grade dysplasia with abnormal p53 immunostaining and p16 loss.

Which interpretation is most accurate?

A. PPI tachyphylaxis causes p53 accumulation

B. Active HSV replication in squamous epithelium produces pseudodysplasia

C. Achalasia-related stasis causes p16 overexpression without cancer risk

D. Tumor-suppressor pathway disruption marks clonal neoplastic progression

E. Eosinophilic degranulation causes reversible atypia only

Answer: D. Tumor-suppressor pathway disruption marks clonal neoplastic progression

Micro-pearl: p53 and p16 abnormalities are progression biomarkers in Barrett neoplasia.

Q12. T1a endoscopic therapy

EMR of a nodular Barrett lesion shows T1a intramucosal adenocarcinoma with clear margins and no lymphovascular invasion.

Why can endoscopic eradication be rational?

A. Mucosal cancers cannot recur after EMR alone

B. Chemotherapy is more effective before tissue diagnosis

C. RFA corrects the reflux mechanism causing cancer

D. All Barrett cancers lack lymphatics regardless of depth

E. Intramucosal confinement has low lymph-node metastatic potential compared with submucosal invasion

Answer: E. Intramucosal confinement has low lymph-node metastatic potential compared with submucosal invasion

Micro-pearl: Depth of invasion predicts nodal risk; T1a selected lesions may be endoscopically treated.

Q13. EoE IL-13/eotaxin

An atopic man has food impaction, rings, furrows, and dense eosinophilia in proximal and distal esophagus.

Which immune micro-pathway is most central?

A. CD8-mediated ganglionitis destroys inhibitory neurons

B. Th1 caseating granulomas destroy the muscularis propria

C. IL-13-driven epithelial eotaxin signaling recruits eosinophils and promotes remodeling

D. Cryoglobulin immune complexes activate classical complement

E. IgG4 plasma cells cause storiform fibrosis of the LES

Answer: C. IL-13-driven epithelial eotaxin signaling recruits eosinophils and promotes remodeling

Micro-pearl: EoE is a type 2, IL-13/eotaxin/eosinophil disease.

Q14. Dupilumab EoE

Severe fibrostenotic EoE with atopic dermatitis persists despite diet, PPI, and swallowed steroid. Dupilumab is started.

Which pathway is targeted?

A. Alpha-4 beta-7 blockade prevents gut lymphocyte homing

B. CCR9 blockade prevents ileal T-cell trafficking

C. TNF-alpha neutralization reduces granulomatous inflammation

D. IL-4 receptor alpha blockade interrupts IL-4 and IL-13 signaling

E. JAK1/3 inhibition blocks common gamma-chain cytokines

Answer: D. IL-4 receptor alpha blockade interrupts IL-4 and IL-13 signaling

Micro-pearl: Dupilumab blocks IL-4R-alpha, reducing type 2 signaling.

Q15. Topical steroid EoE

A patient with EoE is prescribed swallowed budesonide slurry rather than an inhaled pulmonary technique.

Which mechanism is intended?

A. Direct topical glucocorticoid suppression of local esophageal eosinophilic inflammation

B. Neutralization of luminal acid and pepsin

C. Viral DNA polymerase inhibition in epithelial cells

D. Systemic adrenal suppression is required for efficacy

E. Mechanical dilation of fixed fibrotic rings

Answer: A. Direct topical glucocorticoid suppression of local esophageal eosinophilic inflammation

Micro-pearl: Swallowed topical steroids are local anti-inflammatory therapy.

Q16. PPI response in EoE

A man with esophageal eosinophilia improves histologically on high-dose **PPI** despite modest reflux burden.

Which interpretation is best?

A. **PPI** response means eosinophils were **Candida**-related

B. **PPI** response requires complete absence of food antigen signaling

C. **PPI** response confirms **achalasia** pseudo-reflux

D. **PPI** response can reflect anti-inflammatory effects within the **EoE** spectrum, not exclusion of **EoE**

E. **PPI** response proves reflux-only eosinophilia

Answer: D. **PPI** response can reflect anti-inflammatory effects within the **EoE** spectrum, not exclusion of **EoE**

Micro-pearl: **PPI**-responsive eosinophilia is not a separate non-**EoE** diagnosis.

Q17. FLIP in EoE

Symptoms improve in **EoE**, but EndoFLIP shows persistently reduced esophageal **distensibility**.

What does this imply?

A. **IRP** is elevated by definition

B. Fibrostenotic remodeling persists and may maintain food-impaction risk

C. Eosinophils are absent from the mucosa

D. **Candida** plaques are the main obstruction

E. **Acid exposure** is necessarily abnormal

Answer: B. Fibrostenotic remodeling persists and may maintain food-impaction risk

Micro-pearl: Reduced **distensibility** is a remodeling/fibrosis signal.

Q18. Achalasia NO/VIP

A woman has dysphagia to solids and liquids, elevated **IRP**, and absent peristalsis.

Which mechanism is central?

A. **Gastrin** hypersecretion contracts the **LES** through **CCK-B receptors**

B. **IL-13** causes eosinophilic rings at the **EGJ**

C. Loss of inhibitory **NO/VIP** myenteric neurons causes impaired **LES** relaxation and aperistalsis

D. H2-mediated **cAMP** secretion causes esophageal spasm

E. Acid-bile injury creates metaplastic obstruction

Answer: C. Loss of inhibitory **NO/VIP** myenteric neurons causes impaired **LES** relaxation and aperistalsis

Micro-pearl: **Achalasia** is inhibitory neuron failure.

Q19. Type II achalasia

HRM shows elevated **IRP**, absent peristalsis, and panesophageal pressurization after swallows.

What is the best physiologic interpretation?

A. Normal motility with reflux hypersensitivity

B. Absent contractility with hypotensive **LES**

C. Excess contractile vigor with preserved latency

D. Premature distal contractions with normal **EGJ** relaxation

E. Bolus pressurization occurs in a nonperistaltic esophagus against an obstructed **EGJ**

Answer: E. Bolus pressurization occurs in a nonperistaltic esophagus against an obstructed **EGJ**

Micro-pearl: Type II **achalasia** has panesophageal pressurization.

Q20. Type III POEM

A patient has elevated **IRP** and premature spastic distal contractions. POEM is favored over pneumatic dilation.

Why?

A. It blocks **IL-13 receptor** signaling

B. It seals the crural diaphragm anatomically

C. It restores nitrergic neurons directly

D. It avoids all post-procedure reflux

E. POEM permits extended tailored myotomy across both **LES** and spastic distal esophageal body

Answer: E. POEM permits extended tailored myotomy across both **LES** and spastic distal esophageal body

Micro-pearl: Type III needs a longer myotomy targeting spasm plus **EGJ** obstruction.

Q21. Botulinum toxin

A frail elderly patient with **achalasia** receives **LES botulinum** toxin injection as palliation.

Which **micro-mechanism** lowers **LES** pressure?

A. SNARE-mediated inhibition of **acetylcholine** release from excitatory neurons

B. Regeneration of inhibitory NO neurons

C. Covalent **H+/K+-ATPase** inhibition

D. Epithelial **eotaxin** suppression

E. **GABA-B** mediated reduction in **TLESR**

Answer: A. SNARE-mediated inhibition of **acetylcholine** release from excitatory neurons

Micro-pearl: **Botulinum** toxin reduces excitatory cholinergic tone transiently.

Q22. Pseudoachalasia

A 75-year-old man has rapidly progressive dysphagia, major weight loss, and manometry resembling **achalasia**.

Which mechanism must be excluded?

A. Food antigen-mediated eosinophilia only

B. Malignant infiltration or mechanical obstruction at the GEJ causing secondary outflow obstruction

C. Physiologic reflux hypersensitivity

D. Congenital absence of myenteric neurons

E. H2 blocker tachyphylaxis

Answer: B. Malignant infiltration or mechanical obstruction at the GEJ causing secondary outflow obstruction

Micro-pearl: Older age, rapid course, weight loss = **pseudoachalasia** until excluded.

Q23. DES physiology

A woman has intermittent chest pain and dysphagia. HRM shows normal **IRP** with premature contractions and short distal latency.

Which mechanism is most precise?

A. Impaired deglutitive inhibition causes premature smooth-muscle contraction with preserved **EGJ** relaxation

B. Columnar metaplasia of squamous mucosa

C. Hypotensive **LES** from smooth-muscle fibrosis

D. Excess contractile vigor with normal latency only

E. Complete loss of **LES** relaxation and aperistalsis

Answer: A. Impaired deglutitive inhibition causes premature smooth-muscle contraction with preserved **EGJ** relaxation

Micro-pearl: **DES** is premature contraction due to disordered inhibition, not **EGJ** obstruction.

Q24. Jackhammer

A man has chest pain. HRM shows very high **DCI** contractions with normal **IRP** and normal distal latency.

Which mechanism-based label **fit**s?

A. Functional chest pain because HRM is normal

B. Hypercontractile esophagus from excessive contractile vigor without premature timing

C. Type III **achalasia** due to impaired **EGJ** relaxation

D. Scleroderma due to absent contractility

E. **DES** due to shortened distal latency

Answer: B. Hypercontractile esophagus from excessive contractile vigor without premature timing

Micro-pearl: **Jackhammer** = high **DCI**, normal latency, normal **EGJ** relaxation.

Q25. Viral esophagitis biopsy

Two transplant patients have odynophagia. One has small punched-out ulcers; another has large linear distal ulcers.

Which sampling principle reflects viral tropism?

A. Peripheral blood PCR replaces tissue in all cases

B. **Candida** brushing diagnoses both viral ulcers

C. Both are diagnosed best from normal mucosa

D. **HSV** is sampled at ulcer edge; **CMV** is sampled from ulcer base

E. **HSV** is sampled from the base; **CMV** from the edge

Answer: D. **HSV** is sampled at ulcer edge; **CMV** is sampled from ulcer base

Micro-pearl: **HSV** infects squamous epithelial edges; **CMV** inclusions are often in stromal/endothelial cells at the base.

Chapter 2 - Stomach

Q26. H pylori urease

A patient with active chronic gastritis has organisms in the mucus layer despite very low gastric luminal pH.

Which mechanism permits local survival?

A. Somatostatin release raises intragastric pH

B. Bacterial catalase converts acid to chloride

C. CagA directly inhibits parietal-cell proton pumps

D. Urease generates ammonia to buffer the immediate peribacterial microenvironment

E. VacA neutralizes acid by binding hydrogen ions

Answer: D. Urease generates ammonia to buffer the immediate peribacterial microenvironment

Micro-pearl: Urease is a local buffering survival factor.

Q27. CagA signaling

A man with H. pylori gastritis develops intestinal metaplasia. The strain expresses CagA.

Which micro-mechanism is most linked to carcinogenic signaling?

A. VacA activates CCK-B receptors on ECL cells

B. Flagellin irreversibly inhibits H+/K+-ATPase

C. Injected CagA perturbs SHP-2 and epithelial polarity/proliferation pathways

D. Urease directly methylates MLH1 promoter

E. LPS causes MEN1 mutation in chief cells

Answer: C. Injected CagA perturbs SHP-2 and epithelial polarity/proliferation pathways

Micro-pearl: CagA alters intracellular signaling and epithelial phenotype.

Q28. VacA

A virulent H. pylori strain produces epithelial vacuolation and immune modulation.

Which mechanism best fits VacA?

A. Activation of EGFR by TGF-alpha mimicry

B. Formation of intracellular vacuoles with mitochondrial and T-cell functional effects

C. IgA immune-complex deposition in capillaries

D. Direct phosphorylation of beta-catenin by SHP-2

E. Irreversible COX-1 inhibition in epithelial cells

Answer: B. Formation of intracellular vacuoles with mitochondrial and T-cell functional effects

Micro-pearl: VacA is a vacuolating cytotoxin with epithelial and immune effects.

Q29. Duodenal ulcer physiology

A young man has antral-predominant H. pylori and recurrent duodenal ulcer.

Which mechanism best links infection to acid load?

A. CagA blocks bile acid micelles in duodenum

B. VacA causes isolated LES relaxation

C. Urease destroys pancreatic bicarbonate secretion

D. Corpus atrophy produces complete achlorhydria

E. Reduced antral somatostatin increases gastrin-driven parietal-cell acid output

Answer: E. Reduced antral somatostatin increases gastrin-driven parietal-cell acid output

Micro-pearl: Antral H. pylori -> low somatostatin -> high gastrin -> high acid.

Q30. Cancer pathway

A patient has corpus-predominant H. pylori gastritis, atrophy, intestinal metaplasia, and dysplasia.

Which mechanism best explains cancer risk?

A. Acute urease buffering directly transforms cells

B. Type I hypersensitivity produces signet-ring cells

C. Chronic inflammation drives atrophy-metaplasia-dysplasia with genomic injury

D. Transient gastrin elevation creates immediate invasive cancer

E. NSAID COX inhibition creates MALT lymphoma only

Answer: C. Chronic inflammation drives atrophy-metaplasia-dysplasia with genomic injury

Micro-pearl: Gastric adenocarcinoma risk follows chronic inflammatory progression.

Q31. NSAID mucosal injury

A patient on naproxen develops a gastric ulcer without **H. pylori**. The examiner focuses on mucosal defense rather than acid.

Which mechanism is most precise?

A. **Gastrin receptor** activation increases acid and pepsin only

B. **JAK** inhibition suppresses epithelial renewal

C. **IL-13** recruits eosinophils into the antrum

D. **Urease** ammonia causes direct ulceration

E. **COX-1 prostaglandin** depletion reduces mucus, bicarbonate, epithelial restitution, and mucosal blood flow

Answer: E. COX-1 prostaglandin depletion reduces mucus, bicarbonate, epithelial restitution, and mucosal blood flow

Micro-pearl: NSAIDs injure by **prostaglandin** loss plus topical injury.

Q32. Misoprostol

A high-risk NSAID user cannot stop anti-inflammatory therapy. **Misoprostol** is considered but limited by diarrhea.

Which **receptor**-level effect is intended?

A. FXR activation reduces **bile acid** reflux

B. EP **receptor** activation reduces acid **cAMP** signaling and augments mucosal defense

C. M3 blockade increases bicarbonate secretion

D. **CCK-B** blockade suppresses **ECL histamine** release

E. H2 **receptor** agonism improves nocturnal mucosal blood flow

Answer: B. EP **receptor** activation reduces acid **cAMP** signaling and augments mucosal defense

Micro-pearl: **Misoprostol** replaces **prostaglandin** signaling.

Q33. PPI clot stabilization

A bleeding gastric ulcer receives high-dose **PPI** after endoscopic hemostasis.

Which mechanism supports this strategy?

A. **PPI** inhibits thrombin generation

B. Raising intragastric pH improves platelet aggregation and clot stability over the visible vessel

C. **PPI** reduces portal venous pressure

D. **PPI** reverses aspirin platelet inhibition

E. **PPI** directly cross-links fibrin

Answer: B. Raising intragastric pH improves platelet aggregation and clot stability over the visible vessel

Micro-pearl: Acid impairs clot; **PPI** stabilizes hemostasis by pH elevation.

Q34. Gastrinoma diarrhea

A man with refractory ulcers has fasting **gastrin** 2500 pg/mL and gastric pH 1.2 with watery diarrhea.

Which mechanism explains diarrhea?

A. **Gastrin** inhibits motilin **receptor**s

B. **Gastrin** blocks villous **tTG** activity

C. Massive acid load inactivates pancreatic enzymes and injures small-bowel mucosa

D. **Gastrin** opens **CFTR** channels in colonocytes

E. **Gastrin** suppresses **bile acid** synthesis through FXR

Answer: C. Massive acid load inactivates pancreatic enzymes and injures small-bowel mucosa

Micro-pearl: ZES diarrhea is acid-mediated maldigestion and mucosal injury.

Q35. Secretin paradox

A suspected **gastrin**oma patient undergoes secretin stimulation testing.

Which response is pathophysiologically paradoxical?

A. Normal G cells increase **gastrin** after secretin

B. Secretin directly acidifies the stomach

C. Secretin diagnoses **H. pylori** through **urease** activation

D. **Gastrin**oma cells increase **gastrin** secretion after secretin exposure

E. All acid-suppressed patients suppress **gastrin** after secretin

Answer: D. Gastrinoma cells increase **gastrin** secretion after secretin exposure

Micro-pearl: Secretin paradoxically stimulates **gastrin**oma **gastrin** secretion.

Q36. Autoimmune gastritis

A woman has macrocytosis, low B12, high **gastrin**, and corpus-predominant atrophic gastritis.

Which mechanism explains hyper**gastrin**emia?

A. **H. pylori urease** directly secretes **gastrin**

B. Parietal-cell loss causes achlorhydria, removing acid-mediated negative feedback on antral G cells

C. Chief-cell apoptosis increases CCK release

D. Intrinsic factor antibody stimulates **CCK-B receptor**s

E. Antral D-cell excess suppresses **gastrin**

Answer: B. Parietal-cell loss causes achlorhydria, removing acid-mediated negative feedback on antral G cells

Micro-pearl: Achlorhydria removes feedback inhibition and raises **gastrin**.

Q37. Type I gastric NET

A patient with auto**immune** gastritis develops multiple small gastric body neuroendocrine tumors.

Which mechanism drives this tumor pattern?

A. **H. pylori CagA** directly transforms beta cells

B. Ghrelin **receptor** activation prod**uc**es body polyps

C. **Somatostatin** excess stimulates **ECL** proliferation

D. Chronic hyper**gastrin**emia stimulates **ECL**-cell hyperplasia and neoplasia

E. **MEN1** mutation in every **ECL** cell is required

Answer: D. Chronic hyper**gastrin**emia stimulates **ECL**-cell hyperplasia and neoplasia

Micro-pearl: Type I gastric **NET**s are hyper**gastrin**emia/**ECL** driven.

Q38. Menetrier

A man has giant gastric folds, protein-losing gastropathy, hypochlorhydria, and foveolar hyperplasia.

Which **pathway** is implicated?

A. **Gastrin CCK-B** activation expands parietal cells

B. **CagA** ind**uc**es duodenal acid overload

C. KIT mutation drives spindle-cell proliferation

D. **TGF-alpha** mediated **EGFR** activation promotes m**uc**ous cell proliferation

E. **IgA tTG** deposition injures gastric folds

Answer: D. **TGF-alpha** mediated **EGFR** activation promotes m**uc**ous cell proliferation

Micro-pearl: **Menetrier** disease is **EGFR**/**TGF-alpha** linked foveolar hyperplasia.

Q39. GAVE vs PHG

A cirrhotic patient has chronic anemia. Endoscopy shows antral watermelon stripes rather than mosaic fundic m**uc**osa.

Which mechanism best separates **GAVE** from portal hypertensive gastropathy?

A. Both are caused by acid-mediated clot lysis

B. **GAVE** is caused only by high portal pressure and resolves with beta blockers

C. Both require **H. pylori** eradication as definitive therapy

D. **PHG** is isolated antral fibrin thrombi from auto**immune** gastritis

E. **GAVE** is an antral vascular ectasia pattern not primarily corrected by portal-pressure red**uc**tion

Answer: E. **GAVE** is an antral vascular ectasia pattern not primarily corrected by portal-pressure red**uc**tion

Micro-pearl: **GAVE** and **PHG** are mechanistically and endoscopically distinct.

Q40. Gastroparesis D2

A diabetic patient with delayed gastric emptying improves with **metoclopramide** but develops akathisia.

Which mechanism explains both bene**fit** and risk?

A. D2 antagonism enhances cholinergic upper-GI motility but also affects central dopamine **pathway**s

B. **GABA-B** agonism enhances gastric emptying

C. **EGFR** blockade red**uc**es antral folds

D. Motilin **receptor** antagonism accelerates phase III activity

E. H2 **receptor** blockade improves pyloric relaxation

Answer: A. D2 antagonism enhances cholinergic upper-GI motility but also affects central dopamine **pathway**s

Micro-pearl: **Metoclopramide** is a D2 antagonist with CNS dopamine adverse effects.

Q41. Erythromycin
A hospitalized patient with severe gastroparesis improves transiently after **erythromycin**, then loses response.

Which **receptor** explains the initial response?

A. **CCK-B** blockade reducing **gastrin**

B. Motilin **receptor** agonism triggering migrating motor complex-like contractions

C. D2 blockade increasing **acetylcholine** release

D. 5-HT1A agonism improving fundic accommodation

E. NK1 antagonism reducing nausea **pathways**

Answer: B. Motilin **receptor** agonism triggering migrating motor complex-like contractions

Micro-pearl: **Erythromycin** is a motilin agonist; tachyphylaxis limits use.

Q42. Buspirone FD
A woman has postprandial distress syndrome with early satiety and normal endoscopy. **Buspirone** is discussed.

Which mechanism is targeted?

A. D2 blockade causing pyloric contraction

B. 5-HT1A-mediated improvement in fundic accommodation

C. **H+/K+-ATPase** irreversible inhibition

D. **TNF-alpha** neutralization of gastric mucosa

E. Motilin **receptor** activation of antral phase III

Answer: B. 5-HT1A-mediated improvement in fundic accommodation

Micro-pearl: **Buspirone** can improve impaired accommodation.

Q43. MALT lymphoma
Low-grade gastric **MALT** lymphoma is localized and **H. pylori** positive. Eradication is chosen first.

Which mechanism explains potential remission?

A. Direct antibiotic inhibition of BCL2 transcription

B. Removal of chronic antigen-driven B-cell stimulation

C. **Gastrin** reduction **destroys** lymphoma clones universally

D. **Urease** suppression reverses KIT mutation

E. **PPI**-induced apoptosis of monoclonal B cells

Answer: B. Removal of chronic antigen-driven B-cell stimulation

Micro-pearl: Some gastric **MALT** lymphomas are antigen-dependent.

Q44. Diffuse gastric cancer
A young patient with family history of diffuse gastric cancer has signet-ring carcinoma and CDH1 mutation.

Which mechanism is most relevant?

A. **CagA urease** buffers acid directly

B. **APC** loss activates chromosomal instability in adenoma

C. **BRAF** mutation creates serrated gastric polyps

D. **Gastrin** stimulates **ECL** cells only

E. Loss of E-cadherin-mediated cell adhesion promotes diffuse infiltrative growth

Answer: E. Loss of E-cadherin-mediated cell adhesion promotes diffuse infiltrative growth

Micro-pearl: CDH1/E-cadherin loss drives diffuse gastric cancer biology.

Q45. GIST
A gastric subepithelial tumor stains positive for KIT and responds to **imatinib**.

Which mechanism explains therapy?

A. **CCK-B receptor** blockade

B. **EGFR** blockade of **TGF-alpha** signaling

C. H2 **receptor** inverse agonism

D. VEGF neutralization only

E. Tyrosine kinase inhibition of constitutively activated KIT/PDGFRA signaling

Answer: E. Tyrosine kinase inhibition of constitutively activated KIT/PDGFRA signaling

Micro-pearl: **GIST** is kinase-driven; **imatinib** targets KIT/PDGFRA.

Q46. Chromogranin A

A patient on high-dose **PPI** has elevated chromogranin A during **NET** workup.

Which mechanism explains a false signal?

A. **PPI** directly secretes chromogranin from parietal cells

B. Acid suppression induces hypergastrinemia with **ECL**-cell stimulation and **biomarker** elevation

C. **PPI** increases serotonin synthesis by enterochromaffin cells

D. **PPI** blocks **somatostatin receptor**s on **NET** cells

E. **PPI** causes **MEN1** mutation in endocrine cells

Answer: B. Acid suppression induces hypergastrinemia with **ECL**-cell stimulation and **biomarker** elevation

Micro-pearl: **PPI**-induced hypergastrinemia can elevate chromogranin A.

Q47. Stress ulcer

An ICU patient on mechanical ventilation develops gastric bleeding without **H. pylori** or NSAIDs.

Which mechanism is most important?

A. Type 2 eosinophilic **immune** activation

B. MEOS induction with acetaldehyde adducts

C. **APC**-**beta-catenin pathway** activation

D. **CagA**-induced **intracellular** proliferation

E. Mucosal ischemia and impaired defense during critical illness permit acid-peptic injury

Answer: E. Mucosal ischemia and impaired defense during critical illness permit acid-peptic injury

Micro-pearl: Stress ulcers reflect hypoperfusion plus acid-peptic injury.

Q48. Pernicious anemia cancer risk

A patient with autoimmune metaplastic atrophic gastritis asks why endoscopic surveillance may be considered.

Which mechanism creates risk?

A. Intrinsic factor antibodies cause immediate **GIST**

B. H2 **receptor** activation drives squamous cancer

C. **Urease** negativity eliminates cancer risk

D. B12 deficiency directly methylates **KRAS** in antrum

E. Chronic achlorhydria, atrophy, metaplasia, and hypergastrinemia promote adenocarcinoma and type I **NET** risk

Answer: E. Chronic achlorhydria, atrophy, metaplasia, and hypergastrinemia promote adenocarcinoma and type I **NET** risk

Micro-pearl: Autoimmune gastritis carries both intestinal-type cancer and **ECL** **NET** risk.

Q49. Dyspepsia PPI logic

A dyspeptic patient without alarm features has epigastric burning and partial response to **PPI**, but normal endoscopy.

Which mechanism supports acid suppression in this phenotype?

A. **Alpha-4 beta-7** blockade

B. **TNF-alpha** neutralization

C. Motilin **receptor desensitization**

D. Correction of impaired accommodation as the dominant mechanism

E. Reduction of acid-mediated chemosensory stimulation in epigastric pain syndrome

Answer: E. Reduction of acid-mediated chemosensory stimulation in epigastric pain syndrome

Micro-pearl: EPS-type functional dyspepsia may respond to acid suppression.

Q50. Reactive gastropathy

A patient after bile reflux surgery has foveolar hyperplasia, edema, and minimal inflammation.

Which mechanism best explains injury?

A. **Th17** granulomatous inflammation

B. **IgG4** storiform fibrosis

C. Chemical mucosal injury from bile/NSAID-like epithelial damage rather than primary **immune** gastritis

D. **CagA**-driven lymphoid lymphoma

E. HLA-DQ2 gliadin presentation

Answer: C. Chemical mucosal injury from bile/NSAID-like epithelial damage rather than primary **immune** gastritis

Micro-pearl: Reactive gastropathy is chemical injury with little inflammation.

Chapter 3 - Gastrointestinal Bleeding: Upper, Lower and Small Bowel

Q51. Acid and clot

A bleeding duodenal ulcer is clipped successfully, then high-dose **PPI** is started.

Which **micro-mechanism** reduces rebleeding?

A. Higher gastric pH improves platelet aggregation and clot stability at the treated vessel

B. **PPI** reverses aspirin **COX-1** inhibition

C. **PPI** directly constricts the gastroduodenal artery

D. **PPI** activates thrombin through vitamin K

E. **PPI** lowers portal pressure by beta-2 blockade

Answer: A. Higher gastric pH improves platelet aggregation and clot stability at the treated vessel

Micro-pearl: Post-hemostasis **PPI** stabilizes clot by increasing pH.

Q52. Forrest IIa

Endoscopy shows a nonbleeding visible vessel in an ulcer base.

Why is endoscopic therapy indicated?

A. A superficial artery remains exposed with high risk of recurrent arterial hemorrhage

B. Portal hypertensive oozing is the dominant mechanism

C. Adherent clot always has no underlying vessel

D. Flat pigmented spot is equivalent to spurting hemorrhage

E. Clean fibrin base indicates no arterial exposure

Answer: A. A superficial artery remains exposed with high risk of recurrent arterial hemorrhage

Micro-pearl: Visible vessel = exposed artery = high rebleeding risk.

Q53. Epinephrine adjunct

Epinephrine injection stops ulcer bleeding temporarily, but the endoscopist adds clips.

Why is injection alone insufficient?

A. Vasoconstriction and tamponade are transient without durable vessel coaptation or thermal sealing

B. Thermal therapy is needed only for varices

C. Clips only reduce acid secretion

D. Injection causes permanent fibrosis immediately

E. Epinephrine has no effect on local vessels

Answer: A. Vasoconstriction and tamponade are transient without durable vessel coaptation or thermal sealing

Micro-pearl: Epinephrine is adjunctive, not definitive monotherapy.

Q54. Hemostatic powder

Diffuse malignant gastric oozing is treated with hemostatic powder as a bridge.

Which mechanism explains its use?

A. Topical barrier formation and concentration of clotting factors over broad oozing surfaces

B. Portal-pressure reduction via splanchnic vasodilation

C. Selective arterial embolization from the lumen

D. **H. pylori** eradication at the bleeding surface

E. Irreversible inhibition of tumor angiogenesis

Answer: A. Topical barrier formation and concentration of clotting factors over broad oozing surfaces

Micro-pearl: Powder is temporary surface hemostasis for diffuse bleeding.

Q55. Dieulafoy lesion

A patient has massive hematemesis from a tiny normal-appearing gastric mucosal defect with a spurting vessel.

Which mechanism best explains severity?

A. **Immune**-complex vasculitis of venules

B. Large-caliber submucosal artery erodes through a minute mucosal defect

C. Bile reflux causing foveolar hyperplasia

D. Acid-induced wide ulcer crater

E. Diffuse capillary ectasia from portal hypertension

Answer: B. Large-caliber submucosal artery erodes through a minute mucosal defect

Micro-pearl: **Dieulafoy** = big artery, tiny defect.

Q56. Angiodysplasia

An elderly patient with CKD has recurrent painless right-colon bleeding from flat vascular lesions.

Which mechanism is most plausible?

A. Gastrin excess opens colonic vessels

B. Intermittent low-grade venous obstruction and mucosal hypoxia promote ectatic fragile vessels

C. IgA deposition injures arterioles

D. Bile acids deconjugate bilirubin in the colon

E. APC loss causes vascular dysplasia

Answer: B. Intermittent low-grade venous obstruction and mucosal hypoxia promote ectatic fragile vessels

Micro-pearl: Angiodysplasia is acquired ectatic vascular malformation.

Q57. Heyde syndrome

A patient with severe aortic stenosis and recurrent angiodysplasia bleeding has low high-molecular-weight vWF multimers.

Which mechanism explains bleeding?

A. COX-2 excess creates thrombocytosis

B. Shear-induced vWF multimer loss impairs platelet adhesion at fragile angiodysplastic vessels

C. IgG4 infiltrates vascular walls

D. Portal pressure increases colonic venous pressure

E. Bile acid diarrhea causes mucosal erosion

Answer: B. Shear-induced vWF multimer loss impairs platelet adhesion at fragile angiodysplastic vessels

Micro-pearl: Aortic stenosis can cause acquired vWF defect.

Q58. Octreotide in varices

A cirrhotic patient with hematemesis receives octreotide before endoscopy.

Which hemodynamic mechanism is intended?

A. Beta-2 agonism constricts mesenteric arterioles

B. H2 blockade reduces variceal pressure

C. Reduced splanchnic vasodilatory peptide signaling lowers portal venous inflow

D. Alpha-1 blockade reduces intrahepatic resistance

E. Thrombin activation seals varices

Answer: C. Reduced splanchnic vasodilatory peptide signaling lowers portal venous inflow

Micro-pearl: Octreotide reduces portal inflow by splanchnic vasoconstrictive effects.

Q59. Terlipressin

A cirrhotic patient with variceal bleeding and renal dysfunction receives terlipressin.

Which receptor-level effect is most relevant?

A. FXR activation increases bile acid secretion

B. Beta-1 blockade reduces cardiac output only

C. V1-mediated splanchnic vasoconstriction reduces portal inflow and improves effective arterial volume

D. Somatostatin receptor blockade increases mesenteric flow

E. V2-mediated free-water excretion lowers portal pressure

Answer: C. V1-mediated splanchnic vasoconstriction reduces portal inflow and improves effective arterial volume

Micro-pearl: Terlipressin is V1-predominant vasoconstrictive therapy.

Q60. Carvedilol

A patient with large esophageal varices starts carvedilol.

Which combined mechanism explains stronger portal pressure effect than propranolol?

A. FXR blockade improves sinusoidal nitric oxide

B. Selective beta-1 blockade increases splanchnic vasoconstriction

C. Beta-1/beta-2 blockade reduces flow and alpha-1 blockade reduces intrahepatic resistance

D. V1 antagonism reduces portal pressure

E. H2 blockade reduces gastric acid and variceal erosion

Answer: C. Beta-1/beta-2 blockade reduces flow and alpha-1 blockade reduces intrahepatic resistance

Micro-pearl: Carvedilol affects inflow and resistance.

Q61. Band ligation

Variceal banding is performed after active bleeding stops.

Which local mechanism prevents recurrent **variceal** bleeding?

A. Hemospray induces portal decompression

B. **Somatostatin receptor** activation scars the varix

C. Acid suppression collapses portal collaterals

D. Epinephrine permanently destroys varices

E. Mechanical strangulation produces thrombosis, necrosis, and fibrosis of the **variceal** channel

Answer: E. Mechanical strangulation produces thrombosis, necrosis, and fibrosis of the **variceal** channel

Micro-pearl: EVL eradicates varices by ligation-induced thrombosis/fibrosis.

Q62. PHG vs GAVE

A cirrhotic patient has mosaic fundic mucosa with diffuse oozing, not antral stripes.

Which mechanism fits portal hypertensive gastropathy?

A. Eosinophilic mucosal remodeling

B. **CagA**-mediated epithelial dysplasia

C. Portal hypertension causes mucosal and submucosal vascular congestion with impaired defense

D. Antral ectatic vessels independent of portal pressure

E. **Immune**-complex capillaritis with low C4

Answer: C. Portal hypertension causes mucosal and submucosal vascular congestion with impaired defense

Micro-pearl: **PHG** is portal-pressure-related congestion.

Q63. Diverticular bleeding

A patient has sudden painless hematochezia. Colonoscopy shows a diverticulum with an adherent clot.

Which mechanism explains bleeding?

A. Vasa recta injury at the **diverticular** dome/neck causes arterial hemorrhage

B. Mucosal cytokine ulceration from **UC**

C. Tumor angiogenesis in a serrated polyp

D. Venous thrombosis from **ischemic colitis**

E. Radiation endarteritis of rectum

Answer: A. Vasa recta injury at the **diverticular** dome/neck causes arterial hemorrhage

Micro-pearl: **Diverticular** bleeding is arterial vasa recta bleeding.

Q64. Post-polypectomy bleeding

Delayed bleeding occurs 6 days after hot-snare resection of a right-colon sessile polyp.

Which mechanism is most likely?

A. Immediate clip displacement from portal hypertension

B. **Bile acid** deconjugation causing vessel rupture

C. CYP2E1 oxidative injury to colonocytes

D. Thermal injury causes delayed sloughing of coagulum and exposure of submucosal vessels

E. **MMR** deficiency causing delayed bleeding

Answer: D. Thermal injury causes delayed sloughing of coagulum and exposure of submucosal vessels

Micro-pearl: Thermal injury can cause delayed vessel exposure.

Q65. Ischemic colitis bleeding

An elderly woman with hypotension develops crampy pain followed by maroon stools; CT shows segmental left-colon thickening.

Which mechanism best explains bleeding?

A. Adenoma-carcinoma sequence erodes vessels

B. Sphincter spasm raises portal pressure

C. Toxin B glucosylates **Rho GTPases**

D. Low-flow injury in watershed mucosa causes reperfusion-related hemorrhagic inflammation

E. **IgA tTG** deposition injures villi

Answer: D. Low-flow injury in watershed mucosa causes reperfusion-related hemorrhagic inflammation

Micro-pearl: **Ischemic colitis** is low-flow watershed mucosal injury.

Q66. Capsule before deep enteroscopy

A stable patient has recurrent iron deficiency after negative EGD and colonoscopy.

Why is capsule endoscopy often selected before deep enteroscopy?

A. It detects only tumors larger than 5 cm

B. It replaces CT in obstructive symptoms without risk

C. It provides definitive hemostasis for all lesions

D. It reduces portal pressure in small-bowel varices

E. It noninvasively maps small-bowel mucosal bleeding targets to guide directed therapy

Answer: E. It noninvasively maps small-bowel mucosal bleeding targets to guide directed therapy

Micro-pearl: Capsule is localization/triage, not therapy.

Q67. Meckel bleeding

A young adult has painless recurrent maroon bleeding and negative colonoscopy. **Meckel** scan is positive.

Which mechanism explains bleeding?

A. **IgA immune** complexes deposit in vessels

B. Ileal **bile acids** stimulate chloride secretion

C. **NOD2** mutation causes transmural fistula

D. Ectopic gastric mucosa secretes acid causing adjacent ileal ulceration

E. Pancreatic enzymes digest the colon

Answer: D. Ectopic gastric mucosa secretes acid causing adjacent ileal ulceration

Micro-pearl: **Meckel** bleeding is acid injury from ectopic gastric mucosa.

Q68. Small bowel angio and CKD

A dialysis patient has recurrent obscure bleeding from jejunal angioectasias.

Which mechanism best explains recurrence tendency?

A. **APC** mutation creates vascular tufts

B. **Celiac**-associated villous atrophy causes arterial rupture

C. **PPI** therapy causes jejunal varices

D. **H. pylori urease** colonizes jejunal vessels

E. Acquired vascular ectasia plus platelet dysfunction/uremia increases bleeding from fragile lesions

Answer: E. Acquired vascular ectasia plus platelet dysfunction/uremia increases bleeding from fragile lesions

Micro-pearl: CKD promotes angioectasia bleeding and hemostatic dysfunction.

Q69. Rebalanced hemostasis

A cirrhotic patient with GI bleeding has INR 2.1 but normal fibrinogen and platelets 95,000. A junior assumes auto-anticoagulation.

Which concept is correct?

A. Platelet count alone defines coagulation status

B. Vitamin K always normalizes portal bleeding

C. Reduced procoagulant and anticoagulant factors create fragile rebalanced hemostasis not captured by INR alone

D. Cirrhosis completely protects against thrombosis

E. INR precisely predicts bleeding risk in cirrhosis

Answer: C. Reduced procoagulant and anticoagulant factors create fragile rebalanced hemostasis not captured by INR alone

Micro-pearl: INR overstates bleeding tendency in cirrhosis.

Q70. Anticoagulant reversal

A patient on **apixaban** presents with life-threatening upper GI bleeding and shock.

Which principle is most mechanism-based?

A. Reversal targets factor Xa inhibition while endoscopic source control treats the bleeding lesion

B. Platelet transfusion directly removes **apixaban**

C. **PPI** reverses factor Xa binding

D. Vitamin K immediately reverses **apixaban**

E. **Octreotide** neutralizes factor Xa inhibitors

Answer: A. Reversal targets factor Xa inhibition while endoscopic source control treats the bleeding lesion

Micro-pearl: Anticoagulant reversal and source control are distinct mechanisms.

Q71. Lower GI CTA

A patient has brisk ongoing hematochezia and cannot be prepped for colonoscopy.

Why is CTA useful?

A. It detects active contrast extravasation and localizes bleeding for angiographic or surgical targeting

B. It treats **diverticular** bleeding by pH elevation

C. It differentiates **UC** from **Crohn** histologically

D. It identifies all **angiodysplasia**s when not bleeding

E. It measures portal pressure directly

Answer: A. It detects active contrast extravasation and localizes bleeding for angiographic or surgical targeting

Micro-pearl: CTA localizes active bleeding when colonoscopy is impractical.

Q72. IBD bleeding

A young man with severe **UC** has bloody diarrhea, fever, and high **CRP**.

Which mechanism prod**uc**es bleeding?

A. **H. pylori urease** damages colonocytes

B. Transmural fistulization ero**des** vasa recta only

C. Portal pressure creates rectal varices in every **UC** flare

D. Diffuse m**uc**osal ulceration with neutrophilic crypt injury exposes superficial vessels

E. CYP2E1 ROS causes colonic hemorrhage

Answer: D. Diffuse m**uc**osal ulceration with neutrophilic crypt injury exposes superficial vessels

Micro-pearl: **UC** bleeding reflects m**uc**osal inflammatory ulceration.

Q73. Tumor bleeding

An older patient has iron deficiency and intermittent occult blood. Colonoscopy reveals right-sided adenocarcinoma.

Which mechanism best explains occult bleeding?

A. Friable neovascular tumor surface undergoes chronic low-volume m**uc**osal bleeding

B. **IgA immune** complexes rupture capillaries

C. **Bile acid**s dissolve fibrin

D. **Achalasia**-related stasis causes anemia

E. High-output acid secretion inactivates clot

Answer: A. Friable neovascular tumor surface undergoes chronic low-volume m**uc**osal bleeding

Micro-pearl: Right-colon cancers often bleed slowly and occultly.

Q74. Aortoenteric fistula

A man with prior aortic graft has a self-limited herald bleed followed by massive hematemesis.

Which mechanism is most dangerous?

A. Portal hypertensive gastropathy

B. **C. difficile** pseudomembrane sloughing

C. Mechanical erosion between graft/aorta and bowel creates arterial-enteric communication

D. Forrest IIc ulcer clot lysis

E. **Dieulafoy** subm**uc**osal venous ectasia

Answer: C. Mechanical erosion between graft/aorta and bowel creates arterial-enteric communication

Micro-pearl: Herald bleed after aortic graft = aortoenteric fistula until proven otherwise.

Q75. Small bowel varices

A patient with portal vein thrombosis has recurrent melena after negative EGD and colonoscopy. Capsule suggests jejunal varices.

Which mechanism explains bleeding?

A. Portosystemic collateral formation in ectopic small-bowel veins under elevated portal pressure

B. Vasa recta rupture at **diverticular** neck

C. **CagA**-mediated jejunal lymphoma

D. **Bile acid** secretory diarrhea

E. Ectopic gastric m**uc**osa acid ulceration

Answer: A. Portosystemic collateral formation in ectopic small-bowel veins under elevated portal pressure

Micro-pearl: Ectopic varices are portal hypertensive collaterals outside the esophagus/stomach.

Chapter 4 - Small Bowel Diseases, Diarrhea and Malabsorption

Q76. Celiac deamidation

A woman with iron deficiency and diarrhea has villous atrophy and positive **tTG IgA**.

Which molecular step makes gluten more immunogenic?

A. Pancreatic trypsin converts gliadin to **bile acid**

B. IgE crosslinks mast cells in villi

C. **Urease** converts gluten to ammonia

D. FXR suppresses gliadin transport

E. Tissue transglutaminase deamidates gliadin, increasing HLA-DQ2/DQ8 binding

Answer: E. Tissue transglutaminase deamidates gliadin, increasing HLA-DQ2/DQ8 binding

Micro-pearl: **tTG** deamidation enhances HLA binding in **celiac** disease.

Q77. IgA deficiency

A patient has villous atrophy but negative **tTG IgA** and very low total **IgA**.

Which testing trap explains the result?

A. **IgA** deficiency can make **IgA**-based **celiac** serology falsely negative

B. **IgA** deficiency prevents villous injury

C. **IgA** deficiency exclu**des celiac** disease

D. **IgA** deficiency proves **Whipple** disease

E. **IgA** deficiency causes false-positive **tTG IgA**

Answer: A. **IgA** deficiency can make **IgA**-based **celiac** serology falsely negative

Micro-pearl: Check total **IgA** when **celiac** serology is negative but suspicion remains.

Q78. Dermatitis herpetiformis

A man with gluten-sensitive enteropathy has grouped itchy vesic**les** on elbows and knees with granular **IgA** in dermal papillae.

Which antigenic target best **fit**s?

A. ANCA against colonic neutrophils

B. IgE against wheat causing urticaria

C. Epidermal transglutaminase-related **IgA** autoimmunity

D. **H. pylori CagA** cross-reactivity

E. **IgG4** against pancreatic d**uc**ts

Answer: C. Epidermal transglutaminase-related **IgA** autoimmunity

Micro-pearl: Dermatitis herpetiformis is **IgA**/eTG-linked.

Q79. Refractory celiac II

A patient with treated **celiac** disease has persistent villous atrophy and aberrant clonal IELs.

What is the major biologic concern?

A. Antigen-dependent **MALT** lymphoma only

B. Clonal intraepithelial T-cell expansion with risk of enteropathy-associated T-cell lymphoma

C. **H. pylori**-driven diffuse gastric cancer

D. **MEN1** pancreatic **NET**

E. Secretin-responsive **gastrin**oma

Answer: B. Clonal intraepithelial T-cell expansion with risk of enteropathy-associated T-cell lymphoma

Micro-pearl: RCD type II is premalignant clonal IEL disease.

Q80. Olmesartan enteropathy

A patient with sprue-like enteropathy has negative **celiac** serology and no response to gluten withdrawal. Symptoms resolve after sto**ppi**ng olmesartan.

Which mechanism category is most likely?

A. Drug-ind**uc**ed **immune**-mediated enteropathy mimicking villous atrophy

B. HLA-DQ2 obl**iga**te gluten presentation

C. Pancreatic lipase deficiency

D. Bacterial deconjugation of **bile acid**s only

E. Ectopic acid secretion from **Meckel** m**uc**osa

Answer: A. Drug-ind**uc**ed **immune**-mediated enteropathy mimicking villous atrophy

Micro-pearl: Olmesartan can mimic **celiac**-like enteropathy.

Q81. Tropical sprue

A traveler with chronic diarrhea, weight loss, low folate, and B12 deficiency improves with tetracycline and folate.

Which mechanism is most plausible?

A. **Whipple** macrophage infiltration

B. Postinfectious small-bowel m**uc**osal injury with bacterial overgrowth-like features causing malabsorption

C. **tTG**-mediated gliadin presentation only

D. **Bile acid** pool depletion from ileal resection

E. D2 **receptor** antagonism

Answer: B. Postinfectious small-bowel m**uc**osal injury with bacterial overgrowth-like features causing malabsorption

Micro-pearl: Tropical sprue is postinfectious malabsorptive enteropathy.

Q82. Whipple disease

A man has diarrhea, arthralgia, weight loss, hyperpigmentation, and cognitive changes. Duodenal biopsy shows PAS-positive macrophages.

Which mechanism explains disease?

A. **Bile acid** deconjugation from **SIBO** only

B. Bacterial toxin B Rho gl**uc**osylation

C. Mast-cell IgE food allergy

D. Impaired macrophage clearance of Tropheryma **whipple**i with systemic infiltration

E. **IgA** gliadin **immune** injury

Answer: D. Impaired macrophage clearance of Tropheryma **whipple**i with systemic infiltration

Micro-pearl: **Whipple** is systemic macrophage-laden infection.

Q83. SIBO malabsorption

A systemic sclerosis patient has bloating, steatorrhea, and low B12.

Which mechanism is most responsible?

A. Pancreatic acinar **des**tr**uc**tion red**uc**es lipase secretion

B. Excess ileal FGF19 suppresses **bile acid** synthesis

C. HLA-DQ8 gluten presentation

D. Small-bowel stasis permits bacteria to deconjugate **bile acid**s and consume nutrients

E. Brush-border lactase deficiency alone

Answer: D. Small-bowel stasis permits bacteria to deconjugate **bile acid**s and consume nutrients

Micro-pearl: **SIBO** causes **bile acid** deconjugation and nutrient competition.

Q84. Breath testing trap

A patient has rapid orocecal transit and an early hydrogen rise on breath test.

Which interpretation is most cautious?

A. Hydrogen rise always proves **SIBO**

B. Methane exclu**des** constipation

C. Early hydrogen rise may reflect rapid transit rather than true proximal bacterial overgrowth

D. A negative test exclu**des** all dysbiosis

E. Breath testing directly measures **bile acid** pool

Answer: C. Early hydrogen rise may reflect rapid transit rather than true proximal bacterial overgrowth

Micro-pearl: Breath tests can be confounded by transit.

Q85. Bile acid diarrhea

A **Crohn** patient with limited ileal disease has watery diarrhea responsive to cho**les**tyramine.

Which mechanism explains symptoms?

A. Complete **bile acid** pool depletion impairs micel**les**

B. Unabsorbed **bile acid**s reaching colon stimulate secretion and motility

C. Secretin stimulates **gastrin** from a tumor

D. **Celiac** villous atrophy causes osmotic diarrhea

E. Pancreatic lipase excess injures colon

Answer: B. Unabsorbed **bile acid**s reaching colon stimulate secretion and motility

Micro-pearl: Limited ileal **bile acid** malabsorption causes secretory colonic diarrhea.

Q86. Extensive ileal loss

After extensive ileal resection, a patient has steatorrhea worsened by cholestyramine.

Which mechanism explains this change?

A. Gastric acid secretion is abolished

B. **Bile acid** pool depletion impairs micelle formation and fat absorption

C. Bacterial overgrowth cannot occur without ileum

D. **Celiac** serology becomes positive

E. Colonic **bile acid** exposure is still the only problem

Answer: B. **Bile acid** pool depletion impairs micelle formation and fat absorption

Micro-pearl: Extensive ileal loss depletes **bile acid**s, causing steatorrhea.

Q87. Short bowel adaptation

A **short bowel** patient with colon in continuity gradually needs **less** parenteral support.

Which adaptation is most helpful?

A. Complete restoration of ileal **bile acid** transport

B. **Gastrin** suppression increases absorption

C. Pancreatic lipase hypersecretion replaces lost m**uc**osa

D. Colonic fermentation of carbohydrates to short-chain fatty acids salvages calories and fluid

E. **CFTR** closure prod**uc**es villous growth

Answer: D. Colonic fermentation of carbohydrates to short-chain fatty acids salvages calories and fluid

Micro-pearl: Colon in continuity improves energy/fluid salvage.

Q88. D-lactic acidosis

A **short bowel** patient with colon continuity develops episodic confusion after high carbohydrate intake; routine lactate is normal.

Which mechanism explains symptoms?

A. **Bile acid** diarrhea causes hypoglycemia

B. Pancreatic bicarbonate loss causes alkalosis

C. Hepatic failure raises ammonia only

D. **IgA** deficiency causes encephalopathy

E. Colonic bacterial carbohydrate fermentation prod**uc**es D-lactate not detected by standard L-lactate assays

Answer: E. Colonic bacterial carbohydrate fermentation prod**uc**es D-lactate not detected by standard L-lactate assays

Micro-pearl: D-lactic acidosis is a **short bowel**/carbohydrate fermentation trap.

Q89. Intestinal lymphangiectasia

A young patient has edema, hypoalbuminemia, lymphopenia, and low immunoglobulins with dilated intestinal lacteals.

Which mechanism **fit**s?

A. Lymph leakage into the gut causes protein, lymphocyte, and immunoglobulin loss

B. Pancreatic exocrine failure with normal albumin

C. **Bile acid** depletion without **immune** loss

D. Renal albumin leak with preserved lymphocytes

E. Hepatic synthetic failure with high INR only

Answer: A. Lymph leakage into the gut causes protein, lymphocyte, and immunoglobulin loss

Micro-pearl: Lymphangiectasia causes protein-losing enteropathy plus lymphopenia.

Q90. PLE alpha-1 antitrypsin

A patient has edema with normal renal and hepatic evaluation. Stool alpha-1 antitrypsin clearance is elevated.

What does the **biomarker** reflect?

A. Secretory diarrhea through **CFTR**

B. **Bile acid** synthesis rate

C. **Celiac**-specific **tTG** activity

D. Pancreatic protease excess

E. Enteric protein loss because alpha-1 antitrypsin resists intestinal degradation

Answer: E. Enteric protein loss because alpha-1 antitrypsin resists intestinal degradation

Micro-pearl: Alpha-1 antitrypsin clearance detects GI protein loss.

Q91. Osmotic diarrhea

A patient has watery diarrhea that stops with fasting and a high stool osmotic gap.

Which mechanism best **fit**s?

A. Inflammatory ulceration releases blood and pus

B. Active enterocyte chloride secretion persists **des**pite fasting

C. Poorly absorbed luminal solute retains water osmotically

D. Rapid **bile acid** synthesis depletes micel**les**

E. Portal pressure creates colonic edema

Answer: C. Poorly absorbed luminal solute retains water osmotically

Micro-pearl: Osmotic diarrhea improves with fasting and has high osmotic gap.

Q92. Secretory diarrhea

A patient has high-volume diarrhea that persists during fasting with low stool osmotic gap.

Which mechanism **fit**s?

A. Mechanical obstr**uc**tion causes high gap

B. Lactose malabsorption only

C. Gluten-triggered villous atrophy always stops fasting

D. Magnesium ingestion stopped by fasting

E. Active electrolyte secretion or impaired absorption drives water loss independent of intake

Answer: E. Active electrolyte secretion or impaired absorption drives water loss independent of intake

Micro-pearl: Secretory diarrhea persists with fasting and low osmotic gap.

Q93. Microscopic colitis

An older woman on **PPI** has chronic watery diarrhea. Colonoscopy is normal; random biopsies show collagenous colitis.

Why was biopsy essential?

A. Serology is always positive

B. CT angiography is diagnostic

C. The abnormality is histologic with preserved gross m**uc**osal appearance

D. Disease is diagnosed by fecal elastase

E. Capsule is required to see m**uc**osal rings

Answer: C. The abnormality is histologic with preserved gross m**uc**osal appearance

Micro-pearl: Microscopic colitis needs biopsies **des**pite normal colonoscopy.

Q94. Lactase deficiency

A patient develops bloating and diarrhea after milk; symptoms improve with lactose restriction.

Which mechanism explains diarrhea?

A. Bile acid pool depletion

B. IgA tTG deposition in skin

C. Unabsorbed lactose creates osmotic load and bacterial fermentation gases

D. Toxin-mediated Rho GTPase injury

E. Pancreatic lipase deficiency

Answer: C. Unabsorbed lactose creates osmotic load and bacterial fermentation gases

Micro-pearl: Lactose intolerance is osmotic-fermentative.

Q95. Abetalipoproteinemia

A child has fat malabsorption, acanthocytosis, neurologic signs, and very low ApoB-containing lipoproteins.

Which mechanism explains steatorrhea?

A. CYP2E1 ind**uc**tion

B. EGFR activation in foveolae

C. Ileal **bile acid receptor** overactivity

D. Defective microsomal triglyceride transfer prevents chylomicron assembly

E. Urease-mediated villous atrophy

Answer: D. Defective microsomal triglyceride transfer prevents chylomicron assembly

Micro-pearl: ApoB/chylomicron assembly failure causes fat malabsorption.

Q96. CVID enteropathy
A patient with recurrent sinopulmonary infections has chronic diarrhea, nodular lymphoid hyperplasia, and low immunoglobulins.

Which mechanism is central?

A. **CagA** transforms lymph no**des**

B. Humoral immunodeficiency predisposes to infection and **immune**-mediated enteropathy

C. **Bile acid** synthesis is absent

D. **IgA** excess deposits in villi

E. HLA-DQ2 is obl**iga**tory

Answer: B. Humoral immunodeficiency predisposes to infection and **immune**-mediated enteropathy

Micro-pearl: CVID causes infectious and noninfectious enteropathy.

Q97. Amyloid
A patient with systemic amyloidosis has diarrhea, weight loss, and orthostatic symptoms.

Which mechanism explains GI involvement?

A. Amyloid deposition in muscularis, nerves, and vessels disrupts motility and absorption

B. Eosinophilic type 2 m**uc**osal inflammation

C. **Gastrin**-driven acid injury

D. **APC** mutation in enterocytes

E. Bacterial deconjugation of **bile acid**s only

Answer: A. Amyloid deposition in muscularis, nerves, and vessels disrupts motility and absorption

Micro-pearl: Amyloid can cause dysmotility, malabsorption, and vascular fragility.

Q98. Giardia
A **camp**er has foul diarrhea, bloating, and weight loss. Duodenal aspirate shows Giardia.

Which mechanism explains malabsorption?

A. **Bile acid** synthesis stops completely

B. Invasion of portal venu**les** causes vasculitis

C. **IgA tTG** deposition **des**troys crypts

D. Toxin B **des**troys **Rho GTPases**

E. Trophozoite adherence and brush-border injury impair absorptive enzyme function

Answer: E. Trophozoite adherence and brush-border injury impair absorptive enzyme function

Micro-pearl: Giardia causes noninvasive brush-border dysfunction.

Q99. VIPoma
A patient has profound watery diarrhea, hypokalemia, and achlorhydria with very high stool volume.

Which signaling mechanism drives diarrhea?

A. **Somatostatin** closes **CFTR**

B. D2 blockade increases **acetylcholine**

C. Motilin triggers MMC only

D. VIP activates adenylate cyclase-**cAMP** chloride and water secretion

E. **Gastrin** activates **CCK-B** acid secretion

Answer: D. VIP activates adenylate cyclase-**cAMP** chloride and water secretion

Micro-pearl: VIPoma is secretory **cAMP**-mediated diarrhea.

Q100. Fecal elastase
A chronic **pancreatitis** patient has steatorrhea. Fecal elastase is low.

What does this **biomarker** represent?

A. Enteric protein loss

B. **Bile acid** diarrhea in colon

C. Colonic neutrophil inflammation

D. Red**uc**ed pancreatic enzyme output reaching stool

E. Small-bowel villous **immune** injury

Answer: D. Red**uc**ed pancreatic enzyme output reaching stool

Micro-pearl: Fecal elastase is a pancreatic exocrine function marker.

Chapter 5 - Inflammatory Bowel Disease

Q101. NOD2 Crohn

A young man with ileal **Crohn** disease has a **NOD2** risk variant.

Which innate **immune** defect is most relevant?

A. **COX-1 prostaglandin** depletion

B. Impaired bacterial peptidoglycan sensing and Paneth-cell defensin response

C. **V1 receptor**-mediated vasoconstriction

D. **MLH1** promoter methylation causing **MSI**

E. Excess **IL-4 receptor** signaling in squamous epithelium

Answer: B. Impaired bacterial peptidoglycan sensing and Paneth-cell defensin response

Micro-pearl: **NOD2** links microbial sensing to ileal **Crohn** susceptibility.

Q102. ATG16L1

A **Crohn** patient has Paneth-cell abnormalities and an **ATG16L1** risk allele.

Which mechanism is implicated?

A. Defective autophagy/xenophagy alters bacterial handling and epithelial stress responses

B. Constitutive KIT activation

C. Excess H2 **histamine** signaling

D. Viral DNA polymerase inhibition

E. Failed **tTG** deamidation of gliadin

Answer: A. Defective autophagy/xenophagy alters bacterial handling and epithelial stress responses

Micro-pearl: Autophagy genes shape microbial handling in **Crohn** disease.

Q103. IL-23/Th17

A patient with **Crohn** disease responds to selective **IL-23 p19** blockade after anti-TNF failure.

Which **pathway** is targeted?

A. H2 **receptor** acid secretion

B. **CFTR** chloride secretion in **IBS**-C

C. **GABA-B TLESR** suppression

D. **IL-23**-driven maintenance of pathogenic **Th17**-type inflammation

E. IL-5 eosinophil maturation only

Answer: D. **IL-23**-driven maintenance of pathogenic **Th17**-type inflammation

Micro-pearl: **IL-23** sustains **Th17** inflammation; **p19** blockade is selective.

Q104. Anti-TNF

A fistulizing **Crohn** patient improves on **infliximab**.

Which mechanism best explains fistula benefit?

A. **TNF-alpha** neutralization reduces macrophage/T-cell cytokine amplification and tissue destruction

B. **Alpha-4 beta-7** blockade alone closes all fistula tracts

C. **Bile acid** sequestration heals fistulas

D. **Gastrin** suppression improves transmural inflammation

E. **JAK** inhibition is the only fistula mechanism

Answer: A. **TNF-alpha** neutralization reduces macrophage/T-cell cytokine amplification and tissue destruction

Micro-pearl: Anti-TNF is especially useful for fistulizing **Crohn**.

Q105. Anti-drug antibodies

Loss of response to **infliximab** occurs with low trough and high anti-drug antibodies.

Which mechanism explains relapse?

A. **PPI**-induced biologic degradation

B. Mechanistic escape with high trough level

C. **Bile acid** binding of monoclonal antibody

D. **IL-23** overexpression despite adequate TNF blockade only

E. Immunogenic drug clearance lowers effective **TNF-alpha** neutralization

Answer: E. Immunogenic drug clearance lowers effective **TNF-alpha** neutralization

Micro-pearl: Low trough + antibodies = pharmacokinetic immunogenic failure.

Q106. Thiopurine combo

Combination **azathioprine** with **infliximab** is considered early in severe **Crohn** disease.

Which mechanism supports combination therapy?

A. Thiopurines block **alpha-4 beta-7** integrin

B. **Azathioprine** directly neutralizes **TNF-alpha**

C. Reduced anti-drug antibody formation improves biologic durability

D. Thiopurines selectively inhibit **IL-23 p19**

E. **Azathioprine** activates **S1P receptor**s

Answer: C. Reduced anti-drug antibody formation improves biologic durability

Micro-pearl: Thiopurines may reduce immunogenicity to anti-TNF.

Q107. Vedolizumab

A **UC** patient with infection concerns is started on **vedolizumab**.

Which mechanism explains gut selectivity?

A. **TNF-alpha** neutralization throughout tissues

B. **Alpha-4 beta-7** integrin blockade prevents lymphocyte binding to **MAdCAM-1** in gut mucosa

C. Systemic alpha-4 blockade prevents CNS lymphocyte surveillance

D. **S1P receptor** agonism retains lymphocytes

E. **IL-12**/23 **p40** blockade

Answer: B. **Alpha-4 beta-7** integrin blockade prevents lymphocyte binding to **MAdCAM-1** in gut mucosa

Micro-pearl: **Vedolizumab** blocks gut-homing **alpha-4 beta-7**.

Q108. Natalizumab PML

A **Crohn** patient asks why **natalizumab** has a special neurologic infection risk compared with **vedolizumab**.

Which mechanism explains it?

A. Selective gut **MAdCAM-1** blockade increases JC virus entry

B. **S1P** modulation increases CSF lymphocyte trafficking

C. Broader alpha-4 integrin blockade impairs CNS **immune** surveillance and increases PML risk

D. **JAK**1 inhibition causes viral demyelination exclusively

E. TNF blockade directly activates JC virus polymerase

Answer: C. Broader alpha-4 integrin blockade impairs CNS **immune** surveillance and increases PML risk

Micro-pearl: **Natalizumab** is **less** gut-selective than **vedolizumab**.

Q109. Ustekinumab

Crohn disease improves after **ustekinumab**.

Which cytokine unit is blocked?

A. **p19** subunit unique to **IL-23**

B. **TNF-alpha** soluble trimer

C. **p40** subunit shared by **IL-12** and **IL-23**

D. **JAK**1 ATP-binding site

E. **IL-4 receptor** alpha

Answer: C. **p40** subunit shared by **IL-12** and **IL-23**

Micro-pearl: **Ustekinumab** targets **p40**; **risankizumab** targets **p19**.

Q110. Risankizumab

A **Crohn** patient receives a biologic selectively targeting **IL-23** without blocking **IL-12**.

Which target is most consistent?

A. **S1P receptor** 1

B. **IL-12**/23 **p40** subunit

C. **IL-23 p19** subunit

D. **Alpha-4 beta-7** integrin

E. **TNF-alpha**

Answer: C. **IL-23 p19** subunit

Micro-pearl: **p19** blockade is selective **IL-23** inhibition.

Q111. JAK inhibitors

A UC patient responds rapidly to an oral small molecule rather than an antibody infusion.

Which pharmacologic principle is correct?

A. T-cell trappiing through S1P agonism only

B. Integrin blockade of cell trafficking only

C. Extracellular cytokine neutralization of TNF alone

D. Luminal binding of bile acids

E. Intracellular JAK inhibition interrupts multiple cytokine receptor signals

Answer: E. Intracellular JAK inhibition interrupts multiple cytokine receptor signals

Micro-pearl: JAK inhibitors are intracellular signal blockers.

Q112. Tofacitinib risks

Before tofacitinib, a patient is screened for zoster and thrombosis risk.

Which mechanism explains broad efficacy and risk?

A. H2 receptor inhibition

B. Topical epithelial 5-ASA action

C. Pan-JAK cytokine signaling interference affects inflammatory and antiviral/thrombotic pathways

D. Gut-selective integrin blockade

E. IL-23 p19 blockade only

Answer: C. Pan-JAK cytokine signaling interference affects inflammatory and antiviral/thrombotic pathways

Micro-pearl: Broad JAK blockade gives broad immunologic effects and risks.

Q113. Upadacitinib

A refractory UC patient starts a JAK1-preferential inhibitor.

Which signaling concept is intended?

A. Selective inhibition of IL-5 receptor eosinophils

B. Alpha-4 beta-7/MAdCAM blockade

C. TNF-alpha ligand neutralization

D. S1P receptor internalization

E. Preferential blockade of JAK1-dependent cytokine pathways while sparing some JAK2 hematopoietic signaling

Answer: E. Preferential blockade of JAK1-dependent cytokine pathways while sparing some JAK2 hematopoietic signaling

Micro-pearl: JAK selectivity modifies efficacy/toxicity expectations.

Q114. Ozanimod

A UC patient develops lymphopenia after ozanimod.

Which mechanism explains therapy?

A. Direct TNF-alpha apoptosis

B. COX-1 inhibition

C. MAdCAM-1 overexpression

D. IL-13 epithelial blockade

E. S1P receptor modulation retains lymphocytes in lymphoid tissue and reduces gut trafficking

Answer: E. S1P receptor modulation retains lymphocytes in lymphoid tissue and reduces gut trafficking

Micro-pearl: S1P modulators reduce lymphocyte egress.

Q115. Ozanimod bradycardia

First-dose monitoring is considered in a patient with conduction disease before S1P modulator therapy.

Which receptor biology explains concern?

A. Anti-IL23 blocks SA node IL-23

B. Alpha-4 beta-7 blockade slows AV node

C. S1P receptor effects can alter cardiac nodal signaling causing bradyarrhythmia risk

D. TNF neutralization prolongs QT directly

E. 5-ASA inhibits sodium channels

Answer: C. S1P receptor effects can alter cardiac nodal signaling causing bradyarrhythmia risk

Micro-pearl: S1P biology has cardiac conduction implications.

Q116. 5-ASA
A patient with mild distal **UC** improves with rectal **mesalamine**.

Which mechanism is most accurate?

A. Systemic **TNF-alpha** neutralization

B. Pan-**JAK** inhibition

C. **Alpha-4 beta-7** blockade

D. Topical anti-inflammatory effects on epithelial mucosa including **prostaglandin**/leukotriene and NF-kB-related **pathway**s

E. **S1P receptor** internalization

Answer: D. Topical anti-inflammatory effects on epithelial mucosa including **prostaglandin**/leukotriene and NF-kB-related **pathway**s

Micro-pearl: 5-ASA works topically in **UC** mucosa.

Q117. Steroids
IV steroids improve acute severe **UC** within days but are not used for maintenance.

Which mechanism explains induction effect?

A. Selective mucosal healing by epithelial proliferation only

B. Microbiome restoration

C. Integrin blockade preventing trafficking

D. Glucocorticoid **receptor** transcriptional repression of multiple inflammatory genes

E. Permanent deletion of autoreactive T cells

Answer: D. Glucocorticoid **receptor** transcriptional repression of multiple inflammatory genes

Micro-pearl: Steroids are broad transcriptional anti-inflammatory induction therapy.

Q118. Calcineurin rescue
A steroid-refractory acute severe **UC** patient receives **cyclosporine** as rescue therapy.

Which mechanism is targeted?

A. Calcineurin inhibition blocks **NFAT**-dependent **IL-2** transcription and T-cell activation

B. **S1P** modulation traps lymphocytes

C. **TNF-alpha** neutralization

D. **JAK**1 inhibition blocks cytokine **receptor** phosphorylation

E. **IL-23 p19** blockade

Answer: A. Calcineurin inhibition blocks **NFAT**-dependent **IL-2** transcription and T-cell activation

Micro-pearl: Calcineurin inhibitors rapidly suppress T-cell activation.

Q119. Surgery UC
A **UC** patient asks why colectomy can cure colitis but not remove all **immune** complications.

Which mechanism is correct?

A. Removal of the colon removes the target organ for continuous mucosal colitis, but **immune** predisposition can persist

B. Colectomy prevents pouchitis permanently

C. Colectomy restores **IL-23** regulation systemically

D. Colectomy deletes all autoreactive lymphocytes

E. Colectomy reverses PSC in all cases

Answer: A. Removal of the colon removes the target organ for continuous mucosal colitis, but **immune** predisposition can persist

Micro-pearl: **UC** colitis is colon-limited, but systemic/extraintestinal disease may persist.

Q120. Toxic megacolon
A patient with severe colitis develops transverse colon dilation, fever, tachycardia, and systemic toxicity.

Which mechanism is most relevant?

A. Severe transmural inflammatory mediator effect impairs smooth-muscle tone and neuromuscular function

B. **H. pylori urease** paralyzes colon

C. **Bile acid** excess causes mechanical obstruction

D. **APC** mutation causes acute dilation

E. Isolated mucosal aphthae preserve motor tone

Answer: A. Severe transmural inflammatory mediator effect impairs smooth-muscle tone and neuromuscular function

Micro-pearl: Toxic megacolon is inflammatory paralysis and dilation.

Q121. Crohn postoperative recurrence

After ileocolic resection for **Crohn** disease, recurrence occurs at the neoterminal ileum.

Which mechanism explains recurrence pattern?

A. Surgery cures **Crohn** by removing all susceptible m**uc**osa

B. Luminal microbiota and host **immune** susceptibility re-initiate inflammation near the anastomosis

C. TNF blockade creates recurrence

D. **Bile acid** sequestration prevents **immune** recurrence

E. Po**uc**hitis requires retained rectum

Answer: B. Luminal microbiota and host **immune** susceptibility re-initiate inflammation near the anastomosis

Micro-pearl: **Crohn** is not cured by resection; recurrence often starts at the anastomosis.

Q122. Smoking Crohn

A smoker with **Crohn** disease has early postoperative recurrence.

Which interpretation is most accurate?

A. Smoking amplifies **Crohn** recurrence risk through **immune**, vascular, and microbial effects

B. Smoking prevents strictures

C. Smoking acts only by increasing acid secretion

D. Smoking protects **Crohn** but worsens **UC**

E. Smoking directly blocks **IL-23**

Answer: A. Smoking amplifies **Crohn** recurrence risk through **immune**, vascular, and microbial effects

Micro-pearl: Smoking worsens **Crohn**, including postoperative recurrence.

Q123. Colitis cancer field effect

A patient with long-standing extensive **UC** develops multifocal low-grade dysplasia.

Which mechanism explains colectomy discussion?

A. Cancer risk is unrelated to duration or extent

B. A single sporadic adenoma explains all dysplasia

C. Inflammation protects from **p53** mutation

D. Dysplasia in **UC** is always reactive and reversible

E. Chronic inflammation creates a field effect with wi**des**pread molecular injury and synchronous cancer risk

Answer: E. Chronic inflammation creates a field effect with wi**des**pread molecular injury and synchronous cancer risk

Micro-pearl: Colitis-associated neoplasia is often field-based.

Q124. Perianal Crohn

A **Crohn** patient has complex perianal fistulas with rectal inflammation.

Which mechanism supports combined medical and surgical management?

A. Colectomy is always curative

B. **PPI** therapy heals perianal disease

C. Transmural **immune** inflammation maintains tracts while sepsis requires drainage/seton control

D. Antibiotics permanently reverse **NOD2** signaling

E. M**uc**osal inflammation alone closes fistulas

Answer: C. Transmural **immune** inflammation maintains tracts while sepsis requires drainage/seton control

Micro-pearl: Control sepsis mechanically and inflammation biologically.

Q125. Biosimilar switch

A stable **infliximab** patient is switched to a biosimilar under monitoring.

Which pharmacologic principle is correct?

A. Biosimilars act only through **JAK** inhibition

B. Biosimilars are chemically identical generics

C. Biosimilars block a different cytokine by **des**ign

D. Biosimilars cannot form anti-drug antibodies

E. Comparable binding/function is expected, but immunogenicity and trough levels may be monitored in loss of response

Answer: E. Comparable binding/function is expected, but immunogenicity and trough levels may be monitored in loss of response

Micro-pearl: Biologics are comparable, not identical small-molecule generics.

Chapter 6 - Large Bowel Diseases, CRC, Polyps, Polyposis, IBS, Radiation and Ischemic Colitis

Q126. APC beta-catenin

A sporadic tubular adenoma shows **APC** loss.

Which signaling event initiates adenoma growth?

A. **Wnt pathway** activation with **beta-catenin** accumulation and transcriptional proliferation

B. **STK11** hamartomatous stromal overgrowth

C. **KRAS** loss suppressing **MAPK**

D. **p53** activation causing apoptosis

E. **MLH1** methylation causing **MSI** immediately

Answer: A. **Wnt pathway** activation with **beta-catenin** accumulation and transcriptional proliferation

Micro-pearl: **APC** loss activates **Wnt**/**beta-catenin**.

Q127. KRAS step

An adenoma enlarges after acquiring **KRAS** mutation following **APC** loss.

Which **pathway** is amplified?

A. **TGF-beta receptor** overactivation

B. **Bile acid** deconjugation

C. RAS-**MAPK** proliferative signaling that promotes adenoma progression

D. Mismatch repair restoration

E. E-cadherin gain of function

Answer: C. RAS-**MAPK** proliferative signaling that promotes adenoma progression

Micro-pearl: **KRAS** is a progression driver in adenoma-carcinoma sequence.

Q128. p53 late

A villous adenoma progresses to invasive carcinoma with **TP53** loss.

Which interpretation is most accurate?

A. Late loss of DNA-damage checkpoint/apoptosis permits invasive malignant progression

B. **TP53** loss is the earliest initiating **les**ion in all adenomas

C. **TP53** loss proves **Lynch** syndrome

D. **TP53** loss causes hamartoma without dysplasia

E. **TP53** loss prevents chromosomal instability

Answer: A. Late loss of DNA-damage checkpoint/apoptosis permits invasive malignant progression

Micro-pearl: **p53** loss is a late carcinoma progression event.

Q129. Lynch MSI

A right-sided colon cancer in a young patient shows **MSI**-high and loss of **MSH2**/**MSH6** staining.

Which mechanism explains accelerated carcinogenesis?

A. **SMAD4** juvenile polyp stromal expansion

B. **MUTYH** oxidative base-excision failure

C. **APC** germline polyposis with thousands of adenomas only

D. **BRAF**-**CIMP** **MLH1** methylation in every case

E. Mismatch repair failure causes replication slippage and frameshift mutations in microsatellites

Answer: E. Mismatch repair failure causes replication slippage and frameshift mutations in microsatellites

Micro-pearl: **MMR** loss produces **MSI** and frameshift-prone cancer.

Q130. Sporadic MSI

An elderly woman has right-sided **MSI**-high colon cancer with **MLH1** loss, **BRAF** V600E mutation, and **MLH1** promoter methylation.

Which interpretation is best?

A. **Peutz-Jeghers** syndrome is most likely

B. **MUTYH** biallelic disease is diagnostic

C. **APC**-associated **FAP** is proven

D. Germline **MSH2** mutation is confirmed

E. Sporadic serrated/**CIMP** **pathway** is more likely than **Lynch** syndrome

Answer: E. Sporadic serrated/**CIMP pathway** is more likely than **Lynch** syndrome

Micro-pearl: BRAF + **MLH1** methylation supports sporadic **MSI** cancer.

Q131. Serrated pathway

A proximal sessile serrated **les**ion has **BRAF** mutation and CpG island methylator phenotype.

Which mechanism best explains risk?

A. STK11 loss causes arborizing smooth muscle

B. Epige**net**ic silencing including **MLH1** methylation may lead to **MSI**-high carcinoma

C. Classic **APC** first-hit chromosomal instability only

D. E-cadherin loss causes diffuse gastric cancer

E. SMAD4 loss causes juvenile polyps

Answer: B. Epige**net**ic silencing including **MLH1** methylation may lead to **MSI**-high carcinoma

Micro-pearl: Serrated **les**ions can progress through **BRAF**/**CIMP**/**MLH1** methylation.

Q132. FAP

A teenager has hundreds of colorectal adenomas and a germline **APC** mutation.

Which mechanism explains multiplicity?

A. Inherited **APC** loss primes **Wnt** activation; second hits generate numerous adenomas

B. MLH1 methylation causes congenital adenoma burden

C. Biallelic **MUTYH** causes dominant polyposis

D. BRAF mutation in every crypt at birth

E. STK11 causes adenomatous polyps only

Answer: A. Inherited **APC** loss primes **Wnt** activation; second hits generate numerous adenomas

Micro-pearl: FAP is germline **APC** with second-hit adenomas.

Q133. MUTYH

A patient has attenuated polyposis with biallelic **MUTYH** variants.

Which repair defect is central?

A. E-cadherin adhesion failure

B. Mismatch repair failure in microsatellites

C. TGF-beta SMAD4 signaling loss only

D. Wnt activation from germline **APC** only

E. Base-excision repair failure permits oxidative DNA damage mutations

Answer: E. Base-excision repair failure permits oxidative DNA damage mutations

Micro-pearl: MUTYH is recessive base-excision repair polyposis.

Q134. Peutz-Jeghers

A patient has m**uc**ocutaneous pigmentation and hamartomatous polyps with arborizing smooth muscle.

Which gene/**pathway fit**s?

A. BRAF-CIMP serrated **pathway** only

B. MUTYH biallelic repair failure

C. MLH1 methylation only

D. APC loss only

E. STK11/LKB1 tumor-suppressor loss affecting cellular polarity and growth regulation

Answer: E. STK11/LKB1 tumor-suppressor loss affecting cellular polarity and growth regulation

Micro-pearl: Peutz-Jeghers is **STK11** hamartomatous syndrome.

Q135. Juvenile polyposis

A patient with multiple juvenile polyps and AVMs has **SMAD4** mutation.

Which **pathway** is altered?

A. H2 **receptor cAMP** signaling

B. Wnt beta-catenin initiation

C. JAK1 cytokine blockade

D. TGF-beta/BMP signaling dysregulation with hamartomatous growth

E. CYP2E1 oxidative stress

Answer: D. TGF-beta/BMP signaling dysregulation with hamartomatous growth

Micro-pearl: **Juvenile polyposis** involves **SMAD4**/**BMPR1A**.

Q136. Aspirin chemoprevention

A **Lynch** syndrome patient asks why aspirin may reduce CRC risk.

Which mechanism is most plausible?

A. Direct restoration of **MSH2** function

B. Immediate methylation reversal of **MLH1**

C. Selective **BRAF** inhibition in serrated crypts

D. Complete **Wnt pathway** normalization

E. COX/**prostaglandin pathway** modulation reduces inflammation-driven epithelial proliferation and tumor promotion

Answer: E. COX/**prostaglandin pathway** modulation reduces inflammation-driven epithelial proliferation and tumor promotion

Micro-pearl: Aspirin chemoprevention is anti-inflammatory/**prostaglandin** mediated, not **MMR** repair.

Q137. CEA

After curative colon cancer resection, **CEA** is used in surveillance but not as primary screening.

Which **biomarker** principle explains this?

A. **CEA** is tumor-specific and detects all early adenomas

B. **CEA** lacks screening sensitivity/specificity but rising levels may signal recurrence in a known cancer context

C. **CEA** directly measures **Wnt** activation

D. **CEA** normalizes only after colectomy for **UC**

E. **CEA** distinguishes **Lynch** from sporadic **MSI**

Answer: B. **CEA** lacks screening sensitivity/specificity but rising levels may signal recurrence in a known cancer context

Micro-pearl: **CEA** is surveillance **biomarker**, not screening test.

Q138. FIT

A patient asks why **FIT** is better than guaiac testing for lower GI bleeding screening.

Which mechanism is relevant?

A. **FIT** detects upper GI hemoglobin after digestion

B. **FIT** detects bacterial DNA methylation only

C. **FIT** measures **CEA** in stool

D. **FIT** detects human globin from lower GI bleeding with **less** dietary interference

E. **FIT** detects heme peroxidase from any meat source

Answer: D. **FIT** detects human globin from lower GI bleeding with **less** dietary interference

Micro-pearl: **FIT** is human globin immunochemistry.

Q139. IBS visceral hypersensitivity

A patient with **IBS** has normal colonoscopy and exaggerated pain during rectal balloon distension.

Which mechanism explains symptoms?

A. Microscopic ulceration with neutrophils

B. **IgA** villous atrophy

C. Visceral hypersensitivity and altered brain-gut pain processing amplify physiologic stimuli

D. Portal hypertensive colopathy

E. **APC** mutation in nociceptors

Answer: C. Visceral hypersensitivity and altered brain-gut pain processing amplify physiologic stimuli

Micro-pearl: **IBS** is brain-gut interaction with sensory amplification.

Q140. Alosetron

A woman with severe **IBS**-D improves on **alosetron** but is monitored for constipation and **ischemic colitis**.

Which **receptor** explains benefit?

A. Guanylate cyclase-C activation increases secretion

B. Mu-opioid antagonism increases motility

C. **5-HT3** antagonism reduces visceral afferent signaling and slows transit

D. **5-HT4** agonism accelerates transit

E. **TNF-alpha** neutralization heals ulcers

Answer: C. **5-HT3** antagonism reduces visceral afferent signaling and slows transit

Micro-pearl: 5-HT3 blockade helps IBS-D by slowing and sensory modulation.

Q141. Prucalopride

A constipated patient improves with **prucalopride**.

Which mechanism explains prokinetic effect?

A. Mu-opioid agonism decreases transit

B. GC-C activation opens CFTR only

C. Selective 5-HT4 agonism enhances enteric cholinergic peristaltic reflexes

D. JAK inhibition reduces cytokines

E. 5-HT3 blockade slows transit

Answer: C. Selective 5-HT4 agonism enhances enteric cholinergic peristaltic reflexes

Micro-pearl: 5-HT4 agonists stimulate colonic motility.

Q142. Linaclotide

A patient with IBS-C improves with **linaclotide** and reports less pain.

Which intracellular messenger is central?

A. MAPK activation by KRAS

B. cAMP from VIP receptor only

C. IP3-mediated smooth-muscle contraction

D. Guanylate cyclase-C activation increases cGMP, chloride secretion, and analgesic signaling

E. JAK-STAT activation

Answer: D. Guanylate cyclase-C activation increases cGMP, chloride secretion, and analgesic signaling

Micro-pearl: Linaclotide works through GC-C/cGMP.

Q143. Lubiprostone

A patient with chronic idiopathic constipation responds to **lubiprostone**.

Which epithelial effect is intended?

A. Activation of intestinal chloride secretion increases luminal fluid and stool passage

B. S1P receptor modulation traps lymphocytes

C. MLH1 repair restoration

D. COX-1 inhibition lowers prostaglandins

E. 5-HT3 blockade reduces afferents

Answer: A. Activation of intestinal chloride secretion increases luminal fluid and stool passage

Micro-pearl: Lubiprostone increases chloride-rich fluid secretion.

Q144. Eluxadoline

A patient with IBS-D and no gallbladder develops **pancreatitis** after **eluxadoline**.

Which mechanism explains risk?

A. Opioid receptor activity can increase sphincter of Oddi tone and precipitate pancreaticobiliary obstruction

B. GC-C activation raises cGMP

C. TNF-alpha neutralization injures pancreas

D. 5-HT4 agonism accelerates transit

E. Bile acid sequestration blocks ampulla

Answer: A. Opioid receptor activity can increase sphincter of Oddi tone and precipitate pancreaticobiliary obstruction

Micro-pearl: Eluxadoline is risky without gallbladder due to sphincter of Oddi spasm.

Q145. Rifaximin IBS

A patient with bloating-predominant IBS-D improves after **rifaximin**.

Which mechanism is most plausible?

A. Permanent eradication of all colonic bacteria

B. Nonabsorbed antibiotic modulation of gut microbiota and fermentation-related signaling

C. Direct 5-HT3 receptor antagonism

D. H2 receptor blockade

E. APC gene restoration

Answer: B. Nonabsorbed antibiotic modulation of gut microbiota and fermentation-related signaling

Micro-pearl: Rifaximin may modulate microbiota in IBS-D.

Q146. Ischemic colitis

A low-flow episode causes segmental splenic-flexure colitis with hematochezia.

Which vascular concept **fit**s?

A. Radiation causes acute serotonin excess

B. Watershed perfusion vulnerability makes m**uc**osa susceptible to hypoperfusion/reperfusion injury

C. **APC** loss causes sudden infarction

D. Portal vein thrombosis causes every left-sided episode

E. Toxin B directly **des**troys **Rho GTPases**

Answer: B. Watershed perfusion vulnerability makes m**uc**osa susceptible to hypoperfusion/reperfusion injury

Micro-pearl: Watershed zones are **ischemic colitis** traps.

Q147. Radiation proctopathy

Months after pelvic radiation, a patient develops rectal bleeding from telangiectasias.

Which mechanism explains chronic injury?

A. **Bile acid** secretory diarrhea only

B. **MUTYH** repair failure

C. Obliterative endarteritis, ischemia, fibrosis, and fragile neovascular telangiectasia

D. **Th17** transmural inflammation

E. Acute bacterial invasion of crypts

Answer: C. Obliterative endarteritis, ischemia, fibrosis, and fragile neovascular telangiectasia

Micro-pearl: Chronic radiation injury is vascular-ischemic-fibrotic.

Q148. Diverticulitis

A patient has LLQ pain, fever, and CT pericolic fat stranding around sigmoid diverticula.

Which mechanism initiates uncomplicated diverticulitis?

A. Vasa recta rupture causes infection

B. **H. pylori** colonizes sigmoid diverticula

C. **Bile acid**s precipitate calcium bilirubinate

D. **APC** mutation causes abscess

E. Microperforation of a diverticulum triggers localized pericolic inflammation

Answer: E. Microperforation of a diverticulum triggers localized pericolic inflammation

Micro-pearl: Diverticulitis is microperforation/inflammation; **diverticular** bleeding is vasa recta injury.

Q149. C difficile

A hospitalized patient has antibiotic-associated diarrhea and pseudomembranes.

Which molecular injury is central?

A. **BRAF** methylation

B. **IgA tTG** deposition

C. Toxin-mediated gl**uc**osylation of Rho-family GTPases disrupts cytoskeleton and barrier

D. **5-HT3** blockade

E. **Wnt beta-catenin** activation

Answer: C. Toxin-mediated gl**uc**osylation of Rho-family GTPases disrupts cytoskeleton and barrier

Micro-pearl: **C. difficile** toxins disrupt Rho GTPase cytoskeletal signaling.

Q150. Collagenous colitis

A woman with watery diarrhea has normal colonoscopy and a thick subepithelial collagen band on biopsy.

Which mechanism category best **fit**s?

A. Microscopic inflammatory injury with epithelial barrier dysfunction **des**pite normal gross m**uc**osa

B. Transmural granulomatous fistulization

C. Adenoma-carcinoma sequence

D. Portal hypertensive congestion

E. Viral inclusions in endothelial cells

Answer: A. Microscopic inflammatory injury with epithelial barrier dysfunction **des**pite normal gross m**uc**osa

Micro-pearl: Collagenous colitis is histologic, not gross endoscopic disease.

Chapter 7 - Biliary and Pancreas

Q151. Cholesterol stones

An obese multiparous woman has cholesterol gallstones.

Which physicochemical mechanism is most central?

A. Bacterial **beta-glucuronidase** deconjugates bilirubin

B. **Trypsinogen** activates inside acini

C. Hemolysis increases calcium bilirubinate only

D. **IgG4** inflammation narrows bile ducts

E. Biliary cholesterol supersaturation exceeds **bile acid**/phospholipid solubilizing capacity

Answer: E. Biliary cholesterol supersaturation exceeds **bile acid**/phospholipid solubilizing capacity

Micro-pearl: Cholesterol stones require supersaturation, nucleation, and hypomotility.

Q152. Black pigment stones

A patient with hereditary spherocytosis develops multiple black gallbladder stones.

Which mechanism explains stone type?

A. Chronic hemolysis increases bilirubin turnover and calcium bilirubinate precipitation in sterile bile

B. Infected ducts produce brown pigment stones

C. CYP2E1 ROS injures gallbladder

D. Pancreatic reflux causes **choledochal cyst**

E. Cholesterol supersaturation from obesity

Answer: A. Chronic hemolysis increases bilirubin turnover and calcium bilirubinate precipitation in sterile bile

Micro-pearl: Black pigment stones are sterile hemolysis-related pigment stones.

Q153. Brown pigment stones

A patient with recurrent **cholangitis** and biliary stasis develops soft brown CBD stones.

Which mechanism is most precise?

A. Pure cholesterol monohydrate supersaturation

B. Sterile hemolysis in the gallbladder

C. Bacterial **beta-glucuronidase** deconjugates bilirubin, promoting calcium bilirubinate precipitation

D. FXR-driven **bile acid** expansion

E. Eosinophilic duct inflammation

Answer: C. Bacterial **beta-glucuronidase** deconjugates bilirubin, promoting calcium bilirubinate precipitation

Micro-pearl: Brown pigment stones are infection/stasis duct stones.

Q154. Acute cholecystitis

A cystic-duct stone causes RUQ pain, fever, and gallbladder wall thickening.

Which mechanism initiates inflammation?

A. Sphincter of Oddi spasm alone causes gallbladder ischemia

B. Primary bacterial invasion without obstruction is required

C. **IgG4** plasma cells obstruct the cystic duct

D. **Trypsinogen** activates in the gallbladder wall

E. Obstruction causes bile concentration, mucosal injury, **prostaglandin**-mediated inflammation, and secondary infection risk

Answer: E. Obstruction causes bile concentration, mucosal injury, **prostaglandin**-mediated inflammation, and secondary infection risk

Micro-pearl: Cystic duct obstruction initiates acute calculous **cholecystitis**.

Q155. Acalculous cholecystitis

A ventilated septic ICU patient develops gangrenous **cholecystitis** without stones.

Which mechanism is most relevant?

A. Bacterial **beta-glucuronidase** stone formation only

B. Cholesterol supersaturation alone

C. Gallbladder stasis, ischemia, and critical illness impair mucosal defense

D. **IL-13** eosinophilic infiltration

E. **MEN1**-driven endocrine secretion

Answer: C. Gallbladder stasis, ischemia, and critical illness impair mucosal defense

Micro-pearl: Acalculous disease is ischemic/stasis critical illness disease.

Q156. Cholangitis

A patient with CBD stone has fever, jaundice, hypotension, and confusion. ERCP drainage is urgent.

Which mechanism makes drainage essential?

A. V1 antagonism decompresses bile ducts

B. PPI prevents bacteremia by raising gastric pH

C. Bile is sterile because pressure is high

D. Obstruction increases duct pressure causing infected bile reflux into blood and sepsis

E. Antibiotics cannot enter tissues without sphincterotomy

Answer: D. Obstruction increases duct pressure causing infected bile reflux into blood and sepsis

Micro-pearl: **Cholangitis** = infection plus obstruction; drainage is source control.

Q157. Choledocholithiasis labs

A patient with episodic jaundice has CBD stone and cholestatic liver tests.

Which mechanism explains disproportionate ALP/GGT elevation?

A. Pancreatic lipase leaks into bile

B. Hepatocyte necrosis alone releases mitochondrial AST

C. CYP2E1 induction raises GGT only

D. MMR failure increases ALP transcription

E. Biliary obstruction induces cholangiocyte/canalicular enzyme expression and regurgitation

Answer: E. Biliary obstruction induces cholangiocyte/canalicular enzyme expression and regurgitation

Micro-pearl: Obstruction produces cholestatic enzymes through duct/canalicular injury and induction.

Q158. Biliary pancreatitis

A woman develops **pancreatitis** after biliary colic and transient jaundice.

Which mechanism initiates pancreatic injury?

A. Transient ampullary obstruction raises pancreatic duct pressure and promotes premature enzyme activation

B. Bilirubin precipitates inside acinar nuclei

C. Cystic duct obstruction alone activates trypsin

D. Gallbladder mucin directly digests acini

E. IgG4 plasma cells digest duct epithelium

Answer: A. Transient ampullary obstruction raises pancreatic duct pressure and promotes premature enzyme activation

Micro-pearl: Migrating stone at ampulla triggers **pancreatitis**.

Q159. Trypsinogen activation

A patient has early acute **pancreatitis** with acinar injury.

Which **intracellular** event is central?

A. Premature intrapancreatic **trypsinogen** activation overwhelms protective inhibitors and activates digestive enzymes

B. Pancreatic enzymes are fully suppressed

C. **CFTR** overactivity causes autodigestion

D. Insulin **receptor** activation digests acini

E. **Bile acid**s restore lysosomal segregation

Answer: A. Premature intrapancreatic **trypsinogen** activation overwhelms protective inhibitors and activates digestive enzymes

Micro-pearl: Acute **pancreatitis** begins with inappropriate enzyme activation.

Q160. CRP/IL-6

CRP rises 48 hours after acute **pancreatitis** onset and correlates with severity.

Which cytokine-**biomarker** link explains this?

A. **Somatostatin receptor** activation raises **CRP**

B. **TNF-alpha** directly measured as **CRP**

C. **Trypsinogen** converts to **CRP**

D. **IL-6**-driven hepatic acute-phase response induces **CRP** synthesis

E. **CA19-9** induces **CRP** through Lewis antigen

Answer: D. **IL-6**-driven hepatic acute-phase response induces **CRP** synthesis

Micro-pearl: **CRP** is downstream of **IL-6** acute-phase signaling.

Q161. HyperTG pancreatitis

A diabetic patient has triglycerides 2500 mg/dL and **pancreatitis**.

Which mechanism is most relevant?

A. Pancreatic lipase hydrolyzes triglycerides to toxic **free fatty acids** causing microvascular/acinar injury

B. Triglycerides inhibit **CFTR** chloride secretion only

C. Triglycerides mechanically block the ampulla

D. **Bile acid**s precipitate cholesterol stones

E. Chylomicrons neutralize trypsin inhibitors

Answer: A. Pancreatic lipase hydrolyzes triglycerides to toxic **free fatty acids** causing microvascular/acinar injury

Micro-pearl: Severe hypertriglyceridemia causes FFA toxicity and hyperviscosity.

Q162. Chronic pancreatitis pain

A man with calcific chronic **pancreatitis** has severe pain despite ductal decompression.

Which mechanism explains persistent pain?

A. **Bile acid** diarrhea sensitizes pancreas

B. **Gastrin** stimulates nociceptors

C. Acid inactivation of lipase directly causes pain

D. Neural inflammation, fibrosis, and central sensitization maintain pain independent of duct pressure

E. **IL-13** eosinophils invade nerves

Answer: D. Neural inflammation, fibrosis, and central sensitization maintain pain independent of duct pressure

Micro-pearl: Chronic **pancreatitis** pain is neuropathic/inflammatory as well as ductal.

Q163. PRSS1

A family has hereditary **pancreatitis** with early recurrent attacks.

Which mechanism best fits **PRSS1** mutation?

A. Gain-of-function cationic **trypsinogen** increases intrapancreatic trypsin activity

B. **CFTR** over-secretion of bicarbonate

C. **MEN1** mutation activates islet cells

D. **SPINK1** excess blocks trypsin

E. **VHL** loss produces serous cysts

Answer: A. Gain-of-function cationic **trypsinogen** increases intrapancreatic trypsin activity

Micro-pearl: **PRSS1** mutations promote trypsin activation.

Q164. SPINK1

A patient with recurrent **pancreatitis** has a **SPINK1** variant.

Which mechanism is most relevant?

A. Increased **CFTR** bicarbonate secretion

B. **BRAF-CIMP** methylation

C. Decreased enteropeptidase in duodenum

D. **GNAS** mutation in ducts

E. Reduced trypsin inhibitor defense lowers threshold for autodigestive injury

Answer: E. Reduced trypsin inhibitor defense lowers threshold for autodigestive injury

Micro-pearl: **SPINK1** is a protective trypsin inhibitor.

Q165. CFTR pancreatitis

A young adult with recurrent **pancreatitis** has **CFTR**-related duct disease.

Which mechanism predisposes?

A. Cholesterol supersaturation

B. Defective ductal chloride/bicarbonate secretion causes viscous secretions and impaired enzyme flushing

C. **Somatostatin receptor** overexpression

D. Cationic **trypsinogen** gain of function

E. Excess bicarbonate dissolves duct plugs

Answer: B. Defective ductal chloride/bicarbonate secretion causes viscous secretions and impaired enzyme flushing

Micro-pearl: CFTR mutations impair ductal fluid/bicarbonate secretion.

Q166. Exocrine insufficiency

A chronic pancreatitis patient develops steatorrhea and low fecal elastase.

Which mechanism explains symptoms?

A. H. pylori urease injures villi

B. JAK inhibition reduces enterocyte transport

C. Loss of pancreatic lipase delivery impairs triglyceride digestion below the functional threshold

D. Gastrin excess blocks micelles

E. Colonic bile acids increase fat absorption

Answer: C. Loss of pancreatic lipase delivery impairs triglyceride digestion below the functional threshold

Micro-pearl: Lipase loss is central to pancreatic steatorrhea.

Q167. AIP type 1

A man has painless jaundice, diffuse pancreatic enlargement, high IgG4, and steroid response.

Which mechanism fits?

A. Cytotoxic T-cell destruction of beta cells only

B. Premature trypsin activation from gallstones

C. IgG4-related lymphoplasmacytic fibroinflammatory disease involving pancreas and bile ducts

D. Cholesterol supersaturation

E. CagA-mediated pancreatic epithelial dysplasia

Answer: C. IgG4-related lymphoplasmacytic fibroinflammatory disease involving pancreas and bile ducts

Micro-pearl: Type 1 AIP is IgG4-related and steroid-responsive.

Q168. AIP type 2

A younger patient with ulcerative colitis has pancreatitis; biopsy shows granulocytic epithelial lesions without systemic IgG4 disease.

Which mechanism fits?

A. PRSS1 gain-of-function trypsin activation

B. KRAS/SMAD4 carcinoma pathway

C. IgG4-positive storiform fibrosis with salivary involvement

D. Bacterial beta-glucuronidase stone formation

E. Duct-centric neutrophilic epithelial injury characteristic of type 2 autoimmune pancreatitis

Answer: E. Duct-centric neutrophilic epithelial injury characteristic of type 2 autoimmune pancreatitis

Micro-pearl: Type 2 AIP is GEL/IBD-associated, not classic IgG4 disease.

Q169. Pseudocyst vs WON

Five weeks after necrotizing pancreatitis, CT shows a walled collection with fluid and nonliquid debris.

Which diagnosis/mechanism is best?

A. Serous cystadenoma from VHL loss

B. Walled-off necrosis containing necrotic solid material after necrotizing pancreatitis

C. Simple pseudocyst without necrotic debris

D. Choledochal cyst from pancreaticobiliary malunion

E. Mucinous cystic neoplasm with ovarian stroma

Answer: B. Walled-off necrosis containing necrotic solid material after necrotizing pancreatitis

Micro-pearl: Debris means WON, not simple pseudocyst.

Q170. IPMN

A main-duct pancreatic cyst communicates with the duct and produces mucin.

Which molecular/pathologic concept fits?

A. Ovarian-type stroma without duct communication

B. MEN1 islet hyperplasia only

C. Intraductal mucinous neoplasia often involving KRAS/GNAS alterations and ductal obstruction

D. SPINK1 inhibitor failure

E. VHL-driven glycogen-rich microcysts

Answer: C. Intraductal mucinous neoplasia often involving KRAS/GNAS alterations and ductal obstruction

Micro-pearl: **IPMN** is duct-communicating mucinous neoplasia.

Q171. MCN

A middle-aged woman has a pancreatic body-tail mucinous cyst that does not communicate with the duct and has ovarian-type stroma.

Which lesion is most likely?

A. Solid pseudopapillary tumor

B. Branch-duct **IPMN**

C. Pseudocyst

D. Mucinous cystic neoplasm with malignant potential

E. **Serous cystadenoma**

Answer: D. Mucinous cystic neoplasm with malignant potential

Micro-pearl: **MCN**: woman, body/tail, ovarian stroma, no duct communication.

Q172. Serous cystadenoma

A microcystic pancreatic lesion with central scar is found incidentally; cytology suggests glycogen-rich cuboidal cells.

Which **pathway** is classically associated?

A. **GNAS** mutation in mucinous duct neoplasm

B. **KRAS**/**SMAD4** invasive duct cancer sequence only

C. **MEN1** endocrine neoplasia

D. **IgG4** plasma-cell **pancreatitis**

E. **VHL**-related **pathway** in a usually benign serous cystic neoplasm

Answer: E. **VHL**-related **pathway** in a usually benign serous cystic neoplasm

Micro-pearl: **Serous cystadenoma** is **VHL**/glycogen-rich and usually benign.

Q173. Pancreatic cancer stroma

A pancreatic ductal adenocarcinoma has **KRAS** mutation, **SMAD4** loss, and dense **desmoplastic** stroma.

Which mechanism explains treatment resistance partly?

A. Activated pancreatic **stellate cells** generate fibrotic stroma that limits drug delivery and supports tumor signaling

B. **CagA** signaling drives all **pancreatic cancer**s

C. **Bile acid** micelles dissolve chemotherapy

D. **IgG4** fibrosis predicts steroid cure

E. **CFTR** overactivity flushes drugs away

Answer: A. Activated pancreatic **stellate cells** generate fibrotic stroma that limits drug delivery and supports tumor signaling

Micro-pearl: PDAC biology includes **KRAS**, **SMAD4**, and **desmoplastic** stellate-cell stroma.

Q174. CA19-9 trap

A jaundiced patient with suspected **pancreatic cancer** has markedly elevated **CA19-9** before biliary drainage.

Which **biomarker** limitation is most important?

A. **CA19-9** is specific for **pancreatic cancer**

B. **CA19-9** detects all stage I tumors

C. **CA19-9** distinguishes **NET** from adenocarcinoma reliably

D. **CA19-9** is unaffected by biliary obstruction

E. Cholestasis can falsely elevate **CA19-9**, and Lewis antigen-negative patients may not produce it

Answer: E. Cholestasis can falsely elevate **CA19-9**, and Lewis antigen-negative patients may not produce it

Micro-pearl: **CA19-9** is imperfect: cholestasis and Lewis antigen status matter.

Q175. Pancreatic NET

A well-differentiated pancreatic **NET** expresses **somatostatin receptor**s and is evaluated with **receptor** imaging.

Which translational mechanism is exploited?

A. **CA19-9 receptor** binding localizes **NET**s

B. **BRAF-CIMP** drives **receptor** imaging

C. CYP2E1 activation creates radiotracer uptake

D. **KRAS** mutation predicts **octreotide** response

E. **Somatostatin receptor** expression permits functional imaging and peptide **receptor**-targeted therapy

Answer: E. Somatostatin receptor expression permits functional imaging and peptide **receptor**-targeted therapy

Micro-pearl: NET imaging/therapy exploits **somatostatin receptor** biology.

Final Section - 100 Integrated Moderate-to-Long Case Scenarios

Each case uses a longer clinical scenario and close **pathway**-level distractors. The correct answer is the most proximate **micro-mechanism** that explains the final clue, not merely a true statement about the disease.

Case 1 / Q176. Chapter 1 - Esophagus - PPI meal timing - integrated case

A man with LA grade C reflux is told to take omeprazole before breakfast. Symptoms improve when he follows meal timing, but not when he takes it randomly at night. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. **Histamine** H2 **receptor** blockade prevents nocturnal acid escape

B. **Gastrin receptor** blockade peaks only after fasting

C. **GABA-B receptor** activation suppresses transient **LES** relaxations

D. Meal-stimulated recruitment of active canalicular **H+/K+-ATPase** pumps permits irreversible **PPI** binding

E. Direct intragastric acid neutralization requires food buffering

Answer: D. Meal-stimulated recruitment of active canalicular **H+/K+-ATPase** pumps permits irreversible **PPI** binding

Micro-pearl: PPI efficacy depends on active proton pumps exposed after meal stimulation.

Case 2 / Q177. Chapter 1 - Esophagus - PCAB pharmacology - integrated case

A patient with severe nocturnal reflux is switched from a **PPI** to **vonoprazan**-like therapy and develops faster, more sustained acid suppression. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Competitive H2 **receptor** blockade with parietal-cell **cAMP** suppression

B. Irreversible sulfhydryl binding after acid-canaliculus activation

C. Muscarinic M3 blockade reducing vagal **acetylcholine** signaling

D. Potassium-competitive inhibition of **H+/K+-ATPase** without obligatory acid activation

E. **GABA-B** agonism reducing transient **LES** relaxations

Answer: D. Potassium-competitive inhibition of **H+/K+-ATPase** without obligatory acid activation

Micro-pearl: PCABs inhibit the proton pump by potassium-competitive binding, distinct from acid-activated **PPI**s.

Case 3 / Q178. Chapter 1 - Esophagus - H2 blocker tachyphylaxis - integrated case

A woman takes **famotidine** nightly for reflux. It works for 10 days, then loses effect despite adherence. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. **Somatostatin** D-cell activation suppresses antral **gastrin**

B. Loss of **LES** nitrergic neurons causes secondary acid secretion

C. Compensatory **gastrin** and **acetylcholine** acid-secretory signaling bypass **histamine** blockade

D. Irreversible proton pump inhibition requires de novo pump synthesis

E. Permanent destruction of **ECL** cells prevents **histamine** release

Answer: C. Compensatory **gastrin** and **acetylcholine** acid-secretory signaling bypass **histamine** blockade

Micro-pearl: H2 blockers target one acid **pathway**; **gastrin** and **acetylcholine** can maintain secretion.

Case 4 / Q179. Chapter 1 - Esophagus - Baclofen and TLESR - integrated case

A patient on adequate **PPI** has persistent regurgitation. Impedance shows weakly acidic reflux temporally related to transient **LES** relaxations. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. 5-HT4 agonism increasing gastric accommodation

B. Alpha-1 blockade of the crural diaphragm

C. Topical steroid suppression of epithelial IL-13 signaling

D. Irreversible H+/K+-ATPase inhibition of active pumps

E. GABA-B agonism reduces transient lower esophageal sphincter relaxations

Answer: E. GABA-B agonism reduces transient lower esophageal sphincter relaxations

Micro-pearl: Baclofen is a TLESR-targeting strategy for regurgitation/non-acid reflux.

Case 5 / Q180. Chapter 1 - Esophagus - Alginate - integrated case

Postprandial regurgitation persists despite normal acid suppression. An alginate preparation helps more than increasing the PPI dose. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Restoration of LES nitrergic inhibitory neurons

B. Direct neutralization of pepsinogen gene transcription

C. Covalent inhibition of newly synthesized proton pumps

D. Reduction of esophageal eosinophil trafficking through eotaxin blockade

E. Formation of a floating mechanical raft that limits proximal migration of refluxate

Answer: E. Formation of a floating mechanical raft that limits proximal migration of refluxate

Micro-pearl: Alginates are barrier therapy, not receptor pharmacology.

Case 6 / Q181. Chapter 1 - Esophagus - Hiatal hernia barrier - integrated case

An obese man has severe erosive reflux and a large sliding hiatal hernia. HRM shows a weak EGJ barrier. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Excessive nitrergic inhibition prevents esophageal clearance

B. Acid-induced conversion of columnar to squamous mucosa

C. Gastric somatostatin excess increases intragastric pressure

D. IL-13-mediated basal-zone hyperplasia causes reflux

E. Separation of LES and crural diaphragm disrupts the composite anti-reflux barrier

Answer: E. Separation of LES and crural diaphragm disrupts the composite anti-reflux barrier

Micro-pearl: A sliding hernia weakens the EGJ barrier by separating LES from crural diaphragm.

Case 7 / Q182. Chapter 1 - Esophagus - Scleroderma esophagus - integrated case

A woman with systemic sclerosis has severe reflux, absent smooth-muscle peristalsis, and a hypotensive LES. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Cricopharyngeal dysfunction causing Killian dehiscence

B. Spastic distal contractions from impaired deglutitive inhibition

C. Food antigen-driven eosinophil recruitment causing rings

D. Poor reflux clearance plus weak LES from smooth-muscle atrophy and fibrosis

E. Excess ECL histamine release causing isolated acid hypersecretion

Answer: D. Poor reflux clearance plus weak LES from smooth-muscle atrophy and fibrosis

Micro-pearl: Scleroderma creates a low-pressure barrier and ineffective clearance.

Case 8 / Q183. Chapter 1 - Esophagus - Reflux hypersensitivity - integrated case

A woman has normal endoscopy and normal acid exposure, but impedance shows strong symptom association with physiologic weakly acidic reflux. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. PPI failure producing persistent pathological acid exposure

B. EoE-related IL-13/eotaxin eosinophil recruitment

C. Peripheral and central sensitization makes physiologic reflux events painful

D. Loss of myenteric NO/VIP neurons causing EGJ obstruction

E. Candida plaque adherence causing chemical nociception

Answer: C. Peripheral and central sensitization makes physiologic reflux events painful

Micro-pearl: Normal AET with positive symptom association = reflux hypersensitivity.

Case 9 / Q184. Chapter 1 - Esophagus - Functional heartburn - integrated case

A patient with burning chest discomfort has normal endoscopy, normal HRM, normal acid exposure, and negative symptom association on impedance. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which micro-mechanism is the best causal explanation in this case?

A. POEM because IRP is usually elevated

B. Dupilumab because type 2 inflammation is dominant

C. Higher-dose PPI because acid exposure is underestimated

D. Baclofen because symptom association is strongly positive

E. Neuromodulation of visceral pain processing rather than escalation of anti-reflux therapy

Answer: E. Neuromodulation of visceral pain processing rather than escalation of anti-reflux therapy

Micro-pearl: Functional heartburn is pain processing without reflux-symptom coupling.

Case 10 / Q185. Chapter 1 - Esophagus - Barrett metaplasia - integrated case

An obese man with long-standing GERD has intestinal metaplasia in documented columnar-lined distal esophagus. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which micro-mechanism is the best causal explanation in this case?

A. Chronic acid-bile injury reprograms epithelial progenitor differentiation toward intestinal columnar phenotype

B. Gastrin excess from antral G cells causes squamous intestinalization

C. IgE-mediated food allergy creates metaplastic glands

D. Candida invasion converts squamous cells into columnar epithelium

E. Loss of LES nitrergic neurons directly induces goblet cells

Answer: A. Chronic acid-bile injury reprograms epithelial progenitor differentiation toward intestinal columnar phenotype

Micro-pearl: Barrett is metaplastic adaptation to chronic reflux injury.

Case 11 / Q186. Chapter 1 - Esophagus - Barrett p53/p16 - integrated case

A Barrett surveillance biopsy shows low-grade dysplasia with abnormal p53 immunostaining and p16 loss. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which micro-mechanism is the best causal explanation in this case?

A. PPI tachyphylaxis causes p53 accumulation

B. Active HSV replication in squamous epithelium produces pseudodysplasia

C. Eosinophilic degranulation causes reversible atypia only

D. Tumor-suppressor pathway disruption marks clonal neoplastic progression

E. Achalasia-related stasis causes p16 overexpression without cancer risk

Answer: D. Tumor-suppressor pathway disruption marks clonal neoplastic progression

Micro-pearl: p53 and p16 abnormalities are progression biomarkers in Barrett neoplasia.

Case 12 / Q187. Chapter 1 - Esophagus - T1a endoscopic therapy - integrated case

EMR of a nodular Barrett lesion shows T1a intramucosal adenocarcinoma with clear margins and no lymphovascular invasion. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which micro-mechanism is the best causal explanation in this case?

A. RFA corrects the reflux mechanism causing cancer

B. Mucosal cancers cannot recur after EMR alone

C. Chemotherapy is more effective before tissue diagnosis

D. All Barrett cancers lack lymphatics regardless of depth

E. Intramucosal confinement has low lymph-node metastatic potential compared with submucosal invasion

Answer: E. Intramucosal confinement has low lymph-node metastatic potential compared with submucosal invasion

Micro-pearl: Depth of invasion predicts nodal risk; T1a selected lesions may be endoscopically treated.

Case 13 / Q188. Chapter 2 - Stomach - H pylori urease - integrated case

A patient with active chronic gastritis has organisms in the mucus layer despite very low gastric luminal pH. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Somatostatin release raises intragastric pH

B. VacA neutralizes acid by binding hydrogen ions

C. CagA directly inhibits parietal-cell proton pumps

D. Bacterial catalase converts acid to chloride

E. Urease generates ammonia to buffer the immediate peribacterial microenvironment

Answer: E. Urease generates ammonia to buffer the immediate peribacterial microenvironment

Micro-pearl: Urease is a local buffering survival factor.

Case 14 / Q189. Chapter 2 - Stomach - CagA signaling - integrated case

A man with H. pylori gastritis develops intestinal metaplasia. The strain expresses CagA. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Urease directly methylates MLH1 promoter

B. Flagellin irreversibly inhibits H+/K+-ATPase

C. VacA activates CCK-B receptors on ECL cells

D. Injected CagA perturbs SHP-2 and epithelial polarity/proliferation pathways

E. LPS causes MEN1 mutation in chief cells

Answer: D. Injected CagA perturbs SHP-2 and epithelial polarity/proliferation pathways

Micro-pearl: CagA alters intracellular signaling and epithelial phenotype.

Case 15 / Q190. Chapter 2 - Stomach - VacA - integrated case

A virulent H. pylori strain produces epithelial vacuolation and immune modulation. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Irreversible COX-1 inhibition in epithelial cells

B. Formation of intracellular vacuoles with mitochondrial and T-cell functional effects

C. IgA immune-complex deposition in capillaries

D. Activation of EGFR by TGF-alpha mimicry

E. Direct phosphorylation of beta-catenin by SHP-2

Answer: B. Formation of intracellular vacuoles with mitochondrial and T-cell functional effects

Micro-pearl: VacA is a vacuolating cytotoxin with epithelial and immune effects.

Case 16 / Q191. Chapter 2 - Stomach - Duodenal ulcer physiology - integrated case

A young man has antral-predominant H. pylori and recurrent duodenal ulcer. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Reduced antral somatostatin increases gastrin-driven parietal-cell acid output

B. VacA causes isolated LES relaxation

C. Urease destroys pancreatic bicarbonate secretion

D. CagA blocks bile acid micelles in duodenum

E. Corpus atrophy produces complete achlorhydria

Answer: A. Reduced antral somatostatin increases gastrin-driven parietal-cell acid output

Micro-pearl: Antral H. pylori -> low somatostatin -> high gastrin -> high acid.

Case 17 / Q192. Chapter 2 - Stomach - Cancer pathway - integrated case

A patient has corpus-predominant H. pylori gastritis, atrophy, intestinal metaplasia, and dysplasia. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which micro-mechanism is the best causal explanation in this case?

A. Transient gastrin elevation creates immediate invasive cancer

B. Acute urease buffering directly transforms cells

C. NSAID COX inhibition creates MALT lymphoma only

D. Chronic inflammation drives atrophy-metaplasia-dysplasia with genomic injury

E. Type I hypersensitivity produces signet-ring cells

Answer: D. Chronic inflammation drives atrophy-metaplasia-dysplasia with genomic injury

Micro-pearl: Gastric adenocarcinoma risk follows chronic inflammatory progression.

Case 18 / Q193. Chapter 2 - Stomach - NSAID mucosal injury - integrated case

A patient on naproxen develops a gastric ulcer without H. pylori. The examiner focuses on mucosal defense rather than acid. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which micro-mechanism is the best causal explanation in this case?

A. COX-1 prostaglandin depletion reduces mucus, bicarbonate, epithelial restitution, and mucosal blood flow

B. Gastrin receptor activation increases acid and pepsin only

C. Urease ammonia causes direct ulceration

D. IL-13 recruits eosinophils into the antrum

E. JAK inhibition suppresses epithelial renewal

Answer: A. COX-1 prostaglandin depletion reduces mucus, bicarbonate, epithelial restitution, and mucosal blood flow

Micro-pearl: NSAIDs injure by prostaglandin loss plus topical injury.

Case 19 / Q194. Chapter 2 - Stomach - Misoprostol - integrated case

A high-risk NSAID user cannot stop anti-inflammatory therapy. Misoprostol is considered but limited by diarrhea. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which micro-mechanism is the best causal explanation in this case?

A. M3 blockade increases bicarbonate secretion

B. H2 receptor agonism improves nocturnal mucosal blood flow

C. CCK-B blockade suppresses ECL histamine release

D. FXR activation reduces bile acid reflux

E. EP receptor activation reduces acid cAMP signaling and augments mucosal defense

Answer: E. EP receptor activation reduces acid cAMP signaling and augments mucosal defense

Micro-pearl: Misoprostol replaces prostaglandin signaling.

Case 20 / Q195. Chapter 2 - Stomach - PPI clot stabilization - integrated case

A bleeding gastric ulcer receives high-dose PPI after endoscopic hemostasis. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which micro-mechanism is the best causal explanation in this case?

A. PPI reduces portal venous pressure

B. **PPI** reverses aspirin platelet inhibition

C. **PPI** directly cross-links fibrin

D. Raising intragastric pH improves platelet aggregation and clot stability over the visible vessel

E. **PPI** inhibits thrombin generation

Answer: D. Raising intragastric pH improves platelet aggregation and clot stability over the visible vessel

Micro-pearl: Acid impairs clot; **PPI** stabilizes hemostasis by pH elevation.

Case 21 / Q196. Chapter 2 - Stomach - Gastrinoma diarrhea - integrated case

A man with refractory ulcers has fasting **gastrin** 2500 pg/mL and gastric pH 1.2 with watery diarrhea. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. **Gastrin** opens **CFTR** channels in colonocytes

B. **Gastrin** blocks villous **tTG** activity

C. Massive acid load inactivates pancreatic enzymes and injures small-bowel m**uc**osa

D. **Gastrin** suppresses **bile acid** synthesis through FXR

E. **Gastrin** inhibits motilin **receptor**s

Answer: C. Massive acid load inactivates pancreatic enzymes and injures small-bowel m**uc**osa

Micro-pearl: ZES diarrhea is acid-mediated maldigestion and m**uc**osal injury.

Case 22 / Q197. Chapter 2 - Stomach - Secretin paradox - integrated case

A suspected **gastrin**oma patient undergoes secretin stimulation testing. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Normal G cells increase **gastrin** after secretin

B. **Gastrin**oma cells increase **gastrin** secretion after secretin exposure

C. Secretin diagnoses **H. pylori** through **urease** activation

D. Secretin directly acidifies the stomach

E. All acid-suppressed patients suppress **gastrin** after secretin

Answer: B. **Gastrin**oma cells increase **gastrin** secretion after secretin exposure

Micro-pearl: Secretin paradoxically stimulates **gastrin**oma **gastrin** secretion.

Case 23 / Q198. Chapter 2 - Stomach - Autoimmune gastritis - integrated case

A woman has macrocytosis, low B12, high **gastrin**, and corpus-predominant atrophic gastritis. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Parietal-cell loss causes achlorhydria, removing acid-mediated negative feedback on antral G cells

B. Intrinsic factor antibody stimulates **CCK-B receptor**s

C. Antral D-cell excess suppresses **gastrin**

D. Chief-cell apoptosis increases CCK release

E. **H. pylori urease** directly secretes **gastrin**

Answer: A. Parietal-cell loss causes achlorhydria, removing acid-mediated negative feedback on antral G cells

Micro-pearl: Achlorhydria removes feedback inhibition and raises **gastrin**.

Case 24 / Q199. Chapter 2 - Stomach - Type I gastric NET - integrated case

A patient with auto**immune** gastritis develops multiple small gastric body neuroendocrine tumors. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. **Somatostatin** excess stimulates **ECL** proliferation

B. **H. pylori** **CagA** directly transforms beta cells

C. **MEN1** mutation in every **ECL** cell is required

D. Chronic hyper**gastrin**emia stimulates **ECL**-cell hyperplasia and neoplasia

E. Ghrelin **receptor** activation prod**uc**es body polyps

Answer: D. Chronic hyper**gastrin**emia stimulates **ECL**-cell hyperplasia and neoplasia

Micro-pearl: Type I gastric **NET**s are hyper**gastrin**emia/**ECL** driven.

Case 25 / Q200. Chapter 3 - Gastrointestinal Bleeding: Upper, Lower and Small Bowel - Acid and clot - integrated case

A bleeding duodenal ulcer is clipped s**uc**cessfully, then high-dose **PPI** is started. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. **PPI** activates thrombin through vitamin K

B. **PPI** directly constricts the gastroduodenal artery

C. Higher gastric pH improves platelet aggregation and clot stability at the treated vessel

D. **PPI** lowers portal pressure by beta-2 blockade

E. **PPI** reverses aspirin **COX-1** inhibition

Answer: C. Higher gastric pH improves platelet aggregation and clot stability at the treated vessel

Micro-pearl: Post-hemostasis **PPI** stabilizes clot by increasing pH.

Case 26 / Q201. Chapter 3 - Gastrointestinal Bleeding: Upper, Lower and Small Bowel - Forrest IIa - integrated case

Endoscopy shows a nonbleeding visible vessel in an ulcer base. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Adherent clot always has no underlying vessel

B. A superficial artery remains exposed with high risk of recurrent arterial hemorrhage

C. Flat pigmented spot is equivalent to spurting hemorrhage

D. Portal hypertensive oozing is the dominant mechanism

E. Clean fibrin base indicates no arterial exposure

Answer: B. A superficial artery remains exposed with high risk of recurrent arterial hemorrhage

Micro-pearl: Visible vessel = exposed artery = high rebleeding risk.

Case 27 / Q202. Chapter 3 - Gastrointestinal Bleeding: Upper, Lower and Small Bowel - Epinephrine adjunct - integrated case

Epinephrine injection stops ulcer bleeding temporarily, but the endoscopist adds clips. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Injection causes permanent fibrosis immediately

B. Epinephrine has no effect on local vessels

C. Thermal therapy is needed only for varices

D. Clips only red**uc**e acid secretion

E. Vasoconstriction and tamponade are transient without durable vessel coaptation or thermal sealing

Answer: E. Vasoconstriction and tamponade are transient without durable vessel coaptation or thermal sealing

Micro-pearl: Epinephrine is adjunctive, not definitive monotherapy.

Case 28 / Q203. Chapter 3 - Gastrointestinal Bleeding: Upper, Lower and Small Bowel - Hemostatic powder - integrated case

Diffuse malignant gastric oozing is treated with hemostatic powder as a bridge. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Topical barrier formation and concentration of clotting factors over broad oozing surfaces

B. Selective arterial embolization from the lumen

C. Irreversible inhibition of tumor angiogenesis

D. Portal-pressure reduction via splanchnic vasodilation

E. **H. pylori** eradication at the bleeding surface

Answer: A. Topical barrier formation and concentration of clotting factors over broad oozing surfaces

Micro-pearl: Powder is temporary surface hemostasis for diffuse bleeding.

Case 29 / Q204. Chapter 3 - Gastrointestinal Bleeding: Upper, Lower and Small Bowel - Dieulafoy lesion - integrated case

A patient has massive hematemesis from a tiny normal-appearing gastric mucosal defect with a spurting vessel. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Large-caliber submucosal artery erodes through a minute mucosal defect

B. Bile reflux causing foveolar hyperplasia

C. Diffuse capillary ectasia from portal hypertension

D. **Immune**-complex vasculitis of venules

E. Acid-induced wide ulcer crater

Answer: A. Large-caliber submucosal artery erodes through a minute mucosal defect

Micro-pearl: **Dieulafoy** = big artery, tiny defect.

Case 30 / Q205. Chapter 3 - Gastrointestinal Bleeding: Upper, Lower and Small Bowel - Angiodysplasia - integrated case

An elderly patient with CKD has recurrent painless right-colon bleeding from flat vascular lesions. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. **Bile acid**s deconjugate bilirubin in the colon

B. **Gastrin** excess opens colonic vessels

C. **IgA** deposition injures arterioles

D. Intermittent low-grade venous obstruction and mucosal hypoxia promote ectatic fragile vessels

E. **APC** loss causes vascular dysplasia

Answer: D. Intermittent low-grade venous obstruction and mucosal hypoxia promote ectatic fragile vessels

Micro-pearl: **Angiodysplasia** is acquired ectatic vascular malformation.

Case 31 / Q206. Chapter 3 - Gastrointestinal Bleeding: Upper, Lower and Small Bowel - Heyde syndrome - integrated case

A patient with severe aortic stenosis and recurrent **angiodysplasia** bleeding has low high-molecular-weight **vWF** multimers. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. **COX-2** excess creates thrombocytosis

B. **IgG4** infiltrates vascular walls

C. Portal pressure increases colonic venous pressure

D. Shear-induced **vWF** multimer loss impairs platelet adhesion at fragile angiodysplastic vessels

E. **Bile acid** diarrhea causes mucosal erosion

Answer: D. Shear-induced **vWF** multimer loss impairs platelet adhesion at fragile angiodysplastic vessels

Micro-pearl: Aortic stenosis can cause acquired **vWF** defect.

Case 32 / Q207. Chapter 3 - Gastrointestinal Bleeding: Upper, Lower and Small Bowel - Octreotide in varices - integrated case

A cirrhotic patient with hematemesis receives **octreotide** before endoscopy. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the

differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Beta-2 agonism constricts mesenteric arterio**les**

B. H2 blockade red**uc**es **variceal** pressure

C. Alpha-1 blockade red**uc**es intrahepatic resistance

D. Red**uc**ed splanchnic vasodilatory peptide signaling lowers portal venous inflow

E. Thrombin activation seals varices

Answer: D. Red**uc**ed splanchnic vasodilatory peptide signaling lowers portal venous inflow

Micro-pearl: Octreotide red**uc**es portal inflow by splanchnic vasoconstrictive effects.

Case 33 / Q208. Chapter 3 - Gastrointestinal Bleeding: Upper, Lower and Small Bowel - Terlipressin - integrated case

A cirrhotic patient with **variceal** bleeding and renal dysfunction receives **terlipressin**. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Somatostatin receptor blockade increases mesenteric flow

B. V1-mediated splanchnic vasoconstriction red**uc**es portal inflow and improves effective arterial volume

C. V2-mediated free-water excretion lowers portal pressure

D. FXR activation increases **bile acid** secretion

E. Beta-1 blockade red**uc**es cardiac output only

Answer: B. V1-mediated splanchnic vasoconstriction red**uc**es portal inflow and improves effective arterial volume

Micro-pearl: Terlipressin is **V1**-predominant vasoconstrictive therapy.

Case 34 / Q209. Chapter 3 - Gastrointestinal Bleeding: Upper, Lower and Small Bowel - Carvedilol - integrated case

A patient with large esophageal varices starts **carvedilol**. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. H2 blockade red**uc**es gastric acid and **variceal** erosion

B. FXR blockade improves sinusoidal nitric oxide

C. V1 antagonism red**uc**es portal pressure

D. Beta-1/beta-2 blockade red**uc**es flow and alpha-1 blockade red**uc**es intrahepatic resistance

E. Selective beta-1 blockade increases splanchnic vasoconstriction

Answer: D. Beta-1/beta-2 blockade red**uc**es flow and alpha-1 blockade red**uc**es intrahepatic resistance

Micro-pearl: Carvedilol affects inflow and resistance.

Case 35 / Q210. Chapter 3 - Gastrointestinal Bleeding: Upper, Lower and Small Bowel - Band ligation - integrated case

Variceal banding is performed after active bleeding stops. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Somatostatin receptor activation scars the varix

B. Acid suppression collapses portal collaterals

C. Hemospray ind**uc**es portal decompression

D. Epinephrine permanently **des**troys varices

E. Mechanical strangulation prod**uc**es thrombosis, necrosis, and fibrosis of the **variceal** channel

Answer: E. Mechanical strangulation prod**uc**es thrombosis, necrosis, and fibrosis of the **variceal** channel

Micro-pearl: EVL eradicates varices by l**iga**tion-ind**uc**ed thrombosis/fibrosis.

Case 36 / Q211. Chapter 3 - Gastrointestinal Bleeding: Upper, Lower and Small Bowel - PHG vs GAVE - integrated case

A cirrhotic patient has mosaic fundic mucosa with diffuse oozing, not antral stripes. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Portal hypertension causes mucosal and submucosal vascular congestion with impaired defense

B. Eosinophilic mucosal remodeling

C. Antral ectatic vessels independent of portal pressure

D. **CagA**-mediated epithelial dysplasia

E. **Immune**-complex capillaritis with low C4

Answer: A. Portal hypertension causes mucosal and submucosal vascular congestion with impaired defense

Micro-pearl: PHG is portal-pressure-related congestion.

Case 37 / Q212. Chapter 4 - Small Bowel Diseases, Diarrhea and Malabsorption - Celiac deamidation - integrated case

A woman with iron deficiency and diarrhea has villous atrophy and positive **tTG IgA**. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Pancreatic trypsin converts gliadin to **bile acid**

B. FXR suppresses gliadin transport

C. **Urease** converts gluten to ammonia

D. Tissue transglutaminase deamidates gliadin, increasing HLA-DQ2/DQ8 binding

E. IgE crosslinks mast cells in villi

Answer: D. Tissue transglutaminase deamidates gliadin, increasing HLA-DQ2/DQ8 binding

Micro-pearl: tTG deamidation enhances HLA binding in **celiac** disease.

Case 38 / Q213. Chapter 4 - Small Bowel Diseases, Diarrhea and Malabsorption - IgA deficiency - integrated case

A patient has villous atrophy but negative **tTG IgA** and very low total **IgA**. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. **IgA** deficiency excludes **celiac** disease

B. **IgA** deficiency can make **IgA**-based **celiac** serology falsely negative

C. **IgA** deficiency prevents villous injury

D. **IgA** deficiency proves **Whipple** disease

E. **IgA** deficiency causes false-positive **tTG IgA**

Answer: B. **IgA** deficiency can make **IgA**-based **celiac** serology falsely negative

Micro-pearl: Check total **IgA** when **celiac** serology is negative but suspicion remains.

Case 39 / Q214. Chapter 4 - Small Bowel Diseases, Diarrhea and Malabsorption - Dermatitis herpetiformis - integrated case

A man with gluten-sensitive enteropathy has grouped itchy vesicles on elbows and knees with granular **IgA** in dermal papillae. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. **IgG4** against pancreatic ducts

B. Epidermal transglutaminase-related **IgA** autoimmunity

C. **H. pylori CagA** cross-reactivity

D. IgE against wheat causing urticaria

E. ANCA against colonic neutrophils

Answer: B. Epidermal transglutaminase-related **IgA** autoimmunity

Micro-pearl: Dermatitis herpetiformis is **IgA**/eTG-linked.

Case 40 / Q215. Chapter 4 - Small Bowel Diseases, Diarrhea and Malabsorption - Refractory celiac II - integrated case

A patient with treated **celiac** disease has persistent villous atrophy and aberrant clonal IELs. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. **MEN1** pancreatic **NET**

B. Antigen-dependent **MALT** lymphoma only

C. **H. pylori**-driven diffuse gastric cancer

D. Secretin-responsive **gastrin**oma

E. Clonal intraepithelial T-cell expansion with risk of enteropathy-associated T-cell lymphoma

Answer: E. Clonal intraepithelial T-cell expansion with risk of enteropathy-associated T-cell lymphoma

Micro-pearl: RCD type II is premalignant clonal IEL disease.

Case 41 / Q216. Chapter 4 - Small Bowel Diseases, Diarrhea and Malabsorption - Olmesartan enteropathy - integrated case

A patient with sprue-like enteropathy has negative **celiac** serology and no response to gluten withdrawal. Symptoms resolve after stopping olmesartan. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. HLA-DQ2 obligate gluten presentation

B. Drug-induced **immune**-mediated enteropathy mimicking villous atrophy

C. Pancreatic lipase deficiency

D. Bacterial deconjugation of **bile acid**s only

E. Ectopic acid secretion from **Meckel** mucosa

Answer: B. Drug-induced **immune**-mediated enteropathy mimicking villous atrophy

Micro-pearl: Olmesartan can mimic **celiac**-like enteropathy.

Case 42 / Q217. Chapter 4 - Small Bowel Diseases, Diarrhea and Malabsorption - Tropical sprue - integrated case

A traveler with chronic diarrhea, weight loss, low folate, and B12 deficiency improves with tetracycline and folate. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Postinfectious small-bowel mucosal injury with bacterial overgrowth-like features causing malabsorption

B. **Bile acid** pool depletion from ileal resection

C. **tTG**-mediated gliadin presentation only

D. D2 **receptor** antagonism

E. **Whipple** macrophage infiltration

Answer: A. Postinfectious small-bowel mucosal injury with bacterial overgrowth-like features causing malabsorption

Micro-pearl: Tropical sprue is postinfectious malabsorptive enteropathy.

Case 43 / Q218. Chapter 4 - Small Bowel Diseases, Diarrhea and Malabsorption - Whipple disease - integrated case

A man has diarrhea, arthralgia, weight loss, hyperpigmentation, and cognitive changes. Duodenal biopsy shows PAS-positive macrophages. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Impaired macrophage clearance of Tropheryma **whipple**i with systemic infiltration

B. IgA gliadin immune injury

C. Bile acid deconjugation from SIBO only

D. Mast-cell IgE food allergy

E. Bacterial toxin B Rho glucosylation

Answer: A. Impaired macrophage clearance of Tropheryma whipplei with systemic infiltration

Micro-pearl: Whipple is systemic macrophage-laden infection.

Case 44 / Q219. Chapter 4 - Small Bowel Diseases, Diarrhea and Malabsorption - SIBO malabsorption - integrated case

A systemic sclerosis patient has bloating, steatorrhea, and low B12. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. HLA-DQ8 gluten presentation

B. Pancreatic acinar destruction reduces lipase secretion

C. Small-bowel stasis permits bacteria to deconjugate bile acids and consume nutrients

D. Excess ileal FGF19 suppresses bile acid synthesis

E. Brush-border lactase deficiency alone

Answer: C. Small-bowel stasis permits bacteria to deconjugate bile acids and consume nutrients

Micro-pearl: SIBO causes bile acid deconjugation and nutrient competition.

Case 45 / Q220. Chapter 4 - Small Bowel Diseases, Diarrhea and Malabsorption - Breath testing trap - integrated case

A patient has rapid orocecal transit and an early hydrogen rise on breath test. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Methane excludes constipation

B. Early hydrogen rise may reflect rapid transit rather than true proximal bacterial overgrowth

C. A negative test excludes all dysbiosis

D. Hydrogen rise always proves SIBO

E. Breath testing directly measures bile acid pool

Answer: B. Early hydrogen rise may reflect rapid transit rather than true proximal bacterial overgrowth

Micro-pearl: Breath tests can be confounded by transit.

Case 46 / Q221. Chapter 4 - Small Bowel Diseases, Diarrhea and Malabsorption - Bile acid diarrhea - integrated case

A Crohn patient with limited ileal disease has watery diarrhea responsive to cholestyramine. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Complete bile acid pool depletion impairs micelles

B. Secretin stimulates gastrin from a tumor

C. Pancreatic lipase excess injures colon

D. Unabsorbed bile acids reaching colon stimulate secretion and motility

E. Celiac villous atrophy causes osmotic diarrhea

Answer: D. Unabsorbed bile acids reaching colon stimulate secretion and motility

Micro-pearl: Limited ileal bile acid malabsorption causes secretory colonic diarrhea.

Case 47 / Q222. Chapter 4 - Small Bowel Diseases, Diarrhea and Malabsorption - Extensive ileal loss - integrated case

After extensive ileal resection, a patient has steatorrhea worsened by cholestyramine. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. **Celiac** serology becomes positive

B. **Bile acid** pool depletion impairs micelle formation and fat absorption

C. Bacterial overgrowth cannot occur without ileum

D. Gastric acid secretion is abolished

E. Colonic **bile acid** exposure is still the only problem

Answer: B. **Bile acid** pool depletion impairs micelle formation and fat absorption

Micro-pearl: Extensive ileal loss depletes **bile acid**s, causing steatorrhea.

Case 48 / Q223. Chapter 4 - Small Bowel Diseases, Diarrhea and Malabsorption - Short bowel adaptation - integrated case

A **short bowel** patient with colon in continuity gradually needs **less** parenteral support. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Colonic fermentation of carbohydrates to short-chain fatty acids salvages calories and fluid

B. Complete restoration of ileal **bile acid** transport

C. **Gastrin** suppression increases absorption

D. **CFTR** closure produces villous growth

E. Pancreatic lipase hypersecretion replaces lost mucosa

Answer: A. Colonic fermentation of carbohydrates to short-chain fatty acids salvages calories and fluid

Micro-pearl: Colon in continuity improves energy/fluid salvage.

Case 49 / Q224. Chapter 5 - Inflammatory Bowel Disease - NOD2 Crohn - integrated case

A young man with ileal **Crohn** disease has a **NOD2** risk variant. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. **COX-1 prostaglandin** depletion

B. **V1 receptor**-mediated vasoconstriction

C. Excess **IL-4 receptor** signaling in squamous epithelium

D. **MLH1** promoter methylation causing **MSI**

E. Impaired bacterial peptidoglycan sensing and Paneth-cell defensin response

Answer: E. Impaired bacterial peptidoglycan sensing and Paneth-cell defensin response

Micro-pearl: **NOD2** links microbial sensing to ileal **Crohn** susceptibility.

Case 50 / Q225. Chapter 5 - Inflammatory Bowel Disease - ATG16L1 - integrated case

A **Crohn** patient has Paneth-cell abnormalities and an **ATG16L1** risk allele. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Constitutive KIT activation

B. Defective autophagy/xenophagy alters bacterial handling and epithelial stress responses

C. Excess H2 **histamine** signaling

D. Viral DNA polymerase inhibition

E. Failed **tTG** deamidation of gliadin

Answer: B. Defective autophagy/xenophagy alters bacterial handling and epithelial stress responses

Micro-pearl: Autophagy genes shape microbial handling in **Crohn** disease.

Case 51 / Q226. Chapter 5 - Inflammatory Bowel Disease - IL-23/Th17 - integrated case

A patient with **Crohn** disease responds to selective **IL-23 p19** blockade after anti-TNF failure. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. IL-5 eosinophil maturation only

B. **IL-23**-driven maintenance of pathogenic **Th17**-type inflammation

C. **CFTR** chloride secretion in **IBS**-C

D. **GABA-B TLESR** suppression

E. H2 **receptor** acid secretion

Answer: B. **IL-23**-driven maintenance of pathogenic **Th17**-type inflammation

Micro-pearl: **IL-23** sustains **Th17** inflammation; **p19** blockade is selective.

Case 52 / Q227. Chapter 5 - Inflammatory Bowel Disease - Anti-TNF - integrated case

A fistulizing **Crohn** patient improves on **infliximab**. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. **Gastrin** suppression improves transmural inflammation

B. **TNF-alpha** neutralization reduces macrophage/T-cell cytokine amplification and tissue destruction

C. **Alpha-4 beta-7** blockade alone closes all fistula tracts

D. **JAK** inhibition is the only fistula mechanism

E. **Bile acid** sequestration heals fistulas

Answer: B. **TNF-alpha** neutralization reduces macrophage/T-cell cytokine amplification and tissue destruction

Micro-pearl: Anti-TNF is especially useful for fistulizing **Crohn**.

Case 53 / Q228. Chapter 5 - Inflammatory Bowel Disease - Anti-drug antibodies - integrated case

Loss of response to **infliximab** occurs with low trough and high anti-drug antibodies. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. **Bile acid** binding of monoclonal antibody

B. Immunogenic drug clearance lowers effective **TNF-alpha** neutralization

C. Mechanistic escape with high trough level

D. **PPI**-induced biologic degradation

E. **IL-23** overexpression despite adequate TNF blockade only

Answer: B. Immunogenic drug clearance lowers effective **TNF-alpha** neutralization

Micro-pearl: Low trough + antibodies = pharmacokinetic immunogenic failure.

Case 54 / Q229. Chapter 5 - Inflammatory Bowel Disease - Thiopurine combo - integrated case

Combination **azathioprine** with **infliximab** is considered early in severe **Crohn** disease. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. **Azathioprine** activates **S1P receptors**

B. Thiopurines block **alpha-4 beta-7** integrin

C. Thiopurines selectively inhibit **IL-23 p19**

D. **Azathioprine** directly neutralizes **TNF-alpha**

E. Reduced anti-drug antibody formation improves biologic durability

Answer: E. Reduced anti-drug antibody formation improves biologic durability

Micro-pearl: Thiopurines may reduce immunogenicity to anti-TNF.

Case 55 / Q230. Chapter 5 - Inflammatory Bowel Disease - Vedolizumab - integrated case

A **UC** patient with infection concerns is started on **vedolizumab**. Additional data are internally consistent with this diagnosis,

and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. **TNF-alpha** neutralization throughout tissues

B. Systemic alpha-4 blockade prevents CNS lymphocyte surveillance

C. **S1P receptor** agonism retains lymphocytes

D. **IL-12**/23 **p40** blockade

E. **Alpha-4 beta-7** integrin blockade prevents lymphocyte binding to **MAdCAM-1** in gut mucosa

Answer: E. **Alpha-4 beta-7** integrin blockade prevents lymphocyte binding to **MAdCAM-1** in gut mucosa

Micro-pearl: **Vedolizumab** blocks gut-homing **alpha-4 beta-7**.

Case 56 / Q231. Chapter 5 - Inflammatory Bowel Disease - Natalizumab PML - integrated case

A **Crohn** patient asks why **natalizumab** has a special neurologic infection risk compared with **vedolizumab**. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. **S1P** modulation increases CSF lymphocyte trafficking

B. Broader alpha-4 integrin blockade impairs CNS **immune** surveillance and increases PML risk

C. TNF blockade directly activates JC virus polymerase

D. **JAK**1 inhibition causes viral demyelination exclusively

E. Selective gut **MAdCAM-1** blockade increases JC virus entry

Answer: B. Broader alpha-4 integrin blockade impairs CNS **immune** surveillance and increases PML risk

Micro-pearl: **Natalizumab** is **les**s gut-selective than **vedolizumab**.

Case 57 / Q232. Chapter 5 - Inflammatory Bowel Disease - Ustekinumab - integrated case

Crohn disease improves after **ustekinumab**. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. **JAK**1 ATP-binding site

B. **TNF-alpha** soluble trimer

C. **IL-4 receptor** alpha

D. **p40** subunit shared by **IL-12** and **IL-23**

E. **p19** subunit unique to **IL-23**

Answer: D. **p40** subunit shared by **IL-12** and **IL-23**

Micro-pearl: **Ustekinumab** targets **p40**; **risankizumab** targets **p19**.

Case 58 / Q233. Chapter 5 - Inflammatory Bowel Disease - Risankizumab - integrated case

A **Crohn** patient receives a biologic selectively targeting **IL-23** without blocking **IL-12**. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. **Alpha-4 beta-7** integrin

B. **IL-23 p19** subunit

C. **TNF-alpha**

D. **IL-12**/23 **p40** subunit

E. **S1P receptor** 1

Answer: B. **IL-23 p19** subunit

Micro-pearl: **p19** blockade is selective **IL-23** inhibition.

Case 59 / Q234. Chapter 5 - Inflammatory Bowel Disease - JAK inhibitors - integrated case

A **UC** patient responds rapidly to an oral small molecule rather than an antibody infusion. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has

narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. T-cell trapping through **S1P** agonism only

B. Integrin blockade of cell trafficking only

C. Luminal binding of **bile acids**

D. Extracellular cytokine neutralization of TNF alone

E. **Intracellular JAK** inhibition interrupts multiple cytokine **receptor** signals

Answer: E. Intracellular JAK inhibition interrupts multiple cytokine **receptor** signals

Micro-pearl: JAK inhibitors are **intracellular** signal blockers.

Case 60 / Q235. Chapter 5 - Inflammatory Bowel Disease - Tofacitinib risks - integrated case

Before **tofacitinib**, a patient is screened for zoster and thrombosis risk. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. H2 **receptor** inhibition

B. Gut-selective integrin blockade

C. Topical epithelial 5-ASA action

D. Pan-**JAK** cytokine signaling interference affects inflammatory and antiviral/thrombotic **pathways**

E. **IL-23 p19** blockade only

Answer: D. Pan-**JAK** cytokine signaling interference affects inflammatory and antiviral/thrombotic **pathways**

Micro-pearl: Broad **JAK** blockade gives broad immunologic effects and risks.

Case 61 / Q236. Chapter 5 - Inflammatory Bowel Disease - Upadacitinib - integrated case

A refractory **UC** patient starts a **JAK**1-preferential inhibitor. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. **TNF-alpha** ligand neutralization

B. **Alpha-4 beta-7**/MAdCAM blockade

C. Preferential blockade of **JAK**1-dependent cytokine **pathways** while sparing some **JAK**2 hematopoietic signaling

D. Selective inhibition of IL-5 **receptor** eosinophils

E. **S1P receptor** internalization

Answer: C. Preferential blockade of **JAK**1-dependent cytokine **pathways** while sparing some **JAK**2 hematopoietic signaling

Micro-pearl: JAK selectivity modifies efficacy/toxicity expectations.

Case 62 / Q237. Chapter 5 - Inflammatory Bowel Disease - Ozanimod - integrated case

A **UC** patient develops lymphopenia after **ozanimod**. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. **COX-1** inhibition

B. **S1P receptor** modulation retains lymphocytes in lymphoid tissue and reduces gut trafficking

C. **MAdCAM-1** overexpression

D. Direct **TNF-alpha** apoptosis

E. **IL-13** epithelial blockade

Answer: B. S1P receptor modulation retains lymphocytes in lymphoid tissue and reduces gut trafficking

Micro-pearl: S1P modulators reduce lymphocyte egress.

Case 63 / Q238. Chapter 5 - Inflammatory Bowel Disease - Ozanimod bradycardia - integrated case

First-dose monitoring is considered in a patient with conduction disease before **S1P** modulator therapy. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical

team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. **S1P receptor** effects can alter cardiac nodal signaling causing bradyarrhythmia risk

B. 5-ASA inhibits sodium channels

C. **Alpha-4 beta-7** blockade slows AV node

D. Anti-IL23 blocks SA node **IL-23**

E. TNF neutralization prolongs QT directly

Answer: A. **S1P receptor** effects can alter cardiac nodal signaling causing bradyarrhythmia risk

Micro-pearl: **S1P** biology has cardiac conduction implications.

Case 64 / Q239. Chapter 5 - Inflammatory Bowel Disease - 5-ASA - integrated case

A patient with mild distal **UC** improves with rectal **mesalamine**. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Topical anti-inflammatory effects on epithelial mucosa including **prostaglandin**/leukotriene and NF-kB-related **pathway**s

B. **Alpha-4 beta-7** blockade

C. **S1P receptor** internalization

D. Pan-**JAK** inhibition

E. Systemic **TNF-alpha** neutralization

Answer: A. Topical anti-inflammatory effects on epithelial mucosa including **prostaglandin**/leukotriene and NF-kB-related **pathway**s

Micro-pearl: 5-ASA works topically in **UC** mucosa.

Case 65 / Q240. Chapter 5 - Inflammatory Bowel Disease - Steroids - integrated case

IV steroids improve acute severe **UC** within days but are not used for maintenance. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Integrin blockade preventing trafficking

B. Glucocorticoid **receptor** transcriptional repression of multiple inflammatory genes

C. Permanent deletion of autoreactive T cells

D. Microbiome restoration

E. Selective mucosal healing by epithelial proliferation only

Answer: B. Glucocorticoid **receptor** transcriptional repression of multiple inflammatory genes

Micro-pearl: Steroids are broad transcriptional anti-inflammatory induction therapy.

Case 66 / Q241. Chapter 6 - Large Bowel Diseases, CRC, Polyps, Polyposis, IBS, Radiation and Ischemic Colitis - APC beta-catenin - integrated case

A sporadic tubular adenoma shows **APC** loss. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. **KRAS** loss suppressing **MAPK**

B. **p53** activation causing apoptosis

C. **Wnt pathway** activation with **beta-catenin** accumulation and transcriptional proliferation

D. **MLH1** methylation causing **MSI** immediately

E. **STK11** hamartomatous stromal overgrowth

Answer: C. **Wnt pathway** activation with **beta-catenin** accumulation and transcriptional proliferation

Micro-pearl: **APC** loss activates **Wnt**/**beta-catenin**.

Case 67 / Q242. Chapter 6 - Large Bowel Diseases, CRC, Polyps, Polyposis, IBS, Radiation and Ischemic Colitis - KRAS step - integrated case

An adenoma enlarges after acquiring **KRAS** mutation following **APC** loss. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. E-cadherin gain of function

B. RAS-**MAPK** proliferative signaling that promotes adenoma progression

C. Mismatch repair restoration

D. **TGF-beta receptor** overactivation

E. **Bile acid** deconjugation

Answer: B. RAS-**MAPK** proliferative signaling that promotes adenoma progression

Micro-pearl: KRAS is a progression driver in adenoma-carcinoma sequence.

Case 68 / Q243. Chapter 6 - Large Bowel Diseases, CRC, Polyps, Polyposis, IBS, Radiation and Ischemic Colitis - p53 late - integrated case

A villous adenoma progresses to invasive carcinoma with **TP53** loss. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. **TP53** loss prevents chromosomal instability

B. Late loss of DNA-damage checkpoint/apoptosis permits invasive malignant progression

C. **TP53** loss causes hamartoma without dysplasia

D. **TP53** loss is the earliest initiating **les**ion in all adenomas

E. **TP53** loss proves **Lynch** syndrome

Answer: B. Late loss of DNA-damage checkpoint/apoptosis permits invasive malignant progression

Micro-pearl: p53 loss is a late carcinoma progression event.

Case 69 / Q244. Chapter 6 - Large Bowel Diseases, CRC, Polyps, Polyposis, IBS, Radiation and Ischemic Colitis - Lynch MSI - integrated case

A right-sided colon cancer in a young patient shows **MSI**-high and loss of **MSH2**/**MSH6** staining. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. **APC** germline polyposis with thousands of adenomas only

B. Mismatch repair failure causes replication slippage and frameshift mutations in microsatellites

C. **SMAD4** juvenile polyp stromal expansion

D. **BRAF**-**CIMP** **MLH1** methylation in every case

E. **MUTYH** oxidative base-excision failure

Answer: B. Mismatch repair failure causes replication slippage and frameshift mutations in microsatellites

Micro-pearl: MMR loss prod**uc**es **MSI** and frameshift-prone cancer.

Case 70 / Q245. Chapter 6 - Large Bowel Diseases, CRC, Polyps, Polyposis, IBS, Radiation and Ischemic Colitis - Sporadic MSI - integrated case

An elderly woman has right-sided **MSI**-high colon cancer with **MLH1** loss, **BRAF** V600E mutation, and **MLH1** promoter methylation. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. **MUTYH** biallelic disease is diagnostic

B. Germline **MSH2** mutation is confirmed

C. **Peutz-Jeghers** syndrome is most likely

D. **APC**-associated **FAP** is proven

E. Sporadic serrated/**CIMP** **pathway** is more likely than **Lynch** syndrome

Answer: E. Sporadic serrated/**CIMP** **pathway** is more likely than **Lynch** syndrome

Micro-pearl: **BRAF** + **MLH1** methylation supports sporadic **MSI** cancer.

Case 71 / Q246. Chapter 6 - Large Bowel Diseases, CRC, Polyps, Polyposis, IBS, Radiation and Ischemic Colitis - Serrated pathway - integrated case

A proximal sessile serrated **les**ion has **BRAF** mutation and CpG island methylator phenotype. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Classic **APC** first-hit chromosomal instability only

B. Epige**net**ic silencing including **MLH1** methylation may lead to **MSI**-high carcinoma

C. E-cadherin loss causes diffuse gastric cancer

D. **SMAD4** loss causes juvenile polyps

E. **STK11** loss causes arborizing smooth muscle

Answer: B. Epige**net**ic silencing including **MLH1** methylation may lead to **MSI**-high carcinoma

Micro-pearl: Serrated **les**ions can progress through **BRAF**/**CIMP**/**MLH1** methylation.

Case 72 / Q247. Chapter 6 - Large Bowel Diseases, CRC, Polyps, Polyposis, IBS, Radiation and Ischemic Colitis - FAP - integrated case

A teenager has hundreds of colorectal adenomas and a germline **APC** mutation. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. **STK11** causes adenomatous polyps only

B. **BRAF** mutation in every crypt at birth

C. Biallelic **MUTYH** causes dominant polyposis

D. **MLH1** methylation causes congenital adenoma burden

E. Inherited **APC** loss primes **Wnt** activation; second hits generate numerous adenomas

Answer: E. Inherited **APC** loss primes **Wnt** activation; second hits generate numerous adenomas

Micro-pearl: **FAP** is germline **APC** with second-hit adenomas.

Case 73 / Q248. Chapter 6 - Large Bowel Diseases, CRC, Polyps, Polyposis, IBS, Radiation and Ischemic Colitis - MUTYH - integrated case

A patient has attenuated polyposis with biallelic **MUTYH** variants. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Mismatch repair failure in microsatellites

B. **TGF-beta** **SMAD4** signaling loss only

C. **Wnt** activation from germline **APC** only

D. E-cadherin adhesion failure

E. Base-excision repair failure permits oxidative DNA damage mutations

Answer: E. Base-excision repair failure permits oxidative DNA damage mutations

Micro-pearl: **MUTYH** is recessive base-excision repair polyposis.

Case 74 / Q249. Chapter 6 - Large Bowel Diseases, CRC, Polyps, Polyposis, IBS, Radiation and Ischemic Colitis - Peutz-Jeghers - integrated case

A patient has m**uc**ocutaneous pigmentation and hamartomatous polyps with arborizing smooth muscle. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. **MLH1** methylation only

B. **BRAF**-**CIMP** serrated **pathway** only

C. **MUTYH** biallelic repair failure

D. **APC** loss only

E. **STK11**/LKB1 tumor-suppressor loss affecting cellular polarity and growth regulation

Answer: E. **STK11**/LKB1 tumor-suppressor loss affecting cellular polarity and growth regulation

Micro-pearl: **Peutz-Jeghers** is **STK11** hamartomatous syndrome.

Case 75 / Q250. Chapter 6 - Large Bowel Diseases, CRC, Polyps, Polyposis, IBS, Radiation and Ischemic Colitis - Juvenile polyposis - integrated case

A patient with multiple juvenile polyps and AVMs has **SMAD4** mutation. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. H2 **receptor cAMP** signaling

B. **JAK**1 cytokine blockade

C. CYP2E1 oxidative stress

D. **TGF-beta**/BMP signaling dysregulation with hamartomatous growth

E. **Wnt beta-catenin** initiation

Answer: D. **TGF-beta**/BMP signaling dysregulation with hamartomatous growth

Micro-pearl: **Juvenile polyposis** involves **SMAD4**/**BMPR1A**.

Case 76 / Q251. Chapter 6 - Large Bowel Diseases, CRC, Polyps, Polyposis, IBS, Radiation and Ischemic Colitis - Aspirin chemoprevention - integrated case

A **Lynch** syndrome patient asks why aspirin may reduce CRC risk. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. COX/**prostaglandin pathway** modulation reduces inflammation-driven epithelial proliferation and tumor promotion

B. Direct restoration of **MSH2** function

C. Selective **BRAF** inhibition in serrated crypts

D. Complete **Wnt pathway** normalization

E. Immediate methylation reversal of **MLH1**

Answer: A. COX/**prostaglandin pathway** modulation reduces inflammation-driven epithelial proliferation and tumor promotion

Micro-pearl: Aspirin chemoprevention is anti-inflammatory/**prostaglandin** mediated, not **MMR** repair.

Case 77 / Q252. Chapter 6 - Large Bowel Diseases, CRC, Polyps, Polyposis, IBS, Radiation and Ischemic Colitis - CEA - integrated case

After curative colon cancer resection, **CEA** is used in surveillance but not as primary screening. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. **CEA** is tumor-specific and detects all early adenomas

B. **CEA** normalizes only after colectomy for **UC**

C. **CEA** distinguishes **Lynch** from sporadic **MSI**

D. **CEA** directly measures **Wnt** activation

E. **CEA** lacks screening sensitivity/specificity but rising levels may signal recurrence in a known cancer context

Answer: E. **CEA** lacks screening sensitivity/specificity but rising levels may signal recurrence in a known cancer context

Micro-pearl: **CEA** is surveillance **biomarker**, not screening test.

Case 78 / Q253. Chapter 6 - Large Bowel Diseases, CRC, Polyps, Polyposis, IBS, Radiation and Ischemic Colitis - FIT - integrated case

A patient asks why **FIT** is better than guaiac testing for lower GI bleeding screening. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. **FIT** detects heme peroxidase from any meat source

B. **FIT** detects bacterial DNA methylation only

C. **FIT** detects human globin from lower GI bleeding with **less** dietary interference

D. **FIT** detects upper GI hemoglobin after digestion

E. **FIT** measures **CEA** in stool

Answer: C. **FIT** detects human globin from lower GI bleeding with **less** dietary interference

Micro-pearl: **FIT** is human globin immunochemistry.

Case 79 / Q254. Chapter 6 - Large Bowel Diseases, CRC, Polyps, Polyposis, IBS, Radiation and Ischemic Colitis - IBS visceral hypersensitivity - integrated case

A patient with **IBS** has normal colonoscopy and exaggerated pain during rectal balloon distension. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Portal hypertensive colopathy

B. **IgA** villous atrophy

C. **APC** mutation in nociceptors

D. Visceral hypersensitivity and altered brain-gut pain processing amplify physiologic stimuli

E. Microscopic ulceration with neutrophils

Answer: D. Visceral hypersensitivity and altered brain-gut pain processing amplify physiologic stimuli

Micro-pearl: **IBS** is brain-gut interaction with sensory amplification.

Case 80 / Q255. Chapter 6 - Large Bowel Diseases, CRC, Polyps, Polyposis, IBS, Radiation and Ischemic Colitis - Alosetron - integrated case

A woman with severe **IBS**-D improves on **alosetron** but is monitored for constipation and **ischemic colitis**. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Guanylate cyclase-C activation increases secretion

B. **5-HT3** antagonism reduces visceral afferent signaling and slows transit

C. **TNF-alpha** neutralization heals ulcers

D. Mu-opioid antagonism increases motility

E. **5-HT4** agonism accelerates transit

Answer: B. **5-HT3** antagonism reduces visceral afferent signaling and slows transit

Micro-pearl: **5-HT3** blockade helps **IBS**-D by slowing and sensory modulation.

Case 81 / Q256. Chapter 6 - Large Bowel Diseases, CRC, Polyps, Polyposis, IBS, Radiation and Ischemic Colitis - Prucalopride - integrated case

A constipated patient improves with **prucalopride**. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. **5-HT3** blockade slows transit

B. Selective **5-HT4** agonism enhances enteric cholinergic peristaltic reflexes

C. **GC-C** activation opens **CFTR** only

D. Mu-opioid agonism decreases transit

E. **JAK** inhibition reduces cytokines

Answer: B. Selective **5-HT4** agonism enhances enteric cholinergic peristaltic reflexes

Micro-pearl: **5-HT4** agonists stimulate colonic motility.

Case 82 / Q257. Chapter 6 - Large Bowel Diseases, CRC, Polyps, Polyposis, IBS, Radiation and Ischemic Colitis - Linaclotide - integrated case

A patient with **IBS**-C improves with **linaclotide** and reports **les**s pain. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Guanylate cyclase-C activation increases **cGMP**, chloride secretion, and analgesic signaling

B. **JAK**-STAT activation

C. **MAPK** activation by **KRAS**

D. **cAMP** from VIP **receptor** only

E. IP3-mediated smooth-muscle contraction

Answer: A. Guanylate cyclase-C activation increases **cGMP**, chloride secretion, and analgesic signaling

Micro-pearl: **Linaclotide** works through **GC-C**/**cGMP**.

Case 83 / Q258. Chapter 7 - Biliary and Pancreas - Cholesterol stones - integrated case

An obese multiparous woman has cho**les**terol gallstones. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Bacterial **beta-glucuronidase** deconjugates bilirubin

B. Hemolysis increases calcium bilirubinate only

C. **Trypsinogen** activates inside acini

D. Biliary cho**les**terol supersaturation exceeds **bile acid**/phospholipid solubilizing capacity

E. **IgG4** inflammation narrows bile d**uc**ts

Answer: D. Biliary cho**les**terol supersaturation exceeds **bile acid**/phospholipid solubilizing capacity

Micro-pearl: Cho**les**terol stones require supersaturation, n**uc**leation, and hypomotility.

Case 84 / Q259. Chapter 7 - Biliary and Pancreas - Black pigment stones - integrated case

A patient with hereditary spherocytosis develops multiple black gallbladder stones. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Cho**les**terol supersaturation from obesity

B. Infected d**uc**ts prod**uc**e brown pigment stones

C. Chronic hemolysis increases bilirubin turnover and calcium bilirubinate precipitation in sterile bile

D. CYP2E1 ROS injures gallbladder

E. Pancreatic reflux causes **choledochal cyst**

Answer: C. Chronic hemolysis increases bilirubin turnover and calcium bilirubinate precipitation in sterile bile

Micro-pearl: Black pigment stones are sterile hemolysis-related pigment stones.

Case 85 / Q260. Chapter 7 - Biliary and Pancreas - Brown pigment stones - integrated case

A patient with recurrent **cholangitis** and biliary stasis develops soft brown CBD stones. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Sterile hemolysis in the gallbladder

B. Pure cho**les**terol monohydrate supersaturation

C. Bacterial **beta-glucuronidase** deconjugates bilirubin, promoting calcium bilirubinate precipitation

D. FXR-driven **bile acid** expansion

E. Eosinophilic d**uc**t inflammation

Answer: C. Bacterial **beta-glucuronidase** deconjugates bilirubin, promoting calcium bilirubinate precipitation

Micro-pearl: Brown pigment stones are infection/stasis d**uc**t stones.

Case 86 / Q261. Chapter 7 - Biliary and Pancreas - Acute cholecystitis - integrated case

A cystic-duct stone causes RUQ pain, fever, and gallbladder wall thickening. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. **Trypsinogen** activates in the gallbladder wall

B. Primary bacterial invasion without obstruction is required

C. **IgG4** plasma cells obstruct the cystic duct

D. Sphincter of Oddi spasm alone causes gallbladder ischemia

E. Obstruction causes bile concentration, mucosal injury, **prostaglandin**-mediated inflammation, and secondary infection risk

Answer: E. Obstruction causes bile concentration, mucosal injury, **prostaglandin**-mediated inflammation, and secondary infection risk

Micro-pearl: Cystic duct obstruction initiates acute calculous **cholecystitis**.

Case 87 / Q262. Chapter 7 - Biliary and Pancreas - Acalculous cholecystitis - integrated case

A ventilated septic ICU patient develops gangrenous **cholecystitis** without stones. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. **MEN1**-driven endocrine secretion

B. Cholesterol supersaturation alone

C. **IL-13** eosinophilic infiltration

D. Bacterial **beta-glucuronidase** stone formation only

E. Gallbladder stasis, ischemia, and critical illness impair mucosal defense

Answer: E. Gallbladder stasis, ischemia, and critical illness impair mucosal defense

Micro-pearl: Acalculous disease is ischemic/stasis critical illness disease.

Case 88 / Q263. Chapter 7 - Biliary and Pancreas - Cholangitis - integrated case

A patient with CBD stone has fever, jaundice, hypotension, and confusion. ERCP drainage is urgent. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. **PPI** prevents bacteremia by raising gastric pH

B. Bile is sterile because pressure is high

C. Antibiotics cannot enter tissues without sphincterotomy

D. **V1** antagonism decompresses bile ducts

E. Obstruction increases duct pressure causing infected bile reflux into blood and sepsis

Answer: E. Obstruction increases duct pressure causing infected bile reflux into blood and sepsis

Micro-pearl: **Cholangitis** = infection plus obstruction; drainage is source control.

Case 89 / Q264. Chapter 7 - Biliary and Pancreas - Choledocholithiasis labs - integrated case

A patient with episodic jaundice has CBD stone and cholestatic liver tests. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Biliary obstruction induces cholangiocyte/canalicular enzyme expression and regurgitation

B. **MMR** failure increases ALP transcription

C. Hepatocyte necrosis alone releases mitochondrial AST

D. Pancreatic lipase leaks into bile

E. CYP2E1 induction raises GGT only

Answer: A. Biliary obstruction induces cholangiocyte/canalicular enzyme expression and regurgitation

Micro-pearl: Obstruction produces cholestatic enzymes through duct/canalicular injury and induction.

Case 90 / Q265. Chapter 7 - Biliary and Pancreas - Biliary pancreatitis - integrated case

A woman develops **pancreatitis** after biliary colic and transient jaundice. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Bilirubin precipitates inside acinar n**uc**lei

B. **IgG4** plasma cells digest d**uc**t epithelium

C. Gallbladder m**uc**in directly digests acini

D. Cystic d**uc**t obstr**uc**tion alone activates trypsin

E. Transient ampullary obstr**uc**tion raises pancreatic d**uc**t pressure and promotes premature enzyme activation

Answer: E. Transient ampullary obstr**uc**tion raises pancreatic d**uc**t pressure and promotes premature enzyme activation

Micro-pearl: Migrating stone at ampulla triggers **pancreatitis**.

Case 91 / Q266. Chapter 7 - Biliary and Pancreas - Trypsinogen activation - integrated case

A patient has early acute **pancreatitis** with acinar injury. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. **Bile acid**s restore lysosomal segregation

B. **CFTR** overactivity causes autodigestion

C. Insulin **receptor** activation digests acini

D. Pancreatic enzymes are fully suppressed

E. Premature intrapancreatic **trypsinogen** activation overwhelms protective inhibitors and activates digestive enzymes

Answer: E. Premature intrapancreatic **trypsinogen** activation overwhelms protective inhibitors and activates digestive enzymes

Micro-pearl: Acute **pancreatitis** begins with inappropriate enzyme activation.

Case 92 / Q267. Chapter 7 - Biliary and Pancreas - CRP/IL-6 - integrated case

CRP rises 48 hours after acute **pancreatitis** onset and correlates with severity. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. **Trypsinogen** converts to **CRP**

B. **CA19-9** ind**uc**es **CRP** through Lewis antigen

C. **Somatostatin receptor** activation raises **CRP**

D. **TNF-alpha** directly measured as **CRP**

E. **IL-6**-driven hepatic acute-phase response ind**uc**es **CRP** synthesis

Answer: E. **IL-6**-driven hepatic acute-phase response ind**uc**es **CRP** synthesis

Micro-pearl: **CRP** is downstream of **IL-6** acute-phase signaling.

Case 93 / Q268. Chapter 7 - Biliary and Pancreas - HyperTG pancreatitis - integrated case

A diabetic patient has triglyceri**des** 2500 mg/dL and **pancreatitis**. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Chylomicrons neutralize trypsin inhibitors

B. Pancreatic lipase hydrolyzes triglyceri**des** to toxic **free fatty acids** causing microvascular/acinar injury

C. Triglyceri**des** mechanically block the ampulla

D. **Bile acid**s precipitate cho**les**terol stones

E. Triglyceri**des** inhibit **CFTR** chloride secretion only

Answer: B. Pancreatic lipase hydrolyzes triglyceri**des** to toxic **free fatty acids** causing microvascular/acinar injury

Micro-pearl: Severe hypertriglyceridemia causes FFA toxicity and hyperviscosity.

Case 94 / Q269. Chapter 7 - Biliary and Pancreas - Chronic pancreatitis pain - integrated case

A man with calcific chronic **pancreatitis** has severe pain **des**pite d**uc**tal decompression. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. **IL-13** eosinophils invade nerves

B. Neural inflammation, fibrosis, and central sensitization maintain pain independent of d**uc**t pressure

C. **Bile acid** diarrhea sensitizes pancreas

D. Acid inactivation of lipase directly causes pain

E. **Gastrin** stimulates nociceptors

Answer: B. Neural inflammation, fibrosis, and central sensitization maintain pain independent of d**uc**t pressure

Micro-pearl: Chronic **pancreatitis** pain is neuropathic/inflammatory as well as d**uc**tal.

Case 95 / Q270. Chapter 7 - Biliary and Pancreas - PRSS1 - integrated case

A family has hereditary **pancreatitis** with early recurrent attacks. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Gain-of-function cationic **trypsinogen** increases intrapancreatic trypsin activity

B. **MEN1** mutation activates islet cells

C. **CFTR** over-secretion of bicarbonate

D. **VHL** loss prod**uc**es serous cysts

E. **SPINK1** excess blocks trypsin

Answer: A. Gain-of-function cationic **trypsinogen** increases intrapancreatic trypsin activity

Micro-pearl: **PRSS1** mutations promote trypsin activation.

Case 96 / Q271. Chapter 7 - Biliary and Pancreas - SPINK1 - integrated case

A patient with recurrent **pancreatitis** has a **SPINK1** variant. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Red**uc**ed trypsin inhibitor defense lowers threshold for autodigestive injury

B. **BRAF-CIMP** methylation

C. **GNAS** mutation in d**uc**ts

D. Decreased enteropeptidase in duodenum

E. Increased **CFTR** bicarbonate secretion

Answer: A. Red**uc**ed trypsin inhibitor defense lowers threshold for autodigestive injury

Micro-pearl: **SPINK1** is a protective trypsin inhibitor.

Case 97 / Q272. Chapter 7 - Biliary and Pancreas - CFTR pancreatitis - integrated case

A young adult with recurrent **pancreatitis** has **CFTR**-related d**uc**t disease. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. **Somatostatin receptor** overexpression

B. Cho**les**terol supersaturation

C. Cationic **trypsinogen** gain of function

D. Defective d**uc**tal chloride/bicarbonate secretion causes viscous secretions and impaired enzyme flushing

E. Excess bicarbonate dissolves d**uc**t plugs

Answer: D. Defective d**uc**tal chloride/bicarbonate secretion causes viscous secretions and impaired enzyme flushing

Micro-pearl: **CFTR** mutations impair d**uc**tal fluid/bicarbonate secretion.

Case 98 / Q273. Chapter 7 - Biliary and Pancreas - Exocrine insufficiency - integrated case

A chronic **pancreatitis** patient develops steatorrhea and low fecal elastase. Additional data are internally consistent with this

diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. **Gastrin** excess blocks micel**les**

B. **JAK** inhibition red**uc**es enterocyte transport

C. **H. pylori urease** injures villi

D. Colonic **bile acid**s increase fat absorption

E. Loss of pancreatic lipase delivery impairs triglyceride digestion below the functional threshold

Answer: E. Loss of pancreatic lipase delivery impairs triglyceride digestion below the functional threshold

Micro-pearl: Lipase loss is central to pancreatic steatorrhea.

Case 99 / Q274. Chapter 7 - Biliary and Pancreas - AIP type 1 - integrated case

A man has pain**les**s jaundice, diffuse pancreatic enlargement, high **IgG4**, and steroid response. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. Cytotoxic T-cell **des**truc**tion** of beta cells only

B. **CagA**-mediated pancreatic epithelial dysplasia

C. Premature trypsin activation from gallstones

D. **IgG4**-related lymphoplasmacytic fibroinflammatory disease involving pancreas and bile d**uc**ts

E. Cho**les**terol supersaturation

Answer: D. **IgG4**-related lymphoplasmacytic fibroinflammatory disease involving pancreas and bile d**uc**ts

Micro-pearl: Type 1 AIP is **IgG4**-related and steroid-responsive.

Case 100 / Q275. Chapter 7 - Biliary and Pancreas - AIP type 2 - integrated case

A younger patient with ulcerative colitis has **pancreatitis**; biopsy shows granulocytic epithelial **les**ions without systemic **IgG4** disease. Additional data are internally consistent with this diagnosis, and competing explanations have been excluded by appropriate testing. The clinical team has narrowed the differential, but the examiner deliberately places all options within adjacent mechanisms from the same organ system. The key is to identify the single upstream step that most directly explains the final observed phenotype.

Which **micro-mechanism** is the best causal explanation in this case?

A. **KRAS**/**SMAD4** carcinoma **pathway**

B. D**uc**t-centric neutrophilic epithelial injury characteristic of type 2 **autoimmune pancreatitis**

C. **PRSS1** gain-of-function trypsin activation

D. Bacterial **beta-glucuronidase** stone formation

E. **IgG4**-positive storiform fibrosis with salivary involvement

Answer: B. D**uc**t-centric neutrophilic epithelial injury characteristic of type 2 **autoimmune pancreatitis**

Micro-pearl: Type 2 AIP is GEL/**IBD**-associated, not classic **IgG4** disease.

Compact Answer Key

Q - Ans	Q - Ans	Q - Ans	Q - Ans	Q - Ans
1 - A	2 - D	3 - E	4 - E	5 - B
6 - D	7 - A	8 - A	9 - C	10 - A
11 - D	12 - E	13 - C	14 - D	15 - A
16 - D	17 - B	18 - C	19 - E	20 - E
21 - A	22 - B	23 - A	24 - B	25 - D
26 - D	27 - C	28 - B	29 - E	30 - C
31 - E	32 - B	33 - B	34 - C	35 - D
36 - B	37 - D	38 - D	39 - E	40 - A
41 - B	42 - B	43 - B	44 - E	45 - E
46 - B	47 - E	48 - E	49 - E	50 - C
51 - A	52 - A	53 - A	54 - A	55 - B
56 - B	57 - B	58 - C	59 - C	60 - C
61 - E	62 - C	63 - A	64 - D	65 - D
66 - E	67 - D	68 - E	69 - C	70 - A
71 - A	72 - D	73 - A	74 - C	75 - A
76 - E	77 - A	78 - C	79 - B	80 - A
81 - B	82 - D	83 - D	84 - C	85 - B
86 - B	87 - D	88 - E	89 - A	90 - E
91 - C	92 - E	93 - C	94 - C	95 - D
96 - B	97 - A	98 - E	99 - D	100 - D
101 - B	102 - A	103 - D	104 - A	105 - E
106 - C	107 - B	108 - C	109 - C	110 - C
111 - E	112 - C	113 - E	114 - E	115 - C
116 - D	117 - D	118 - A	119 - A	120 - A
121 - B	122 - A	123 - E	124 - C	125 - E
126 - A	127 - C	128 - A	129 - E	130 - E
131 - B	132 - A	133 - E	134 - E	135 - D
136 - E	137 - B	138 - D	139 - C	140 - C
141 - C	142 - D	143 - A	144 - A	145 - B
146 - B	147 - C	148 - E	149 - C	150 - A
151 - E	152 - A	153 - C	154 - E	155 - C
156 - D	157 - E	158 - A	159 - A	160 - D
161 - A	162 - D	163 - A	164 - E	165 - B
166 - C	167 - C	168 - E	169 - B	170 - C
171 - D	172 - E	173 - A	174 - E	175 - E
176 - D	177 - D	178 - C	179 - E	180 - E
181 - E	182 - D	183 - C	184 - E	185 - A
186 - D	187 - E	188 - E	189 - D	190 - B
191 - A	192 - D	193 - A	194 - E	195 - D
196 - C	197 - B	198 - A	199 - D	200 - C
201 - B	202 - E	203 - A	204 - A	205 - D
206 - D	207 - D	208 - B	209 - D	210 - E
211 - A	212 - D	213 - B	214 - B	215 - E
216 - B	217 - A	218 - A	219 - C	220 - B
221 - D	222 - B	223 - A	224 - E	225 - B
226 - B	227 - B	228 - B	229 - E	230 - E
231 - B	232 - D	233 - B	234 - E	235 - D
236 - C	237 - B	238 - A	239 - A	240 - B
241 - C	242 - B	243 - B	244 - B	245 - E
246 - B	247 - E	248 - E	249 - E	250 - D
251 - A	252 - E	253 - C	254 - D	255 - B
256 - B	257 - A	258 - D	259 - C	260 - C
261 - E	262 - E	263 - E	264 - A	265 - E
266 - E	267 - E	268 - B	269 - B	270 - A
271 - A	272 - D	273 - E	274 - D	275 - B

Chapter mapping note: Q1-Q175 are chapter-based **micro-mechanism** traps. Q176-Q275 are integrated case scenarios across the same seven chapters.