

Infectious Enterocolitis

Mechanisms • morphology • clinicopathologic correlation

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Learning objectives

- Link pathogen localization and virulence strategy to the diarrheal phenotype
- Recognize mechanisms of secretory, inflammatory, and malabsorptive injury
- Distinguish common bacterial, viral, and parasitic infections
- Interpret histology without overcalling an organism-specific diagnosis

Clinical spectrum: One syndrome, many mechanisms

- Diarrhea may coexist with pain, urgency, perianal discomfort, incontinence, or bleeding
- Small bowel infection often produces watery diarrhea and malabsorption
- Invasive colonic disease more often causes dysentery and systemic inflammation
- Clinical phenotype narrows—but does not prove—the causal pathogen

Etiologic families and dominant patterns

Group	Typical setting	Usual pathological response
Bacterial	Food, water, host-to-host exposure	Secretory injury or inflammatory colitis
Viral	Close-contact outbreaks; Pediatric infection	Enterocyte injury, transient villous dysfunction
Protozoal	Contaminated water; Immune deficiency	Surface adherence or invasive ulceration
Helminthic	Soil / food exposures	Eosinophilia, mucosal injury, obstruction

Host context changes the causal spectrum

- Age and nutrition change susceptibility and consequences
- Immune status influences organism clearance and dissemination
- Geography, sanitation, and access to clean water modify exposure
- Travel, antibiotic exposure, and food history are diagnostically informative

Read the stool phenotype as a mechanism

Phenotype	Mechanistic clue	Illustrative pathogens
Profuse watery	Active electrolyte secretion	Vibrio cholerae, ETEC
Bloody / exudative	Invasion or toxin-associated mucosal injury	Shigella, Campylobacter, EHEC
Malabsorptive / prolonged	Impaired enterocyte function or lymphatic drainage	Giardia, Whipple disease
Post-antibiotic watery	Dysbiosis and toxin injury	Clostridioides difficile

Three pathogen–mucosa relationships



- Noninvasive toxins can drive major fluid loss with little histologic injury
- Tissue invasion instead recruits neutrophils, causes epithelial injury, and can produce bleeding

Anatomic localization helps interpretation

Predominant site	Examples	Clinical / tissue clue
Small intestine	Cholera, ETEC, EPEC, Giardia	Watery diarrhea or malabsorption
Colon	Campylobacter, Shigella, EHEC, C. Difficile	Inflammation, blood, or pseudomembranes
Ileum / right colon	Yersinia, typhoid, Cryptosporidium	Peyer patch involvement or focal ileitis

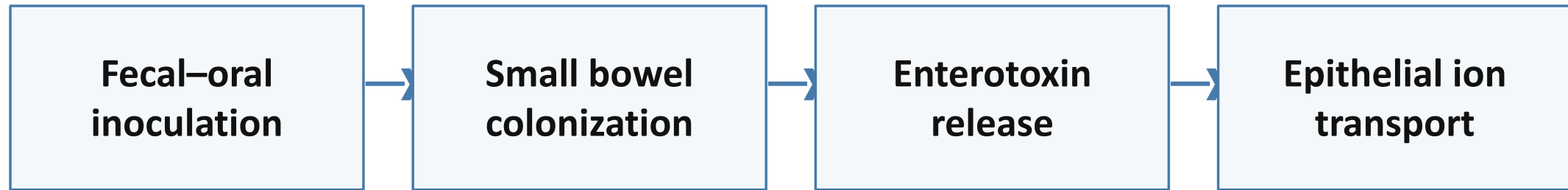
Beyond stool frequency: Major complications

- Fluid and electrolyte loss may cause hypotension or shock
- Epithelial damage may result in hemorrhage or toxic megacolon
- Invasive pathogens can disseminate through lymphatic or blood vessels
- Immune-mediated sequelae can persist after intestinal symptoms resolve

Vibrio cholerae: Exposure and tissue niche

- Comma-shaped gram-negative organisms inhabit aquatic reservoirs, including shellfish and plankton
- Fecally contaminated water is a major route of epidemic spread
- Loss of sewage infrastructure increases risk of large outbreaks
- Disease targets the small intestine without direct mucosal invasion

Cholera colonization precedes toxigenic diarrhea

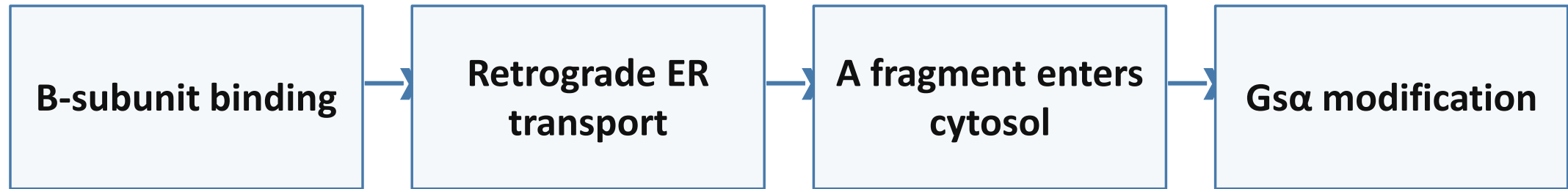


- Organism motility and adherence support intestinal colonization
- Bacterial detachment and shedding help onward transmission

Cholera toxin is an A–B5 complex

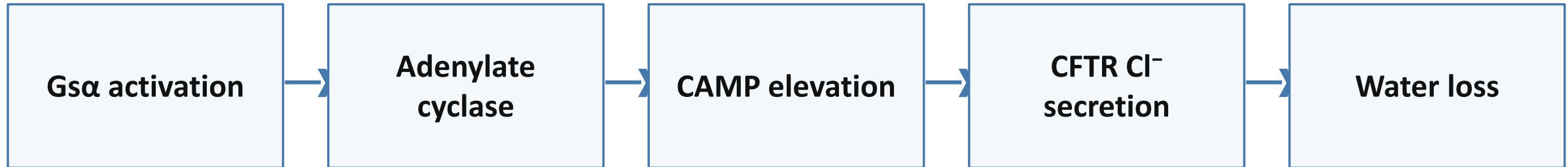
- Five B subunits engage GM1 ganglioside on enterocytes
- A subunit is responsible for intracellular enzymatic signaling
- The toxin is encoded by a bacterial virulence phage
- Severe diarrhea reflects disrupted host ion transport—not deep invasion

Cholera toxin entry pathway



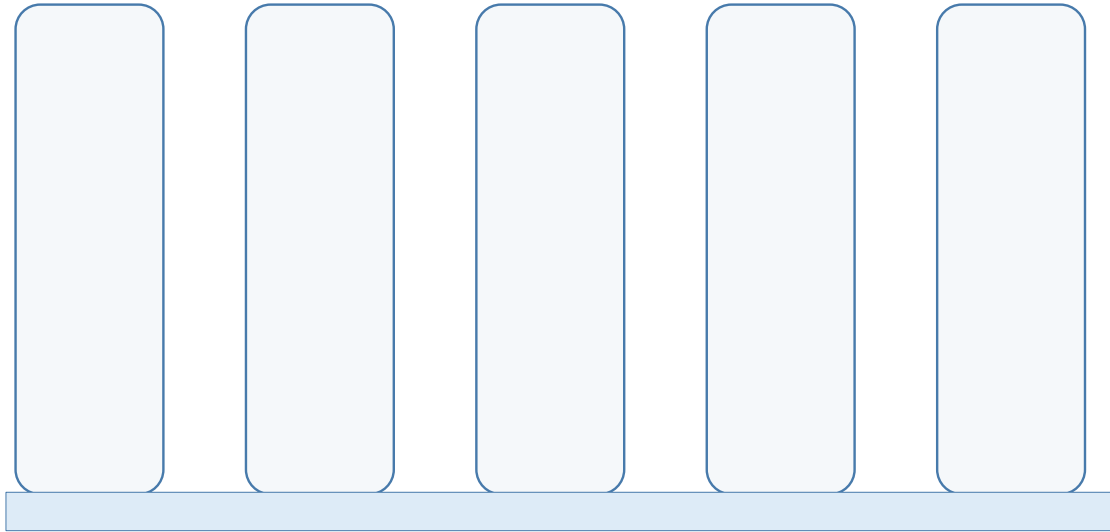
- Protein disulfide isomerase processes the A subunit in the ER
- Host machinery returns the catalytically active fragment into the cytosol

Cholera: From Gsα to luminal water



- Toxin-mediated ADP ribosylation locks Gsα in its active state
- CAMP also suppresses absorptive ion transport, amplifying net secretion

Severe fluid loss with subtle histology



Preserved mucosal architecture

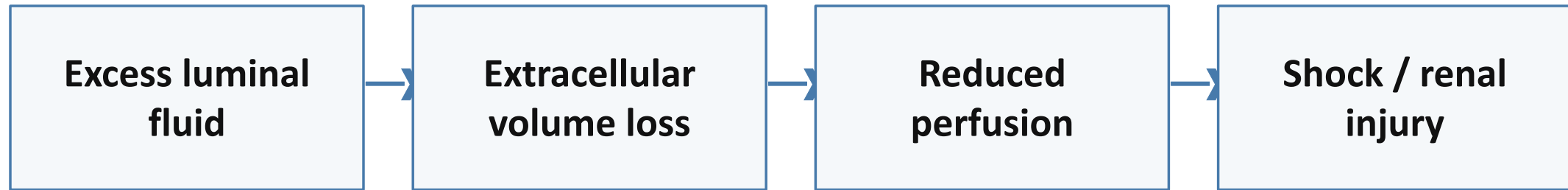
Schematic — not a histologic specimen

- Massive secretory diarrhea can coexist with minimally altered villi and crypts
- A near-normal biopsy cannot exclude cholera
- Clinical dehydration severity does not track the degree of mucosal destruction

Cholera clinical syndrome

- Severe cases begin abruptly with vomiting and voluminous watery stool
- “Rice-water” stools reflect profound fluid-rich output
- Hypotension, cramps, oliguria or anuria, and shock follow rapid fluid depletion
- Dehydration is the immediate life-threatening pathophysiology

Fluid depletion explains systemic manifestations



- Electrolyte imbalances and muscular cramping accompany volume depletion
- Time-critical fluid replacement reverses the principal physiological defect

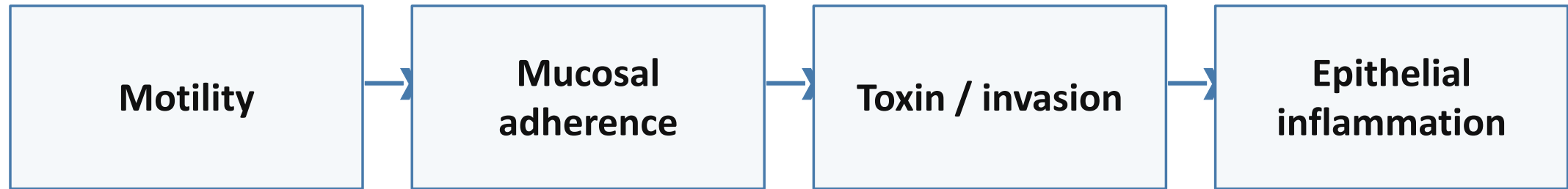
Secretory diarrhea: Key distinctions

Finding	Cholera	Invasive bacterial colitis
Bacterial location	Luminal, noninvasive	Mucosal epithelial / lamina propria invasion
Typical stool	High-volume watery	Often inflammatory or bloody
Biopsy	Usually minimal change	Cryptitis, erosions, neutrophils
Major threat	Hypovolemia	Mucosal damage ± systemic consequences

Campylobacter: Food and animal exposure

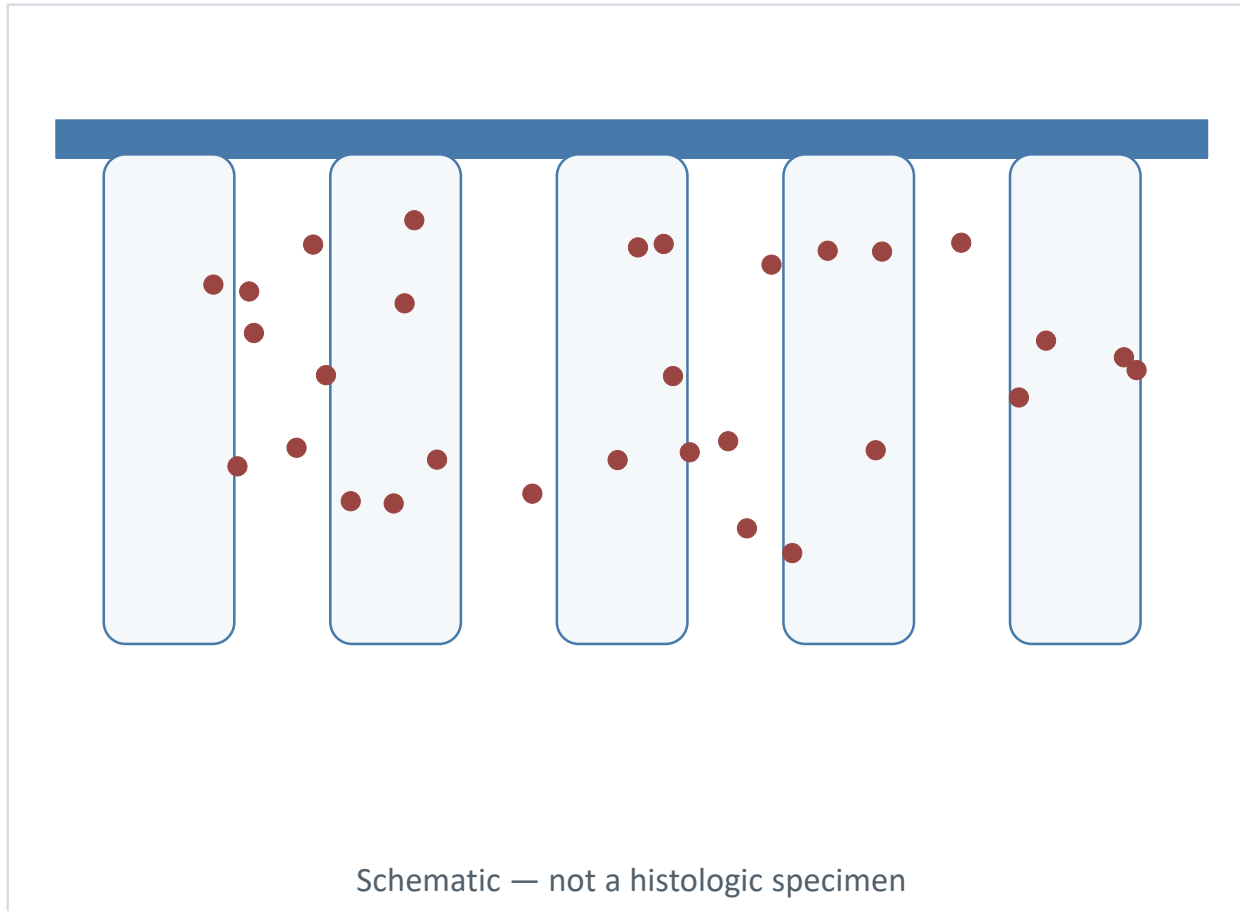
- C. Jejuni is a prominent enteric pathogen in high-resource settings
- Undercooked poultry, unpasteurized milk, and contaminated water are major exposures
- Farm animals and pets can transmit infection
- Direct person-to-person spread is relatively uncommon

Campylobacter virulence is multifactorial



- Flagella enhance intestinal colonization
- Some strains cause direct epithelial injury; Invasive strains can produce dysentery

Campylobacter: Acute self-limited colitis



- Neutrophils infiltrate superficial epithelium and crypts
- Crypt abscesses may form from intra-crypt neutrophils
- Overall crypt architecture often remains preserved
- This pattern is not specific for Campylobacter

Campylobacter clinical and immune sequelae

Manifestation	Biological connection
Watery diarrhea	Inflammatory or enterotoxigenic epithelial dysfunction
Dysentery	Invasive bacterial phenotype
Reactive arthritis	Postinfectious immune complication; HLA-B27 association
Guillain–Barré syndrome	Ganglioside-directed cross-reactivity after infection

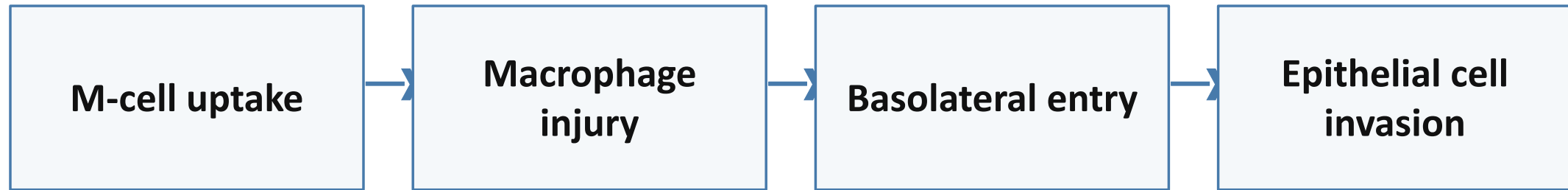
Campylobacter: Symptoms and diagnosis

- A prodrome may precede abdominal pain and watery diarrhea
- Some patients develop bloody stools, especially children
- Culture-based stool testing establishes the organism
- Biopsy demonstrates acute colitis but usually cannot identify the pathogen

Shigella: Efficient fecal–oral spread

- Humans are the recognized reservoir
- Acid resistance and a low infective dose facilitate transmission
- Crowded settings and inadequate sanitation increase exposure
- Shigellosis frequently produces dysentery

Shigella traverses the mucosal barrier

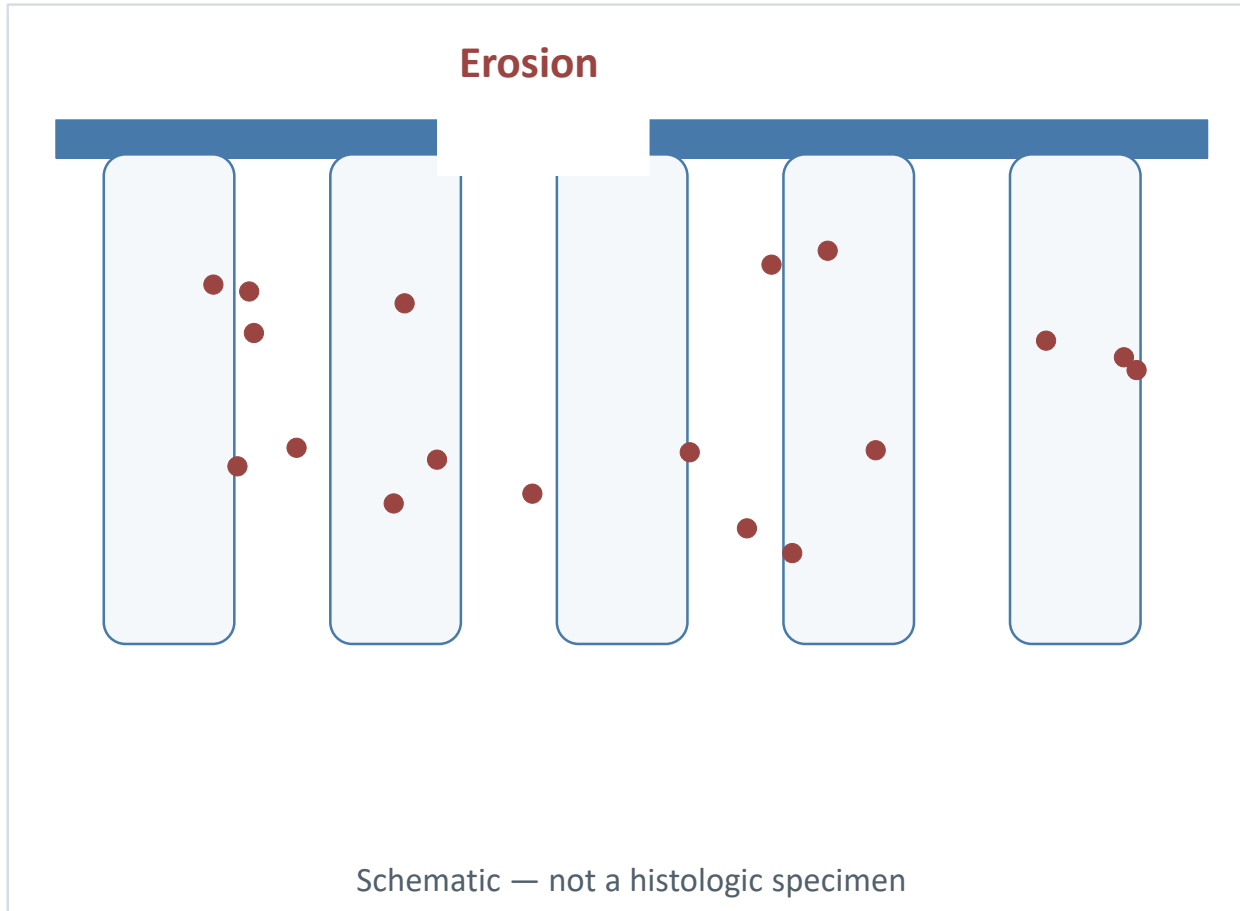


- The inflammatory response disrupts surface integrity
- Type III secretion machinery assists delivery of bacterial effectors into host cells

Shiga toxin adds cytotoxic damage

- *Shigella dysenteriae* serotype 1 can produce Shiga toxin
- Toxin inhibits eukaryotic protein synthesis and kills host cells
- Severe mucosal injury underlies bleeding and ulceration
- Shiga toxin may be complicated by hemolytic uremic syndrome

Shigella: Ulcerative inflammatory colitis



- The left colon is commonly affected; Ileal involvement is possible
- Hemorrhage, ulceration, and occasional pseudomembranes may be seen
- Aphthous ulcers can resemble Crohn disease
- Architecture and disease distribution must be interpreted with clinical context

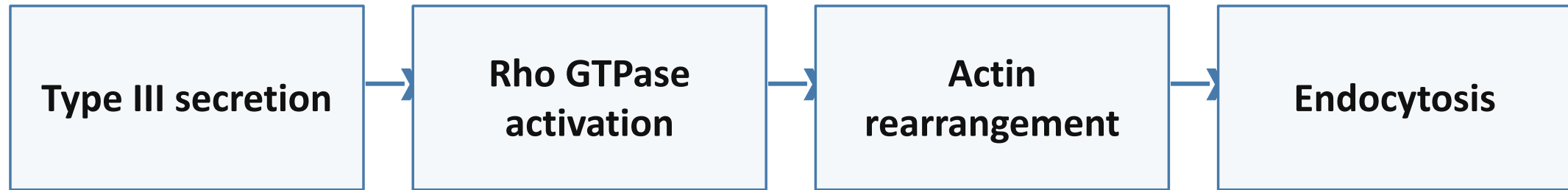
Shigellosis: Clinical consequences

- Fever, cramps, diarrhea, and bloody stools develop during acute infection
- Reactive arthritis may be accompanied by urethritis and conjunctivitis
- Severe toxin-associated disease can cause hemolytic uremic syndrome
- A subacute presentation may mimic inflammatory bowel disease

Nontyphoidal Salmonella: Foodborne infection

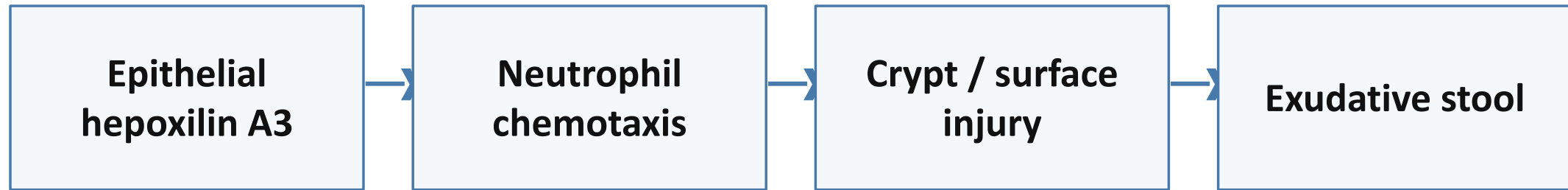
- Raw or undercooked meat, poultry, eggs, and milk are common sources
- Young children and older adults are especially affected
- Food handling and delayed refrigeration can facilitate outbreaks
- The illness is commonly self-limited gastroenteritis

Salmonella promotes enterocyte uptake



- Intracellular bacterial survival enables mucosal infection
- Innate sensors TLR4 and TLR5 amplify host inflammation

Recruitment of neutrophils damages mucosa



- Neutrophils help control infection but intensify epithelial damage
- Inflammatory signaling supports the dysenteric phenotype

Nontyphoidal salmonellosis: Clinical range

- Symptoms range from loose stool to profuse diarrhea or dysentery
- Stool testing distinguishes it from other acute enteric pathogens
- Bacterial shedding may persist beyond clinical recovery
- Immunocompromised hosts face greater risk of invasive complications

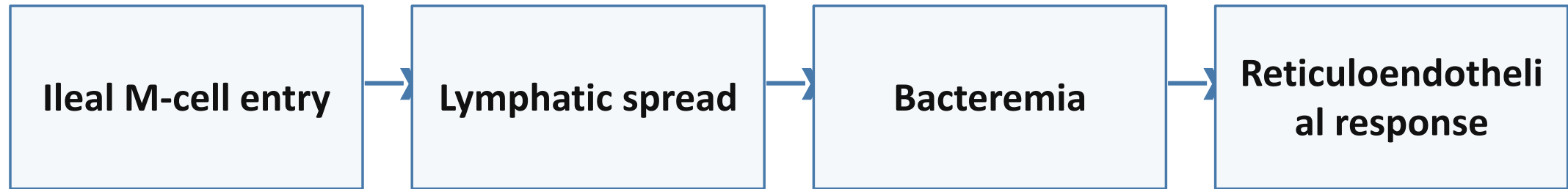
Host defense determines dissemination risk

- Th1 and Th17 responses contribute to bacterial clearance
- Impaired cell-mediated immunity increases the risk of systemic infection
- Hemolytic anemia, sickle cell disease, and other comorbidities can worsen outcomes
- Postinfectious arthritis and bowel dysfunction are recognized sequelae

Enteric fever is not simple salmonellosis

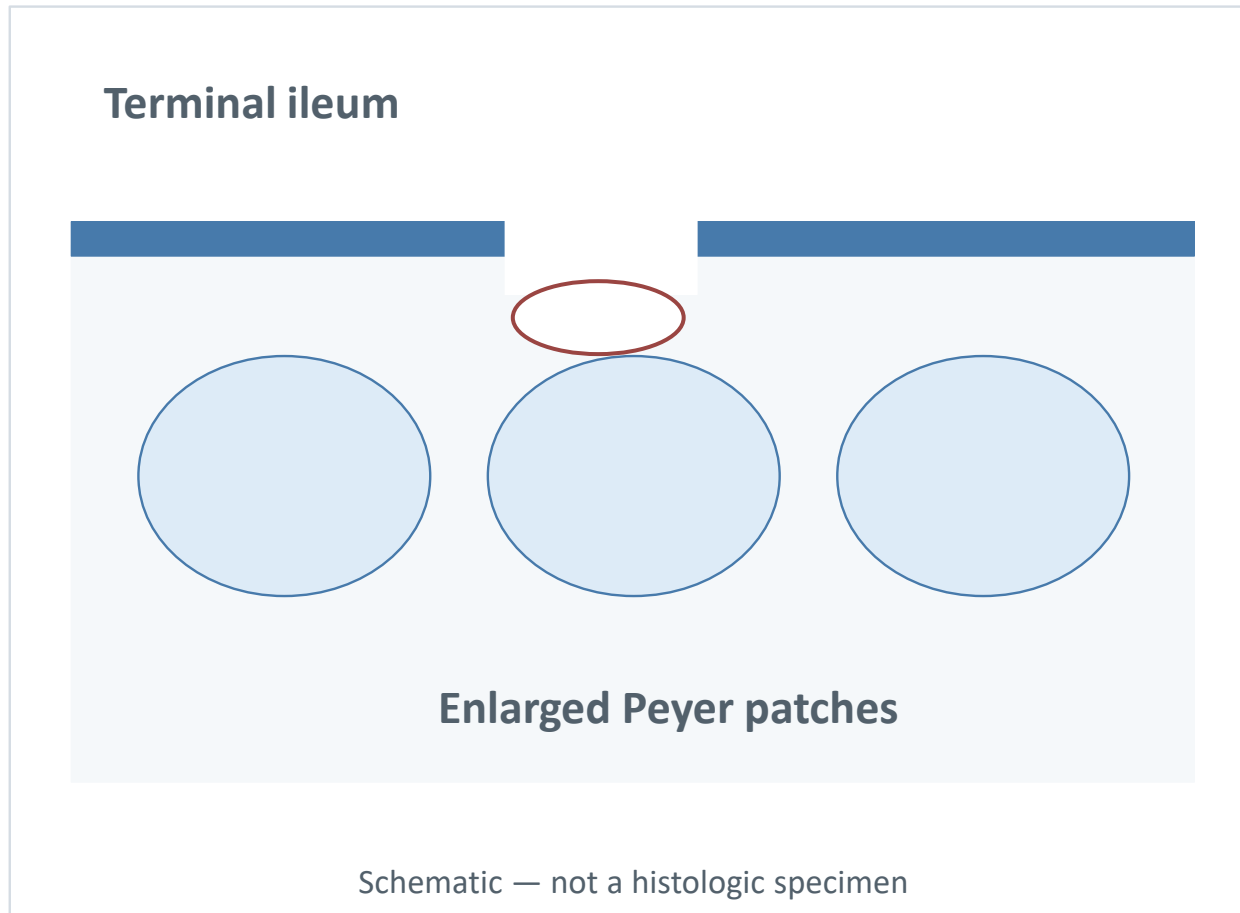
Feature	Nontyphoidal Salmonella	S. Typhi / Paratyphi
Typical pattern	Acute intestinal gastroenteritis	Systemic enteric fever
Distribution	Small bowel and colon	Small bowel with systemic spread
Bacteremia	In selected high-risk hosts	Integral to illness evolution
Tissue response	Neutrophilic enterocolitis	Mononuclear phagocyte / lymphoid response

Typhoid: Mucosal entry to systemic disease



- Humans are the principal reservoir for typhoidal Salmonella
- Gallbladder colonization can support chronic carriage

Typhoid morphology: The Peyer patch lesion



- Peyer patches enlarge within the terminal ileum
- Macrophage-rich inflammation and epithelial loss may create longitudinal ulcers
- Ulcers may penetrate the bowel wall and perforate
- Regional lymph nodes and spleen show reactive enlargement

Systemic morphology in enteric fever

- The spleen may be enlarged, soft, and rich in phagocytes
- Typhoid nodules are macrophage-rich hepatic lesions with focal necrosis
- Reticuloendothelial involvement reflects systemic dissemination
- Intestinal perforation is a serious consequence of deep ulceration

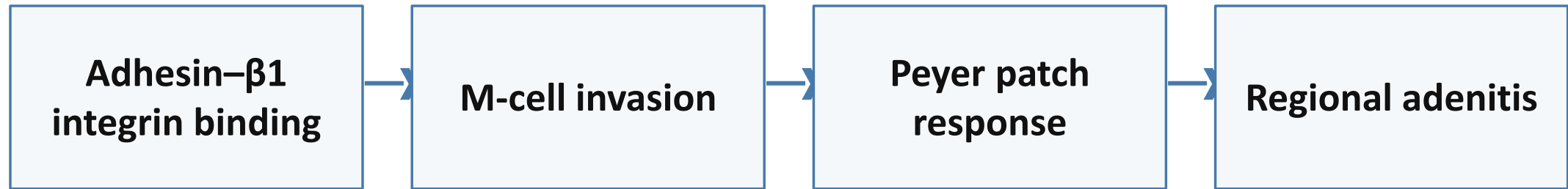
Typhoid fever: Changing clinical phases

- Gastrointestinal symptoms can precede an interval of systemic fever
- Bacteremia produces constitutional illness; Rose spots may occur
- Extraintestinal complications include neurologic and cardiac involvement
- Blood cultures contribute to microbiologic confirmation during febrile disease

Yersinia: Right-sided enterocolitis

- Y. Enterocolitica and Y. Pseudotuberculosis cause intestinal infection
- Exposure is linked to pork, raw milk, and contaminated water
- Ileum, appendix, and right colon are favored sites
- Lymphoid involvement can simulate acute appendicitis

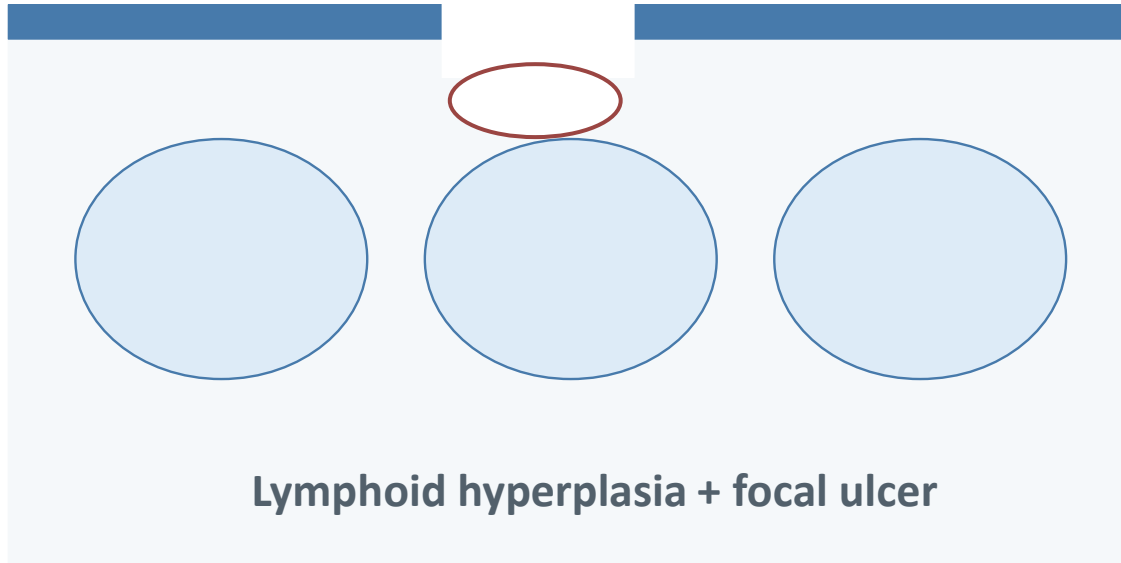
Yersinia targets mucosal lymphoid tissue



- Lymphoid tissue supports bacterial proliferation and inflammation
- Iron acquisition systems can increase virulence and systemic spread

Yersinia: An infectious Crohn mimic

Ileal / appendiceal region



Schematic — not a histologic specimen

- Focal aphthous ulcers and granulomas can occur
- Lymphoid hyperplasia, neutrophils, and bowel-wall thickening may coexist
- A right-sided distribution supports but does not establish Yersinia
- Culture and exposure history prevent a mistaken chronic IBD diagnosis

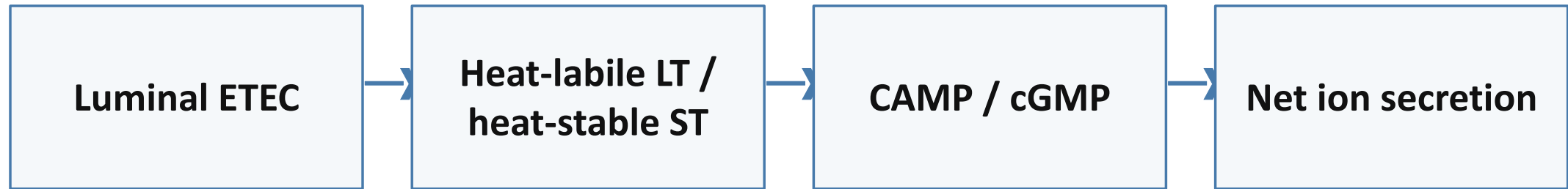
Yersinia clinical presentation

- Abdominal pain and tenderness can dominate over diarrhea
- Mesenteric lymphadenitis produces pseudoappendicitis
- Postinfectious reactive arthritis and erythema nodosum are recognized
- Stool culture may require organism-selective conditions

E. Coli pathotypes are mechanistically distinct

Pathotype	Main interaction	Characteristic syndrome
ETEC	Secreted LT / ST enterotoxins	Watery traveler's diarrhea
EPEC	Attaching-and-effacing injury	Infant watery diarrhea
EHEC	Shiga-like toxin-associated damage	Hemorrhagic colitis ± HUS
EIEC	Intracellular epithelial invasion	Inflammatory diarrhea
EAEC	Aggregative adherence	Sometimes prolonged nonbloody diarrhea

ETEC: Two routes to secretory diarrhea

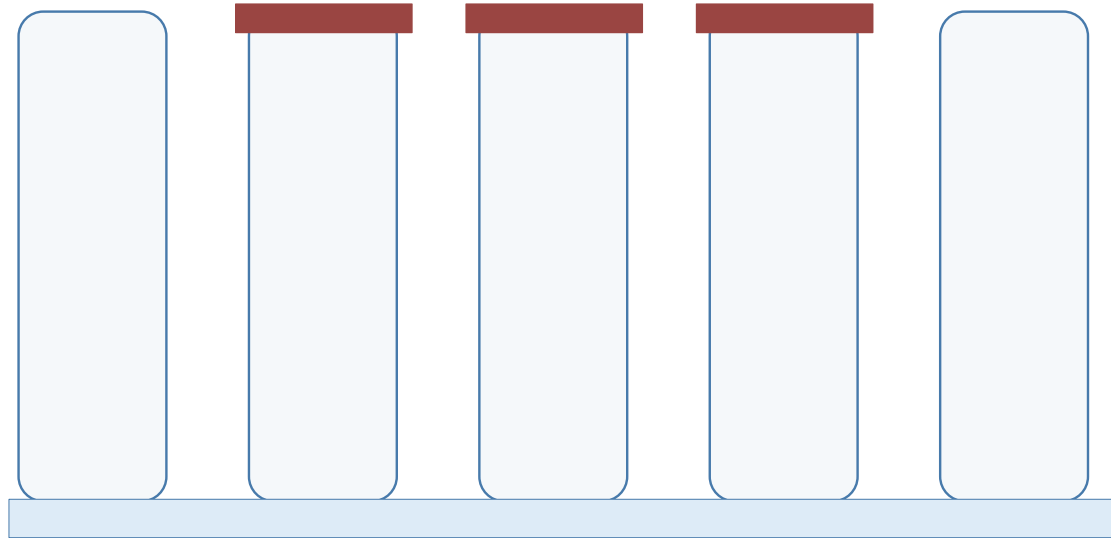


- ETEC remains noninvasive
- Histologic change is often mild despite abundant watery stool

Cyclic nucleotide mechanisms

Toxin	Host signal	Principal consequence
Cholera toxin	Activated Gs α $\rightarrow$ adenylate cyclase $\rightarrow$ cAMP	CFTR-associated chloride and water secretion
ETEC heat-labile toxin	Adenylate cyclase $\rightarrow$ cAMP	Chloride-rich watery output
ETEC heat-stable toxin	Guanylate cyclase $\rightarrow$ cGMP	Altered epithelial ion transport

EPEC produces attaching-and-effacing lesions



Apical adherence / microvillus effacement

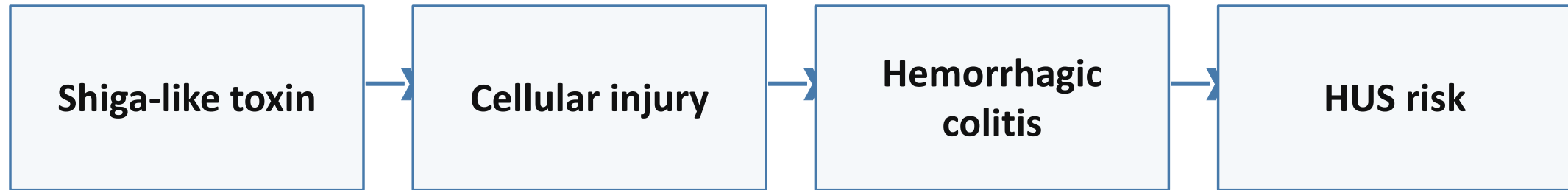
Schematic — not a histologic specimen

- Bacteria adhere intimately to the enterocyte apical surface
- Adjacent microvilli are effaced rather than invaded deeply
- Loss of brush-border function contributes to watery diarrhea
- Bacterial factors responsible for adherence can aid molecular diagnosis

EHEC: Exposure and toxin-mediated colitis

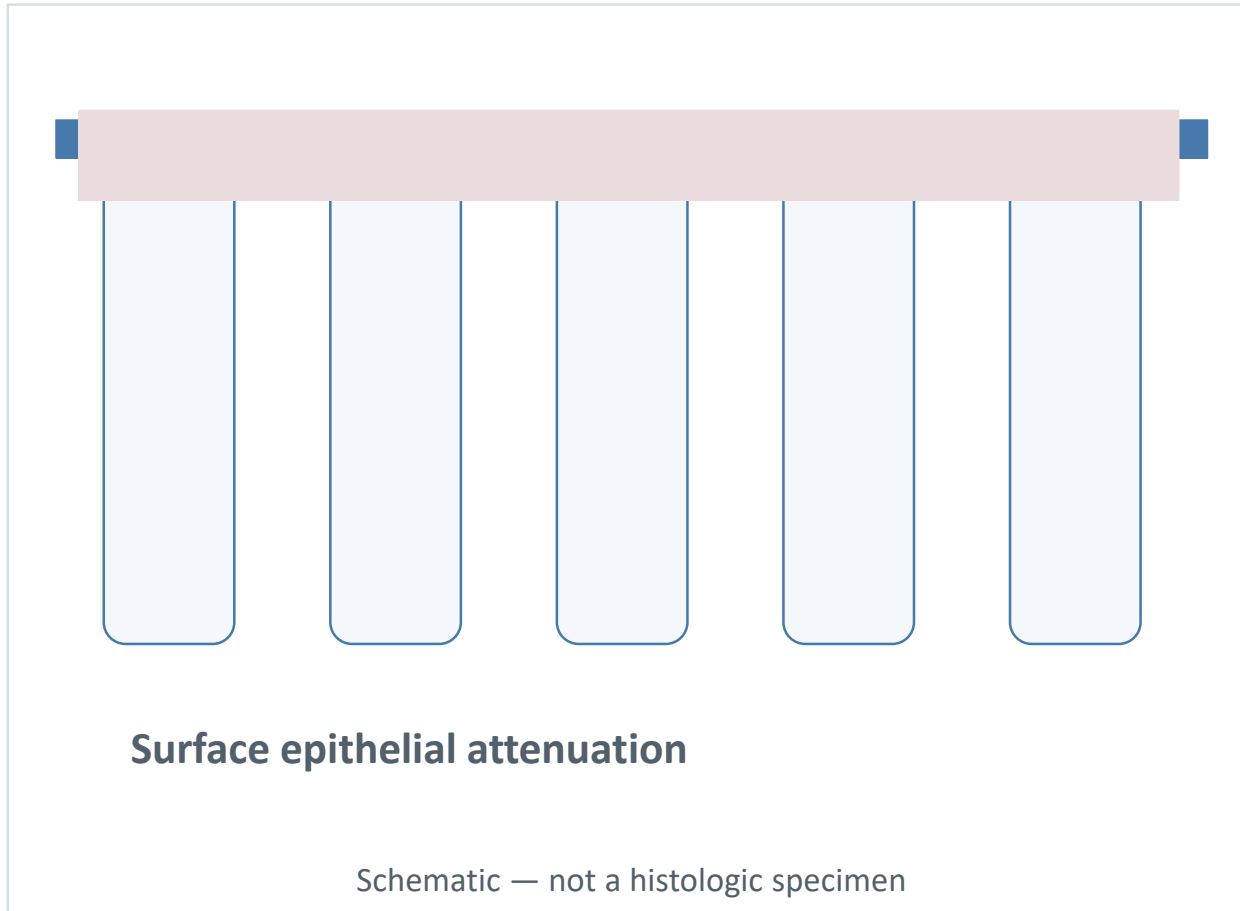
- Cattle are an important reservoir; Undercooked beef and contaminated produce transmit infection
- O157:H7 and other serotypes produce Shiga-like toxins
- EHEC may cause hemorrhagic diarrhea and systemic toxicity
- Recognition matters because toxin-associated HUS is a major complication

EHEC: Mucosal toxin to microangiopathy



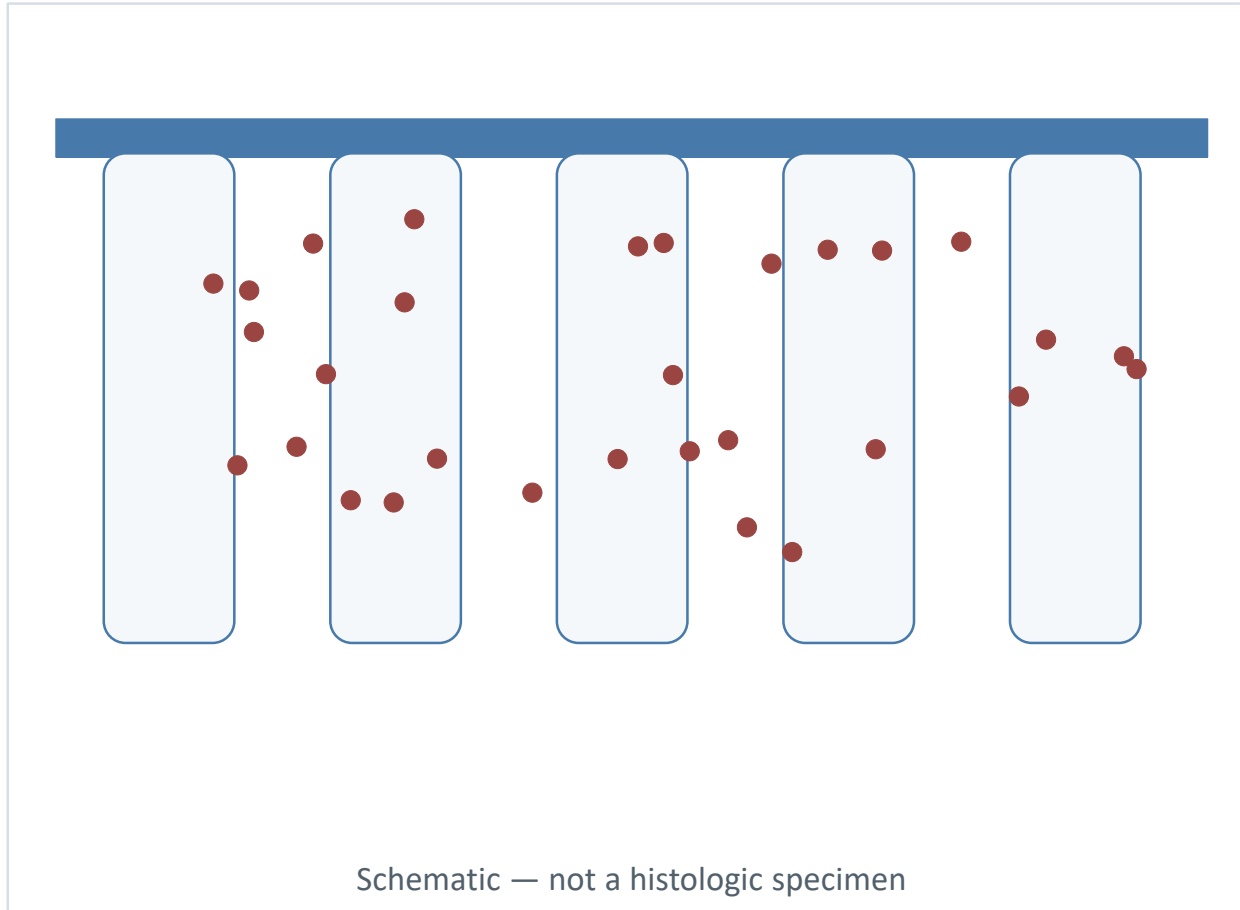
- The mechanism can resemble ischemic injury in colonic biopsies
- Source text warns that antibiotics may enhance toxin release and HUS risk

EHEC may mimic ischemic injury



- Surface epithelial atrophy and erosion can predominate
- Ischemia-like morphology does not prove primary vascular insufficiency
- Correlate with bloody diarrhea and epidemiologic exposure
- Stool microbiology and toxin detection resolve etiologic uncertainty

EIEC: Inflammation without chronic distortion



- EIEC invades the intestinal epithelium much like *Shigella*
- Acute self-limited colitis includes cryptitis and intraepithelial neutrophils
- Preserved crypt spacing helps differentiate acute from chronic injury
- Inflammatory histology is not pathotype-specific

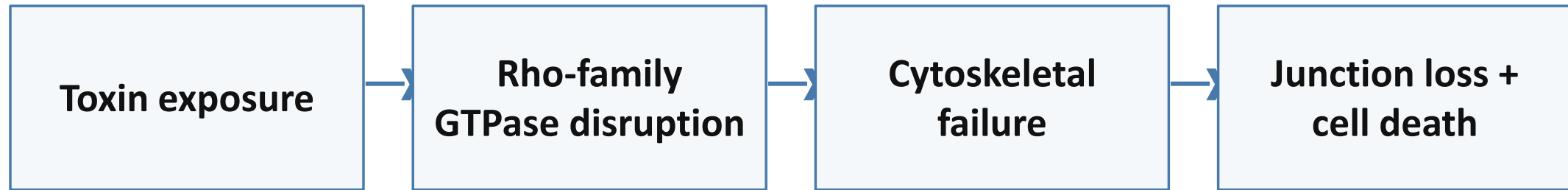
EAEC: Adherence with limited tissue damage

- Aggregative fimbriae support epithelial attachment
- Dispersin reduces electrostatic repulsion at the bacterial surface
- Nonbloody diarrhea may persist, particularly with immune dysfunction
- Biopsy changes may be minimal

C. Difficile follows loss of microbial resistance

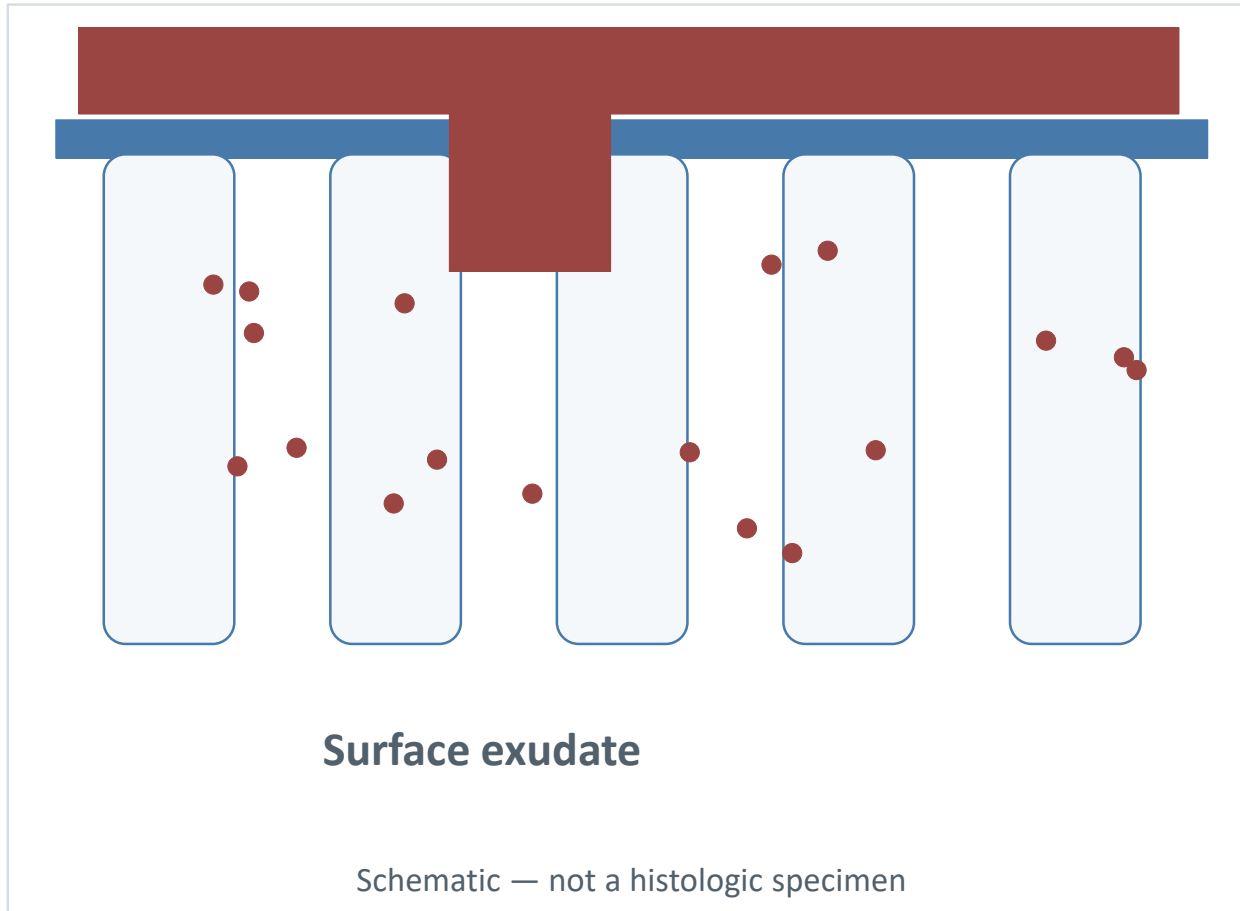
- Antibiotics disrupt normal colonic microbial communities
- C. Difficile can overgrow and elaborate toxins
- Hospital exposure, older age, and impaired immunity increase susceptibility
- Colonization without symptomatic disease must be distinguished from colitis

C. Difficile toxins break epithelial integrity



- Proinflammatory cytokines and neutrophils amplify injury
- Barrier disruption enables inflammatory exudate to reach the surface

The pseudomembrane “volcano” pattern



- Damaged, dilated crypts release a column of mucopurulent material
- Neutrophils, fibrin, and necrotic epithelial debris accumulate on the surface
- Coalescent exudates form pale adherent pseudomembranes
- Schematic illustrates morphology; It is not a histologic specimen

Pseudomembranes are a pattern, not a microbiologic test

Observation	Interpretation
Surface exudate of fibrin and neutrophils	Suggests severe superficial epithelial injury
Crypt-associated “volcano” lesion	Strongly favors C. Difficile in appropriate context
Similar membranes in ischemia or necrotizing infections	Morphology is not universally organism-specific
Positive organism detection without symptoms	May indicate colonization rather than active toxin disease

C. Difficile: Clinical and dangerous variants

- Watery diarrhea, cramps, fever, and leukocytosis are typical
- Hypoalbuminemia may result from protein-losing mucosal injury
- Extensive colonic damage can cause toxic megacolon
- Recurrent symptomatic episodes are an important clinical problem

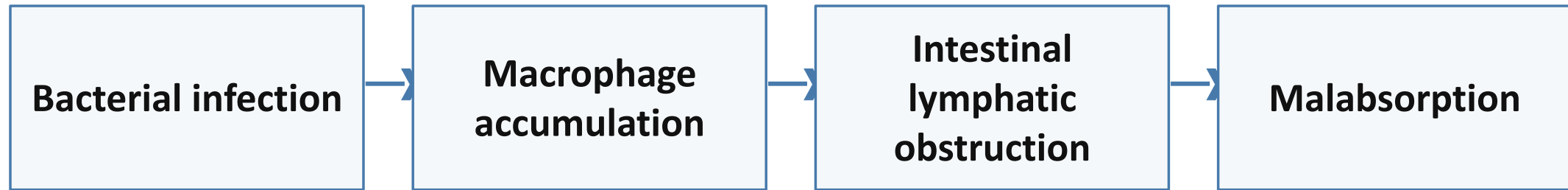
Correlate toxin tests with the syndrome

- The supplied textbook emphasizes stool toxin detection over culture alone
- Interpretation requires compatible diarrhea and risk factors
- A characteristic biopsy can support but should not substitute for infection testing
- Histologic pseudomembranes have a differential diagnosis

Whipple disease: Intracellular organisms and malabsorption

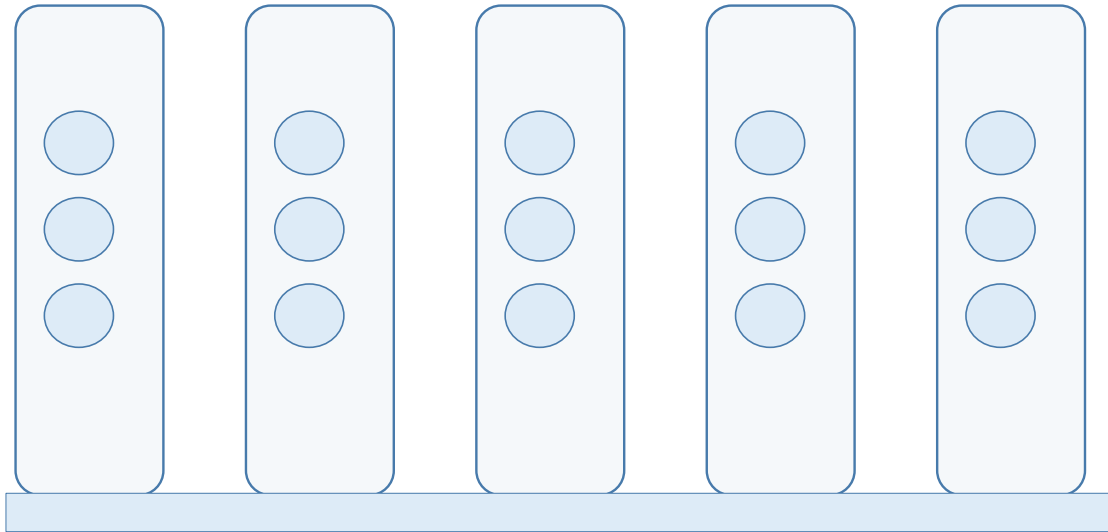
- *Tropheryma whipplei* is associated with chronic, multisystem infection
- Macrophages accumulate in small-intestinal lamina propria and mesenteric nodes
- Lymphatic outflow obstruction contributes to malabsorptive diarrhea
- Weight loss and arthralgia may accompany digestive symptoms

Whipple pathogenesis: Lymphatic obstruction



- Foamy histiocytes expand villi and replace normal lamina propria
- Extraintestinal macrophage accumulation explains multisystem manifestations

Whipple histology: PAS-positive macrophages



Lamina propria macrophage expansion

Schematic — not a histologic specimen

- The lamina propria becomes crowded with distended foamy macrophages
- Intracellular granules stain PAS-positive and resist diastase
- Expansion of villi creates a broad, shaggy mucosal appearance
- Authentic micrographs are required for definitive morphologic recognition

Whipple versus intestinal mycobacterial infection

Finding	T. Whipplei	Intestinal mycobacteria
Lamina propria	Foamy macrophages	Foamy macrophages possible
PAS stain	Granules positive	May also be positive
Acid-fast stain	Negative	Positive in acid-fast organisms
Interpretation	Tissue stain + context	Microbial confirmation needed

Whipple: Recognize systemic involvement

- Arthritis or arthralgia may precede intestinal symptoms
- Lymphadenopathy, fever, and weight loss may occur
- Central nervous system, cardiac valves, and other sites can be involved
- Consider the disease in otherwise unexplained malabsorption with systemic findings

Viruses injure enterocytes without classic dysentery

- Norovirus, rotavirus, and enteric adenovirus are major causes of gastroenteritis
- Watery stool and vomiting are common clinical features
- Epithelial dysfunction or loss impairs nutrient absorption
- Viral biopsies are frequently nonspecific

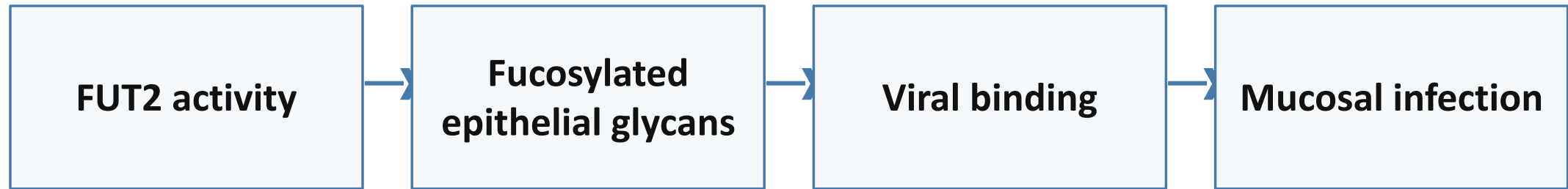
Norovirus: Rapid transmission and outbreaks

- Fecal–oral transmission and contaminated surfaces facilitate spread
- Institutional outbreaks occur in schools, hospitals, care facilities, and ships
- A very small infectious inoculum contributes to transmission
- Virus can be shed before symptoms and after clinical recovery

Norovirus: Acute syndrome and persistence

- Acute vomiting, cramps, and watery diarrhea typically resolve rapidly
- Immunosuppressed patients may develop prolonged diarrhea and shedding
- Extensive strain diversity makes durable cross-protective immunity difficult
- Clinical resolution does not necessarily mark immediate virologic clearance

Norovirus and host mucosal susceptibility



- Some FUT2 loss-of-function nonsecretors resist selected norovirus strains
- Viral antigenic diversity also influences population susceptibility

Norovirus: Modest, nonspecific small-bowel changes

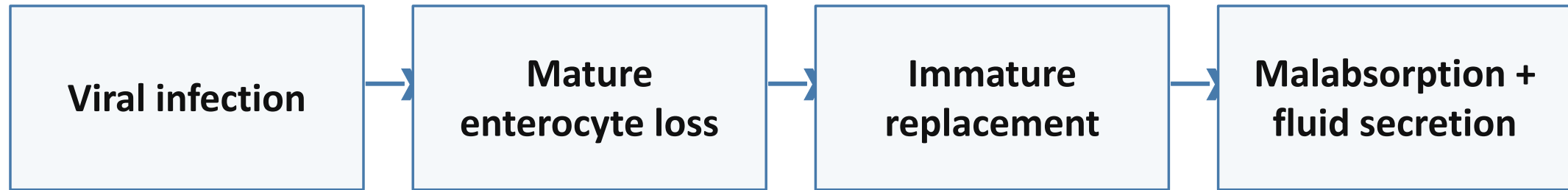


Shortened villi / functional enterocyte loss

Schematic — not a histologic specimen

- Mild villous shortening and epithelial vacuolization may be present
- Crypt enlargement and mixed lamina propria inflammation can occur
- Brush-border enzyme reduction adds transient malabsorption
- Tissue morphology is supportive, not diagnostic of norovirus

Rotavirus damages mature villous enterocytes



- NSP4 may contribute to epithelial apoptosis
- Loss of enzymes and absorption creates an osmotic component to watery diarrhea

Rotavirus: Age and clinical disease

- Young children are a vulnerable group
- Spread in daycare and inpatient settings is efficient
- Vomiting and watery diarrhea follow a short incubation period
- The source describes vaccination as an important prevention strategy

Enteric adenovirus: Pathology and course

- In children and immunocompromised adults, adenovirus can cause diarrhea
- Villous atrophy and reactive crypt hyperplasia are relatively nonspecific
- Epithelial degeneration is variable, and viral inclusions are uncommon
- Symptoms may include vomiting, pain, fever, and weight loss

SARS-CoV-2 may involve intestinal epithelium

- Gastrointestinal symptoms can accompany respiratory infection
- ACE2 and TMPRSS2 expression provides a potential route for epithelial infection
- Epithelial cytotoxicity and immune injury may both contribute
- GI symptoms should not be equated with a distinct histologic diagnostic pattern

Common viral enteritides: Focused comparison

Pathogen	Mechanism / site	Histologic clue
Norovirus	Small bowel epithelial dysfunction	Mild villous change; Nonspecific
Rotavirus	Loss of mature villous enterocytes	Functional malabsorption and epithelial repair
Adenovirus	Enterocyte degeneration	Villous atrophy, crypt hyperplasia
SARS-CoV-2	Possible epithelial infection + inflammation	No defining routine pattern in cited text

Major enteric parasites and injury patterns

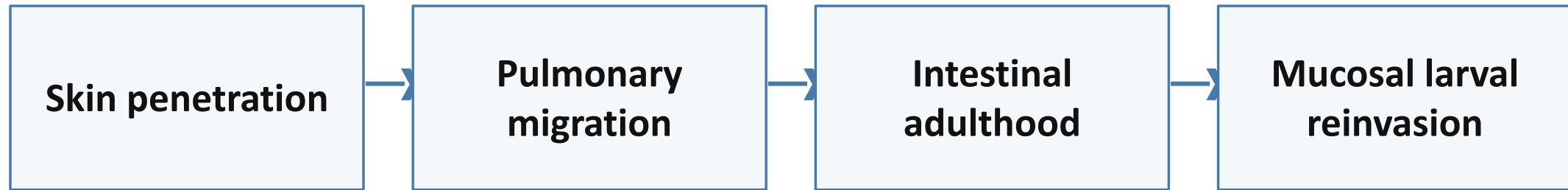
Category	Examples	Dominant tissue effect
Nematodes	Ascaris, Strongyloides, hookworm	Eosinophilic injury, bleeding, obstruction
Tapeworms	Taenia, Diphyllbothrium	Usually intraluminal; Nutritional competition
Amoebae	Entamoeba histolytica	Invasion and deep ulceration
Flagellates / coccidia	Giardia, Cryptosporidium	Brush-border dysfunction and watery stool

Ascaris undergoes lung–gut migration



- Adult worms can cause eosinophil-rich inflammation and bowel or biliary obstruction
- Eggs in stool often establish the diagnosis

Strongyloides autoinfection enables persistence



- Internal autoinfection allows infection to persist long term
- Immune suppression can produce overwhelming disseminated infection

Hookworms produce chronic intestinal blood loss

- Larvae enter through intact skin and migrate via the lungs
- Adult worms attach to duodenal mucosa and feed on blood
- Erosions and repeated bleeding can cause iron-deficiency anemia
- Fecal eggs support diagnosis

Intestinal nematodes: Focused clinical clues

Worm	Location / behavior	Distinguishing manifestation
Trichuris trichiura	Colonic whipworm; Heavy burden	Bloody diarrhea, possible prolapse
Enterobius species	Intraluminal; Nocturnal perianal eggs	Pruritus ani and repeat household transmission
Ascaris lumbricoides	Small intestinal adult worms	Obstruction / biliary migration
Strongyloides	Autoinfection across mucosa	Hyperinfection with immune suppression

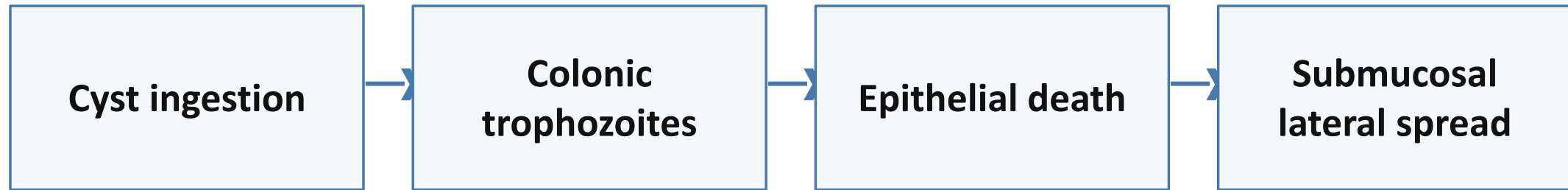
Schistosomiasis: Eggs, not worms, drive bowel injury

- Adult worms reside in mesenteric veins
- Eggs retained in mucosa and submucosa trigger inflammation
- Granulomatous reaction may cause bleeding and obstruction
- Parasitic granulomas require appropriate exposure and organism evidence

Intestinal cestodes are largely luminal

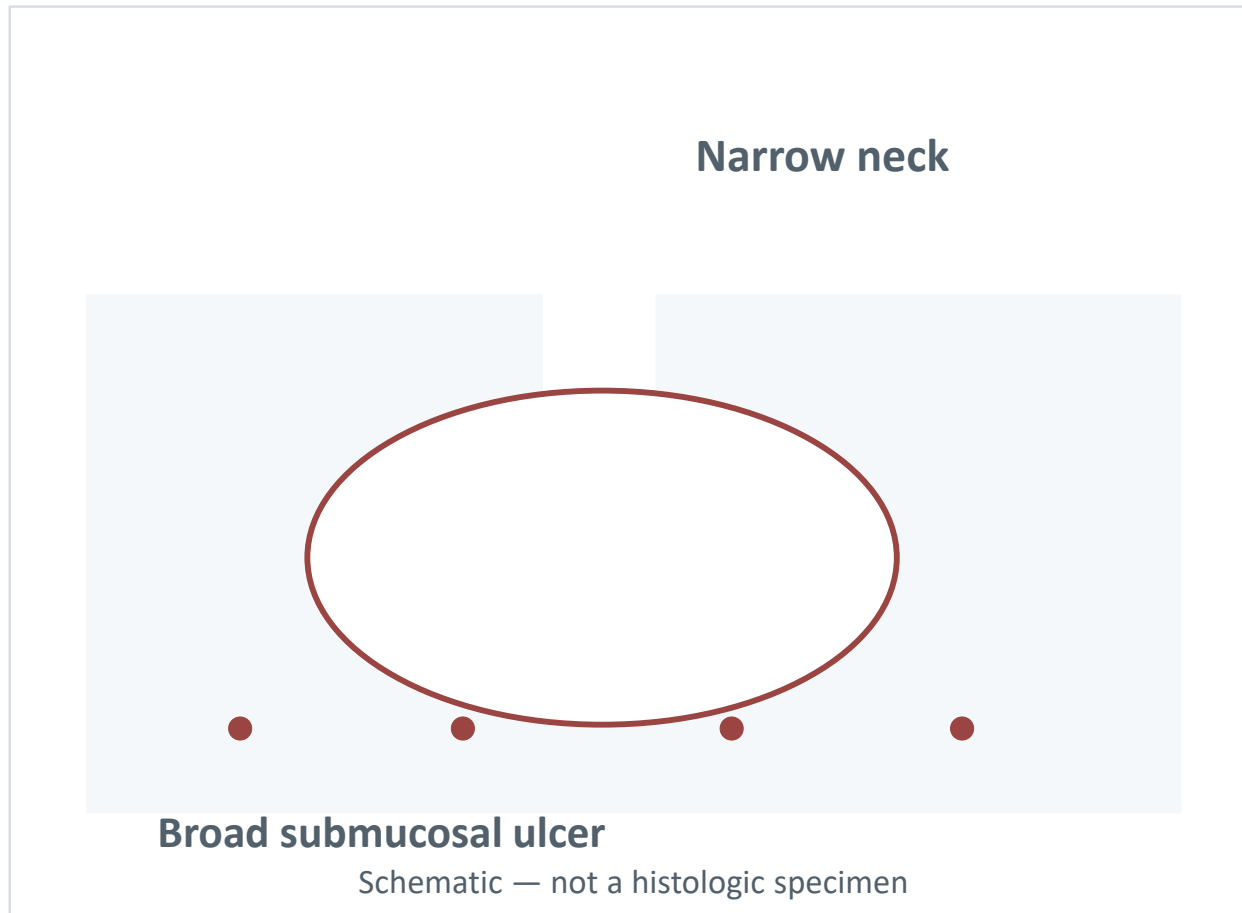
- Fish, pork, and other tapeworms attach by a scolex
- Most do not invade host intestinal tissues
- Eggs and proglottids shed in stool allow identification
- Diphyllbothrium may consume dietary vitamin B12 and cause deficiency

Entamoeba histolytica creates flask-shaped ulcers



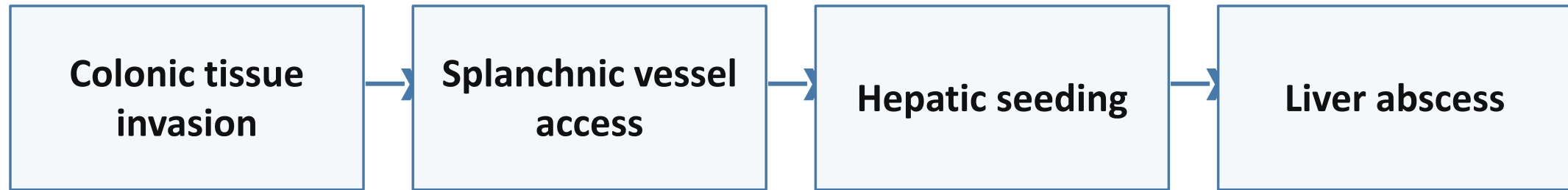
- The deep ulcer base can be wider than the surface opening
- Inflammation, hemorrhage, and dysentery follow tissue invasion

Amebiasis: Recognize the ulcer topology



- Narrow mucosal opening overlies broader submucosal destruction
- Trophozoites can resemble macrophages on routine microscopy
- Ingested erythrocytes within trophozoites provide a useful morphologic clue
- Cecal and right-colonic involvement is common

Amebiasis can disseminate to the liver

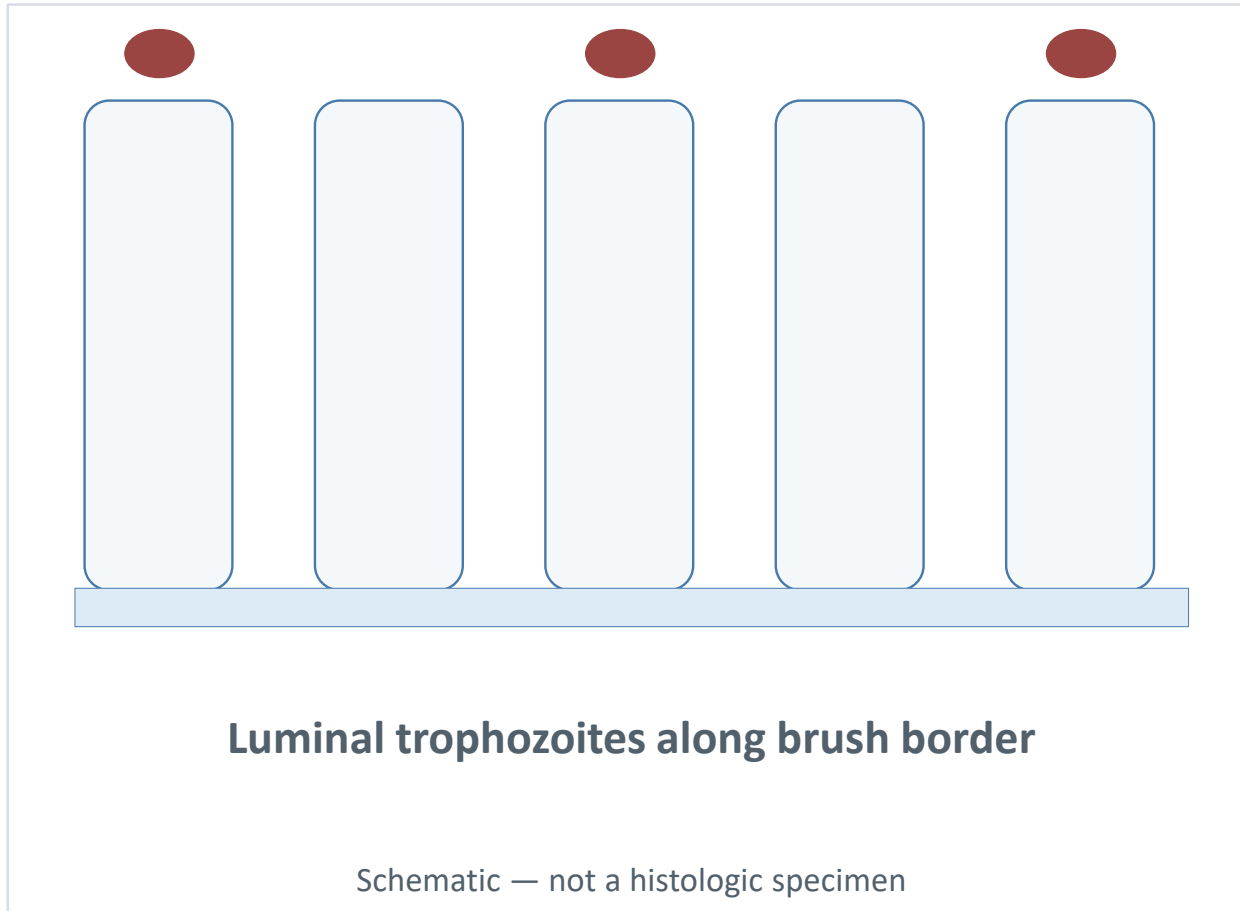


- A hepatic abscess can persist after intestinal symptoms subside
- Spread beyond the liver is uncommon but documented

Giardia: Surface adherence, not deep invasion

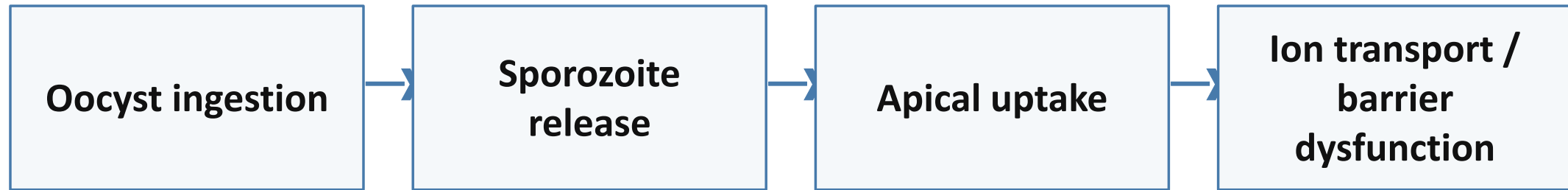
- Fecally contaminated water transmits resistant cysts
- Trophozoites adhere to the small-bowel brush border
- Brush-border enzyme loss, epithelial injury, and malabsorption occur
- Severe or persistent infection is more likely with antibody deficiency

Giardia: Organisms can overlay normal villi



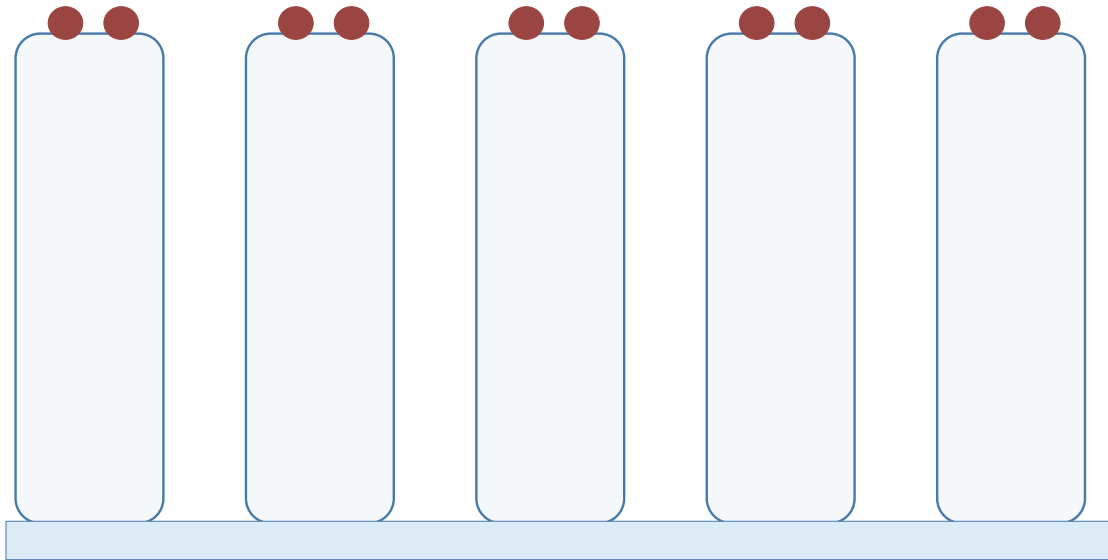
- Pear-shaped trophozoites have two similarly sized nuclei
- Numerous luminal organisms may accompany nearly normal mucosa
- Heavy infection can cause mild blunting and intraepithelial lymphocytosis
- Lack of tissue invasion distinguishes it from amebiasis

Cryptosporidium occupies an apical intracellular niche



- Parasites sit within an epithelial-derived vacuole near the brush border
- Malabsorption, chloride secretion, and junction leak produce watery diarrhea

Cryptosporidium: Deceptively surface-associated



Apical parasite-associated vacuoles

Schematic — not a histologic specimen

- Tiny organisms appear to sit on the luminal surface
- They are actually enveloped by a thin layer of host cytoplasm
- Heavy infection can cause villous atrophy and crypt hyperplasia
- The terminal ileum and proximal colon are commonly involved

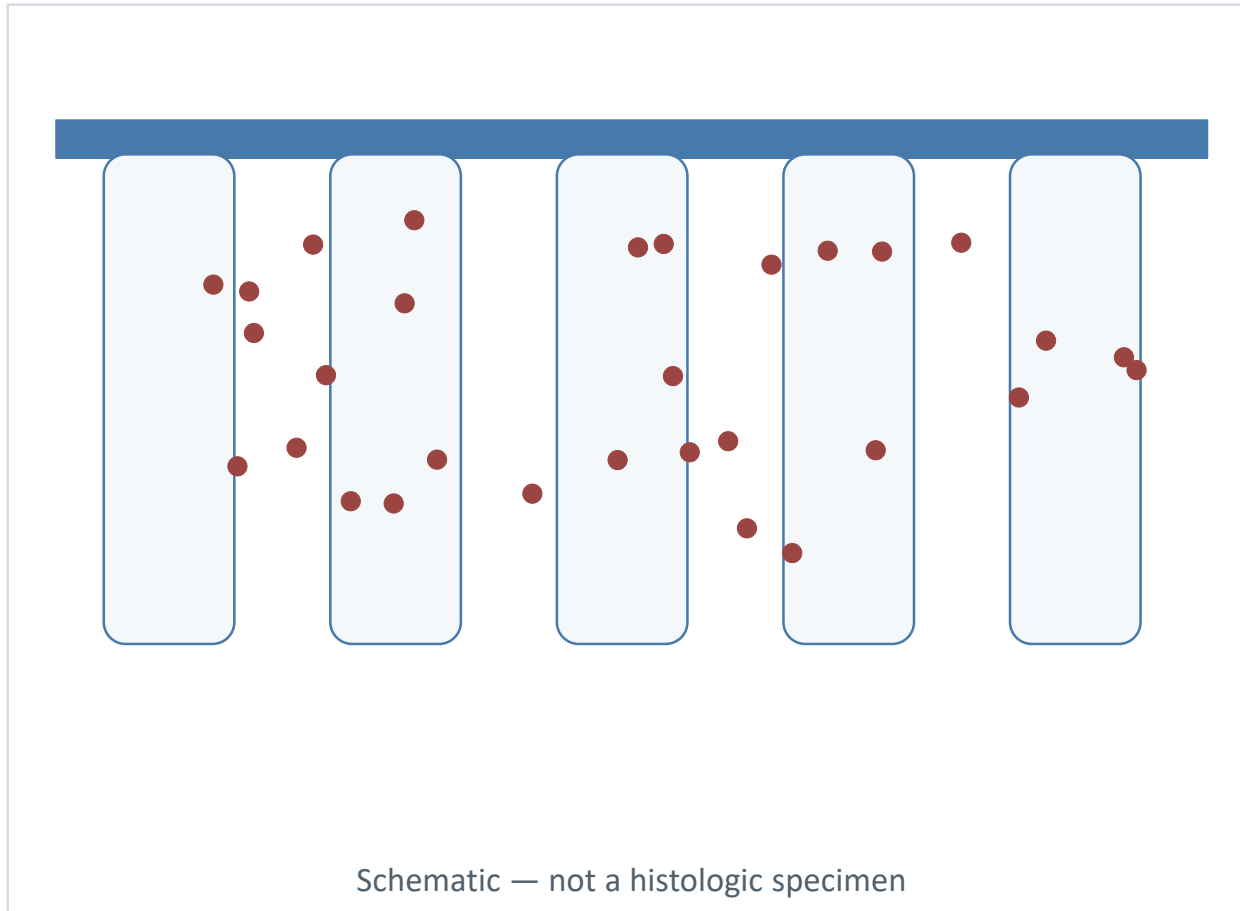
Three protozoa: Morphology versus mechanism

Organism	Mode of injury	Diagnostic clue
Entamoeba	Invasion; Deep ulcers	Flask ulcer; RBC-ingesting trophozoites
Giardia	Small-bowel surface adherence	Paired nuclei; Luminal pear-shaped organisms
Cryptosporidium	Apical vacuolar infection	Small surface-associated bodies; Stool oocysts

Biopsy pattern: Use it to constrain the differential

Pattern	Likely mechanisms	Potential causes
Intact villi / minimal injury	Secretory toxin, surface adherence	Cholera, ETEC, Giardia
Acute cryptitis; Preserved spacing	Acute invasive infection	Campylobacter, Shigella, EIEC
Pseudomembranes / crypt eruptions	Severe epithelial toxin injury	C. Difficile; Ischemia in differential
Foamy lamina propria cells	Macrophage-rich infection	Whipple; Mycobacterial mimic

Acute colitis does not equal chronic IBD



- Neutrophilic cryptitis and crypt abscesses are shared by many infections
- Preserved crypt architecture supports an acute self-limited process
- Infection can produce aphthous ulcers or granulomas and mimic Crohn disease
- Biopsy timing, distribution, and microbiology remain essential

A pseudomembrane is not organism proof

- Classic crypt-associated eruptions strongly suggest C. Difficile
- Ischemic injury and other necrotizing disorders may also produce membranes
- Tissue morphology should be correlated with toxin testing
- Avoid labeling C. Difficile solely from an isolated membrane

Stool testing is pathogen- and context-dependent

- Bacterial stool cultures help identify organisms with overlapping colitis patterns
- Stool toxin testing is central to C. Difficile assessment in the source
- Eggs and parasites, cysts, or oocysts may be sought in helminthic / protozoal disease
- Blood cultures are informative in suspected systemic enteric fever

Case: Acute febrile bloody diarrhea

Question: Which mechanisms and organisms best fit neutrophilic cryptitis with preserved crypt spacing?

- A patient develops fever, abdominal cramping, and bloody diarrhea after a food exposure
- Colon biopsy shows cryptitis and focal crypt abscesses without chronic distortion
- Consider invasive bacterial colitis before diagnosing inflammatory bowel disease

Case interpretation: Acute inflammatory colitis

- Campylobacter, Shigella, Salmonella, and EIEC are plausible mechanisms
- Histology alone cannot separate most acute bacterial colitides
- Exposure history and appropriate stool testing determine etiology
- EHEC also needs consideration when hemorrhagic disease predominates

Case: Watery diarrhea with little tissue injury

Question: Why can a near-normal intestinal biopsy accompany severe dehydration?

- A patient develops sudden copious watery stools following contaminated-water exposure
- Mucosa shows little structural destruction
- Enterotoxin-driven electrolyte secretion is more plausible than an invasive ulcerative process

Case interpretation: Dissociation of function and form

- Cholera toxin activates $G_{s\alpha}$ and cAMP-dependent chloride secretion
- ETEC produces related enterotoxin-mediated ion transport defects
- Massive luminal water flow need not produce prominent neutrophilic injury
- Rapid fluid loss is the immediate clinical danger

Six integrative principles

- Watery versus bloody diarrhea reflects distinct dominant injury mechanisms
- Organism tropism and exposure history are diagnostically informative
- Histology is a pattern, not usually a species-level diagnosis
- Some microbes cause systemic infection, HUS, or immune sequelae
- Immune status changes severity and persistence
- Test interpretation must distinguish infection from colonization

The final diagnostic distinction

- Clinical syndrome directs the initial pathogen differential
- Exposure history and immune status refine pretest probability
- Histologic pattern helps identify mechanisms and dangerous mimics
- Microbiologic tests establish the causative organism when morphology is nonspecific