

Ulcerative Colitis

Inflammatory bowel disease: mechanisms, morphology and clinicopathologic interpretation

A pathology teaching lecture

Dr Abu Suraih Sakhri

MBBS, MD (Pathology)

www.abusuraihsakhri.com

Learning objectives

- Identify the characteristic continuous, rectum-based distribution of ulcerative colitis.
- Explain the immune, microbial and epithelial components of the multifactorial pathogenesis.
- Recognize gross and microscopic evidence of activity and chronic mucosal injury.
- Distinguish ulcerative colitis from Crohn disease and discuss major complications.

Definition: Chronic inflammatory disease of the colon

- Ulcerative colitis is a chronic, relapsing form of inflammatory bowel disease.
- Inflammation extends continuously proximally from the rectum.
- Disease primarily involves the mucosa, with superficial submucosal extension in severe cases.
- The usual distribution is confined to the colon and rectum.

Ulcerative colitis in the inflammatory bowel disease spectrum

Feature	Ulcerative colitis	Crohn disease
Principal site	Colon and rectum	Any gastrointestinal site
Typical pattern	Continuous	Discontinuous (“skip”)
Inflammatory depth	Mucosal	Often transmural
Typical complication	Severe colitis / toxic megacolon	Stricture / fistula

Distribution begins at the rectum

Segmental map of large bowel (schematic)



Distal → proximal

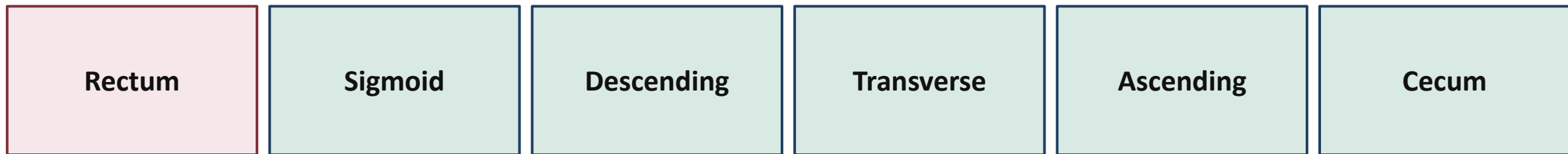
 Involved mucosa

Inflammation is continuous; Normal bowel is not ordinarily interposed between diseased segments.

Colored segments convey disease distribution, not anatomical shape or segment length.

Ulcerative proctitis: Disease confined distally

Segmental map of large bowel (schematic)



Distal → proximal

 Involved mucosa

Proctitis describes ulcerative colitis restricted to the rectum.

Colored segments convey disease distribution, not anatomical shape or segment length.

Proctosigmoiditis and left-sided colitis

Segmental map of large bowel (schematic)



Distal → proximal

 Involved mucosa

Distal phenotypes may involve rectum and sigmoid or extend through the descending colon.

Colored segments convey disease distribution, not anatomical shape or segment length.

Pancolitis: Extensive colonic involvement

Segmental map of large bowel (schematic)



Distal → proximal

 Involved mucosa

Pancolitis denotes involvement of the entire colon; It is relevant to complications and surveillance.

Colored segments convey disease distribution, not anatomical shape or segment length.

Backwash ileitis does not imply Crohn disease

- The small bowel is usually spared in ulcerative colitis.
- Mild distal ileal mucosal inflammation can accompany severe pancolitis.
- This phenomenon is termed backwash ileitis.
- Interpret ileal inflammation alongside colonic distribution and overall morphology.

Cecal red spot: An important distribution caveat

Segmental map of large bowel (schematic)



Distal → proximal

 Involved mucosa

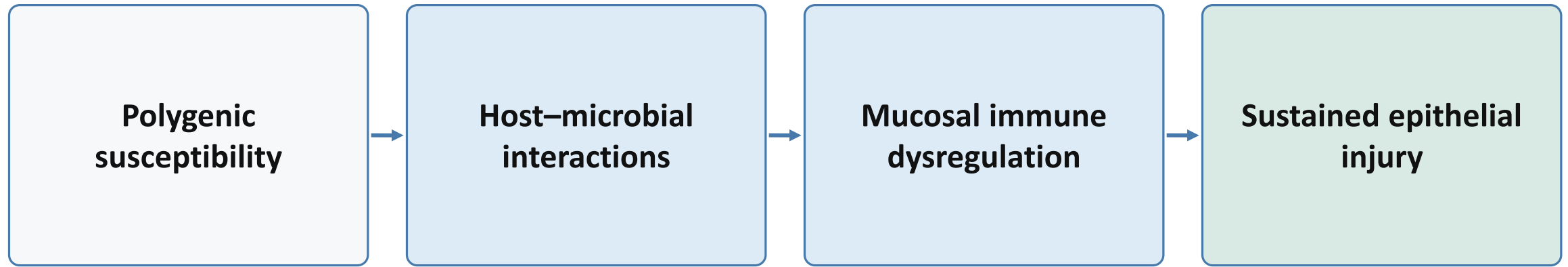
A focal appendiceal/cecal focus may accompany left-sided ulcerative colitis without typical Crohn-type skip disease.

Colored segments convey disease distribution, not anatomical shape or segment length.

Epidemiology and clinical onset

- Ulcerative colitis commonly presents in adolescence or early adulthood but can begin at any age.
- Inflammatory bowel disease is prevalent in North America, northern Europe and Australia.
- Incidence is also rising in regions where inflammatory bowel disease was historically uncommon.
- Population and environmental trends support a contribution from host–environment interactions.

Multifactorial pathogenesis: Interacting systems



No single pathogen or single-gene model explains ordinary ulcerative colitis.

Schematic causal framework; Associations should not be interpreted as established single-step mechanisms.

Genetic susceptibility is polygenic

- More than 200 inflammatory bowel disease risk alleles have been identified.
- Known variants account for only a minority of overall disease risk, particularly in ulcerative colitis.
- Many variants are shared by ulcerative colitis and Crohn disease.
- Risk loci implicate immune signaling, bacterial responses and host defense.

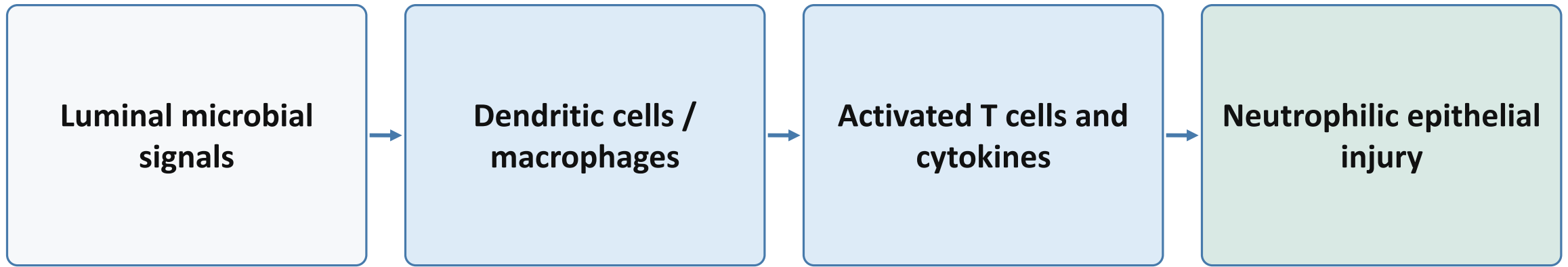
Shared genetic architecture does not mean identical risk

Genetic observation	Clinicopathologic significance
Many shared risk polymorphisms	Common inflammatory pathways underlie both disorders
NOD2 susceptibility variants	Strongly linked to Crohn disease, not typical ulcerative colitis
PTPN22 risk variants	Opposing risk directions between the two conditions
Ulcerative colitis extent	May correlate with aggregate genetic associations

Interpreting genetic association

- A genetic association signals susceptibility, not inevitability of disease.
- Risk-allele prevalence and effect sizes differ between populations.
- Regulatory-region loci may alter expression without changing protein sequence.
- Pathology reflects combined genetic, environmental, microbial and immune influences.

Mucosal immunity: The cellular inflammatory circuit



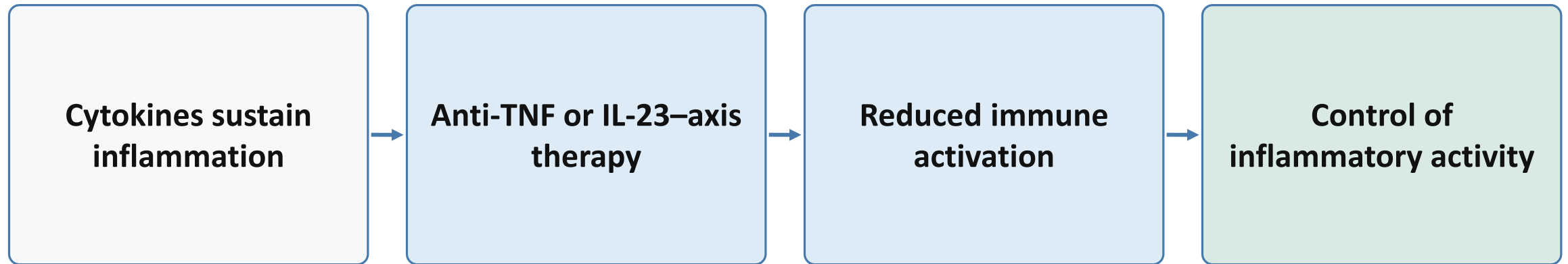
This is a conceptual immune circuit; The initiating microbial species remain uncertain.

Schematic causal framework; Associations should not be interpreted as established single-step mechanisms.

T-cell pathways in inflammatory bowel disease

- Th1 and Th17 inflammatory responses are implicated in both major forms of inflammatory bowel disease.
- Ulcerative colitis also shows a limited Th2-associated component.
- Cytokine-mediated immune recruitment perpetuates epithelial damage.
- Morphologic activity is manifested by neutrophils injuring crypt epithelium.

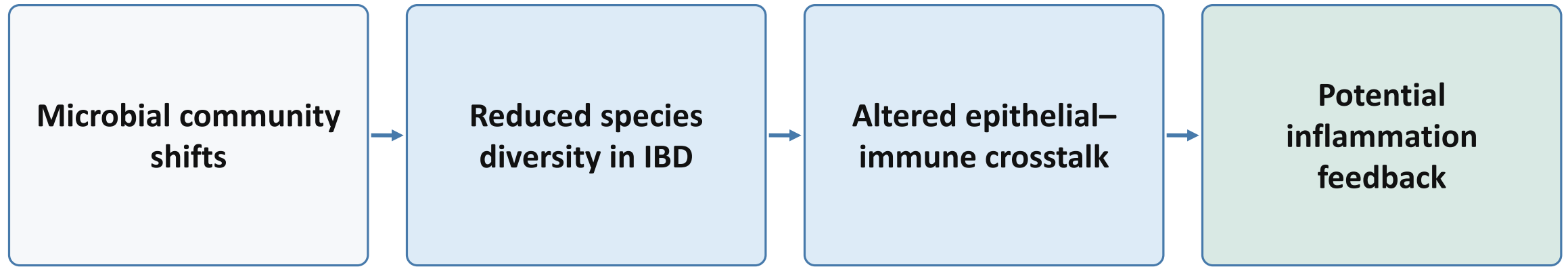
Therapeutic responses support immune involvement



Treatment efficacy supports an immune contribution; It does not establish one universal pathogenesis.

Schematic causal framework; Associations should not be interpreted as established single-step mechanisms.

Microbiome: Dysbiosis is associated with disease



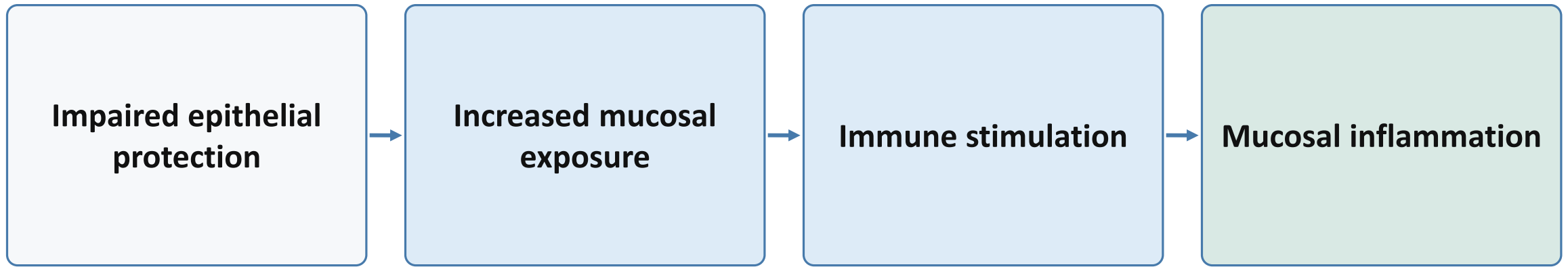
Whether dysbiosis precedes inflammation or results from it is often unresolved.

Schematic causal framework; Associations should not be interpreted as established single-step mechanisms.

Microbial findings: Observation versus inference

Observed or proposed	Interpretation
Dysbiosis in patients with IBD	Association documented
Persistent immune responses to commensals	Plausible pathogenic mechanism
Specific universal microbial trigger	Not established
Microbial metabolites modifying immunity	Active area of investigation

Barrier function links lumen and mucosal immunity



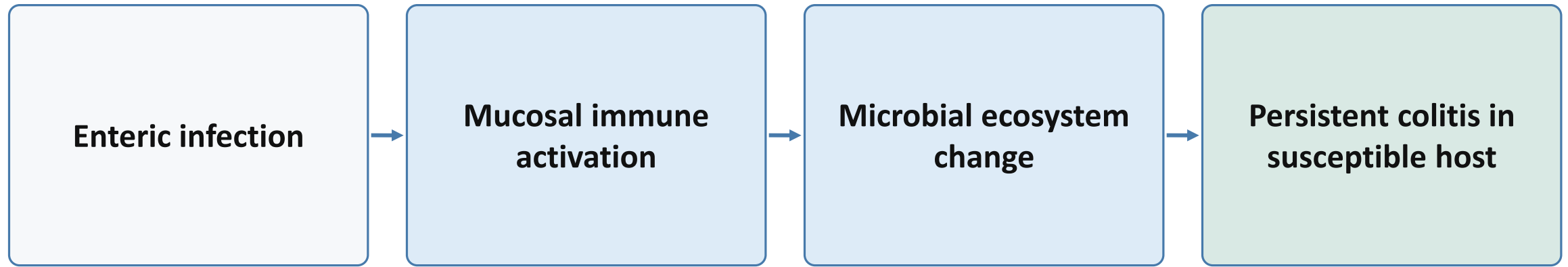
Epithelial function is one contributor; Barrier data are especially clear in Crohn disease.

Schematic causal framework; Associations should not be interpreted as established single-step mechanisms.

What remains unknown in ulcerative colitis

- Exact triggers of onset in previously healthy individuals are not known.
- No single causative organism accounts for the disease.
- Dysbiosis may be either cause or consequence of intestinal inflammation.
- Immune, barrier and host-genetic models remain incomplete.

A possible infectious antecedent



Proposed mechanism, not a proven sequence for every patient.

Schematic causal framework; Associations should not be interpreted as established single-step mechanisms.

Observed environmental associations require caution

Observation	Interpretive caution
Psychological stress can precede disease or relapse	Association does not establish direct etiology
Symptom onset after smoking cessation	Clinical association; Not a recommendation to smoke
Infectious enteritis can precede onset	Possible trigger in a susceptible patient
Regional incidence has increased	Several environmental explanations remain possible

Gross pathology follows a continuous gradient

Segmental map of large bowel (schematic)



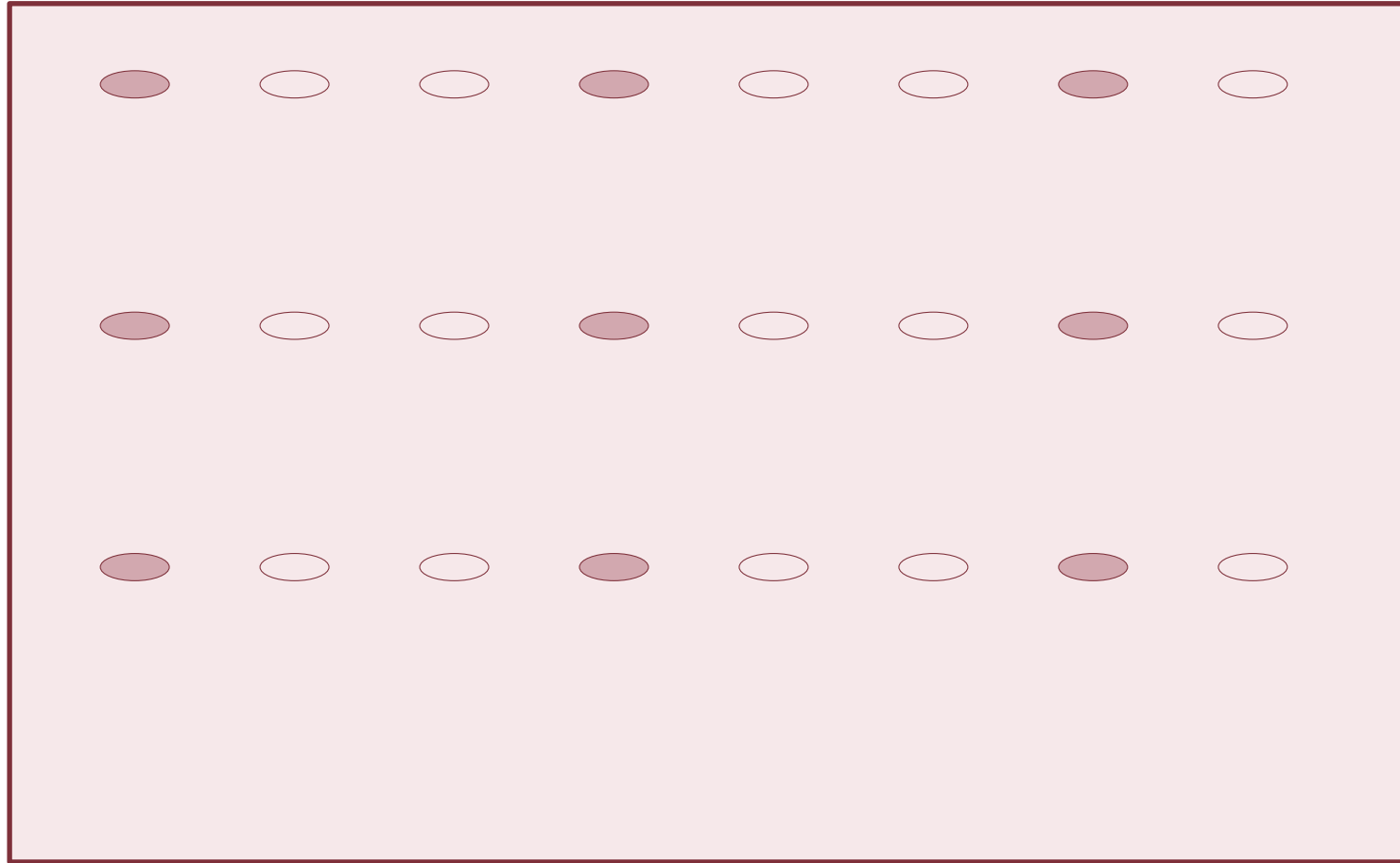
Distal → proximal

 Involved mucosa

The boundary between inflamed and uninvolved colon may be abrupt, despite continuous disease proximally from the rectum.

Colored segments convey disease distribution, not anatomical shape or segment length.

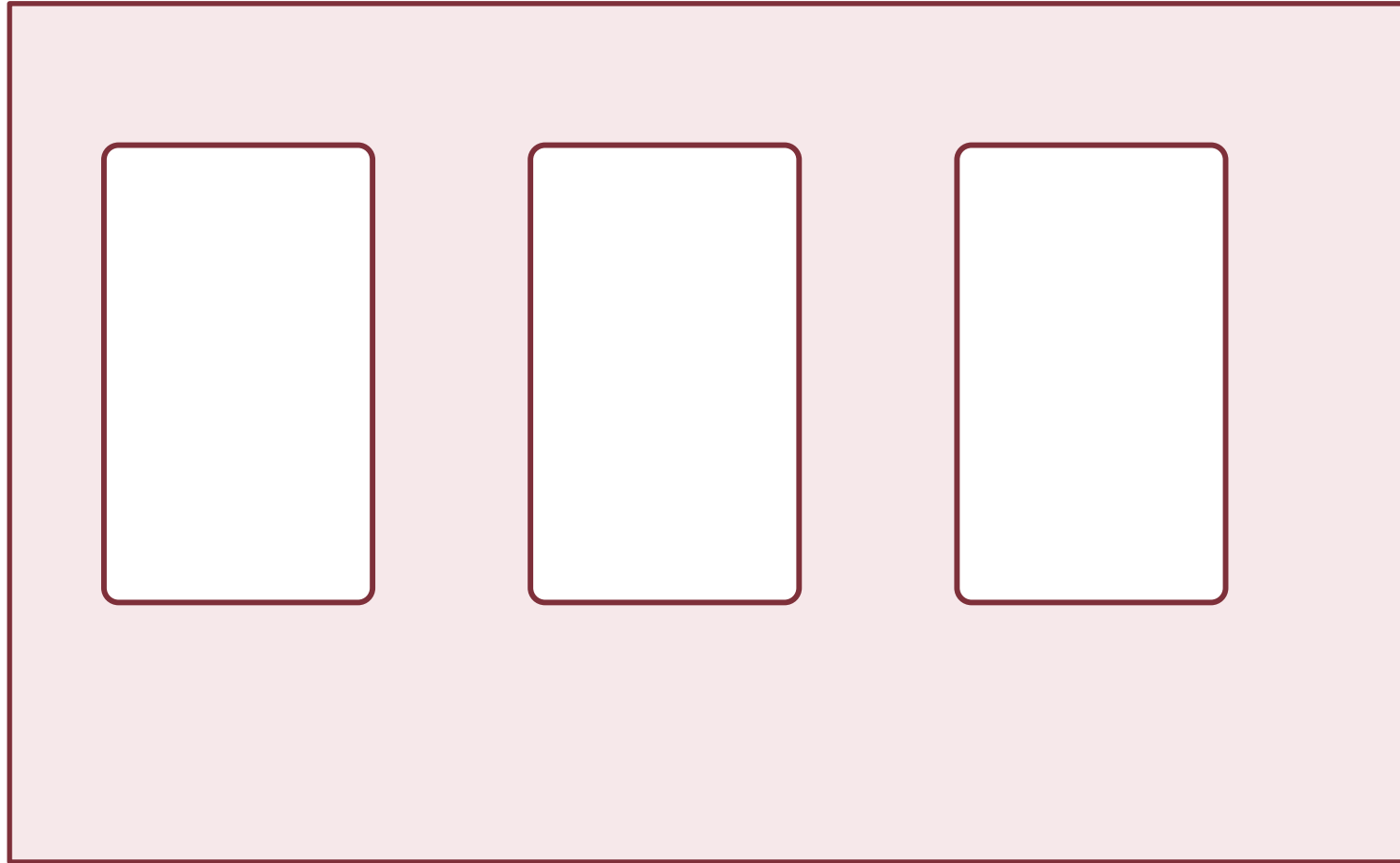
Active colitis: Red, granular mucosal surface



Erythema and granularity reflect mucosal inflammation. These changes vary in intensity along the involved colon.

Schematic, not a gross pathology specimen

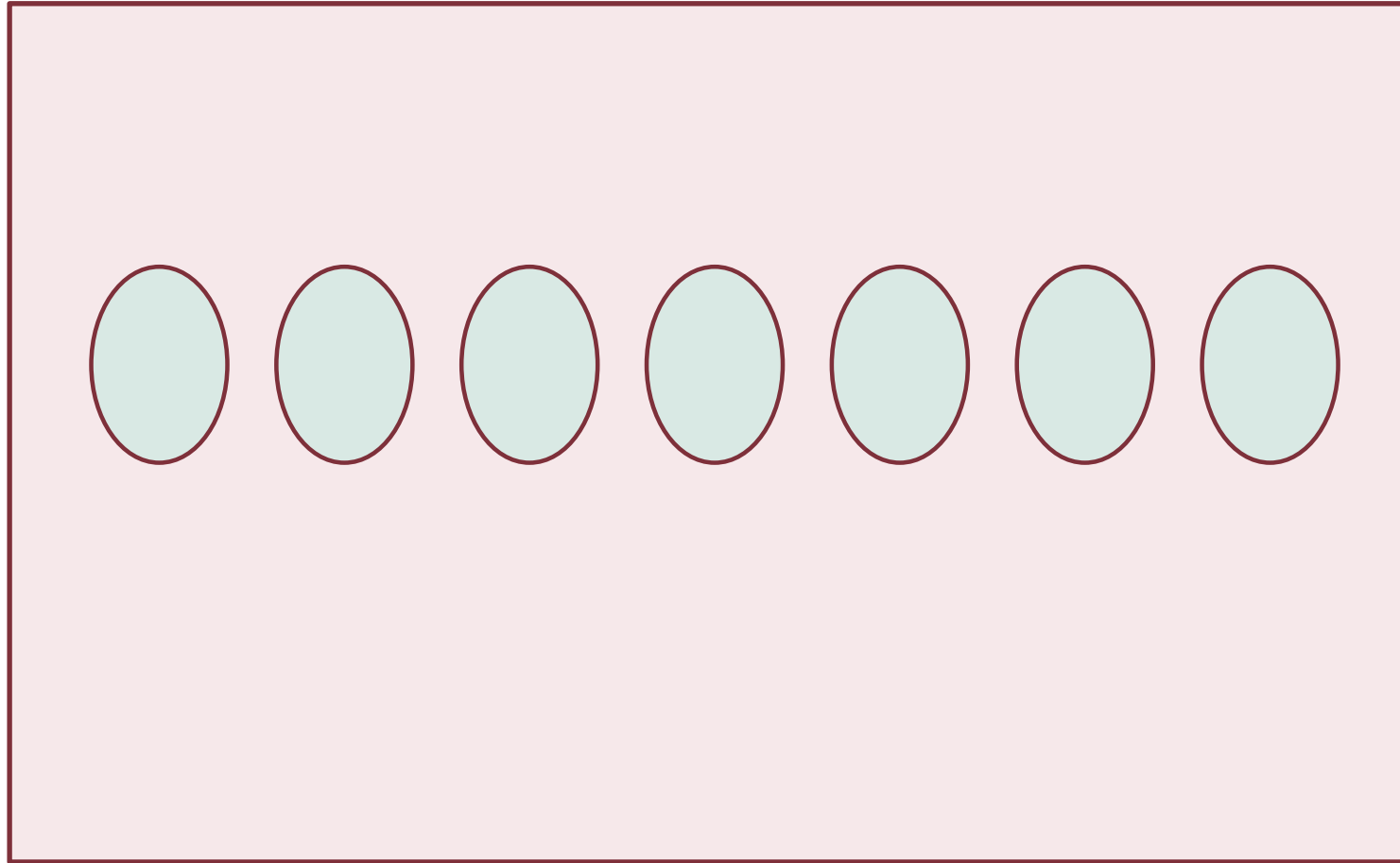
Ulcerative colitis produces broad-based ulcers



Ulceration may be extensive and broad based rather than the narrow, deep fissures characteristic of Crohn disease.

Schematic, not a gross pathology specimen

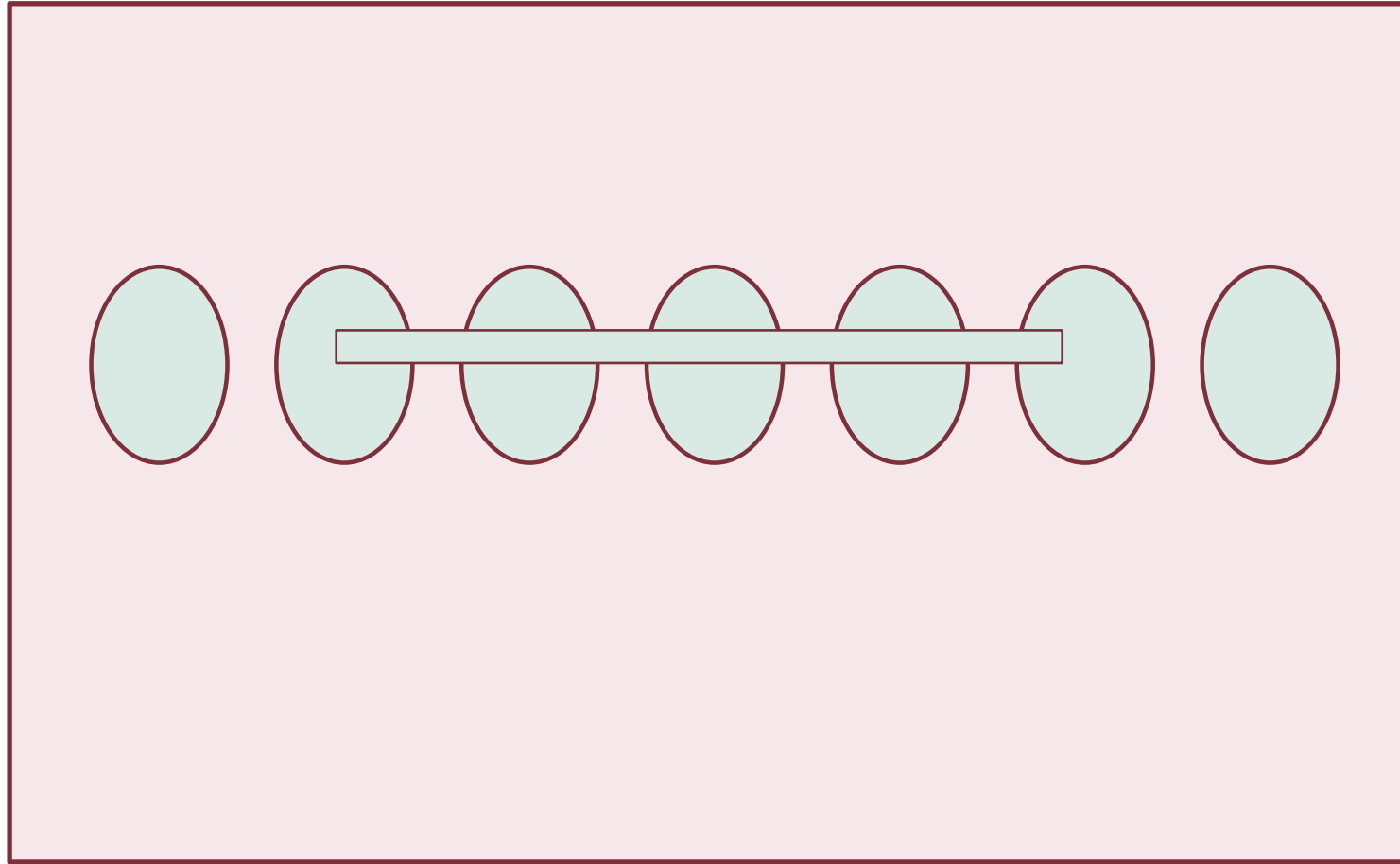
Inflammatory pseudopolyps are regenerative islands



Residual or regenerating mucosa protrudes between regions of ulceration and is not itself evidence of epithelial neoplasia.

Schematic, not a gross pathology specimen

Mucosal bridges can join pseudopolyps



The tips of inflammatory polyps may become connected by bridges of residual/regenerating mucosa.

Schematic, not a gross pathology specimen

Chronic mucosal atrophy may erase normal folds



Repeated mucosal injury and repair can produce a smooth, atrophic surface with reduced normal folding.

Schematic, not a gross pathology specimen

Superficial disease explains the usual normal wall thickness

Mucosa	Mucosa affected; Deeper wall usually preserved.
Submucosa	
Muscularis propria	
Serosa	

Inflammation is primarily mucosal.

Layer cross-section schematic; Relative layer thickness is illustrative.

Why strictures point toward an alternative diagnosis

Feature	Ulcerative colitis	Crohn disease
Typical bowel-wall fibrosis	Mild / minimal	More prominent
Fibrostenotic narrowing	Uncommon	Characteristic complication
Wall thickening	Not a defining feature	Often substantial
Fistulas	Not characteristic	Common with penetrating disease

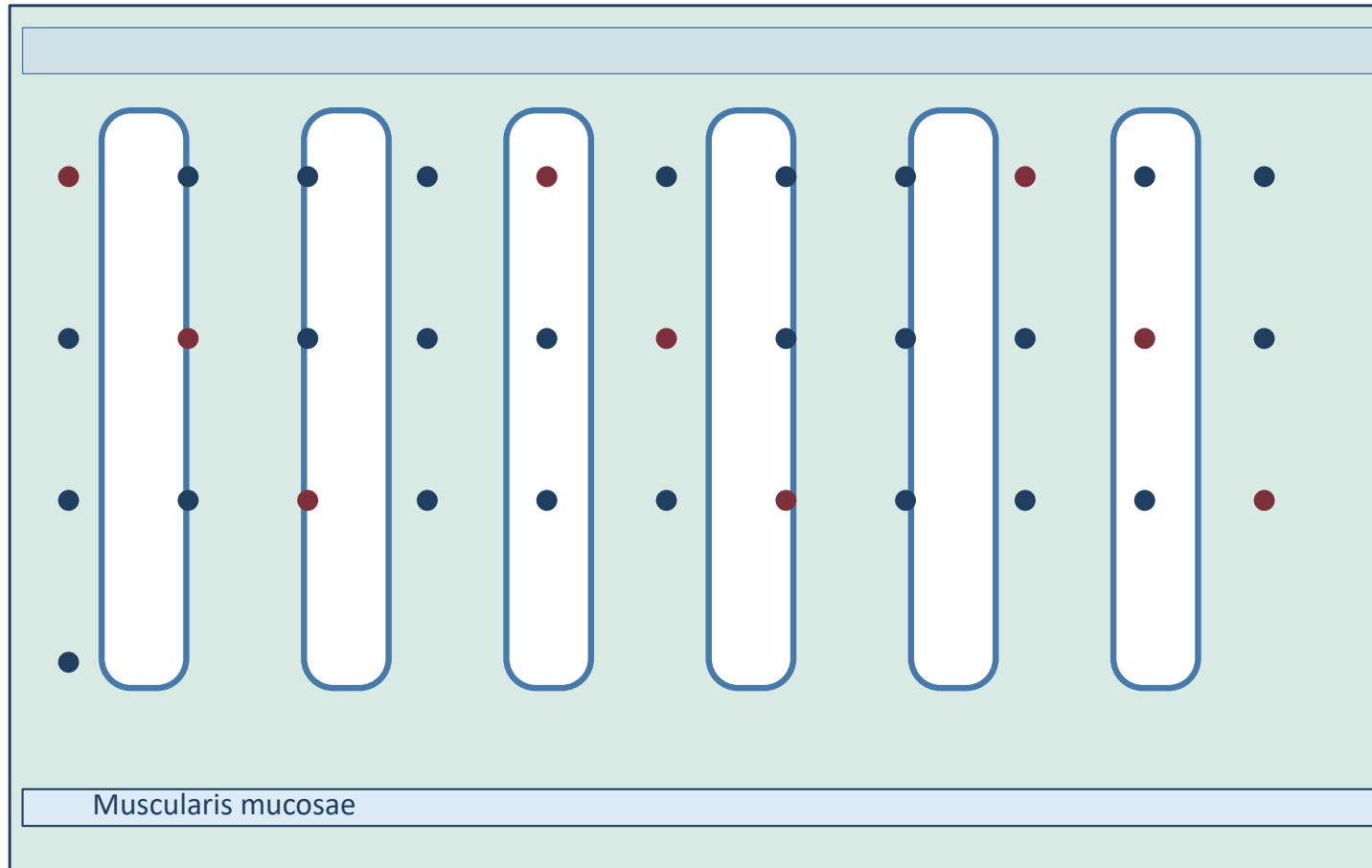
Microscopic inflammation is mainly mucosal

Mucosa	Lamina propria inflammation with crypt injury dominates.
Submucosa	
Muscularis propria	
Serosa	

Inflammation is primarily mucosal.

Layer cross-section schematic; Relative layer thickness is illustrative.

Inflammatory infiltrates populate the lamina propria

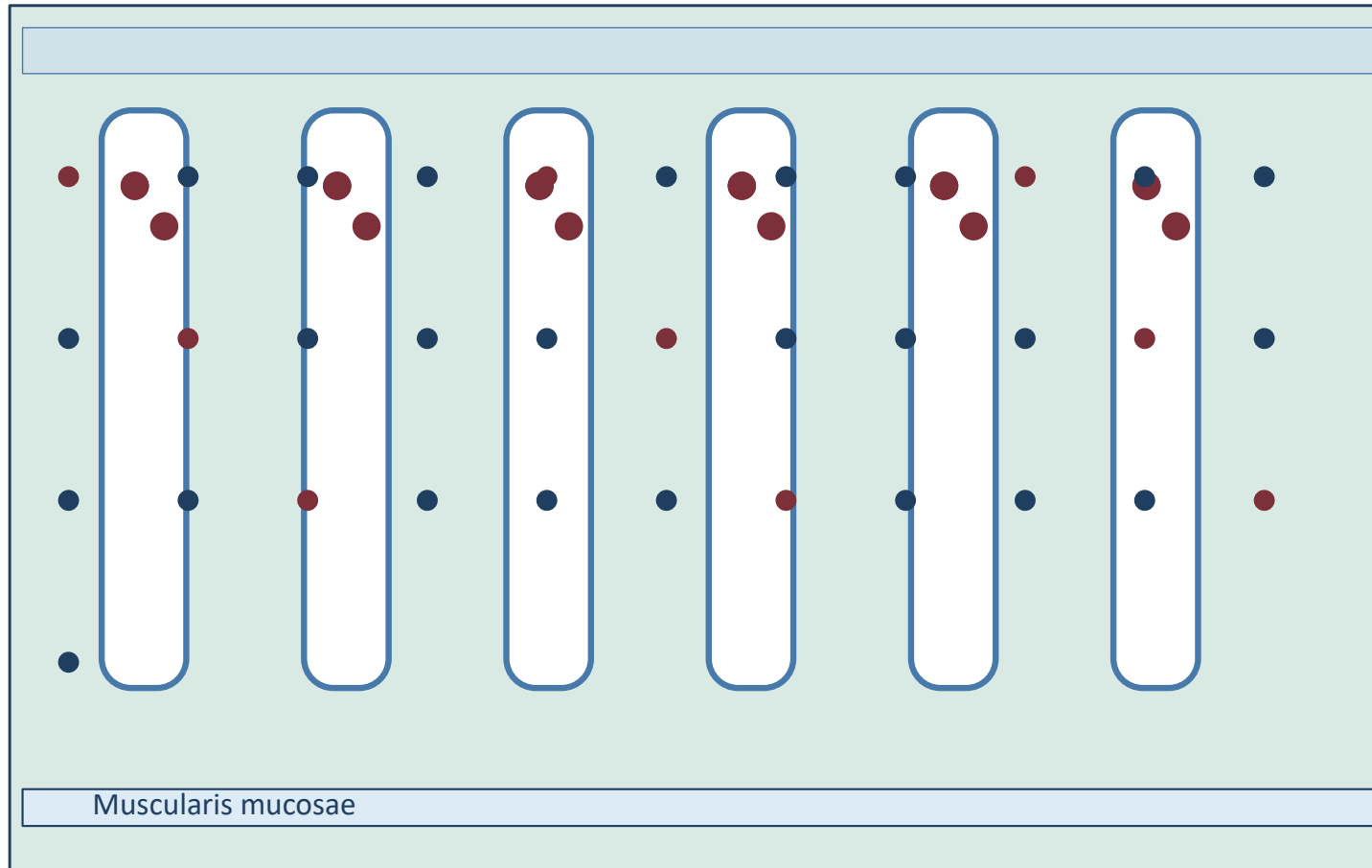


Microscopic interpretation

Increased mucosal inflammatory cells accompany glandular injury. Assess both chronic inflammation and neutrophilic activity.

Illustrative crypt architecture — not a tissue photomicrograph

Cryptitis: Neutrophils invade crypt epithelium

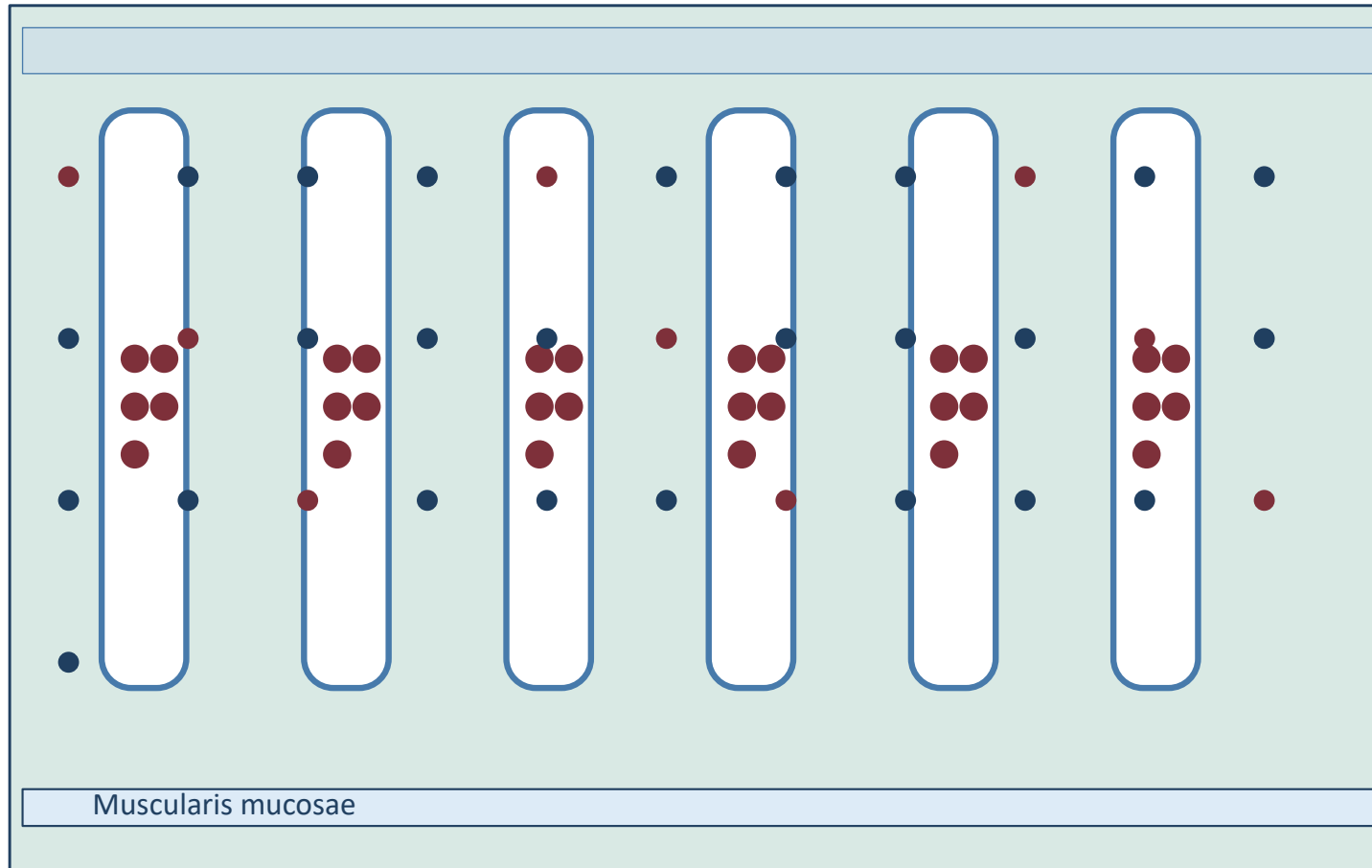


Microscopic interpretation

An active inflammatory change. Neutrophils breach the glandular epithelium and injure epithelial cells.

Illustrative crypt architecture — not a tissue photomicrograph

Crypt abscess: Neutrophils accumulate in crypt lumina

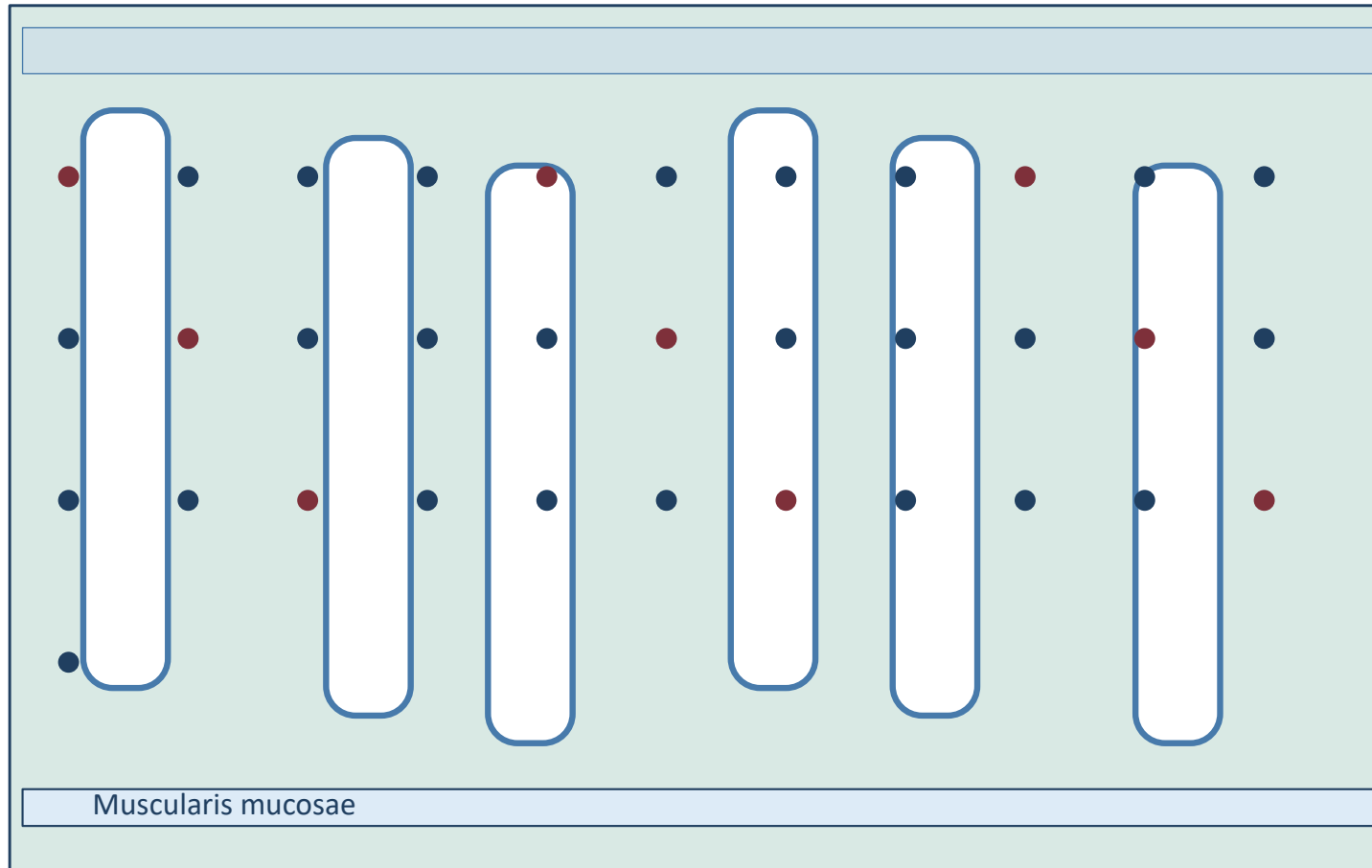


Microscopic interpretation

Clusters of neutrophils within gland lumina signify active crypt injury. They are not specific to ulcerative colitis.

Illustrative crypt architecture — not a tissue photomicrograph

Repeated injury distorts crypt architecture



Microscopic interpretation

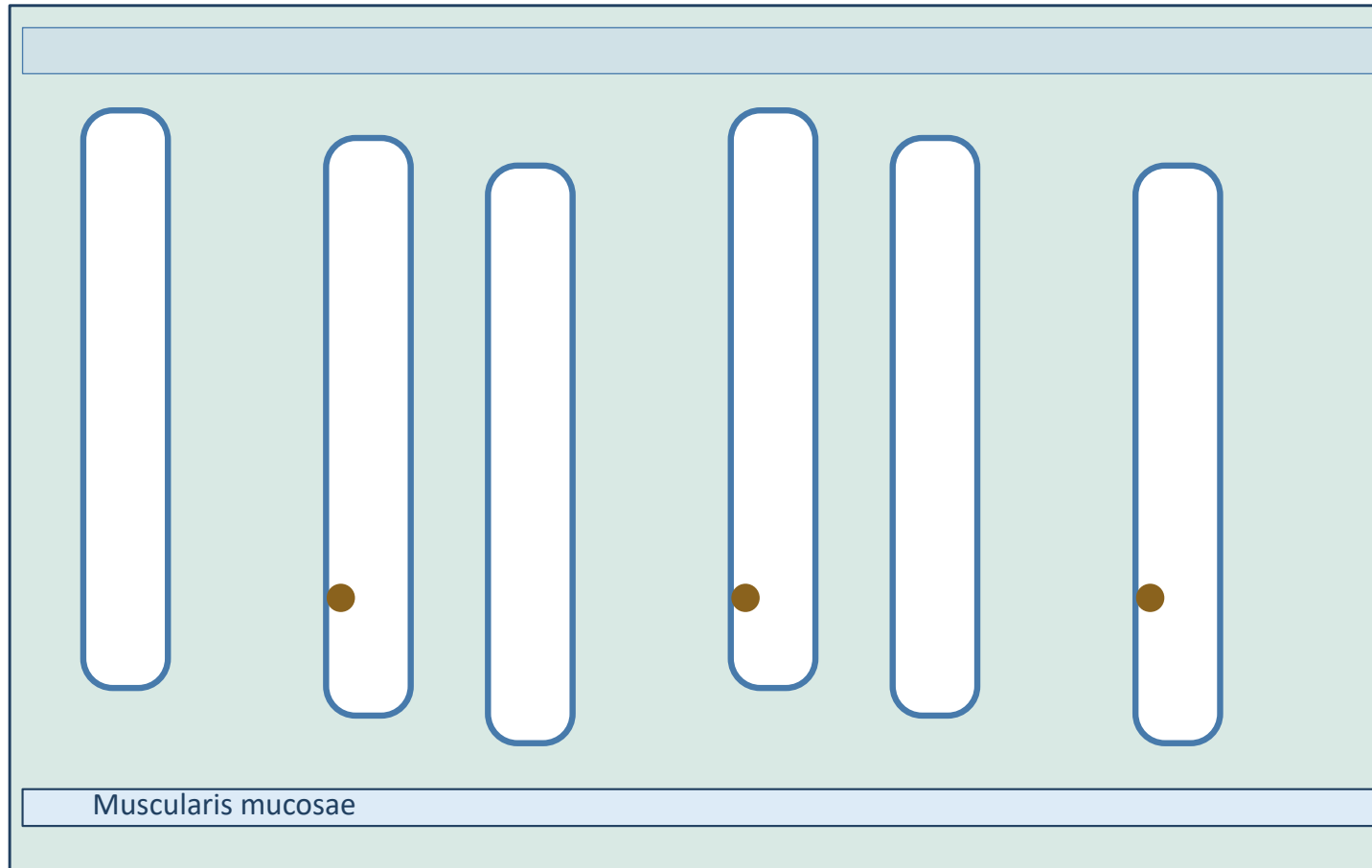
Long-standing injury and regeneration cause abnormal crypt orientation, branching and spacing.

Illustrative crypt architecture — not a tissue photomicrograph

Metaplastic changes indicate chronic injury

Change	Meaning in chronic colitis
Paneth cell metaplasia in left colon	Paneth cells appear where normally absent
Pseudopyloric metaplasia	Glands resemble gastric antral-type glands
Architectural distortion	Residual evidence of repeated crypt destruction and repair
Mucosal atrophy	Reduced crypt population after longstanding injury

Paneth cell metaplasia in distal colonic mucosa



Microscopic interpretation

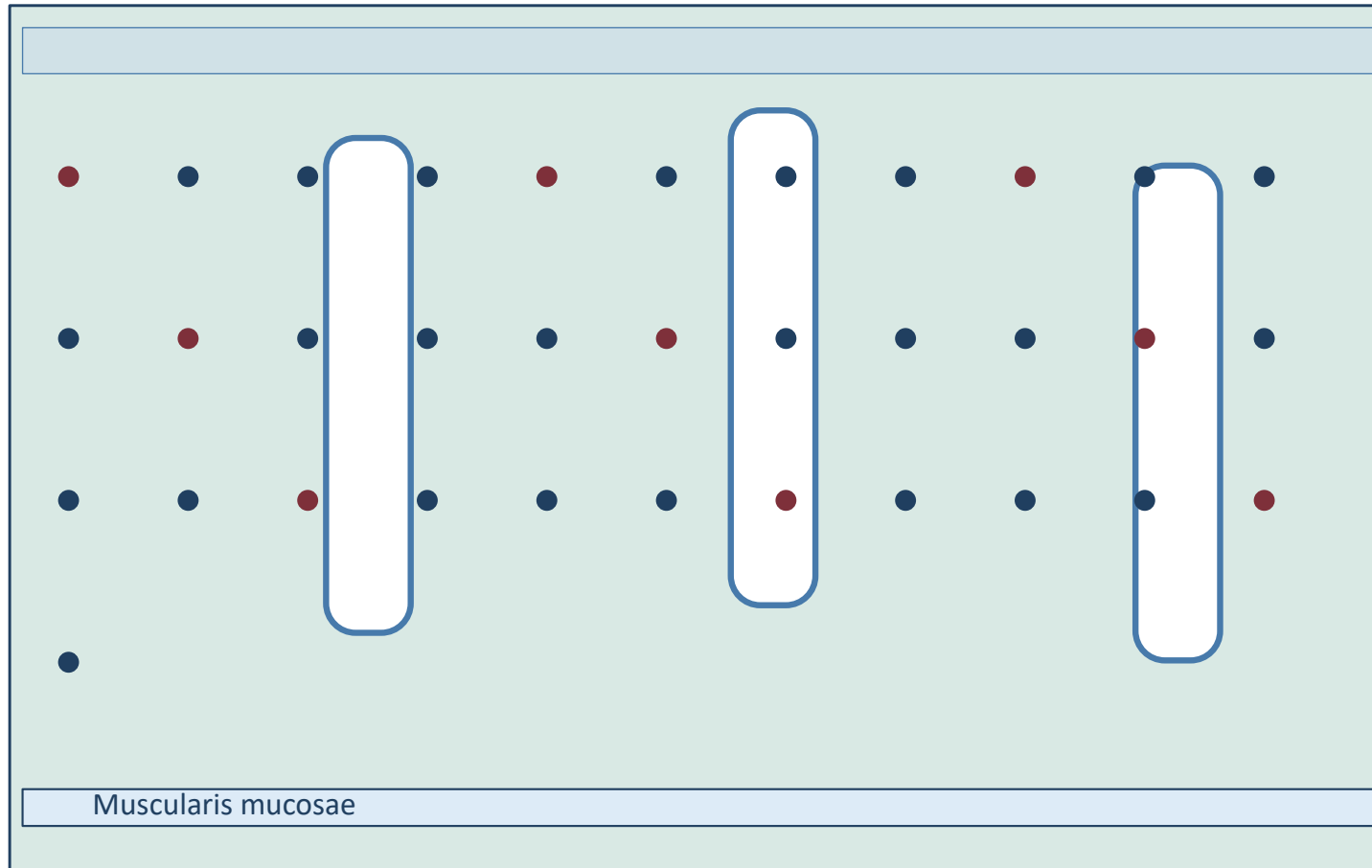
Paneth cells are normally absent from much of the left colon. Their presence there supports chronic mucosal injury.

Illustrative crypt architecture — not a tissue photomicrograph

Pseudopyloric metaplasia as a marker of repair

- Involved colonic mucosa can show glands with gastric antral-like differentiation.
- It emerges in the setting of repeated epithelial injury and regeneration.
- It is not an isolated, pathognomonic marker of ulcerative colitis.
- Interpret with the distribution and other histologic findings.

Mucosal atrophy results from prolonged injury



Microscopic interpretation

Loss of crypts and altered gland spacing may persist after activity decreases. This is a marker of chronic tissue damage.

Illustrative crypt architecture — not a tissue photomicrograph

Severe ulcers may reach the submucosa

Mucosa
Submucosa
Muscularis propria
Serosa

Severe mucosal
destruction can
penetrate
superficially.

Schematic layer distribution is simplified.

Layer cross-section schematic; Relative layer thickness is illustrative.

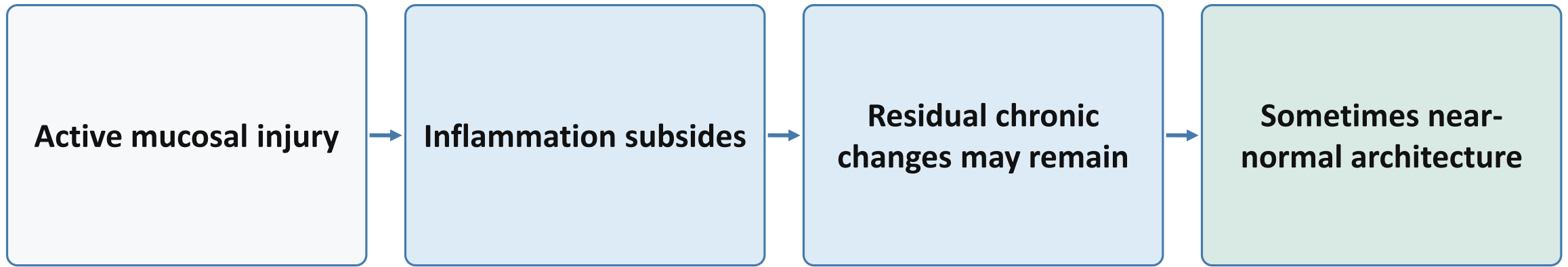
Granulomas are a key differential clue

Finding	Interpretation
Well-formed noncaseating granulomas	Suggest Crohn disease or an alternative granulomatous colitis
Typical ulcerative colitis biopsy	No Crohn-type granulomas expected
Crypt rupture-associated granulomatous reaction	Interpret in an appropriate tissue context
Absent granulomas	Does not by itself exclude Crohn disease

Recognizing activity versus chronicity

Active inflammation	Chronic injury
Neutrophilic cryptitis	Architectural crypt distortion
Crypt abscesses	Metaplasia of epithelial glands
Surface epithelial injury and ulceration	Crypt loss and mucosal atrophy
Current inflammatory damage	Evidence of prior recurrent damage

Histologic healing may be incomplete or extensive



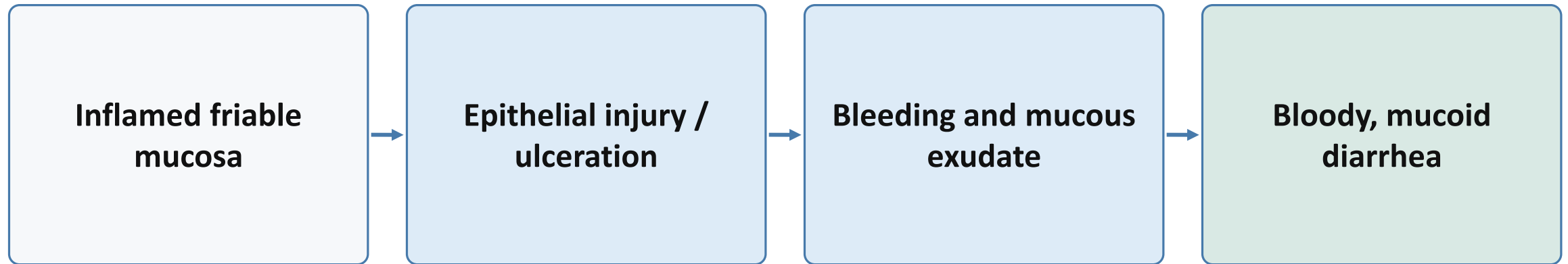
Avoid equating endoscopic remission with obligatory microscopic normalization.

Schematic causal framework; Associations should not be interpreted as established single-step mechanisms.

Classic symptomatic attack

- Bloody diarrhea is often mixed with stringy mucoid material.
- Lower abdominal pain and cramping are frequent.
- Cramps may be temporarily relieved by defecation.
- Attacks may persist for days to months before symptoms subside.

Why blood and mucus accompany active colitis



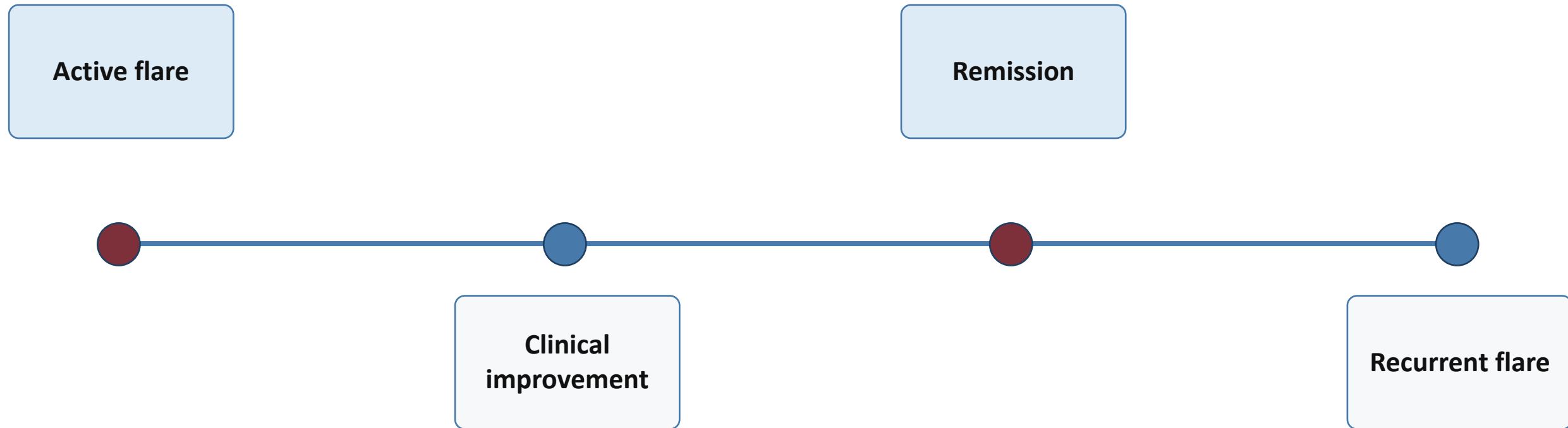
This mechanistic schema relates the classic clinical finding to observed mucosal injury.

Schematic causal framework; Associations should not be interpreted as established single-step mechanisms.

Symptoms reflect inflammation of the distal colon

- Distal mucosal injury contributes to rectal bleeding and urgency.
- Lower abdominal cramping often accompanies active bowel movements.
- Rectal involvement is an important clue when clinical findings are interpreted.
- The intensity of symptoms can fluctuate across relapses and remissions.

Relapsing disease: Activity alternates with remission

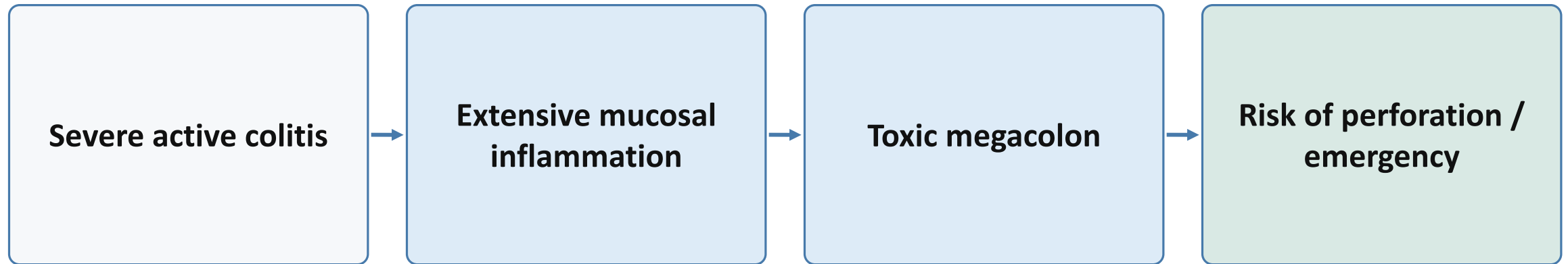


The cycle is variable; Individual episodes may last days, weeks or months.

Disease burden varies substantially

- More than half of patients have clinically mild disease description.
- However, most patients experience at least one relapse over a ten-year period.
- An initial episode can occasionally be severe enough to require urgent care.
- Severity must be assessed clinically rather than inferred from the diagnosis alone.

Life-threatening deterioration requires recognition



Toxic megacolon is an uncommon but important complication of fulminant disease.

Schematic causal framework; Associations should not be interpreted as established single-step mechanisms.

Toxic megacolon: A severe colonic complication

Marked colonic dilation in severe colitis

**Severe colonic
inflammation**



**Systemic toxicity /
emergency**

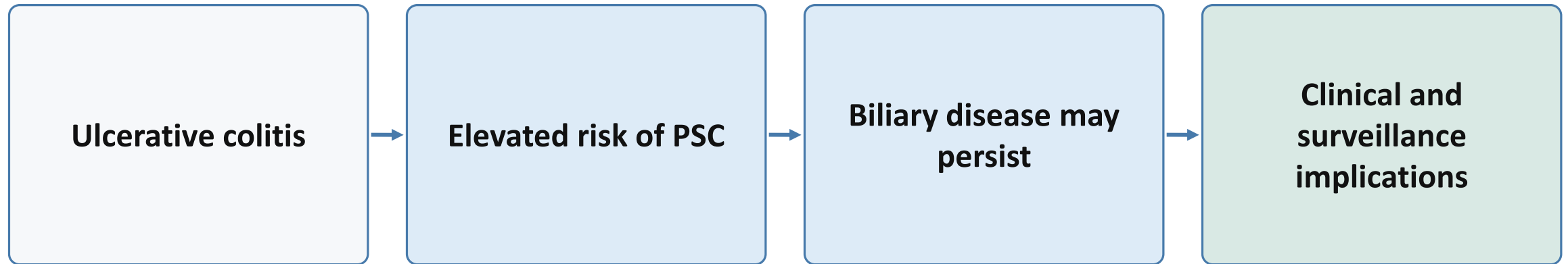
Perforation is not a routine feature of ulcerative colitis

- Deep transmural injury is not the usual pattern of ulcerative colitis.
- Perforation is uncommon outside severe cases progressing to toxic megacolon.
- The presence of fistulas or penetrating sinus tracts favors Crohn disease.
- Acute deterioration warrants assessment for urgent complications.

Extraintestinal manifestations extend beyond the bowel

System	Examples
Musculoskeletal	Migratory polyarthrititis; Sacroiliitis; Ankylosing spondylitis
Ocular	Uveitis
Skin	Inflammatory skin lesions
Hepatobiliary	Primary sclerosing cholangitis

Primary sclerosing cholangitis: Strong association



Primary sclerosing cholangitis affects approximately 5% of patients with ulcerative colitis.

Schematic causal framework; Associations should not be interpreted as established single-step mechanisms.

Ulcerative colitis versus Crohn disease: Gross anatomy

Criterion	Ulcerative colitis	Crohn disease
Distribution	Rectum-based, continuous	Skip lesions frequent
Affected organ	Colon	Any GI segment
Ulcers	Broad and superficial	Often linear / fissuring
Bowel wall	Usually not thickened	Often thickened
Perianal fistula	Not characteristic	May be present

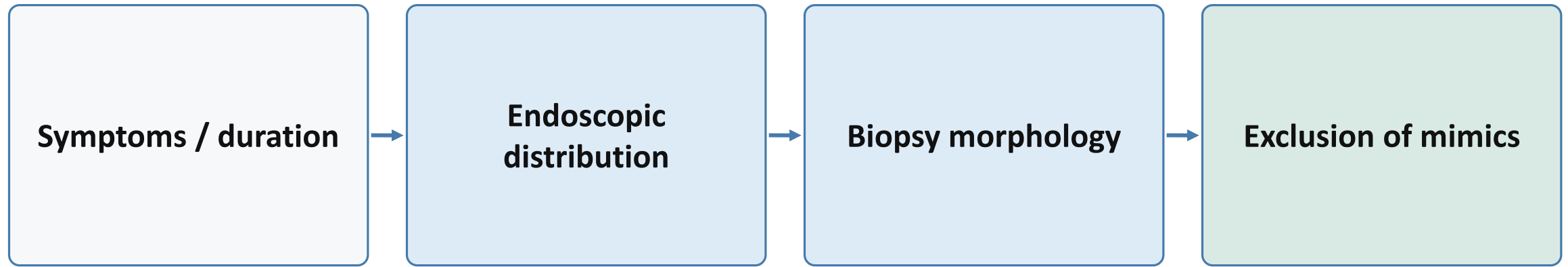
Ulcerative colitis versus Crohn disease: Microscopy

Criterion	Ulcerative colitis	Crohn disease
Inflammatory depth	Mainly mucosa	Frequently transmural
Crypt abscesses	May occur	May occur
Architectural distortion	May occur	May occur
Noncaseating granulomas	Absent in typical UC	May be found
Fibrosis	Mild / minimal	Can be prominent

Serology: Supportive association, not a diagnostic definition

Marker	Association in source	Limitation
P-ANCA	Reported in up to 75% of UC	Insufficient to establish diagnosis alone
P-ANCA in Crohn disease	Reported in fewer than 10%	Negative finding does not classify IBD
Anti-Saccharomyces cerevisiae	Often found in Crohn disease	Not a stand-alone diagnostic discriminator

Diagnosis integrates several independent data streams



No isolated histologic sign or serologic marker is universally definitive.

Schematic causal framework; Associations should not be interpreted as established single-step mechanisms.

Biopsy interpretation: Report activity and chronicity

Assess	Pertinent histologic questions
Activity	Are neutrophils present in crypts, or is there ulceration?
Chronicity	Are glands distorted, lost or metaplastic?
Distribution	Is disease diffuse or patchy across sampled sites?
Alternatives	Are granulomas, infections or other patterns present?

Pitfalls in differentiating the colitides

- Crypt abscesses and distortion occur in both ulcerative colitis and Crohn disease.
- Medical treatment and healing can reduce activity or alter the apparent distribution.
- Backwash ileitis and the cecal red spot are recognized ulcerative colitis caveats.
- Multiple biopsy sites and the clinical pattern are needed for synthesis.

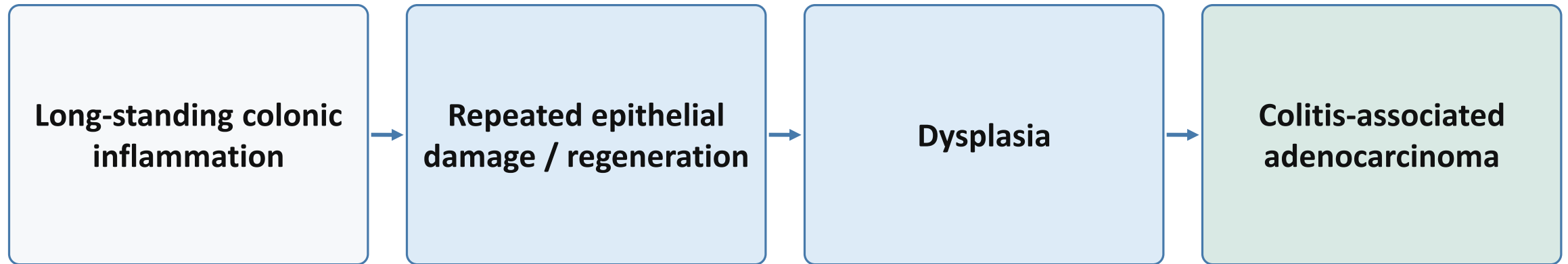
Indeterminate colitis: A legitimate diagnostic category

Typical ulcerative colitis	Indeterminate colitis
Characteristic continuous colonic disease	Continuous disease may coexist with atypical features
No typical granulomas	Patchy microscopic changes may create ambiguity
No Crohn-type perianal disease	Perianal lesions or Crohn family history may coexist
Confident assignment possible	Cannot confidently assign to UC or Crohn disease

Differential diagnosis: Not every colitis is IBD

- Infectious enterocolitis can cause diarrhea, bleeding and neutrophilic mucosal injury.
- Other forms of colitis may produce overlapping architectural or inflammatory patterns.
- Morphology alone must be integrated with history, disease distribution and microbiology.
- Failure to exclude a treatable infectious cause can misclassify a patient.

Chronic inflammatory injury can precede neoplasia



Dysplasia is a recognized precursor; Progression is not inevitable in every patient.

Schematic causal framework; Associations should not be interpreted as established single-step mechanisms.

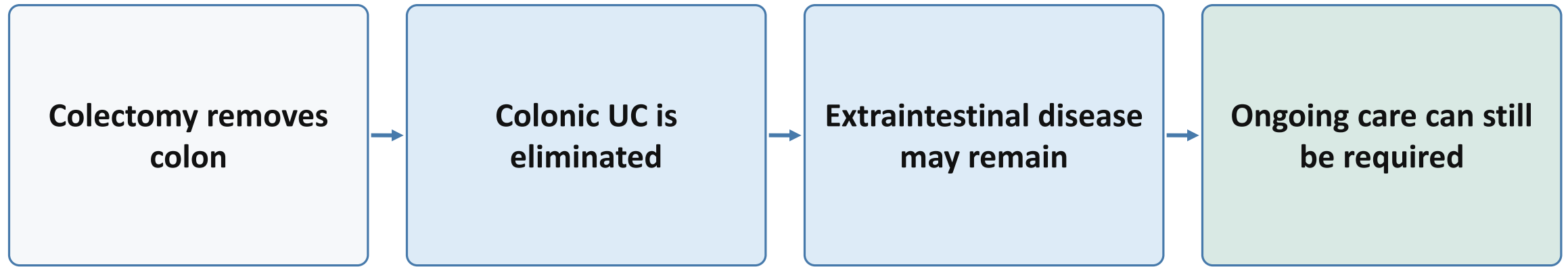
Risk of colitis-associated neoplasia varies

Higher-risk feature	Why it matters
Longer disease duration	Risk rises especially after prolonged disease
More extensive colonic involvement	Pancolitis generally confers greater risk
Frequent/severe active inflammation	Cumulative mucosal injury is relevant
Associated primary sclerosing cholangitis	Additional risk and earlier surveillance

Surveillance targets dysplasia rather than symptoms

- Colitis-associated dysplasia may develop in endoscopically inconspicuous flat mucosa.
- High-resolution endoscopy and chromoendoscopy can target suspicious areas.
- Histologic examination remains essential to establish and grade dysplasia.
- Surveillance plans reflect disease duration, extent, inflammation and coexisting PSC.

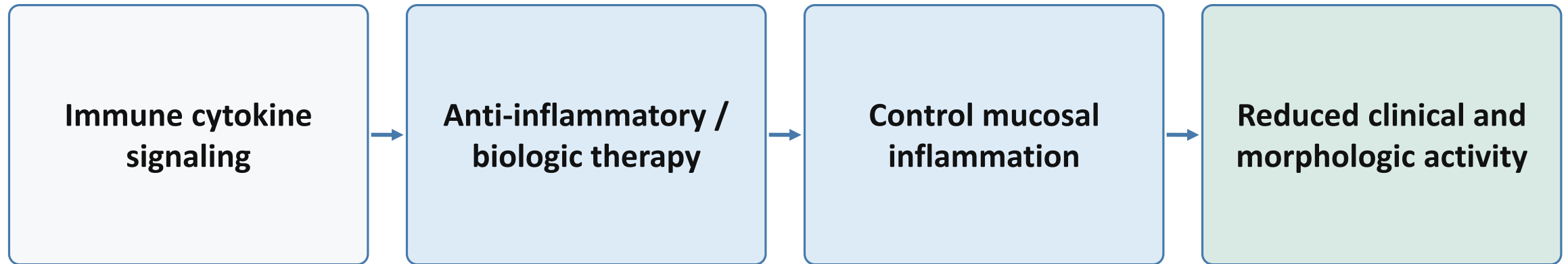
Colectomy and the distinction between disease sites



In contrast to Crohn disease, typical intestinal ulcerative colitis does not recur in another GI segment.

Schematic causal framework; Associations should not be interpreted as established single-step mechanisms.

Treatment mechanisms correspond to disease biology



Robbins also discusses JAK inhibition and altered lymphocyte trafficking as therapeutic targets.

Schematic causal framework; Associations should not be interpreted as established single-step mechanisms.

Applied case: A continuous colitis

A young adult has repeated episodes of bloody, mucoid diarrhea. Colonoscopy describes disease extending continuously from the rectum through the left colon. Biopsy shows crypt abscesses and glandular distortion.

Which findings most strongly support ulcerative colitis?

Case interpretation: Ulcerative colitis is favored

- Rectum-based continuous disease is a characteristic distribution.
- Crypt abscesses indicate active glandular injury.
- Crypt architectural distortion supports chronicity rather than an isolated acute event.
- Crypt abscesses are not specific; Clinical and endoscopic context remains essential.

Applied case: The granuloma problem

A patient with chronic colitis has patchy involvement, a thickened bowel wall, and a well-formed noncaseating granuloma away from a ruptured crypt.

Which alternate inflammatory bowel disease is favored?

Case interpretation: Crohn disease is favored

- Patchiness and bowel-wall thickening contrast with usual ulcerative colitis.
- An appropriately situated noncaseating granuloma supports Crohn disease.
- Transmural features are more characteristic of Crohn disease.
- Classification still depends on the full clinical and pathologic assessment.

Core discriminators for examination and practice

Domain	Ulcerative colitis clue
Distribution	Continuous colitis beginning in the rectum
Depth	Mucosal-predominant inflammation
Gross	Granularity, broad ulcers, pseudopolyps
Microscopic	Crypt activity plus chronic distortion; No typical granulomas
Complication	Toxic megacolon and colitis-associated neoplasia

Integrated summary

- Ulcerative colitis is a mucosal, rectum-based, continuous form of inflammatory bowel disease.
- Complex immune–microbial–epithelial interactions act on a genetically susceptible background.
- Activity is marked by neutrophilic crypt injury; Chronicity by distortion, metaplasia and atrophy.
- Accurate diagnosis and prognostic assessment require distribution, histology and clinical context.

References and teaching-source limitations

- Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th edition (2026), Chapter 17, pp. 727–733.
- Morphologic distinctions draw on textbook Table 17.8 and descriptions corresponding to Figs. 17.35, 17.39 and 17.40.
- Colitis-associated neoplasia is introduced only as a complication; its dedicated unit provides fuller coverage.
- Drawings are original editable schematics; no genuine photomicrographs or textbook figures are reproduced.