Diverticular Disease-Related Colitis

**TERMINOLOGY**
- Segmental colitis-associated diverticulosis (SCAD)

**ETIOLOGY/PATHOGENESIS**
- Unknown, TNF-α may play role

**CLINICAL ISSUES**
- Presents with hematochezia, abdominal pain, diarrhea
- Median age: 64 years
  - Range: 40-86 years
- Predominately involves descending and sigmoid colon (with rectal sparing)
- Treatment directed toward diverticular disease suppresses symptoms

**MACROSCOPIC**
- Mucosal changes are mild and nonspecific
- Mural changes are related more to underlying diverticulosis coli rather than SCAD

**MICROSCOPIC**
- Chronic colitis-like changes mimicking inflammatory bowel disease
- Ulcerative colitis-like variant shows changes confined to mucosa
  - Diverticulitis may or may not be present in these cases
- Crohn disease-like variant shows mural lymphoid aggregates
- Changes in both variants confined to segment involved with diverticulosis coli

**TOP DIFFERENTIAL DIAGNOSES**
- Ulcerative colitis, Crohn disease, infectious colitis, diversion colitis, NSAID-associated colitis

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*(Left)* The mucosa surrounding the openings of diverticula into the colonic lumen is erythematous and granular, consistent with diverticular disease-associated colitis (DDAC). *(Right)* It is not uncommon to find some inflammation or erosions around the luminal opening of a colonic diverticulum. To be diagnostic of DDAC, inflammation must involve the mucosa in the interdiverticular region.

*(Left)* A chronic colitis pattern of inflammatory infiltrate is seen in both the ulcerative colitis-like and Crohn disease-like variant of DDAC. The mucosal changes are indistinguishable from true inflammatory bowel disease (IBD). *(Right)* A band of lymphoplasmacytic infiltrate is present beneath the base of the crypts in the mucosa. The distinction between DDAC and true IBD can only be made by knowing the distribution of disease involvement.
Diverticular Disease-Related Colitis

**TERMINOLOGY**

**Abbreviations**
- Diverticular disease-associated colitis (DDAC)

**Synonyms**
- Segmental colitis associated with diverticulosis (SCAD)

**Definitions**
- Chronic colitis involving interdiverticular mucosa in colonic segment with diverticulosis
  - Histologic findings may mimic ulcerative colitis or Crohn disease

**ETIOLOGY/PATHOGENESIS**

**Exact Pathogenetic Mechanism Unknown**
- Immune-mediated injury may play role

**Immunologically Mediated**
- Stasis of colonic contents may promote bacterial proliferation that acts as trigger for mucosal inflammation
- Disproportionate immune response in genetically susceptible host
- Similar to inflammatory bowel disease (IBD), TNF-α has been postulated to play role in pathogenesis of SCAD

**May Be Related to Severity of Diverticulitis**
- Early mucosal inflammation around opening of diverticula into lumen, which then spreads to interdiverticular mucosa

**CLINICAL ISSUES**

**Epidemiology**
- **Incidence**
  - Estimated: ~ 0.36%
- **Age**
  - Median: 64 years (range: 40-86 years)
  - Later age of onset compared to patients with IBD
- **Sex**
  - Equal incidence in both sexes
- **Ethnicity**
  - Geographical differences are related to differences in prevalence of diverticulosis coli, which is higher in West

**Site**
- Most common in sigmoid colon; rare in other segments
- Rectum is typically spared

**Presentation**
- Hematochezia
- Crampy, abdominal pain
- Diarrhea
- Fistula tract formation and intestinal obstruction may be present in cases associated with severe diverticulitis

**Endoscopic Findings**
- Changes confined to segment involved with diverticulosis coli
  - Colonic mucosa proximal and distal to diverticular segment is normal
  - Patchy areas of erythema or exudate or diffuse mucosal granularity

**Natural History**
- Clinical course is related to severity of disease
- Endoscopic disease severity scoring system has been proposed
- Mild cases may not need any intervention, other than follow-up colonoscopy
- Severe cases or patients with continued symptoms treated with antiinflammatory medications or steroids
- Resection restricted to patients with severe symptoms unresponsive to medical therapy

**Treatment**
- **Options, risks, complications**
  - Treatment directed toward diverticular disease may suppress symptoms
    - Decrease intraluminal pressure by increasing stool bulk (high-fiber diet)
    - Surgical intervention usually dictated by severity of diverticulosis rather than SCAD
  - Drugs
    - Antibiotics for treatment of active diverticulitis
    - Oral aminosalicylates and probiotics for mild SCAD
    - Immunosuppressives for severe SCAD
      - Sulfasalazine
      - 5-aminosalicylic acid
      - Topical steroids

**Prognosis**
- Depends on patient symptoms, severity of disease, and response to medical intervention

**IMAGING**

**CT Findings**
- Colonic wall thickening in segment involved with diverticulosis and associated luminal narrowing
- Diverticular abscess, fistula, or perforation may be seen

**MACROSCOPIC**

**General Features**
- Findings related to diverticulosis coli
  - Ostia or openings of diverticula on mucosal surface
  - Sac-like outpouchings ± fecaliths
  - Peridiverticular abscesses may be present
  - Bowel wall thickening or perforation depending on severity of disease
- Findings related to SCAD
  - Mucosal erythema or granularity involving interdiverticular segments of colonic mucosal surface
  - Erosions or ulcers in severe cases

**MICROSCOPIC**

**Histologic Features**
- Chronic colitis-like mucosal changes mimicking IBD
  - Basal lymphoplasmacytosis
  - Crypt architectural disarray
  - Paneth cell metaplasia
  - Variable active inflammation with erosion or ulcer
- Mucosal and mural changes confined to segment involved with diverticulosis coli; other parts of colon are normal
Diverticular Disease-Related Colitis

**Predominant Pattern/Injury Type**
- Inflammatory, chronic

**DIFFERENTIAL DIAGNOSIS**

**Ulcerative Colitis**
- Key to diagnosis is recognizing that colitis in SCAD involves only segment with diverticulosis
- Inflammation above or below segment involved with diverticulosis colitis suggests infection or IBD as underlying etiology
- Rectum is almost always spared in SCAD but involved in ulcerative colitis

**Crohn Disease**
- Also patchy segmental colitis like SCAD
- Diagnosis of Crohn disease in segment involved with diverticulosis colitis should be made with great caution
- Clinical or radiographic evidence of disease involvement beyond diverticular segment favors Crohn disease
- Terminal ileal or upper Gl involvement favors Crohn disease

**Infectious Disease**
- *Shigella* and *Salmonella* infections can present as segmental colitides
- Stool cultures diagnostic

**Diversion Colitis**
- Clinical setting helps in making this distinction
- Morphologic findings may be similar to SCAD
- Changes in diversion colitis are confined to segment of colon removed from fecal stream
- Diversion colitis resolves with restitution of bowel stream

**NSAID-Associated Colitis**
- Can occur after only weeks of use
- May also present with hematochezia or abdominal pain
- Symptoms usually resolve with cessation of NSAIDs
- Pancolonic involvement favors NSAID-induced colitis
- Changes confined to segment involved with diverticulosis is diagnostic of SCAD

**DIAGNOSTIC CHECKLIST**

**Clinically Relevant Pathologic Features**
- Endoscopic and pathologic findings limited to segment involved with diverticulosis colitis

**Pathologic Interpretation Pearls**
- Inflammation within diverticulum ("diverticulitis") is not considered SCAD
- SCAD is defined by inflammation of flat mucosa between openings of diverticula (interdiverticular region) into colonic lumen
- Inflammation in SCAD shows chronic colitis pattern similar to IBD

**SELECTED REFERENCES**

**Diverticular Disease-Related Colitis**

**Ulcerative Colitis-Like Variant**

(Left) Marked lymphoplasmacytosis of the lamina propria and neutrophilic cryptitis and crypt abscesses are characteristic of ulcerative colitis-like variant of DDAC. (Right) In this biopsy from the sigmoid colon in a patient with DDAC, all features of a chronic colitis, such as basal lymphoplasmacytosis, architectural disarray, and Paneth cell metaplasia, are present.

**Ulcerative Colitis-Like Variant**

(Left) A chronic inactive colitis pattern may be seen in some patients where architectural disarray and metaplastic features dominate the findings, and there is minimal increase in lamina propria inflammation. Note the crypt branching and disarray and the Paneth cells in this sigmoid colon biopsy. (Right) Compact, transmural lymphoid aggregates reminiscent of Crohn disease may be seen in some resections performed for diverticulosis coli.

**Peridiverticular Abscess**

(Left) In cases where mural lymphoid aggregates raise the possibility of Crohn disease, the presence of peridiverticular abscesses, with foreign body type giant cell reaction, favors the diagnosis of diverticular disease associated colitis. (Right) Deep fissuring ulcers away from the segment involved with diverticulosis, as seen in this example, are diagnostic of Crohn disease.
Nonsteroidal Antiinflammatory Drug (NSAID) Damage

**TERMINOLOGY**
- Gastrointestinal (GI) tract injury resulting from NSAID use

**ETIOLOGY/PATHOGENESIS**
- NSAIDs: Salicylates, propionic and acetic acid derivatives, selective cyclooxygenase 2 (COX-2) inhibitors
- Toxicity to GI mucosa: 2 mechanisms of pathogenesis
  - Direct contact/irritation: Increased mucosal permeability
  - Drug action: ↓ prostaglandin synthesis, ↓ blood flow

**CLINICAL ISSUES**
- Widespread NSAID use (prescription, over the counter)
  - GI damage in 30-50% of users (mostly elderly, women)
- Symptoms: Odynophagia, dyspepsia, heartburn, abdominal pain, diarrhea, malabsorption, iron-deficiency anemia
- Endoscopy: Erosions, ulcers, exudates, hemorrhage
- GI complications with both short- and long-term treatment
  - Life-threatening GI bleeding: Highest mortality
- Rx: Discontinue use, prevent injury (alternate formulations)

**MACROSCOPIC**
- Erythema, erosions, ulcers, hemorrhage throughout GI
- Small bowel: Diaphragm disease (classic NSAID injury)
  - Thin, concentric, web-like folds with pinhole lumina

**MICROSCOPIC**
- Active inflammation, erosions, ulcers throughout GI tract
- Esophagus: Pill-induced esophagitis, sloughing esophagitis
- Stomach: Chemical/reactive gastropathy, erosive gastritis
- Small intestine: NSAID enteropathy/enteritis, “diaphragms”
- Large intestine: NSAID colopathy/colitis, focal active colitis

**TOP DIFFERENTIAL DIAGNOSES**
- *H. pylori* gastritis: Epithelial neutrophil, surface lymphocyte
- Peptic duodenitis: Surface gastric foveolar metaplasia
- Inflammatory bowel disease/Crohn disease
  - Chronic crypt distortion, basal lymphoplasmacytosis
- Infectious colitis: Lamina propria PMNs, pseudomembranes
- Ischemic colitis: Hyalinized lamina propria, withered crypts

**Chemical/Reactive Gastropathy**
(Left) High-power H&E-stained section shows histologic features of chemical gastropathy: Foveolar hyperplasia \(\rightarrow\) (with corkscrew appearance), surface mucin depletion \(\rightarrow\), and relative paucity of inflammation. (Right) Low-power H&E-stained section shows a small bowel ulcer caused by nonsteroidal antiinflammatory drugs (NSAIDs), which is classically well demarcated \(\rightarrow\) (“punched out”) from surrounding intestinal mucosa and, when chronic, associated with submucosal fibrosis \(\rightarrow\).

**Focal Active Colitis**
(Left) High-power H&E-stained section shows focal cryptitis with neutrophils \(\rightarrow\) in the colonic epithelium near a lymphoid follicle \(\rightarrow\) (aphthous lesion). One of many causes may be NSAIDs. (Right) High-power H&E-stained section shows colon mucosa with surface neutrophilic exudate \(\rightarrow\), fibrin \(\rightarrow\), hyalinized lamina propria \(\rightarrow\), and withered crypts \(\rightarrow\) with enlarged hyperchromatic nuclei \(\rightarrow\). These ischemic-type histologic changes may be due to NSAID injury.

**NSAID Enteritis/Enteropathy**

**NSAID-Related Ischemic-Type Injury**
TERMINOLOGY
Abbreviations
• Nonsteroidal antiinflammatory drugs (NSAIDs)

Synonyms
• NSAID-induced gastroduodenal damage
  □ Including chemical/reactive gastropathy
• NSAID-related enteropathy/enteritis
  □ Including diaphragm disease
• NSAID-related colopathy/colitis

Definitions
• Gastrointestinal (GI) tract injury resulting from NSAID use

ETIOLOGY/PATHOGENESIS
Environmental Exposure
• NSAIDs used for relief of inflammation, pain, edema, fever
  □ Heterogeneous class of medications, including
    ○ Nonselective cyclooxygenase (COX) inhibitors
      – Salicylates, propionic and acetic acid derivatives
    ○ Selective COX-2 inhibitors: Celecoxib, etc.
      – ↓ GI side effects but cardiovascular complications
    ○ Toxicity to GI mucosa: 2 mechanisms of pathogenesis
    ● Toxic effect on GI mucosa due to direct contact, irritation
      □ Acidic nature of drugs irritates and damages mucosa
        – NSAID-induced injury is pH dependent
      □ Esophagus: Acid reflux aids absorption of drugs
        – Leads to toxic effect within epithelial cells
    ○ Intestinal tract: Increased mucosal permeability
      □ NSAIDs and bile synergistically injure intestinal mucosa
        – Bile duct ligation prevents intestinal NSAID damage
      □ Small bowel: Enterohepatic circulation
        – Allows prolonged, repeated exposure to chemicals
      □ Direct damage to cell membrane phospholipids
      □ Cellular injury, loss of function in tight junctions
      □ Subsequent intracellular damage to mitochondria
      □ Intracellular Ca release → free radical generation
      □ Leads to ↑ permeability by bacteria, antigens, bile
      □ ↑ nitric oxide (NO), cytotoxic peroxynitrite output
      □ All culminate in increased inflammatory response
        – Colon: Local toxicity from slow-release NSAIDs
        □ Increased permeability → immune response
        – Rectum: Toxicity from NSAID suppositories
      □ Toxic effect from actual drug action (mostly in stomach)
        ○ COX-1: Constitutively expressed in GI mucosa normally
        – Local inhibition of COX-1 enzyme
          □ Decreased prostaglandin (PG) synthesis
            – PGs normally maintain mucosal integrity
            – Via mucus and bicarbonate production
          □ Decreased mucosal blood flow in upper/lower GI tract
            – Results in focal and localized ischemia
            – Via neutrophil-mediated vascular endothelial injury
          □ Also interferes with epithelial regeneration
            – Results in mucosal erosion, even ulcers
          ○ Selective COX-2 inhibitors: ↓ gastric ulcer/hemorrhage
            – Also ↓ gastroduodenal toxicity, ↓ lower GI tract injury
          ○ Inhibition of thromboxane synthesis by platelets
            – Leads to decreased platelet aggregation → bleeding
          ○ Large intestine: NSAID-mediated PG inhibition
            – Main toxic mechanism (over direct contact)
            – PGs promote ulcer healing, disease stability
              □ NSAIDs/COX-2 inhibitors exacerbate inflammatory bowel disease (IBD) colitis

Genetic Polymorphism
• Variation in gene encoding cytochrome P450 2C9 enzyme
  □ Leads to delayed NSAID metabolism

CLINICAL ISSUES
Epidemiology
• Incidence
  ○ Widespread NSAID use (prescription, over the counter)
    – 70% of elderly patients use 1x/week, 34% use daily
  ○ NSAID-related upper GI events: 2.5-4.5% of patients/year
    – 1.0-1.5% annual incidence of serious GI complications
  ○ GI damage occurs in 30-50% of regular NSAID users
  ○ Injury to esophagus less common than rest of GI tract
    – 41% of pill-induced esophagitis is due to NSAIDs
  ○ Gastric injury in 10-45% of patients on long-term NSAIDs
    – 50% develop erosions, 10-30% develop ulcers
  ○ Small intestinal injury is very common
    – Seen in up to 50-70% of long-term NSAID users
  ○ NSAID colitis: Up to 10% of new colitis patients
    – Proportion of patients with significant disease is small
• Sex
  □ NSAID use is reportedly more common in women
• Age
  □ Usually affects elderly more

Site
• Esophagus: Pill-induced esophagitis
  – At anatomic site of narrowing: Middle esophagus
• Stomach: Reactive/chemical (NSAID) gastropathy
  – Most commonly seen in gastric antrum
• Small Intestine: NSAID enteropathy/enteritis
  □ NSAID-related erosions/ulcers commonest in distal ileum
  □ Diaphragm disease: Rare but distinctive form
    – Mostly in ileum; ~ 30% in proximal colon
• Large intestine: NSAID colopathy/colitis, focal active colitis
  – Mostly occurs in right colon

Presentation
• Symptoms can present months to years after use
• Upper GI tract: Odynophagia, dysphagia, dyspepsia, heartburn, bloating, nausea, vomiting, malabsorption
• Lower GI tract: Abdominal pain/cramps, mild diarrhea
  – Hypoalbuminemia, vitamin B12 deficiency
• Both: Chronic blood loss → iron deficiency anemia

Endoscopic Findings
• Little correlation with symptoms and presentation
  ○ ~ 50% of patients with GI complications: Asymptomatic
  ○ ~ 50% of patients with dyspepsia: Normal endoscopy
• Esophagus: Erosions, ulcers, exudates
  ○ Esophagitis dissecans superficialis (sloughing)
    – Large, tubular epithelial casts sloughing off wall
• Stomach: Erosions, ulcers, hemorrhage
  ○ Erosions more often located in gastric body/fundus
  ○ Ulcers mainly found in antrum

Nonsteroidal Antiinflammatory Drug (NSAID) Damage
Nonsteroidal Antiinflammatory Drug (NSAID) Damage

Natural History
- Gastric fundus/body erosions tend to heal within days
- Gastric antrum ulcers tend to be more chronic
- Susceptible to bleeding and perforation

Treatment
- Options, risks, complications
  - GI complications in ~ 4% of NSAID users in 1st year
    - Risk with both short- and long-term treatment
    - Life-threatening GI bleeding: Worst complication
    - Strictures, obstruction, perforation
    - Malabsorption: Bile acids, protein (hypoalbuminemia)
  - Exacerbation of quiescent, inactive IBD
    - Seen in ~ 40% of IBD patients using NSAIDs
  - Risk factors for GI complications
    - Age > 60-70 years, longer duration of therapy
    - High-dose or multiple NSAID use
    - Past GI adverse event (ulcer, hemorrhage)
    - Comorbidities: Renal failure, cerebrovascular disease
    - Concurrent glucocorticoids/anticoagulant use
    - Concurrent Helicobacter pylori infection (controversial)
    - Tobacco and alcohol use, stress, depression
- Treatment options
  - Discontinue use: 10% of patients stop due to side effects
  - Adverse effects can last for > 1 year after cessation
  - Surgery for perforation, bleeding, and obstruction
  - Endoscopic dilation of strictures
- Injury prevention: ↓ toxicity with alternate formulations
  - Enteric-coated or soluble preparations
    - Reduce gastric residence/mucosal contact time
  - Buffered preparations, nonacidic prodrugs
  - Rectal, parenteral administration
  - Selective COX-2 inhibitors, NO-releasing NSAIDs
- Gastroprotection with adjuvant therapy
  - H2-receptor antagonists, proton pump inhibitors
  - Misoprostol: Protection against ↑ intestinal permeability
  - Metronidazole, sulfasalazine: ↓ intestinal inflammation

Prognosis
- Depends on treatment: modality and complications
- Long-term use may lead to tubulointerstitial renal disease
- Reye syndrome: Acute liver failure in children on salicylates
- Overall mortality depends on age, comorbidities
  - 5.5/1,000 person years after upper GI event
  - 17.7/1,000 person years after myocardial infarction
  - 21.8/1,000 person years after cerebrovascular accident

MACROSCOPIC

General Features
- Upper endoscopy and colonoscopy may be normal
- Erythema, erosions, and ulcers throughout GI tract
  - Patchy, most common in ileocecal region
  - Multiple discrete ulcers with intervening normal mucosa
  - Rectal ulcers/proctitis with NSAID suppositories
- Heavy, long-term NSAID users may develop long strictures
- Diaphragm-like strictures (diaphragm disease)
  - Most common in jejunum and ileum
  - Multiple, thin, concentric, web-like septa/folds
    - 1-4 mm thick with small, pinpoint lumina
- Perpendicular to longitudinal axis of GI tract
  - Project/protrude into gut lumen
  - Unevenly distributed along bowel length
  - Can cause narrowing, occlusion, obstruction
  - Lumen dilation proximal to stricture
  - Endoscopic capsule often gets stuck proximally
  - Virtually pathognomonic for NSAID-related injury

MICROSCOPIC

Histologic Features
- Active inflammation, erosions, ulcers throughout GI tract
- Esophagus: Pill-induced esophagitis
  - Crystalline pill fragments amidst ulcer/granulation tissue
  - Spongiosis, epithelial necrosis, intraepithelial neutrophils
- Esophagus: Esophagitis dissecans superficialis
  - a.k.a. sloughing esophagitis
  - Hyperkeratosis, necrosis of superficial epithelium
  - Bullae-like fluid cysts, little associated inflammation
  - Underlying viable epithelium is pale and edematous
    - Imparts characteristic 2-tone appearance
- Stomach: Chemical/reactive (NSAID) gastropathy
  - Foveolar hyperplasia of surface epithelium
    - Corkscrew-appearing glands
  - Loss of intracellular mucin (mucin depletion)
  - Diffusely enlarged, hyperchromatic nuclei
  - Smooth muscle fiber proliferation
    - Bundles extending toward gastric surface
  - Splay apart mucous glands in lamina propria
  - Lamina propria congestion, edema, telangiectasia
  - Generally little to no inflammation
- Stomach: Acute erosive (hemorrhagic) gastritis
  - Surface erosion with fibrin exudates
  - Neutrophilic infiltrates in epithelium, lamina propria
  - Reactive atypia, nuclear hyperchromasia
  - Mucin depletion, low nuclear:cytoplasmic (N:C) ratio
- Small intestine: NSAID-induced enteropathy/enteritis
  - Mild villous atrophy (mefenamic acid, sulindac)
    - Diffuse villous blunting not feature of NSAID injury
  - Increased intraepithelial lymphocytes
  - Superficial erosions; may progress to deep ulcers
    - Often multiple (in > 50% of cases)
    - Classically well demarcated, “punched out”
  - Nonspecific neutrophilic and plasmacytic infiltrates
  - Mucosa over strictures may be normal or ulcerated
  - Prominent submucosal fibrosis
  - Pyloric gland metaplasia seen with chronic injury
- Small intestine: Diaphragm disease
  - Submucosal fibrous bands protrude into lumen
    - Perpendicularly to mucosal surface
    - Smooth muscle, nerves, vessels also contained
      - "Neuromuscular vascular hamartoma" in old reports
  - Due to recurrent ulceration and healing with scarring
  - Overlying mucosa with reactive epithelial changes
    - Erosions often seen at tip of protruding column
- Large intestine: NSAID-induced colopathy/colitis
  - Mild, mixed inflammatory infiltrate in lamina propria
    - May be predominantly neutrophilic/lymphocytic
    - Eosinophils also described; may be prominent
    - Mildly increased intraepithelial lymphocytes
Nonsteroidal Antiinflammatory Drug (NSAID) Damage

- Focal active colitis: Neutrophils in crypt epithelium
  - Mild, focal variation in crypt distribution and size
  - Lack of diffuse crypt architectural distortion
    - No branching or shortening
  - Regenerative surface epithelium
    - Mucin depletion, nuclear enlargement, visible nucleoli
    - Ischemic-like changes in erosive areas
    - Lamina propria hyalinization, hyaline thrombi
  - Increase in apoptotic bodies within intestinal crypts
    - > 5 intraepithelial apoptoses per 100 crypts
    - Moderate levels (up to 24 apoptoses/100 crypts) seen

### DIFFERENTIAL DIAGNOSIS

#### Iron Pill-Induced Gastritis/Esophagitis
- Usually show luminal or stromal by iron deposits

#### Helicobacter pylori-Associated Gastritis
- Neutrophils in gastric foveolar and glandular epithelium
- Organisms attached to surface mucous cells
- Superficial lymphoplasmacytosis and lymphoid follicles

#### Collagenous/Lymphocytic Gastritis
- More prominent collagen band/intraepithelial lymphocytes
- Usually lack erosions, ulcers, reactive changes

#### Peptic Duodenitis
- Component may be due to NSAIDs (vs. gastric acid injury)
- Surface gastric foveolar metaplasia with neutral mucin
- Brunner gland hyperplasia, villous blunting
- Increased infiltrates of neutrophils, plasma cells
- Mucin depletion, nuclear hyperchromasia
- Increased mitoses in surface epithelium
- Erosion/ulceration only in severe cases

#### Inflammatory Bowel Disease/Crohn Disease
- Chronic inflammatory changes
  - Crypt architectural distortion (crypt branching, shortfall)
  - Significant lymphoplasmacytic infiltrate, especially basal
- Focally marked cryptitis/crypt abscesses, granulomas (Crohn disease)
- Pyloric gland metaplasia, inflammatory pseudopolyps
- Aphthous lesions may occur in both Crohn disease and NSAID damage

#### Infections
- Acute, self-limited colitis, pseudomembranous
  - ↑ neutrophils, histiocytes, lymphocytes in lamina propria
- Resolving phase: Focal active colitis
  - May be indistinguishable from NSAID injury
  - Patchy lamina propria inflammation
  - Slightly increased intraepithelial lymphocytes
- Crypts: Neutrophils, abscesses, rupture, no distortion
- Surface erosions/ulcers, but intervening mucosa involved
- Viral inclusions (cytomegalovirus, herpes simplex virus); fungal pseudomycophae
  - Giardia in duodenum may mimic NSAID injury

#### Vasculitis
- Mixed vascular/perivascular necrotizing
  - Granulomatous inflammation may be present
  - Fibrinoid necrosis of vessel walls with thrombosis
- Submucosal edema/hemorrhage
- Clinical history of autoimmune diseases
  - Systemic lupus erythematosus, rheumatoid arthritis

### Bowel Preparation Artifact
- Surface epithelium usually normal
- Neutrophils near/over lymphoid follicles (aphthoid lesion)
- Focal active colitis; indistinguishable from NSAID injury
- Minimal extension of inflammation into lamina propria
- Increased apoptosis in base of crypts
- Lamina propria edema and focal hemorrhage

#### Behçet Disease
- Colonic ulcers deeper than those induced by NSAIDs
- Fibrinous necrosis and lymphocytic infiltration of vessels

#### Ischemic Colitis
- Predominantly left colon: Splenic flexure most common
- Superficial mucosal necrosis, pseudomembranes
- Withered crypts with reactive cytologic atypia
- Lamina propria edema, hemorrhage, and hyalinization

#### Radiation-Induced Enteritis/Colitis
- Clinical history of radiation
- Acute radiation injury
  - Eosinophilic cryptitis, increased crypt apoptosis
  - Nuclear enlargement and hyperchromasia
  - Flattened surface epithelium, submucosal edema
- Chronic radiation injury
  - Enlarged fibroblasts, cytoplasmic vacuolization
    - Larger hyperchromatic nuclei, normal N:C ratio
  - Intimal proliferation of small/medium-sized arteries
    - Occlusion of lumina → mucosal ischemic changes
    - Hyalinization of lamina propria
    - Especially around dilated mucosal vessels
  - Crypt distortion (especially around areas of stricture
  - Serosal adhesions

#### Microscopic Colitis (Collagenous/Lymphocytic)
- More prominent collagen band/intraepithelial lymphocytes
- Usually lack erosions, ulcers, ischemic-type injury

### DIAGNOSTIC CHECKLIST

#### Pathologic Interpretation Pearls
- Patchy process, can affect entire GI tract (upper and lower)
- Erosions, ulcers, and mild (usually acute) inflammation
- Little crypt architectural distortion or chronic changes
- Few surface/crypt epithelial or lamina propria lymphocytes

### SELECTED REFERENCES

Multiple Organs

Nonsteroidal Antiinflammatory Drug (NSAID) Damage

(Left) Medium-power H&E-stained section shows an esophageal ulcer with acute inflammatory exudate, fibrin, reactive, bizarre stromal cells, and crystalline pill fragments (possibly NSAIDs) causing this injury. (Right) High-power H&E-stained section shows hyperkeratosis, hyalinization, and necrosis of the superficial squamous epithelium in the esophagus, which is in contrast to the underlying viable epithelium, giving it a 2-tone appearance.

(Left) High-power H&E-stained section shows the classic corkscrew appearance of the gastric antral mucosa due to foveolar hyperplasia in the setting of chemical gastropathy. Note the relative absence of inflammation. (Right) High-power H&E-stained section shows a gastric erosion with acute inflammatory exudate, disruption of the surface epithelium, and reactive epithelial atypia (withered crypts, large hyperchromatic nuclei, mucin loss).

(Left) High-power H&E-stained section shows duodenal mucosa with an erosion: Disrupted surface epithelium, fibrin, and regenerative atypia (large hyperchromatic nuclei, loss of goblet cells). GI tract erosions are commonly due to NSAID use. (Right) Medium-power H&E-stained section shows the base of ileal mucosa with pyloric gland metaplasia and submucosal fibrosis, indicating chronic mucosal damage, often seen with long-term NSAID use.

Pill-Induced Esophagitis

Sloughing Esophagitis

Chemical/Reactive Gastropathy

Acute Erosive (Hemorrhagic) Gastritis

Duodenal Erosion

NSAID Enteritis/Enteropathy
Nonsteroidal Antiinflammatory Drug (NSAID) Damage

**Diaphragm Disease**

(Left) Gross specimen photograph of a small bowel segment shows multiple, concentric, ring-like folds in the wall that result in stenotic “diaphragms,” which may cause obstruction. This appearance is characteristic of NSAID intestinal injury. (Right) Low-power H&E-stained section shows small bowel “diaphragms,” which are thought to result from repeated rounds of injury/erosion followed by healing and submucosal scarring, leading to fibrous bands protruding into the gut lumen.

**NSAID Enteritis/Enteropathy**

(Left) Medium-power H&E-stained section shows ileal mucosa with an erosion at the top of mucosal folds, suggestive of NSAID use. Similar lesions may be seen at the tips of the folds in diaphragm disease. (Right) Medium-power H&E-stained section shows jejunal mucosa with a discrete ulcer sharply delineated from the surrounding uninvolved mucosa, suggestive of NSAID injury.

**Ischemic-Type Colonic Injury**

(Left) High-power H&E-stained section shows ischemic-type injury in the colon with withered crypts and hyalinized lamina propria. (Right) High-power H&E-stained section shows healing colonic erosion with crypt loss, flat regenerative surface epithelium (absence of goblet cells, hyperchromatic nuclei, mucin loss), and hyalinized lamina propria. NSAIDs are a common cause of localized small erosions, especially in the ileocecal valve and proximal colon.