INFLAMMATORY BOWEL DISEASE

By Dr. Swathi Swaroopa. B

- Inflammation and ulceration of the lining of the intestines with unknown etiology

- 2 types
  1. Ulcerative colitis (UC)
  2. Crohn’s disease (CD)

- Crohn disease most commonly affects the distal small intestine and proximal colon, but can affect any area of the GI tract from the esophagus to the anus

- ulcerative colitis is confined to the colon and rectum

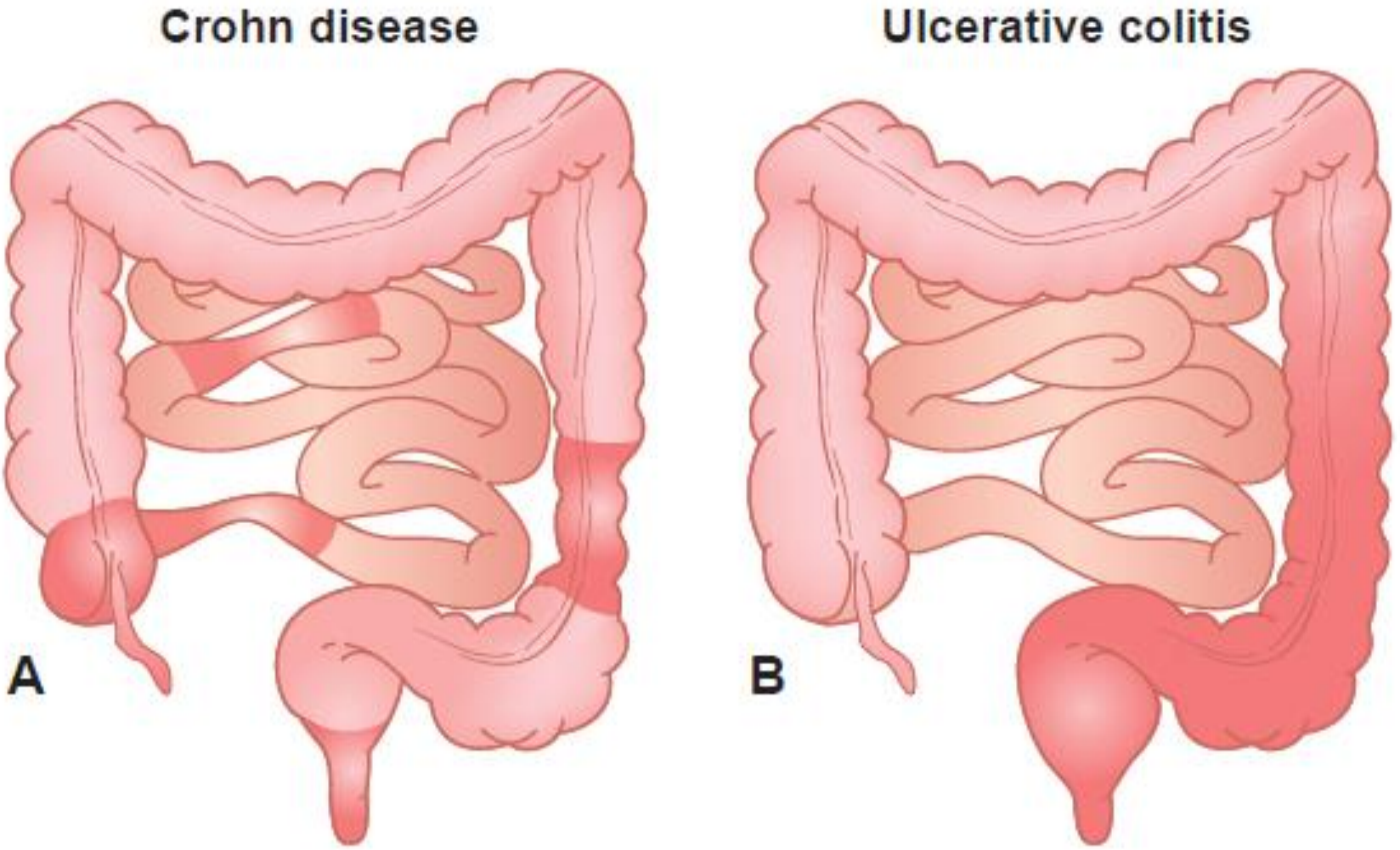


FIGURE 45.7 • Distribution patterns of disease with (A) skip lesions in Crohn disease and (B) continuous involvement of the colon, beginning with the rectum, in ulcerative colitis.

- These two condition share many common features like
  - Diarrhea
  - Bloody stools
  - Weight loss
  - Abdominal pain
  - Fever and fatigue

  but each has unique features

TABLE 45.1 DIFFERENTIATING CHARACTERISTICS OF CROHN DISEASE AND ULCERATIVE COLITIS

CHARACTERISTIC	CROHN DISEASE	ULCERATIVE COLITIS
Types of inflammation	Granulomatous	Ulcerative and exudative
Level of involvement	Primarily submucosal	Primarily mucosal
Extent of involvement	Skip lesions	Continuous
Areas of involvement	Primarily ileum, secondarily colon	Primarily rectum and left colon
Diarrhea	Common	Common
Rectal bleeding	Rare	Common
Fistulas	Common	Rare
Strictures	Common	Rare
Perianal abscesses	Common	Rare
Development of cancer	Uncommon	Relatively common

- Both diseases produce inflammation of the bowel, both lack confirming evidence of a proven causative agent

- As in many other autoimmune disorders, the pathogenesis of Crohn disease and ulcerative colitis involves a failure of immune regulation, genetic predisposition, and an environmental trigger, especially microbial flora

ETIOLOGY

Genetics

- Profound disorders of mucosal immunity
- IBD1 locus on chromosome 16 has recently been shown to contribute to Crohn disease
- NOD2 / CARD15 mutations that are associated with Crohn disease
- IBD3 on chromosome 6 linked to Crohn disease and ulcerative colitis.
- IBD5 on chromosome 5
- Human leukocyte antigen (HLA) associations HLA) DR2, HLA-DR3 for UC
- (ABCB/MDR 1) on chromosome 7 is a potential susceptibility gene for ulcerative colitis.

Environmental Factors :

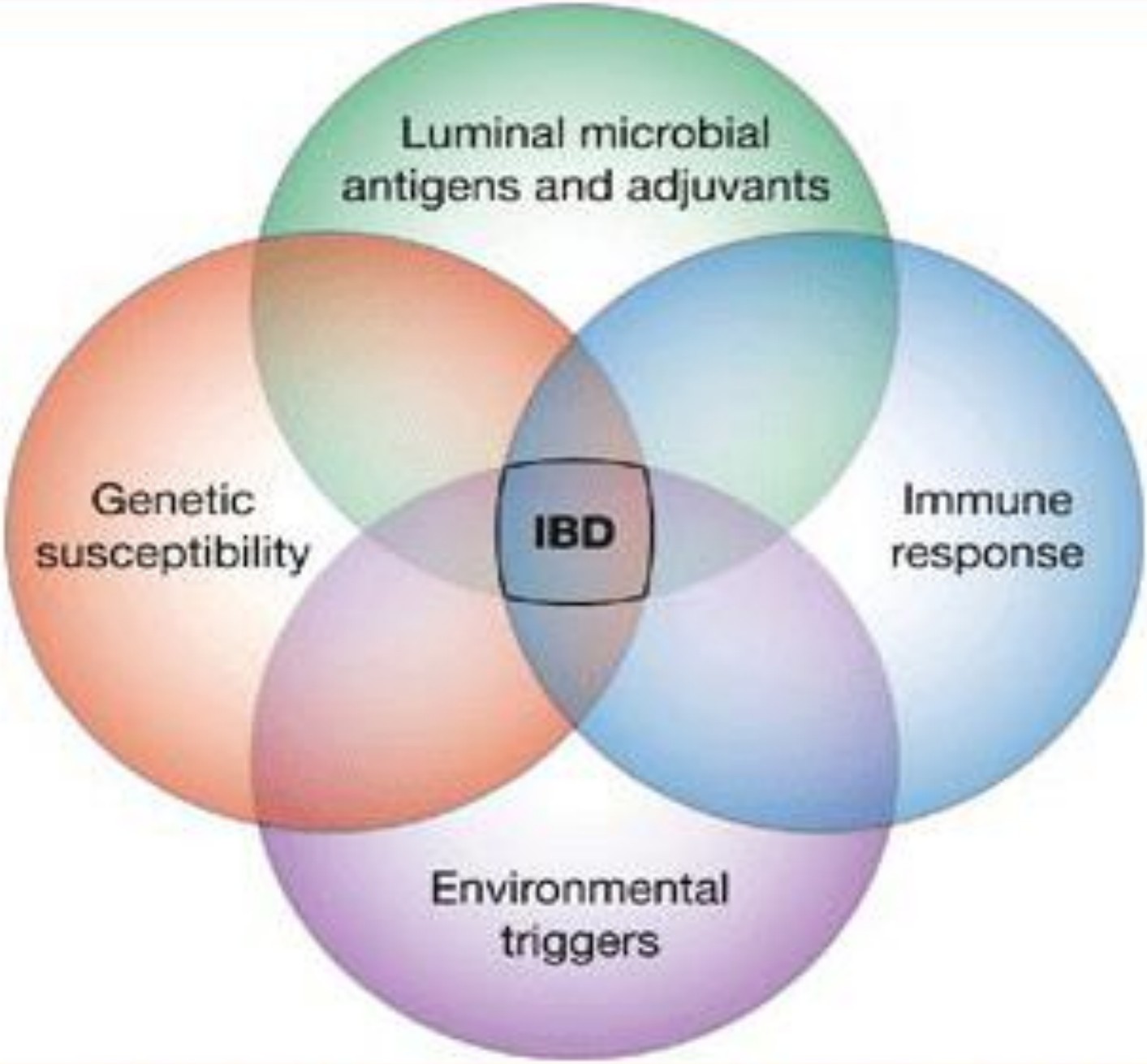
- Microbes –
  - Escherichia coli
  - Mycobacterium paratuberculosis
- Smoking (Crohn's disease)

Immune defects :

- Altered host defence
- Immune-mediated mucosal damage
- alterations in mucosal T-cell and B-cell function
- Deregulation of cytokine release.
- Mucosal immune dysregulation

Psychological factors :

- Stress
- Emotional or physical trauma
- Occupation



Source: Nat Clin Pract Gastroenterol Hepatol © 2006 Nature Publishing Group

Pathophysiology

- NOD2 protein is expressed in many types of leukocytes as well as epithelial cells and is thought to act as an intracellular receptor for lipopolysaccharides on microbes.

- On binding microbial products, it may trigger the NFκβ pathway, which leads to the production of cytokines and other proteins involved in the innate immune defense against microorganisms.

- NOD2 mutations that are associated with Crohn disease may reduce the activity of the protein, resulting in persistence of intracellular microbes and prolonged immune responses.

- IBD5 rich in genes encoding several cytokines that may contribute to the disease.

- Smoking- Due to coagulopathies occurring in the intestine or as a result of an immune response.
- Microbes- Provide the antigen trigger for an unregulated immune response.
- Bacteria produce toxins (necrotoxins, hemolysins, and enterotoxins) that cause mucosal damage.
- Bacteria elaborate peptides (e.g., formyl-methionyl-leucylphenylalanine) that have chemotactic properties and that cause an influx of inflammatory cells with subsequent release of inflammatory mediators and tissue destruction.

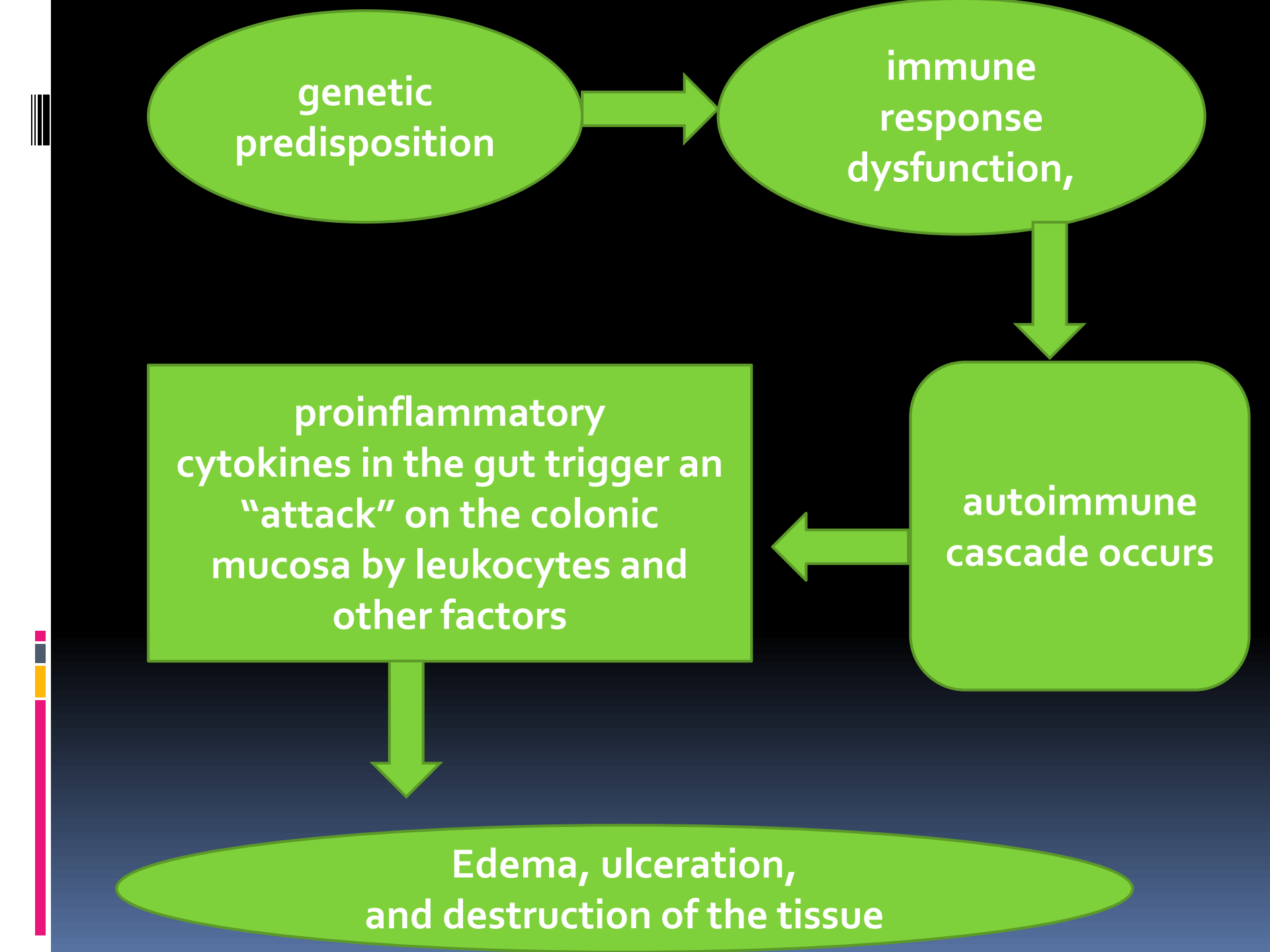
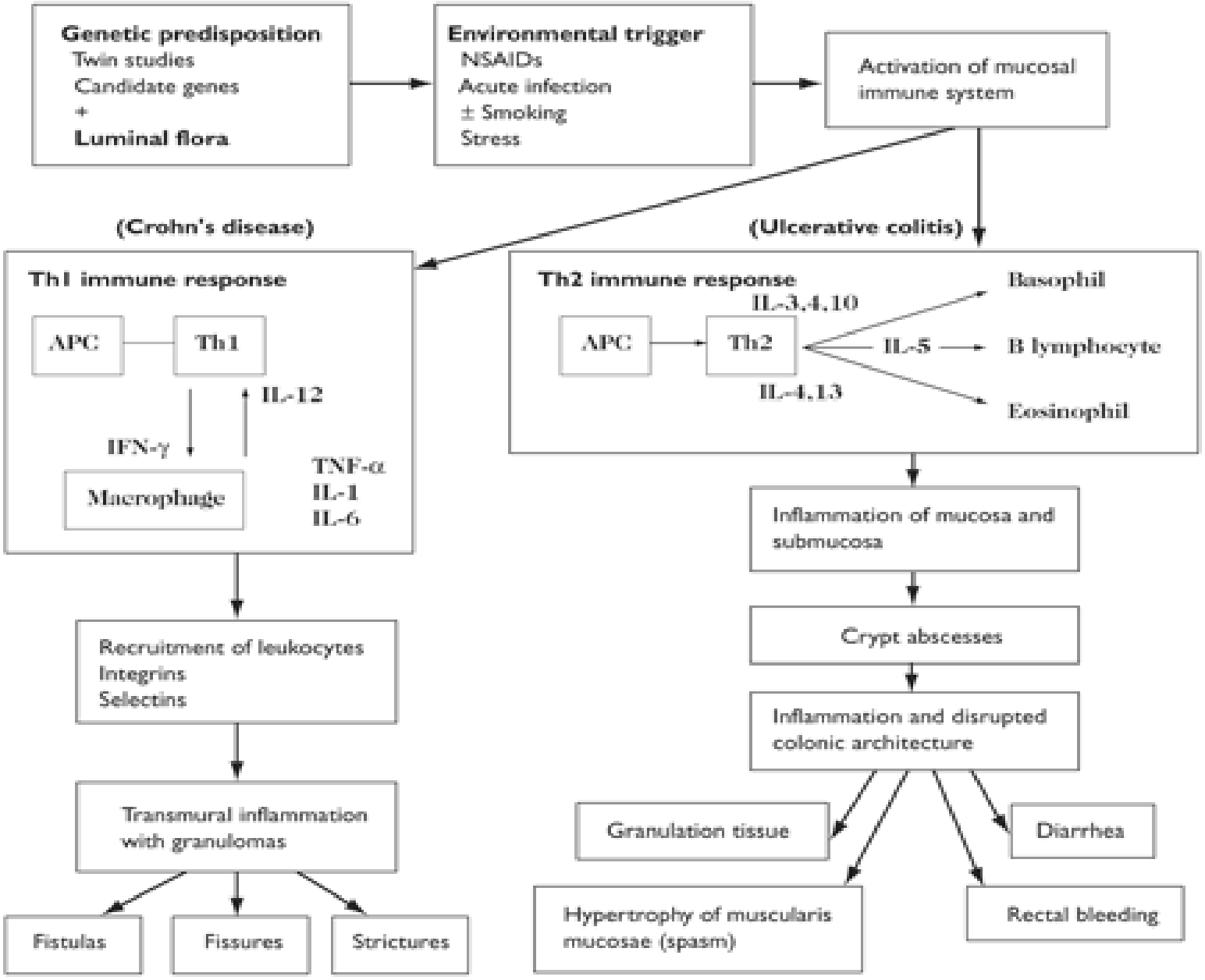
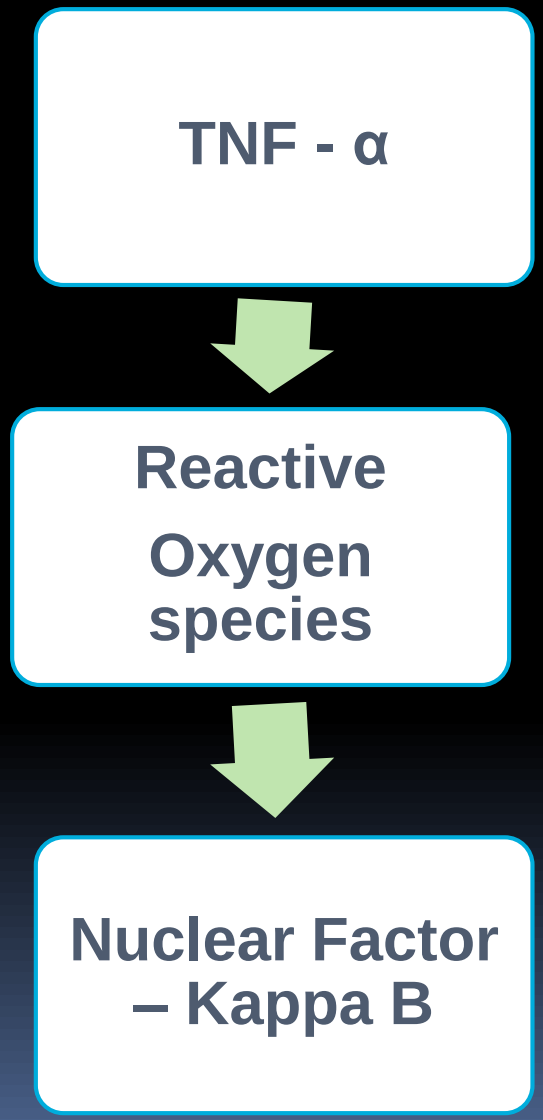

genetic predisposition
immune response dysfunction,
autoimmune cascade occurs
proinflammatory cytokines in the gut trigger an "attack" on the colonic mucosa by leukocytes and other factors
Edema, ulceration, and destruction of the tissue

Figure. Pathogenesis of Inflammatory Bowel Disease



APC indicates antigen-presenting cell; IFN-γ, interferon γ; IL, interleukin; NSAIDs, nonsteroidal anti-inflammatory drugs; Th, T helper; and TNF-α, tumor necrosis factor α.

2. Signs of oxidative stress



Abnormal glycosaminoglycan (GAG) content of the mucosa:

- GAGs are abundant in the basement membrane, lamina propria, and submucosa of the GI tract
- Ulcerative colitis yielded a distinctly abnormal distribution of GAGs
- Whether it is a result of, or cause of, inflammation remains to be determined

↑ sulfide production (sulfide-induced colonocyte toxicity)

In the colon, H_2S is produced both endogenously and by naturally occurring sulfate-reducing bacteria (SRB).

CLINICAL PRESENTATION

ULCERATIVE COLLITIS-The inflammation is limited to the mucosa

- Crypt abscesses
- necrosis of the epithelium
- Edema
- Hemorrhage
- surrounding accumulations of chronic inflammatory cells
- granular, and erythematous, with or without ulceration.

- Chronic, loose, bloody stools
- tenesmus (urge to defecate)
- Abdominal pain
- Severe disease is defined as more than six bloody stools a day, fever, tachycardia, anemia, or an ESR greater than 30

- A major complication is toxic megacolon, which is a segmental or total colonic distension of >6 cm with acute colitis and signs of systemic toxicity.

CROHN'S DISEASE

- CD is a chronic, transmural, patchy, granulomatous, inflammatory disease that can involve the entire GI tract, from mouth to anus, with discontinuous ulceration (so-called skip lesions), fistula formation, and perianal involvement.

- Predominantly inflammatory
- Stricturing, or fistulizing
- Abdominal pain and chronic, often nocturnal, diarrhea
- Weight loss, low-grade fever, and fatigue are also common
- Abdominal masses or abscesses and fistulae
- Enterocutaneous and enterorectal fistulae are common

TABLE 36-3 Clinical Presentation of Ulcerative Colitis

Signs and symptoms

- Abdominal cramping
- Frequent bowel movements, often with blood in the stool
- Weight loss
- Fever and tachycardia in severe disease
- Blurred vision, eye pain, and photophobia with ocular involvement
- Arthritis
- Raised, red, tender nodules that vary in size from 1 cm to several centimeters

Physical examination

- Hemorrhoids, anal fissures, or perirectal abscesses may be present
- Iritis, uveitis, episcleritis, and conjunctivitis with ocular involvement
- Dermatologic findings with erythema nodosum, pyoderma gangrenosum

Laboratory tests

- Decreased hematocrit/hemoglobin
- Increased erythrocyte sedimentation rate
- Leukocytosis and hypoalbuminemia with severe disease

TABLE 36-4 Clinical Presentation of Crohn's Disease

Signs and symptoms

- Malaise and fever
- Abdominal pain
- Frequent bowel movements
- Hematochezia
- Fistula
- Weight loss
- Arthritis

Physical examination

- Abdominal mass and tenderness
- Perianal fissure or fistula

Laboratory tests

- Increased white blood cell count and erythrocyte sedimentation rate

Extraintestinal manifestations of IBD

- Reactive arthritis,
- Uveitis,
- Ankylosing spondylitis,
- Pyoderma gangrenosum, and
- Primary sclerosing cholangitis.