

Inflammatory Bowel  
Disease (IBD)

# Introduction

- **What is IBD?**
- Chronic inflammatory condition of the gastrointestinal (GI) tract.
- Two main types:
  - **Ulcerative Colitis:** Limited to the colon.
  - **Crohn Disease:** Can affect any part of the GI tract.
- **Pathogenesis:** Involves immune and microbial factors, but remains unclear

# Definitions of Ulcerative Colitis

- **Ulcerative Colitis (UC):**
  - Chronic inflammation of the colon's mucosal layer.
- **Disease Extent:**
  - **Ulcerative Proctitis:** Limited to the rectum.
  - **Proctosigmoiditis:** Involves rectum and sigmoid colon.
  - **Left-sided Colitis:** Extends from rectum up to the splenic flexure.
  - **Extensive Colitis:** Extends beyond splenic flexure.

# Disease Activity and Risk in Ulcerative Colitis

- **Severity Levels:**

Mild, Moderate, Severe.

- **Risk Classification:**

- **Low-risk:** Minimal inflammation, lower chance of complications.

- **High-risk:** Significant inflammation, higher risk of complications like colectomy.

# Definitions of Crohn Disease

- **Crohn Disease (CD):**

  - Involves full-thickness (transmural) inflammation.

- **Skip Lesions:**

  - Areas of normal bowel between inflamed sections.

- **Commonly Affected Areas:**

  - Ileum and proximal colon.

- **Complications:**

  - **Strictures:** Narrowing of the intestines.

  - **Fistulas:** Abnormal connections between organs.

# Genetic Factors in IBD

- **Genetic Susceptibility:**

- IBD is **polygenic** (many genes involved).
- **200+ genetic loci** linked to increased risk.
- **NOD2 Gene:** First susceptibility gene identified in Crohn Disease.

- **Family Risk:**

- Higher risk with a first-degree relative with IBD.
- 20x more likely to develop if a family member is affected.

# Epidemiology - Global Prevalence

- **Prevalence:**

- 1990: 3.7 million cases.
- 2017: 6.8 million cases globally.

- **Regional Variations:**

- Highest in **North America**: 422 cases per 100,000.
- Lowest in **Caribbean**: 6.7 cases per 100,000.

- **Emerging Trends:**

Increasing incidence in newly industrialized countries.

# Epidemiology – Demographic Trends

- **Age of Onset:**

- Most common between ages 15-30.
- Possible second peak: Ages 50-80.

- **Sex Differences:**

- **Crohn Disease:** Slight female predominance.
- **Ulcerative Colitis:** Slight male predominance.

- **Ethnic and Racial Variations:**

- Higher prevalence among Jewish populations.
- Lower prevalence in Hispanic and Black populations.

# Clinical Risk Factors - Lifestyle

- **Smoking:**

- **Crohn Disease:** Increased risk and complications.

- **Ulcerative Colitis:** May reduce risk but worsens symptoms upon cessation.

- **Physical Activity:**

- Reduced risk for Crohn Disease with higher activity levels.

- **Dietary Factors:**

- **Fiber:** Protective in Crohn Disease.

- **High Fat:** Increased risk for both conditions.

- **Vitamin D:** Low levels associated with higher IBD risk.

# Clinical Risk Factors – Sleep and Infection

- **Sleep Duration:**

- <6 or >9 hours linked to higher ulcerative colitis risk.

- **Infection:**

- Acute gastroenteritis increases IBD risk.
- Infections with pathogens like **Salmonella** may predispose individuals to IBD.

# Clinical Risk Factors - Medications

- **Antibiotics:**

- Higher IBD risk, especially for Crohn Disease.

- **NSAIDs:**

- Small increased risk for both UC and CD.

- **Oral Contraceptives:**

- Slightly increased risk, especially for UC.

- **Isotretinoin:**

- Possible link with IBD, especially if combined with antibiotics.

# Ulcerative Colitis

- **Key Symptoms:**

- Diarrhea (often with blood)
- Frequent, small-volume bowel movements
- Abdominal pain, urgency, and incontinence
- Potential constipation with blood/mucus discharge for distal disease

# Disease Severity in Ulcerative Colitis

- **Mild Disease:**

- $\leq 4$  stools/day, mild symptoms, no severe pain or weight loss.

- **Moderate Disease:**

- Frequent bloody stools, mild anemia, low-grade fever.

- **Severe Disease:**

- $\geq 6$  bloody stools/day, cramps, systemic symptoms (fever, anemia, weight loss).

# Assessment Tools for Disease Severity

- **Montreal Classification:**

- Categories for mild, moderate, and severe cases.

- **Mayo Scoring System:**

- Used for disease monitoring (0-12 scale, higher = more severe).

# Acute Complications

- **Severe Bleeding:**

- Up to 10% of patients; may require surgery.

- **Fulminant Colitis and Toxic Megacolon:**

- Risk for  $\geq 10$  stools/day, toxic symptoms.

- **Perforation:**

- Can be life-threatening; higher mortality if it leads to peritonitis.

# Extraintestinal Manifestations

- **Musculoskeletal:**

- Arthritis (joint pain, large joints), risk of osteoporosis.

- **Eye:**

- Uveitis, episcleritis, with symptoms like redness and burning.

- **Skin:**

- Erythema nodosum, pyoderma gangrenosum.

- **Hepatobiliary:**

- Primary sclerosing cholangitis, fatty liver disease.

# Other Systemic Complications

- **Hematopoietic:**

- Increased risk of thromboembolism, anemia.

- **Pulmonary:**

- Rare; airway inflammation, lung disease, bronchiectasis.

- **Autoimmune Reactions:**

- Hemolytic anemia and other systemic autoimmune issues.

# Laboratory Findings: Blood Tests

- **Complete Blood Count (CBC)**

- Detects anemia due to blood loss or inflammation
- Low hemoglobin/hematocrit levels, particularly in severe cases

- **Erythrocyte Sedimentation Rate (ESR)**

- Elevated ESR ( $\geq 30$  mm/hour) in active or severe inflammation

- **Albumin and Electrolytes**

- Low albumin indicates malnutrition or inflammation
- Electrolyte imbalances due to dehydration from diarrhea

# Laboratory Findings: Stool Markers

- **Calprotectin and Lactoferrin**

- Elevated levels indicate intestinal inflammation
- Useful for distinguishing inflammatory from non-inflammatory diarrhea

- **Limitations**

- Nonspecific markers that may be elevated in other inflammatory conditions

# Imaging in Ulcerative Colitis

- **When and Why**

- Imaging not always needed for diagnosis
- Helps assess disease severity or complications (e.g., toxic megacolon)

- **Imaging Types**

- Abdominal X-rays, Barium Enema, CT, MRI, and Ultrasound

# Abdominal X-ray Findings

- **Mild to Moderate Disease**

- Typically normal but may show signs like constipation or mucosal thickening

- **Severe Disease**

- Colonic dilation and “thumbprinting” due to mucosal edema
- Helpful for identifying toxic megacolon

# Double Contrast Barium Enema

- **Mild Disease**

- May appear normal or show a reticulated pattern

- **Moderate to Severe Disease**

- Shows more specific findings: “collar button” ulcers, loss of haustra, luminal narrowing, pseudopolyps

- **Limitations**

- Avoid in severely ill patients to prevent risk of toxic megacolon

# CT and MRI Scans

- **Utility in Ulcerative Colitis**

- Shows bowel wall thickening, but findings are nonspecific
- MRI and CT are more effective in severe or established disease

- **Limitations**

- Lower sensitivity for early mucosal disease compared to barium enema

# Evaluation: Diagnostic Criteria

- **Initial Symptoms**

- Chronic diarrhea (lasting >4 weeks)
- Endoscopic and biopsy evidence of inflammation

- **Exclusion of Other Causes**

- Requires ruling out infections, ischemia, medication-induced colitis, etc.

# Laboratory Studies for Differential Diagnosis

- **Infectious Causes**

- Stool cultures for pathogens (e.g., Salmonella, Shigella, C. difficile)
- PCR for specific infections (e.g., CMV in immunocompromised patients)

- **Other Conditions**

- Testing for sexually transmitted infections in high-risk individuals

# Endoscopy and Biopsy

- **Endoscopic Findings**

- Loss of vascular markings, erythema, granularity, spontaneous bleeding
- In severe cases, macro-ulcerations and pseudopolyps

- **Biopsy Findings**

- Crypt abscesses, mucosal atrophy, increased lamina propria cellularity
- Basal plasmacytosis and other signs suggesting chronic inflammation

# Endoscopic Patterns and Involvement

- **Continuous and Circumferential Involvement**

- Disease usually starts in the rectum and progresses proximally

- **Patchy Involvement in Severe Disease**

- Occasional “cecal patch” or “backwash ileitis” observed in some cases

# Histologic Characteristics on Biopsy

- **Key Features**

- Crypt architectural distortion, Paneth cell metaplasia, basal lymphoid aggregates

- **Relapse Predictors**

- Basal plasmacytosis may predict relapse in patients in remission

# Factors Influencing Disease Course

- **Age at Diagnosis:**

- Older patients more likely to have remission

- **Smoking:**

- Smoking cessation linked to increased UC severity

- **Extent and Severity of Disease:**

- Proctitis vs. pancolitis

# Complications of Ulcerative Colitis

- **Chronic Complications:**

- Strictures (risk of obstruction, malignancy suspicion)
- Dysplasia and Colorectal Cancer (CRC) risks

# Impact on Survival and Mortality Rates

- **Overall Mortality:**

- Slightly higher than the general population

- **Risk Factors:**

- Severe disease, CRC, infections

- **Current Trends:**

- Improved outcomes due to better management

Induction of  
Remission in  
Ulcerative Colitis

# Goals of Therapy

- Achieve clinical and endoscopic remission in active UC.
- Focus on complete mucosal healing.
- Symptomatic improvement: resolution of diarrhea and bleeding.
- Histologic improvement is emerging as important for remission.
- Response is monitored through symptoms, lab tests, and endoscopy.

# Initial Treatment of Ulcerative Colitis

- Treatment based on severity and extent of disease.
- Mild to moderate UC typically responds to 5-ASA with or without glucocorticoids.
- Focus on patient's specific type of UC: proctitis, proctosigmoiditis, left-sided, or extensive colitis.

# Ulcerative Proctitis or Proctosigmoiditis

- First-line treatment:
  - Topical mesalamine (suppository or enema).
- Enemas effective for proximal sigmoid colon; suppositories for rectal disease.
- Dosage:
  - Mesalamine suppository: 1g once daily, increase to 2x daily if needed.
  - Mesalamine enemas: 1x daily, increase to 2x daily if no improvement.

# Symptomatic Improvement Timeline

- Improvement in symptoms (bleeding, stool frequency) usually within a week.
- Clinical remission may take 4-6 weeks or longer.
- Continue treatment to maintain remission.

# Alternative Therapy Options

- Topical glucocorticoids if mesalamine is not tolerated.
- Oral 5-ASA agents for patients unwilling to use topical treatments.
- Consider high-dose mesalamine for effective induction therapy.

# Left-sided or Extensive Colitis Initial Therapy

- Combination therapy: Oral 5-ASA + rectal mesalamine.
- High-dose mesalamine (>3 grams daily) preferred.
- Symptomatic improvement expected within 2-4 weeks.

# Subsequent Therapy Options

- If no improvement after combination therapy:
  - Add topical glucocorticoid or oral 5-ASA.
  - Consider systemic glucocorticoids if necessary.

# For moderate to severe Ulcerative Colitis

- **Options include:**
  - **Biologic Agents** (with or without immunomodulators).
  - **Oral S1P Receptor Modulators.**
  - **Glucocorticoids.**

# Example Induction Regimens

- **Anti-TNF Agents:** (e.g., Infliximab, Adalimumab).
  - Recommended for patients with coexisting inflammatory diseases.
- **Anti-Interleukin Therapy** (e.g., Ustekinumab/Mirikizumab)
  - For those with psoriasis.
- **S1P Receptor Modulators:** (e.g., Ozanimod & Etrasimod)
  - Preferred in patients with demyelinating conditions.
- **Older Patients:**
  - Prefer vedolizumab or anti-interleukin agents.

# Glucocorticoids

- **Use:**

- Immediate symptom relief, not for long-term maintenance.

- **Commonly Used:**

- Oral prednisone at 40 mg daily.

- **Expected Improvement:**

- Within one week; tapering based on response.

Maintenance of  
Remission in  
Ulcerative Colitis

# Goals of Maintenance Therapy

- **Primary Goal:**

- Prevent clinical and endoscopic relapse after achieving clinical remission.
- Importance of long-term management strategies for sustained remission.

# Indications for Maintenance Therapy

- **Patients requiring maintenance therapy:**

- Ulcerative proctitis with  $>1$  flare/year.
- All patients with ulcerative proctosigmoiditis.
- All patients with left-sided colitis or extensive colitis.

- **Exceptions:**

- Ulcerative proctitis with  $\leq 1$  flare/year responding to topical mesalamine may not require maintenance therapy.

# Maintenance Therapy Choices

- **Factors Influencing Choices:**

- Induction agent used.
- Distribution of disease.
- Patient and clinician preferences.
- Insurance coverage/cost.

- **Common Agents:**

- Topical mesalamine.
- Oral 5-ASA agents.

# Maintenance Therapy for Ulcerative Proctitis

- **Induction with Topical Mesalamine:**

- Maintenance: 1 gram mesalamine suppository every night for patients with >1 flare/year.

- **Dosing Adjustments:**

- Frequency may be reduced based on patient willingness or tolerance.

# Maintenance Therapy for Ulcerative Proctosigmoiditis

- **Induction with Topical Mesalamine:**
  - Maintenance: 1 mesalamine enema nightly for patients who responded well.

# Oral 5-ASA Therapy

- **Use of Oral 5-ASA agents:**

- For patients who achieved remission with oral 5-ASA, maintain at induction doses (>3 grams daily).
- For frequent relapses ( $\geq 2$  flares/year), consider higher doses.

Treatment strategies differ based on the initial response to therapy.

- **Anti-TNF Agent-Induced Remission**

- Continue anti-TNF therapy long-term.

- **Vedolizumab-Induced Remission**

- Continue vedolizumab long-term.

- **Anti-Interleukin Agent-Induced Remission (Ustekinumab, Mirikizumab) :**

- Continue for long-term maintenance

- **Glucocorticoid-Induced Remission**

- Not used for maintenance.
- Taper glucocorticoids while initiating thiopurines or biologics for long-term therapy.

# Monitoring During Remission

- **Regular Assessments:**

- Clinical evaluations and colonoscopy every 6 to 12 months.

- **Biomarkers:**

- Measure CRP and fecal biomarkers (e.g., fecal calprotectin) to assess mucosal healing.

# Additional Therapeutic Options

- **Antidiarrheal Medications:**

- Short courses for mild symptoms; avoid opioids and NSAIDs.

- **Nutritional Considerations:**

- Importance of dietary management in IBD patients.

# Cancer Screening Guidelines

- **Colorectal Cancer:**

- Screening based on disease extent and duration.

- **Other Screenings:**

- Cervical and skin cancer screenings for at-risk patients.

# Clinical Features of Crohn's Disease (CD)

- **Abdominal Pain:**

- A common manifestation of CD, often described as crampy.
- Right lower quadrant pain is typical in those with distal ileal disease.
- Transmural inflammation can lead to fibrotic strictures, resulting in abdominal pain, bowel obstruction, and possibly fistula formation.
- Patients may remain asymptomatic until luminal narrowing occurs, leading to pain and changes in bowel habits.

- **Diarrhea:**

- A prevalent symptom that often fluctuates.
- Persistent, intermittent diarrhea without gross blood alongside other IBD features (skin, eye, joint issues) may indicate CD.
- Causes include:
  - Fluid secretion and impaired absorption due to inflammation.
  - Bile salt malabsorption from inflamed terminal ileum.
  - Steatorrhea due to bile salt loss.
  - Enteroenteric fistulas bypassing absorptive areas.
- Microscopic blood may be present, with some patients experiencing grossly bloody stools, especially those with colonic involvement.

- **Systemic Symptoms:**

- **Fatigue:** Common due to chronic illness.
- **Weight Loss:** Often results from decreased food intake due to pain and malabsorption.
- **Fever:** Less common; may indicate inflammation or complications like abscesses.

# Features of Transmural Inflammation

- **Fistulas**

- Fistulas form due to sinus tracts penetrating the bowel wall, often manifesting indolently rather than acutely. Types include:
  - **Enteroenteric:** May be asymptomatic or present as a mass.
  - **Enterovesical:** Leads to recurrent UTIs and pneumaturia.
  - **Retroperitoneal:** Can result in abscesses or ureteral obstruction.
  - **Enterovaginal:** May present with gas or fecal passage through the vagina.
  - **Enterocutaneous:** Causes bowel contents to drain to

- **Inflammatory Mass/Abscess**

- Not all sinus tracts result in fistulas; some present as a palpable inflammatory mass.
- Abscesses can lead to peritonitis with fever, pain, and tenderness.

- **Perianal Disease**

- Occurs in about one-third of CD patients, presenting with pain, drainage, or abscess formation.

# Establishing the Diagnosis

- The diagnosis of CD relies on:
  - **Radiologic Findings:** Imaging studies showing segmental and transmural inflammation.
  - **Endoscopic Findings:** Direct visualization of the intestinal tract.
  - **Histologic Findings:** Biopsies showing inflammatory changes consistent with CD.

# Approach to Testing

- **Laboratory Studies**

- Complete Blood Count (CBC)
- Blood Chemistry (electrolytes, renal function, liver function)
- Serum Iron, Ferritin, Vitamin D, Vitamin B12 levels
- Serum Albumin
- C-Reactive Protein (CRP)

- **Stool Studies**

- **Testing for Enteric Pathogens:**

- Culture, examination for ova and parasites, and Clostridioides difficile toxin.

- **Stool Inflammatory Markers:**

- Fecal calprotectin and lactoferrin to differentiate intestinal inflammation from functional bowel disease.
- Elevated fecal calprotectin indicates a likelihood of IBD.

# Imaging Studies

- **Small Bowel Imaging:**

- Computed Tomography Enterography (CTE) or Magnetic Resonance Enterography (MRE).
- Both methods are used to evaluate disease extent and complications.

- **Endoscopic Procedures:**

- **Ileocolonoscopy:**

- Includes mucosal biopsies to assess for focal ulcerations, nodular changes, and histologic evidence of inflammation.

- **Upper Endoscopy:**

- For patients with upper gastrointestinal symptoms.

# Grading Systems for Crohn Disease

- **Commonly Used Tools:**
  - **Crohn Disease Activity Index (CDAI)**
  - **Harvey-Bradshaw Index (HBI)**

# Management of the Acutely Ill Patient

- **Indications for Hospitalization:**

- Complications like bowel obstruction, peritonitis, or disease flare.

- **Initial Management Strategies:**

- Intravenous fluid and electrolyte replacement.
- Broad-spectrum antibiotics.
- Nutritional assessment.
- Possible consultation with gastrointestinal surgeons.
- Consideration of glucocorticoids or biologic therapy.

# Factors Influencing Induction Therapy

- **Patient Preferences**
- **Patient Characteristics**
  - Age, prior treatments.
- **Disease Characteristics**
  - Fistulizing or penetrating disease.
- **Response to Previous Therapies**

Induction of  
Remission in  
Crohn's Disease

# Mild Crohn's Disease with Ileum and/or Proximal Colon Involvement

- **First-Line Treatment:** Enteric-coated budesonide.
- **Dosage:** 9 mg daily for at least four weeks, tapering after achieving remission.
- **Tapering Schedule:** Decrease by 3 mg every 2-4 weeks over 8-12 weeks.
- **Recommendation:** Do not use budesonide for more than 12 weeks per course

# Alternative Agents

- **Prednisone**

- **Use:** For patients who do not respond to budesonide.
- **Dosage:** Start with 40 mg daily for one week, then taper by 5-10 mg weekly.
- **Considerations:** Long-term use is discouraged due to significant side effects.

- **5-Aminosalicylates (5-ASA)**

- **Controversy:** Limited use in mild Crohn's disease; better for those avoiding glucocorticoids.
- **Dosage:** Slow-release oral 5-ASA (e.g., mesalamine).
- **Efficacy:** Mixed results, with some studies suggesting higher doses may be more effective.

# Induction Options

- **Biologic Agents with or without Immunomodulators**

- Anti-TNF agents (e.g., infliximab, adalimumab)
- Anti-interleukin or anti-integrin therapies.

- **Combination Therapy**

- Anti-TNF agents with immunomodulators for fistulizing disease.

# Importance of Combination Therapy

- **Mechanisms of Action**

- Synergistic effects targeting different pathways.

- **Reduction of Immunogenicity**

- Lower risk of developing antibodies against biologics.

- **Improvement of Pharmacokinetics**

# Anti-TNF Agents Overview

- **Available Anti-TNF Therapies**

- **Infliximab**

- Chimeric monoclonal antibody.
- Administered intravenously.

- **Adalimumab**

- Recombinant human monoclonal antibody.
- Administered subcutaneously.

- **Certolizumab Pegol**

- Humanized monoclonal antibody fragment.
- Administered subcutaneously.

# Anti-Interleukin Therapy

- **Risankizumab**

- Targets IL-23, effective for induction and maintenance.

- **Ustekinumab**

- Targets IL-12 and IL-23; used for patients naïve to biologics or with previous non-response.

# Anti-Integrin Therapy

- **Vedolizumab**

- Effective in inducing and maintaining remission; low immunogenicity.

- **Natalizumab**

- Reserved for select patients due to risk of serious side effects.

# JAK Inhibitors

- **Upadacitinib**

- Approved for patients with prior anti-TNF therapy failure.
- Fast-acting with flexible dosing options.

# Monitoring and Follow-Up

- **Ileocolonoscopy**

- Recommended 6-12 months post-induction.

- **Regular Monitoring**

- Assess liver enzymes, therapeutic drug levels, and patient symptoms

Achieving and  
Maintaining  
Remission

# Maintenance Therapy

- **Thiopurines**

- For patients with glucocorticoid remission or non-response to biologics.
- Regular monitoring for toxicity; TPMT genotype testing recommended.

- **Methotrexate**

- Alternative for patients intolerant to thiopurines.
- Initiation and gradual dose adjustment, with folic acid supplementation to reduce side effects.

Treatment strategies differ based on the initial response to therapy.

- **Anti-TNF Agent-Induced Remission**

- Continue anti-TNF therapy long-term.

- **Vedolizumab-Induced Remission**

- Continue vedolizumab long-term.

- **Anti-Interleukin Agent-Induced Remission (Ustekinumab, Mirikizumab) :**

- Continue for long-term maintenance