INFLAMMATORY BOWEL DISEASE
(CROHN’S DISEASE, ULCERATIVE COLITIS)

Crohn’s disease (regional enteritis, regional ileitis, granulomatous ileocolitis)

General Considerations
- Involvement: alimentary tract anywhere from the mouth to the anus
- Principal site of the disease: ileum ± colon and jejunum
- Incidence: young adults, intermittent clinical course with mild to severe disability and frequent complications

Etiology
Autoinflammatory disease: NODS mutation of granulocytes leads to uncontrolled molecular pattern recognition

Genetic factors: higher than normal incidence in monozygotic twins, greater than random familial incidence. The most common familial pattern involves two or more siblings. Regional enteritis and ulcerative colitis occur in the same family.

Infectious origin: no agent to date has been substantiated. Studies suggested transmission of an agent from tissues with regional enteritis into immunologically deficient mice and rabbits.

Pathology

Various clinical patterns
- Indolent and symptomatology mild
- Toxic: fever, toxic erythema, arthralgia, anemia.
- Complicated: stricture or perforations of the bowel, suppurative complications of intra-abdominal perforation.

Clinical signs and symptoms
- Exacerbations and remissions
- Colicky, steady abdominal pain: right lower quadrant or periumbilical area; at some time during the course of the disease; mild to severe.
- Diarrhea: usually with intervening periods of normal bowel function or constipation.
- Milk products, chemically or mechanically irritating food: aggravate symptoms.
- Abdominal tenderness: especially in the right lower quadrant, with signs of peritoneal irritation;
- Abdominal and pelvic mass in the same area. Mass: sausage like thickened intestine to matted loops of intestine.
- Fever: low-grade or rarely, spiking with chills.
- Anorexia, flatulence, malaise, weight loss
Extra-intestinal manifestations
- Pyoderma gangrenosum
- Erythema nodosum
- Polyarthritis
- Ankylosing spondilitis
- Anemia
- Pleuropericarditis
- Extra-intestinal manifestations 2
  - Ocular lesions (episcleritis, iritis, uveitis)
  - Oral ulcers
  - Liver disease (pericholangitis, sclerosing cholangitis)
  - Thrombophlebitis
  - Impaired growth in children

Laboratory findings
- ↑ESR, leukocytosis with shift to the left, ↑CRP
- Occult blood in the stool.
- Hypochromic anemia: macrocytic due to vitamin B12 malabsorption.
- Specific autoantibodies:
  - Anti-streptomyces sacch. (ASCA)

Imaging
Small bowel x-ray: mucosal irregularity (“cofflesones”), ulceration, stiffening of the bowel wall, luminal narrowing.

Barium enema: fissuras, ulcers. Eccentric involvement, skipped areas of involvement, strictures → Crohn's disease of the colon is suggested.

CT: Marked thickening of the colonic wall (to the left of the bladder) CT is good at detecting fistulas.

Endoscopic examination: Edematous hyperemic mucosa; when colon is involved - discrete ulcers.

Differential diagnosis
- Acute appendicitis.
- Location in the terminal ileum: intestinal tuberculosis, Yersinia enterocolitica infection, lymphomas.
- In immunodeficient patients: Mycobacterium avium-intracellulare.
- Regional enteritis involving the colon: idiopathic ulcerative colitis, amebic colitis, ischemic colitis, infectious disease of the colon.
- Definitive diagnosis: cultures, examinations of the stool for parasites, biopsy in selected instances. Sigmoidoscopic and x-ray criteria - not absolute.

Complications
- Ischiorectal, perianal fistulas: frequent. Fistulas to the bladder, vagina, even to the skin in the area of a previous scar.
- Mechanical intestinal obstruction.
- Malabsorption, maldigestion (decreased bile salt pool) → sprue-like syndrome.
- Generalized peritonitis: rare. Perforation occurs slowly, is locally contained, or results in internal fistula formation.
• Migratory peripheral synovitis, axial arthropathy: indistinguishable from ankylosing spondilitis.
• Fistula formation in Crohn’s disease

The incidence of colorectal or small bowel cancer: normal population → regional enteritis → ulcerative colitis.

**Treatment**

**A. Remission induction and maintenance**

• Prednisone, prednisolone, methylprednisolon IV, PO or rectally
• Sulfasalazine (sulfapyridine + 5-amunosalicylic acid)
• Azathioprin

**B. Biological (anti-cytokine) therapy**

• Anti-TNFα agents
• infliximab
• adalimumab
• golimumab

**C. General Measures**

• Diet: high in calories and vitamins and adequate protein. Nonresidue, well balanced diet: to maintain nutrition until obstructive symptoms subside. Raw fruits and vegetables: avoid in patients with obstructive symptoms.
• Anemia, dehydration, diarrhea, avitaminosis: treatment as indicated
• When terminal ileal disease is present: vitamin B12, calcium supplementation

**D. Antimicrobial Agents**

• Only for specific infectious problems: abscess, fistulas.
• Antibiotics: In cases of acute suppuration (manifested by tender mass, fever, leukocytosis): ampicillin; clindamycin or metronidazole (for anaerobs) and aminoglycosides.
• In cases where internal fistula formation has led to a defunctionalized loop with bacterial overgrowth or where stricture formation has led to small bowel stasis with malabsorption: tetracycline + correction of absorptive malfunction.

**E. Surgical Measures**

• Indication: management of complications
• Resection of small bowel (especially, the resection is extensive) → "short bowel syndrome" (malabsorption of vitamin B12, hyperoxaluria, steatorrhea, osteomalacia, macrocytic anemia - due to folic acid and vitamin B12 deficiency)
• Stricuroplasty

**Ulcerative colitis**

• Chronic inflammatory disease of the colon with unknown cause.
• Characterization: bloody diarrhea, tendency to remissions and exacerbations.
• Involvement: mainly, the left colon.
• Incidence: primarily in adolescents and young adults, but onset may be in age group.

**Pathology**

• Acute nonspecific inflammation of the colonic mucosa, particularly the rectosigmoid area.
• Multiple ulcerations
• Repeated episodes → thickening of the wall tissue with scar formation
• Proliferative changes in epithelium → polypoid structure; pseudopolyps → severe ulceration
• Diffuse chronic inflammation of the lamina propria with crypt distortion.
• Crypt abscess

Clinical signs and symptoms
• Fever, weight loss, evidence of toxemia: vary with the severity of the disease.
• Abdominal tenderness: mild; without signs of peritoneal irritations.
• Abdominal distension: in the fulminating form; poor prognosis.
• Rectal examination: perianal irritation, fissure, hemorrhoids. Uncommonly, fistulas, abscesses.
• Variations: from mild cases with relatively minimal symptoms to acute and fulminating cases with severe diarrhea and prostration.
• Remissions - exacerbations.
• Diarrhea: characteristic. Up to 10-25 discharges daily, with blood and mucus in the stools. Blood or mucus may occur without feces. Nocturnal diarrhea is usually present when daytime diarrhea is prominent.
• Blood in the stool is the cardinal manifestation.
• The small intestine is almost never involved.
• Rectal tenesmus. Anal incontinentia.
• Cramping lower abdominal pain: mild
• Anorexia, malaise, weakness, fatigability.

Extraintestinal manifestations
• Pyoderma gangrenosum
• Erythema nodosum
• Polyarthritis
• Ankylosing spondilitis
• Ocular lesions (episcleritis, iritis, uveitis)
• Oral ulcers
• Liver disease (pericholangitis, sclerosing cholangitis)
• Anemia
• Pleuropericarditis
• Thrombophlebitis
• Impaired growth and sexual development in children.

Laboratory findings
• Stool: blood, mucus, pus; but no pathogens.
• Hypochromic anemia due to blood loss.
• Polymorphonuclear leukocytosis: in acute disease.
• ↑ESR, ↑CRP
• Hypoproteinemia.
• Electrolyte disturbance in fulminating cases.
• Antibody: xANCA positivity (not specific)

Imaging
• Air contrast barium enema (avoid in actively symptomatic patients!)
Involvement: regional or generalized.
• Irritability and fuzzy margins or pseudopolyps
• Decreased size of colon, shortening and narrowing of the lumen, loss of haustral markings.
• When the disease is limited to the rectosigmoid area, the barium enema may even be normal
• Sigmoideoscopy: Discloses rectal involvement in over 95% of cases. In mild cases: mucosal hyperemia, petechiae, minimal granularity. In severe cases: polypoid changes. The mucose may appear grossly normal, it is friable when wiped with a cotton sponge.
• Colonoscopic examination: Not in actively symptomatic patients! Useful in defining the extent ulcerative colitis. Highly recommended: annually after the tenth year of disease colonoscopy with multiple biopsies - looking for dysplasia and cancer.

Differential diagnosis
• Imperative: any cultures and parasitology specimens be obtained before barium enema.
• Bacterial dysentery: culture for specific stool pathogens.
• Amebiasis: indirect hemagglutination test and biopsy.
• When rectal strictures have developed lymphogranuloma venerum is ruled out by history and complement fixation test.
• Other enteritis: functional diarrhea, granulomatous colitis, diverticulitis.
• Intestinal neoplasm,

Complications
• Colonic perforation
• Massive hemorrhage
• Toxic dilatation of colon (toxic megacolon)
• Carcinoma. The incidence of carcinoma is significantly greater in patients with ulcerative colitis. Involvement: the entire colon - greater risk than minimal disease. Disease confined to the rectum is unassociated with higher risk of cancer. Duration: The risk rises from approximately 0.2% at 1 year to 2.8% at 15 years, 4.5% at 20 years and 13.5% at 30 years.

Treatment
Goals
• Terminate the acute attack
• Prevent recurrent attacks
• Promote healing of the damaged mucosa

General Measures
• Restore circulating blood volume with fluids, plasma, and blood as indicated.
• Discontinue opiates and anticholinergics.
• Correct electrolyte abnormalities.
• Discontinue all oral intake. Nasogastric suction if the colon has become dilated.

Medical treatment
• Corticosteroids
• Sulfasalazine
• Antimicrobial therapy: Ampicillin, cephalosporin, clindamycin, metronidazole, gentamicin: singly or in appropriate combinations.
• Biological therapy (as in Crohn’s disease)
Surgery

- Refractory disease
- Toxic colonic dilatation: not improve in 24 hours → colonic resection.
- Severe extracolonic complications (growth suppression)
- Prolonged widespread colon disease
- Massive hemorrhage
- Extensive perirectal disease
- Fulminant disease but not toxic: iv therapy for 5-7 days. No response or deterioration: colectomy

Prognosis

Permanent and complete cure on medical therapy is unusual. Life expectancy is shortened. Close follow-up → potential complications. After 10 years of the disease, colonoscopy be performed annually, multiple biopsies should be examined for dysplasia. Dysplasia is considered a preacancerous lesion and if severe is thought to be an indication for surgery.

Differences between Crohn’s disease and ulcerative colitis

<table>
<thead>
<tr>
<th>Clinical</th>
<th>Crohn’s disease</th>
<th>Ulcerative colitis</th>
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<tbody>
<tr>
<td>Systemic toxicity</td>
<td>Rare</td>
<td>Occasional</td>
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<tr>
<td>Bleeding</td>
<td>Rare</td>
<td>Common</td>
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<tr>
<td>Perianal disease</td>
<td>Common</td>
<td>Rare</td>
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<tr>
<td>Fistula</td>
<td>Common</td>
<td>Rare</td>
</tr>
<tr>
<td>Perforation</td>
<td>Common</td>
<td>Rare</td>
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<tr>
<td>Sigmoidoscopy</td>
<td>Discrete, occasionally diffuse</td>
<td>Diffuse, friable superficial ulceration</td>
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<tr>
<th>X-ray</th>
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<tr>
<td>Distribution</td>
<td>Segmental</td>
<td>Continuous</td>
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<tr>
<td>Mucosa</td>
<td>Fissures to deep ulcers</td>
<td>Serrated</td>
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<tr>
<td>Stricture</td>
<td>Common</td>
<td>Rare</td>
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<thead>
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<th>Pathology</th>
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<tbody>
<tr>
<td>Transmural involvement, granulomas</td>
<td>Mucosal microabscesses</td>
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