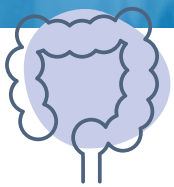
INFLAMMATORY BOWEL DISEASE (IBD)

Jens Rasenack

INT



Falk FOUNDATION e.V.

Scientific editor

Prof. Dr. Jens Rasenack

Formerly
University Medical Center Freiburg,
Hugstetter Str. 55, 79106 Freiburg, Germany,
Department of Internal Medicine II

Provided by
Falk Foundation e.V.
Leinenweberstraße 5 | 79108 Freiburg im Breisgau | Germany
Media@falkfoundation.org

www.falkfoundation.org

1st international edition 2025

Table of contents

Cardinal signs of Crohn's disease and ulcerative colitis

If the following signs and symptoms are present, inflammatory bowel disease must be considered:

- More than 2 bowel movements a day
- Liquid stools
- Blood or mucus in the stool
- Diarrhea lasting more than 4 weeks
- Cramp-like abdominal pain
- Recurring episodes of such symptoms
- Increased urge to defecate
- Defecation at night
- Feeling of incomplete defecation
- Perianal fistulas/abscesses
- Fever
- Malnutrition/weight loss/delayed growth (in children)

Differential diagnosis:

- Infections (*Yersinia, Campylobacter jejuni, Clostridioides difficile, Chlamydia*, parasitic infections, tuberculosis, AIDS-related opportunistic infections)
- Pseudomembranous colitis
- Eosinophilic gastroenteritis
- Ischemic colitis
- Microscopic colitis (collagenous and lymphocytic colitis)
- Diversion colitis
- Graft-versus-host disease
- Radiation colitis
- Drug-induced adverse events
- Celiac disease
- Behcet's disease
- Irritable bowel syndrome
- Diverticulitis
- Gynecological symptoms
- Food intolerance

Etiology and pathogenesis

Inflammatory bowel disease (IBD) is characterized by destructive inflammation of the small and/or large intestines with a relapsing-remitting clinical course. It includes the 2 most common forms, Crohn's disease (CD) and ulcerative colitis (UC), as well as the less frequently diagnosed types: collagenous colitis, lymphocytic colitis, and incomplete microscopic colitis. Due to several unique features, microscopic colitis is not covered by this booklet. Crohn's disease and ulcerative colitis differ in terms of their pattern of inflammation, and their macroscopic and histological presentation.

Crohn's disease can occur in segments in all sections of the digestive tract, from the esophagus to the rectum, and it affects all layers of the luminal wall. Ulcerative colitis begins in the rectum, and from here can extend to all sections of the colon, affecting only the mucosal layer in a continuous pattern. Often, IBD can only be definitively diagnosed once the disease becomes chronic. It is not always possible to distinguish between CD and UC (CD: involvement of the small intestine, possibly no rectal involvement, fistulas, granulomas).

The causes of IBD are still unknown. Genetic factors play an important role, as demonstrated by epidemiological studies in monozygotic twins. The combined concordance rate from 3 studies was 37% for CD in monozygotic twins, in contrast to 7% in dizygotic twins; in the case of UC, these figures were 10% and 3% respectively. In 2.2–16.2% of people with CD the condition is also present in a first-degree relative; the corresponding figure for IBD is 5.2–22.5%. Among patients with UC, 5.7–15.5% also have a first-degree relative with UC, and 6.6–15.8% have one with an IBD. Almost 200 different genes and gene loci have now been identified as being associated with IBD, with the most well-known of these being the NOD2/CARD15 gene. The NOD2 protein is strongly associated with the epithelial defense/barrier function.

Furthermore, IBD genes are also involved in the control of adaptive immunity, non-specific tissue destruction and protein synthesis. Several IBD-associated genes play a role in the body's reaction to gut bacteria. In some patients with IBD, changes to the microbiome composition have been observed with a reduction in *Bacteroidetes* and *Firmicutes* and an increase in *Proteobacteria*.

In addition to genetic predisposition, the following factors are also considered in connection with IBD:

Crohn's disease	
Viral infections	Measles virus
Bacterial infections	*Chlamydia, Listeria monocytogenes,* Pseudomonas species, *Mycobacterium paratuberculosis*
Environmental factors	Early weaning, higher socioeconomic status, ovulation inhibitors, non-steroidal anti-inflammatory drugs (NSAIDs), refined sugars, too little fresh fruit and vegetables, titanium oxide (e.g., from tooth-paste), smoking
Other	Psychological factors

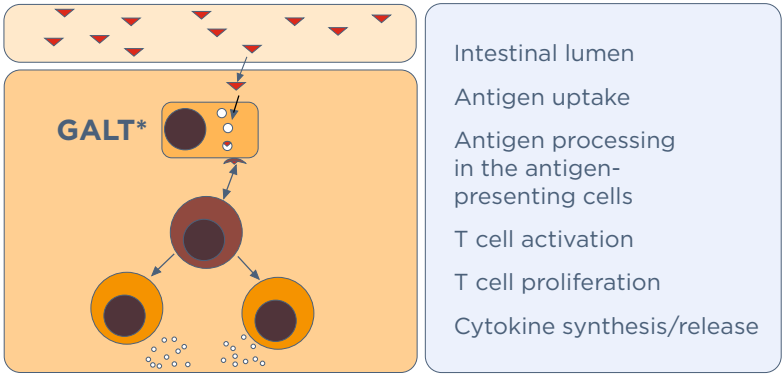
Ulcerative colitis	
Viral infections	Herpes viruses
Bacterial infections	Certain strains of *E. coli*
Environmental factors	Cow's milk, ovulation inhibitors

New immunology-based models explaining disease pathogenesis may have practical implications for medical approaches to the disease.

Genetics and gene functions

To date, almost 200 different genes and gene loci have been linked to IBD. The most well-researched of these is NOD2/CARD15, which is expressed in monocytes, dendritic cells, Paneth cells, and mucosal epithelial cells. NOD2/CARD15 is an intracellular molecule that recognizes specific bacterial components known as proteoglycans, leading to the activation of NF-κB through several intermediate steps. NOD2/CARD15 may serve as an anti-bacterial factor essential for immune defense, with mutations potentially resulting in weakened defenses. However, in animal studies, NOD2/CARD15 mutations do not spontaneously cause IBD, suggesting it acts only as a cofactor in disease development.

It is possible that NOD2/CARD15 modulates the secretion of defensins – endogenous antimicrobial proteins produced by mucosal epithelial cells. NOD2/CARD15 is located in the Paneth cells near granules, and mutations may impair defensin release. Mutations in the NOD2/CARD15 gene are associated with forms of CD predominantly affecting the terminal ileum and are often linked with stenosis.



*gut-associated lymphoid tissue (the gut's immune system)

Fig. 1: Induction of immune response in the intestine and possibilities for immunological intervention (mod. based on Zeitz 1997)

In this immunological model, the inflammatory cascade causing IBD begins with antigen exposure in the intestine (Fig. 1). Macrophages and dendritic cells take up the antigen, partially break it down, and present it on their surface to specific immune cells. This process activates inflammation-promoting messengers (cytokines) and ultimately leads to the destruction of the intestinal mucosa through the release of secondary inflammatory factors. In addition, further immune-competent cells are recruited from the bloodstream. In this model, each patient has their own individual set of disease-triggering antigens.

Unlike in a healthy person, in patients with IBD there is a significant disruption of the balance between inflammation-triggering and inflammation-inhibiting cytokines. Dysfunction in the regulation of the immune response leads to excessive activation of inflammation-promoting cytokines. In patients with CD, the pathologically extended lifespan of disease-promoting T lymphocytes causes the disease to become chronic.

Thus, in IBD, the immune system is not weakened; rather, the intestinal immune response is excessively activated and prolonged. One of the aims of all immunomodulatory therapies is to restore balance to this immune system through targeted suppression.

These research findings explain the proven efficacy of treatments such as systemic corticosteroids and topical corticosteroids (budesonide), azathioprine therapy, and modern biologic therapies (such as monoclonal antibodies) targeting specific immune processes.

Pathogenic and symbiotic bacteria

Bacterial antigens are currently believed to play an important role. The gastrointestinal tract contains many antigens, including food components, bacteria, as well as viruses and fungi. Although the small intestine is only colonized to a small extent, the large intestine harbors 10^{10}–10^{12} bacteria per gram of stool, comprising 60% of the stool mass.

Using simple detection methods, 400–500 species from approximately 30 genera can be observed. These are separated from the "inside of the body" by only a single layer of cells. The immune system of the mucous membrane constantly interacts with the intestinal contents, allowing for the tolerance of location-specific bacteria and food components within this interaction.

In the last few decades, various pathogens have been proposed to be responsible for the development of IBD: *Mycobacterium paratuberculosis, Listeria monocytogenes, Chlamydia trachomatis,* cytomegalovirus, measles virus, *Saccharomyces cerevisiae*, specific *E. coli* strains, *Yersinia enterocolitica*, and *Yersinia pseudotuberculosis*. However, this data has not yet been confirmed, and antibiotics were not effective in large studies.

Recent research suggests that the normal gut flora, which exists in a symbiotic relationship with the gastrointestinal tract, plays an important role in the development and persistence of IBD. This is supported by the observation that surgically bypassing intestinal loops (thereby removing contact with the intestinal contents) can lead to the resolution of inflammation in these bowel segments. However, signs of inflammation often return once intestinal continuity is restored.

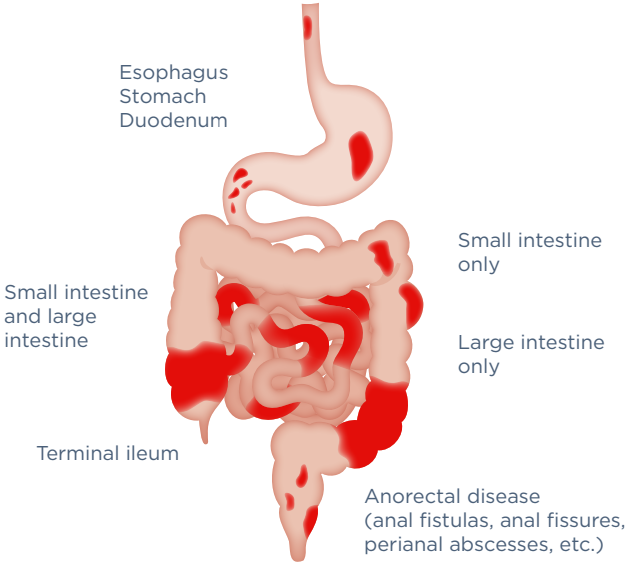
Changes in the physiological flora, such as a decrease in *Lactobacillus* or anaerobic bacteria, can be observed in active CD, but not in inactive CD. In an experimental colitis model, most animals do not develop inflammation if they are kept under germ-free conditions.

The total number of bacteria also appears to be important.

Location and endoscopic findings of Crohn's disease

Location

Patterns of segmental, discontinuous inflammation observed in different intestinal regions



Endoscopic findings

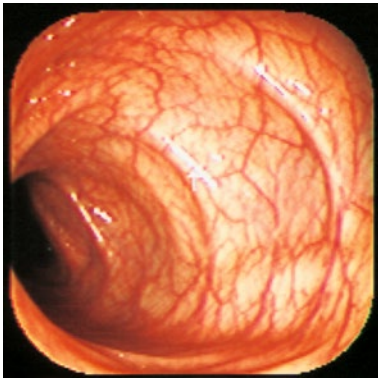


Fig. 2: Normal

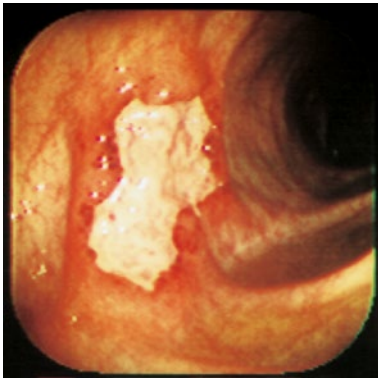
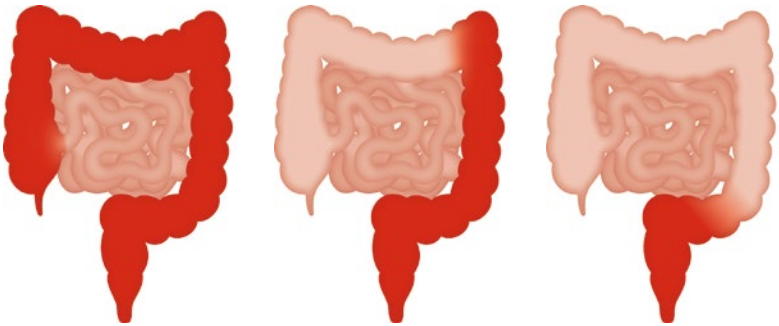


Fig. 3: Crohn's disease
"Map-like" ulcer with red, raised edge

Location and endoscopic findings of ulcerative colitis

Location

Frequency of inflammation spread in the colon
(acc. to Riegler et al. 2000)



Entire colon 22%

Up to left colic (splenic) flexure 22%

Rectosigmoid 57%

Endoscopic findings

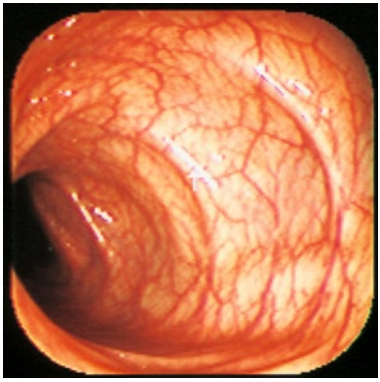


Fig. 4: Normal
Smooth mucous membrane, vascular pattern normal

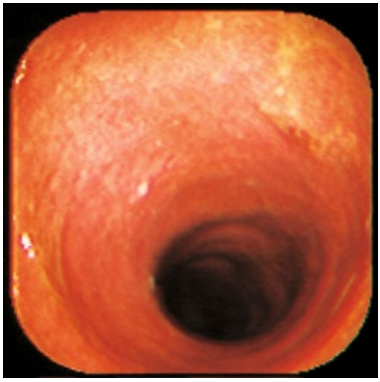


Fig. 5: Ulcerative colitis
Reduced vascular markings, granulation, velvet-like redness

Histological, radiological, and ultrasound features of Crohn's disease

Histology

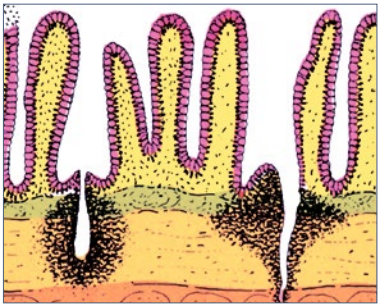


Fig. 6: Heterogeneous, discontinuous transmural inflammation; granulomas

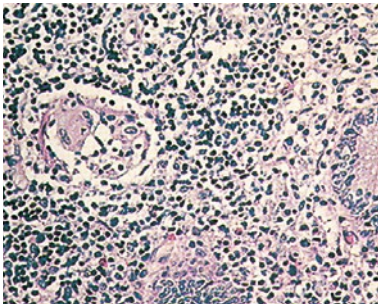


Fig. 7: Transmural lymphocytic infiltration, discontinuous pattern; focal, lymphoid hyperplasia; fibrosis in all wall layers; fissures; epithelioid granulomas (30–60%) in the submucosa; in rare cases crypt abscesses, intact goblet cells (colon)

X-ray

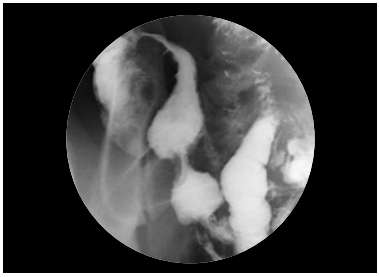


Fig. 8: Terminal ileum, segmental stenosis, cobblestone appearance

Ultrasound

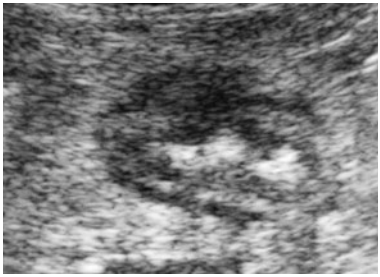


Fig. 9: Wall thickening of low echogenicity, typically eccentric

Histological, radiological, and ultrasound features of ulcerative colitis

Histology

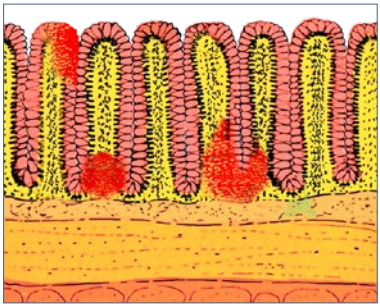


Fig. 10: Homogeneous, continuous mucosal inflammation; crypt abscesses

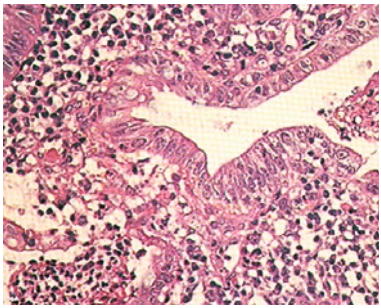


Fig. 11: Continuous, polymorphonuclear infiltration, limited to the mucosa, crypt abscesses, goblet cell mass reduced

X-ray

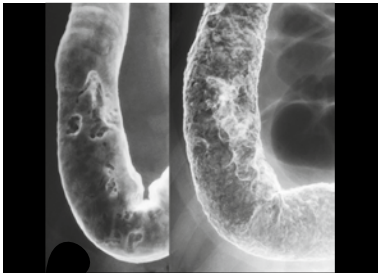


Fig. 12: Loss of colonic haustra, "rigid tube," pseudopolyps

Ultrasound

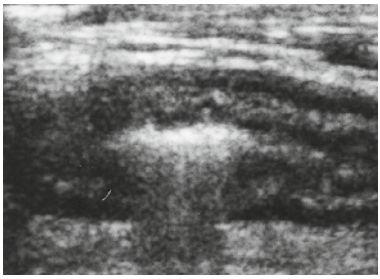


Fig. 13: Active ulcerative colitis with moderate wall thickening. The wall layers are intact.

Clinical presentation and advice for practitioners

Overview of clinical presentation

Crohn's disease

- CD involves segmental, discontinuous, subacute or chronic inflammation, which may affect the **entire** digestive tract from the mouth to the anus, but most commonly the terminal ileum and proximal colon. Pathologically, anatomically, and histologically, the **transmural** inflammation is segmentally localized with micro-erosions, fissures, large, deep and serpentine ulcers, granulomas, infiltrations, and dilated lymphatic vessels. Typical symptoms include cramp-like pain, diarrhea, fever, and weight loss.

Cardinal signs at disease onset

Intestinal		Extraintestinal	
• Abdominal pain	77%	• Weight loss	54%
• Diarrhea	73%	• Fever	35%
• Bleeding	22%	• Anemia	27%
• Anal fistulas	16%	• Arthralgia	38%
		• Eye involvement	10%
		• Erythema nodosum	8%

Epidemiology (Zhao 2021)

- Incidence in Europe: 0.4 to 22.8 cases/100,000 person-years
- Increasing incidence of CD. However, in high-prevalence Northern countries including Iceland and Finland, the incidence of CD has stabilized.
- Prevalence in Europe: 1.5 (Romania) to 331 (The Netherlands)/100,000
- Peak onset: 20–40 years of age

Disease activity

In patients with CD, inflammation is transmural. The deeper tissue layers of the intestines can be more severely affected. The clinical manifestation of the disease does not necessarily correlate with the endoscopic and histological findings, or with individual laboratory values. For this reason, indexes have been developed to determine disease activity and guide therapy. One of the most well-known of these is the Crohn's Disease Activity Index (CDAI), described on page 15. Other indexes have been developed, with

endoscopic findings increasingly considered in recent years. One of the most commonly used endoscopic indexes is the Simple Endoscopic Score for Crohn's Disease (SES-CD), shown on page 16.

Ulcerative colitis

- Ulcerative colitis is a relapsing, inflammatory disease of the colon and the rectum with ulcerations. Typically, the disease is most pronounced in the distal regions, and spreads proximally to varying extents. Pathologically and histologically, it presents as diffuse inflammation of the intestinal mucosa with ulcerations, crypt abscesses, infiltrates, and a reduced goblet cell count. The deeper layers of the large intestine wall are usually not affected. Patients exhibit bloody diarrhea, cramp-like pain, loss of appetite, and weight loss.
- The terminal ileum is rarely affected (backwash ileitis).

Active stage:	Granulocytic inflammation with reduced goblet cell count
In remission:	Normal findings possible, but often distorted crypt architecture; isolated pseudopolyp growth
Chronic colitis:	Epithelial dysplasia possible –> carcinoma development

Cardinal signs

Intestinal			Extraintestinal	
	Initial	1st year	• Fever	20%
• Bleeding	80%	100%	• Anemia	30–50%
• Diarrhea	52%	85%	• Arthralgia	30%
• Abdominal pain	47%	35%	• Weight loss	30%
• Anal fissures	4%	4%	• Eye involvement	10%
• Anal fistulas	0%	0%	• Erythema nodosum	8%

Epidemiology (Zhao 2021)

- Incidence in Europe: 2.4 to 44.0 cases/100,000 person-years
- Prevalence in Europe: approx. 2.4 (Romania) to 432 (Scotland)/100,000
- Peak onset: 20–40 years of age, although the peak in UC occurs five to 10 years later than in CD

Disease activity

In patients with UC, the inflammation is continuous and circumferential. The endoscopic and histological findings therefore

correlate somewhat better with the disease activity than in CD. Various indexes have been developed to assess activity, in which clinical and laboratory parameters and/or endoscopic findings are used. Two of the most widely used indexes are the partial Mayo score for clinical activity and the Mayo endoscopic score (MES) for endoscopic findings (see page 17).

Classification of Crohn's disease

Classification according to age, location, and disease behavior

Montreal classification	
Age at diagnosis	A1 ≤ 16 years A2 17–40 years A3 > 40 years
Location	L1 Ileal L2 Colonic L3 Ileocolonic L4 Isolated upper disease (in addition to L1–3)
Disease behavior	B1 Non-stricturing, non-penetrating B2 Stricturing (stenosis/strictures) B3 Penetrating (abscesses/fistulas) p Perianal disease (in addition to B1–3)

Paris classification (children)	
Age at diagnosis	A1a 0 – < 10 years A1b 10 – < 17 years A2 17–40 years A3 > 40 years
Location	L1 Distal third of ileum ± cecum L2 Colonic L3 Ileocolonic L4a Upper disease proximal to ligament of Treitz L4b Upper disease distal to ligament of Treitz and proximal to distal third of ileum
Disease behavior	B1 Non-stricturing, non-penetrating B2 Stricturing (stenosis/strictures) B3 Penetrating (abscesses/fistulas) B2B3 Stricturing and penetrating p Perianal disease (in addition to B1–3)
Growth	G0 No evidence of growth delay G1 Growth delay

Classification by disease activity (Crohn's Disease Activity Index [CDAI])

Variables 1–8 are recorded based on the information provided and multiplied by the weighting factors.

		Weighting factor	Subtotal
1	Number of liquid or soft stools (sum of previous 7 days)	× 2 =	
2	Abdominal pain (sum of previous 7 days)	× 5 =	
3	General well-being (sum of previous 7 days) (0 = generally well to 4 = terrible)	× 7 =	
4	Other symptoms associated with Crohn's disease (Please tick all that apply) ☐ Iritis Uveitis ☐ Erythema nodosum, pyoderma gangrenosum, aphthous stomatitis ☐ Joint pain Arthritis ☐ Anal fissure – fistulas – abscesses ☐ Other fistulas ☐ Temperatures above 37.5°C during the previous week Number of boxes ticked	× 20 =	
5	Anti-diarrheal treatment If yes	1 × 30 =	
6	Abdominal mass 0 = none 2 = possible 5 = present	× 10 =	
7	☐ Hematocrit Women: 42 - hct Men: 47 - hct	× 6 =	
8	☐ Weight (kg) ☐ Standard weight (kg) $1 - \frac{\text{Weight}}{\text{Standard weight}}$ (Note correct sign)	× 100 =	

Interpretation:
Total ≤ 150 = quiescent disease (remission)
Total > 150 = active disease

Sum CDAI value

Classification by endoscopic findings
(Simple Endoscopic Score – Crohn's Disease [SES-CD])

Variable	0	1	2	3
Size of ulcers	None	Aphthous ulcers (0.1–0.5 cm)	Large ulcers (0.5–2 cm)	Very large ulcers (> 2 cm)
Ulcerated surface	None	< 10%	10–30%	> 30%
Affected surface	Unaffected	< 50%	50–75%	> 75%
Presence of narrowings	None	Single, can be passed	Multiple, can be passed	Cannot be passed

Interpretation: 0–2 = Remission; 3–6 = Mild; 7–15 = Moderate; ≥ 16 = Severe

Classification of ulcerative colitis

Classification by extent and severity

Montreal classification		
Extent	E1	Ulcerative proctitis (limited to the rectum)
	E2	Left-sided colitis (distal to the splenic flexure)
	E3	Extensive colitis (proximal to the splenic flexure)
Severity	S0	Remission (asymptomatic)
	S1	Mild (≤ 4 stools/day ± blood, no signs of systemic disease, normal ESR[1])
	S2	Moderate (> 4 stools/day, minimal signs of systemic disease)
	S3	Severe (≥ 6 bloody stools/day, heart rate ≥ 90 bpm, temperature ≥ 37.5°C, hemoglobin < 10.5 g/dl, ESR ≥ 30 mm after 1 hour)

Paris classification (children)		
Extent	E1	Ulcerative proctitis (limited to the rectum)
	E2	Left-sided colitis (distal to the splenic flexure)
	E3	Extensive colitis (distal to the hepatic flexure)
	E4	Pancolitis
Severity	S0	Never severe (PUCAI[2] < 65)
	S1	Always severe

[1] ESR: erythrocyte sedimentation rate; [2] PUCAI: Pediatric Ulcerative Colitis Activity Index

Classification by disease activity (partial Mayo score)

Variable	0	1	2	3
Stool frequency (past 3 days)	Normal	1–2 more than normal	3–4 more than normal	5+ more than normal
Rectal bleeding	No blood seen	Streaks of blood with stool less than half the time	Obvious blood with stool most of the time	Blood passed alone
Physician's global assessment	Normal	Mild disease	Moderate disease	Severe disease

Interpretation: 0–1 = Inactive; 2–4 = Mild; 5–6 = Moderate; 7–9 = Severe

Classification by endoscopic findings (Mayo Endoscopic Score [MES])

Grade	Endoscopic findings
0 (normal)	None
1 (mild)	Erythema, decreased vascular pattern, mild friability
2 (moderate)	Marked erythema, absent vascular pattern, friability, erosions
3 (severe)	Spontaneous bleeding, ulceration

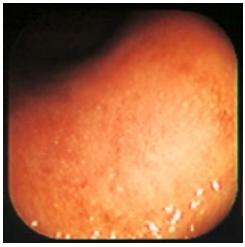


Fig. 14: Grade 1

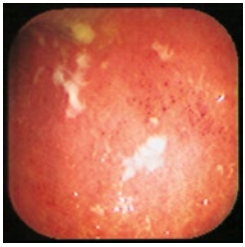


Fig. 15: Grade 2

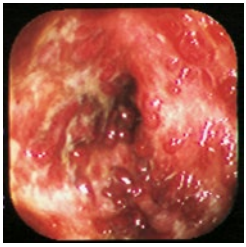


Fig. 16: Grade 3

Diagnosis and follow-up in primary care

Initial diagnosis

In many patients, the time period from the onset of symptoms until a diagnosis of IBD (such as CD or UC) is often very long (too long).

Diagnosis can sometimes be challenging because the cardinal clinical sign, "diarrhea," is often masked by more prominent extra-intestinal manifestations, with intestinal symptoms appearing only as secondary signs.

Basic diagnosis	
Medical history	• Number/consistency of stools/day • Diarrhea lasting more than 4 weeks • Blood in the stool • Mucus in the stool • Cramp-like pain • Recurring episodes of such symptoms • Increased urge to defecate • Defecation at night • Feeling of incomplete defecation • Fever • Skin problems • Joint pain • Eye pain • Aphthous ulcers • Use of certain medications (e.g., antidiarrheals, analgesics) • Travel abroad • Weight loss • Fatigue • Reduced physical strength • Edemas • Family history of IBD
Examination findings	• Reduced general condition • Height • Weight • Puberty status • Pallor • Skin problems (pyoderma gangrenosum, erythema nodosum)

Basic diagnosis	
Examination findings (continued)	• Bowel sounds • Abdominal mass • Tenderness on palpation in the abdomen • Joint swelling • Aphthous ulcers in the mouth • Fistulas
Laboratory	Inflammation parameters • ESR • CRP • Anemia • Thrombocytosis • Serum iron • (Ferritin) • Transferrin saturation • Creatinine • AST, ALT • Alkaline phosphatase Stool test for suspected infection Serology for suspected *Salmonella, Yersinia, Campylobacter jejuni/coli* Stool *Clostridioides difficile* toxin test Calprotectin in stool
Abdominal ultrasound	Characteristic ultrasound finding: • Intestinal wall thickening as a result of inflammatory or tumorous infiltration • Abscess • Intra-abdominal adhesions
Additional tests	For suspected: • Lactose intolerance: lactose H2 breath test • Malabsorption: D-xylose absorption test • Diverticulosis/diverticulitis: colonoscopy, CT • Celiac disease: anti-gliadin IgA antibody, anti-transglutaminase antibody

Referral to gastroenterologist/hospital	
For suspected:	• Acute flare-up • Toxic megacolon (UC) • Chronic refractory course

Follow-up tests for known disease	
Clinical Laboratory	(Activity indexes) • Blood count • AST, ALT • Calprotectin (if symptoms increase) • Vitamin D • Vitamin B_{12} (CD) • Folic acid

Diagnosis and follow-up by a gastroenterologist and at hospital

Outpatient examination

- Ultrasound
- Rectoscopy
- Sigmoidoscopy
- Complete ileocolonoscopy with segmental biopsies
- Upper endoscopy
- (Balloon-assisted enteroscopy)
- (Small bowel barium enteroclysis)
- MR enterography
- (Video capsule endoscopy, with patency capsule beforehand if needed)
- Pelvic MRI scan
- MR fistulography
- Computed tomography (CT)
- Transrectal endosonography
- Colon contrast enema

IBD is diagnosed based on a combination of clinical findings, disease progression, as well as endoscopic, histological, laboratory, and biochemical findings.

Crohn's disease

If signs of CD are present, a comprehensive diagnosis (upper endoscopy, small bowel barium enteroclysis, MR enterography, ileocolonoscopy) should be performed before starting treatment. This ensures that all affected intestinal segments are identified, especially in cases where the disease presents in a segmental pattern.

Ulcerative colitis

If signs of UC are present, a complete ileocolonoscopy should be carried out before initiating therapy in order to determine the exact extent of involvement (rarely discontinuous) both macroscopically and by histology. This is also important for planning treatment (topical vs. systemic).

Inpatient treatment

- Toxic colitis (with or without megacolon)
- Suspected sepsis
- Suspected contained or free perforation
- Subileus/ileus
- Poor general condition

Follow-up

Primarily based on clinical presentation, laboratory parameters, and endoscopic findings if necessary.

It is usually possible to distinguish between CD and UC. Above all, endoscopic findings with location and type of involvement play a prominent role here. Histological findings are only of secondary importance.

Findings	Ulcerative colitis	Crohn's disease
Abdominal pain	Frequent prior to defecation	Frequent
Bloody stools	Frequent	Occasional
Mucus in the stool	Frequent	Occasional
Abdominal "tumor" palpable	Rare	Frequent (when the ileocecal region is involved)
Subileus	Rare	Occasional
Involvement of the rectum	Almost always	Occasional
Perianal lesions	Rare	Frequent
Fistulas	Very rare	Frequent
Toxic dilation (megacolon)	Rare	Very rare
Relapse after curative surgery	Very rare	Frequent

Endoscopic findings	Ulcerative colitis	Crohn's disease
Aphthous ulcers	No	Frequent
Longitudinal ulcers	No	Frequent
Continuous involvement	Regular	Rare
Involvement of the terminal ileum	No	Frequent (> 80%)
Involvement of the rectum	95–100%	25–50%
Involvement of the mucous membrane	Superficial	Transmural
Ileocecal valve	Usually normal	Often stenosed
Pseudopolyps	Frequent	Rare
Strictures	Rare	Frequent
Epithelioid granulomas	No	Present (40%)

Extraintestinal manifestations

Extraintestinal signs of IBD occur in approx. 60% of patients and may be prominent, often involving the joints, skin, eyes, liver and bile ducts. Other organs (lung, heart, kidneys) are less commonly affected.

The signs may occur as initial indicators, particularly joint pain and erythema nodosum. Occasionally, a diagnosis of primary sclerosing cholangitis (PSC) leads to a diagnosis of ulcerative colitis.

In rare cases (< 1%), pancreatitis, vasculitis, pericarditis, myocarditis, autoimmune hemolytic anemia, and thrombotic diseases may occur.

Extraintestinal manifestations	
Skin	Erythema nodosum, pyoderma gangrenosum
Joints	Polyarthritis, monoarthritis, sacroiliitis
Eyes	Iridocyclitis, uveitis
Lung	Alveolitis, pulmonary fibrosis
Heart	Myopericarditis
Liver	Fatty liver disease, primary sclerosing cholangitis (PSC), overlap syndrome
Kidneys	Nephrolithiasis
Skeleton	Osteoporosis
Blood	Thromboembolism, autoimmune hemolytic anemia
Tissue	Amyloidosis
Psychological	Fatigue

Extraintestinal manifestations often accompany flare-ups (also known as “flares” or “attacks”), though not always. Consistent treatment of the underlying disease may therefore be accompanied by an improvement in the extraintestinal signs (exceptions: pyoderma gangrenosum, PSC, ankylosing spondylitis).

Extraintestinal complications

Extraintestinal complications are mainly caused by a deficiency, or (rarely) an excess of exogenous and endogenous substances in the body as a result of impaired intestinal function. Here, vitamins, trace elements, proteins, bile acids, oxalic acid, and water are extremely important. Deficiencies can lead to the following symptoms: anemia, osteomalacia, sensory disturbances, nyctalopia (zinc deficiency, vitamin A, D, E, K and B deficiency).

Changes in intestinal absorption can cause gallstones (reduced bile acid absorption) and kidney stones.

To detect deficiencies before signs occur, regular (e.g. annual) checks of the following parameters are recommended: Fe, Ca, Mg, Zn, ferritin, folic acid, vitamin A, B_{12}, D, E, K. Early testing for vitamin B_{12} deficiency can determine whether continuous supplementation is necessary. Specific ophthalmologic and rheumatic diagnostic procedures are indicated in patients with eye or joint issues. Liver manifestations, gallstones and kidney stones can often be detected by ultrasound. Primary sclerosing cholangitis (PSC) is diagnosed through endoscopic retrograde cholangiopancreatography (ERCP) or through MR cholangiography.

The adverse effects caused by the medications used and the interactions between these medications should be taken into account (e.g., reduced absorption: calcium [glucocorticoids], folic acid [sulfasalazine, methotrexate]).

Extraintestinal complications

1. Deficiencies
   a) Vitamin deficiency (A, B_{12}, C, D, E, K): osteomalacia, muscle atrophy, nyctalopia, sensory function disorders, hyperkeratosis, anemia
   b) Mineral deficiency (iron, calcium, magnesium, zinc): anemia, osteomalacia, growth disorder, oligospermia, immune deficiency
   c) Protein deficiency: edema
2. Changes in absorption
   a) Hyperoxaluria, dehydration: kidney stones
   b) Bile acid deficiency: gallstones

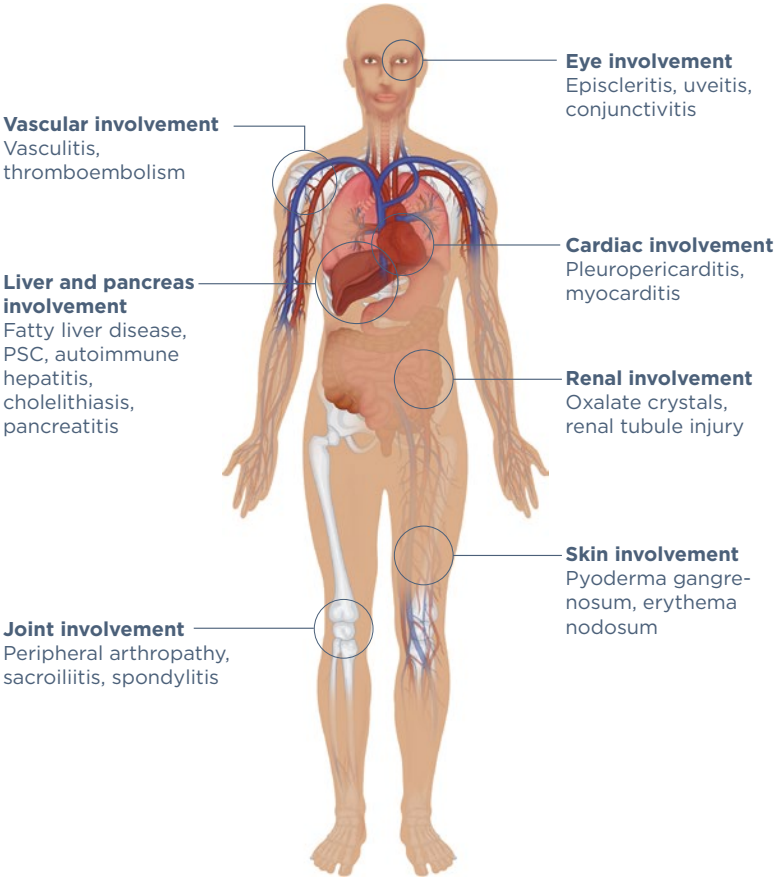


Fig. 17: Extraintestinal manifestations and complications in inflammatory bowel disease

Management of inflammatory bowel disease in adults

Crohn's disease (CD) and ulcerative colitis (UC) are chronic conditions that require lifelong treatment that aims to improve the patient's health and quality of life and reduce the risk of complications such as cancer or obstruction. This section provides information on common medical and surgical treatment options for CD and UC in adults, together with a summary of the latest evidence-based treatment guidelines published by the European Crohn's and Colitis Organisation (ECCO) and the British Society of Gastroenterology (BSG).

Medical treatment of inflammatory bowel disease

General approach to the medical management of inflammatory bowel disease

The overall therapeutic goal in IBD is for patients to achieve both symptom relief (clinical remission) and reduction of intestinal inflammation (endoscopic remission). However, a lack of correlation between symptoms and inflammation often complicates effective management of IBD in clinical practice. The international Selecting Therapeutic Targets in IBD (STRIDE) program has devised recommendations for a treat-to-target management strategy in IBD. For CD, this approach focuses on the resolution of abdominal pain and diarrhea, healing of endoscopic ulceration or resolution of inflammation on cross-sectional imaging, and normalization of C-reactive protein (CRP) and calprotectin levels (Peyrin-Biroulet 2015, Turner 2021). For UC, STRIDE targets include resolution of rectal bleeding and diarrhea and achieving a Mayo endoscopic subscore of 0–1. A recent update of the STRIDE recommendations has added absence of disability and restoration of quality of life as long-term targets in IBD; in addition, transmural healing and histological healing, while not considered formal targets, are recommended for estimating the depth of remission in CD and UC, respectively. Following induction of remission, maintenance therapy should be carried out to prevent relapses and optimize long-term outcomes.

Induction and maintenance therapy should be individualized based on factors such as disease location, disease activity and severity, response to previous therapy, complications such as perianal disease or fistulas, and other prognostic risk factors such

as the patient's age, health status, and any comorbidities which may have a bearing on the treatment benefit/risk ratio. Adopting an individualized approach will mean that a patient with severe or disseminated disease may be eligible for biologic therapy up front, with or without the addition of an immunomodulator (a "top-down" strategy), whereas a patient with mild or localized disease may receive initial treatment with 5-aminosalicylic acid (5-ASA) and/or a topical corticosteroid, with immunomodulators or biologics added as needed ("step-up" therapy). Combination therapy with different drug classes may be required to achieve the patient's individual therapeutic targets.

Approved medical treatment options for inflammatory bowel disease

Aminosalicylates

5-aminosalicylates (5-ASA) remain a cornerstone of UC treatment. For mild to moderate UC, oral mesalazine at doses of up to 4.8 g daily are effective and well tolerated. Combined oral and topical (rectal) 5-ASA treatment exhibits a significant additional benefit in extensive disease, while 5-ASA enema treatment alone can maintain remission in mild to moderate distal ulcerative colitis, i.e., proctitis and left-sided colitis. 5-ASAs have a favorable safety profile and are typically associated with low rates of serious adverse effects.

For CD, aminosalicylates including mesalazine and sulfasalazine have shown limited or no efficacy for inducing or maintaining remission.

Corticosteroids

Local and systemic corticosteroids are another mainstay of IBD drug therapy. The use of conventional systemic corticosteroids such as prednisolone is limited by significant adverse effects, especially in younger patients. In contrast, budesonide undergoes rapid and extensive first-pass metabolism in the liver, resulting in limited systemic bioavailability and fewer adverse effects. Modified-release formulations that deliver budesonide directly to the ileum and colon are effective for inducing remission in mild to moderate CD and UC, respectively.

In Europe, prednisolone and methylprednisolone are the most widely used systemic corticosteroids for induction of remission in moderate to severe CD and UC. Both budesonide and prednisolone are also available as rectal formulations for topical administration, for inducing remission in active inflammation limited to the rectum and sigmoid colon.

Although corticosteroids are highly effective for inducing remission in IBD, they have limited efficacy in maintenance therapy of CD with no evidence in UC. For this reason, and given the well-documented toxicity profile of systemic corticosteroids, international guidelines recommend their use in IBD only for induction therapy.

Thiopurines

Thiopurine analogues (azathioprine and 6-mercaptopurine) are immunosuppressive agents that have been associated with clinical benefit in maintenance treatment of IBD patients as monotherapy or as an adjunct to biologic anti-TNF therapy. Individual variation in thiopurine metabolism may limit the clinical benefit and increase the risk of adverse effects with thiopurine metabolites. Therefore, monitoring thiopurine metabolite levels, along with dose adjustment, split dosing, and/or combination therapy with allopurinol or 5-ASA may be advisable. For some patients, switching from azathioprine to 6-mercaptopurine can improve tolerability. Most thiopurine-related adverse effects appear early on and may be transient; hence a personalized approach of starting on a lower dose and gradually increasing up to the recommended level under close monitoring may be considered.

Methotrexate

Methotrexate was initially developed as a treatment for cancer but was later found to have immunosuppressive properties. Today, it is widely used to manage rheumatoid arthritis and other conditions involving systemic inflammation. In IBD, intramuscular methotrexate can maintain remission in patients with CD at standard doses of 15 mg/week, whereas low-dose methotrexate or combination therapy with infliximab are not effective. There is no data to show that methotrexate at standard doses is effective for inducing remission in CD, nor has any clinical benefit of methotrexate been shown in UC.

Biologic therapies

Anti-TNF-alpha therapy

Anti-TNF therapy is recommended as a first-line treatment option for both CD and UC, for patients with moderate to severe active disease who are refractory or intolerant to conventional non-biologic therapy. Multiple randomized controlled studies and meta-analyses have confirmed the efficacy of TNF inhibition in induction of clinical remission in CD and UC. Anti-TNF therapy has also demonstrated high levels of efficacy when administered as maintenance therapy in CD and UC patients after achieving remission.

The primary anti-TNF agents used in IBD treatment are infliximab, adalimumab, and golimumab. The choice of anti-TNF agent is largely determined by local availability and patient preference.

Anti-IL-23 therapy

Several monoclonal antibody therapies target interleukin (IL)-23 or the common p40 subunit of IL-12 and IL-23. Ustekinumab is a monoclonal antibody that binds to the p40 subunit shared by IL-12 and IL-23 and is effective for induction and maintenance of remission in patients with moderate to severe CD or UC. Risankizumab and mirikizumab selectively bind to IL-23 and are both approved for UC, while risankizumab is also approved for CD.

Anti-integrin (α4β7) therapy

Vedolizumab is a monoclonal antibody that blocks lymphocyte trafficking in the gastrointestinal tract by inhibiting the binding of integrin α4β7 to MAdCAM-1, resulting in suppression of T cell-mediated inflammation. Intravenous vedolizumab is effective as induction therapy in moderate to severe CD and UC. A subcutaneous formulation of vedolizumab is effective as maintenance therapy in CD and UC.

JAK inhibitors

Janus kinase (JAK) inhibitors are a class of small, orally administered molecules that target additional inflammatory mechanisms in IBD, primarily in UC. Several members of this class, including tofacitinib, are effective as induction therapy as well as in the maintenance setting in moderate to severe UC. However, some safety concerns have been raised regarding JAK inhibitors which must be considered.

Sphingosine-1-phosphate receptor modulators

Sphingosine-1-phosphate (S1P) receptor modulators exert immunomodulatory effects by reducing lymphocyte migration. The oral S1P receptor modulators ozanimod and etrasimod have been shown to be effective in inducing and maintaining remission in moderate to severe UC.

Specific guideline recommendations – medical management of inflammatory bowel disease

The following treatment strategies are derived from published clinical practice guidelines, specifically from guidelines issued by the European Crohn's and Colitis Organisation (ECCO) in 2022 (Raine 2022) and 2020 (Torres 2020) as well as by the British Society of Gastroenterology (BSG) (Lamb 2019). They are intended to provide an introductory overview to approaching the management of IBD; for more details, please consult local guidance.

Crohn's disease

Induction therapy, mild to moderate Crohn's disease

Oral budesonide is recommended for inducing clinical remission in patients with mild to moderate CD limited to the ileum and/or ascending colon. The BSG guidelines advise that mild to moderate CD can be treated either with systemic corticosteroids to induce remission, or alternatively with exclusive enteral nutrition (EEN) for patients where steroid avoidance is desired.

There is no evidence to support a consistent treatment benefit of antibiotics in mild to moderate CD.

Induction therapy, moderate to severe Crohn's disease

In patients with moderate to severe CD, systemic corticosteroids can be used for the induction of clinical response and remission. Anti-TNF therapy is recommended for inducing remission in patients with moderate to severe CD who have not responded to conventional therapy (i.e., corticosteroids and/or thiopurines).

Ustekinumab and vedolizumab are both recommended induction therapy options for moderate to severe CD in patients who fail to achieve a satisfactory response to conventional therapy and/or prior anti-TNF therapy.

Maintenance therapy

Thiopurine analogues are recommended for maintaining remission in patients with steroid-dependent CD, and parenteral methotrexate can also be used in this setting.

For CD patients who have achieved remission on a biologic, maintenance therapy using the same agent is recommended. CD patients who have achieved long-term remission on combination therapy with an anti-TNF and immunosuppressant should be offered to continue maintenance therapy with infliximab or adalimumab as monotherapy, subject to a discussion of the risks and benefits for the individual patient.

Perianal fistulizing disease

Infliximab is the recommended option for induction and maintenance of remission in CD patients with complex perianal fistulas; adalimumab can also be used in this setting.

Ulcerative colitis

Induction therapy, mild to moderate ulcerative colitis

In mild to moderate UC, oral 5-ASA at a dose of ≥ 2 g daily is recommended to induce remission. For active distal colitis, topical (rectal) 5-ASA is recommended as induction therapy, and is preferred over topical (rectal) corticosteroids. An oral colonic-release corticosteroid (budesonide MMX) can be used as induction therapy for mild to moderate UC extending beyond the rectum.

The BSG guidelines suggest that the mesalazine dose may be increased up to 4.8 g daily orally alongside topical (rectal) 5-ASA for UC patients who flare while on 5-ASA. For patients with mild to moderate UC who are refractory or intolerant to 5-ASA, the BSG guidelines recommend budesonide MMX as a means of avoiding systemic corticosteroids.

Induction therapy, moderate to severe ulcerative colitis

Oral prednisolone is recommended as induction therapy for non-hospitalized patients with moderate to severe UC. For patients with moderate to severe UC who are refractory or intolerant to conventional therapy (i.e., 5-ASA, steroids, and thiopurines), induction therapy with an anti-TNF, ustekinumab or vedolizumab, or tofacitinib is recommended.

Maintenance therapy, mild to moderate ulcerative colitis

Oral 5-ASA at a dose of ≥ 2 g daily should be used to maintain remission in UC; in distal UC topical (rectal) 5-ASA can be used. For UC patients who are steroid-dependent or intolerant to 5-ASA, thiopurine analogue monotherapy is recommended as maintenance therapy.

Maintenance therapy, moderate to severe ulcerative colitis

For UC patients who have achieved remission on biologic therapy or JAK inhibitor therapy, maintenance therapy using the same agent is recommended.

Acute severe ulcerative colitis

Intravenous corticosteroids are recommended as initial treatment in acute severe UC (ASUC) to induce clinical remission and reduce mortality. Patients with steroid-refractory acute severe UC should receive either infliximab or cyclosporine depending on local experience, with a plan for post-cyclosporine maintenance therapy if applicable.

The BSG guidelines recommend that patients with ASUC should be hospitalized for assessment and intensive management. Patients with ASUC who fail to respond to infliximab or cyclosporine rescue therapy within 7 days, or patients who deteriorate or develop complications in this time (including toxic megacolon, severe hemorrhage or perforation) should undergo colectomy.

Therapeutic class	Target/mode of action
Locally-acting corticosteroids	Anti-inflammatory and immunomodulatory effect through downregulation of inflammatory cytokines and NF-κB production
Systemic corticosteroids	Anti-inflammatory and immunomodulatory effect through downregulation of inflammatory cytokines and NF-κB production
Anti-TNF antibodies	Multiple mechanisms of action, including neutralization of TNF-α, reverse signaling, apoptosis, and cytotoxicity
Anti-IL-12/23 antibodies	Bind specifically to the p40 protein subunit shared by IL-12 and IL-23, thus preventing binding to the IL-12Rβ1 receptor expressed on the surface of immune cells
Anti-α4β7 integrin antibodies	Inhibiting the binding of integrin α4β7 to MAdCAM-1, resulting in suppression of T cell-mediated inflammation
Thiopurine analogues	Immunosuppressive effect through inhibition of purine synthesis
Methotrexate	Immunomodulatory effect through multiple mechanisms, including inhibition of purine and pyrimidine synthesis, transmethylation reactions, translocation of NF-κB, JAK-STAT signaling, and NO production
Aminosalicylates	Local anti-inflammatory effect in the intestinal mucosa – unknown mechanism of action
JAK inhibitors	Anti-inflammatory effect through blockade of the JAK-STAT pathway
Sphingosine-1-phosphate receptor agonists	Immunomodulatory effect through inhibition of lymphocyte migration

[1]As of September 2024.

Table 1: Overview of selected drugs and drug classes approved for IBD management. Not all active compounds are indicated for all settings listed. This table does not constitute treatment recommendations. Please refer to local guidelines.

	Active compounds approved for IBD treatment[1]	Route(s) of administration	Setting
	Budesonide	Oral, topical (rectal)	Induction therapy of mild to moderate CD. Induction therapy of mild to moderate UC
	Prednisolone, methylprednisolone, prednisone	Oral	Induction therapy of moderate to severe CD. Induction therapy of moderate to severe UC
	Infliximab, adalimumab, golilumumab, certolizumab pegol	iv and sc injection	Induction and maintenance therapy of moderate to severe CD Induction and maintenance therapy of moderate to severe UC
	Ustekinumab, risankizumab, mirikizumab	iv and sc injection	Induction and maintenance therapy of moderate to severe CD Induction and maintenance therapy of moderate to severe UC
	Vedolizumab	iv infusion	Induction and maintenance therapy of moderate to severe CD Induction and maintenance therapy of moderate to severe UC
	Azathioprine, mercaptopurine	Oral	Maintenance therapy of steroid-dependent CD
	Methotrexate	im or sc injection	Maintenance therapy of steroid-dependent CD
	Mesalazine (5-ASA)	Oral, topical (rectal)	Induction and maintenance therapy of mild to moderate UC
	Tofacitinib, filgotinib, upadacitinib	Oral	Induction and maintenance therapy of moderate to severe UC
	Ozanimod, etrasimod	Oral	Induction and maintenance therapy of moderate to severe UC

Surgery for inflammatory bowel disease

IBD patients who fail to respond to medical therapy, or who develop complications such as strictures, abscesses or fistulas, may require surgery. Surgery can lead to resolution of ongoing symptoms, reduce the need for hospitalization and immunosuppressive therapy, and prevent cancer. However, surgical intervention may lead to loss of bowel function, which may be difficult for the patient to accept. A multidisciplinary approach involving specialists with a good understanding of the social and psychologic burden of IBD is essential.

Preoperative optimization

As with any other type of surgery, several factors have been linked to an increased risk of poor outcomes and complications, such as smoking and malnutrition. Patients undergoing elective surgery for CD or UC should be assessed and any risk factors addressed prior to surgery and as part of multidisciplinary management to achieve acceptable long-term functional outcomes and minimize peri- and postoperative complications. This includes drainage and antibiotic treatment of abscesses, correction of anemia, and nutritional support as required. Patients treated with corticosteroids should be weaned or have their dose tapered to the lowest possible dose, as systemic corticosteroid therapy is known to increase the risk of surgical complications including infections, wound-healing problems and anastomotic insufficiency. In contrast, treatment with thiopurine analogues anti-TNF agents, ustekinumab, and vedolizumab can be safely continued. While data on other biologics and small molecules is emerging, knowledge about their impact on postoperative outcomes in IBD is as yet limited, underlining the importance of multidisciplinary management and decision-making.

Other preoperative measures include thromboprophylaxis to reduce the risk of thromboembolic complications, and tapering or cessation of preoperative opioid analgesics to optimize postoperative pain management.

Surgical options for inflammatory bowel disease

The following treatment strategies are derived from published clinical practice guidelines, specifically from guidelines issued by the European Crohn's and Colitis Organisation (ECCO) in 2022 (Spinelli 2022) and 2020 (Adamina 2020) as well as by the British Society of Gastroenterology (Lamb 2019). They are intended to provide an introductory overview to approaching the management of IBD. For more details, please consult local guidance.

Minimally invasive surgery is now the standard of care for IBD owing to lower rates of wound infections, anastomosis leak, and reintervention compared with open surgery.

Crohn's disease

Abdominal Crohn's disease

Endoscopic balloon dilation (EBD) may be considered for patients with CD-associated fibrotic strictures in the small intestine that are endoscopically accessible, and for anastomotic strictures. EBD is associated with a high success rate and low rates of perforation and hemorrhage; however, a sizable proportion of patients will require re-dilation and/or resection. For strictures that are unsuitable for EBD, strictureplasty may offer an alternative to resection that can spare bowel length and reduce the risk of developing short bowel syndrome.

Bowel resection or small bowel bypass can be performed as an alternative to biologic therapy for CD patients with inflammatory strictures, or patients with fibrotic strictures where bowel-sparing surgery is not feasible. In addition to the type and extent of the disease, the choice of surgical technique should also take into account the length of the strictures, the size of the resection margin, the decision to include the mesentery, and the choice between an end-to-end hand-sewn or side-to-side anastomosis.

Acute perforation usually requires emergency surgery involving resection of the affected bowel segment together with a temporary or permanent stoma. In addition, abscesses that cannot be accessed for percutaneous drainage may require surgical drainage, and bowel resection and a temporary stoma may be indicated.

For patients with extensive and/or treatment-refractory CD, creating a defunctioning stoma can help control the active inflammation, and also help to buy time for preoperative optimization prior to bowel resection.

For selected CD patients with pancolitis, an ileal pouch-anal-anastomosis (IPAA) procedure may be considered, provided there is no evidence of existing or previous perianal or small bowel CD. IPAA is usually associated with excellent functional outcomes, but complications such as strictures and pouchitis can lead to pouch failure. An alternative option is the Kock pouch or continent ileostomy, which can be used as a primary procedure for patients unsuitable for IPAA or as a salvage option following a failed pelvic pouch.

Perianal Crohn's disease

The management of perianal CD patients should be multidisciplinary and aim for symptom reduction with preservation of continence. Perianal abscesses may be managed by surgical drainage, with antibiotics as needed. Simple, asymptomatic perianal fistulas generally require no surgical intervention, whereas complex perianal fistulas usually require combined medical therapy and surgical intervention, including drainage through seton placement and/or local fistula repair using fibrin glue or a fibrin plug, advancement flaps, or the ligation of intersphincteric track (LIFT) procedure. Notably, the treatment of complex anorectovaginal fistulas should be reserved for an expert multidisciplinary team in experienced centers.

In recent years, mesenchymal stem cell (MSC) therapy has emerged as a promising therapeutic option for complex perianal CD. Intrafistular injections of bone marrow-derived MSCs were associated with high rates of fistula closure and mucosal healing in CD patients with complex perianal fistulas. More recently, a significant benefit has been shown with allogeneic adipose tissue-derived MSCs (darvadstrocel) versus placebo.

For CD patients with treatment-refractory complex perianal fistulas, temporary fecal diversion through a defunctioning stoma may be required for symptom relief; in very severe cases proctectomy may be indicated.

Ulcerative colitis

Up to 25% of patients with UC require a surgical intervention in their lifetime. Subtotal colectomy using minimally invasive techniques is indicated as an emergency intervention for ASUC when the acute inflammation does not respond to medical therapy or there are signs of life-threatening complications including hemorrhage, bowel perforation, or toxic megacolon. Subtotal

colectomy also offers an option for patients with treatment-refractory UC or a history of frequent relapses, although surgical management of moderate to severe refractory UC is more varied compared with that of ASUC and there is currently less consensus. In this setting, subtotal colectomy followed by ileal pouch-anal anastomosis (IPAA) is considered to be the gold standard and is usually associated with good functional and quality of life outcomes. Ileorectal anastomosis (IRA) is a technically simpler procedure which may be considered for selected patients with little or no rectal inflammation and no family history of colorectal cancer. For patients who are unwilling or unable to have a pelvic pouch after undergoing subtotal colectomy, a Kock pouch may be an option.

References

Adamina M, Bonovas S, Raine T, Spinelli A, Warusavitarne J, Armuzzi A, et al. ECCO Guidelines on Therapeutics in Crohn's Disease: Surgical Treatment. J Crohns Colitis. 2020;14(2):155–68. doi: 10.1093/ecco-jcc/jjz187.

Lamb CA, Kennedy NA, Raine T, Hendy PA, Smith PJ, Limdi JK, et al. British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults. Gut. 2019;68(Suppl 3):s1–106. doi: 10.1136/gutjnl-2019-318484.

Peyrin-Biroulet L, Sandborn W, Sands BE, Reinisch W, Bemelman W, Bryant RV, et al. Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE): Determining Therapeutic Goals for Treat-to-Target. Am J Gastroenterol. 2015;110(9):1324–38. doi: 10.1038/ajg.2015.233.

Raine T, Bonovas S, Burisch J, Kucharzik T, Adamina M, Annese V, et al. ECCO Guidelines on Therapeutics in Ulcerative Colitis: Medical Treatment. J Crohns Colitis. 2022;16(1):2–17. doi: 10.1093/ecco-jcc/jjab178.

Riegler G, Tartaglione MT, Carratú R, et al. Age-related clinical severity at diagnosis in 1705 patients with ulcerative colitis: a study by GISC (Italian Colon-Rectum Study Group). Dig Dis Sci. 2000;45(3):462–465. doi: 10.1023/a:1005424603085.

Spinelli A, Bonovas S, Burisch J, Kucharzik T, Adamina M, Annese V, et al. ECCO Guidelines on Therapeutics in Ulcerative Colitis: Surgical Treatment. J Crohns Colitis. 2022;16(2):179–89. doi: 10.1093/ecco-jcc/jjab177.

Torres J, Bonovas S, Doherty G, Kucharzik T, Gisbert JP, Raine T, et al. ECCO Guidelines on Therapeutics in Crohn's Disease: Medical Treatment. J Crohns Colitis. 2020;14(1):4–22. doi: 10.1093/ecco-jcc/jjz180.

Turner D, Ricciuto A, Lewis A, D'Amico F, Dhaliwal J, Griffiths AM, et al. STRIDE-II: An Update on the Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE) Initiative of the International Organization for the Study of IBD (IOIBD): Determining Therapeutic Goals for Treat-to-Target strategies in IBD. Gastroenterology. 2021;160(5):1570–83. doi: 10.1053/j.gastro.2020.12.031.

Zeitz M. Neue Therapiemöglichkeiten bei den chronisch entzündlichen Darmerkrankungen (IBD) [New therapeutic possibilities in chronic inflammatory bowel diseases]. Praxis (Bern 1994). 1997;86(25–26):1071–4. German. PMID: 9289806.

Zhao M, Gonczi L, Lakatos PL, Burisch J. The Burden of Inflammatory Bowel Disease in Europe in 2020. Journal of Crohn's & colitis. 2021;15(9):1573–87.

Quiz

Your knowledge about IBD:

Have you been able to refresh your medical expertise on IBD with the help of this brochure? Test your knowledge!

This QR code (Microsoft Form) will take you to 10 questions. Only 1 answer out of 5 possible is correct.

Good luck!

S3E 1-2/2025 HOF

Together we know more. Together we do more.
Falk Foundation e.V. | Leinenweberstr. 5 | 79108 Freiburg | Germany