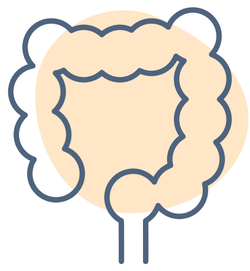
ULCERATIVE COLITIS

EPIDEMIOLOGY – CLINICAL PRESENTATION – DIAGNOSIS AND MONITORING – THERAPY



CLINICAL PRESENTATION

- UC is a life-long disease of the colon and rectum, characterized by a relapsing-remitting course of inflammation with ulceration.
- The presenting symptoms of UC depend on the extent and severity of the colonic inflammation.
- The most common presenting symptom is rectal bleeding (> 90% of patients).
- EIMs can occur in up to one in three patients, in many cases prior to confirmation of UC. EIMs may be triggered by UC exacerbations or occur independently.

EIMs: extra-intestinal manifestations

GASTROINTESTINAL SYMPTOMS OF UC

- Increased stool frequency (diarrhea with mucus and/or blood)
- Rectal bleeding
- Decreased stool consistency (loose, watery stools)
- Bowel urgency, including at night
- Tenesmus
- Fecal incontinence
- Cramp-like abdominal pain

EPIDEMIOLOGY IN EUROPE

Incidence (annual rate of new cases):
Up to 44 cases per 100,000 population per year

Prevalence (number of existing cases):
Up to 505 cases per 100,000 population

INITIAL DIAGNOSIS AND MONITORING

The diagnosis of ulcerative colitis (UC) is based on a combination of symptoms and biochemical, endoscopic, and histological parameters. There is no single reference standard for the diagnosis of UC.

Diagnostic investigations

- At diagnosis, patients should undergo biochemical evaluation, including but not limited to complete blood count, assessment of inflammatory markers such as CRP, electrolytes, liver enzymes, and stool analysis.
- Fecal calprotectin appears to be the most sensitive marker of intestinal inflammation in IBD, but has a low specificity (cannot be used to distinguish IBD from differential diagnoses).

Endoscopy

UC characteristically affects the rectum and the colon to a variable extent (Figure 4–6) in a continuous, circumferential manner with clear demarcation between inflammation and healthy mucosa.

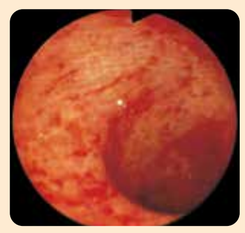


Figure 1: Mild UC

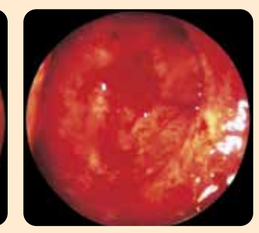


Figure 2: Moderately active UC

Histology

Two or more biopsies from inflamed regions showing focal or diffuse basal plasmacytosis, crypt architectual distortion (branching, shortening, irregular spacing), crypt abcesses, goblet cell depletion, submucosal hypertrophy, and/or mucosal atrophy. Additional biopsies from inflamed and uninflamed colonic segments including the rectum may support the UC diagnosis.

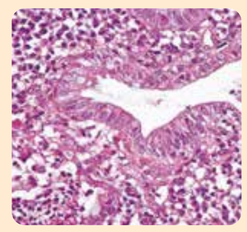


Figure 3: Histology

Differential diagnosis

Gastrointestinal infections (e.g., *Clostridium difficile*), ischemic colitis, drug-induced colitis (e.g., from checkpoint inhibitors or NSAIDs), microscopic colitis, colorectal cancer, functional bowel disorders including IBS, radiation proctitis, GvHD, common variable immunodeficiency, traumatic proctitis, diverticulosis, Crohn's disease, and more.

IBS: irritable bowel syndrome; NSAIDs: nonsteroidal anti-inflammatory drugs; GvHD: graft-versus-host disease

DISEASE ACTIVITY ASSESSMENT

By Location

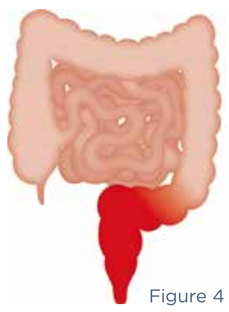


Figure 4

Proctitis:
Inflammation limited to the rectum

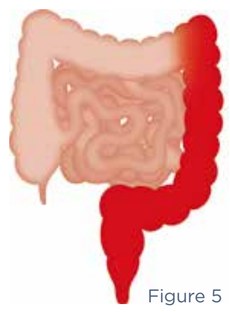


Figure 5

Left-sided colitis:
Inflammation past the rectum but not beyond the splenic flexure

Figure 6

Extensive or pan-colitis:
Inflammation past the splenic flexure or involving the entire colon

Scoring Systems

The Mayo Endoscopy Score (MES), a subcomponent of the full Mayo Score, is commonly used to assess endoscopic disease activity in clinical practice and clinical studies.* The full Mayo Score consists of four components: three clinical parameters (stool frequency, rectal bleeding, and physician's global assessment), which together form the Partial Mayo Score (pMayo), and the MES as the fourth, endoscopic component.

Classification by disease activity (partial Mayo score)

	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

*Alternatively, the Ulcerative Colitis Endoscopic Index of Severity (UCEIS) is also available for assessing disease activity.

DISEASE MONITORING & SURVEILLANCE

In 2015, the STRIDE consensus identified both clinical and endoscopic remission as key goals in the medical management of UC, laying the foundation for a treat-to-target strategy in IBD. The STRIDE-II update confirmed the long-term targets, while adding absence of disability, improved quality of life, and normal growth in children as additional treatment targets as well as introducing symptomatic relief and biomarker normalization as short-term objectives.

Short-term targets ▼	**Symptomatic response**
Short-term/intermediate targets ▼	**Symptomatic remission and normalization of CRP**
Intermediate targets ▼	**Decrease in calprotectin to acceptable range**
Long-term targets ▼	**Endoscopic healing, normalized QoL and absence of disability**

QoL=Quality of Life; CRP = C-reactive Protein; Adapted from Turner et al, Gastroenterology, 2021, Fig. 2.

OVERVIEW OF SELECTED DRUGS AND DRUG CLASSES APPROVED FOR UC

This table does not constitute treatment recommendations. Please refer to local guidelines.

Therapeutic class	Target/mode of action	Active compounds approved for IBD treatment	Route(s) of administration	Setting
Second-generation corticosteroids**	Broad anti-inflammatory and immunomodulatory effects through downregulation of inflammatory cytokines and modulation of leucocyte activity and function.	Budesonide	Oral, topical (rectal)	Induction therapy of mild to moderate UC
First-generation corticosteroids	Broad anti-inflammatory and immunomodulatory effects through downregulation of inflammatory cytokines and modulation of leucocyte activity and function.	Prednisolone, methylprednisolone, prednisone	Oral	Induction therapy of moderate to severe UC
Anti-TNF antibodies	Multiple mechanisms of action, including neutralization of TNF-α, reverse signaling, apoptosis, and cytotoxicity.	Infliximab, adalimumab, golilumab, certolizumab pegol	IV and SC injection	Induction and maintenance therapy of moderate to severe UC
Anti-IL-12/23 antibodies	Binds 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.	Ustekinumab, risankizumab, mirikizumab	IV and SC injection	Induction and maintenance therapy of moderate to severe UC
Anti-α4β7 integrin antibodies	Inhibiting the binding of integrin α4β7 to MAdCAM-1, resulting in suppression of T-cell-mediated inflammation.	Vedolizumab	IV infusion	Induction and maintenance therapy of moderate to severe UC
Aminosalicylates	Local anti-inflammatory effect in the intestinal mucosa – unknown mechanism of action.	Mesalazine (5-ASA), sulfasalazine, balsalazide, olsalazine	Oral, topical (rectal)	Induction and maintenance therapy of mild to moderate UC
JAK inhibitors	Anti-inflammatory effect through blockade of the JAK-STAT pathway.	Tofacitinib, filgotinib, upadacitinib	Oral	Induction and maintenance therapy of moderate to severe UC
Sphingosine-1-phosphate receptor agonists	Immunomodulatory effect through inhibition of lymphocyte migration.	Ozanimod, etrasimod	Oral	Induction and maintenance therapy of moderate to severe UC

**Second-generation corticosteroids refer to synthetic corticosteroids that have been structurally modified to enhance their potency, selectivity, and safety profile

Together we know more. Together we do more.

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