# INFLAMMATORY BOWEL DISEASES: DIFFERENTIAL DIAGNOSIS OF CROHN'S DISEASE AND ULCERATIVE COLITIS

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**Abstract**

**Background:** Crohn's disease and ulcerative colitis are the two principal forms of inflammatory bowel disease (IBD), sharing overlapping symptoms of chronic diarrhea, abdominal pain, and rectal bleeding but differing fundamentally in anatomical distribution, depth of inflammation, and complication profile, such that correct differentiation is essential to guide treatment and prognosis.

**Methods:** This narrative review synthesizes current evidence on the clinical, endoscopic, histological, and serological differentiation of Crohn's disease and ulcerative colitis, drawing on major gastroenterology reference guidelines and recent comparative reviews of both conditions.

**Results:** Crohn's disease can affect any segment of the gastrointestinal tract from mouth to anus in a discontinuous, "skip lesion" pattern with transmural inflammation that predisposes to fistula, stricture, and abscess formation, whereas ulcerative colitis is confined to the colon and rectum, producing continuous, mucosa-limited inflammation beginning at the rectum. Ileocolonoscopy with segmental biopsy remains the diagnostic cornerstone for both conditions, with cross-sectional small-bowel imaging added when Crohn's disease is suspected; despite a thorough work-up, approximately 10 to 15% of patients with isolated colitis cannot be definitively classified and are labelled as having IBD-unclassified. Histological and serological findings, including granulomas and ASCA positivity in Crohn's disease versus crypt abscesses and p-ANCA positivity in ulcerative colitis, provide supportive but not individually definitive evidence.

**Conclusion:** Because Crohn's disease and ulcerative colitis require different surgical thresholds, carry different complication risks, and respond somewhat differently to certain therapies, systematic application of endoscopic, histological, and, where needed, radiological criteria remains essential for accurate differentiation, an approach that is both feasible and important to apply consistently in resource-limited settings such as Uzbekistan, where ileocolonoscopy with biopsy is the most widely available and highest-yield diagnostic tool.

**Keywords**

Inflammatory bowel disease, Crohn's disease, ulcerative colitis, differential diagnosis, ileocolonoscopy, transmural inflammation, skip lesions, IBD-unclassified, ASCA, p-ANCA.

**Methods**

This work was prepared as a narrative literature review. A literature search was conducted in September 2026 using PubMed and major gastroenterology reference databases, with the search terms "Crohn's disease," "ulcerative colitis," "inflammatory bowel disease differential diagnosis," "IBD-unclassified," and "ileocolonoscopy," combined with filters for publication in English between 2011 and 2026. Priority was given to major comparative reviews of Crohn's disease and ulcerative colitis, diagnostic and classification studies, and histopathology-focused comparative series; narrative summaries from established clinical reference sources were included for foundational background. Case reports and articles without accessible full text were excluded. A total of twelve sources meeting these criteria were selected and synthesized for this review.

**Introduction**

Crohn's disease and ulcerative colitis are the two principal, clinically distinct forms of inflammatory bowel disease, both characterized by chronic, relapsing immune-mediated inflammation of the gastrointestinal tract but differing substantially in their anatomical distribution, depth of tissue involvement, and long-term complication profile. Both conditions can present with overlapping symptoms — chronic diarrhea, abdominal pain, rectal bleeding, weight loss, and fatigue — making symptom-based diagnosis alone unreliable and correct classification dependent on a structured combination of endoscopic, histological, radiological, and, at times, serological findings.

Accurate differentiation is not merely an academic exercise: the two conditions carry different risks of specific complications, different indications and outcomes for surgery, and, for certain therapeutic agents, different expected efficacy, such that misclassification can meaningfully affect patient management. At the same time, despite a thorough diagnostic work-up, a clinically important minority of patients with isolated colonic disease

cannot be confidently assigned to either category and are appropriately classified as having IBD-unclassified, a designation that itself carries management implications.

*The aim of this review is to summarize the key anatomical, endoscopic, histological, and serological features that differentiate Crohn's disease from ulcerative colitis, and to outline the structured diagnostic pathway used to distinguish them, with attention to their relevance to gastroenterology and internal medicine practice in Uzbekistan.*

Correctly differentiating Crohn's disease from ulcerative colitis is relevant across several areas of clinical practice, including:

- Gastroenterology (endoscopic and histological classification, medical therapy selection)
- General and colorectal surgery (differing surgical indications and approaches for each condition)
- Radiology (interpretation of cross-sectional small-bowel imaging in suspected Crohn's disease)
- Pathology (recognition of granulomas, crypt architecture, and transmural inflammation on biopsy)
- Primary care and internal medicine (early recognition of chronic diarrhea or rectal bleeding warranting referral)

**Anatomical Distribution: The Central Distinguishing Feature**

The single most fundamental distinction between the two conditions is anatomical: Crohn's disease can involve any segment of the gastrointestinal tract from the mouth to the anus, most commonly the terminal ileum and proximal colon, and characteristically does so in a discontinuous, "skip lesion" pattern in which segments of diseased bowel alternate with segments of entirely normal mucosa; the rectum is frequently, though not always, spared. Ulcerative colitis, by contrast, is confined to the colon and rectum and does not extend into the small bowel (with the exception of mild, non-specific "backwash ileitis" in some cases of pancolitis), and its inflammation is continuous, beginning at the rectum and extending proximally without skip areas, with disease severity typically greatest distally.

This difference in distribution is compounded by a difference in depth: Crohn's disease is transmural, involving the full thickness of the bowel wall, which predisposes to fistula formation, abscesses, and fibrotic strictures, whereas ulcerative colitis is limited to the mucosa and submucosa, so that deep transmural complications such as fistulas are not a feature of uncomplicated disease. These anatomical and depth-based distinctions, which underlie nearly all of the clinical, endoscopic, and complication differences between the two conditions, are illustrated in Figure 1.

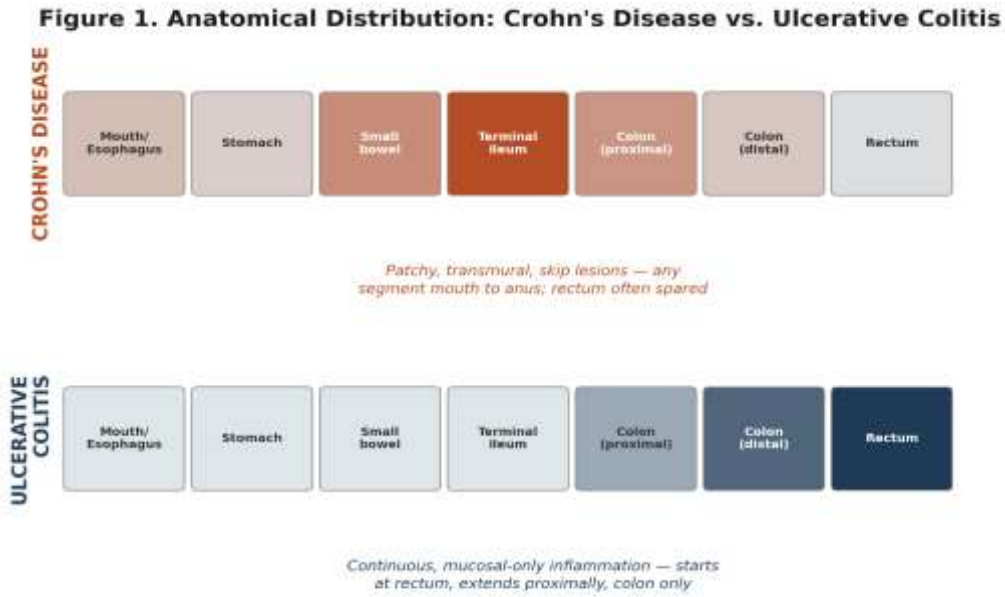


*Figure 1. Crohn's disease produces patchy, transmural, skip-lesion involvement anywhere from mouth to anus, while ulcerative colitis produces continuous, mucosa-limited inflammation confined to the colon, beginning at the rectum.*

**Diagnostic Work-Up and Classification**

Ileocolonoscopy with intubation of the terminal ileum and systematic segmental biopsy of each colonic segment and the terminal ileum, regardless of whether mucosa appears grossly normal or abnormal, is the diagnostic cornerstone for distinguishing the two conditions, since histological involvement can be present even where gross appearance is deceptively normal, and conversely gross appearance alone can be misleading. Endoscopically, Crohn's disease typically shows cobblestoning, deep linear or serpiginous ulcers, and stricturing, while ulcerative colitis shows friable, granular mucosa with diffuse superficial ulceration and loss of the normal vascular pattern, generally without the skip areas or deep ulceration characteristic of Crohn's disease.

Histologically, non-caseating granulomas, when present, are a relatively specific though insensitive finding for Crohn's disease, seen in only a minority of biopsy specimens, alongside transmural lymphoid aggregates; ulcerative colitis instead shows crypt abscesses and crypt architectural distortion with diffuse, continuous mucosal inflammation and no granulomas. Serological markers offer supportive but not individually diagnostic information: anti-Saccharomyces cerevisiae antibodies (ASCA) are more often positive in

Crohn's disease, while perinuclear anti-neutrophil cytoplasmic antibodies (p-ANCA) are more often positive in ulcerative colitis, though neither test is sufficiently sensitive or specific to be used in isolation. When Crohn's disease is suspected, particularly with small-bowel involvement, magnetic resonance or computed tomography enterography is added to assess for disease beyond the reach of the colonoscope and to detect fistulas, abscesses, or strictures not visible endoscopically.

Despite this structured, multi-modal approach, approximately 10 to 15% of patients with isolated colonic inflammatory bowel disease cannot be definitively classified as either Crohn's disease or ulcerative colitis even after complete work-up, and are appropriately designated as having IBD-unclassified (previously termed indeterminate colitis); clinical features that should raise suspicion of this possibility, or of Crohn's disease masquerading as ulcerative colitis, include an active smoking history and rectal sparing in a patient who otherwise meets criteria for ulcerative colitis. This overall diagnostic sequence, from initial clinical suspicion through classification and treatment guidance, is summarized as a recurring clinical cycle in Figure 2.

**Figure 2. The IBD Differential Diagnosis Cycle**

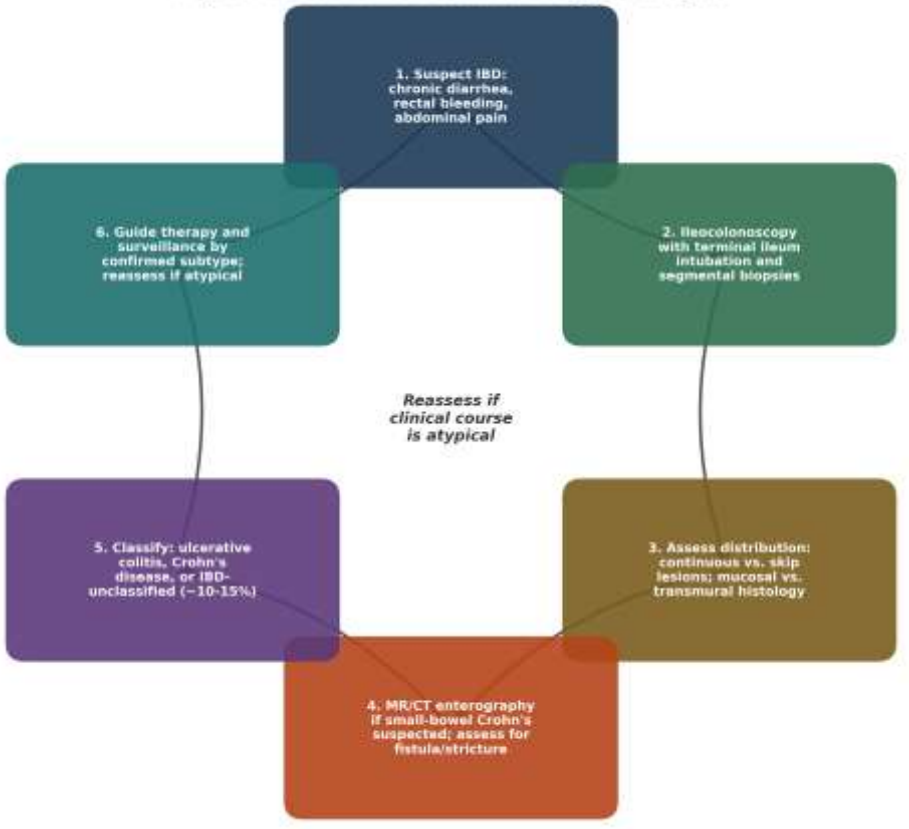


*Figure 2. The recurring IBD differential diagnosis cycle: clinical suspicion, ileocolonoscopy with segmental biopsy, assessment of distribution and histology, small-*

*bowel imaging when indicated, classification (including IBD-unclassified), and subtype-guided treatment with reassessment if the course proves atypical.*

The distinguishing features summarized in this review, spanning anatomical, endoscopic, histological, and serological domains, are consolidated in Table 1 for practical reference.

**Table 1. Key Differentiating Features of Crohn's Disease and Ulcerative Colitis**

| Feature | Crohn's Disease | Ulcerative Colitis |
|---|---|---|
| **Anatomical extent** | Any segment of the GI tract, mouth to anus; terminal ileum most common | Colon and rectum only; never extends into small bowel (except mild "backwash ileitis") |
| **Pattern of involvement** | Discontinuous, "skip lesions" with intervening normal mucosa; rectum often spared | Continuous inflammation beginning at the rectum and extending proximally without skips |
| **Depth of inflammation** | Transmural (full bowel-wall thickness); predisposes to fistula, abscess, stricture | Mucosal and submucosal only; deep transmural injury is not a feature |
| **Endoscopic appearance** | Cobblestoning, deep linear/serpiginous ulcers, strictures | Friable, granular mucosa with diffuse superficial ulceration; loss of vascular pattern |
| **Histology** | Non-caseating granulomas (in a minority); transmural lymphoid aggregates | Crypt abscesses, crypt distortion; diffuse, continuous mucosal inflammation; no granulomas |
| **Typical complications** | Fistulas, perianal disease, abscesses, strictures, small-bowel obstruction | Toxic megacolon, massive hemorrhage, colonic dysplasia/cancer with long-standing disease |
| **Serology (adjunctive)** | ASCA more often positive | p-ANCA more often positive |

| Feature | Crohn's Disease | Ulcerative Colitis |
|---|---|---|
| **Effect of smoking** | Worsens disease course and increases relapse risk | Associated with lower incidence; may modestly improve disease course |

In healthcare systems with constrained access to cross-sectional small-bowel imaging or serological panels — a relevant consideration for gastroenterology practice in Uzbekistan — the practical priority is to ensure that ileocolonoscopy with terminal ileum intubation and systematic segmental biopsy, rather than gross visual impression alone, is performed rigorously in every patient with suspected IBD, since this single step provides the great majority of the information needed for accurate classification even where more advanced imaging or serological testing is not always available.

**Conclusion**

Crohn's disease and ulcerative colitis, though both forms of chronic inflammatory bowel disease with overlapping symptoms, are anatomically and pathologically distinct conditions — one patchy and transmural, capable of affecting any part of the gastrointestinal tract, the other continuous and mucosa-limited, confined to the colon and rectum — and this distinction underlies nearly all of the differences in their complications, surgical indications, and treatment approach.

For clinical practice, this translates into two actionable priorities: performing systematic ileocolonoscopy with terminal ileum intubation and segmental biopsy in every patient with suspected IBD rather than relying on gross endoscopic impression alone, and recognizing that a definitive classification is not always achievable, so that IBD-unclassified is used appropriately rather than forcing an uncertain case into either category. Continued application of these principles, adapted to local resource constraints, holds substantial potential to improve diagnostic accuracy and guide appropriate treatment for patients with inflammatory bowel disease, including within the healthcare system of Uzbekistan.

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