

# The Differential Diagnosis of Acute Colitis: Clues to a Specific Diagnosis



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## KEYWORDS

- Acute colitis • Infectious colitis • Drug-induced colitis • Hemorrhagic colitis
- Pseudomembranous colitis • Ischemic colitis

## Key points

- Colonic biopsy specimens from patients with acute colitis are usually obtained in patients with a prolonged clinical course or who do not respond as expected to treatment.
- Five basic histologic patterns are identified: acute colitis, focal active colitis, pseudomembranous colitis, hemorrhagic colitis, and ischemic colitis.
- These patterns are associated with certain etiologic considerations that influence therapeutic decisions.
- Acute colitis patterns should be differentiated from those associated with chronic inflammatory disorders.

## ABSTRACT

**T**his review describes a systematic approach to the interpretation of colonic biopsy specimens of patients with acute colitis. Five main histologic patterns are discussed: acute colitis, focal active colitis, pseudomembranous colitis, hemorrhagic colitis, and ischemic colitis. For each pattern, the most common etiologic associations and their differential diagnoses are presented. Strategies based on histologic analysis and clinical considerations to differentiate acute from chronic colitides are discussed.

## OVERVIEW

Most patients with acute colitis are diagnosed and treated based on a combination of clinical and

laboratory findings without need for colonoscopy and mucosal biopsy analysis. For the most part, patients with acute colitic symptoms only undergo endoscopic evaluation if they have a severe or atypical clinical presentation, do not improve within an expected timeframe, or fail to respond to treatment. Pathologists are most helpful when they are able to generate a circumscribed differential diagnosis based on interpretation of inflammatory patterns; descriptive diagnoses, such as “acute and chronic inflammation” or “nonspecific inflammation,” do not contribute substantially to patient care. Such designations may be used to describe a variety of circumstances ranging from normal mucosa to inflammatory bowel disease. In this article, a brief review of the normal histology of the colonic mucosa is followed by a discussion of the most frequent histologic patterns of acute colonic injury encountered in biopsy specimens.

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## HISTOLOGY OF THE NORMAL COLONIC MUCOSA

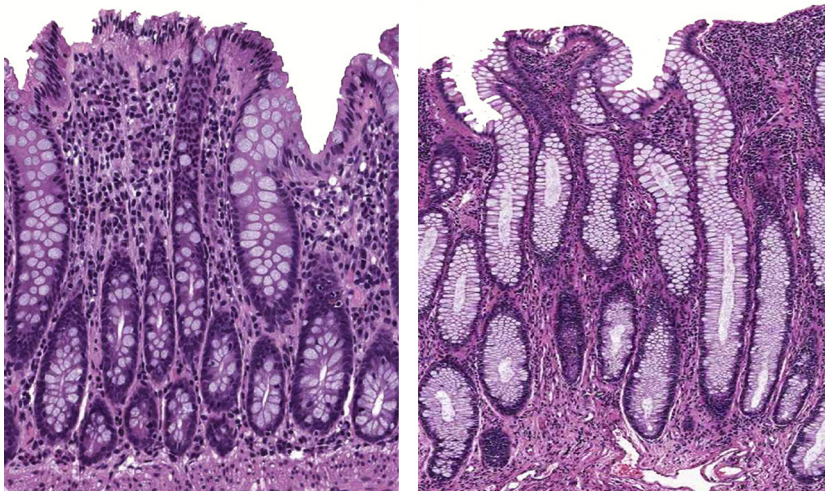
The colonic mucosa comprises epithelial cells, stromal cells, and “inflammatory” cells. Straight tubular crypts composed of absorptive and goblet cells extend perpendicularly from the surface to the muscularis mucosae. These crypts are evenly spaced resembling test tubes in a rack. Crypts of the left colon and rectum contain many more goblet cells than those of the right colon where absorptive cells predominate (**Fig. 1**). When cut tangentially, their even distribution can be compared with a pack of cigarettes opened at the top (**Fig. 2**). Occasional branched crypts may be encountered in an otherwise normal colonic mucosa. Paneth cells are confined to the right colon in adults where their numbers vary from none to a few cells within a single crypt. Because these cells play a role in immune modulation, apoptosis, autophagy, and regeneration, their numbers are probably related to environmental factors. In young children, Paneth cells are normally encountered in the transverse colon and rectum and tend to decrease in number with increasing age.<sup>1</sup> Mitotic figures are confined to the lower third of the crypts. Regenerative crypts may show mitotic figures in the middle or upper thirds of the crypts or more than 2 mitotic figures per crypt in tangentially cut sections.

The lamina propria normally contains plasma cells, eosinophils, lymphocytes, and few histiocytes. The density of these cells and their relative proportions vary considerably among different populations, reflecting environmental and sanitary conditions. The colonic lamina propria from asymptomatic individuals living in underdeveloped

countries tends to be more cellular compared with that of those living in developed nations. The number of eosinophils present in the lamina propria is also highly variable. People living in the northern United States tend to have fewer eosinophils than those living in southern states.<sup>2</sup> Eosinophil numbers throughout the colon show slight seasonal variation, which may reflect allergen exposure.<sup>3</sup> The density of all inflammatory cell types is more pronounced in the right colon compared with the distal colorectum. Plasma cells tend to be more abundant in the luminal third of the mucosa and decrease toward the deep mucosa, although this pattern is obscured in the cecum where a transmucosal distribution of plasma cells is frequently present. Mildly increased mononuclear cells in the lamina propria of the proximal colon should not be taken as evidence of a chronic inflammatory disorder if there are no other features that support this interpretation. The superficial regions of the crypts and luminal epithelium normally contains CD3<sup>+</sup>/CD8<sup>+</sup> intraepithelial lymphocytes. Although variable, their number rarely exceed 5 per 100 colonic epithelial cells.

## HISTOLOGIC PATTERNS ASSOCIATED WITH ACUTE COLITIS

There are no generally accepted classifications for the histologic patterns encountered in colonic biopsy specimens from patients with acute colitis, although 2 basic patterns may be recognized based on mechanisms of disease: inflammatory and ischemic. Infiltration of the mucosa by inflammatory cells characterizes the former pattern, whereas hypoperfusion explains the ischemic pattern. Decreased perfusion may result from



**Fig. 1.** Normal colonic mucosa. Evenly distributed straight crypts extend from the luminal surface to the muscularis mucosae. Goblet cells are less abundant in the right colon (*left panel*) compared with the sigmoid colon and rectum (*right panel*). Inflammatory cells predominate in the luminal third of the lamina propria. (H&E, original magnification  $\times 100$ )

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