Contemporary Morphologic Definition of Backwash Ileitis in Ulcerative Colitis and Features That Distinguish It From Crohn Disease

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Abstract

Terminal ileum (TI) sections from 250 ulcerative colitis (UC) total colectomy specimens resected during 3 periods and endoscopic TI biopsy specimens from 100 contemporary chronic UC and 100 Crohn disease (CD) patients were reviewed. The respective proportions of cases resected during the 3 periods with moderately or markedly active cecal UC were 72%, 34%, and 2% and with moderate or marked backwash ileitis (BWI), 21%, 18%, and 0%. The activity level of BWI correlated with level of cecal UC. In contemporary initial endoscopic TI biopsy specimens, 6% of chronic UC patients had BWI, all with moderately to markedly active cecal chronic UC. In CD cases, 75% had chronic or active enteritis, consisting of patchy lamina propria edema containing mildly active inflammation, crypt disarray, and focally blunted or flattened villi. Mucous gland metaplasia was present in 27% of CD biopsy specimens. BWI should be restricted to active enteritis that involves the ileum in a contiguous pattern from the cecum that has a similar or greater degree of active inflammation. Mild BWI predominantly involves the superficial mucosa in a contiguous pattern. Focal isolated ileal erosions, mucous gland metaplasia, or patchy edema with mild active inflammation are features of CD.

Involvement of the distal ileum in ulcerative colitis (UC) is termed backwash ileitis (BWI). It generally is accepted as a distinct pathologic process in patients with UC.[1-3] However, the morphologic features and clinicopathologic associations of BWI are vague. Many of the pathologic studies on BWI were published before 1965 when medical therapy for UC was less advanced and Crohn colitis was not as well characterized.[4-8] Whether BWI continues to be a feature seen in medically controlled, contemporary UC patients and the extent to which Crohn enteritis morphologically resembles BWI are unknown. An updated and revised definition of BWI in the context of distinguishing BWI from Crohn Disease (CD) in endoscopically procured mucosal biopsy specimens is needed.

To achieve these goals, 2 studies were conducted. We studied archival UC total colectomy specimens to characterize the morphologic features of BWI from a historic perspective. The findings from this review were applied to endoscopically procured, ileal mucosal biopsy specimens from patients with UC and patients with CD.

Materials and Methods

Terminal Ileum Attached to Chronic UC Colectomy Specimens

The William Beaumont Hospital (Royal Oak, MI) surgical pathology computer was searched for total or subtotal (without rectum) colectomy specimens with the diagnosis of UC for the period January, 1, 1960, through December 30, 2004. Specimens were divided into groups based on the year of resection: 1960 through 1979, 1980 through 1997, and

1998 through 2004. The 1997-1998 cut point was used arbitrarily so that at least 50 cases were included in the 1998-2004 case group. We randomly selected 100 colectomy specimens from each of the first 2 periods, and we identified 50 cases in the most recent period. Slides of these cases were retrieved from the department archives.

Cases were reviewed if a sufficient number of representative colon mucosa sections from all regions were available for review, the surgical pathology gross description described the presence or absence of ileal ulcers, and the attached ileal segment was completely or extremely thoroughly submitted for histologic evaluation. Beginning in approximately 1975 and in sporadic cases preceding this date, the entire ileum was submitted for histologic examination in almost all cases with a block key that facilitated histologic reconstruction and composite measurements. In many of the pre-1975 cases with more than 7 cm of nonulcerated ileum attached to the ileum, 1 or 2 longitudinally oriented strips of the entire ileum were submitted for histologic evaluation.

Cases were excluded from the study after review if there was high-grade dysplasia or malignancy in the specimen. Cases in which the status of the ileum could not be almost completely evaluated were excluded. Cases with too few colon slides to reliably establish a diagnosis of UC were excluded. Cases of fulminant colitis, toxic megacolon, and markedly autolyzed specimens with no or minimal residual mucosa and submucosa were excluded; however, cases of markedly active UC with extensive ulceration in which a definite UC diagnosis could be established (see the next paragraph) were retained in the study.

The morphologic features used to establish a diagnosis of definite UC and, therefore, include a specimen in the study were diffuse disease of the large intestine, involvement of the rectum, more proximal colonic disease occurring in continuity with an involved rectum (no gross or histologic skip lesions), no mural sinus tracts, no fissural ulcers, no transmural lymphoid aggregates in an area not deeply ulcerated, and the absence of nonnecrotizing granulomas.[9-18] Terminal ileal involvement (if present), in the context of characterizing BWI while excluding cases of CD, had to be most severe distally and be a diffuse process in continuity with the cecum and a mucosal-based inflammatory process. Features of the terminal ileum (TI) that were used to exclude a case were mural sinuses or tracts, deep fissural ulcers, transmural lymphoid aggregates in the absence of deep ulcerations, neural hyperplasia,[19] thickened (hypertrophic and hyperplastic) muscularis mucosae,[20] and nonnecrotizing granulomas.[21]

The following morphologic features were recorded in each case:

1. Level of colonic UC disease activity, evaluated separately in the rectosigmoid and cecum. Activity was assessed by using the 5-tiered Geboes activity scoring system.[22] Briefly, the system is as follows: minimal (grade 1) UC, any increase in lymphoplasmacytic inflammation in the lamina propria; mildly active (grade 2) UC, granulocytes (neutrophils or eosinophils) confined to the lamina propria; moderately active (grade 3) UC, neutrophils within the epithelium (crypt or surface) without crypt abscesses; markedly active (grade 4) UC, neutrophilic crypt destruction; and severely active (grade 5) UC, erosions or ulcerations.
2. Level of ileal mucosal inflammation. Because of the acknowledged problems associated with distinguishing between normal immune system inflammatory cells and pathologic inflammation and the inhomogeneous nature of ileal histologic activity, components of the D'Haens CD activity scoring system were used to score inflammatory changes.[23] Component factors evaluated separately were lamina propria lymphocytes and plasma cells (scored as normal, moderately increased, or markedly increased), lamina propria neutrophils and eosinophils (scored as normal, moderately increased, or markedly increased), neutrophils within the epithelium (scored as in the surface epithelium, crypts, or forming crypt abscesses), and the presence of granulomas (scored as absent or present). A moderate increase of inflammatory cells was twice the number of cells that normally can be expected in that location, and a marked increase was more than twice the normal number of cells. Activity was scored in the region of greatest inflammation.
3. Presence and length of ileal mucosal ulceration, measured in a proximal (cephalad) direction from the ileocolonic mucosal junction.
4. Presence of patchy lamina propria edema, defined as a well-delineated zone of looser-than-normal areolar lamina propria connective tissue with no to sparse inflammation.
5. Presence of architectural changes, defined as broadened or blunted villi and/or crypt disarray (scored as normal, moderately disturbed, or markedly disturbed).
6. Presence of mucous (pyloric) gland metaplasia.[24,25]

Terminal Ileum Endoscopic Biopsy Specimens

TI biopsy specimens from initial colonoscopy procedures performed from July 1, 1998, through June 30, 2002, for an inflammatory bowel disease (IBD) diagnosis in 100 patients who, over time, were determined to have classic pan-colonic chronic UC were obtained from the surgical pathology files of William Beaumont Hospital. The cases were identified by reviewing the histories of consecutively accessioned specimens from patients with chronic UC undergoing dysplasia surveillance colonoscopy from January 1, 2003, through June 1, 2004. Similarly, the TI biopsy specimens from the initial IBD diagnostic colonoscopy procedure performed from January 1, 1998, through December 30, 2002, from 100

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patents in whom complicated stenosing-type ileal CD subsequently developed were retrieved from the surgical pathology files of William Beaumont Hospital. These cases were identified by reviewing the histories of consecutive patients undergoing surgical resection of the ileal stenosis from January 1, 2002, through June 30, 2004. The cases were reviewed in a blinded manner without knowledge of whether they were from a patient with UC or a patient with CD.

The list of morphologic features for colectomy specimens was used to evaluate endoscopic biopsy specimens. Some features could not be evaluated in small endoscopic biopsy specimens owing to their limited size and scope. Morphologic features that could be evaluated in endoscopic biopsy specimens that were recorded in each case included extent of erosions, number of microscopic foci of active inflammation, and presence of foci composed of active inflammation within a background of lamina propria edema.

Results

Terminal Ileum Attached to Chronic UC Colectomy Resections

The length of distal ileum attached to the 250 colectomy specimens varied through the years of the study. The mean length of ileum was 7.5 cm (range, 3.0-14.0 cm) in the 1965-1979 specimens, 4.5 cm (range, 2.0-8.0 cm) in 1980-1997 specimens, and 3.3 cm (range, 1.2-5.0 cm) in 1998-2004 specimens.

The level of active inflammation in the rectosigmoid region of colectomy specimens decreased across the 3 periods **Table 1**. None of the specimens resected during the 1960-1979 period had quiescent colitis in the rectosigmoid region, whereas 22 (22.0%) of specimens resected during the 1980-1997 period and 10 (20%) of 50 specimens resected during the 1998-2004 period had quiescent colitis in the rectosigmoid region. The proportion of specimens with moderate to marked active chronic UC in the cecum also decreased from 72 (72.0%) of 100 cases resected during the 1960-1979 period to 1 (2%) of 50 cases resected during the 1998-2004 period.

Patterns of Terminal Ileum Injury in Chronic UC Colectomy Resection Specimens

An initial review of the 250 ileal specimens was performed. As a single specimen group, the extent and degree of TI injury ranged from none to marked. A consistent relationship among the level of active inflammation, erosions or ulcers, and length of injured ileum could be noted generally across the specimens as a group. Based on these observations, 4 general, broad categories or grades of increasing ileal injury were established **Table 2**. We classified cases into 1 of 4

Table 1
Chronic Ulcerative Colitis Activity in Total Colectomy Specimens*

	Chronic Ulcerative Colitis Disease Activity					
	Rectum			Cecum		
Period	Quiescent	Mild	Moderate-Marked	Quiescent	Mild	Moderate-Marked
1960-1979 (n = 100)	0 (0.0)	16 (16.0)	84 (84.0)	0 (0.0)	28 (28.0)	72 (72.0)
1980-1997 (n = 100)	22 (22.0)	32 (32.0)	46 (46.0)	20 (20.0)	46 (46.0)	34 (34.0)
1998-2004 (n = 50)	10 (20)	23 (46)	17 (34)	27 (54)	22 (44)	1 (2)

* Data are given as number (percentage).

Table 2
Morphologic Features of Backwash Ileitis Grades

	Backwash Ileitis Grade			
Morphologic Feature	Minimal	Mild	Moderate	Marked
Active inflammation	Few villus tips	Villi and lamina propria	Crypt abscesses	Surface fibrinopurulent debris
Lymphoplasmacytic inflammation	None	Mild in lamina propria	Confluent	Confluent in lamina propria extending into submucosa
Villous blunting	None	Slight	Prominent	Extensive
Erosions or ulcers	None	None	Focal and superficial	Extensive ulceration of distal ileum
Mucosal injury pattern	1-5 villi	≤5 mm; no zonation injury pattern	Approximately 5-2 mm length of mucosal injury; zonation injury pattern appreciable; predominantly intact mucosa with focal erosions in distal ileum	Several centimeters of mucosal injury; zonation injury pattern appreciable; extensive erosions in distal ileal mucosa
Mean length of injured mucosa, mm (range)	Microscopic	3.6 (2.0-5.0)	10.3 (7.0-21.0)	22.4 (10.0-37.0)

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groups based on the general, overall, composite findings of the specimen, rather than a single, unique factor or criterion. This BWI grading system was created for the sole purpose of classifying and grouping data and comparing results in the present study. It has no clinical usefulness, and we did not intend that it be used clinically. The BWI grade was not intended to be a rigidly and strictly applied ordinal variable nor were its grouping criteria exclusionary.

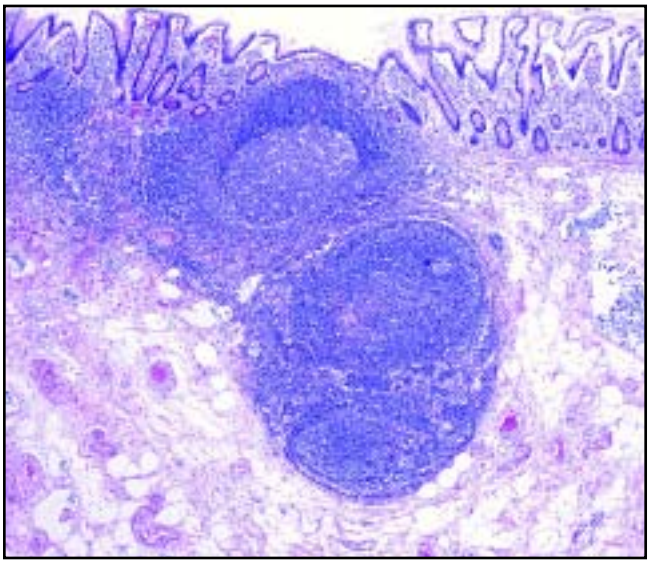

Image 1 Normal terminal ileum from a 1989 quiescent cecal chronic ulcerative colitis resection specimen. Villi are arranged uniformly. Lymphoid follicles overlap but remain discernible (H&E, ×4).

BWI Grades

The grades of BWI used for the present study were as follows:

- Normal mucosa **Image 1**
- Minimally active BWI **Image 2**, central feature of scattered neutrophils in the tips of a small number of villi immediately adjacent to the ileocecal mucosal junction
- Mildly active BWI **Image 3** and **Image 4**, active inflammation present in villi and the lamina propria, involved villi blunted and shorter than noninflamed villi, lymphoplasmacytic inflammation present in the lamina propria between lymphoid follicles, inflammation confined to an approximately 5-mm length of distal TI, and no zonation pattern of the abnormalities was detected
- Moderately active BWI **Image 5**, approximately 5 to 12 mm of distal ileal mucosal injury, including edema and erythema; distal ileal mucosal surface predominantly intact with interspersed focal erosions that were predominantly confined to the mucosa and rarely extended down through the muscularis mucosae; feature distinguishing moderate from marked BWI was the length of ileal mucosa injury and extent of mucosal ulceration in the most actively involved area, with a predominantly intact mucosa containing small erosions characteristic of moderate BWI; zonation pattern of mucosal injury present with the most severely injured mucosa located most distally; in the most severely

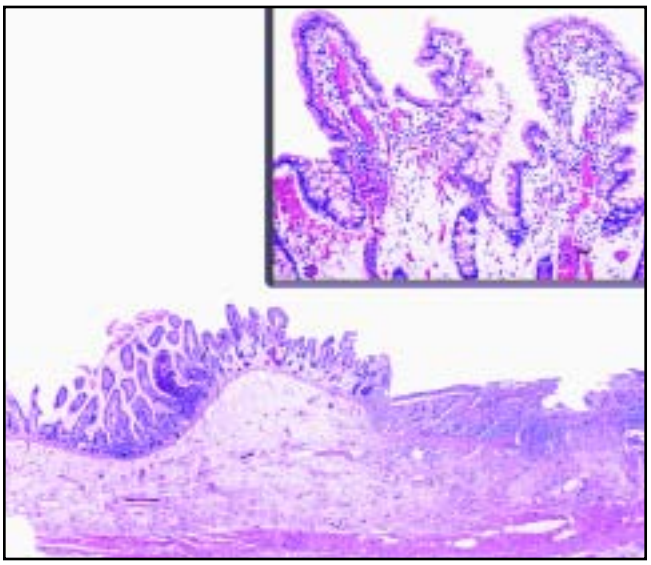

Image 2 Minimal backwash ileitis in a 1972 markedly active cecal chronic ulcerative colitis resection specimen. Active mucosal injury with ulceration stops abruptly at the ileocecal valve (H&E, ×2). Inset, High magnification of most-distal ileal mucosa. There are rare neutrophils in the tips of edematous villi (H&E, ×128).

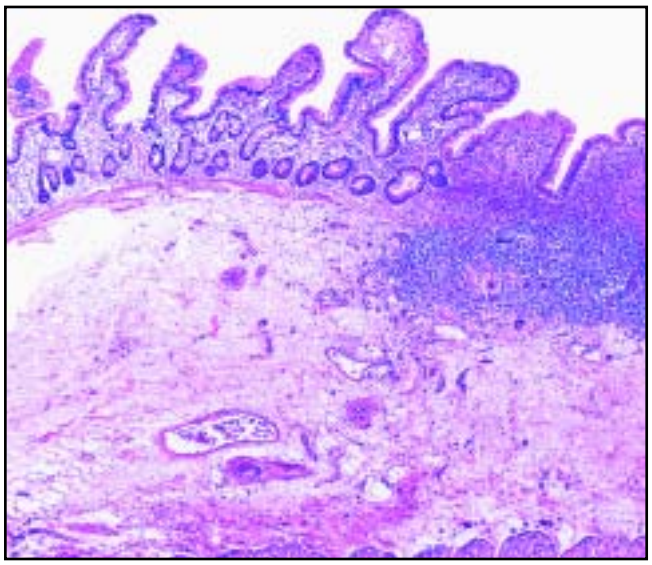

Image 3 Mild backwash ileitis in a 1985 moderately active cecal chronic ulcerative colitis resection specimen. The mucosa of the distal 1.5 cm of ileum is edematous, and villi are slightly wider and flatter than the normal villi of the more proximal ileum (left side of image) (H&E, ×2).

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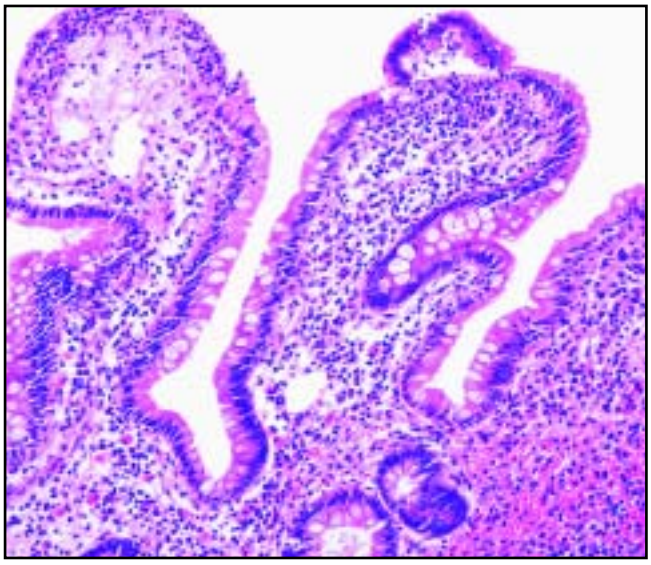

Image 4 Mild backwash ileitis. High magnification of Image 3. Junction of ileocecal mucosa. Most of the active colitis stops abruptly at the transition point between the 2 mucosae. The 2 most distal villi have the greatest degree of injury, including blunting, edema, and neutrophils in the lamina propria and surface epithelium (H&E, ×128).

involved distal mucosa, production of many crypt abscesses by abundant mucosal active inflammation; lamina propria expanded by lymphoplasmacytic inflammation that extended down into the middle to deep regions of the submucosa; villi extensively shorted due to edema and inflammation in the mucosa proximal to the erosions

- Markedly active BWI **Image 6** and **Image 7**, markedly active injury with extensive ulceration and a surface layer of fibrinopurulent debris and usually several centimeters of ileal injury; zonation pattern of injury present with ulceration of the most distal mucosa, moderately active enteritis with numerous crypt abscesses, and an intact surface epithelium proximal to the ulcerated mucosa, which gradually became less active in more proximal mucosa

None of the distal ileal mucosa cases had foci of mucous gland (so-called pyloric gland) metaplasia, regardless of the degree of BWI.

BWI in Specimens From Different Periods

Of 100 cases resected during the 1960-1979 period, 72 (72.0%) had moderately to markedly active cecal chronic UC **Table 3**. Of these 72 cases, 8 (11%) had marked BWI, 13 (18%) had moderate BWI, 21 (29%) had mild BWI, and 18 cases (25%) had minimal BWI. Among the 34 specimens with moderately to markedly active cecal chronic UC resected during the 1980-1997 period, 10 cases (29%) had marked BWI, 8 (24%) had moderate BWI, and 10 (29%) had mild BWI. None of the specimens with mild active cecal chronic UC from the 3 resection periods had moderate or marked BWI.

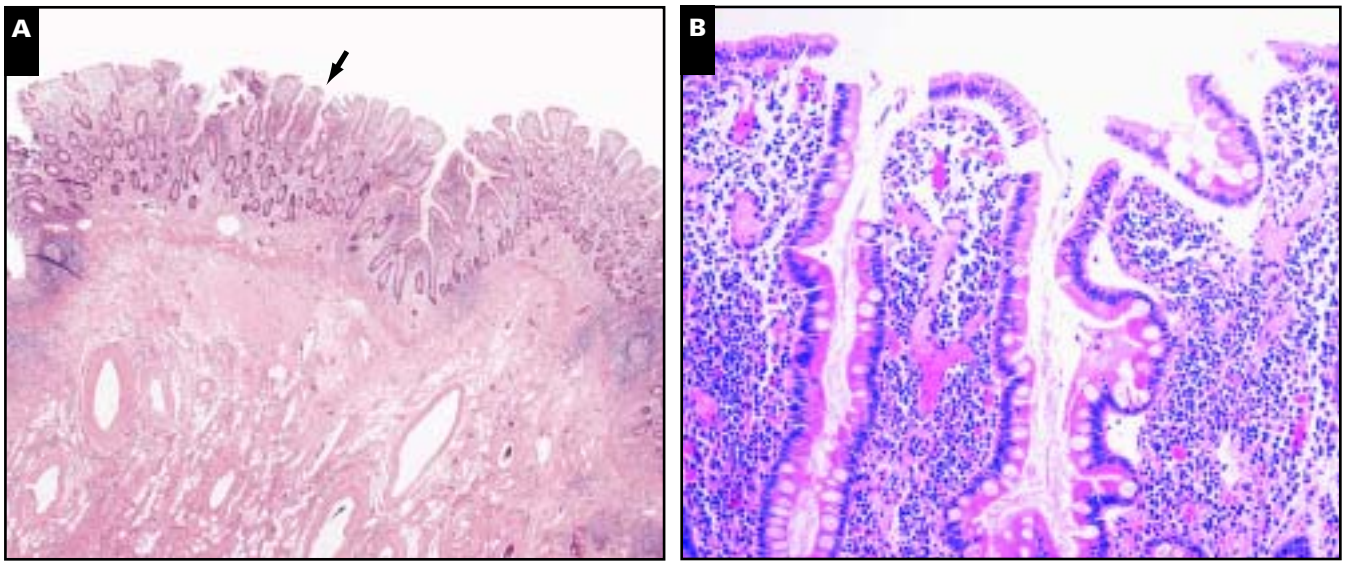

Image 5 **A**, Moderate backwash ileitis in a 1967 markedly active cecal chronic ulcerative colitis resection specimen. Ulcerated cecum is on the left. Normal ileum is on the far right of the image. Backwash ileitis involves the distal 1.5 cm of ileum. The most-distal 2 mm of ileum is ulcerated. Ileum proximal to the ulceration has increased lamina propria lymphoplasmacytic inflammation, and villi are uniformly abnormally wide. Note the zonation effect from abnormal to normal with the most severe injury in the most distal ileum adjacent to the cecum (H&E, ×2). The arrow designates the area shown in **B**. **B**, Villi proximal to ulceration have edema and moderate numbers of neutrophils (H&E, ×128).

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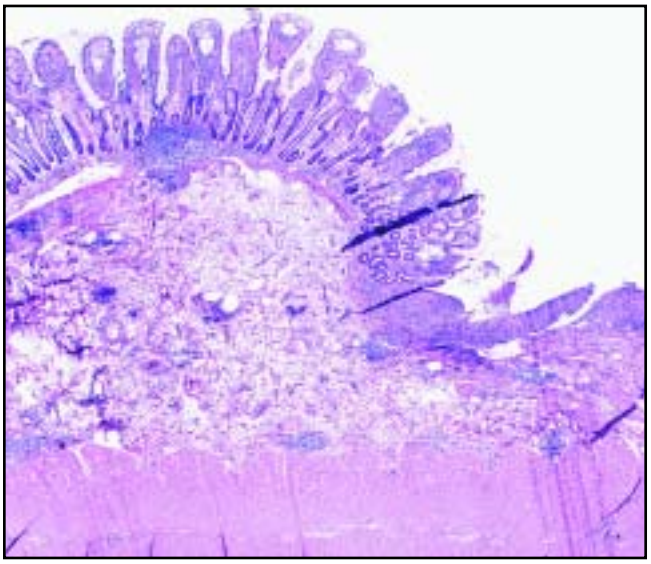

Image 6 Marked backwash ileitis in a 1973 markedly active cecal chronic ulcerative colitis resection specimen. The most distal segment of the ileum is ulcerated. Villi with abnormal inflammation extend for approximately 2 cm proximally. A zonation process can be seen with the most severely involved ileum located distally (H&E, ×2).

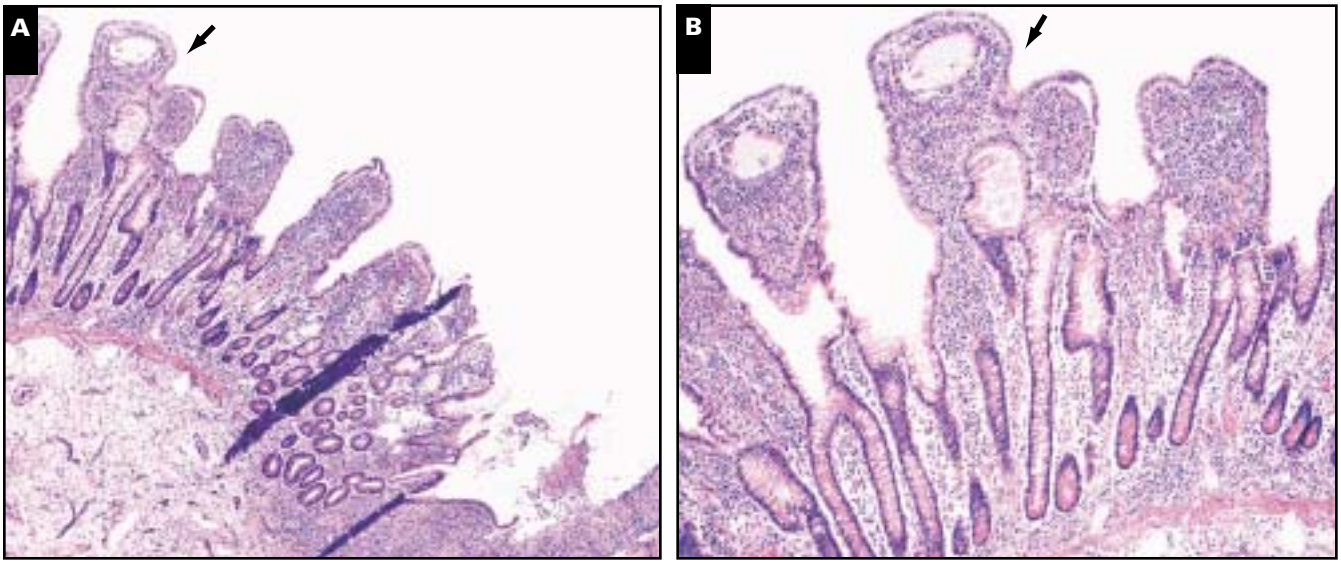

Image 7 **A**, Marked backwash ileitis. Medium magnification of Image 6. Mucosa proximal to the ulcerated region shows uniform injury. Villi are fused and widened secondary to inflammation and edema (H&E, ×128). **B**, Higher magnification of intact ileal mucosa proximal to ileal ulceration. There is uniform expansion of the lamina propria by inflammatory cells. Crypts are arranged uniformly, and there is no mucous gland metaplasia (H&E, ×256).

Table 3
Backwash Ileitis and Cecal Disease Activity by Resection Period*

		Backwash Ileitis Activity Grade				
Cecal Chronic UC Activity	**No. of Cases**	**None**	**Minimal**	**Mild**	**Moderate**	**Marked**
1960-1979 (n = 100)						
Mild	28	14 (50)	12 (43)	2 (7)	0 (0)	0 (0)
Moderate-marked	72	12 (17)	18 (25)	21 (29)	13 (18)	8 (11)
1980-1997 (n = 100)						
Quiescent	20	20 (100)	0 (0)	0 (0)	0 (0)	0 (0)
Mild	46	16 (35)	20 (43)	10 (22)	0 (0)	0 (0)
Moderate-marked	34	2 (6)	4 (12)	10 (29)	8 (24)	10 (29)
1998-2004 (n = 50)						
Quiescent	27	27 (100)	0 (0)	0 (0)	0 (0)	0 (0)
Mild	22	21 (95)	1 (5)	0 (0)	0 (0)	0 (0)
Moderate-marked	1	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)

UC, ulcerative colitis.
* Data are given as number (percentage).

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BWI and Cecal Chronic UC Activity in All Specimens

When combined as a single group of 250 specimens, none of the 47 TI sections with quiescent cecal chronic UC had BWI **Table 4**. Of the 96 specimens with mildly active cecal chronic UC, 45 (47%) had minimal or mild BWI and none had moderate or marked BWI. Of the 107 specimens with moderately to markedly active cecal chronic UC, 39 (36.4%) had moderate or marked BWI, 53 (49.5%) had minimal or mild BWI, and 15 (14.0%) had no BWI.

Terminal Ileum Endoscopic Biopsy Specimens

The mean number of ileal mucosa tissue fragments examined per chronic UC case was 1.4 (range, 1-6 fragments) **Table 5**. The TI was normal in 94 (94.0%) of 100 chronic UC cases. Six chronic UC cases (6.0%) had BWI. The BWI was minimal in 3 cases. In the other 3 cases, more substantial changes involved the majority of 1 tissue fragment including active inflammation in villus tips (mild BWI) **Image 8**. The injury pattern was greatest on villus tips and was uniform across the breadth of the tissue fragment. None had patchy lamina propria edema, focal crypt disarray, or mucous gland metaplasia. The 6 BWI chronic UC cases had moderately or markedly active cecal chronic UC.

The mean number of ileal mucosa tissue fragments examined per CD case was 3.5 (range, 2-12 fragments). Of the 100 CD TI cases, 75 (75.0%) had chronic enteritis with focal, variable changes **Image 9** and **Image 10**. Chronic enteritis changes consisted of patchy lamina propria edema, crypt disarray, focally blunted or flattened villi, and confluent lymphoplasmacytic inflammation that did not form follicles. Of these 75 cases, 42 had minimal or mild activity, consisting of sparse to scattered neutrophils within foci of edema, most often in the lamina propria and occasionally within villi. Mucous gland metaplasia was present in 27 cases (27.0%) **Image 11** and **Image 12**. The TI was normal in 25 CD cases.

Discussion

Distal ileal inflammation and injury in UC was first recognized and given the name BWI during the latter half of the 19th century. A large number of studies on BWI were published during the last century, and it is generally considered to be a distinct pathologic entity.[4-8,26-29] Although BWI is a conceptually clear-cut lesion, in application, many of the morphologic

Table 4
Backwash Ileitis and Cecal Disease Activity for All Periods*

		Backwash Ileitis Activity Grade				
Cecal Chronic UC Activity	No. of Cases	None	Minimal	Mild	Moderate	Marked
Quiescent	47	47 (100)	0 (0)	0 (0)	0 (0)	0 (0)
Mild	96	51 (53)	33 (34)	12 (13)	0 (0)	0 (0)
Moderate-marked	107	15 (14.0)	22 (20.6)	31 (29.0)	21 (19.6)	18 (16.8)
Total	250	113 (45.2)	55 (22.0)	43 (17.2)	21 (8.4)	18 (7.2)

UC, ulcerative colitis.
* Data are given as number (percentage).

Table 5
Ileitis and Cecal Disease Activity in Endoscopic Biopsy Specimens From Contemporary Patients With Inflammatory Bowel Disease*

		Ileitis Activity Level				
Cecal Colitis Activity Level	No. of Cases	None	Minimal	Mild	Moderate	Marked
Ulcerative colitis						
Quiescent	23	23 (100)	0 (0)	0 (0)	0 (0)	0 (0)
Mild	28	28 (100)	0 (0)	0 (0)	0 (0)	0 (0)
Moderate	43	41 (95)	2 (5)	0 (0)	0 (0)	0 (0)
Marked	6	2 (33)	1 (17)	3 (50)	0 (0)	0 (0)
Total	100	94 (94.0)	3 (3.0)	3 (3.0)	0 (0.0)	0 (0.0)
Crohn disease						
Quiescent	42	23 (55)	8 (19)	9 (21)	2 (5)	0 (0)
Mild	34	2 (6)	6 (18)	12 (35)	10 (29)	4 (12)
Moderate	21	0 (0)	0 (0)	7 (33)	8 (38)	6 (29)
Marked	3	0 (0)	0 (0)	0 (0)	1 (33)	2 (67)
Total	100	25 (25.0)	14 (14.0)	28 (28.0)	21 (21.0)	12 (12.0)

* Data are given as number (percentage).

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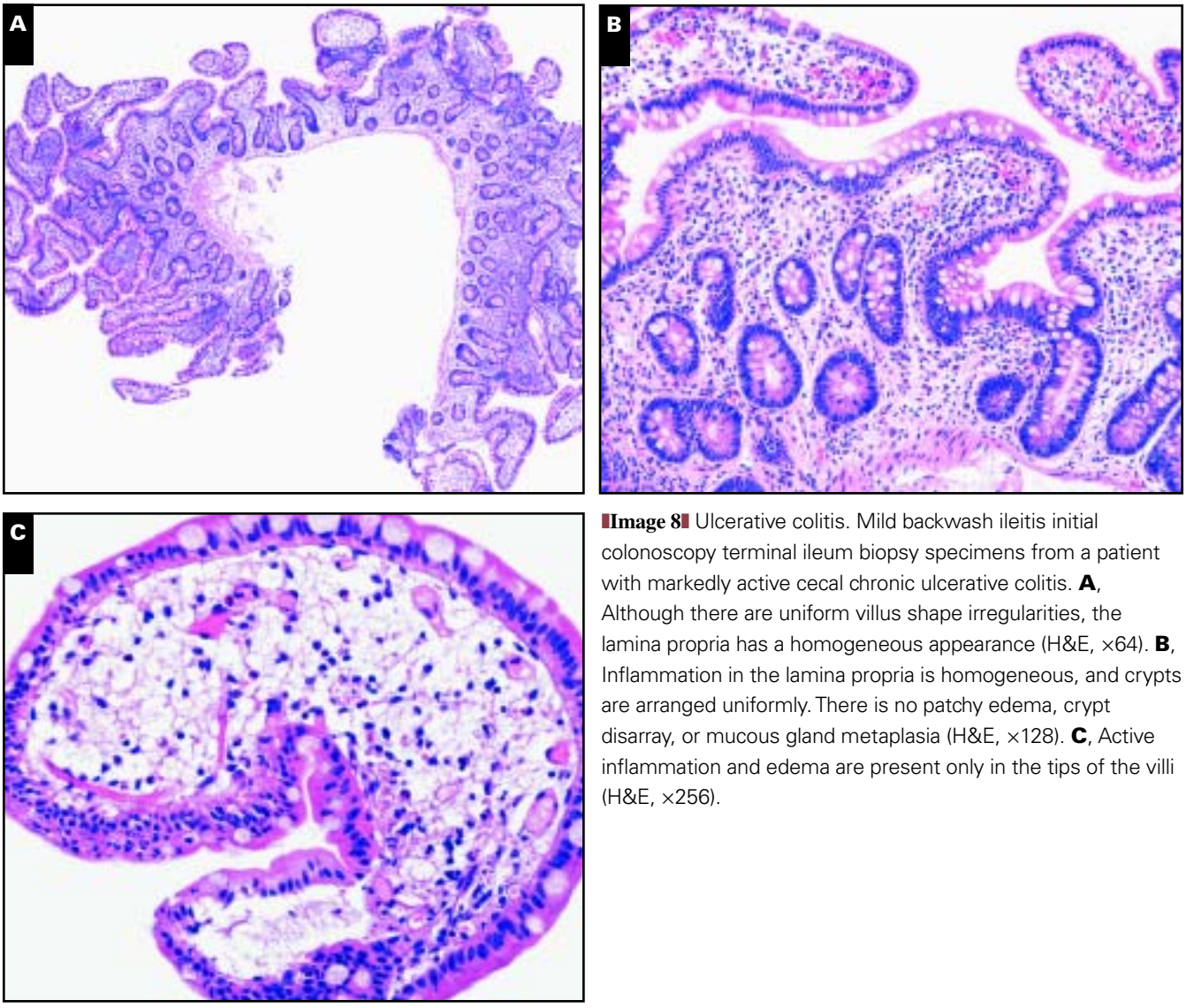

Image 8 Ulcerative colitis. Mild backwash ileitis initial colonoscopy terminal ileum biopsy specimens from a patient with markedly active cecal chronic ulcerative colitis. **A**, Although there are uniform villus shape irregularities, the lamina propria has a homogeneous appearance (H&E, ×64). **B**, Inflammation in the lamina propria is homogeneous, and crypts are arranged uniformly. There is no patchy edema, crypt disarray, or mucous gland metaplasia (H&E, ×128). **C**, Active inflammation and edema are present only in the tips of the villi (H&E, ×256).

features ascribed to BWI are shared by CD. Approximately 5% to 33% of the cases purported to be chronic UC with BWI and used by authors to characterize the morphologic features of BWI were CD.[4,7,8,30] This is not surprising; colonic CD was not a recognized entity before 1960.[26,31-33] In addition, the 2 diseases can have identical clinical manifestations, and they share many morphologic features.[9,16,34,35]

Of the 250 cases in our study, 82 (32.8%) had mildly to markedly active BWI. The presence of BWI correlated with the colitis activity level in the cecum. Of 107 moderately to markedly active cecal chronic UC cases, 70 (65.4%) had mild to marked BWI compared with 12 (13%) of 96 mildly active cecal UC cases and none of the quiescent cecal UC cases. The activity level of the BWI also correlated with the colitis activity level in the cecum. In all BWI cases, the level of active inflammation and degree of mucosal injury or ulceration was similar or less in the distal ileum than in the immediately proximal cecum. In addition, BWI in all cases involved the ileum as a contiguous, uniform process in direct continuity with the colitis in the cecum. We did not encounter a case of BWI that involved the distal ileum in a patchy, discontinuous manner with intervening regions of normal ileal mucosa or in which the activity and injury level in the ileum was greater than in the cecum. These findings have been reported consistently in studies of BWI from all periods of study and are the most reproducible features of BWI among authors throughout the decades.[4,5,7,8,29,36-38]

We noted that the level of active cecal UC in colectomy specimens decreased across the 4.5 decades of the study. Of the 100 cases resected during the 1960-1979 period, only 28.0% had mildly active or quiescent cecal chronic UC, whereas 22 (44%) of 50 cases resected during the 1998-2004 period had mildly active cecal chronic UC and 27 (54%) had quiescent colitis. Concurrent with the decrease in cecal colitis activity over time, the incidence of BWI also decreased such

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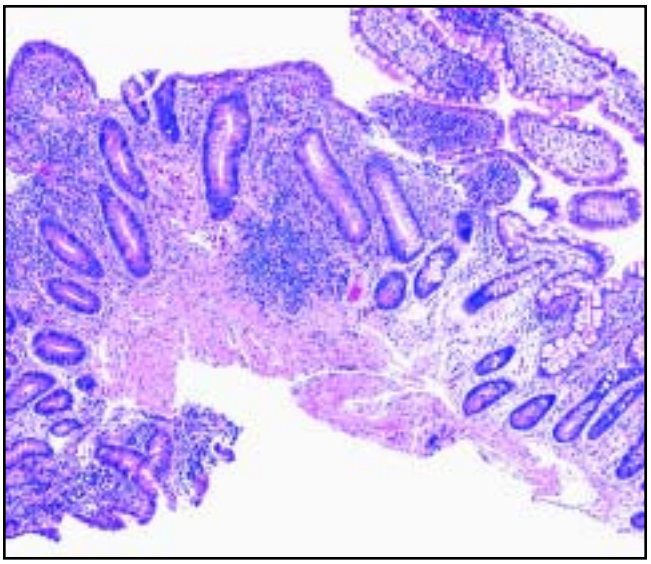

Image 9 Crohn enteritis. Initial colonoscopy terminal ileum biopsy specimens. There is patchy lamina propria edema, crypt disarray, and focal villous blunting. The focality and lamina propria–centered process distinguishes Crohn disease from confluent villus-predominant injury with minimal lamina propria edema and crypt disarray of backwash ileitis (H&E, ×32).

that only 1 case (2%) of the 50 recently resected colon specimens had BWI. It is important to point out that this incidence may not reflect the overall incidence of BWI in contemporary chronic UC patients. We excluded cases of markedly active colitis with luminal dilation and transmural ischemia from the study. The incidence of BWI reported by authors has decreased over time. Most authors from the early part of the 20th century reported the incidence of BWI as 20% to 35%,[5,6,8,28,39-41] whereas the incidence in contemporary patients is approximately 5% to 10%.[29,36,42] Together, these results suggest that BWI is uncommon in contemporary patients with inactive or mildly active chronic UC.

The decreasing prevalence of BWI is most likely related to UC, which as a disease entity has not been static. Across the decades, advances in radiologic, endoscopic, and medical therapies have changed the clinical face of UC. Whereas patients with moderate or severe pan-UC could be offered only a total colectomy in decades past, the majority now are treated medically and often keep their colons.[43-51]

Improved maintenance therapy has reduced the relapse rate and the severity of colitis flares.[52,53] Other authors have noted the impact of improved medical therapy on the morphologic features of UC.[54,55] The resultant effect can be seen in the level of colitis activity in specimens resected during the 45 years represented by the present study. The degree of active colitis decreased in the rectum and cecum over time; however, the magnitude of the decrease was substantially greater in the cecum than the rectum. In the rectum, the proportion of cases with moderately or markedly active chronic UC had the greatest decrease between 1960-1979 and 1980-1997 intervals (from 84.0% to 46.0% of specimens). In the cecum, the proportion of cases with moderately or markedly active chronic UC also decreased substantially across all 3 periods such that only 2% of contemporary resection specimens had markedly active cecal colitis.

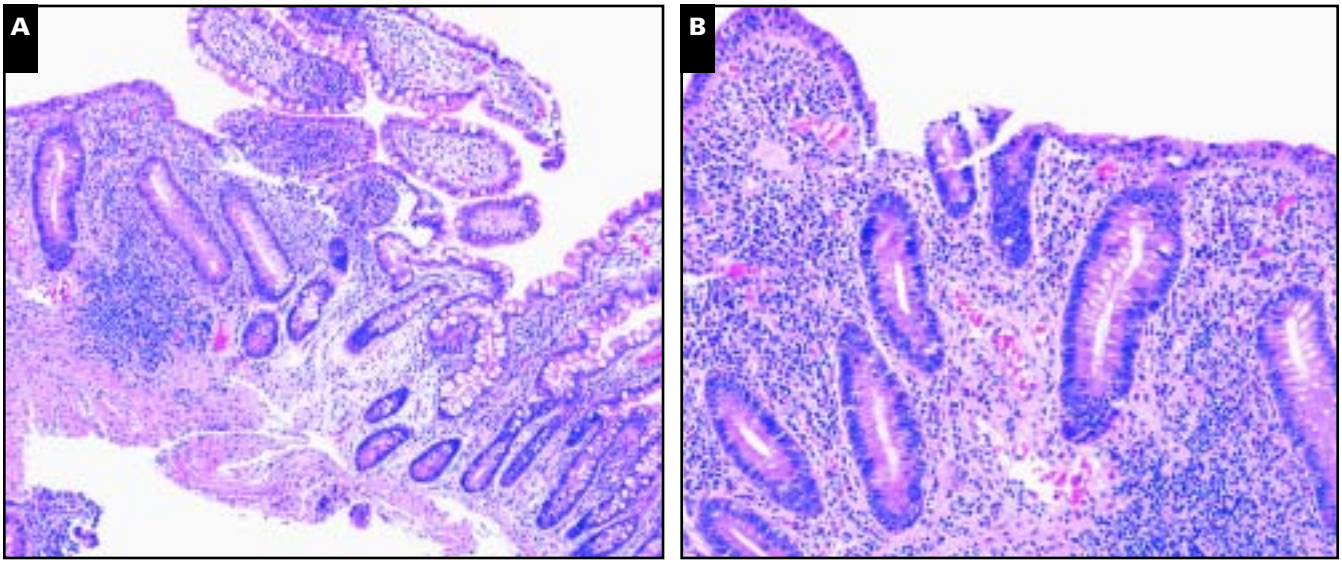

Image 10 Crohn enteritis. Higher magnifications of Image 9. **A**, Crypts to the left of the focal lamina propria edema are disarrayed, whereas those to the immediate right are arranged uniformly (H&E, ×64). **B**, Flattened surface lined by regenerative epithelium with active inflammation adjacent to lymphoid aggregate suggests this focus is a recently healed aphthoid erosion (H&E, ×128).

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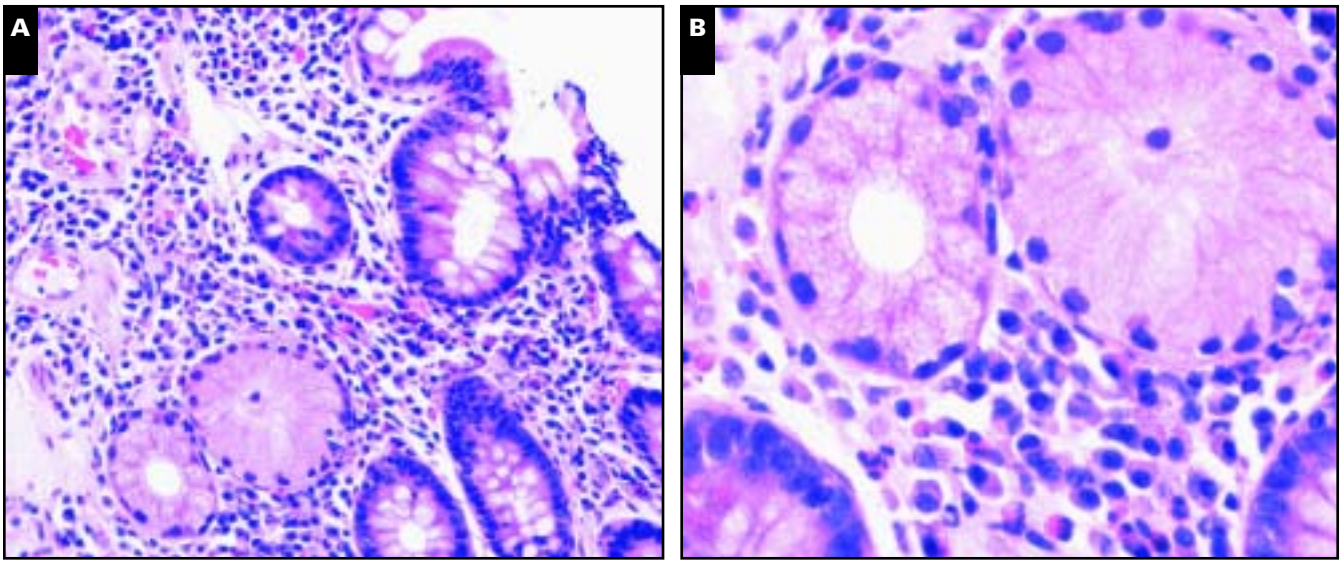

Image 11 Crohn enteritis. Initial colonoscopy terminal ileum biopsy specimens. **A**, Mucous gland metaplasia is present in the lower half of the lamina propria. This gland stands out from the normal ileal crypts that surround it (H&E, ×128). **B**, Columnar mucin cells, high magnification (H&E, ×256).

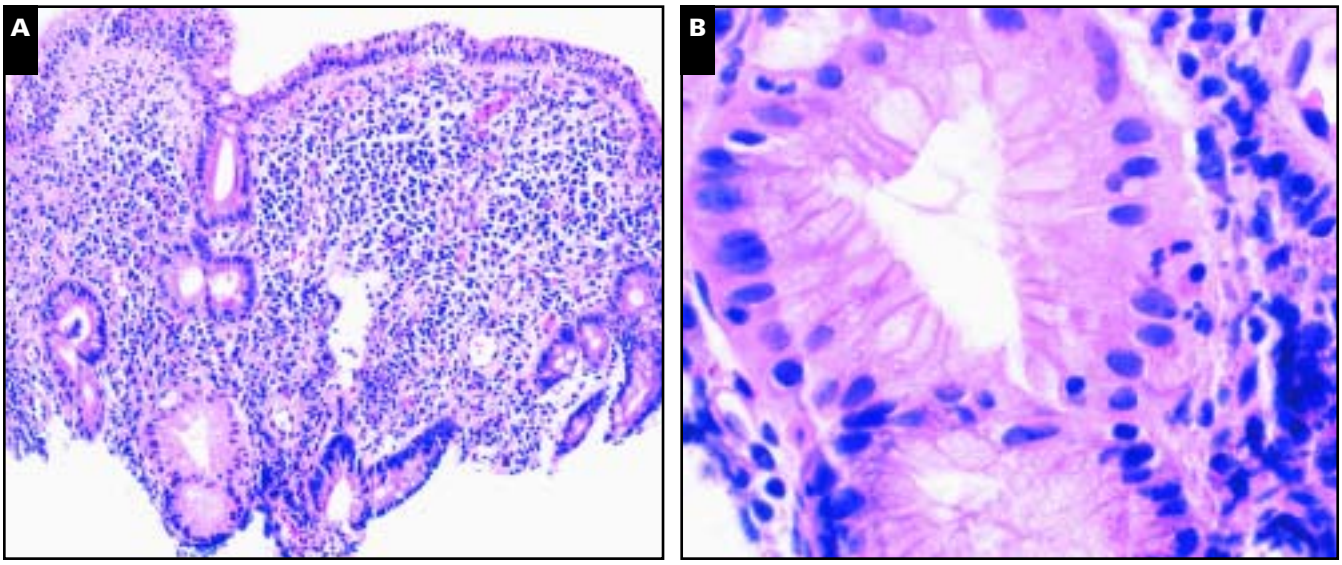

Image 12 Crohn enteritis. Initial colonoscopy terminal ileum biopsy specimens. **A**, Single gland of mucous gland metaplasia in the deep lamina propria. A metaplastic single gland was typical in endoscopic ileal biopsy specimens (H&E, ×128). **B**, Columnar mucin cells, high magnification (H&E, ×256).

In our opinion, the low incidence of BWI in contemporary resection specimens is a reflection of the low proportion of cases with moderately or markedly active chronic UC in the cecum. Most of the active colitis in contemporary patients with chronic UC who undergo colectomy for secondary complications of long-term immunosuppressive therapy or chronic unremitting pancolitis is located in the distal colon and rectum.

Contemporary TI endoscopic biopsy specimens from patients with chronic UC showed a similar range of alterations as distal ileal sections from colectomy specimens resected during the most recent period. Of 100 cases, 6 (6.0%) had minimally or mildly active BWI in association with moderately or markedly active cecal chronic UC. In contrast, 75 of 100 CD TI cases had chronic enteritis, of which 42 had had minimal or mild patchy activity consisting predominantly of patchy lamina propria edema, focal villous flattening, focal crypt disarray, and sparse neutrophils centered in or around areas of patchy edema. Of the 100 CD TI biopsy specimens, 27 (27.0%) had mucous (pyloric) gland metaplasia, which is similar to the 22% incidence reported

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by other authors.[24] Mucous gland metaplasia was seen only in TI biopsy specimens from CD cases.

Contemporary BWI Definition

Most authors agree that BWI has a similar morphologic pattern of mucosal inflammation and injury to UC and does not have the features typical of CD. Beyond these points, there is no agreement on the morphologic definition of BWI and the features that distinguish it from CD or reclassify the IBD as indeterminate colitis.[1-3,11,17,29,30,37,38,56-60]

Features that favor a diagnosis of CD rather than chronic UC with BWI, in our opinion, are an extensive length of involved small bowel, involvement of the jejunum, proximally located regions of active ileitis separated by skip regions of uninvolved cecum or distal ileum, greater inflammatory activity and mucosal injury in the ileum than the cecum, transmural ileal inflammation with granulomas and neural hyperplasia, and mucous gland (so-called pyloric gland) metaplasia of the ileal mucosa.

In endoscopic biopsy specimens, features that suggest a diagnosis of CD include mucous gland metaplasia or the constellation of focal lamina propria edema with crypt disarray and no to mild active inflammation that involves a small region of a tissue fragment surrounded by normal small bowel mucosa. Mild BWI consists of active inflammation and edema that is located predominantly in villus tips without significant lamina propria focal edema or crypt disarray. In BWI, mild ileal mucosal injury is found in association with moderate or markedly active cecal colitis. Focal ileal erosions with mild active inflammation seen in association with mildly active cecal colitis should be considered CD.

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