45
IBD Diagnosis and Evaluation

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Key Concepts

- Familiarity with modes of clinical presentation of ulcerative colitis and Crohn's disease allows the clinician to promptly select the most efficient combination of tests.
- Knowledge of histologic findings of ulcerative colitis and Crohn's disease facilitates discussion with other physicians of the care team and tailors specific medical and surgical therapies.
- Serologic tests such as ASCA, pANCA, and fecal markers such as calprotectin are increasingly becoming utilized for diagnosis and treatment effectiveness monitoring.
- High definition images, chromoendoscopy, confocal laser endomicroscopy, and double balloon enteroscopy add to the ability to diagnose and treat ulcerative colitis and Crohn's.
- Capsule endoscopy, computerized tomography and computerized tomography enterography, magnetic resonance imaging, and magnetic resonance enterography provide previously unimagined ability to visualize disease and are revolutionizing the care of the IBD patient.

Inflammatory Bowel Disease: Diagnosis and Evaluation

Historical Context

The purpose of this chapter is to describe modalities and points of information that will aid the surgeon in the diagnosis and evaluation of the inflammatory bowel diseases.

Crohn's disease and ulcerative colitis are collectively referred to as inflammatory bowel diseases. Inflammation plays a significant role in each entity. Though largely different in the distribution of disease and the manner in which inflammation affects the gastrointestinal tract, occasionally the diseases overlap both in behavior and in their responses to similar treatments.

The consideration of ulcerative colitis and Crohn's disease together as inflammatory bowel diseases is beautifully described in a historical review in the Mt. Sinai Journal of Medicine, "Although clinical descriptions of diarrhea with or without blood go back thousands of years, clear distinctions between enteritis and ulcerative colitis were possible only in the nineteenth century." [1] The term "ulcerative colitis" was mentioned in 1888 by Dr. Hale-White in his paper, "On simple ulcerative colitis and other rare incidental ulcers" [2]. As described by Dr. Lockhart Mummery in 1905, the introduction of the electric sigmoidoscope made it possible to make proper diagnosis of ulcerative colitis and distinguish it from infective dysentery, membranous mucous or catarrhal colitis, and nervous diarrhea [3]. The entity now known as Crohn's disease has a politicized origin. Drs. Ginzburg and Oppenheimer "in conjunction with Dr. Burrill B. Crohn" presented a definitive paper, "Non-specific Granulomata of the Intestine," on May 2, 1932, to the American Gastro-Enterological Association and the paper "Regional Ileitis: A Pathologic and Chronic Entity," under the authorship of Crohn, Ginzburg, and Oppenheimer," was published later that year [4].

Ulcerative Colitis

The classic presentation of ulcerative colitis is the new passage of bloody diarrhea. The work-up must include a careful history. The importance of rapidity of onset, fecal consistency, frequency of defecation, continence, and exposure to infectious agents, weight loss, other concurrent associated symptoms, and family history are all important and may hint at diagnosis. The goal of investigation is to make a specific, prompt diagnosis to facilitate early treatment. Past medical history is always crucial. Patients with prior immunosuppression, foreign travel, or antibiotic use may be more likely to have an infectious colitis and prior perianal infection may suggest Crohn's disease. Physical exam is important to evaluate signs of toxicity that might mandate prompt surgical

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TABLE 45-1. Extra-intestinal manifestations of ulcerative colitis [6]

Site	Manifestation	% of UC patients
Skin	Erythema nodosum	3
	Pyoderma gangrenosum	1.4–5
	Aphthous stomatitis	4
Hepatopancreatobiliary	Primary sclerosing cholangitis	5
	Cholangiocarcinoma	Rare
	Primary biliary cirrhosis	Rare
	Autoimmune hepatitis	Rare
	Portal vein thrombosis	Rare
	Pancreatitis	Rare
Musculoskeletal	Peripheral arthritis	20–40
	Axial	5
	Metabolic bone disorders	2–40
	Myopathy	Rare
Ocular	Episcleritis	Rare
	Uveitis	Rare
	Scleritis	Rare
	Optic neuritis	Rare
Hematologic	Anemia	8–73
Vascular	Venous thromboembolism	Rare
Genitourinary	Urolithiasis	Rare
Pulmonary	Bronchiolitis	Rare
Cardiac	Pericarditis	Rare

evaluation and treatment. Evaluation of vital signs is critical looking for tachycardia specifically. Careful abdominal examination and rectal exam must be performed. External anal examination should be performed evaluating signs of anal Crohn's disease (waxy thickened skin tags, fistulae). Rectal tone should be evaluated and documented. The nature of the anus should receive focus. Is there any sign of anal structuring or fibrosis, or is the musculature supple? Is there a mass? The contents of the rectal vault should be noted for stool consistency and the nature of the bleeding.

Infectious colitides that mimic ulcerative colitis must be evaluated via stool culture. Shigella, Salmonella, Yersinia, Clostridia *difficile*, and Cytomegalovirus must be specifically queried (see Chap. 52 for further details about infectious colitides).

The colon must be evaluated by colonoscopy. The extent of disease and characteristics of the mucosa are critical. Classically, ulcerative colitis begins in the distal rectum and extends proximally. The inflammation progresses in a confluent manner and affects only the mucosa, without fissuring, or skip areas. An activity index for ulcerative colitis is seen in Table 45-1 [5]. Extra-intestinal manifestations can be associated with both ulcerative colitis and Crohn's disease (Table 45-2) [6].

TABLE 45-2. A simple clinical colitis activity index. Scoring system for the Powell-Tuck Index [5]

Symptoms and signs		Score
Symptoms		
Bowel frequency	3–6	1
	>6	2
Stool consistency	Formed	0
	Semi-formed	1
	Liquid	2
Abdominal pain	Before/after bowel motions	1
	Prolonged	2
	Anorexia	1
	Nausea/vomiting	1
General health	Normal	0
	Slightly impaired	1
	Activities restricted	2
	Unable to work	3
Extracolonic manifestations	One/mild	1
	More than one/severe	2
Signs		
Abdominal tenderness	Mild	1
	Marked	2
	Rebound	3
Body temperature (°C)	<37.1	0
	37.1–38	1
	>38	2
Blood in stool	Trace	1
	More than trace	2
Sigmoidoscopy	Non-hemorrhagic	0
	Friable	1
	Spontaneous bleed	2

Crohn's Disease

Crohn's disease can affect anywhere in the digestive tract from the mouth to the anus and the inflammatory process of Crohn's involves the full thickness of the bowel wall.

TABLE 45-3. Macroscopic features used for the diagnosis of IBD [13]

	Ulcerative colitis	Crohn's disease
Localization GI tract	Especially colon and rectum	Whole GI tract
Ileum	Not except in backwash ileitis	Often involved
Colon	Left > right	Right > left
Rectum	Commonly involved	Typically spared
Distribution GI tract	Diffuse (continuous)	Segmental (discontinuous)
Ulcers	Superficial ulcers	Aphthoid ulcers, confluent deep linear ulcers
Pseudopolyps	Common	Uncommon
Skip lesions	Absent	Present
Cobblestone pattern	Absent	Present
Deep fissures	Absent except in fulminant colitis	Present
Fistulae	Absent except in fulminant colitis	Present
Mucosal atrophy	Marked	Minimal
Thickness of the wall	Normal	Increased
Fat wrapping	Absent	Present
Strictures	Uncommon	Present

These properties contribute to the clinical behavior of the disease and the varied manners of presentation.

The most common site of Crohn's disease is an ileocolic distribution though anal, intestinal, or colonic disease alone are also regularly seen. As Crohn's disease involves the full thickness of the bowel wall, stricture and obstruction, fistula formation, and abscess formation are important sequelae that might result in presenting symptoms, point to diagnosis, and might mandate intervention. Discontinuous skip areas of involvement are common and a clear differentiating behavior from ulcerative colitis.

The work-up of Crohn's disease begins similarly to ulcerative colitis. History and physical exam provide evidence of the diagnosis.

IBD Histology

A basic knowledge of the histological features in inflammatory bowel disease is essential for the practicing colorectal surgeon. The combination of clinical disease activity, endoscopic findings, and histology generates accurate diagnosis. Communication with an experienced IBD pathologist is vital for making correct treatment decisions in many situations.

Ulcerative Colitis

The classic macroscopic finding in ulcerative colitis (UC) is contiguous mucosal inflammation extending from the rectum proximally for a variable distance in the colon. Other portions of the gastrointestinal tract are not involved. Macroscopic features of UC are shown in Table 45-3. Clinicians should be aware of certain instances where macroscopic inflammation in UC may not be in a continuous pattern. These situations are often confused with Crohn's disease. The cecal cap or patch is an isolated area of inflammation surrounding the appendix [7, 8]. Backwash ileitis is contiguous ileal inflammation in UC from reflux through the ileocecal valve. It is correlated with severity of cecal inflammation. The incidence of backwash ileitis is decreasing, likely due to improved medical management and reductions in severe right-sided colitis [9]. Patchy or noncontiguous ileal involvement should raise suspicion for Crohn's disease. Rectal mucosal sparing is often thought to result from enema topical therapy. Among medically treated UC patients, both oral and per rectum, 33–44% have been shown to have some patchy distribution of inflammation [10].

The hallmark of microscopic ulcerative colitis is widespread crypt distortion in a continuous pattern of inflammation (Figure 45-1). The severity of inflammation is worse distally in the colon. It is mucosal limited, with occasional extension into the superficial submucosa. In situations of fulminant UC, ulcer penetration to the muscularis propria with serositis can occur, making it difficult to discriminate from Crohn's disease. Crypt abscesses occur more frequently in UC (41%) than in Crohn's disease (19%) [11]. Mucin depletion is much more common in UC than in Crohn's [12]. Basal plasmacytosis is an early feature of UC and can be used to help differentiate it from infectious colitis [13].

Crohn's Disease

Crohn's disease (CD) can affect any portion of the gastrointestinal tract. Mostly commonly the ileocolon is involved. "Creeping fat" at the mesenteric edge of the bowel is due to transmural inflammation and is strongly correlated with Crohn's. "Creeping fat" is nonspecific and is found in other inflammatory conditions, including diverticular disease [14]. Aphthous ulcers are one of the early gross mucosal findings in Crohn's. Ulcers are often surrounded by edematous, but otherwise normal tissues. Coalescence and spread of the ulcers leads to the classic cobblestoned mucosal appearance (Figure 45-2). Inflammatory pseudopolyps caused by inflammation and

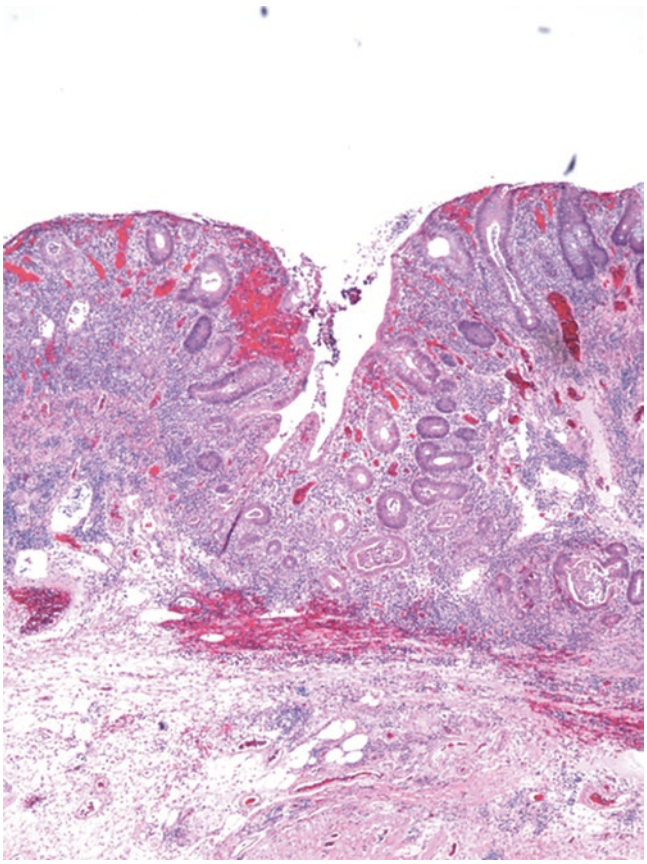

FIGURE 45-1. Low-power view of ulcerative colitis showing inflammatory infiltrate confined to the mucosa.

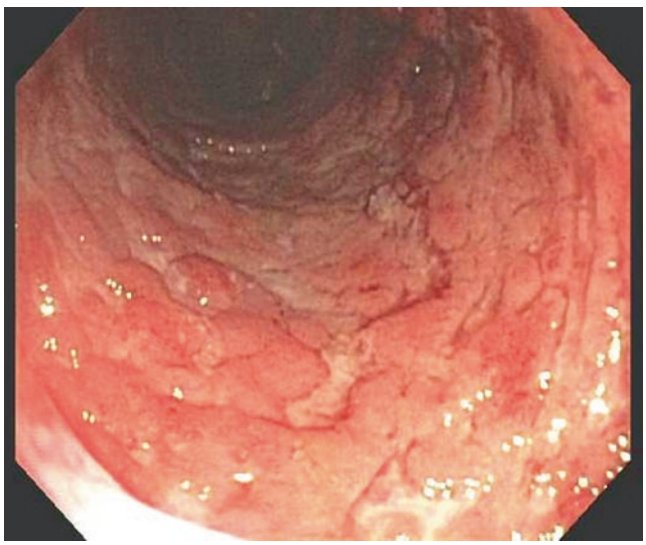

FIGURE 45-2. Crohn's disease with cobblestone appearance of the mucosa.

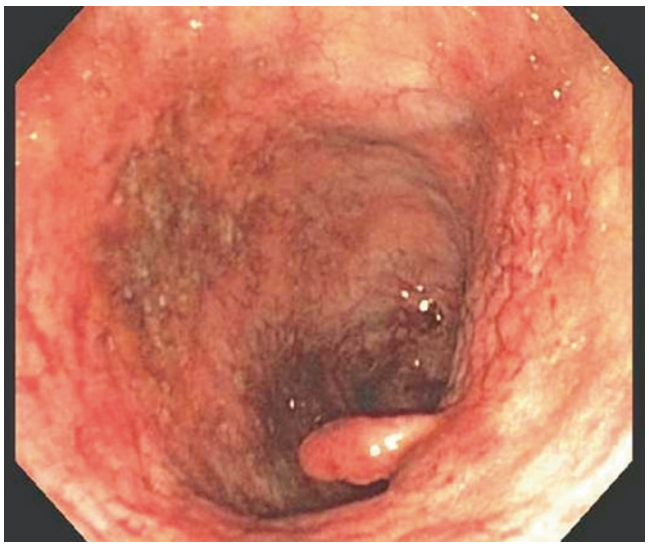

FIGURE 45-3. Pseudopolyp in Crohn's disease.

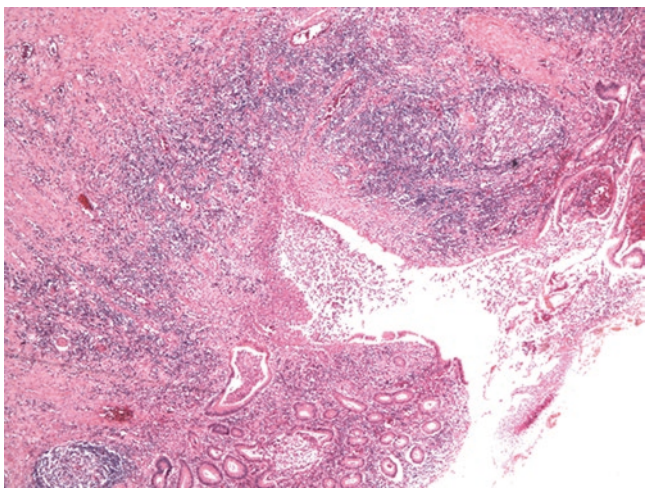

FIGURE 45-4. Low-power view of Crohn's disease with lymphocytic infiltration and mucosal ulceration.

reactive hyperplasia, although more common in UC, also occur in Crohn's colitis (Figure 45-3).

Focal chronic inflammation, granuloma, and localized crypt distortion are some of the commonly accepted microscopic features in Crohn's. Plasma cells and lymphocytes in the lamina propria are hallmarks of colonic inflammation (Figures 45-4 and 45-5). Lymphoid aggregates are common and transmural. Granulomas, although highly suggestive, are not specific for Crohn's, being present in a few as 18% of samples in some studies (Figure 45-5) [11]. Granulomas can

occur at the site of ruptured crypts in UC and are also found in infectious colitis and intestinal tuberculosis. Microscopic differences between UC and CD are listed in Table 45-4.

Indeterminate Colitis

Often the clinical and histologic features of a patient's disease course may share that of both UC and Crohn's. One common situation is fulminant UC mimicking CD with deep transmural inflammation. Indeterminate colitis (IC) was first described by Kent in 1970 [15] and more formally by Price in 1978 [16]. The Montreal Working Party recommended that the term indeterminate colitis should be reserved only for those cases where colectomy has been performed and pathologists are unable to make a definitive diagnosis of either CD or UC after full examination [17]. The term "inflammatory bowel disease, type unclassified" (IBDU) is suggested for patients in whom there is evidence on clinical and endoscopic grounds for chronic inflammatory bowel disease affecting the colon, without small bowel involvement, and no definitive histological or other evidence to favor either CD or UC [17].

The distinct delineation of disease carries becomes surgically relevant when considering a patient with an IC or IBDU diagnosis for a restorative proctectomy. Higher rates of pelvis sepsis, pouch fistula, and pouch failure have been reported in patients with IC undergoing ileal pouch-anal anastomosis (IPAA), compared to a UC cohort [18]. When the patients ultimately diagnosed with CD were excluded, outcomes for the IC patients were similar to the UC group. Functional status and quality of life have been reported to be similar between IC and UC patients post-IPAA, along with similar pouch failure rates [19].

Ultimately, most patients with an initial IC diagnosis will be found to have UC [20]. In the absence of current or historical clinical features of Crohn's disease, most IC patients could be considered for IPAA, with expectations of functional outcome and pouch retention rates similar to that of UC patients [21].

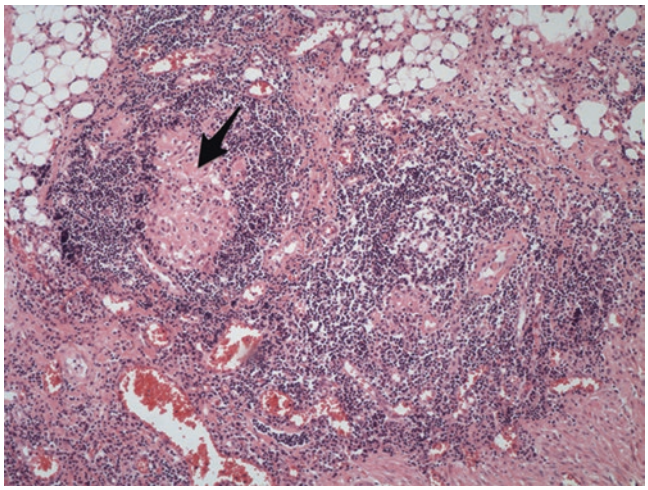

FIGURE 45-5. Crohn's disease with full-thickness inflammatory change and lymphocytic infiltration into the serosa and granuloma (*arrow*).

Serology and Markers of Disease

ASCA and pANCA

Anti-*Saccharomyces cerevisiae* antibodies (ASCA) and perinuclear anti-neutrophil cytoplasmic antibodies (pANCA) have been extensively studied as biomarkers in IBD. Due to

TABLE 45-4. Microscopic features used for the diagnosis of IBD [13]

	Ulcerative colitis	Crohn's disease
Crypt architectural irregularity	Diffuse (continuous)	Focal (discontinuous)
Chronic inflammation	Diffuse (continuous) Decrease proximally	Focal (discontinuous) Variable
Patchiness	Uncommon	Common
Localization	Superficial Transmucosal Sometimes in submucosa	Transmural
Serositis	Absent except in fulminant colitis	Present
Lymphoid aggregates	Frequent in mucosa, submucosa	Common, transmural
Granulomas	Absent, except with ruptured crypts	Present
Acute inflammation	Diffuse (continuous)	Focal (discontinuous)
Crypt epithelial polymorphs	Diffuse (continuous)	Focal (discontinuous)
Crypt abscesses	Common	Uncommon
Mucin depletion	Present, pronounced	Uncommon, mild
Neuronal hyperplasia	Rare	Common
Muscular hypertrophy	Absent	Present
Paneth cell metaplasia	Present	Uncommon
Pyloric gland metaplasia	Rare	Present

their presence in other inflammatory conditions, such as vasculitis or rheumatoid arthritis, they are not useful as screening measures. pANCA-positive values range from 2 to 28% in CD patients, while 20–85% of UC patients are positive for pANCA, resulting in a sensitivity of 56% and a specificity of 89% in UC patients [22]. ASCA positivity is found in 39–69% of CD patients and in 5–15% of UC patients [22]. One clinical situation where biomarkers could be extremely useful would be in indeterminate colitis. Unfortunately, in one study of 97 IC patients nearly half (48.5) were ASCA−/pANCA−, thus providing no useful clinical information [23]. ASCA+/pANCA− status was able to predict CD in 80% and ASCA−/pANCA+ predicted UC in 63.3%. One small study of IPAA patients showed ASCA+/pANCA− patients had 44% of developing postoperative fistulas and were more likely to have their diagnosis changed to CD [24]. Elevated levels of pANCA in UC patients undergoing IPAA have been shown to predict the incidence of chronic pouchitis. The cumulative risk of developing chronic pouchitis among patients with high-level pANCA (56%), defined as >100 EU/ml, before IPAA was significantly higher than in patients with medium level (22%), low level (16%), and those who were pANCA−ANCAsi [25].

Fecal Markers

Calprotectin is a small calcium-binding protein, found in abundance in neutrophilic granulocytes, in which it accounts for 60% of the cytosolic fraction, as well as in monocytes and macrophages [26]. Calprotectin is stable in feces for up to 7 days at room temperature and is homogenously distributed [26]. The presence of calprotectin in stool implies mucosal inflammation, which is nonspecific, and can also occur with mucosal bleeding. This can occur in non-IBD situations like NSAID damage or malignancy. Lactoferrin is similar to calprotectin in that it is neutrophil derived and found in the stool. Like calprotectin, it can be measured by commercial ELISA. Lactoferrin testing tends to be more affordable than calprotectin [27]. Calprotectin has been used in a variety of clinical situations for IBD patients, including diagnosis, prediction of clinical course, monitoring response to therapy, and postoperative surveillance. Although primarily assayed via stool sample, measurement via serum samples has been studied, but correlation to stool values is weak [28].

Initial use of fecal calprotectin was in attempting to differentiate between patients with IBD and irritable bowel syndrome, a non-inflammatory condition. This has been fairly extensively studied in both the adult and pediatric populations, with a goal of reducing the need for invasive testing. A meta-analysis showed good sensitivity (93%) and specificity (96%) of fecal calprotectin to diagnose IBD in adult patients, although specificity (76%) was much lower for pediatric patients [29]. The authors calculated in a hypothetical population of 100 adults with suspected inflammatory bowel disease (and an overall mean prevalence of 32%) three patients without the disease would go on to have endoscopy and two patients with the disease would be missed [29]. They conclude that increased fecal calprotectin levels could be used to guide more urgent endoscopic evaluation, but caution that negative values in a patient with persistent rectal bleeding do not exclude the presence of IBD.

There is mounting evidence that mucosal healing is a better target in IBD treatment, rather than clinical symptom control, as it can alter the course of disease, reducing hospitalizations and rates of future surgery [30]. Calprotectin would be a desirable marker for following mucosal healing, as repeated endoscopic evaluation is not practicable for patients. One study of IBD patients in clinical remission with normalized calprotectin levels showed 38 of 45 had complete mucosal healing [31]. Data from the STORI trial showed that of CD patients in stable remission on infliximab and immunomodulator who stopped biologic treatment, 43.9% would relapse at 1 year [32]. Fecal calprotectin ≥300 μg/g was shown to be predictive of relapse on multivariable regression (hazard ratio 2.5). In general, fecal calprotectin has been more effective in predicting the clinical course of UC patients or in CD patients with colonic involvement [26].

Fecal calprotectin has also been studied in the surgical IBD cohort. In a prospective study of 90 patients admitted with acute UC, calprotectin was shown to be predictive of the need for colectomy [33]. All patients received high-dose steroid therapy, with 23% receiving infliximab. 34.4% of patients required colectomy due to failure of medical management. Fecal calprotectin was significantly higher in patients who had failed medical therapy compared to those who escaped surgery (1200.0 vs. 887.0 μg/g; $P=0.04$). Using a cutoff point of 1922.5 μg/g at mean follow-up around 1 year, 87% of patients required colectomy. In post-resection CD, fecal calprotectin >200 μg/g has been shown to be predictive of endoscopic recurrence after 12 months [34]. Recurrence after surgical resection for CD may also be predicted by calprotectin levels. In a prospective study, levels of calprotectin greater than 100 μg/g indicated endoscopic recurrence with 89% sensitivity and 58% specificity and a negative predictive value of 91% [35]. Calprotectin was superior to CRP and a clinical disease index (CDAI) for detection of recurrence and monitoring response to treatment. Serial calprotectin measurement may represent a less invasive and costly method for the postoperative management of CD patients.

Inflammatory Markers

C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and albumin are three common serum measures of the acute phase of inflammation. IBD intestinal inflammation is clearly a trigger for elevation of these measures, but remains nonspecific, as other inflammatory conditions can

elevate them as well. Albumin has a long half-life (5 days), limiting its clinical usefulness. CRP is made by hepatocytes, and a primary trigger for release is IL-6. CRP has a short half-life (19 h) compared with other acute-phase proteins and will therefore rise early after the onset of inflammation and rapidly decrease after resolution of the inflammation [36]. CRP tends to be elevated more in CD, rather than UC [37]. ESR is the rate at which erythrocytes settle in the plasma. ESR is an indirect measurement of plasma acute-phase protein concentrations and can be greatly influenced by the size, shape, and number of erythrocytes, as well as by other plasma constituents such as immunoglobulins or fibrinogen [38]. Compared with CRP, ESR will peak much less rapidly and may also take several days to decrease, even if the clinical condition of the patient or the inflammation resolves [36].

These inflammatory markers have been studied in a variety of clinical IBD situations. They allow for excluding IBD diagnosis in patients with functional bowel disorders without invasive study, in whom there may be some overlap of clinical symptoms. One study of patients presenting with abdominal symptoms showed elevations in CRP and ESR in all patients eventually diagnosed with CD and in 50% of those eventually diagnosed with UC [39]. No patients with functional bowel disorders had elevated inflammatory markers. A more recent study showed a cutoff value of 2.3 mg/l had a sensitivity of 100% and a specificity of 67% in differentiating functional disease from new cases of IBD [40]. CRP tends to be a less reliable predictor of endoscopic disease in the postoperative CD patient [35, 41].

Genetic-Based Testing

In 2001, two groups simultaneously reported on NOD2/CARD15 gene mutations on chromosome 16 that conferred susceptibility to Crohn's disease [42, 43]. NOD2 plays a role in the nuclear factor NF-κβ pathway that is responsible for the cellular response to bacteria. This has provided a genetic model for the dysregulated response of the immune system that occurs in IBD. In retrospective clinical studies, NOD2 mutations have been shown to be more frequently associated with ileal CD and severe pouchitis in UC patients after IPAA [44, 45]. NOD2/CARD15 mutations are actually quite common in asymptomatic patients, with prevalence between 2.4 and 11.5% in a white population, with wide geographic variability [46]. Even patients with double NOD2/CARD15 mutations did not have elevated risk of IBD [46]. This underscores the fact that genetics in conjunction with environmental exposure is necessary for the clinical expression of IBD. In fact, another burgeoning area of genetic research in IBD involves the microbial environment of the gut [47]. Although the clinical utility of genetic testing remains limited currently, it is clear that research in this field will shape the future of IBD diagnosis and treatment.

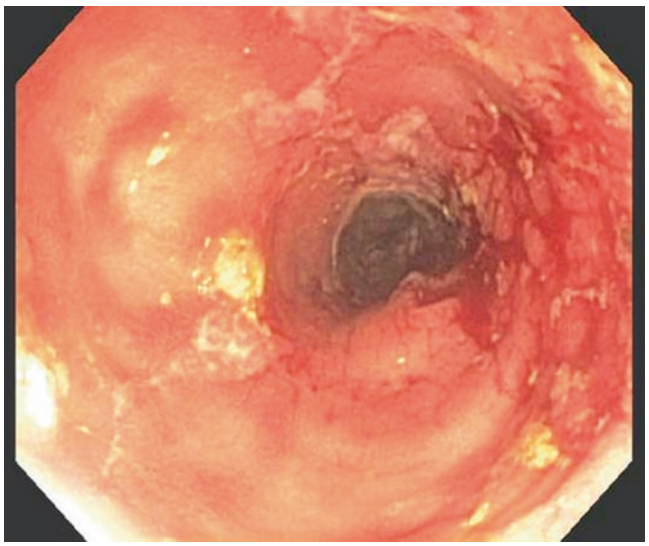

FIGURE 45-6. Crohn's colitis of transverse colon.

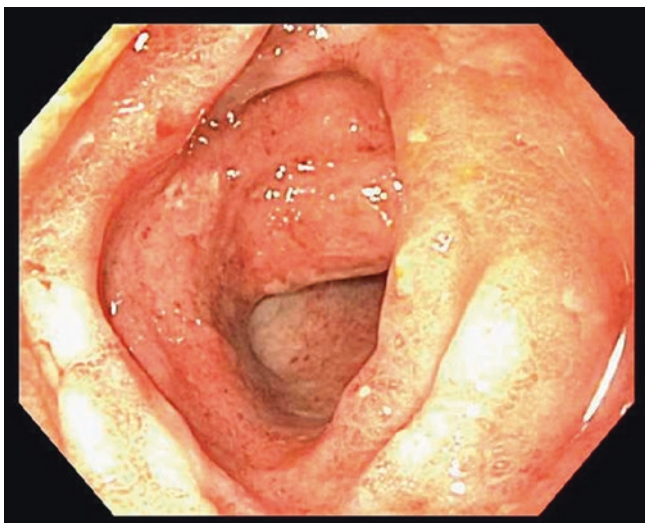

FIGURE 45-7. Sigmoid colon in ulcerative colitis.

Endoscopy in IBD

Flexible Endoscopy

Flexible endoscopy remains a gold standard technique in the initial diagnosis and follow-up management of patients with suspected or established inflammatory bowel disease. Figures 45-6 and 45-7 show the endoscopic appearance and subtle differences between Crohn's colitis (patchy) and ulcerative colitis (diffuse and contiguous). Endoscopy allows for mucosal inspection and, importantly, tissue sampling for histology. Therapeutic interventions, such as balloon dilations of strictures, can also be performed. Patients with symptoms suggestive of IBD should undergo colonoscopy. Intubation and biopsy of the terminal ileum is especially

important in patients with suspected Crohn's disease. Endoscopically abnormal areas of the colon should be sampled. Biopsy of normal areas is important as well, as presence or absence of microscopic colitis can aid in differential diagnosis. Particular attention should be made in areas of colonic stricture, with historical studies showing 24% of UC and 6% of CD strictures may be malignant [48, 49]. Colonoscopy is overall a safe procedure, but it is invasive and carries risk of serious complications. IBD patients are known to carry higher risks of procedural complications. This is especially true in patient with advanced age, severe colitis, or during therapeutic interventions. Risk of perforation in one national database study for IBD patients was 1%, with age, female gender, and therapeutic dilation being predictors of complication [50]. Upper endoscopy plays a role in the smaller subset of Crohn's patients who present with esophagogastroduodenal involvement. Newer techniques of single and double balloon enteroscopy allow advanced endoscopists to reach far into the small bowel, in both antegrade and retrograde directions. Double balloon enteroscopy has been shown to be similar to CT enterography for the evaluation of Crohn's small bowel disease [51]. Double balloon enteroscopy is invasive, however, and carries risk of perforation, with major complication rates of around 1% and interventional procedure complication rates of 4–5% [52]. One major advantage is that it can be used for stricture dilation or retained video capsule removal, with relatively good rates of success [53, 54]. Double balloon enteroscopy remains an advanced endoscopic technique and may not be available in all centers.

Beyond initial diagnosis, endoscopy is used for evaluating the response of IBD to medical therapy, for monitoring recurrence after surgery, and for dysplasia surveillance in UC. There are no specific guidelines for routine colonoscopy during medical therapy for IBD [55]. Colonoscopy is indicated when there is a major change in symptoms. It is debated whether colonoscopy should be done for the clinically asymptomatic patient. It is well established that clinical symptoms and endoscopic findings may not be congruent, and clinicians are often poor at predicting disease extent based on symptoms alone. Colonoscopy is useful in the decision to withdraw medical therapy in stable CD [55]. Endoscopic mucosal healing has been shown to reduce twofold the risk of relapse after infliximab withdrawal in CD patients on immunosuppression with steroid-free remission [32]. Colonoscopy is recommended 6–12 months after surgery for CD, as anastomotic recurrence (Figure 45-8) is common (60–90% at 1 year) [55]. Fecal calprotectin may be a useful screening trigger to prompt earlier colonoscopy (see Fecal markers section) [55]. Early medical intervention in the postoperative CD setting is associated with lower rates of endoscopic recurrence and higher rates of complete mucosal healing [56]. There are a number of endoscopic grading systems used to describe mucosal findings in CD, including the Crohn's Disease Endoscopic Index of Severity (CDEIS) and

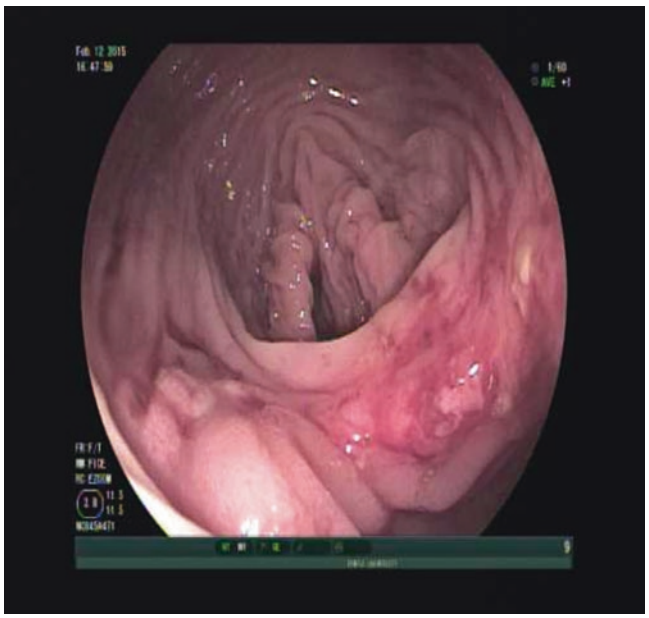

FIGURE 45-8. Anastomotic recurrence 2 months after ileocolic resection.

the Simple Endoscopic Score for Crohn's Disease (SES-CD) [57, 58]. None are widely or routinely used outside of research settings. However, it is important to standardize endoscopic reporting including severity, location and extent of inflammation, and presence of strictures or other lesions. The Rutgeerts endoscopic score (Table 45-5) has been shown to predict the recurrence of symptoms and need for repeat surgery based on the endoscopic appearance of the neoterminal ileum and ileocolonic anastomosis [59]. 85% of patients with i0 or i1 lesions 6–12 months postoperatively will have no endoscopic progression at 3 years [60]. i3 or i4 patients had progressive or very severe endoscopic progression 92% of the time [60]. Clinical recurrence occurred in less than 5% of patients with i0/i1 lesions, 15% with i2, 40% with i3, and >90% with i4 [60]. There are at least 9 endoscopic scoring systems described for UC [30]. Two of the most commonly used are the Baron and Mayo scores (Table 45-6) [61, 62]. The Baron score relies on the assessment of mucosal bleeding during colonoscopy, and the Mayo score evaluates the overall appearance of the mucosa, with respect to erythema, vascular pattern, friability, bleeding, erosions, and ulcerations.

Colonoscopy is recommended for patients with chronic colitis for dysplasia surveillance. The risk of colorectal cancer surpasses that of the general population after 8–10 years of disease [63]. It is important to note that this period begins at the onset of symptoms, rather than time of histological diagnosis. Although a meta-analysis demonstrated the cumulative risk of colorectal cancer for UC patients to be 2.1% at 10 years, 8.5% at 20 years, and 17.8% at 30 years, population-based series have reported lower annual incidence rates of 0.06–0.2%. Despite this, it is generally

TABLE 45-5. Rutgeerts score of postoperative endoscopy for CD [59] and corresponding CTE scoring system for postsurgical examination [92]

Rutgeerts	Endoscopic findings	CTE	CTE findings
i0	No lesion in the neoterminal ileum	CTE0	No findings
i1	<5 aphthoid ulcers	CTE1	Minor mucosal irregularities with slight wall thickening and mural contrast enhancement
i2	>5 aphthoid ulcers with normal mucosa in between, or skip areas or larger lesions related to anastomosis	CTE2	Mucosal hyperdensity with distinct bowel wall thickening, no stenosis, or stenosis without prestenotic dilatation
i3	Diffuse aphthoid ileitis, with mucosa extensively inflamed	CTE3	Major mucosal abnormalities, distinct bowel wall thickening with target sign and extravisceral signs such as perienteric stranding, comb sign, fibrofatty proliferation, stenosis with prestenotic dilatation, and/or the presence of complications
i4	Diffuse inflammation, large ulcers, nodules, and/or stenoses		

TABLE 45-6. Baron and Mayo scores for ulcerative colitis

	Baron score	Mayo score
Score 0	Normal mucosa, ramifying vascular pattern clearly visible throughout, no spontaneous bleeding, no bleeding to light touch	Normal or inactive disease
Score 1	Abnormal but not hemorrhagic: appearances between "0" and "2"	Mild disease (erythema, decreased vascular pattern, mild friability)
Score 2	Moderately hemorrhagic: bleeding to light touch, but no spontaneous bleeding seen ahead of instrument on initial inspection	Moderate disease (marked erythema, absent vascular pattern, friability, erosions)
Score 3	Severely hemorrhagic: spontaneous bleeding seen ahead of instrument at initial inspection, and bleeds to light touch	Severe disease (spontaneous bleeding, ulceration)

accepted that chronic UC is associated with an increased risk of malignancy [64]. Studies on dysplasia and cancer in UC are more widely available than those on CD; thus surveillance and treatment paradigms are often similar in the two groups despite the differing disease pathophysiology [65]. The Crohn's and Colitis Foundation of America (8–10 years), the American College of Gastroenterology (8–10 years), and the American Society of Colon and Rectal Surgeons (8 years) all have similar recommendations for initial surveillance colonoscopy in chronic colitis [64, 66, 67]. After a negative study, most recommend 1–2 year interval for repeat examination. After two negative exams, follow-up time can be 1–3 years. After 20 years of disease, recommendations are again every 1–2 years [66]. Patients with primary sclerosis cholangitis (PSC) have higher rates of malignancy and should undergo yearly evaluation [68].

The traditional recommendation for endoscopic biopsy for dysplasia surveillance is four-quadrant sampling every 10 cm [64, 66]. Particular attention should be paid to raised lesions or strictures, with sampling of any normal surrounding areas to allow for histologic comparison. Significant pseudopolyposis may make surveillance unreliable by obscuring the mucosa or being too numerable to sample [67]. Particularly in UC, consideration of sampling every 5 cm in the distal colon is reasonable given the worsening severity of inflammation and higher rates of malignancy in this area [66]. A typical endoscopic biopsy samples 0.05% of the mucosal surface [69]; accordingly multiple samples must be taken for adequate sampling. A minimum of 33 random biopsies has been shown to result in 80–90% sensitivity for detecting dysplasia, with 64 required for 95% [70].

Recent advances in endoscopic technology are changing how dysplasia surveillance is performed. The American Society for Gastrointestinal Endoscopy (ASGE) has recently made strong recommendations that high definition video equipment be used when using traditional white-light colonoscopy [71]. One retrospective study showed twice as many dysplastic lesions were detected with high definition equipment rather than standard definition [72]. Chromoendoscopy involves the use of dye applied to colonic mucosa to improve epithelial surface detail and allow for targeted sampling. Diluted indigo carmine and methylene blue are the two most commonly used dyes. Two prospective tandem colonoscopy studies have shown the increased ability of chromoendoscopy to detect dysplastic lesions, being 1.8–3.5 times more likely positive than conventional four-quadrant biopsy technique [71, 73, 74]. One study found no dysplasia in 2904 non-targeted biopsies, versus 9 in 157 chromoendoscopy-targeted biopsies [73]. The improvement in efficiency using chromoendoscopy is clear. It is not clear that this has had any effect on reducing rates of progression to cancer. The St Mark's Hospital recently reported on the outcomes of their UC surveillance screening program originating in 1971. From 2002 to 2012 twice as many dysplastic lesions were found using chromoendoscopy (8.4%) vs. white-light colonoscopy (4%) [75]. The post-colonoscopy colorectal cancer rate was lower following chromoendoscopy compared with white-light endoscopy, although this did not reach statistical significance [75]. Chromoendoscopy has been given a strong recommendation over white-light colonoscopy by the ASGE [71]. Currently there is no evidence to support routine use of digital enhancement techniques, such as narrow band imaging (NBI).

One study of NBI vs. white-light colonoscopy actually found fewer total dysplastic lesions were detected with NBI [76].

Confocal laser endomicroscopy (CLE) is a newly introduced modality which captures images of "virtual histology" of the gastrointestinal mucosa during endoscopy [77]. At present, CLE can be performed with two devices: one integrated into an endoscope (Pentax, Tokyo, Japan) and one as a mini-probe through the scope (Cellvizio, Mauna Kea Technologies, Paris, France) [77]. Confocal microscopy consists of focusing a laser ray onto the mucosal surface and filtering the returned light by means of a small pinhole which rejects out-of-focus light [77]. This technology allows for real-time interpretation of histology and, in theory, could eliminate the need for endoscopic biopsy. It can also detect microscopic evidence of ongoing inflammation in normal appearing colonic mucosa. One study found 4.75-fold more dysplastic lesions using chromoendoscopy-guided CLE with 50% fewer biopsy specimens [78]. This technique will require further investigation and study before it can be considered for integration into screening paradigms.

Capsule Endoscopy

Video capsule endoscopy (VCE) was introduced in 2001 as a noninvasive method to evaluate the small bowel that remains outside the reach of contemporary flexible endoscopy [79]. The technique consists of a pill-sized device with self-contained lighting, video capture, and transmission capability. After a 12 h fast, the patient consumes the camera with a sip of water. Bowel preparation regimens are variable, but a meta-analysis showed a combination of polyethylene glycol and simethicone provided optimum image quality [80]. Patients should abstain from NSAIDs for a month prior to examination, as these can induce mucosal ulcerations and confound image interpretation. Patients wear image capture sensors and belt, avoid consumption of fluids for 4 h, and do not have to limit physical activity. The capsule itself passes naturally with bowel movement and is usually excreted within 24–72 h [79].

For the IBD patient, evaluation of small bowel CD is the most common indication for VCE. Meta-analysis has shown VCE to have higher diagnostic yield than colonoscopy, push enteroscopy, conventional enterography, and CT enterography [81, 82]. VCE was found to be similar to MR enterography in those same reviews. One important consideration in many VCE studies is that patients with suspected or known structuring CD were excluded, due to fear of capsule retention. Capsule retention is a rare, but feared, complication of VCE. Reported rates of capsule retention in CD patients are around 13%, with one review showing that established CD diagnosis increased the risk of capsule retention ninefold [83, 84]. A slowly dissolvable patency capsule exists (Agile PC, Given Imaging) and is intended to assess patency of the small bowel prior to VCE [79]. The European Society of Gastrointestinal Endoscopy (ESGE) has recommended that VCE be done if deemed necessary to change management in CD and only after cross-sectional imaging and patency capsule evaluation are done to exclude stricture [83].

FIGURE 45-9. Fluoroscopic enterography study showing terminal ileal stricture in Crohn's disease.

Radiology in IBD

Plain Radiography

Plain radiographs remain a standard for rapid assessment of the IBD patient presenting with acute abdominal symptoms. Free air from hollow viscus perforation, toxic megacolon, or small bowl obstruction from stricture or adhesion are diagnoses that can rapidly and inexpensively be confirmed. Fluoroscopic gastrointestinal imaging, once the gold standard for IBD evaluation, has rapidly been supplanted by advanced imaging techniques and flexible endoscopy. In the 1960s and 1970s, before CT or MRI, single contrast and then double contrast enema imaging was the primary method to evaluate both the upper and lower GI tracts. Historically, small bowel follow-through (SBFT) studies have been the standard approach to assess active disease [85]. Early mucosal changes and strictures can be seen with fluoroscopic studies (Figure 45-9). Although well-supervised SBFT studies allow for excellent visualization of the bowel mucosa, small bowel enteroclysis offers a more sensitive and accurate assessment of mucosal abnormality and strictures [85]. Standard enteroclysis is typically performed with placement of a nasojejunal tube with fluoroscopic guidance. Barium along with air or methylcellulose, for double contrast, is instilled to provide opacification and distension of the small bowel [86].

Computed Tomography

Computed tomography (CT) imaging has revolutionized the diagnosis and management of abdominal diseases. Findings of small and large bowel mural thickening, abscess, and

fistulae were evident on the earliest generation of CT scanners in early studies of IBD patients [87]. CT imaging for UC patients is mostly limited to situations of severe or fulminant colitis. CT for CD allows non-interventional assessment of the small and large bowel, as well as possible extra-intestinal manifestations of disease. In addition to standard axial image acquisition, CT enteroclysis and enterography are also possible. CT scanning is a primary modality for image-guided percutaneous biopsy of abscesses in CD. A study using a nationwide database showed 29% of CD abscesses were treated with percutaneous drainage in 2007, up from 7% in 1998 [88]. In that same time period, surgical drainage fell from 59 to 32%.

CT enterography (CTE) requires specialized preparation. Neutral intraluminal contrast agents (such as water) are required to enable adequate visualization of enhancing mucosal lesions which would otherwise be masked by positive contrast agents such as barium [85]. Because luminal collapse can mimic bowel wall thickening, large volume ingestion is necessary. A typical prep consists of 1 L of a polyethylene glycol solution followed by 1 L of water. This can be consumed orally (enterography) or via nasojejunal tube (enteroclysis) given 1 h before scanning. Intravenous contrast is given to enhance inflammatory changes in the mesentery and bowel wall. Anti-spasmodics are often given to reduce bowel motion artifact.

CTE has been shown to be as specific as conventional enteroclysis in diagnosis of Crohn's small bowel lesions, with somewhat less sensitivity [89]. Enteroclysis can pick up some early changes of disease (thickened folds, aphthoid ulcers) that CTE does not have the resolution to identify, and there may be clinical situations where a combination of the techniques is helpful. CTE has been shown to alter clinical decision making in CD. One cohort study of 273 established or suspected IBD patients showed CTE changed management in 51% of cases [90]. Of those with established disease, 48% had management change, including 24% with medication changes. Another study showed poor correlation between CTE findings and clinical assessment of IBD symptoms [91]. 16% of CTE identified strictures in this study were not suspected by expert clinical assessors. No scoring systems for CTE are in wide use, but one has been developed for imaging postsurgical resection [92] (Table 45-5). This has been evaluated prospectively, and been shown to accurately predict need for reoperation, similar to Rutgeerts endoscopic score [93].

MRI

Magnetic resonance imaging (MRI) allows for acquisition of images, similar to CT, but does so by manipulating the nuclear properties of hydrogen atoms and thereby avoids exposing the patient to the ionizing radiation that CT requires. MRI also allows for obtaining images with specific contrast profiles to allow for differentiation between inflammation and fibrosis or suppressing surrounding fatty tissues. One issue with MRI is increased complexity, longer time for image acquisition, and generally more limited availably, when compared to CTE. The increased soft tissue resolution delivered by MRI over CT has made it the preferred imaging technique when imaging is required for complex fistulizing perianal CD.

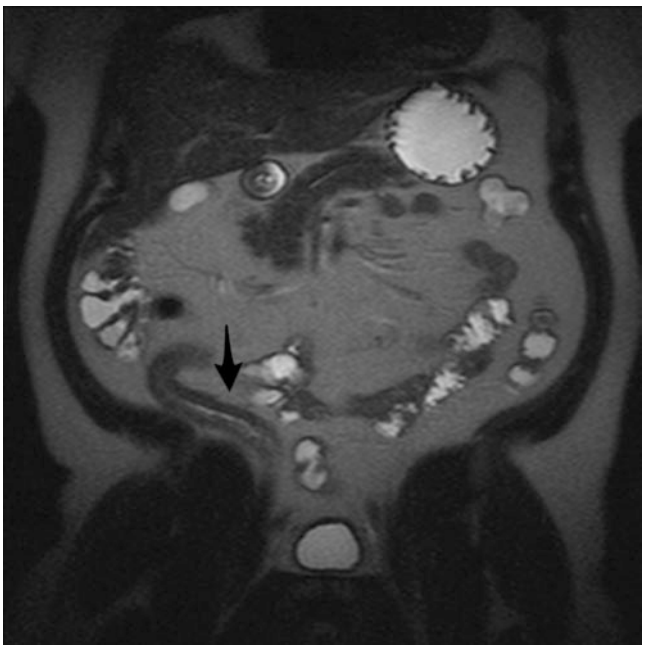

FIGURE 45-10. MRE in Crohn's disease. Coronal T2-weighted images demonstrate segmental mural thickening of the terminal ileum (*black arrow*).

Patient preparation for MRE is similar to that of CTE. Oral purgatory solution and large volume negative contrast solution are consumed. MR enteroclysis can be performed, but enterography is preferred by patients and has been shown to produce similar image quality [94]. Gadolinium is used as an IV contrast medium. MRE is much more sensitive to motion artifacts than CTE, so 1 mg of glucagon is often used. Multiple image acquisition sequences are taken including T1, T2, and diffusion weighted (Figures 45-10, 45-11, and 45-12). Breath holding is necessary for most sequences and the entire time of image acquisition takes around 30–35 min [94].

The presence of bowel wall thickening in conjunction with asymmetric mural hyperenhancement is essentially pathognomonic for Crohn's disease images (Figure 45-10) [95]. The "comb sign" refers to engorgement of the vasa recta and is highly suggestive of active inflammation [95]. The ability of MRE and CTE to detect Crohn's lesions is similar. One study showed sensitivity of MRE to be 90.5% and 95.2% in CTE for detecting active small bowel Crohn's disease [96]. In this study, MRE image quality scores were rated significantly worse than CTE, underlying the increased technical challenge of image acquisition for MRE. Three indexes of activity based on adequate external references have been proposed: the

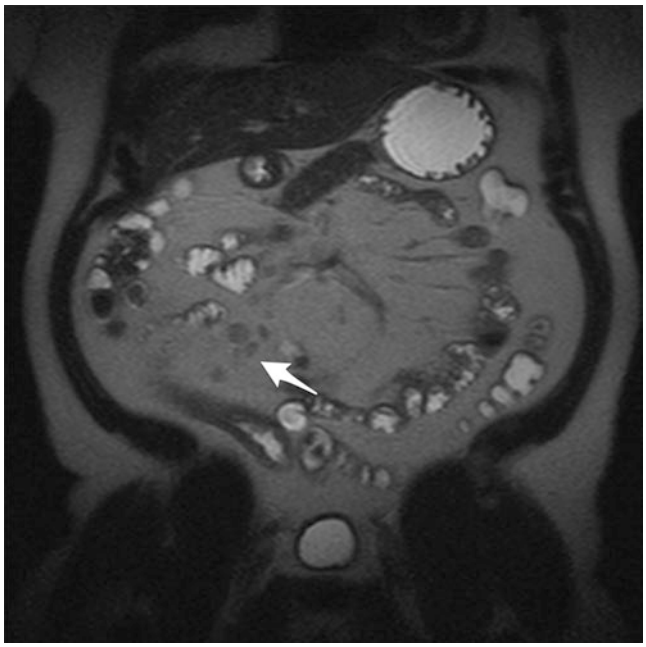

FIGURE 45-11. MRE in Crohn's disease. Coronal T2-weighted images with surrounding fibrofatty proliferation and ileocolic lymph nodes (*white arrow*).

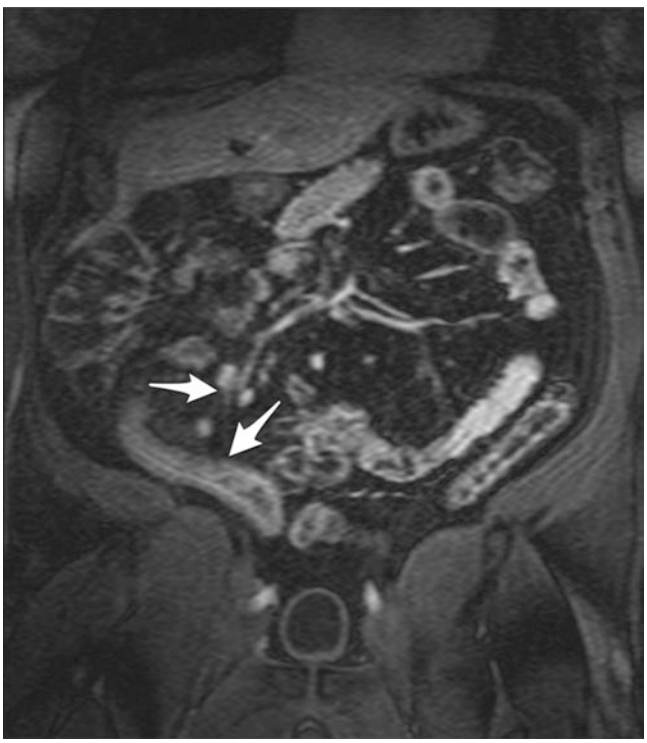

FIGURE 45-12. MRE in Crohn's disease. Gadolinium-enhanced coronal T1-weighted image demonstrate mucosal hyper-enhancement as well as enhancement of the ileocolic lymph nodes, indicative of active Crohn's disease (*arrows*).

Magnetic Resonance Index of Activity (MaRIA) score, the Crohn's disease MRI Index (CDMI) score, and the Nancy score [97]. The MaRIA and CDMI scores are the most commonly used in research settings, but neither has yet transitioned to routine clinical practice [97]. The accuracy of the MaRIA, CDMI, and Nancy scores for detecting inflammatory activity is in the range of 80–90%, with MaRIA accuracy of predicting mucosal healing being 83% [97].

Ultrasound

Ultrasound (US) could, in theory, represent an ideal imaging technique for the IBD patient. US is widely available, is relatively low cost, is noninvasive, and does not require ionizing radiation. However, US is a highly operator-dependent imaging method and correct interpretation of sonographic findings requires adequate experience in abdominal and bowel sonography [98]. Both oral and intravenous contrast agents are available to enhance images. Bowel wall thickness >3–5 mm detected with US is the primary cutoff for postoperative CD recurrence in many studies, with a wide range of sensitivity and specificity reported [99]. One study looked at bowl wall thickness of the anastomosis in postoperative CD, showing patients with thickness >3 mm had twice the risk of further surgical intervention [100].

Nuclear Medicine

Currently nuclear medicine plays a limited role in the initial imaging assessment of patients with CD, depending on local practice [85]. Radiolabeled white cells have been used to quantify degree of bowel inflammation, but are limited by poor anatomical correlation and failure to detect strictures and fistulae [85]. PET/CT has also been evaluated in CD, with higher standardized uptake values (SUV) correlating with worsening inflammation [101]. One small study of 13 patients showed the addition of PET to CTE was able to detect additional areas of inflammation or fistula in 23% of patients [102]. In general, concerns over radiation exposure have limited the use of many nuclear medicine techniques in routine clinical practice.

Evolving Role of CTE and MRE

There has been recent concern among medical professionals and the media regarding increasing exposure of patients to ionizing radiation and subsequent risk of malignancy. IBD patients represent a cohort at particular risk for repeated studies employing ionizing radiation. The young IBD patient represents a particular concern. Younger patients are inherently more radiosensitive and have longer life spans for radiation-induced cancers to develop [103]. One retrospective study looking at radiation exposure in children with IBD

estimated that 60% would exceed 50 mSv by age 35 [104]. There is direct evidence from epidemiologic studies that organ doses in the range of 30–90 mSv result in an increased risk of cancer [103]. Given the similar clinical usefulness of both CTE and MRE, many advocate for the use of MRE in most situations where imaging is required, especially in the adolescent IBD patient. Surgeons, gastroenterologists, and emergency medicine physicians caring for IBD patients should be particularly aware of this issue and coordinate care so that unnecessary radiologic studies can be avoided.

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