Diagnostic Criteria for Inflammatory Bowel Disease in Adults

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Inflammatory bowel disease comprises disorders of unknown etiology. The diagnosis is made on the association of symptoms and signs and sometimes on the family history of the subject, since there is at present no specific clinical, morphological, or biological diagnostic test. The diagnosis is usually easier when it is obvious that the disease is chronic than it is during the first episode, although differential diagnoses (or associated diagnoses in patients with established inflammatory bowel disease) must always be considered.

When Should Inflammatory Bowel Disease Be Suspected?

Inflammatory bowel disease is usually revealed by gastrointestinal symptoms [1, 2]. The frequency of intestinal transit disturbances, abdominal pain, abnormal stools, and other symptoms in patients with ulcerative colitis and Crohn’s disease is summarized in Table 1. Anoperineal lesions can reveal Crohn’s disease [3]. Extraintestinal symptoms which may reveal ulcerative colitis or Crohn’s disease include peripheral or axial arthritis, oral aphthae, skin lesions such as erythema nodosum or pyoderma gangrenosum, ocular diseases (uveitis, episcleritis), and sclerosing cholangitis (inflammatory bowel disease is present in 70% of patients with this disorder). It is easy to suspect inflammatory bowel disease when there are associated intestinal symptoms but more difficult when they are isolated (since each can have many causes). The presence of other cases of inflammatory bowel disease in the family and the absence of other causes are important arguments in favor of inflammatory bowel disease [4].
Table 1. Frequency of the main symptoms in patients with inflammatory bowel disease

<table>
<thead>
<tr>
<th>Symptom or sign</th>
<th>Ulcerative colitis</th>
<th>Crohn’s disease</th>
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<tbody>
<tr>
<td>Blood in stools</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Abdominal mass</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>Fistulae</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>Perianal destructive lesions</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>Weight loss</td>
<td>+</td>
<td>++</td>
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In the presence of blood in the stools, the clinician must search for rectal or colonic lesions. Endoscopic examination shows the presence of inflammatory lesions (that is, colitis), and rules out other diseases, especially tumors. It is, however, sometimes difficult to recognize minimal mucosal lesions such as a loss of the vascular pattern, and it is thus important not to forget to perform a rectal biopsy for histological examination. The next step is to establish the cause of colitis (see below).

The diagnosis of inflammatory bowel disease, especially Crohn’s disease, is also usually made rapidly in patients with major intestinal transit disturbances associated with pain (colic), an abdominal mass, and sometimes fever and weight loss. Every physician will perform abdominal investigations in such cases including either ultrasound scanning or computed tomography, or endoscopy of the lower intestinal tract which will disclose the lesions of inflammatory bowel disease. The causes of acute and chronic ileitis are discussed below.

In patients with moderate intestinal transit disturbances, moderate pain, blood in stools, and without extraintestinal symptoms, the most frequent diagnosis is irritable bowel syndrome, though there is no specific sign for this common disorder which affects 15% of the population. Endoscopy and radiological examination of the small bowel usually allows one to differentiate inflammatory bowel disease from irritable bowel syndrome, but the latter is so common that the decision to perform these invasive examinations is often delayed or restricted to patients with more severe symptoms [5].

Diagnosis of Inflammatory Bowel Disease in Practice

The diagnosis of inflammatory bowel disease is usually done by (i) demonstration of the presence of inflammatory lesions in the gastrointestinal tract; (ii) exclusion of other causes for the lesions (infections and so on); often helped by (iii) chronicity of the symptoms or lesions, and sometimes by (iv) a positive family history (as about 10% of the subjects with inflammatory bowel disease have a family history of inflammatory bowel disease).
Demonstration of the Presence of Inflammatory Lesions of the Gastrointestinal Tract

The presence of inflammatory lesions in the gastrointestinal tract can be established by physical examination for oral and perineal lesions, but most of the time it is detected only by imaging techniques. Endoscopy is better than radiology at detecting and defining the extent of mucosal lesions [6]. I have described the mucosal and architectural abnormalities in inflammatory bowel disease in an earlier chapter. Phosphate-cleansing solutions should be avoided for the preparation of the colon as they may induce superficial lesions similar to those of inflammatory bowel disease [7]. Biopsies should be performed on the lesions, but also if the colon and ileum appear normal [8]. Endoscopy shows macroscopic lesions of the upper gastrointestinal tract in less than 15% of the subjects with Crohn’s disease, and in none of those with ulcerative colitis. However, histological lesions of gastritis without the presence of Helicobacter pylori (the most frequent cause of gastritis in the general population) are found in more than 30% of the subjects with Crohn’s disease, and this may be a useful guide in some difficult diagnoses [9]. Push enteroscopy may be of interest in a limited number of patients with Crohn’s disease.

Histological examination of biopsies is of paramount importance for the diagnosis of inflammatory bowel disease. However, none of the microscopic lesions (including noncaseating granulomata) is specific for Crohn’s disease or ulcerative colitis [10].

Radiological examination is used to study the parts of the gastrointestinal tract that cannot be reached by endoscopy, either because of the presence of stenosis or because they are too far from the anus or from the mouth. The small bowel can be studied using a barium small bowel follow-through, sometimes with enteroclysis. The most frequent radiological appearance of ileitis includes ulceration, narrowing and irregularity of the lumen, and separation of the intestinal loops (which reflects thickening of the bowel wall). Fistulae are also well studied using radiological methods.

Ultrasonography and computed tomography are useful techniques to study abdominal masses or intestinal obstruction. They have a good accuracy in differentiating inflammatory masses from abscesses, they can detect the site of intestinal obstruction, and they show the thickening of the bowel wall, the creeping fat, and some fistulae. They are increasingly used in diagnostic assessment of Crohn’s disease (but not in ulcerative colitis, as they are not accurate for studying the mucosa). Nuclear magnetic resonance is the procedure of choice for detection of pararectal fistulae and abscesses. Transrectal endosonography is also good but is limited by the experience of the investigator and the tolerance of the patient for the procedure.

Autologous radionuclide-labeled leukocyte scintigraphy is used by some teams to generate scanning images of inflamed intestinal areas [11].
Table 2. Main causes of acute pain in the lower right abdominal quadrant with fever

- Appendicitis
- Mucocele
- Tubo-ovarian abnormalities
  - Ectopic pregnancy
  - Ovarian cysts or tumors
- Salpingitis
- Mesenteric adenitis
- Typhilitis
- Yersiniosis
- Lymphoma
- Cecal diverticulitis

Exclusion of Other Causes for Inflammatory Lesions

The differential diagnosis depends on the site of the lesions, and differs between acute or chronic ileitis or ileocolitis and isolated colitis. The main causes of acute pain in the lower right abdominal quadrant with fever, chronic ileitis, and colitis are shown in Tables 2–4. Exclusion of the other causes requires a search for drug-induced lesions [12, 13]. Many drugs can induce diarrhea and some can cause colitis (Table 4). The most common of these are nonsteroidal anti-inflammatory drugs (NSAID) and antibiotics. NSAID-induced ulceration of the ileum and colon is the most commonly encountered drug-related enterocolitis, owing to the prevalence of NSAID use [12, 13]. The incidence of subclinical NSAID-induced damage to the gut mucosa is high (over one third of exposed individuals).

Stool examination for pathogens is also often necessary, especially when the patient has fever, has been in contact with infected subjects, or is a traveler (salmonellae, shigellae, campylobacter, some *Escherichia coli* including O-157 H-7, *Clostridium difficile*, and *Entamoeba histolytica*). Most bacterial pathogens (except tuberculosis) and viral pathogens produce a self-limiting disease lasting less than 14 days, irrespective of the symptoms, and the lesions of the gut mucosa may be indistinguishable from those of ulcerative colitis or Crohn’s disease. Syphilis, gonorrhea, and lymphogranuloma venereum also induce proctitis in male homosexuals. HIV diarrhea should be excluded by serologic studies in patients with suspected exposure. Specific additional tests are only used in selected situations.
**Table 4. Main causes of acute colitis**

<table>
<thead>
<tr>
<th>Infections</th>
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<tbody>
<tr>
<td>Bacterial</td>
</tr>
<tr>
<td><em>Salmonella</em></td>
</tr>
<tr>
<td><em>Shigella</em></td>
</tr>
<tr>
<td><em>Campylobacter</em></td>
</tr>
<tr>
<td><em>Escherichia coli</em> (enterohemorrhagic, ...)*</td>
</tr>
<tr>
<td><em>Clostridium difficile</em></td>
</tr>
<tr>
<td><em>Klebsiella oxytoca</em></td>
</tr>
<tr>
<td>Parasitic</td>
</tr>
<tr>
<td><em>Entamoeba histolytica</em></td>
</tr>
<tr>
<td><em>Cryptosporidium</em></td>
</tr>
<tr>
<td>Viral</td>
</tr>
<tr>
<td><em>CMV</em></td>
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</tbody>
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<table>
<thead>
<tr>
<th>Drugs</th>
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</thead>
<tbody>
<tr>
<td>Antibiotics</td>
</tr>
<tr>
<td>Chemotherapy</td>
</tr>
<tr>
<td>Estrogens (ischemia)</td>
</tr>
<tr>
<td>Non-steroidal anti-inflammatory</td>
</tr>
<tr>
<td>Potassium chloride</td>
</tr>
<tr>
<td>Gold compounds</td>
</tr>
<tr>
<td>Cathartic laxatives</td>
</tr>
<tr>
<td>Many rectal preparations</td>
</tr>
<tr>
<td>Ticlopidine</td>
</tr>
</tbody>
</table>

**Inflammatory Bowel Disease versus Infectious Colitis in Patients with a First Attack of Proctitis or Colitis**

Many patients with inflammatory bowel disease of recent onset have just traveled or taken antibiotics, and many have fever, so the past medical history and physical examination often cannot accurately discriminate inflammatory bowel disease from infectious colitis [14]. The macroscopic appearance of the lesions is often similar. Some histologic features probably help to differentiate inflammatory bowel disease from infectious colitis [14–18], for example basal plasmacytosis, crypt distortion, more than two vertical crypt branches, villous mucosa, mucosal atrophy, epithelioid granuloma, and Paneth cell metaplasia. The differential diagnosis on histology is difficult when biopsies are performed in the first 15 days of colitis because at that time only the basal plasmacytosis may be present. If the clinician and histopathologist cannot make a definite diagnosis of inflammatory bowel disease and use the term “unclassified colitis”, the risk of relapse (and thus of inflammatory bowel disease) is about 50% [19].
Table 5. A scheme for the diagnosis of Crohn’s colitis; a simple scoring system may be used and Crohn’s colitis defined as three criteria (++) or one criterion plus granulomata (+️) (from Lennard-Jones [30], with permission)

<table>
<thead>
<tr>
<th>Clinical/endoscopy</th>
<th>X-ray</th>
<th>Biopsy</th>
<th>Operation specimen</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Distribution</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mouth/upper gut</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Anus</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Discontinuous</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><strong>Transmural</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fissuring ulcer</td>
<td></td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Abscess</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Fistula</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><strong>Fibrosis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stricture</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><strong>Histology</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphoid ulcers</td>
<td></td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Lymphoid aggregates</td>
<td></td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Undamaged glands</td>
<td></td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Granuloma</td>
<td>️</td>
<td>️</td>
<td></td>
</tr>
</tbody>
</table>

Ulcerative Colitis versus Crohn’s Disease in Patients with Colitis

It is usually easy to differentiate Crohn’s disease from ulcerative colitis as only Crohn’s disease presents with small intestine involvement, skip lesions, fistulae, or granulomas. However, Crohn’s disease may simulate ulcerative colitis (sometimes for long periods). Thus in some patients the diagnosis may be altered during follow-up from ulcerative colitis to Crohn’s disease when signs appear that are not observed in ulcerative colitis (such as ileal involvement, fistulae, granulomas, and so on). The main reason for making a definitive differential diagnosis is that surgical treatment is (at least classically) not the same for the two diseases; thus the type of surgery generally used in ulcerative colitis is total colectomy with ileo-anal pouch anastomosis, an operation which has for a long time been considered strictly contraindicated in Crohn’s disease [20, 21]. The signs which are taken into account in the differential diagnosis are shown in Table 5.

New biological tests have also recently been proposed. Some investigators have suggested that the immunohistochemical detection of increased expression of CD44 variant 6 (CD44v6) on colonic crypt epithelium is positive in ulcerative colitis but not in Crohn’s disease [22]. However, this has not been confirmed in other trials in which neither colonic nor serum sCD44v6 facilitate the differential diagnosis between ulcerative colitis and Crohn’s disease [23]. Another (and prob-
ably more useful) new tool is based on the presence of serum antibodies. Perinuclear antineutrophil cytoplasmic autoantibodies (P-ANCA) are more often found in patients with ulcerative colitis than Crohn’s disease. On the other hand, antibodies to oligomannosidic epitopes of the yeast *Saccharomyces cerevisiae* (ASCA) are more often associated with Crohn’s disease. In a recent study, the combination of a positive P-ANCA test and a negative ASCA test yielded a sensitivity, specificity, and positive predictive value for ulcerative colitis of 57, 97, and 92.5%, respectively [24], while the combination of a positive ASCA test and a negative P-ANCA test yielded a sensitivity, specificity, and positive predictive value for Crohn’s disease of 49, 97, and 96%, respectively. Interestingly (and fortunately for the patients), recent studies have shown that the functional results of ileo-anal pouch anastomosis in patients with indeterminate colitis or ulcerative-colitis-like Crohn’s disease, or even Crohn’s disease without small bowel and anal involvement [21] do not differ from those in patients with ulcerative colitis, so the debate, although important, may not have dramatic clinical consequences.

**Diagnostic Criteria for Inflammatory Bowel Disease Used in Clinical Trials in Adults**

A common language is necessary in carrying out therapeutic trials on inflammatory bowel disease. There is at present no pathognomonic feature of either Crohn’s disease or ulcerative colitis. The diagnosis of these diseases in clinical trials is based on clinical and pathologic features and the exclusion of alternative disease states. The terms “cryptogenetic colitis” (or proctitis) and “ulcerative colitis” are often used as synonyms; however, there is a tendency to use the term cryptogenetic colitis for the first episode of colitis, and to use the term ulcerative colitis only in patients with chronic (or relapsing) disease. Some authors have proposed classification or scoring systems that allow one to distinguish Crohn’s disease from ulcerative colitis [10, 25, 26] (Table 5), or to determine the probabilities [25, 27–29] but these are rarely used in published reports.

**References**

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Discussion

Dr. Ziegler: I’m just curious about the current status of alternative therapies, like cyclosporine which you mentioned. I believe there are trials of nicotine? Are there other ongoing trials on IL-10 and TNF antagonists?

Dr. Marteau: That’s a difficult question because we haven’t discussed the usual treatment! Briefly, the usual treatment of ulcerative colitis is topical treatment of the mucosa with 5-aminosalicylic acid or 4-aminosalicylic acid, which is very well tolerated and works in about 70% of cases. In the most severe forms of the disease you need to add steroids. In the majority of patients, it’s not very difficult to treat ulcerative colitis. A few cases, say 10–20%, have a resistant form of the disease and in these cases cyclosporine has been used. Its place in ulcerative colitis is to try to save the colon. In severe forms of the disease it is usual to remove the colon if there has been no improvement with steroids and nutritional management after about 5 days. In 80% of such cases you can save the colon with cyclosporine. Unfortunately most require surgery within a year, so the effects are temporary. Nicotine is more effective than a placebo to treat acute episodes but not to prevent relapses.

Treatment of Crohn’s disease is much more difficult. The risk-benefit ratio of the drugs used is not easy to determine. Aminosalicylates are not very effective, with only about 40% efficacy in acute episodes and maybe somewhat more for maintenance treatment. Steroids are very effective for acute episodes, but they are, of course, dangerous in the long term, so we need alternatives. Budesonide has a lower bioavailability and is less efficient than classical steroids at high dosage, but it’s as effective as the classical steroids at medium or low dosage and is better tolerated. For maintenance treatment the main drug is azathioprine. It’s very efficient, about 70% efficacy, but there is 15% intolerance and a 1% risk of excessive immunosuppression. We need to develop alternatives, so there is an important place for new drugs, among which is anti-TNF.

Dr. Alpers: I’d like your comment on the use of the Crohn’s disease activity index. Many of us don’t rely on that for clinical purposes because it so selectively overscores diarrhea, and many of our patients don’t have diarrhea. There are many other scores for Crohn’s disease. Could you comment on the relative value of those and how you think these should be used for the research classification of Crohn’s disease?

Dr. Marteau: Yes, that’s an important question and a very difficult one to answer. In our everyday practice we can tailor our surveillance of the patients to their individual progress. But for research, of course, you need homogeneous groups of patients and you need to use indexes. None of the indexes is perfect. I think the indexes we use in ulcerative colitis are better than those used in Crohn’s disease because the symptoms of ulcerative colitis are nearly always the same. That’s not true for Crohn’s disease, so there are difficulties. Of course, with subgroups of Crohn’s disease patients, for example patients with anal lesions, indexes may be more useful.

Dr. Ferry: There’s also a Pediatric Crohn’s Disease Activity Index which I think has been reasonably well validated [1]. It is weighted a bit more towards growth because it has both height and weight parameters. It’s also weighted a bit more towards laboratory evaluation because it includes hematocrit, albumin, and ESR. Its disadvantage is that the growth parameters are relatively slow to change, requiring 6-month intervals. For research, especially on younger children, it may turn out to be more useful than the adult CDAI.

Dr. Alpers: But it’s interesting that you bring that up because the thing that’s lacking from all the scores that I’ve seen is a longitudinal measure of disease. Somehow I think we have to get that into the score.

Dr. Marteau: Many indexes are only useful in studying the effect of drugs when the endpoint is to obtain remission, which clearly can be defined. The main problem with indexes is the lack of comparability between patients with diseases like Crohn’s disease.
Dr. Ekbom: I want to bring up the question of cancer risk in patients with inflammatory bowel disease. The figures you presented are from historical materials, illustrating a time that’s past. What the Copenhagen group has taught us is that the risk of cancer is affected by the treatment received by the patient. Thus since the introduction of maintenance therapy, there is now reason to believe that the risk of cancer is substantially lower than was previously thought in patients with ulcerative colitis. We have just done a survey in Stockholm which shows that colorectal cancer in patients with ulcerative colitis is currently extremely rare, but the combination of previous Crohn’s disease and colorectal cancer is getting increasingly frequent. We have to alter our risk estimates in future because we are in a dynamic process. The recommendations we are giving currently with regard to surveillance may well not be a good mirror of what’s really happening.

Dr. Marteau: I agree it’s very difficult to state the risk of colonic cancer precisely, but it is certainly higher than in the general population. Maybe the risk has been overestimated but we should not forget there is a risk.

Dr. Ekbom: I don’t think we’ve overestimated the risk previously. It’s just that the risk has been altered by new drug regimens.

Dr. Grimble: The cancer risk was a very interesting facet of your talk. Some studies have shown that 5-aminosalicylic acid actually inhibits NFκB, and works as an anti-inflammatory agent at that level. In terms of the cancer risk, could it be that the treatment of patients is so much better now that antioxidant status is better protected, so the oxidants produced in the inflammatory process are not damaging K-RAS and P53 genes to the same extent?

Dr. Marteau: I’m not certain that the risk is really decreasing. I don’t think we have enough data to prove that. I know the hypothesis that 5-ASA or sulfasalazine may be responsible for reduced cancer risk but it’s certainly not proven yet. We need to be careful that this theory does not push us towards the increased use of maintenance treatment in ulcerative colitis or Crohn’s disease without a sound basis.

Dr. Belli: As pediatric gastroenterologist, I find it not always easy to differentiate between Crohn’s disease and ulcerative colitis early on in the illness. In your opinion, what is the present percentage of adults who are diagnosed as having ulcerative colitis but who in fact have Crohn’s disease? My second question is related. You spoke about mouth ulcers as a sign of ulcerative colitis, but when these are biopsied they often contain granulomas. Hence for me mouth ulcers are more closely related to Crohn’s disease. Do you think this implies that the two diseases occur at the same time in those cases?

Dr. Marteau: The problem of differentiating Crohn’s disease from ulcerative colitis is not a frequent one. The problem arises in cases of Crohn’s disease involving the colon and rectum, without skip lesions. That’s a very rare situation. In such cases you will also find a high proportion in whom there is only one episode so the origin was probably infective. I very much doubt whether as many as 10% of cases of supposed ulcerative colitis turn out to have Crohn’s disease. As to mouth ulcers, probably they are more common in Crohn’s disease but they are seen in ulcerative colitis so they don’t help to differentiate the two diseases. I have no experience with biopsies of oral lesions.

Dr. Jeejeebhoy: There are at least two prospective longitudinal studies that I know of that have shown that patients who have received long-term 5-ASA treatment have a significantly lower incidence of cancer of the colon [2]. This is very much in line with the finding that people taking aspirin on a long-term basis also have a lower incidence of cancer of the colon [3]. There’s some evidence also that giving folate may reduce cancer risk [4]. So I think there’s very strong epidemiological evidence that treatment is altering the risks. In our own unit at St. Michael’s Hospital we’ve got probably 1,800 patients with inflammatory bowel disease who’ve been followed for a mean of about 15 years, and we have only seen 1 case of cancer.

Dr. Marteau: But there is no controlled study showing that there is a decrease in the risk of colonic cancer. It may be a cohort effect.

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Dr. Van Gossum: It’s not proven that endoscopic surveillance can decrease the risk of cancer, so would you really recommend it?

Dr. Marteau: Maybe Dr. Ekbom can answer that. We still write in textbooks of the need to perform endoscopic surveillance because it decreases the risk.

Dr. Ekbom: The surveillance program is probably one of the most difficult things to assess. I must make the point that what we are talking about is not avoiding colorectal cancer; we are talking about avoiding death from colorectal cancer, which is a different outcome. What we found in a retrospective case-control study in Sweden is a clear indication that there is a beneficial effect from entering a surveillance program. However, there is a major problem in keeping patients within the program: it’s hard to get them to the second surveillance endoscopy; it’s very difficult to get them to the third; it’s almost impossible to get them to a fourth. These are the facts of life which we have to face. But this is presently the only thing we have to offer this patient group besides clinical surveillance. We should bear in mind though that we probably will not fulfill the promise that this will avoid death from rectal cancer in all cases.

Dr. Rolandelli: I’d like to offer a surgeon’s perspective on some of the topics that we’ve been discussing.

With regard to colonic surveillance, of course the alternative is a colectomy for many of these patients and that’s proven to be the cure of this disease. A recent meta-analysis of 12 surveillance colonoscopy series involving 1,912 patients found 92 cancers [5]. If the goal of surveillance is to detect how patients evolve from low-grade dysplasia, through high-grade dysplasia to cancer, they should get the surgery before they develop cancer. In fact the programs were successful in only 12% of patients because by the time they were operated on these patients had Dukes C or more advanced cancer and were incurable. Many had a diagnosis of cancer made outside the surveillance program, by CT scan or barium enema for example, so it is debatable how effective it is.

Another issue I want to mention is about pouchitis. It is true that pouchitis can occur in up to 40% of patients, but it’s only a problem in about 5% of patients, when it becomes recurrent. If you study those patients, you often will find a reason for the pouchitis becoming recurrent – for example, some form of stasis in the small intestine, either a pouch outlet obstruction from a mechanical problem or a partial small obstruction; once that is dealt with, the recurrent pouchitis resolves in up to half the patients. There is a small group of patients who eventually may lose the pouch to recurrent pouchitis.

With reference to Crohn’s disease and cancer: during the evolution of surgery for Crohn’s disease we went through a period when we did bypass surgery for fear of complications secondary to resection. We noticed that those patients developed small bowel cancer in the bypass segments. Recently we have tried to minimize this surgery and avoid resection, and in a selected group of patients we can do that by doing strictureplasies. There is already a reported case of cancer developing at a strictureplasty site. It is a matter of concern leaving behind small bowel that’s been diseased for so long.

A last comment is the use of the Crohn’s disease activity index in patients whose chief symptoms are perianal disease. I find that it fairly misleading in those circumstances and I wonder if you have any comments about that?

Dr. Marteau: I agree with all your comments and especially the last one. It has been said already that the CDAI is not a very good index in patients with anal lesions. Of course, the majority of people with severe anal lesions also have severe lesions higher up the gut, so you will find a correlation with the CDAI. But if your endpoint is to cure the anal lesions, then you need to add a special index to describe the lesions, such as the Cardiff system, for example [6].

Dr. Rolandelli: We often fail to show granulomas or histological signs of Crohn’s disease in the anal lesions. We find that sometimes when you treat the disease elsewhere in the small or large bowel the perianal disease gets better, as if it were either an extraintestinal manifestation within the gastrointestinal tract or it has a different pathogenic mechanism.
Dr. Marteau: It really depends on the lesions. Some lesions in the anus can be nonspecific lesions, just due to diarrhea – superficial ulceration, skin lesions and so on – but when you have abscesses, fistulae, deep ulceration coming from the rectum then mostly it’s due to the disease, with superinfection and so on in addition. Your chance of finding a granuloma when you biopsy a Crohn’s lesion is about 30%, not more. Maybe that’s why you didn’t get them.

Dr. Noel: We have noticed a decrease in the incidence of cancer in patients with ulcerative colitis that may be related to treatment, but largely in patients with chronic relapsing disease poorly responsive to therapy. I think the timely colectomy probably has as much to do with the reduction in the incidence of colon cancer as drug treatment.

Dr. Marteau: A study on 130 patients with pancolitis in France showed that even after colectomy there were still cases of colonic cancer. So it still occurs despite surgery. The series was published last year [7].

Dr. Lochs: At this year’s World Congress of Gastroenterology an international working group presented a phenotypic classification of Crohn’s disease, as you might know, and they proposed three categories: age at onset, location of disease, and disease behavior. Would you like to comment on that? Do you think this is useful for the classification of our patients and do you think we should try to use that more often?

Dr. Marteau: Yes, for sure there is a need for classification; people with Crohn’s disease do not all have exactly the same disease, so it’s interesting, for example, to see whether some drugs or treatments are more effective in certain subgroups of patients. At present, treatment does not depend on these classifications, so this classification has no immediate impact for the clinician in my view.

Dr. Van Gossum: The classification mentioned by Dr. Lochs is probably more useful for clinical trials than for everyday practice. Many clinical trials have involved patients with different presentations, which is probably why the results are often contradictory.

Dr. Seidman: I think that your talk is one of the most controversial topics today. The reason I think it’s so important and controversial is because everything that we’ve talked about today – in terms of studies on epidemiology, genetics, immunoregulatory abnormalities, response to treatments – all depend upon a proper diagnosis of ulcerative colitis versus Crohn’s disease. It’s very easy to make a diagnosis of Crohn’s disease but it can be very difficult to make a diagnosis of ulcerative colitis, particularly in children. When people publish studies on genetics or epidemiology, or even on immunology of inflammatory bowel disease, they often cite a 1970 paper stating that they’ve used the standard criteria to make a diagnosis of ulcerative colitis or Crohn’s disease. I maintain that in pediatrics that is inappropriate and inadequate. I’d like to take Dr. Belli’s comments further, that patients who have pancolitis, who have ulcers in their mouth, or who have perianal disease in fact do have Crohn’s disease and if one looks for it, one will find it. It’s all a matter of how much investigation the patient undergoes. Most patients with aphthous ulcers in the mouth also have aphthous ulcers in the stomach, duodenum, or esophagus, and in the 60% who don’t have aphthous ulceration, there is histological evidence of Crohn’s disease in the upper gastrointestinal tract. It’s much more difficult to make a diagnosis of ulcerative colitis, and for study purposes that’s a major point. For example, for study purposes the diagnosis is sometimes made on the basis of the last colonoscopy, but we know that in patients with ulcerative colitis treated with topical 5-ASA the rectum is no longer histologically abnormal. Furthermore, people don’t use standard criteria. For example, a patient could have superficial pancolitis microscopically, but with the cecum and ascending colon more severely involved than the rectum and sigmoid; if you took a census in this room I’m sure you would find that people would disagree on the ultimate diagnosis of that type of colitis.

Dr. Marteau: The more signs you have, the easier it is. It’s very difficult to stick Crohn’s or ulcerative colitis labels on patients, but as a clinician I would say that it’s not very important most of the time. It’s very important for research, and it’s important for the clinician...
when considering surgery. But when you consider the usual medical treatment, most of the
time we can treat patients with inflammatory bowel disease without knowing whether it’s
Crohn’s disease or ulcerative colitis.

Dr. Ferry: One of the other factors that we need to take into account in pediatrics is the
broad age range we see, from birth up to 18 or 20 years of age. We may need to stratify the
disease by age range, perhaps pre- and postpuberty. There’s always been a view that really
young patients, 5 or 6 years of age, may be more difficult to treat, but as you know many
publications just list the entire age range without breaking it down. This is something we
need to be thinking about in the future.

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