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Colonoscopy of Acute Colitis

A Safe and Reliable Tool for Assessment of Severity

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Complications that might lead to surgery in severe attacks of ulcerative colitis have been found to be correlated with the depth of colonic ulcerations as measured by pathological examination of colectomy specimens. In order to evaluate the value of colonoscopy for the assessment of colonic ulcerations, we have reviewed the clinical, biological, colonoscopic, and anatomical findings in 85 consecutive patients with attacks of ulcerative colitis involving at least the rectosigmoid and part of the descending colon, seen in our center between 1981 and 1989. All had colonoscopy performed by a senior endoscopist at entry. Extensive deep colonic ulcerations were diagnosed in 46 of them, and moderate endoscopic colitis in 39. No complication related to colonoscopy occurred except for one colonic dilatation. Forty-three of the 46 patients with severe endoscopic colitis were operated upon: 38 of them failed to improve with high-dose corticosteroids and five had a toxic megacolon. Extensive ulcerations reaching at least the circular muscle layer were found at pathological examination of colectomy specimen in 42 of the 43 patients. Conversely, 30 of 39 patients with moderate endoscopic colitis went into clinical remission with medical treatment, and only nine patients needed further surgery because of medical treatment failure. Six of these nine patients underwent another colonoscopy prior to colectomy, and all six showed features of severe endoscopic colitis. Deep ulcerations reaching the circular muscle layer were found at pathological examination in five of these six patients and in one additional patient whose colonoscopy had been performed 21 days before colectomy. We conclude that, in expert hands, colonoscopy is safe and accurately selects patients with high risk of surgical complications who need early surgery in case of failure of medical treatment.

KEY WORDS: ulcerative colitis; colonoscopy; pathology; acute colitis.

The management of severe attacks of ulcerative colitis (UC) remains difficult. The main question is indication and time of colectomy. Although it is well accepted that patients with severe attacks of UC should be managed initially medically, numerous studies have clearly demonstrated that in nonresponding patients, early surgery is necessary to avoid high rates of morbidity and mortality (1). For most authors, colectomy is indicated in patients selected by the clinical and biological severity criteria proposed by Truelove and Witts (2) and others (7) and unresponsive to intensive medical therapy. Nevertheless, Buckell et al (8) have shown that in patients colectomized for toxic megacolon, perforation, or failure to improve with drug therapy, clin-

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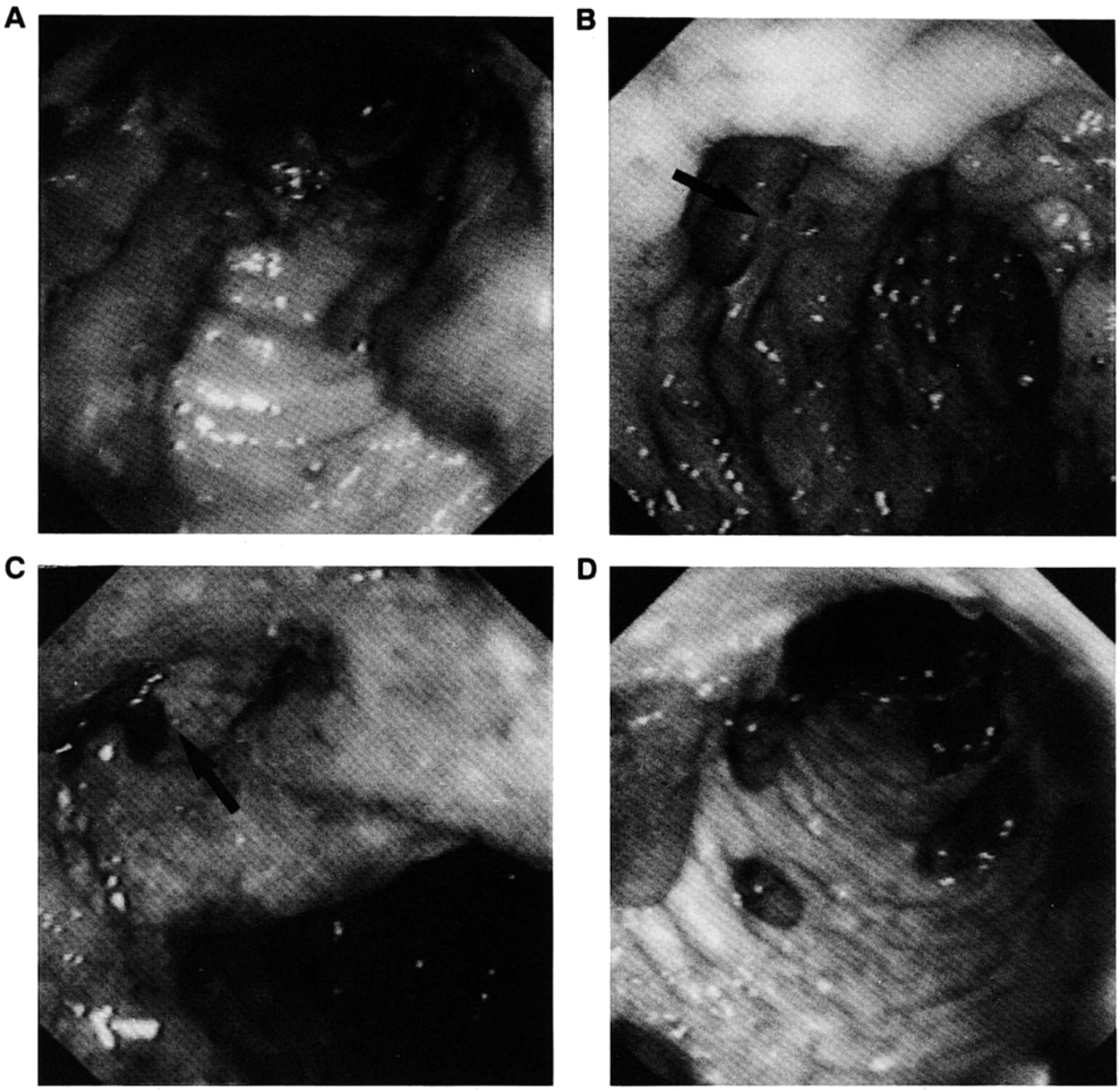

Fig 1. Severe colonoscopic lesions. (A) deep and extensive ulcerations, bounded by swollen mucosa. (B) Mucosal detachment (arrow), which could be demonstrated by insertion of the biopsy forceps under the edge of the ulceration. (C) Well-like ulcerations (arrow), visible as very deep ulcerations with a small diameter. (D) Large mucosal abrasions, formed by the junction of several deep ulcerations.

ical and biological criteria were poorly indicative of depth of colonic ulcerations, which correlated well with complications and prognosis. Thus, there is obviously a need for a direct assessment of the severity of colonic lesions in such patients. Plain abdominal radiographs can show colonic wall alterations, but the typical images are often difficult to recognize and may be missing. In a study of 11 patients with UC attacks, it has been suggested that extensive undermining of the mucosa on barium enema carried a poor prognosis (9). Colonoscopy is now the most sensitive method for assessing colonic mucosal lesions. Since 1981, it has been routinely performed at entry for all patients with acute attacks of UC admitted to our department. The aims of this study were to evaluate the safety of colonoscopy in such circumstances, to determine its accuracy by comparing endoscopic to pathological findings in colectomized patients, and to assess its usefulness for decision making.

MATERIALS AND METHODS

Patients. We reviewed medical records of the 85 patients admitted to our department between 1981 and 1989 for an attack of presumed UC involving at least the rectosigmoid and part of the descending colon. The preoperative diagnosis of UC rested on the following criteria: negative stool examination for bacteria and parasites at the first attack, no evidence of anal or small bowel involvement, rectal involvement, continuous rectocolonic lesions with no interval of normal mucosa on endoscopy, no granulomas on biopsy specimen, and no previous diagnosis of Crohn's disease. According to the pathological study of colectomy specimens, the diagnosis of UC was maintained in 15 of the 52 operated cases, 17 patients were considered as unclassified colitis, and 20 as possible Crohn's disease. However, the follow-up of the 52 colectomized patients (median duration four years) revealed only three overt cases of Crohn's disease. All the 85 patients were thus kept in the study because they initially presented as UC.

Colonoscopy. All colonoscopies were performed by a senior endoscopist belonging to our department. After the absence of pneumoperitoneum had been checked, patients received 3–4 liters of PEG-4000 solution given orally or through a nasogastric tube. Tolerance of the first liter of PEG was assessed before the rest of the solution was given. The presence of at least one of the following signs in any segment of the rectocolon defined severe endoscopic colitis (SEC): (1) extensive deep ulcerations, (2) mucosal detachment on the edge of these ulcerations, (3) well-like ulcerations, and (4) large mucosal abrasion (Figure 1). These lesions were always located in an area of continuous inflammatory process and could be associated with less severe lesions (see description above) and pseudopolypi. Conversely, colonoscopic moderate lesions were defined as: (1) erythematous and swollen mucosa, (2) superficial ulcerations, and (3) deep ulcerations covering less than 10% of the mucosal area. The diagnosis of moderate endoscopic colitis (MEC) was made in the presence of one or several of these signs, and exclusion of any sign indicative of SEC. The endoscopic criteria of severity were defined by one of us (A.B.) before the beginning of this series, on the basis of his preliminary experience. Endoscopic data were reviewed from colonoscopy reports which, in our center, always mention the diagnosis of SEC or MEC. As seen later, total colonoscopy and ileoscopy were often attempted in order to distinguish between CD and UC. In patients with acute colonic dilatation (transverse colonic diameter exceeding 7 cm), colonoscopy was not attempted beyond the splenic flexure.

Clinical and Biological Severity Criteria. The following clinical and biological criteria of severity were quoted at the moment of colonoscopy: (1) "severe diarrhea," ie, the emission of at least six bloody motions daily; (2) fever (mean evening body temperature exceeding 37° 5 C or a temperature of 37° 8 C or more on at least two days out of four); (3) tachycardia (mean pulse rate of more than 90/min); (4) anemia (hemoglobin less than 75% of normal value); (5) erythrocyte sedimentation rate of more than 30 mm/hr; and (6) serum albumin lower than 35 g/liter. Truelove and Witts' criteria of severe colitis were defined as the combination of the first five criteria listed above (2) and the modified Oxford criteria as the combination of "severe diarrhea" with one or several of the other criteria (11).

Outcome of Patients. Response to medical treatment and need for colectomy were reviewed. Decision for surgery was made by the same medicosurgical team, taking into account clinical and biological, radiological, and endoscopic severity criteria at entry and failure to improve under medical treatment, ie, high-dose corticosteroids (1 m/kg of prednisolone equivalent during at least five days), with or without total parenteral nutrition. In colectomized patients, mortality and morbidity was analyzed as well as further operative procedures performed and occurrence of lesions indicative of Crohn's disease.

Pathological Examination of Colectomy Specimens. Colectomy specimens were fixed in 10% buffered formalin, routinely processed, and stained with hematein eosin safran (HES). All colectomy specimens were reviewed by the same pathologist (A.L.), without knowledge of the endoscopic diagnosis. At least 15 regularly distributed samples of the colectomy specimen were examined for each patient. For each area of the colon, the deepest ulcerations were considered and graded according to the scale of Buckell et al (8): grade A, ulcerations confined to the mucosa; grade B1, ulcerations involving a part of the submucosa; grade B2, ulcerations involving the entire thickness of the submucosa; grade C1, ulcerations involving a part of the circular muscle coat (Figure 2); grade C2: ulcerations involving the whole thickness of the circular muscle coat or the longitudinal muscle; and grade D: ulcerations extending beyond the outer part of the circular muscle coat. Colectomy specimens exhibiting grade B2, C1, C2, or D ulcerations were considered to indicate a severe anatomical colitis (SAC), and those with grade A or B1 ulcerations to indicate a moderate anatomical colitis (MAC). Colonoscopic findings were compared in a blinded fashion to the depth of ulcerations in colectomy specimens. For those patients who underwent two colonoscopies, comparisons between anatomical and endoscopic findings were made with the latest colonoscopy.

Statistical Analysis. Clinical characteristics of MEC and SEC patients were compared using χ^2 and Student's t tests, when appropriate. Five percent was considered as the level of significance value. Values were expressed as mean ± standard deviation (SD).

RESULTS

Colonoscopy

According to our criteria, 46 cases of SEC and 39 cases of MEC were diagnosed. Six patients whose first colonoscopy indicated MEC underwent another colonoscopy, 9–25 days after the first one, because of medical treatment failure; this second colonoscopy indicated SEC in all cases. However, these six patients are classified as MEC. Clinical

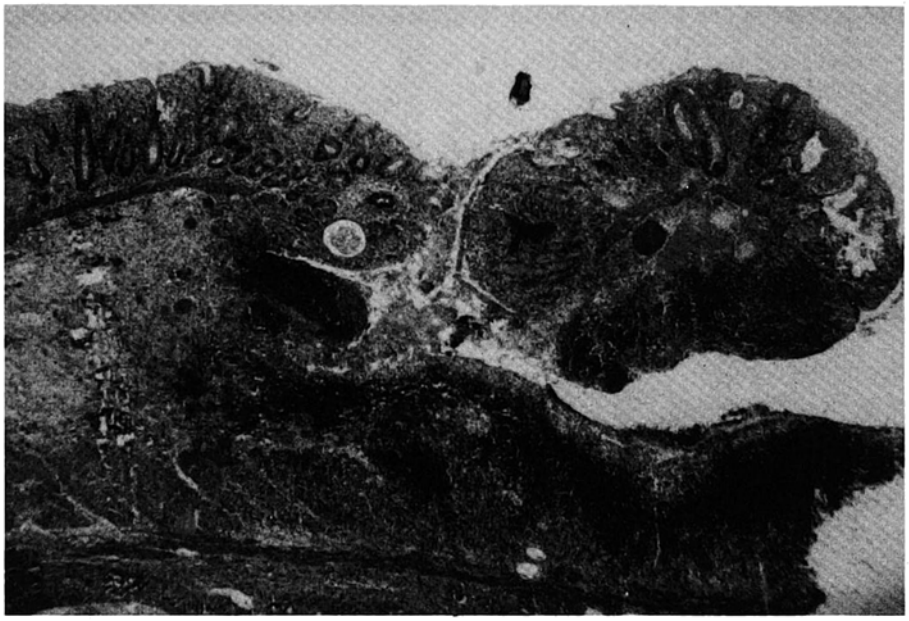

Fig 2. Deep ulceration reaching circular layer of muscularis propria with wide detachment along submucosa. HES ×70.

characteristics of the 85 patients are summarized in Table 1.

Patients with SEC. No complication related to colonoscopy occurred in this group except for one patient who developed an acute colonic dilatation 24 hr after colonoscopy. This patient was colectomized, and his postoperative course was uneventful; pathological examination of his colectomy specimen disclosed extensive grade D ulcerations. Among the 46 patients with SEC, colonoscopy reached the ileum in 18 cases (39%), the cecum in 34 (74%), the transverse colon in 36 (78%), and the splenic flexure in 46 (100%). Colonoscopy revealed deep and extensive ulcerations in 43 of the 46 cases (93%), mucosal detachment in 14 (30%), large mucosal abrasion in 12 (26%), and well-like ulcerations in 8 (17%). Figure 3 shows the distribution of endoscopic lesions along the colon. Twelve of the 34 patients who underwent complete colonoscopy (35%) were found to have endoscopic pancolitis.

Patients with MEC. No complication related to colonoscopy occurred in these patients. Among the 39 patients with MEC, colonoscopy reached the ileum in 25 (64%) and the cecum in 39 (100%). Colonoscopy disclosed erythematous and swollen mucosa in all patients, superficial ulcerations in 30

TABLE 1. CLINICAL CHARACTERISTICS OF PATIENTS WITH SEVERE OR MODERATE ENDOSCOPIC COLITIS

	SEC (N = *46*)	*MEC* (N = *39*)	P
Age (years)	38 ± 16	31 ± 10	0.02
Sex (F/M)	1.4	1	NS
First attacks	16 (35%)	10 (25%)	NS
Length of history (years)	4.7 ± 8.2	3.5 ± 4.0	NS
Duration of the attack (weeks)	8.9 ± 7.1	9.9 ± 10.6	NS
Patients referred from another hospital	21 (46%)	5 (13%)	<0.01
High-dose steroids prior to admission (>5 days)	28 (61%)	9 (23%)	<0.01

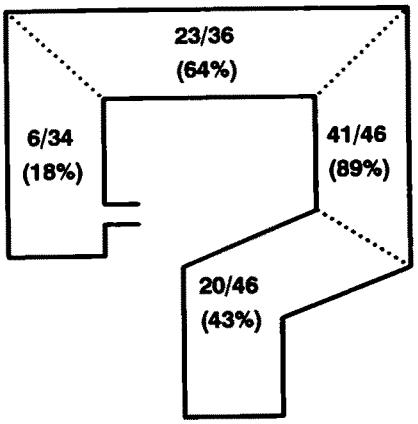

Fig 3. Distribution of severe endoscopic lesions along the colon. For each colonic segment, the number represents the proportion of severe lesions among cases examined by colonoscopy.

TABLE 2. COMPARISON OF CLINICAL AND BIOLOGICAL SEVERITY CRITERIA WITH COLONOSCOPIC SEVERITY CRITERIA WITH PATHOLOGICAL EXAMINATION OF COLECTOMY SPECIMENS IN OPERATED PATIENTS (N = 52)

Ulceration depth	*Truelove and Witts' criteria*	*Modified Oxford criteria*	*SEC (N = 49)*	*MEC (N = 3)*
Grade A (*N* = 2)	0	0	0	2
Grade B1 (*N* = 2)	0	0	2	0
Grade B2 (*N* = 12)	1	9	12	0
Grade C1 (*N* = 33)	7	23	32	1
Grade C2 (*N* = 1)	0	0	1	0
Grade D (*N* = 2)	0	0	2	0

(77%), and deep but nonextensive ulcerations in three (8%). Nineteen of the 39 patients (49%) were found to have pancolitis.

Clinical and Biological Severity Criteria

Truelove and Witts' criteria of severe colitis were found in 8/46 patients with SEC (17%) and the modified Oxford criteria in 30/46 (65%) (Table 2). In 28 of the 46 patients with SEC, clinical and biological criteria were recorded after high-dose corticosteroids had been started. Among the patients with MEC, two patients displayed the Truelove and Witts' criteria of severe colitis (5%), and 16 had the modified Oxford criteria (41%).

Outcome of Patients

Patients with SEC. Only three patients (7%) rapidly improved under intravenous high-dose corticosteroids (methylprednisolone or hydrocortisone hemisuccinate) and were not operated. Among them, a 65-year-old woman with long-standing UC and cryptogenic cirrhosis experienced a relapse 16 weeks later and died of sepsis; no colonoscopy or autopsy was performed. Forty-three of the 46 patients with SEC were colectomized (93%), and there was no death in this group. Thirty-eight of these patients were operated upon after they had failed to improve under high-dose corticosteroid treatment, often started before referral and given either orally (prednisolone, $N = 10$) or parenterally (intravenous methylprednisolone or hydrocortisone hemisuccinate, $N = 22$; intramuscular betamethasone, $N = 6$) at a dose equivalent to 1 m/kg prednisolone. Five other patients were emergently colectomized because they presented at entry with a toxic megacolon. For the whole SEC group, the mean interval between colonoscopy and surgical intervention was 3.7 ± 5.4 days (range 0–15 days); 34 of the 46 patients with SEC (74%) had colectomy within five days after colonoscopy. Emergency surgical operations were: colectomy sparing the rectum with provisional ileostomy and sigmoidostomy in 33 (77%), ileal pouch anal anastomosis in seven patients (16%), and proctocolectomy with ileostomy in three (7%). Thirteen of the 43 patients (30%) had complications after surgery: acute intestinal obstruction ($N = 5$), perineal abscess ($N = 1$), hemoperitoneum ($N = 1$), sigmoidostomy leakage ($N = 1$), massive hematochezia ($N = 1$), gram negative septicemia ($N = 2$), and pulmonary embolism ($N = 2$). Among the 33 patients who underwent a colectomy sparing the rectum, 18 later had an ileorectal anastomosis, eight had an ileoanal anastomosis, and four had a permanent ileostomy; due to persistent severe lesions of the rectum, continuity was delayed in three, who still had an ileostomy and sigmoidostomy. None of the operated patients has been so far lost to follow-up (4–122 months, median duration: 48 months). Only three patients experienced a clinical recurrence consisting of anal lesions, suggesting the diagnosis of Crohn's disease.

Patients with MEC. Twenty-nine of 39 patients with MEC (74%) went into complete clinical remission on medical treatment. Among these patients, 29 (74%) were given oral prednisone, while the other 10 (26%) were treated by 5-aminosalicylates with ($N = 5$) or without ($N = 5$) steroid enemas. Nine patients were operated upon: three of these patients were dependent on corticosteroids, two of them underwent a colectomy sparing the rectum (with a subsequent ileorectal anastomosis in one case and an ileal pouch anal anastomosis in one case), and one patient underwent a proctocolectomy with ileal pouch anal anastomosis (interval between colonoscopy and colectomy: 9–21 days). Six patients were resistant to corticosteroids and underwent a preoperative colonoscopy, which showed features of SEC in all instances (deep and extensive ulcerations in five, mucosal detachment in two, mucosal abrasion in one); five of these six patients underwent a colectomy sparing the rectum with a subsequent ileorectal anastomosis, and one patient had a proctocolectomy with a permanent ileostomy. No complication occurred among the nine operated patients.

Pathological Examination of Colectomy Specimens

Among the 49 operated patients with the final diagnosis of SEC (including the six patients whose first colonoscopy disclosed features of MEC), 47

TABLE 3. FREQUENCY OF CLINICAL AND BIOLOGICAL SEVERITY CRITERIA IN PATIENTS WITH SEVERE ENDOSCOPIC COLITIS (SEC) AND WITH MODERATE ENDOSCOPIC COLITIS (MEC)

Criteria	*SEC*	*MEC*
Severe diarrhea	0.70	0.51
Fever	0.67	0.28
Tachycardia	0.63	0.41
Anemia	0.35	0.20
ESR > 30 mm	0.74	0.54
Albuminemia < 35 g/liter	0.93	0.64
Truelove and Witts' criteria*	0.17	0.05
Modified Oxford criteria	0.65	0.41

*All the five criteria present.

were classified as SAC (grade B2, $N = 12$; grade C1, $N = 32$; grade C2, $N = 1$; grade D, $N = 2$) and two as MAC (grade B1) (Table 3). Of the five operative specimens from patients with acute colonic dilatation, three showed grade C1 ulcerations and two grade D lesions. Among the three operated patients with the final diagnosis of MEC, two were classified as MAC (grade A) and the other one as SAC (grade C1). In the latter case, colonoscopy had been performed 21 days before colectomy. The distribution of severe anatomic lesions along the different colonic segments is shown in Figure 4. Clinical and biological severity criteria in both patients with SAC and MAC are shown on Table 3.

DISCUSSION

To our knowledge, this study is the first to describe precisely endoscopic lesions observed in patients with severe attacks of UC and to investigate the safety, accuracy, and usefulness of colonoscopy in the management of such patients. Owing to the potential risk of perforation and toxic megacolon, several authors consider that colonoscopy is contraindicated in severe attacks of colitis (12–15). In spite of this, Alemayehu and Jarneröt recently reported that 14 patients with severe UC lesions underwent complete or partial colonoscopy without complications (10). In the present series of 85 patients with attacks of UC, including 48 patients with severe colonic lesions, no perforation occurred after colonoscopy. One patient developed acute colonic dilatation the day after colonoscopy, and this complication is possibly related to the procedure; pathological examination of the colectomy specimen showed ulceration reaching the serosa which, in any case, warranted emergency colectomy. The need for total colonoscopy can be questioned since, as shown in Figure 3, 92% of the SEC lesions have been disclosed by colonoscopy up to the splenic flexure. In the present study, total colonoscopy was often attempted in order to rule out the diagnosis of obvious Crohn's disease, whose response to medical treatment is better (7). However, total colonoscopy is probably not mandatory for patients in whom the diagnosis of UC has been previously firmly established. In such patients, colonoscopy could be stopped as soon as severe lesions have been discovered.

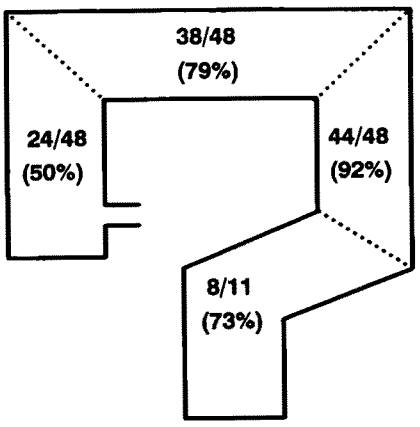

Fig 4. Distribution of severe anatomic lesions along the colon on colectomy specimens. For each colonic segment, the number represents the proportion of severe lesions at pathological examination.

The comparison of endoscopic with anatomical findings in operated patients demonstrates the accuracy of colonoscopy in the assessment of severity of lesions. The diagnosis of SEC in 43 patients correctly predicted the severity of anatomical lesions in 42, hence a positive predictive value of 42/43 (0.98); furthermore, all occurrences of acute colonic dilatation were found in this group. On the other hand, the value of colonoscopy cannot be evaluated in patients with MEC due to the lack of operative specimens in the majority of them. However, it is probable that most of these patients were free of severe anatomical lesions since 75% of them responded to standard medical therapy, consisting of 5-aminosalicylates in 25%, and no acute colonic dilatation or other surgical complications occurred in this group. A second colonoscopy performed because of corticosteroid resistance in six patients showed a definite worsening of the colonic mucosa pattern and lesions of SAC were found in five patients.

By comparison to colonoscopy, clinical and biological severity criteria were less predictive of severe anatomical lesions since only eight of 49 (16%)

patients with SAC fulfilled all five criteria of Truelove and Witts and 32 of 49 (65%) the modified Oxford criteria (Table 3). However, these criteria are probably best adapted to patients seen early in an attack of UC, and not to the increasing number of patients seen at referral centers from other centers, after they failed to improve on corticosteroids. In these patients, the initial clinical and biological severity is not well known, and it is often difficult to choose between colectomy and continuation of medical treatment. Our study suggests that colonoscopy might be very useful in such circumstances. Because colonoscopy correctly predicts severe anatomical lesions and thus selects patients at high risk of developing complications (8), it might help the clinician in deciding on colectomy. Conversely, since most patients with MEC respond to standard therapy, the finding of mild endoscopic lesions should lead to the continuation of medical treatment. It cannot be stated, however, that all patients with MEC will enter into remission and will not need further surgery since 25% of them ultimately underwent surgery. It is noteworthy that among the nine patients with MEC who required colectomy, a second colonoscopy, performed in six cases, disclosed SEC in all instances, five of them showing SAC lesions. These recommendations are consistent with the results of Alemayehu and Jarneröt, who have studied 34 patients with attacks of UC fulfilling Truelove and Witts' criteria and were resistant to intensive corticosteroid treatment. They were submitted to colonoscopy, and surgical intervention was postponed in the 17 patients with mild endoscopic lesions and 12 of them eventually improved. Management of these patients according to Oxford criteria alone would have led to undue colectomy. It is unlikely that any of the usual adjuvant treatments would have been useful in our patients with corticosteroid-resistant SEC since several controlled studies have proven the inefficiency of total parenteral nutrition in patients with UC (7, 16, 17) and of antibiotics in severe acute colitis (11, 18). Due to its long delayed action, azathioprine is of little value in severe colitis (19). Furthermore, total absorption of oral prednisolone is similar in acute colitis patients and healthy volunteers (20), thus, it is likely that the parenteral route of administration of steroids does not confer a significant advantage comparing to the oral route. Recently, a randomized placebo-controlled trial of intravenous cyclosporine has given very encouraging results in severe attacks of UC (21). Consequently, this drug must be now considered as an option in patients who failed to improve with high dose corticosteroids. Obviously, some of our patients would have been potential candidates for this drug.

Although we only selected patients who presented with the least disputable signs of UC, many cases were classified after the pathological examination of colectomy specimen as indeterminate colitis or even possible Crohn's disease (only one patient exhibited granuloma). This result is not surprising, as it is well known that disease activity greatly affects the assessment of pathological features (22), especially in severe acute colitis. In spite of this high prevalence of possible Crohn's disease and unclassified cases, follow-up of operated patients eventually showed a small proportion with unequivocal Crohn's disease. We decided to maintain these cases in the present study because they presented with all the criteria of UC at entry and were treated like the other patients.

In conclusion, the present study indicates that, in expert hands, colonoscopy is safe and provides a reliable tool to assess the severity of colonic lesions in acute attacks of UC. In our opinion, colonoscopy is especially useful for patients already treated by steroids and/or who failed to respond to intensive medical therapy, in order to select candidates for prompt colectomy. Total colonoscopy is not mandatory for patients in whom the diagnosis of UC has been previously firmly established; it could be stopped as soon as severe lesions have been discovered. Yet the question of whether endoscopic criteria of severity *per se* should indicate colectomy, before assessing the clinical response to corticosteroids and possibly cyclosporine, has to be answered in further studies.

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