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DIFFERENCES IN PATHOGENESIS, INCIDENCE AND OUTCOME OF PERFORATION IN INFLAMMATORY BOWEL DISEASE

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PERFORATION is an uncommon but lethal complication of inflammatory intestinal disease. It occurs more frequently in ulcerative colitis than in Crohn's disease irrespective of whether the latter originates in the small or large intestine. Despite early reports to the contrary (1), perforation in ulcerative colitis is usually preceeded by colonic dilation (2–6). In Crohn's disease, perforation without dilation of the small or large intestine is more common (7). The incidence and outcome of perforation with and without toxic megacolon in the two forms of inflammatory intestinal disease are compared herein.

MATERIAL AND METHODS

The records of 1,623 patients with inflammatory intestinal disease admitted to The Mount Sinai Hospital between 1960 and 1980 were reviewed retrospectively: there were 613 patients with ulcerative colitis (UC) and 1,010 with Crohn's disease (CD). Of the patients with CD, 457 had ileocolitis (IC), 166 had Crohn's colitis (CC) and 387 regional enteritis (RE). Seventy-five patients had colonic dilation, 61 with UC and 14 with CD, and 29 patients with UC and 20 patients with CD had either a free or sealed off perforation.

DEFINITIONS

The diagnosis of granulomatous disease was based upon criteria published previously (8–10). The clinicopathologic diagnosis of ulcerative colitis was made on the basis of mucosal colitis extending proximally from the rectum in the absence of transmural disease, fissures, fistulas or skip areas. Free perforation was defined as spontaneous rupture of the small or large intestine with spillage of intestinal contents into the general peritoneal cavity and resulting peritonitis. A sealed perforation was occasionally recognized preoperatively as a tender palpable mass and established at laparotomy as an area of localized perforation sealed by adherent mass of omentum or peritoneum. Toxic dilation was based upon criteria similar to that described in one study (4) and included one or more of these findings: abdominal distension, signs of peritonitis, temperature of more than 101 degrees F., tachycardia of more than 120 per minute and a leukocyte count of more than 11,000 white blood cells per millimeter cubed. The diagnosis of colonic dilation was accepted if the colon measured 6.0 centimeters or more in diameter on a roentgenogram or 6.5 centimeters in diameter on barium enema. Mortality was defined as a death occurring during the same hospital admission. Analysis of the ulcerative colitis and Crohn's disease data (Table I) was calculated using the programmed 2 XK chi square contingency table of a 9815A Hewlett-Packard calculator.

RESULTS

Perforation in ulcerative colitis. Twenty-nine of 613 patients with ulcerative colitis (4.7 per cent) sustained a perforation (Fig. 1). Twenty-two of these occurred among 61 patients with toxic dilation (TCD) (36 per cent). Seven occurred among the remaining 552 patients without toxic dilation (1.3 per cent).

Thirteen of 29 patients with UC died; nine of 22 with TCD and four of seven without TCD. Among the patients with TCD, 13 sustained a free perforation with five deaths and nine a sealed perforation with four deaths. Thus, the mortality was similar for patients with and without toxic colonic dilation and was also similar irrespective of whether the perforation was free or sealed at the time of operation. All patients with free perforation except one were operated upon within

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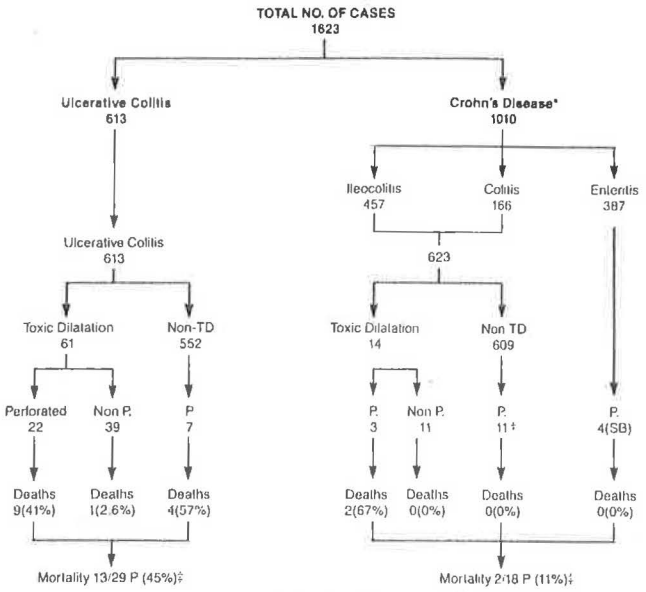

FIG. 1. Comparison of the incidences of perforation and mortality in 613 patients with ulcerative colitis and 1,010 patients with Crohn's disease. *, Two additional deaths in perforation in recurrent disease in ileocolitis, one in the small intestine and one in the colon. †, Ten colonic (one with two ileal perforations), one small intestine. ‡, In perforated instances (excluding recurrent disease *).

one to nine hours of the presumed perforation, whereas the patients with a sealed perforation had severe symptoms for an average of two days before operation.

In UC without colonic dilation, massive bleeding developed in four patients with perforation who later died. Three had a decreased platelet count and increased partial thromboplastin time consistent with disseminated intravascular coagulation (DIC). By contrast, DIC developed in only two of nine patients with a perforated UC and toxic colonic dilation who later died. Perforation in patients with toxic megacolon was likely to be multiple and occured predominantly (52 per cent) in the transverse colon including the hepatic and splenic flexures; 20 per cent occurred in the sigmoid colon.

Perforation in Crohn's disease. A free perforation developed in twenty of 1,010 patients with Crohn's disease (2 per cent) (Table II and Fig. 1). Fourteen occurred among 623 patients with colonic involvement (CDC), four developed in 387 patients with regional enteritis (RE) and two patients had perforations through areas of recurrent disease (one in the ileum proximal to an ileostomy and one in the sigmoid colon). Toxic dilation occurred in 14 of 623 patients with CDC and colonic involvement (2.24 per cent); five occurred in ileocolitis (1.1 per cent) and nine in granulomatous colitis (5.4 per cent). Perforation occurred in three of 14 patients with CDC and toxic dilation. One perforation was free and two were sealed. The two patients with sealed perforations and toxic colonic dilation died. The one patient with the free perforation survived.

Among the 609 patients with CDC, spontaneous free perforation with peritonitis occurred in an additional 11 patients (nine in the colon alone, one in the ileum alone and one synchronously in the ileum and colon) without mortality. Seven were single perforations; one had four simultaneous synchronous perforations of ascen-

TABLE I.—A COMPARISON OF INCIDENCES OF TOXIC MEGACOLON, PERFORATION AND MORTALITY IN ULCERATIVE COLITIS AND CROHN'S DISEASE

	U.C.	*Per cent*	*C.D.*	*Per cent**	*C.D.C.*	*Per cent†*	X^2	*P value*
Toxic megacolon								
UC versus CD	61/613	10	14/1010	1.4			63.49	0.001
UC versus CDC	61/613	10			14/623	2.2	30.1	0.001
UC versus CC	61/613	10			9/166	5.4	3.28	NS†
UC versus IC	61/613	10			5/457	1.1	35.49	0.001
Perforation								
All	29/613	4.7	20/1010	2.0			9.9	0.005
Colon	29/613	4.7			13/623	2.1	6.2	0.02
Of TM	22/613	3.6			3/623	0.5	14.4	0.005
In TM‡	22/61	36			3/14	21	2.83	NS
Mortality								
Perforation of colon	13/613	2			3/623	0.5	6.3	0.02
Free perforation, no TM	4/7	57			0/10	0	7.47	0.01
Free perforation§, no TM	4/7	57	0/15	0			10.47	0.005
Perforation in TM	9/22	41			2/3	67	0.71	NS
All primary perforation	13/29	45	2/18	11			5.81	0.02
All perforations[a]	13/29	45	4/20	20			3.22	NS[b]

UC, Ulcerative colitis, 613 patients.
*CD, Crohn's disease, 1010 patients.
†CDC, Crohn's colitis (CC) and ileocolitis (IC), 623 patients.
‡TM, Toxic megacolon, 75 patients—61 UC and 14 CDC.
§Free perforation without toxic megacolon in 20 patients.
[a]Includes two mortalities in recurrent Crohn's disease.
[b]Failed to reach statistical significance.

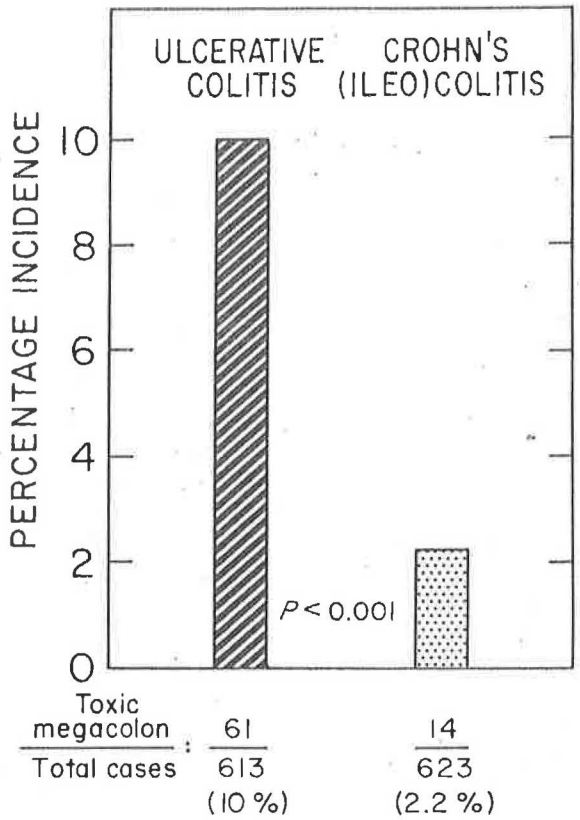

FIG. 2. A significant greater incidence of toxic megacolon in ulcerative colitis than in Crohn's disease involving the colon is shown (Crohn's disease and ileocolitis).

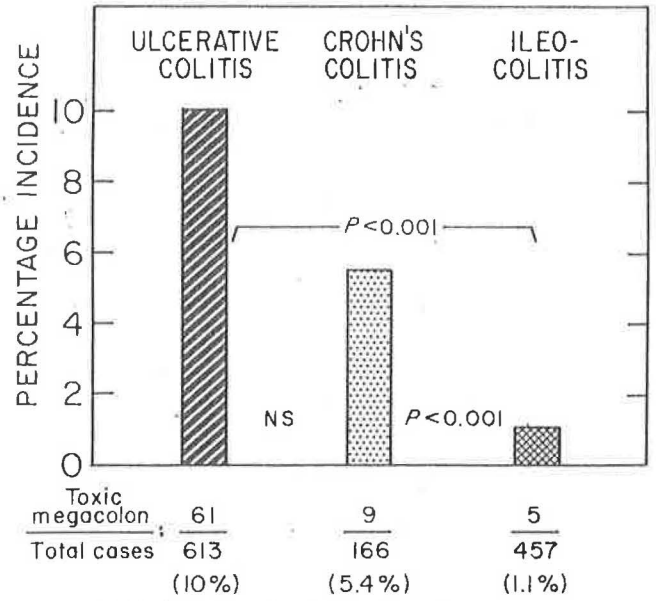

FIG. 3. Toxic megacolon is significantly more common in ulcerative colitis than in ileocolitis and Crohn's colitis than in ileocolitis. Although the incidence is approximately twice as high in ulcerative colitis than in Crohn's colitis, a significant difference could not be demonstrated.

ding, transverse, descending and sigmoid colon, and one had metachronous perforations each in the descending colon.

Four of 383 patients with regional enteritis (1.04 per cent) sustained a spontaneous free perforation. Two occurred in the jejunum in jejunoileitis and two in the ileum in regional ileitis. All four patients had evidence of dilation with stricture distal to the site of perforation. Three had a segmental small intestine or ileocolic resection and one resection with ileostomy and distal mucous fistula. The latter underwent subsequent successful reanastomosis. The four patients survived, as did the patient with synchronous ileal and colonic perforations. Thus, the 15 patients with spontaneous free perforation with peritonitis without toxic colonic dilation in CD all survived; this compares favorably with two deaths among three patients with toxic dilation in Crohn's disease and nine deaths among 22 patients with toxic colonic dilation in UC.

Management of patients with perforation. Nine of 11 patients with colitis or ileocolitis in Crohn's disease had resection with a proximal diverting ileostomy in eight and a colostomy in one. The other two had suture and proximal colectomy and exteriorization with proximal colostomy, respectively.

A comparison of the incidence of toxic megacolon in UC and CD. In this series, the incidence of toxic megacolon was significantly greater in UC than in CD (Fig. 2), CDC or IC (Fig. 3). In addition, the incidence of toxic megacolon was significantly greater for Crohn's colitis when compared with patients with ileocolitis (nine of 166 versus five of 457, DF=1; $X^2=10.38$; $p<0.001$) (Fig. 3). However, when patients with disease confined to the colon were compared, although colonic dilation in UC was almost twice as common as in CC (UC 10 versus CC 5.4 per cent) a significant difference in TCD could not be demonstrated (Fig. 3) (Table I).

A comparison of perforations of large or small intestine. In UC, the incidence of perforation was

TABLE II.—PERFORATION IN CROHN'S DISEASE ALL CROHN'S DISEASE 20 OF 1,010

—COLITIS AND ILEOCOLITIS— N=16 of 623		—REGIONAL ENTERITIS— N=4 of 387	
Site	*No.*	*Site*	*No.*
Ileum	1	Ileum	2
Colon*	10	Jejunum	2
Colon with TM (2†)	3		
Recurrent disease (2‡)	2		

*One with two concomitant ileal perforations.
†Mortalities: 2 of three in toxic megacolon-sealed perforations.
‡Both with recurrent disease-free perforations (one ileum and one colon).
TM, Toxic megacolon.

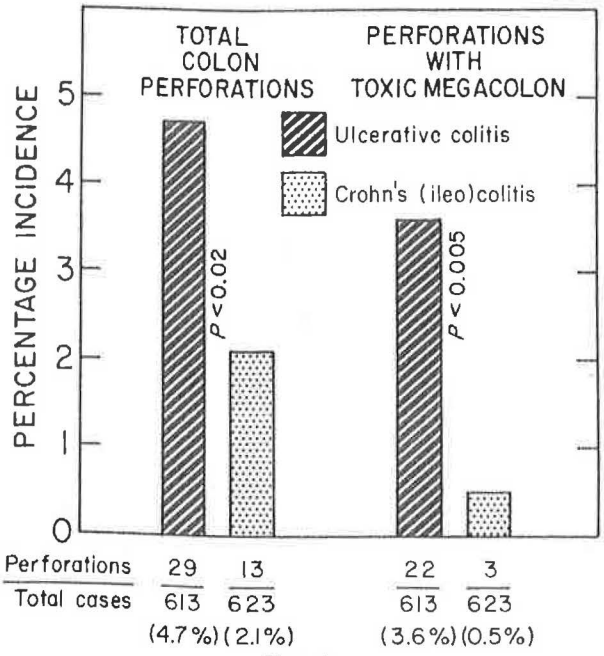

FIG. 4

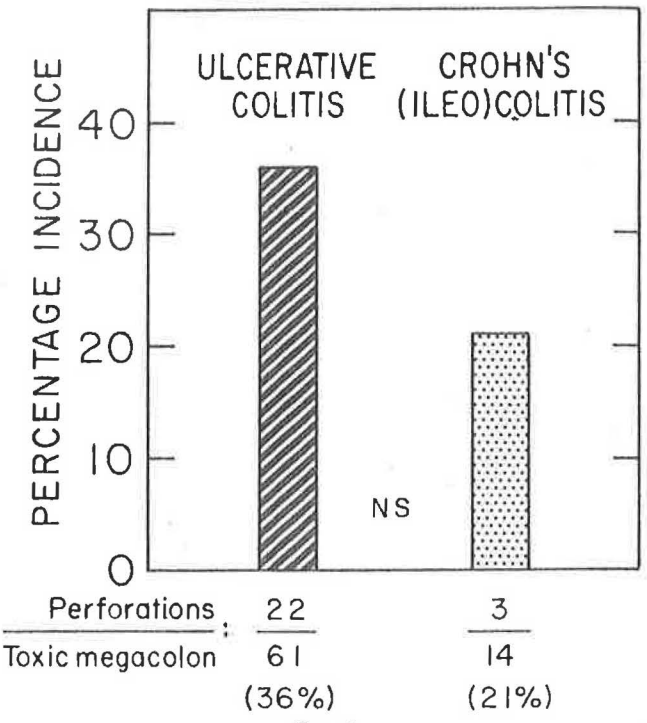

FIG. 5

FIG. 4. A signficantly greater incidence of total colonic perforation and perforation with toxic megacolon in ulcerative colitis compared with Crohn's disease involving the colon is shown (colitis and ileocolitis) when considered as a proportion of the total series.

FIG. 5. Perforation in toxic megacolon is not significantly different in ulcerative colitis and Crohn's colitis involving the colon when it is considered as a proportion of all patients with megacolon.

28 times as frequent in patients with TCD than in those without; compared with ten times the frequency in patients with CD and TCD (Table I). Within the context of the total series, colonic perforation in patients with disease confined to the colon and patients with perforation in toxic megacolon were both significantly greater in patients with UC (Fig. 4). The increase in perforation in UC was due to the higher incidence and proportion of toxic megacolon in UC and probably also to the higher proportion of perforation in patients with UC and TCD (36 versus 21 per cent) (Fig. 5). However, if one examines only the 75 patients with toxic megacolon with UC and CD, although the proportion of patients who had perforations was almost twice as great in the former, the difference was not statistically significant in this series (Fig. 5). The incidence of colonic perforation in the absence of toxic megacolon was similar in the two series (seven of 552 for UC, 1.2 per cent versus 11 of 607 with CDC, 1.8 per cent).

Comparison of mortality. The over-all mortality for perforations of the colon as a proportion of the total series was four times greater in UC than in CDC (2 versus 0.5 per cent) and the difference was statistically significant (Table I). If one examines all 47 primary spontaneous perforations, omitting the two deaths which occurred with recurrent disease, there is a significant difference in mortality between UC and CD (Fig. 6). With the addition of the two perforations in recurrent Crohn's disease, the results of the chi square test fail to reach statistical significance.

Mortality was significantly greater in patients with perforation in UC than in those with Crohn's disease in both the over-all series and in the absence of toxic megacolon, but not in toxic megacolon if examined separately. A comparison of free perforation in the absence of toxic dilation revealed a highly significant difference between the two groups (Fig. 7). More than one-half of the patients with UC died—four of seven patients, 57 per cent. This incidence is comparable with the 41 per cent mortality for perforation in UC with toxic megacolon. All 15 patients with Crohn's disease (including all ten patients with free colonic perforation and five with free small intestinal perforation) (Table II) survived (Fig. 7.) Mortality was no different in toxic megacolon

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