Toxic Megacolon Complicating Crohn's Colitis

MICHAEL B. GRIECO, M.D., DENNIS L. BORDAN, M.D., ALAN C. GEISS, M.D., ARTHUR R. BEIL, JR., M.D.

From the Departments of Surgery, North Shore University Hospital, Manhasset, New York, and Cornell University Medical College, New York, New York

Toxic megacolon complicating ulcerative colitis has been a well-recognized entity since its original description in 1950. The presence of toxic megacolon frequently has precluded a diagnosis of Crohn's colitis. Recent literature, however, has demonstrated that the incidence of toxic megacolon associated with Crohn's colitis (4.4–6.3%) may be higher than that in ulcerative colitis (1–2.5%). Differentiation between these two catastrophic forms of colitis is important in respect to prognosis and long-term results. Medical management of toxic megacolon may be initially successful in either type of colitis. Surgical intervention is indicated if the patient's condition does not improve within 48–72 hours. A subtotal colectomy with an ileostomy and mucous fistula is probably the treatment of choice for most of these extremely ill patients. The influence of the type of colitis on the results of subsequent management of the rectal stump remains unresolved.

TOXIC MEGACOLON, or toxic dilatation of the colon, is a well-known complication of chronic ulcerative colitis. Since its original description by Marshak in 1950,[39] toxic megacolon had been assumed to occur only in patients with ulcerative colitis. Recently there has been documentation of this entity complicating amebic colitis, ischemic colitis, pseudomembranous enterocolitis, and bacillary dysentery.[10,13,20,36,46,58] In 1967, Schachter presented the first detailed case report of toxic megacolon occurring in a patient with Crohn's disease of the colon.[48] We have found only 66 additional cases from a collection of reported series.[6,8,11-14,21,25,27,30,31,34,38,40,42,45,48,50,51] However, some authors have proposed that many cases originally thought to have been ulcerative colitis actually may have been Crohn's colitis.[25,26] It is the purpose of this paper to review the literature and to describe the experience at North Shore University Hospital of toxic megacolon complicating Crohn's colitis.

Materials and Methods

Between 1970 and 1978 there were 165 patients hospitalized at the North Shore University Hospital for treatment of Crohn's disease of either the large or small intestine. Eighty-seven patients had involvement of the small intestine, 29 patients the colon (Crohn's colitis), and 49 patients both the large and small intestine concurrently (ileocolitis). Of the 78 patients with Crohn's colitis and ileocolitis, five patients developed toxic megacolon for an incidence of 6.4% (Table 1). During this same eight-year period 64 patients were hospitalized for treatment of nonspecific ulcerative colitis, and four of these developed toxic megacolon for an incidence of 6.3%.

A diagnosis of Crohn's colitis was based on the antecedent history, clinical presentation, and gross and histopathologic findings.[11] Toxic megacolon does not have as well-defined limits; accordingly, its diagnosis was formulated from less well-known criteria. First, the patients must be acutely-ill with a rapid deterioration in their overall condition. Second, they must be toxic by demonstrating at least two of the following: tachycardia greater than 120/minute, oral temperature above 38.0 C, ESR of 30 mm or more in the first hour (Wintrobe), and white cell count of 10,000/mm or greater.[11,47,53] Third, the diameter of the midtransverse colon of nonoperative cases must be greater than 5.5 cm on a plain radiograph of the abdomen.[32] In pathologic specimens a megacolon is characterized by a midtransverse colon diameter of at least 10 cm in the unopened, formalin-fixed specimen.[11]

Recent literature has favored the use of the descriptive phrase of toxic dilatation of the colon in preference to the older term of toxic megacolon. The newer term has been used to avoid confusion with congenital megacolon or Hirschsprung's disease. However, as emphasized by Menguy,[41] this newer, bland alternative fails to instill the same fear that one normally associates with toxic megacolon. Although these terms can be used interchangeably, we prefer to use toxic megacolon. We also prefer Crohn's colitis, or Crohn's disease of the colon, rather than granulomatous colitis, because granulomas are not invariably present in all specimens.

Case Report

V.M., a 36-year-old white man, was in good health until January, 1977, when he developed diffuse, crampy, abdominal pain and

Reprint requests: Michael B. Grieco, M.D., Department of General Surgery, Lahey Clinic Foundation, Boston, Massachusetts 02215.

Submitted for publication: July 2, 1979.

0003-4932/80/0100/0075 $00.80 © J. B. Lippincott Company

TABLE 1. *Clinical Series*

Patient, Age and Sex	Duration of Crohn's Disease (Months)	Duration of Documented Colonic Dilatation (Days)	Barium Enema	Mid-transverse Colon Diameter (cm)		Colonic Perforation	Granulomas	Primary Operative Procedure	Present Condition	Early Complications	Late Complications
				X-ray	Unopened Specimen						
1. VM, 36M	12	7	8 mo preop	11	13	None	Present	STC-IM*	Asymptomatic 2 yr postop	Small bowel obstruction	None
2. GK, 59M	2	10	9 mo preop	10	13	None	None	Aylett† Procedure	Asymptomatic 2 yr after closure of loop ileostomy at 8 mo postop	None	None
3. LC, 45M	8	4	None	9	11	Walled-off	Present	STC-IM*	Asymptomatic 5 yr postop	Wound infection	None
4. LJ, 53F	30	8	None	10	12	None	Present	STC-IM*	Lost to follow-up	Wound infection, U.T.I.	None
5. SR, 39M	16	5	None	12	‡	None	None	STC-IM*	Asymptomatic 4 yr postop	None	Small bowel obstruction

* Subtotal colectomy—ileostomy, mucous fistula.
† Total colectomy—primary ileorectal anastomosis, loop ileostomy.
‡ Data not available.

nonbloody diarrhea. The patient was treated for peptic ulcer disease with antacids and dietary restrictions without any improvement. A barium enema demonstrated subtle changes in the transverse colon that were suggestive of "colitis." Sigmoidoscopy and an upper gastrointestinal series were normal. The abdominal pain and diarrhea gradually subsided until December, 1977, when the patient was hospitalized with an acute exacerbation of symptoms. Treatment for presumed "colitis" was initiated with broad spectrum antibiotics, systemic corticosteroids, and intestinal intubation.

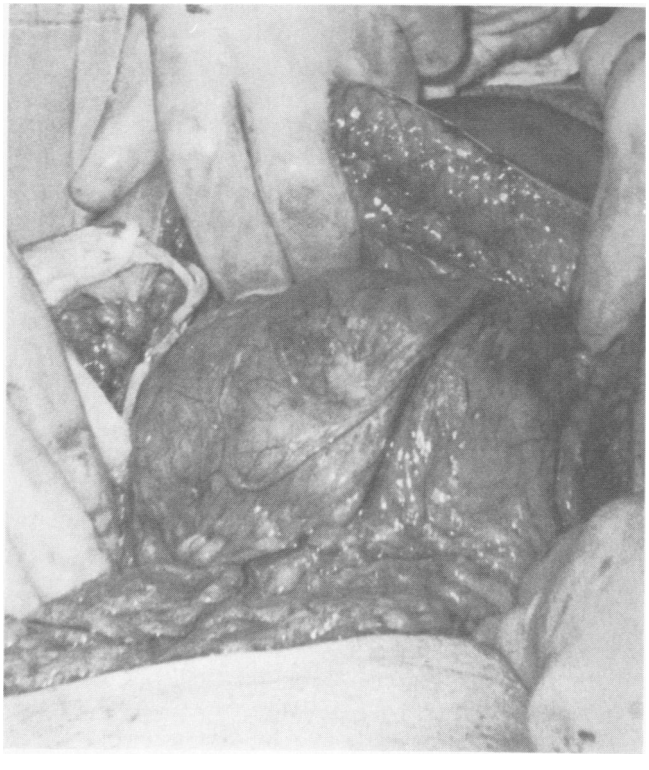

FIG. 1. Operative view of greatly distended transverse colon. The diameter of the midtransverse colon measured approximately 18 cm before needle decompression was performed.

During a one-month hospitalization the patient lost 30 pounds, had 15–20 watery, nonbloody stools per day, and suffered an exacerbation of his symptoms whenever he ate. The patient then was transferred to North Shore University Hospital for further evaluation and total parenteral nutrition.

Physical examination revealed a cachectic, dehydrated, alert man with a rectal temperature of 39.0 C, pulse of 125, respirations of 16, and a BP of 110/80. Pertinent physical findings were limited to the abdomen, which was distended, tympanitic, and diffusely tender. There were no bowel sounds, masses, or organ enlargement. Proctosigmoidoscopy revealed a minimally-inflamed mucosa without ulcerations and a guaiac positive stool. Abnormal laboratory values were: hematocrit 32%, white blood cell count 6,100 including 34 bands, total protein 5.4, and protime 13.6/11.6. Flat and upright abdominal radiographs demonstrated a greatly-distended transverse colon that measured 11 cm in diameter in the midline. Despite vigorous medical treatment with systemic antibiotics, corticosteroids, and intestinal long tube decompression, the patient remained septic. Within 72 hours of transfer to North Shore University Hospital, the patient underwent an exploratory laparotomy. A greatly-distended transverse colon was present (Fig. 1) with relatively normal-appearing proximal ascending, distal descending, and sigmoid colon (Fig. 2). The entire small intestine was normal. There was no evidence of sealed or free perforations. A subtotal colectomy with formation of an end ileostomy and mucous fistula was accomplished. Histopathologic examination revealed a transmural cicatrizing process with granulomas consistent with a diagnosis of Crohn's colitis. The patient had an uncomplicated postoperative course and presently has a well-functioning ileostomy without evidence of recurrent disease.

Discussion

Colitis was first described in the English literature in 1875 by Wilks and Moxon of London.[57] For the next 50 years physicians assumed that only one type of colitis existed—namely, ulcerative colitis. In 1930, Bargen and Weber described another type of colitis that occurred in different segments of the colon.[4] Crohn, in 1932, published his classic paper in which he stated that

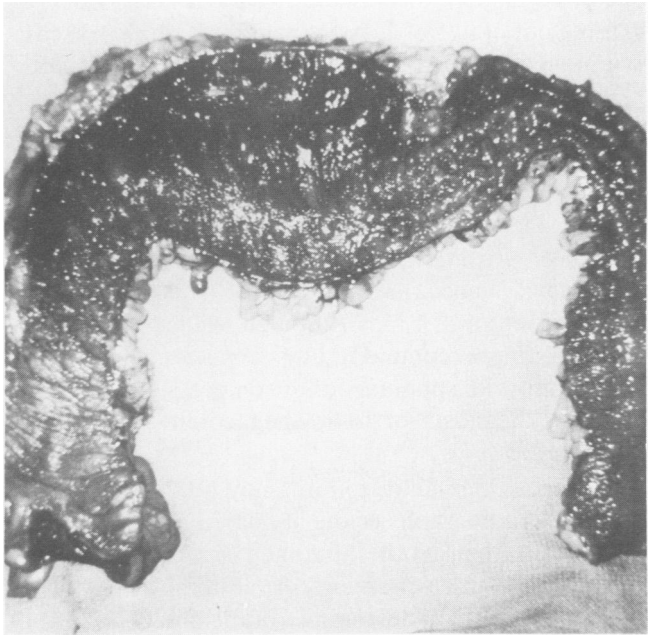

FIG. 2. Subtotal colectomy specimen. Proximal ascending, distal descending, and sigmoid colon are grossly normal. The transverse colon demonstrates features typical of Crohn's colitis.

granulomatous disease only affected the small intestine.[19] Four years later, Crohn reported that "Crohn's disease" could exist in the colon independently of or simultaneously with disease in the small intestine.[19] In 1950, Marshak first described toxic dilatation of the colon or "megacolon" as a distinct clinical entity complicating ulcerative colitis.[39] Several years later, Roth coined the descriptive term "toxic megacolon."[47] For the next 15 years it was assumed that toxic megacolon only occurred in patients with ulcerative colitis. However, Wruble, in 1966, presented the first case report of a patient with toxic megacolon not associated with ulcerative colitis; his patient had amebiasis.[58] In the same year, Hawk and Turnbull[31] first reported cases of toxic megacolon complicating granulomatous colitis, and Schachter,[48] in 1967, presented the first detailed case report of such an occurrence.

The incidence of toxic megacolon complicating ulcerative colitis has been variously reported in numerous retrospective studies,[20,30] but it is probably in the range of 1–2.5% of patients.[28] This entity complicating Crohn's disease of the colon has been appreciated more slowly. Some recent surveys have suggested that its incidence actually may be somewhat higher than in ulcerative colitis.[11,21,30] An examination of the only large series published (Table 2) reveals an incidence of toxic megacolon of between 4.4–6.3% in cases of Crohn's colitis. This is comparable to our incidence of 6.4% despite our exacting criteria for diagnosis. Further scrutiny of these data demonstrates the propensity for toxic megacolon to occur when Crohn's disease is confined to the colon.

The etiology of toxic megacolon associated with ulcerative or Crohn's colitis is largely speculative. Several reports have implicated the performance of a barium enema with the subsequent appearance of toxic megacolon.[30,38,41,44,48] It has been suggested that the tannic acid in the barium mixture is the etiologic agent, but this has been disproven.[35] The threat of perforation is a more important reason for not performing a barium enema in the acute phase of inflammatory bowel disease. Anticholinergics, antidiarrheals, and opiates may exacerbate this condition by further decreasing colonic muscular tone.[10,27,30,41,45] Hypokalemia is now believed to be the result of, and not the cause of, toxic megacolon.[20,41] Distal stenosis and aerophagia also have been offered as contributing factors.[47]

Irrespective of the cause or causes of toxic megacolon complicating any form of colitis, the basic pathologic process consists of rapid damage involving all layers of the colonic wall.[30,50] Menguy has suggested that unknown toxins cause a breakdown of the protective mucosal barrier thus exposing the susceptible muscularis propria.[41] Bockus has presented evidence that there is destruction of ganglion cells and swelling of nerve fibers in the myenteric plexus.[7] Cello and Meyer believe that destruction of colonic musculature by widespread inflammation is most important.[13] Ultimately, there is an almost complete paralysis of the diseased segment of colon with loss of smooth muscle substance, tone, and motility.[26]

Macroscopically, "cobblestone" mucosa, longitu-

TABLE 2. *Review of Recent Literature*

Author	Year	Total Cases	Total Number of Patients With Toxic Megacolon	Pattern of Distribution	
				Ileocolitis	Colitis
Buzzard[11]	1974	190	12 (6.3%)	1 Patient*	11 Patients*
Greenstein[30]	1975	160	7 (4.4%)	3/130 (2.3%)	4/30 (13.3%)
Farmer[21]	1975	418	23 (5.5%)	5/252 (2.0%)	18/166 (10.8%)
N.S.U.H.	1978	78	5 (6.4%)	2/49 (4.1%)	3/29 (10.3%)

* Additional data not available.

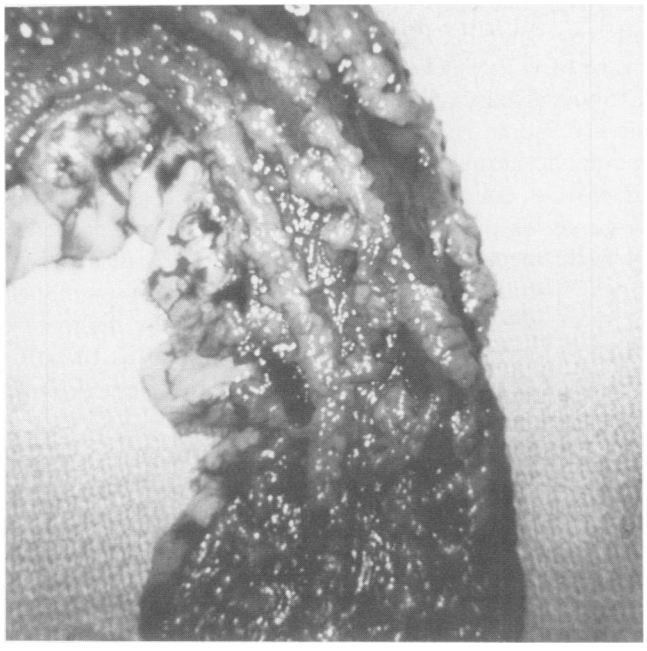

FIG. 3. Close-up of splenic flexure of resected specimen. Longitudinal "rake" ulcers, "cobblestone" mucosa, and thickened colonic walls are evident.

dinal "rake" ulcers, and thickened colonic walls as discontinuous or diffuse disease characterize the opened specimen of toxic megacolon in Crohn's disease (Figs. 2 and 3). Histopathologic examination may reveal transmural inflammatory reaction often with extension to the serosa, crypt abscesses, necrosis of smooth muscle fibers, variable areas of fibrosis, transmural fissures, noncaseating granulomas and disintegration of ganglion cells of the myenteric or submucosal plexuses. The presence of sarcoid-like, noncaseating granulomas is most important in distinguishing between toxic megacolon occurring in Crohn's colitis and in ulcerative colitis. These granulomas do not occur in nonspecific ulcerative colitis and have been reported in 50[12,56] to 100%[17] of Crohn's colitis specimens. Three out of five of our patients with toxic megacolon complicating Crohn's disease of the colon had granulomas in the pathologic specimen (Table 1).

Toxic megacolon characteristically occurs during the acute and early manifestations of Crohn's colitis[56] before extensive fibrosis ensues. The transmural, proliferative and cicatrizing nature of Crohn's disease is thought to preclude the late occurrence of toxic megacolon by preventing dilatation of the colon.[31,38,48,50] This is in contradistinction to chronic ulcerative colitis in which toxic megacolon more commonly complicates an acute exacerbation occurring at any time during the course of the disease,[23] although it may occur as an initial event in 24–40% of patients.[13] In Buzzard's series, of the 12 patients with toxic megacolon complicating Crohn's colitis, ten had a relatively short preoperative history of less than two years.[11] However, in three out of five of Javett's patients with this disease, symptoms had been present for more than two years.[34]

Patients with toxic megacolon usually appear severely ill with tachycardia, pyrexia, dehydration, abdominal pain, electrolyte disturbances, and leukocytosis. These septic patients may have anemia, hypoalbuminemia, mental aberrations, diarrhea, hypotension, signs of peritoneal irritation, paradoxical decrease in stool frequency[13,20] and, rarely, intestinal hemorrhage[13,30] or free perforation.[25,30,34,49] Although walled-off perforations are more common, it is conceivable that free perforation with spontaneous decompression may occur before a diagnosis of toxic megacolon is even contemplated.

Visible abdominal distention may not be prominent; therefore, radiographs of the abdomen are a necessity. Daily plain films of the abdomen are probably more reliable than measurement of abdominal girth.[20,26] Patchy loss of "cobblestoning" of the mucosa and subserosal air sometimes can be observed on abdominal radiographs before actual dilatation occurs.[9] Colonic dilatation can be segmental or total, and the transverse colon is most commonly involved.[13,20,26,30,43,45,50] Hywel Jones and Chapman[32] presented evidence that the maximum diameter of the normal transverse colon in the midline on a plain radiograph of the abdomen is 5.5 cm. The authors thus defined megacolon as a midtransverse colon whose diameter was greater than 5.5 cm. In their 15 patients with toxic megacolon complicating "colitis," the mean diameter of the transverse colon was 8.2 cm, which is similar to Neschis' results (8.4 cm).[43]

Initial management of patients with toxic megacolon complicating either Crohn's colitis or ulcerative colitis consists of correction of fluid and electrolyte abnormalities, systemic broad spectrum antibiotics, parenteral corticosteroids, intubation with a long intestinal tube, and daily plain radiographs of the abdomen. Barium enema examination, and the use of opiates, anticholinergics, and antidiarrheals should be avoided. Proctosigmoidoscopy without air insufflation is useful in differentiating Crohn's disease from ulcerative colitis. Greenstein states that more than 75% of these patients with Crohn's colitis will respond well to this conservative approach unlike the situation in ulcerative colitis. He concludes, however, that most of these patients ultimately will require surgery for continuing symptoms or relapses.[30] In contrast, acute toxic dilatation limited to the ileum in Crohn's disease, an entity which can easily be confused with toxic megacolon, may be more likely to respond to conservative treatment.[29]

If these conservative measures fail to control the clinical and radiologic progression within 48–72 hours after the onset of symptoms, then surgical intervention is mandatory.[30] Many authors have emphasized the

importance of early diagnosis, avoidance of precipitating factors and prompt surgery in cases of toxic megacolon.[1,5,13,16,20,26] Protracted medical management leading to perforation is probably the major contributing factor to the high mortality associated with toxic megacolon. Cello and Meyer have stated that the incidence of free perforation is as high as 50% after 72 hours of unsuccessful conservative treatment.[13] A recent survey of the literature on toxic megacolon revealed an incidence of perforation of 24%. The overall medical mortality was 27%, and the overall surgical mortality was 19.5%. The operative mortality without perforation was only 8.8% while it was 41% for patients with perforation.[51] Binder reported an overall nonoperative mortality of 30% that rose to 82% once perforation of a toxic megacolon occurred despite vigorous medical treatment.[5] It should also be noted that free perforation has been reported in Crohn's colitis in the absence of toxic megacolon.[54]

The operative management of toxic megacolon is a controversial topic regardless of the type of colitis present. A cecostomy[37] or a completely diverting ileostomy alone[30] are usually inadequate procedures. Additionally, a single stage total proctocolectomy is probably too extensive an operation for these critically ill patients;[30,33] mortality rates of 14–30% have been reported.[22] A total or subtotal colectomy with an end ileostomy and mucous fistula is most likely the procedure of choice.[51] In selected cases of suspected walled-off perforations, the so-called Turnbull ileostomy-blowhole colostomy may be used. Turnbull reported 25 survivors out of 26 patients in which this procedure of diversion, decompression, and drainage was used.[55] Fazio's follow-up of these patients yielded the same excellent results with only a 2% mortality.[22]

Of our five patients with toxic megacolon complicating Crohn's colitis (Table 1), four have had subtotal colectomy with ileostomy and mucous fistula as a primary procedure. None of these four patients has had a subsequent reanastomosis despite a normal-appearing rectum on sigmoidoscopy. The fifth patient underwent a total colectomy with primary ileorectal anastomosis and a diverting, loop ileostomy. The ileostomy was closed eight months postoperatively, and he has remained asymptomatic.

Although the various procedures are similar for toxic megacolon associated with either Crohn's or ulcerative colitis, the long-term results and prognosis are not. It is well-known, for instance, that total proctocolectomy will cure patients with ulcerative colitis but not Crohn's disease.[15] A point of some contention is the place of an ileorectal anastomosis as either a primary or staged procedure in either type of colitis. All of Buzzard's 12 patients with toxic megacolon complicating Crohn's colitis underwent total colectomy and ileorectal anastomosis with a relieving ileostomy as a staged procedure. Of these patients, only four had functioning ileorectal anastomoses as of the report in 1974.[11] These results are certainly less favorable than the report of Baker[3] for the same procedure performed for toxic megacolon in ulcerative colitis. Therefore, it would appear that it is of some benefit relative to long-term results to know whether one is treating ulcerative colitis or Crohn's colitis in cases of toxic megacolon. Tompkins, on the other hand, states that the duration of symptoms is more important than the type of colitis present in predicting success of a rectum-retaining operation.[52] Regardless, distinguishing between these two diseases is not essential for making a decision whether or not to operate in a case of toxic megacolon.

Conclusions

Toxic megacolon can complicate Crohn's disease of the colon; in fact, its incidence may be even higher than that occurring in instances of ulcerative colitis. Statements concerning prognosis and long-term results of treatment in cases of toxic megacolon are contingent upon differentiation of these two forms of colitis. For example, total proctocolectomy will cure patients with ulcerative colitis but not those with Crohn's disease involving the colon.[15] In contrast, the initial management of patients with toxic megacolon is identical regardless of the type of colitis present, although in some instances medical treatment has been more successful in cases of Crohn's colitis.[30] However, protracted medical management must be avoided to prevent colonic perforation.

The state of the colon and condition of the patient at the time of laparotomy should indicate the type of operative procedure to be employed. A single-stage total proctocolectomy, the Turnbull ileostomy-blowhole colostomy, and the Aylett procedure[2] are indicated in selective situations. We recommend utilization of a total or subtotal colectomy with an ileostomy and mucous fistula as the procedure of choice in these seriously ill patients regardless of the form of colitis present. The question of subsequent surgical therapy is problematic because of the controversy concerning the place of rectum-retaining operations as an alternative to excision of the rectum. The influence of the type of colitis present on these additional procedures awaits further trials.

Acknowledgment

The authors wish to express their appreciation to Ms. Janet Lehmann for her assistance in the preparation of this manuscript.

References

1. Adams JT. Toxic dilatation of the colon. Arch Surg 1973; 106:678.

2. Aylett SO. Delayed ileorectal anastomosis in the surgery of ulcerative colitis. Br J Surg 1970; 57:812.
3. Baker WNW. The results of ileorectal anastomosis at St. Mark's Hospital from 1953 to 1968. Gut 1970; 11:235.
4. Bargen JA Weber HM. Regional migratory chronic ulcerative colitis. Surg Gynecol Obstet 1930; 50:964.
5. Binder SC, Patterson JF, Glotzer DJ. Toxic megacolon in ulcerative colitis. Gastroenterology, 1974; 66:909.
6. Bockus HL. Gastroenterology. Philadelphia, W. B. Saunders Company, 1976. p. 581.
7. Bockus HL, Roth JL, Bachman E, et al. Ulcerative colitis I. Classification of types, clinical behavior, life history, prognosis. *In* Avery Jones F, (ed.) Modern Trends in Gastroenterology. New York, Paul B. Hoeber, Inc., 1958, p. 296.
8. Brooke BN. Crohn's disease of the large bowel. Br Med J 1972; 1:310.
9. Brooke BN, Sampson PA. An indication for surgery in acute ulcerative colitis. Lancet 1964; 2:1272.
10. Brown CH, Ferrante WA, Davis WD, Jr. Toxic dilatation of the colon complicating pseudomembranous enterocolitis. Am J Dig Dis 1968; 13:813.
11. Buzzard AJ, Baker WNW, Needham PRG, Warren RE. Acute toxic dilatation of the colon in Crohn's colitis. Gut 1974; 15:416.
12. Cello JP, Meyer JH. Crohn's disease of the colon. *In* Sleisenger, MH, Fordtran JS (eds.) Gastrointestinal Disease. Philadelphia, W. B. Saunders Company, 1978. p. 1658.
13. Cello JP, Meyer JH. Ulcerative colitis. *In* Sleisenger MH and Fordtran JS (eds.) Gastrointestinal Disease. Philadelphia, W. B. Saunders Company, 1978, p. 1597.
14. Clark AW. Dilatation of colon in Crohn's disease. Br Med J 1972; 4:233.
15. Colcock BP. Regional enteritis. Curr Probl Surg June, 1965.
16. Collier RL, Wylie JH, Gomez J. Toxic megacolon: a surgical disease. Am J Surg 1971; 121:283.
17. Cook MG, Dixon MF. An analysis of the reliability of detection and diagnostic value of various pathological features in Crohn's disease and ulcerative colitis. Gut 1973; 14:255.
18. Crohn BB, Berg AA. Right-sided (regional) colitis. JAMA 1938, 110:32.
19. Crohn BB, Ginzburg L, Oppenheimer GD. Regional ileitis; pathological and clinical entity. JAMA 1932; 99:1323.
20. Editorial: Toxic megacolon may complicate Crohn's disease. Br Med J 1975; 3:723.
21. Farmer RG, Hawk WA, Turnbull RB. Clinical patterns in Crohn's disease: a statistical study of 615 cases. Gastroenterology 1975; 68:627.
22. Fazio V, Turnbull RB, Goldsmith M. Ileostomy-colostomy for the megacolon phase of toxic ulcerative colitis. *In* Clearfield HR, Dinoso VP, Jr (eds.) Gastrointestinal Emergencies. New York, Grune and Stratton, Inc. 1976. p. 209.
23. Ferrante WA, Egger J. Toxic megacolon complicating chronic ulcerative colitis. South Med J 1965; 58:969.
24. Fielding JF, Truelove SC. Crohn's disease of the large bowel. Br Med J 1972; 1:310.
25. Fisher J, Mantz F, Calkins WG. Colonic perforation in Crohn's disease. Gastroenterology 1976; 71:835.
26. Foley WJ, Weaver DK, Coon WW. Toxic megacolon and granulomatous colitis, report of two cases. Am Surg 1971; 37:67.
27. Garrett JM, Saver WG, Moertel CG. Colonic motility in ulcerative colitis after opiate administration. Gastroenterology. 1967; 53:93.
28. Gilat T, Lilos P, Zemishlany Z, et al. Ulcerative colitis in the Jewish population of Tel-Aviv. Yafo. III. Clinical Course. Gastroenterology 1976; 70:14.
29. Greene L, Kresch L, Held B. Acute toxic dilatation limited to the ileum in Crohn's disease. Am J Dig Dis 1972; 17:439.
30. Greenstein AJ, Kark AE, Dreiling DA. Crohn's disease of the colon. III. Toxic dilatation of the colon in Crohn's colitis. Am J Gastroenterol 1975; 63:117.
31. Hawk WA, Turnbull RB, Jr. Granulomatous colitis, pathogenic concepts. Gastroenterology 1966; 51:802.
32. Hywel Jones J, Chapman M. Definition of megacolon in colitis. Gut 1969; 10:562.
33. Jagelman DG, Fazio VW, Turnbull RB. Toxic Megacolon in Crohn's disease. Br Med J 1975; 4:459.
34. Javett SL, Brooke BN. Acute dilatation of colon in Crohn's disease. Lancet 1970; 2:126.
35. Judd ES. Current surgical aspects of toxic megacolon. Surgery 1969; 65:401.
36. Kirsner JB. Problems in the differentiation of ulcerative colitis and Crohn's disease of the colon: the need for repeated diagnostic evaluation. Gastroenterology 1975; 68:182.
37. Klein SH, Edelman S, Kirschner PA, et al. Emergency cecostomy in ulcerative colitis with acute toxic dilatation. Surgery 1960; 47:399.
38. Leoutsakos B, Pedridis G. Toxic megacolon complicating Crohn's disease of the colon. Am J Proctol 1970; 21:258.
39. Marshak RH, Lester LJ, Friedman AI. Megacolon, a complication of ulcerative colitis. Gastroenterology 1950; 16:768.
40. McGovern VJ, Goulston SJM. Crohn's disease of the colon. Gut 1968; 9:164.
41. Menguy R. The surgery of toxic megacolon. *In* Bercovitz ZT, Krisner, JB, Lindner AE, et al. (eds.) Ulcerative and Granulomatous Colitis. Springfield, Charles C Thomas, 1973. p. 293.
42. Mir-Madjlesis SH, Farmer RG. Behcet's syndrome, Crohn's disease and toxic megacolon. Clev Clin 1972; 39:49.
43. Neschis M, Siegelman S, Parker J. Diagnosis and management of the megacolon of ulcerative colitis. Gastroenterology 1968; 55:251.
44. Odyniec NA, Judd ES, Sauer WG. Toxic megacolon; significant improvement in surgical management. Arch Surg 1967; 94: 638.
45. Papp JP, Pollard HM. Toxic dilatation of the colon in granulomatous colitis. Am J Dig Dis 1970; 15:1105.
46. Ripstein CB, Wiener EA. Toxic megacolon. Dis Colon Rectum 1973; 16:402.
47. Roth JLA, Valdes-Dapena A, Stein GN, Bockus HL. Toxic megacolon in ulcerative colitis. Gastroenterology 1959; 37: 239.
48. Schachter H, Goldstein MJ, Kirsner JB. Toxic dilatation complicating Crohn's disease of the colon. Gastroenterology 1967; 53:136.
49. Shahmanesh M, Wilken BJ. Perforated Crohn's. Lancet, 1970; 2:363.
50. Soll EL, Ferrante WA, Gathright JB, Jr. Toxic dilatation of the colon due to granulomatous colitis (Crohn's disease). South Med J 1971; 64:349.
51. Strauss RJ, Flint GW, Platt N, et al. The surgical management of toxic dilatation of the colon. Ann Surg 1976; 184:682.
52. Tompkins RK, Weinstein MH, Foropzan P, et al. Reappraisal of rectum-retaining operations for ulcerative and granulomatous colitis. Am J Surg 1973; 125:159.
53. Truelove SC, Witts LJ. Cortisone in ulcerative colitis. Br Med J 1955; 2:1041.
54. Tugwell P, Southcott D, Walmesley P. Free perforation of the colon in Crohn's disease. Br J Clin Pract 1972; 26:44.
55. Turnbull RB, Jr, Weakley FL, Hawk WA, Schofield P. Choice of operation for the toxic megacolon phase of nonspecific ulcerative colitis. Surg Clin North Am 1970; 50:1151.
56. Veidenheimer MC, Nugent FW, Haggitt RC. Ulcerative colitis or Crohn's colitis, is differentiation necessary? Surg Clin North Am 1976; 56:721.
57. Wilks S, Moxon W. Lectures in Pathological Anatomy. Second edition, London, J., and A. Churchill, Ltd., 1875, p. 681.
58. Wruble LD, Duckworth JK, Duke DD, Rothschild JA. Toxic dilatation of the colon in a case of amebiasis. N Engl J Med 1966; 275:926.