

## CLINICAL REVIEWS

# A New Look at Toxic Megacolon: An Update and Review of Incidence, Etiology, Pathogenesis, and Management

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### ABSTRACT

Toxic megacolon (TM) is an infrequent but devastating complication of colitis. Numerous forms of colonic inflammation can give rise to TM but the majority occur in individuals with inflammatory bowel disease (IBD). Recently there has been a marked increase in the number of reports of TM associated with pseudomembranous colitis. Because of the associated high morbidity and mortality, early recognition and management of TM is of paramount importance. The mechanisms involved in development of TM are not clearly delineated, but chemical mediators such as nitric oxide and interleukins may play a pivotal role in the pathogenesis. New evidence suggests that TM and its associated morbidity may be predicted by the extent of small bowel and gastric distension in patients with colitis. CT scanning may also play an important role the management of TM, in that it may be the only noninvasive mode to detect subclinical perforations and abscesses. Management involves close medical attention, supportive care, and treatment of the underlying colitis. Possible exacerbating factors such as narcotic and anticholinergic medications must be withdrawn, and colonic decompression via tube drainage or positional techniques must be considered. Signs of progression or complications of the disease must be treated aggressively with surgical intervention, as delay is associated with even greater risk of mortality. (Am J Gastroenterol 2003;98:2363–2371. © 2003 by Am. Coll. of Gastroenterology)

### INTRODUCTION

Toxic megacolon (TM) is a well recognized, potentially fatal complication of colitis. First recognized as a clinical entity by Marschak *et al.* in 1950 (1), it is defined as segmental or total colonic distension of >6 cm in the presence of acute colitis and signs of systemic toxicity. Given the many other causes of colonic distension (*e.g.*, intestinal pseudo-obstruction and Hirschsprung's disease), TM must be differentiated from these other processes by its inflammatory trigger and its accompanying toxic manifestations.

### INCIDENCE

The incidence of TM is difficult to determine from the literature and is dependent on the cause in question. In addition, most studies are referral center-based, thus skewing the results. The incidence of TM in inflammatory bowel disease (IBD) has been the most extensively reported. One study estimated that the lifetime incidence of TM in individuals with ulcerative colitis (UC) is 1–2.5% (2). In a study of 1236 IBD patients admitted to hospital over a 19-yr period, Greenstein *et al.* reported that TM was noted on 6% of hospital admissions (3). More specifically, TM was present on 10% of UC and 2.3% of Crohn's disease patient admissions (3). A more recent study of 180 patients with severe UC who were admitted to a tertiary care facility found an incidence of 17% in this selected population (4). However, a prospective study from 1995 to 2000 by the same group reported an overall incidence of 7.9% of UC patients admissions (5).

TM has a reported incidence of 0.4–3% in patients with pseudomembranous colitis (PMC), and this is expected to increase in proportion to the rapidly increasing prevalence of disease (6–9). Recent data suggest a dramatic doubling of overall incidence of PMC in some centers (10), which is likely related to an increase in use of broad-spectrum antibiotics. Colectomy and mortality related to PMC have also increased at an alarming rate, and a substantial number of these patients have evidence of TM (10). The development of TM in PMC is often devastating in that there is a reported mortality of 38–80% (6, 7, 11, 12). TM resulting from other infections and causes tends to be exceedingly rare.

### ETIOLOGY

Classically, toxic megacolon was thought to be a complication solely of ulcerative colitis. However, Crohn's colitis was then recognized as a cause, and gradually it became evident that almost any inflammatory condition of the colon could predispose patients to toxic dilation (Table 1). These include pseudomembranous colitis (7, 13–20), Salmonella (21–25), Shigella (26–30), Campylobacter (31–37), Entamoeba (38–40), and ischemic colitis (41–43). In patients with

HIV or AIDS, TM has been reported as a consequence of CMV colitis, Cryptosporidia, Salmonella, and Kaposi's sarcoma (44–46). In addition to underlying colitis, risk factors for occurrence include discontinuation of 5-aminosalicylate (5-ASA) agents or steroids (47), barium enemas (48), and any drugs that slow colonic motility (narcotic, antidiarrheal, or anticholinergic preparations). Several authors have noted anecdotal reports of colonoscopy as a trigger (49, 50) and, despite isolated reports of its safety as a diagnostic and prognostic technique in ulcerative colitis (51), full colonoscopy is generally frowned upon in severe colitis (52). Finally, there are case reports of chemotherapy as a possible inducing factor in TM (53, 54) (Table 1). Interestingly, there have been no reported cases of radiation or graft-versus-host disease-induced TM.

### NATURAL HISTORY

The mortality from toxic megacolon has been extensively documented over the past 50 yr. Recent population studies of mortality in IBD suggest TM is an uncommon cause of death overall. A European study of 796 patients revealed an incidence of TM-related death of only 0.2% in UC over a 4-yr follow-up. However, this represented 50% of total deaths due to UC. No deaths from TM were reported in patients with Crohn's disease (55). Furthermore, in a Danish cohort of 374 Crohn's disease patients there were no deaths reported from toxic megacolon (56).

In the patients who develop TM, mortality rates are high. In a large review of the early literature totaling >600 patients, Strauss *et al.* reported an overall mortality of 19% (57). In that study, mortality in medically managed patients was slightly higher than in those managed with early surgery (27% vs 19.5%). Mortality was significantly higher if the patient experienced perforation (41.5% vs 8.8% without perforation) (57). This is echoed in several studies showing a higher mortality in those patients requiring emergent surgery for perforation (3, 58, 59). Work to identify other risk factors of mortality has been variable. Interestingly, the two largest single-center studies assessing risk factors in management of TM differ in their findings. Jalan *et al.* observed an overall mortality of 45% and found no significant predictive value in age, sex, albumin levels, or potassium levels (58). However, Greenstein *et al.* found several factors that were significantly associated with mortality (3). Age >40 yr and female sex both independently predicted a higher mortality as did a lower albumin level, low serum CO<sub>2</sub>, and a high BUN (3). Mortality did not seem to be significantly affected by the total duration of IBD in either study. Clinical features such as bloody diarrhea, fever, weight loss, and abdominal symptoms also did not influence mortality rates (3).

Remarkably, mortality does not seem to be related to the extent of underlying disease. Although TM does indeed tend to occur in patients with pancolitis, mortality is similar in groups with pancolitis or with limited colitis (3, 58, 60).

**Table 1.** Causes and Associations With Toxic Megacolon

Inflammatory
Ulcerative colitis
Crohn's disease
Infectious
<i>Clostridium difficile</i>
Salmonella, Shigella, Yersinia, Campylobacter
Cryptosporidium
Entameba
Cytomegalovirus
Ischemia
Malignancy
Kaposi's sarcoma
Potential triggers and exacerbating factors
Hypokalemia, hypomagnesemia
Barium enema
Discontinuation of steroids
Narcotics
Anticholinergics
Chemotherapy
Colonoscopy

This suggests that mortality is related more to the process of TM rather than to the colitis itself. In one study, in fact, mortality was higher in the group with partial or segmental colitis (55%) than in the group with pancolitis (44%) (58). Greenstein *et al.* found lower overall mortality, but rates were similar regardless of the extent of disease (16% in the pancolitis group vs 20% in the limited colitis group) (3).

For those who survive a course of TM with medical management alone, long-term follow-up has shown a relatively poor prognosis. One study found that of patients who were successfully managed with medical treatment, 57% of those available to for long-term follow-up required a colectomy (3). Another study from the Mayo Clinic found a 29% recurrence of either fulminant colitis or toxic megacolon (61). Over an average follow-up of 13 yr, almost one half (47%) of the 38 patients with an initially successful medical management of TM required a colectomy. The majority of those patients (83%) required surgery on an urgent or emergent basis, and thus the investigators concluded that medical intervention should be considered only as a preparation for surgery (61). It should be noted, however, that these conclusions are based on data that predate the modern era of antimetabolite therapies.

### PATHOGENESIS

Although the exact mechanism of toxic megacolon is not known, a number of reasons for an apparent dysmotility of the colon have been postulated. Several studies have reported abnormal colonic motility in patients with nontoxic colitis. These included findings of defective smooth muscle contraction (62), lowered basal pressure in the colonic lumen, and an inhibited gastro-colic reflex (63, 64). Further research suggests that these effects may be the result of changes in colonic response to vasoactive intestinal polypeptide, substance P, neurotensin, leukotrienes, and ni-

tric oxide (65–68). A recent study compared levels of IL-1 $\beta$  in controls and in the muscularis propria of UC patients. IL-1 $\beta$  levels were significantly elevated in the UC samples, and smooth muscle contraction was notably reduced. The reduction in muscle fiber shortening could be duplicated in the control tissue by the addition of similar levels of IL-1 $\beta$ . Furthermore, the reduction could be partially attenuated by means of catalase, a hydrogen peroxide scavenger, suggesting that hydrogen peroxide could be one of the mediators of dysmotility (69). These significant changes in motility may predispose the patient to the toxic changes that occur in TM and may be the first step in a progressive phenomenon.

It is then postulated that more severe inflammation and damage to the colonic wall are necessary for the development of TM. Buckell *et al.* graded 40 patients who required colectomy for ulcerative colitis and found a correlation between the depth of involvement and the presence of toxic colonic dilation (70). It seems that although in uncomplicated ulcerative colitis the inflammation does not generally extend past the submucosa, in toxic megacolon the inflammation spreads into the circular and longitudinal muscle layers (52, 70). This direct damage may induce neural injury in the colonic wall, resulting in dysmotility and dilation. Specifically, some but not all studies have also found destruction of the myenteric and Auerbach's plexus (71). Hypokalemia and other electrolyte abnormalities secondary to diarrhea and steroid use are reported to contribute to colonic dysmotility (72). Alternatively, these abnormalities may simply be surrogate markers of severe colitis rather than true causes of the disease (49).

Caprilli proposed that the pathogenic mechanism of TM was actually driven by soluble inflammatory mediators, which had downstream inhibitory effects on colonic muscle tone (73). Nitric oxide (NO), which is purported to be the most important nonadrenergic, noncholinergic neurotransmitter in the gut, may be the one of the key players in this theory. Studies show that NO has similar smooth-muscle relaxing effects in the gut as it does in the vasculature. Mourelle *et al.* examined the presence of NO synthase in the colonic mucosa and muscularis propria in patients undergoing colectomy for toxic megacolon, nontoxic ulcerative colitis, and colon cancer (74). Inducible NO synthase was found in high amounts in colonic tissue from TM patients, whereas that in uncomplicated colitis and tumor controls was low or undetectable. Whether this is simply a marker of increased inflammation or whether NO production is truly involved in the pathogenesis of TM is unclear. However, in a rat colitis model, inducible NO synthase activity could be reduced with bowel decontamination with oral antibiotic pretreatment (75), and selective NO synthase inhibition successfully increased intracolonic pressure in colitic rats but not in control rats.

Another set of inflammatory mediators in colonic dysmotility could be the oxidants formed by the inflamed mucosa. Prasad *et al.* studied the effects of monochloramine (NH<sup>2</sup>Cl), a membrane-permeable oxidant formed in in-

**Table 2.** Diagnosis of Toxic megacolon

Clinical presentation
Diarrhea, bloody diarrhea
Constipation, obstipation
Abdominal pain and tenderness
Abdominal distension
Decreased bowel sounds
Radiographic findings
Dilation of transverse or ascending colon >6cm
Small bowel and gastric distension
CT : colonic dilation, diffuse colonic wall thickening, submucosal edema, pericolic stranding, ascites, perforations, abscesses, ascending pyelophlebitis
Jalan's criteria
1) Fever >101.5°F (38.6°C)
2) Heart rate >120 beats/min
3) White blood cell count >10.5 (10 <sup>9</sup> /L)
or
4) Anemia
• Plus one of the following criteria: dehydration, mental changes, electrolyte disturbances, or hypotension

flamed colon because of the large amounts of luminal NH<sub>3</sub>, on ionic currents in the muscularis mucosa. This molecule was found to activate Ca<sup>++</sup> gated K<sup>+</sup> channels in rabbit mucosa. These effects would directly interfere with smooth muscle function and could thereby inhibit colonic motility (76)

## CLINICAL FEATURES

TM can occur in any patient with colitis, young or old. Often patients present during a relapse of established IBD, but a substantial number present during their first flare or within 2–3 months of diagnosis. The mean duration of disease has been reported to be 3–5 yr (57, 58).

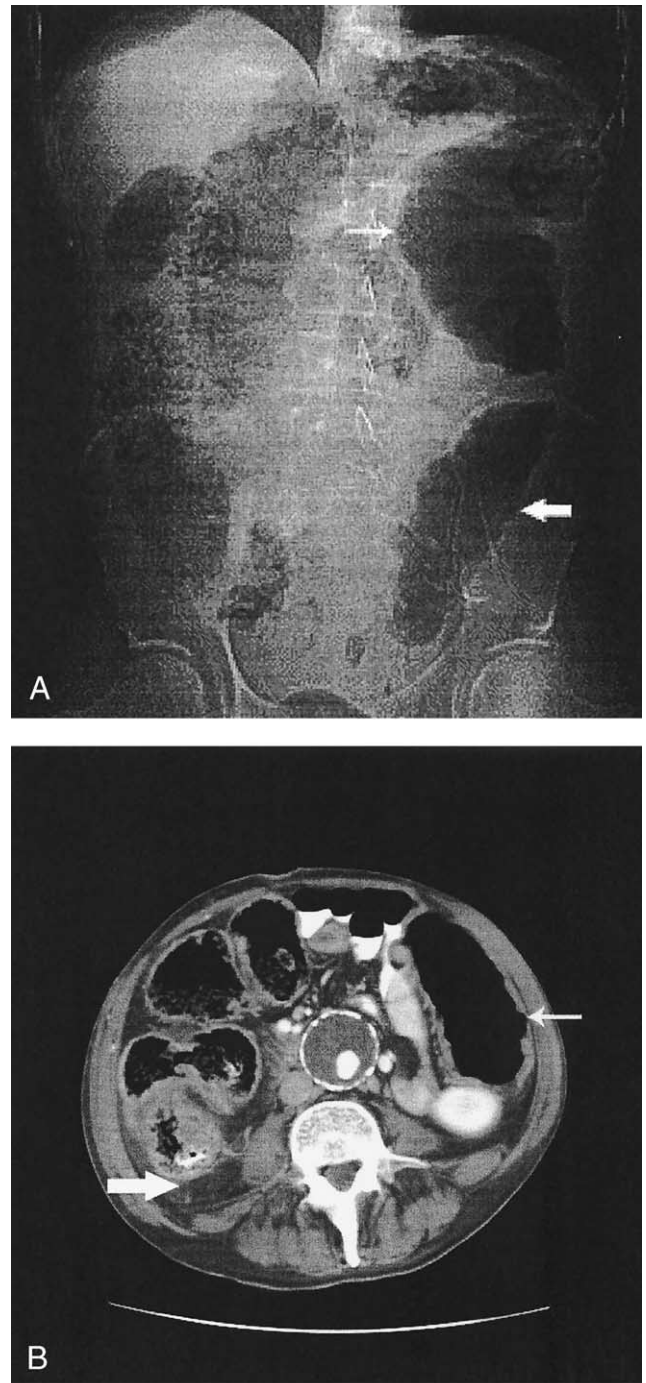
The majority of patients present in the midst of an ongoing bout of severe colitis. It is the signs of colitis that therefore predominate the clinical picture before the onset of TM. These include diarrhea (often bloody), fevers, chills, and abdominal cramping. The onset of TM is inconsistent but may be heralded by abdominal distension, constipation, obstipation, reduced bowel sounds, and constitutional symptoms such as fever, tachycardia, or hypotension. The abdomen can be extremely tender either locally or diffusely, but these signs and others may be masked by high-dose corticosteroids or a decreased level of consciousness.

Diagnosis of TM is made on the basis of clinical information and plain x-rays of the abdomen (Table 2). Jalan *et al.* described the best-accepted clinical criteria for diagnosis as any three of the following: fever >101.5°F (>38.6°C), heart rate >120 beats/min, white blood cell count >10.5 (×10<sup>9</sup>/L) or anemia. Patients should furthermore have one of the following criteria: dehydration, mental changes, electrolyte disturbances, or hypotension (58).

Radiological diagnosis (dilation of transverse or ascending colon to >6 cm) is based on consensus and clinical data that suggests the transverse colon and the ascending colon

are usually the most prone to dilation (77, 78). Kramer and Wittenberg found that air tends to sequester in the transverse colon because of its anterior and superior location when the patient is in the supine position (79). It will then redistribute to the descending and ascending colon when the patient is placed in the prone position. Dilation of  $>6$  cm is suggestive of the diagnosis, and dilations of as much as 15 cm are not uncommon. (Fig. 1A) Colonic air fluid levels are often present on upright films and the normal haustral patterns may be absent. A study of 69 patients with severe colitis demonstrated an increased risk of TM in patients with increased small intestinal gas on abdominal films as documented by planimetric studies (80). Specifically, small bowel distension was defined as small intestinal gas shadow areas significantly greater than  $36.5$  cm<sup>2</sup>. Of patients with this finding, 20% developed TM, whereas none of the 38 patients with normal intestinal gas developed toxic dilation. A prospective follow-up study found that of 45 patients with severe UC, 53% had evidence of small bowel and gastric distension. Of those patients, seven (29%) either had or developed TM and two developed multiorgan dysfunction and died. In contrast, none of the patients without small bowel and gastric distension had any complications. The authors concluded that small bowel and gastric distension is a significant predictor of TM and multiorgan dysfunction in severe ulcerative colitis (5). It is not known, however, whether the small intestinal air is simply a marker of the disease process or actually a precipitant. In centers lacking digital planimetric imaging, the authors have suggested that the number of dilated small bowel loops and the duration of dilation may be helpful in assessing the severity and predicting outcome in those with UC and TM (Renzo Caprilli, Universita la Sapienza Di Roma, personal communication, 2002).

Literature on the use of CT to diagnose TM is scant. In a recent paper by Imbriaco and Balthazar (81), experience in 18 patients with TM was reviewed. The cohort involved 12 patients with PMC, four with UC, and two with CMV colitis. CT proved useful in both the diagnosis of severe acute colitis and the diagnosis of TM and its complications. Findings of diffuse colonic wall thickening (mean 7.2 mm, range 2–17 mm), submucosal edema, and pericolic stranding were all indicative of severe colitis (Fig. 1B). Furthermore, associated dilation of the transverse colon (mean 7.7 cm, range 6–10 cm) with abnormal haustral pattern predicted the development of TM. Many patients (72%) had ascites, but this did not correlate with outcome. Four of 12 patients (33%), with PMC-associated TM had intra-abdominal complications not detected by plain films. Of these four patients, perforations were detected in two patients, one of whom had an adjacent abscess. Ascending pyelophlebitis with septic emboli was diagnosed in two other patients. Three of the four patients died of the complications despite colectomies. Despite the poor outcome of these patients, it is still recommended that all patients in whom the diagnosis is being entertained receive an abdominal CT (81). It is



**Figure 1.** A 68 yr-old man with toxic megacolon secondary to pseudomembranous colitis. (A) Plain view of a notably dilated (7 cm) descending colon (large arrow) with evidence of mucosal edema and thumbprinting (small arrow). (B) CT scan of the abdomen of the same patient. This cut demonstrates dilation of the descending colon (small arrow), mucosal wall thickening, and stranding around the affected colon (small arrow).

hoped that further studies on the role of CT in colitis and TM may provide us with more definitive prognostic criteria.

Laboratory studies usually reveal evidence of the severe underlying colitis. Patients may be anemic because of blood

**Table 3.** Management of Toxic Megacolon

General
Intravenous fluid support
Correct electrolyte abnormalities
Complete bowel rest
Discontinue anticholinergics and narcotics
Rule out infectious etiology
Decompression
Rectal tube
Nasogastric or long nasointestinal tube
Repositioning maneuvers
Medical care
Specific treatment for infections
Intravenous corticosteroids for inflammatory bowel disease
Broad spectrum antibiotics
Radiology
Frequent assessment with plain films
Computed tomographic scanning may aid in management
Surgical intervention
Failed medical care
Progressive toxicity or dilation
Signs of perforation

loss or chronic disease. White blood count may be elevated, often with a left shift, and this may be precipitated or exaggerated by use of steroids. Electrolyte abnormalities are common, and hypokalemia and hypoalbuminemia in particular reflect significant diarrhea and volume depletion. Both may portend a poor prognosis (82). Stool samples should be sent for culture, sensitivity, and *Clostridium difficile* toxin assay. Blood cultures should be considered, as bacteremia occurs in up to 25% of patients with TM (58).

Endoscopy may be of value in cases when the underlying diagnosis (51) is in question; but *extreme* caution is advised, as perforation may ensue. It is hoped that histological diagnosis has been achieved before the onset of toxic megacolon. If required, limited sigmoidoscopy may differentiate underlying colitides, particularly if the patient has no known IBD or if infective causes such as pseudomembranous or CMV colitis are in the differential diagnosis. As noted above, limited disease may have as grim a prognosis as pancolitis, and therefore knowledge of the extent of disease should not affect management. Based on anecdotal evidence (47), we would recommend advancing the sigmoidoscope only as far as is necessary to make a diagnosis. Air insufflation should be strictly minimized. Full colonoscopy cannot be recommended unless used for endoscopic decompression in a nonsurgical candidate.

## MANAGEMENT

### General Management

The management of TM must involve both medical and surgical modalities in a coordinated fashion (Table 3). Normal supportive care should be routine in all patients with TM. Patients should be placed on complete bowel rest and patients should receive adequate supplementation with intravenous fluids. Electrolytes should be closely monitored,

and any abnormalities should be corrected. All narcotic, antidiarrheal, and anticholinergic agents (including, for example, antidepressants) should be withdrawn.

Several techniques have been recommended for decompression. Although there is no firm evidence that decompression actually changes prognosis and outcome, it does have theoretical benefit and may facilitate surgery if that end is required. Nasogastric or long tube suction are both common place in management. Long intestinal tubes are reported to be more effective than nasogastric tubes in colonic decompression (60), but must be placed into the ileum under fluoroscopic guidance.

There are two reports of patient repositioning as a technique of decompression of the megacolon. Based on the previously cited study by Kramer and Wittenburg (79) of colonic gas redistribution, the first study (83) looked at 19 patients with TM were examined who were otherwise treated in the usual manner. The patients were instructed to roll into the prone position for 10–15 min every 2–3 h and were encouraged to pass gas. Efficacy was 100% after a mean time of 4.9 days. Two patients died of sepsis-related causes despite adequate decompression, and four patients still required elective colectomy. In the second study, Panos *et al.* (84) reported two patients successfully treated with frequent turning to the prone knee-elbow position, which moves the rectum to the highest point in the body. Although these techniques have never been verified in a controlled fashion, they are logically sound means of gas redistribution and should be attempted. It should be noted that although the techniques may be relatively easy in the patient who is cooperative, they become difficult nursing issues in the obtunded or intubated patient in the intensive care unit.

One case report exists on the use of a hyperbaric oxygen chamber for the purpose of colonic decompression (85). After 7 days of treatment the investigators reported a marked reduction of colonic gas and improvements in systemic markers of inflammation. The postulated mechanisms were the positive effects on the nitrogen diffusion gradient in the colon and compression of intestinal gas with subsequent improvement in mucosal circulation. This technique has not been replicated at other centers although one group has used hyperbaric oxygen in the successful treatment of a refractory case of nontoxic ulcerative colitis (86).

Endoscopic decompression has been reported in at least three patients (87, 88). The first patient, who refused surgery, was successfully decompressed by means of an indwelling endoscopically placed colonic tube. Topical steroids were infused through the tube and surgery was obviated. It must be reiterated, however, that TM is an entity that is completely different from pseudo-obstructive processes such as Ogilvie's syndrome and that endoscopic decompression is not part of the usual regimen. As stated before, endoscopy may actually worsen the disease course and does not in any way replace proper medical and surgical management.

### Medical Management

In general, controlled evidence for different medical regimens in TM is almost nonexistent. Current recommendations and practice are based on retrospective data and expert opinion.

Although there is some controversy over the use of corticosteroids in these patients, several conclusions can be made from the literature. First, although TM will often develop after the initiation of high-dose intravenous steroids, there is little to suggest that steroid therapy actually precipitates TM, which was a known complication of colitis before the steroid era, and it continues to occur in the presence of steroids. Nor is it believed that steroids increase the risk of perforation in colitis. Judicious re-evaluation of patients on corticosteroids must be maintained, however, as overt physical signs of perforation may be masked by the use of these medications, and overly zealous reliance on this therapy may delay surgery when clinically indicated.

In a retrospective study assessing the use of steroids in UC-associated TM, Jalan *et al.* compared 10 patients treated supportively with 35 patients treated with steroids (58). Nine of the 10 patients treated supportively died. In contrast, the 35 patients treated with steroids had an overall mortality of 34%, with mortality mostly due to those patients requiring urgent surgery. Six patients in the steroid-treated group attained remission, and 17 improved enough to allow elective surgery. In contrast, a third group of 10 patients treated with early colectomy had a similar 40% mortality rate; but all deaths occurred after 5 months postoperatively, and all were attributable to complications of repeat operations. On the basis of this study and others, most investigators recommend that patients who are not already initiated on steroids be started on either hydrocortisone, 100 mg every 8 h, methylprednisolone 15 mg every 6 h, or corticotropin (ACTH) 40 U every 8 h (49, 58, 89).

Antibiotics are recommended by many investigators, not as primary therapy for IBD or for toxic dilation but rather to reduce mortality should the perforation—the most dreaded endpoint—occur (47, 58, 60, 90). Furthermore, bacteremia can often be present even in the absence of perforation and carries with it a high mortality (58). It is likely that patients should be placed on broad-spectrum antibiotics; however, there is no evidence to support this.

Intravenous parenteral nutrition (IPN) and total bowel rest have been examined in the setting of acute colitis but never specifically in TM. In a classic paper by Dickinson *et al.*, no difference in outcome was determined in a randomized controlled trial of intravenous hyperalimentation and corticosteroids when compared with corticosteroids alone (91). Although nutritional status was shown to be preserved with IPN, the rate of surgical intervention and mortality was unchanged by this intervention. In addition, complications of IPN included pneumothoraces and line sepsis. The authors concluded that IPN is not an appropriate primary therapy for acute colitis but may be useful as an adjunctive

preparative therapy for patients being considered for surgery.

Use of 5-ASA products are not appropriate in this condition. Patients with TM are too severely ill to expect a positive effect from these medications and may paradoxically worsen upon their institution.

Immunosuppressants have never been studied specifically in the setting of TM. Based on a small randomized trial by Lichtiger *et al.* (92), cyclosporine has clear evidence for use in refractory colitis; but unfortunately, its effects in TM are unknown, and therefore this agent cannot be recommended. Given its strong immunosuppressive effects and potential renal toxicities, cyclosporine may even have deleterious effects in these potentially septic patients. Similarly, although certain immunosuppressive agents have been found to be effective in Crohn's colitis, there is no evidence supporting their use in TM.

Medical therapy for toxic megacolon related to non-IBD-related colitis is directed specifically to the disease process. In particular, pseudomembranous colitis should be aggressively treated with withdrawal of offending antibiotics, and either oral or intravenous metronidazole or oral vancomycin should be initiated. Surgery should not be delayed if clinical parameters continue to worsen. A recent study examined the use of decompressive colonoscopy and intracolonic vancomycin infusion for treatment in seven patients with pseudomembranous colitis-induced TM. Although four of the seven patients had a complete response and one had a partial response, mortality remained extremely high (71%) because of comorbid disease (93).

### Surgical Management

The issue of timing of surgery in patients with TM has fueled a substantial amount of debate in the literature. Absolute indications for colectomy include perforation, uncontrollable bleeding, and progressive dilation. Based on a high mortality rate in patients with perforation and on the results in several patients treated medically early in their course, several investigators have proposed that operative management be performed as soon as the diagnosis is made. Because of high mortality rates in patients with perforation and a lower short-term mortality rate among patients with early surgery, Jalan *et al.* recommended surgery shortly after diagnosis but did not preclude a short trial of medical therapy with corticosteroids (58). Goligher's often quoted dictum to "save the patient, not the colon" was based on a study that reduced the rate of perforation from 32.5% to 11.6% and mortality from 20% to 7% by means of early surgery (99). The investigators concluded that surgery should be performed shortly after diagnosis (99).

Not all evidence would concur with such an aggressive approach, and most experts would agree that a trial of medical therapy is the best initial regimen. This is based on studies showing a low mortality with medical management. Katzka *et al.*, (94), for example, reported 19 patients who were medically managed with antibiotics and corticoste-

roids for up to 7 days and noted a greater than 50% salvage of colons. There was no mortality and the majority of patients were well up to 11 yr in follow-up. Present *et al.* (95) had similar results with 68% of 19 patients being successfully managed with a mean follow-up of 6.5 yr. These studies suggest that medical treatment can be continued for at least 7 days as long as there is evidence of clinical improvement. If there is no improvement, elective surgery is far preferable to emergent surgery for complications, given the dramatic difference in outcome. Greenstein *et al.* (3) found a significantly decreased mortality in those undergoing elective surgery (5%) versus emergent (30%). Furthermore, prolonged periods of delay (>1 month) resulted in an even higher mortality (40%).

When indicated, the surgical procedure of choice in more elective situations is a total colectomy and ileostomy. In urgent situations, however, most surgeons favor a subtotal colectomy, mucous fistula, and ileostomy, as this approach is associated with a lower morbidity and mortality than is total proctocolectomy. In addition, this allows for the potential creation of a pouch at a later date. Unfortunately, there remains a high perioperative perforation rate associated with this procedure that is believed to result from iatrogenic disruption of the bowel at sites of previously walled-off perforation. The fecal soilage and sepsis that ensue are often the cause of postoperative mortality. For this reason, Turnbull *et al.* (96, 97) have suggested that in cases in which these sealed perforations are found, colectomy should be abandoned in favor of a decompression procedure referred to as a "less than colectomy" or "blowhole" operation. In essence, this is a temporary ileostomy and transverse colostomy performed to diffuse the toxicity of the situation and to allow the proper bowel cleansing necessary for a safe definitive procedure. The results of Turnbull *et al.* were impressive, with only one death in a series of 42 patients. All patients subsequently underwent elective colectomies or were awaiting such an operation at the time of publication. Not all patients were completely stabilized by the procedure, as may have been expected given the continued presence of a fulminant sigmoid colitis. Despite decompression, four patients continued to show signs of toxicity and required more expedient colectomy after 12–18 days. Khoo *et al.* (98) described an alternative form of decompression by means of a chest tube inserted into cecum through the terminal ileum. This obviated immediate surgery and allowed opportunity for preparation of the colon. Although this approach was stated to be successful in TM, actual results were not presented.

In summary, surgical intervention remains a mainstay in the management of TM. Although short trials of medical therapy are certainly warranted, any sign of complication (either clinically or on CT scan), worsening, or failure to improve should be indication for colectomy. Surgeons should be consulted early in the course of the disease, and frequent surgical reevaluation is crucial. Excessive delays will likely lead to unnecessary morbidity and mortality.

## CONCLUSIONS

TM is a dreaded complication of fulminant colitis that carries with it a high morbidity and mortality. Diagnosis is made on clinical and radiological bases and warrants immediate initiation of medical management. New evidence exists regarding the importance of early radiological clues in the prediction of this outcome. Special attention should be paid in all UC patients for the signs of significant small bowel and gastric distention on plain film. CT scans should be performed in all patients in whom the diagnosis is considered, as several complications can be identified before clinical or plain film findings. Medical therapy is directed at the underlying cause, whether inflammatory or infectious. The timing of surgery may be crucial, and delay in surgical management can result in perforation and the poor prognosis that accompanies it. The long-term prognosis of medically managed, ulcerative colitis–related TM is poor, with high rates of eventual colectomy and recurrence, and begets consideration as to the futility of medical therapy.

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