# Toxic megacolon

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## INTRODUCTION

Toxic megacolon is total or segmental nonobstructive colonic dilatation that occurs in the context of systemic toxicity [1-3]. Although toxic megacolon is most commonly considered a complication of inflammatory bowel disease, especially ulcerative colitis and, to a lesser extent, Crohn's disease, in reality almost any inflammatory or infectious condition of the colon can lead to toxic dilatation ( table 1) [4].

Colonic dilatation is also observed in patients with other disease processes. However, the lack of systemic toxicity distinguishes these presentations from true toxic megacolon. (See 'Differential diagnosis' below.)

In this topic, we discuss the clinical manifestations, diagnosis, and treatment of toxic megacolon. The management of severe or fulminant ulcerative colitis, Crohn's disease, and *Clostridioides difficile* colitis, which can lead to toxic megacolon, is also discussed in other topics:

- (See "Management of the hospitalized adult patient with severe ulcerative colitis".)
- (See "Medical management of moderate to severe Crohn disease in adults".)
- (See "Surgical management of Clostridioides difficile colitis in adults".)

## EPIDEMIOLOGY

The precise incidence of toxic megacolon is unknown. However, the adult population at risk to develop toxic megacolon is possibly shifting from those with inflammatory bowel disease (IBD) to older patients with comorbidities [5].

Historically, 1 to 5 percent of patients with IBD developed toxic megacolon [6]. The reported rate is higher in patients with ulcerative colitis in some studies [4,7] but in Crohn's patients in other studies [6]. The prevalence of toxic megacolon has decreased in contemporary series of inflammatory bowel disease.

Approximately 1 percent of all hospitalized patients have symptomatic *C. difficile* infection [8-10]. The incidence of *C. difficile*-colitis-related toxic megacolon has increased from 0.4 to 3 percent before 1990 to 4.3 percent after 1990, in proportion to the rapidly increasing prevalence of the disease [4,7]. (See "*Clostridioides difficile* infection in adults: Epidemiology, microbiology, and pathophysiology".)

## ETIOLOGY

Toxic megacolon can occur with many infectious or inflammatory etiologies ( table 1).

- Patients with inflammatory bowel disease (IBD) usually present with abdominal pain, bloody diarrhea, perianal disease, and/or symptoms outside of the gastrointestinal tract. (See "Clinical manifestations, diagnosis, and prognosis of ulcerative colitis in adults" and "Clinical manifestations, diagnosis, and prognosis of Crohn disease in adults".)

- Risk factors for the development of severe colitis in patients with *C. difficile* infection include malignancy, chronic obstructive pulmonary disease, immunosuppressive therapy, renal failure, or exposure to antiperistaltic medications or clindamycin [8,11]. Toxic megacolon has been described in patients with recurrent *C. difficile* [12].

- *Salmonella* [13], *Shigella* [14], and *Campylobacter* colitis [15] can also lead to toxic dilatation and can usually be differentiated from IBD by histology and endoscopic biopsy [16]. Toxic megacolon may also arise from hemorrhagic colitis and hemolytic uremic syndrome secondary to infection with *Escherichia coli* O157 [17].

- Amoebic infection can cause fulminant colitis in a small percentage of patients, including possible toxic megacolon. The use of loperamide in amoebic colitis may precipitate toxic megacolon [18].

- Disseminated cytomegalovirus (CMV) infection is a cause of toxic megacolon in patients with HIV infection or IBD [19]. In one series, for example, 6 of 46 resected colons in

patients with ulcerative colitis showed evidence of CMV infection; 5 of these 6 patients had toxic dilatation compared with only 2 of the remaining 40 patients without CMV infection [20]. (See 'HIV/AIDS patients' below.)

## PATHOGENESIS AND RISK FACTORS

Toxic megacolon is characterized by colonic dilatation, which can be caused by a few potential mechanisms [1]:

- Colonic inflammation increases the production of inducible nitric oxide (NO) synthase by macrophage and smooth muscle cells [21]. NO inhibits smooth muscle tone, which contributes toward colonic dilatation [1].
- While only the mucosa is inflamed in typical ulcerative colitis, the smooth muscle layer is inflamed and paralyzed in toxic megacolon, which can contribute toward colonic dilatation. It is inconclusive whether the myenteric plexus of the colon is damaged in toxic megacolon.
- Risk factors that could precipitate toxic megacolon include hypokalemia, antimotility agents, opiates, anticholinergics, antidepressants, abrupt cessation of glucocorticoids, barium enemas, and colonoscopy/bowel preparation [22].
- Sulfasalazine and 5-ASA compounds can precipitate toxic megacolon and therefore have no role in treating patients with inflammatory bowel disease-related toxic megacolon. They should be initiated or continued only after the symptoms of toxic megacolon have resolved.

## CLINICAL MANIFESTATIONS

Toxic megacolon affects all ages. Inflammatory bowel disease (IBD)-related toxic megacolon occurs early in the disease progression and not infrequently at initial presentation [3]. Of those patients with IBD who develop toxic megacolon, approximately 30 percent develop toxic dilatation within three months of diagnosis, and approximately 60 percent within the first three years. Compared with ulcerative colitis, Crohn's disease is even more susceptible to developing into toxic megacolon during the acute and early phase, before extensive fibrosis develops, which prevents dilatation of the colon [6].

Patients typically present with severe bloody diarrhea that is refractory to therapy for at least one week prior to acute colonic dilatation; diarrhea may improve after the development of megacolon. One study of patients with *C. difficile* colitis and toxic megacolon found that diarrhea was a complaint in 100 percent of cases, malaise in 91 percent, and abdominal pain and distention in 82 percent [9].

A thorough history is crucial. Knowledge of prior attacks of IBD, the extent and type of disease, details of prior therapy, extraintestinal manifestations of IBD, recent travel, HIV status, occupational exposure (eg, day care workers), and medications (eg, chemotherapy, antibiotics, or antimotility agents) is very helpful.

Physical examination invariably reveals a toxic-appearing patient with altered sensorium, fever, tachycardia, hypotension, and distended and tender abdomen with or without peritoneal signs. However, corticosteroids, analgesics, or a clouded sensorium may mask the signs or symptoms of toxic megacolon.

## DIAGNOSIS

Toxic megacolon should be suspected in patients with abdominal distension and diarrhea. The diagnosis is made based on clinical signs of systemic toxicity combined with radiographic evidence of colonic dilatation (diameter >6 cm) [7]. The most widely used criteria are [3]:

- Radiographic evidence of colonic dilation (diameter >6 cm)
- PLUS at least three of the following:
  - Fever >38ºC
  - Heart rate >120 beats/min
  - Neutrophilic leukocytosis >10,500/microL
  - Anemia
- PLUS at least one of the following:
  - Dehydration
  - Altered sensorium
  - Electrolyte disturbances

- Hypotension

## DIAGNOSTIC EVALUATION

The initial evaluation should be aimed at establishing the diagnosis of toxic megacolon and at determining the underlying etiology to help institute specific therapeutic measures.

**Imaging studies** — Although a "megacolon" is defined radiographically by a maximum diameter of >6 cm, the diagnosis of toxic megacolon has more to do with the clinical condition of the patient than with the colonic diameter. (See 'Diagnosis' above.)

In contemporary practice, an abdominopelvic computed tomography (CT) with oral and intravenous contrast is typically first performed to establish the diagnosis and exclude complications that may require immediate surgery; rectal contrast is contraindicated in this patient population. Serial plain abdominal films are then performed to follow the progression of colonic dilatation. CT can be repeated if there is a concern for evolving complications (eg, abscess) in patients who deteriorate or fail to improve.

Baseline plain abdominal films should be obtained upon admission. Plain abdominal radiographs are critical for diagnosing toxic megacolon and for following its course. There are several typical features ( image 1):

- The degree of dilatation is usually the greatest in the transverse or right colon, followed by the descending colon, the sigmoid colon, and the rectum. The diameter of the transverse and right colon is frequently greater than 6 cm and occasionally up to 15 cm on supine films [2].
- By contrast, the location of air is not as important as the degree of dilatation, as repositioning of the patient can result in redistribution of air in the colon.
- The normal colonic haustral pattern is either absent or severely disturbed.
- Multiple air-fluid levels can be seen in the colon.
- Deep mucosal ulcerations may appear as air-filled crevices between large pseudopolypoid projections extending into the colonic lumen.
- Some studies suggest that toxic megacolon can be predicted by an increase of small bowel gas on abdominal films [4,23].

- Ultrasonography and CT may aid in overall management [24]. Abdominal CT is more reliable in evaluating both the length and severity of colitis and the presence of colonic dilatation than plain abdominal radiographs [25]. CT may even be able to distinguish toxic megacolon (segmental colonic wall thinning, air-filled colonic distension over 6 cm with abnormal haustral pattern, nodular pseudopolyps, and associated small bowel distension) from severe acute colitis (diffuse colonic wall thickening, submucosal edema, pericolonic fat stranding, and ascites) [26]. Furthermore, CT can also identify complications of megacolon, such as perforation or vascular compromise, and is helpful for excluding other causes of colonic distension, such as mechanical obstruction [27]. However, CT is generally unable to determine the etiology of the inflammatory process or predict the clinical outcome.

**Laboratory studies** — There may be multiple nonspecific laboratory abnormalities associated with toxic megacolon:

- Leukocytosis with a neutrophil predominance occurs frequently, especially with *C. difficile* infection. By contrast, immunocompromised (eg, AIDS [acquired immunodeficiency syndrome] patients) or septic patients may exhibit neutropenia. In addition, patients with toxic megacolon may develop anemia from gastrointestinal blood loss.

- Patients may develop hypokalemia and metabolic alkalosis due to diarrhea and colonic inflammation [28]. Metabolic acidosis suggests the presence of ischemic colitis.

- Hypoalbuminemia (<3 g/dL) is common due to protein loss, chronic inflammation, and malnutrition.

- Inflammatory markers such as erythrocyte sedimentation rate and serum C-reactive protein are usually increased.

- In addition, stool specimens should be sent for culture, microscopic analysis, and *C. difficile* toxin.

**Limited endoscopy for selected patients** — We suggest that a complete colonoscopy should generally be avoided in patients with toxic megacolon because it can cause colonic perforation. However, one study has reported it safe in patients with severe ulcerative colitis [29].

A limited endoscopic examination without bowel preparation (eg, proctoscopy or sigmoidoscopy) is safer and can be used to diagnose an inflammatory (eg, inflammatory bowel disease [IBD]) or infectious process (eg, cytomegalovirus [CMV] or *C. difficile* colitis) in the rectum or sigmoid colon. However, limited sigmoidoscopy can miss CMV inclusion bodies that

may only be present in the right colon [30]. Similarly, while a proctoscopic finding of pseudomembrane may allow rapid diagnosis of *C. difficile* colitis, the rectum may be spared in up to 40 percent of patients with *C. difficile* colitis. (See "*Clostridioides difficile* infection in adults: Clinical manifestations and diagnosis", section on 'Endoscopy'.)

If performed, either limited or complete lower endoscopy should be done cautiously, with minimal or no air insufflation, to avoid worsening ileus or distention/perforation of the colon.

**Pathology** — The gross pathologic features of fulminant colitis and toxic megacolon are similar in both ulcerative colitis and Crohn's disease, with marked dilatation of the colon, thinning of the bowel wall, and deep ulcers. The histologic hallmark is acute inflammation in all layers of the colon with varying degrees of degeneration, necrosis, and replacement by granulation tissue infiltrated by histiocytes, neutrophils, lymphocytes, and plasma cells. The muscle fibers are frequently shortened and rounded with aggregates of eosinophilic cytoplasm. The preservation of colonic submucosal and myenteric plexi is a common feature and is strong evidence against a neuropathic process [31].

The pathologic appearance of toxic megacolon associated with other disorders is as follows:

- In toxic megacolon secondary to *C. difficile* (or, rarely, ischemia), the characteristic pathologic features include diffuse ulcerations, raised mucosal nodules, yellowish-white superficial plaques with normal intervening mucosa (typical "pseudomembrane" appearance), and extensive denudation ( picture 1).
- Similar findings may also be seen in fulminant amoebic colitis, in addition to the characteristic "wet blotting paper" appearance of the involved bowel segments, punched-out ulcers, and presence of trophozoites in biopsy specimens.
- CMV colitis is characterized by the presence of inclusion bodies in biopsy specimens.

## DIFFERENTIAL DIAGNOSIS

Toxic megacolon may be differentiated from other chronic nontoxic processes leading to colonic dilatation by its inflammatory trigger and accompanying toxic manifestations. These processes include:

- Congenital megacolon (Hirschsprung's disease) (see "Congenital aganglionic megacolon (Hirschsprung disease)")

- Acquired megacolon (eg, due to chronic constipation) (see "Etiology and evaluation of chronic constipation in adults", section on 'Megacolon and megarectum')
- Chagas megacolon (see "Chagas gastrointestinal disease", section on 'Colonic manifestations')
- Colonic pseudo-obstruction (Ogilvie syndrome) (see "Acute colonic pseudo-obstruction (Ogilvie's syndrome)")
- Diffuse gastrointestinal dysmotility (see "Chronic intestinal pseudo-obstruction: Etiology, clinical manifestations, and diagnosis")

Colonic dilatation and systemic toxicity are also seen in patients with acute colonic obstruction from diverticulitis, volvulus, pelvic tumors, and intraluminal obstructing tumors. In these patients, a history of acute or chronic diarrhea is unusual, and air is absent in the colon below the point of obstruction. Barium enema or colonoscopy is often required to diagnose the level and type of obstruction.

## TREATMENT

The treatment of toxic megacolon is aimed at reducing colonic inflammation, restoring normal colonic motility, and decreasing the likelihood of perforation [1]. The initial therapy is supportive and medical, which is successful in preventing surgery in up to 50 percent of patients [2]. However, surgery is required for the rest of the patients.

The timing of surgery in toxic megacolon is still a matter of controversy and varies by the underlying etiology of the toxic megacolon. Although the principal objective of all medical therapy is to circumvent the need for surgery, delaying surgery may ultimately increase the risk of complications such as bowel perforation or abdominal compartment syndrome [32] heralding a poor prognosis [7].

**Supportive therapy** — The patient typically requires intensive care because of systemic toxicity. Routine laboratory tests and abdominal radiographs are checked twice a day until the patient is stabilized, then continued daily. Patients are repleted with blood products, intravenous fluids, and electrolytes (eg, potassium).

Patients are initially placed at complete bowel rest, and nasogastric tube decompression may be required at the discretion of the treating clinician. Total parenteral nutrition (TPN) may be necessary for patients who cannot tolerate enteral nutrition but has not been shown to decrease the need for surgery or the length of hospital stay in patients with acute colitis due to

ulcerative colitis [33]. Enteral feeding, which hastens mucosal healing and stimulates normal motility, can be started as soon as the patient's condition improves.

Patients should be given broad-spectrum antibiotics to treat sepsis and, in case of colonic perforation, histamine-2 blockers or proton pump inhibitors for ulcer prophylaxis and venous thromboembolism prophylaxis. All medications that can impede colonic motility (eg, opiates, anticholinergics) should be stopped.

Intermittent rolling maneuvers [34] or the knee-elbow position [35] may help redistribute and expel gas in the colon. These techniques may be particularly useful when colonic dilatation persists despite the resolution of systemic toxicity.

**Etiology-specific therapy** — The specific medical/surgical therapy for toxic megacolon must target the underlying etiology:

**Inflammatory bowel disease**

**Glucocorticoids** — We suggest intravenous glucocorticoids (hydrocortisone 100 mg or equivalent every six to eight hours or by continuous infusion) as the first-line therapy for all patients with IBD-related toxic megacolon; this does not increase the risk of perforation [31]. However, this approach is based on limited observational data and clinical experience.

Medical therapy is successful when the patient appears to be less toxic, requires fewer fluid or blood products, has less abdominal and colonic dilatation, and has improved laboratory parameters. By contrast, persistent fever after 48 to 72 hours of glucocorticoid therapy suggests possible complications (eg, abscess or perforation), in which case repeat abdominal CT and surgical consultation should be obtained.

Absolute indications for surgery at any time include:

- Frank intraperitoneal perforation
- Life-threatening hemorrhage or increasing transfusion requirements
- Worsening systemic toxicity
- Worsening colonic dilatation

In addition, most surgeons recommend colectomy if there is persistent colonic distention after 48 to 72 hours since older studies have shown the incidence of free perforation to be as high as 50 percent after 72 hours of unsuccessful conservative treatment [6]. However, those studies were performed without the benefit of modern medications such as cyclosporine and biologics (eg, infliximab).

**Infliximab or cyclosporine** — Patients with IBD-related toxic megacolon who do not respond to intravenous glucocorticoids within three days should be considered for a trial of infliximab or cyclosporine as second-line therapy. (See "Medical management of moderate to severe Crohn disease in adults" and "Management of the hospitalized adult patient with severe ulcerative colitis", section on 'Complications'.)

Whereas most patients who develop IBD-related toxic megacolon have ulcerative colitis, some have Crohn's colitis or indeterminate colitis. Since these three entities may not be readily distinguishable during an acute flare-up such as toxic megacolon, we suggest treating all IBD-related toxic megacolon with the same approach. (See 'Pathology' above.)

Infliximab is the preferred second-line treatment for all patients with IBD-related toxic megacolon. Cyclosporine should be reserved for those who cannot tolerate infliximab (eg, due to drug allergy), and there is only evidence for its effectiveness in ulcerative colitis, not Crohn's disease.

**Surgery** — Patients who fail to respond to one of the second-line agents (infliximab or cyclosporine) after another three days require surgery. Patients who develop toxic megacolon while on either infliximab or cyclosporine should undergo surgery without delay.

For patients who require emergency surgery for IBD-related toxic megacolon, we suggest subtotal colectomy with end ileostomy rather than a single-stage proctocolectomy [4]. Subtotal colectomy has a lower morbidity and mortality and permits subsequent anastomosis in most patients. The surgical mortality is much lower without than with colonic perforation (2 to 8 versus 40 percent or more) [36]. (See "Surgical management of ulcerative colitis" and "Surgical management of Crohn disease".)

**C. difficile colitis** — The inciting antibiotics should be stopped in patients with *C. difficile* colitis-related toxic megacolon. Steroids are **not** used for infectious colitis.

**Medical therapy** — Medical therapy is the first-line treatment for fulminant *C. difficile* colitis. The details of medical therapy for severe or fulminant *C. difficile* colitis are presented in this table ( table 2) and another topic. (See "*Clostridioides difficile* infection in adults: Treatment and prevention".)

Fecal microbial transplantation has been used successfully in *C. difficile* patients with severe colitis including toxic megacolon [37,38], but the indications, outcomes, and risks of this approach have not been well defined [39]. (See "Fecal microbiota transplantation for treatment of *Clostridioides difficile* infection".)

**Surgery** — Surgery is indicated for colonic perforation, necrosis, or full-thickness ischemia, intra-abdominal hypertension or abdominal compartment syndrome, clinical signs of peritonitis or worsening abdominal examination despite adequate medical therapy, and end-organ failure (eg, vasopressor requirement, intubation and mechanical ventilation, or acute renal failure) ( table 3). In addition, white blood cell count >50,000 cell/mL and serum lactate level of >5 mmol/L are relative indications for surgery. Early colectomy before the onset of septic shock was associated with a reduction of 30 day mortality from 45 to 21 percent [40]. (See "Surgical management of Clostridioides difficile colitis in adults", section on 'When to perform surgery?'.)

Several operative approaches have been advocated in the management of patients with *C. difficile* colitis who meet the criteria for surgical therapy as outlined before. Total abdominal colectomy used to be the standard procedure and remains the procedure of choice for patients with colonic perforation, necrosis, or abdominal compartment syndrome. For others, diverting loop ileostomy/colonic lavage is an alternative that has been associated with decreased mortality in limited studies. Partial or segmental colectomy is no longer performed, due to a higher reoperative and mortality rate. These surgical procedures are discussed in detail in this algorithm ( algorithm 1) and another topic. (See "Surgical management of Clostridioides difficile colitis in adults", section on 'Which procedure to perform?'.)

## SPECIAL POPULATIONS

**HIV/AIDS patients** — Toxic megacolon may develop in patients with HIV (human immunodeficiency virus) infection due to various infectious and noninfectious causes. Among these, cytomegalovirus (CMV) colitis or *C. difficile* infection often does not respond to medical therapy and requires surgery [41,42]. In one report, however, four of five such patients died despite emergency colectomy [41]. Critically ill patients who would not be able to withstand surgery, as well as patients with terminal AIDS, could possibly be managed by careful colonic decompression, antibiotics, and supportive therapy.

**Pregnant women** — Women with known risk factors for toxic megacolon (most commonly ulcerative colitis) should plan conception during a state of remission [43]. Patients who are in remission at the conception are likely to remain in remission during pregnancy. When toxic megacolon develops during pregnancy due to ulcerative colitis, 75 percent of the cases resolve with high-dose intravenous glucocorticoid therapy (the equivalent of 60 to 120 mg/day of prednisone); the rest will require either infliximab or surgery [44,45]. (See 'Inflammatory bowel disease' above.)

It is more difficult to diagnose toxic megacolon during pregnancy because of the interference of the physical examination from a gravid uterus and the limited choices of imaging modalities [46]. In addition, laboratory tests such as hemoglobin and serum albumin concentrations fall during pregnancy, while the erythrocyte sedimentation rate and serum C-reactive protein levels increase; thus, these tests are not reliable measures of disease activity. The choice of anti-inflammatory and immunosuppressive medications during pregnancy should be based on their relative safety and efficacy. Urgent colon surgery is associated with higher risks of preterm delivery and spontaneous abortions. (See "Fertility, pregnancy, and nursing in inflammatory bowel disease".)

## OUTCOME

The mortality rates in patients who develop toxic megacolon are trending down. In a historic study from the last century, the mortality rate of toxic megacolon was 27 and 19 percent with medical and surgical treatment, respectively [47]. The in-hospital mortality for toxic megacolon further decreased from 9.2 to 6.5 percent during the observation period of 2010 through 2014 [48]. Colonic perforation is associated with a significantly worse prognosis, with the mortality rate increasing by three- to fivefold [4,27,48,49].

It used to be generally accepted that colonic dilatation due to infectious colitis had a better prognosis than toxic megacolon occurring in patients with inflammatory bowel disease (IBD) who have been treated with biologics; however, this conclusion was largely based upon small studies or case reports. The prognosis is particularly good when colonic dilatation complicates acute self-limited colitis and is treated aggressively [50].

However, the mortality rates dropped dramatically to between 0 and 2 percent in patients with IBD, probably due to early recognition of toxic megacolon, early escalation from glucocorticoid therapy to biologics (or cyclosporine), increasing use of biologics and accelerated dosing, and improved medical and surgical care [36].

Variations in mortality rates may also be related to the specialty biases of the published literature. Two studies from the medical literature have shown that 68 to 75 percent of cases of toxic megacolon treated medically did not require a colectomy later and have remained in remission for up to six years [4,36]. Surgical studies report up to a 50 percent rate of future colectomy in patients with toxic megacolon who had presumably responded to medical treatment alone [2,51]. Early surgery decreased the mortality rate from 22 to 1.2 percent in one report [52].

One study between 1968 and 1992 associated *C. difficile*-related toxic megacolon with an overall mortality of 31 to 35 percent, 42 percent for those treated with surgery and 18 percent for those treated medically [9]. In more contemporary studies, the overall mortality from severe *C. difficile* colitis/toxic megacolon was 64 to 67 percent, and 71 to 100 percent for surgically treated patients [8,9]. These studies suggest that patients who develop toxic megacolon during *C. difficile* infection can survive with medical therapy alone, and surgery may offer a very limited benefit. On the other hand, surgery should not be extensively delayed in acutely ill patients. In a contemporary series of colectomies performed for toxic megacolon, a 30 day mortality of approximately 15 percent was achieved in patients with either IBD or *C. difficile* infection [53].

## SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Ulcerative colitis in adults".)

## SUMMARY AND RECOMMENDATIONS

- **Etiologies** – Toxic megacolon is a life-threatening complication of inflammatory or infectious colitis that is characterized by total or segmental nonobstructive colonic dilatation plus systemic toxicity. Although inflammatory bowel disease (IBD) and *Clostridioides difficile* colitis are the two most common causes, other inflammatory or infectious conditions of the colon can also lead to toxic dilatation ( table 1). (See 'Introduction' above and 'Etiology' above.)

- **Clinical manifestations** – Of patients with IBD who develop toxic megacolon, approximately 30 percent develop toxic dilatation within three months after diagnosis and approximately 60 percent within the first three years. Severe bloody diarrhea is the most common presenting symptom. (See 'Clinical manifestations' above.)

- **Diagnosis** – Toxic megacolon should be suspected in all patients with abdominal distension and diarrhea. The diagnosis is made based on clinical signs of systemic toxicity combined with radiographic evidence of colonic dilatation (maximum diameter >6 cm). (See 'Diagnosis' above.)

  - **Imaging** – Abdominopelvic CT with oral and intravenous contrast is typically first performed to establish the diagnosis and exclude complications that may require

immediate surgery. Serial plain abdominal films are then performed to follow the progression of colonic dilatation. (See 'Imaging studies' above.)

- **Role of endoscopy** – Bowel preparation, barium enema, and complete colonoscopy are contraindicated because they can cause colonic perforation. An unprepped, limited endoscopic examination of the rectum and sigmoid colon can be performed to diagnose an inflammatory (eg, IBD) or infectious process (eg, cytomegalovirus [CMV] or *C. difficile* colitis). (See 'Limited endoscopy for selected patients' above.)

- **Supportive therapy** – Supportive therapy should be instituted for all patients with toxic megacolon, regardless of etiology, and includes intensive care unit monitoring, fluid resuscitation and correction of laboratory abnormalities, administration of broad-spectrum antibiotics, complete bowel rest, and a surgical consultation. Bowel decompression with a nasogastric tube can be performed at the discretion of the treating clinician. (See 'Supportive therapy' above.)

- **Definitive therapy for IBD-related toxic megacolon** – For patients with IBD-related (ulcerative colitis, Crohn's colitis, or indeterminate colitis) toxic megacolon, we prefer the following approach (see 'Inflammatory bowel disease' above and "Management of the hospitalized adult patient with severe ulcerative colitis", section on 'Complications'):

  - Intravenous glucocorticoid therapy for three days.

  - Either infliximab (preferred) or cyclosporine (alternative for ulcerative colitis only) for another three days, if the patient does not respond to glucocorticoids.

  - Surgery (usually subtotal colectomy and ileostomy) if the patient again fails to respond or develops toxic megacolon while already on glucocorticoid, infliximab, or cyclosporine therapy.

- **Definitive therapy for *C. difficile*-related toxic megacolon** – For patients with toxic megacolon from *C. difficile,* medications are first-line therapy. Surgery is indicated for colonic perforation, necrosis, or full-thickness ischemia, intra-abdominal hypertension or abdominal compartment syndrome, clinical signs of peritonitis or worsening abdominal examination despite adequate medical therapy, and end-organ failure (eg, vasopressor requirement, intubation and mechanical ventilation, or acute renal failure) and can be performed as either total abdominal colectomy or diverting ileostomy with colonic lavage. (See 'C. difficile colitis' above and "*Clostridioides difficile* infection in adults: Treatment and prevention" and "Surgical management of Clostridioides difficile colitis in adults".)

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Topic 1381 Version 22.0

## GRAPHICS

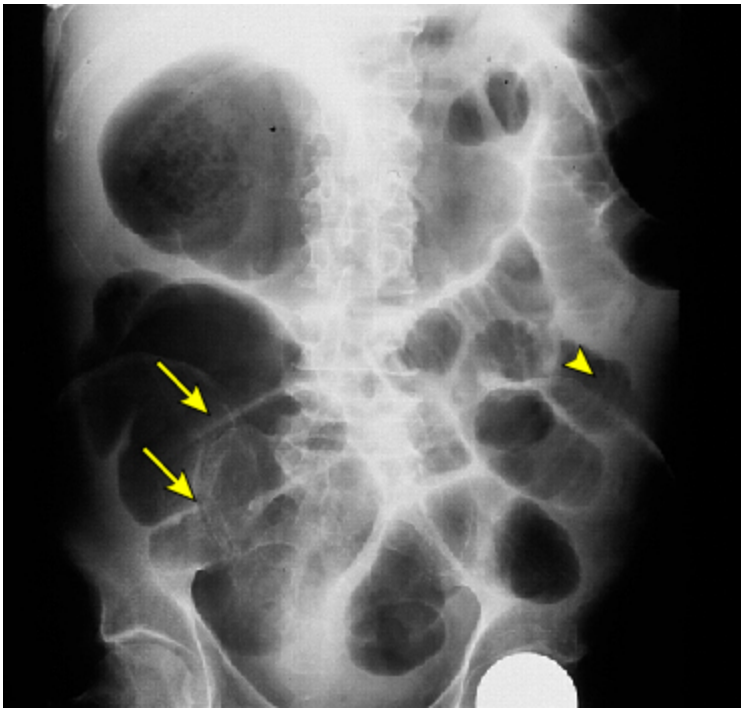
### Causes of toxic megacolon

| |
|---|
| **Inflammatory** |
| Ulcerative colitis |
| Crohn's colitis |
| **Infectious** |
| Bacterial |
| *Clostridioides difficile* pseudomembranous colitis |
| *Salmonella* - typhoid and nontyphoid |
| *Shigella* |
| *Campylobacter* |
| *Yersinia* |
| Parasitic |
| *Entameba histolytica* |
| *Cryptosporidium* |
| Viral |
| CMV colitis |
| Self-limited colitis (culture negative) |
| **Other** |
| Pseudomembranous colitis secondary to methotrexate therapy |
| Kaposi's sarcoma |

CMV: cytomegalovirus.

Graphic 72629 Version 3.0

## Toxic megacolon in *Clostridioides difficile*



Plain film of the abdomen from a patient with toxic megacolon associated with *Clostridioides* (formerly *Clostridium*) *difficile* infection. The large and small intestines are grossly dilated. Dilatation of the small bowel, which has the thin transverse folds of the valvulae conniventes (arrowhead), is seen best in the left lower quadrant. Large bowel dilatation occupies most of the right lower quadrant and has characteristic thick haustral markings that do not extend across the entire lumen (arrows).

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*Courtesy of J Thomas Lamont, MD.*

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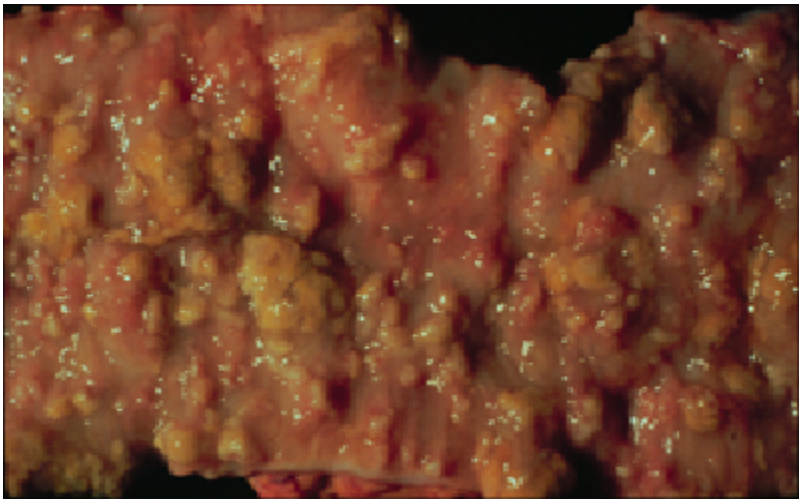
Graphic 59217 Version 8.0

## Pseudomembranous colitis



Gross appearance of the colon from a patient with pseudomembranous colitis. The pseudomembranes are yellow or off-white raised plaques 0.2 to 2.0 cm in diameter, which are scattered over fairly normal-appearing intervening mucosa.

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*Courtesy of J Thomas Lamont, MD.*

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Graphic 62422 Version 2.0

## Treatment of *Clostridioides difficile* infection (CDI) in adults

| Clinical condition | Treatment |
|---|---|
| **Nonfulminant disease** | |
| **Initial episode (nonsevere or severe disease)** | Management of an initial CDI episode consists of treatment with an antibiotic regimen. |
| **Nonsevere disease** is supported by the following clinical data: White blood cell count ≤15,000 cells/mL and serum creatinine level <1.5 mg/dL<br><br>**Severe disease*** is supported by the following clinical data: White blood cell count >15,000 cells/mL and/or serum creatinine level ≥1.5 mg/dL | **Antibiotic regimens:**<br>▪ Fidaxomicin[¶] 200 mg orally twice daily for 10 days<br>▪ Vancomycin[Δ] 125 mg orally 4 times daily for 10 days<br>▪ For nonsevere disease, alternative regimen if above agents are unavailable:<br>• Metronidazole[◇] 500 mg orally 3 times daily for 10 to 14 days |
| **Recurrent episode**[§] | Management of a recurrent CDI episode consists of treatment with an antibiotic regimen, in addition to adjunctive bezlotoxumab[¶] if feasible. |
| **First recurrence** | **Antibiotic regimens:**<br>▪ Fidaxomicin[¶]<br>• 200 mg orally twice daily for 10 days, **OR**<br>• 200 mg orally twice daily for 5 days, followed by once every other day for 20 days<br>▪ Vancomycin[Δ] in a tapered and pulsed regimen, for example:<br>• 125 mg orally 4 times daily for 10 to 14 days, then<br>• 125 mg orally 2 times daily for 7 days, then<br>• 125 mg orally once daily for 7 days, then<br>• 125 mg orally every 2 to 3 days for 2 to 8 weeks<br>▪ Vancomycin[Δ] 125 mg orally 4 times daily for 10 days<br><br>**Adjunctive treatment:** Bezlotoxumab[¶ ¥] 10 mg/kg intravenously, given once during administration of standard antibiotic regimen. |
| **Second or subsequent recurrence** | **Antibiotic regimens:**<br>▪ Fidaxomicin[¶]<br>• 200 mg orally twice daily for 10 days, **OR** |

| | |
|---|---|
| | • 200 mg orally twice daily for 5 days, followed by once every other day for 20 days<br>▪ Vancomycin[Δ] in a tapered and pulsed regimen (example as above)<br>▪ Vancomycin[Δ] followed by rifaximin:<br>• Vancomycin 125 mg orally 4 times daily by mouth for 10 days, then<br>• Rifaximin 400 mg orally 3 times daily for 20 days<br>**Adjunctive treatment:** Bezlotoxumab[¶ ¥] 10 mg/kg intravenously, given once during administration of standard antibiotic regimen.<br>**Role of fecal microbiota transplantation (FMT):** For patients who have received appropriate antibiotic treatment for at least 3 CDI episodes (ie, initial episode plus 2 recurrences), who subsequently present with a fourth or further CDI episode (third or subsequent recurrence), we favor FMT in regions where available[‡]. Pending referral for FMT, we treat with an antibiotic regimen as outlined above. |
| **Fulminant disease** | |
| **Fulminant disease*** is supported by the following clinical data: Hypotension or shock, ileus, megacolon | ▪ Absence of ileus: Enteric vancomycin plus parenteral metronidazole[†]:<br>• Vancomycin[Δ] 500 mg orally or via nasogastric tube 4 times daily, **AND**<br>• Metronidazole 500 mg intravenously every 8 hours<br>▪ If ileus is present, additional considerations include:<br>• FMT (administered rectally)** **OR**<br>• Rectal vancomycin (administered as a retention enema 500 mg in 100 mL normal saline per rectum; retained for as long as possible and readministered every 6 hours)[¶¶] |

The standard course of treatment for an initial episode of CDI is 10 days. Some patients, particularly those treated with metronidazole or with severe disease, may have a delayed response; in such circumstances, treatment may be extended to 14 days. For patients with inflammatory bowel disease, an extended duration of 14 days is also appropriate. If continuation of antibiotic(s) for a primary infection is essential, we continue CDI treatment for one week after completion of other antibiotics.

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* The criteria proposed for defining severe or fulminant CDI are based on expert opinion and may need to be reviewed upon publication of prospectively validated severity scores for patients with CDI. Patients with severe or fulminant CDI also warrant assessment for surgical indications; refer to UpToDate topic on treatment of CDI for further discussion.

¶ For patients with nonfulminant disease, we suggest a fidaxomicin-based regimen over a vancomycin-based regimen. In addition, for patients with nonfulminant recurrent disease and prior CDI in the last 6 months, we suggest adjunctive bezlotoxumab. Use of fidaxomicin or bezlotoxumab

have each been associated with a small benefit with respect to CDI recurrence rates (10 to 15% decrease). In the setting of cost constraints, we prioritize use of these agents for patients at greatest risk for CDI recurrence (age ≥65 years, severe CDI, or immunosuppression). Vancomycin remains an acceptable agent for treatment of initial and recurrent CDI.

Δ Systemic absorption of enteral vancomycin can occur in patients with mucosal disruption due to severe or fulminant colitis; this consideration is particularly important for patients with kidney insufficiency (creatinine clearance <10 mL/minute). Therefore, monitoring serum vancomycin levels is warranted for patients with kidney failure who have severe or fulminant colitis and require a prolonged course (>10 days) of enteral vancomycin therapy.

◇ Metronidazole should be avoided in patients who are frail, age >65 years, or who develop CDI in association with inflammatory bowel disease. Caution is also warranted during pregnancy and lactation.

§ The approach to antibiotic management of nonfulminant recurrent CDI is the same regardless of severity, but varies depending on the number of recurrences, as outlined above. For patients with a recurrent episode of CDI that is severe, refer to UpToDate topic on treatment of CDI for further discussion.

¥ The bezlotoxumab prescribing information in the United States warns that in patients with a history of congestive heart failure, the drug should be reserved for use when the benefit outweighs the risk, given reports of increased heart failure exacerbations and associated deaths in such patients. In addition, data for use of bezlotoxumab combined with fidaxomicin are limited.

‡ In contrast to the above approach, some favor FMT for patients who have received antibiotic treatment for at least 2 CDI episodes (ie, initial episode plus one recurrence), who subsequently present with a third or further CDI episode (second or subsequent recurrence)[1].

† Continue dosing for 10 days. If recovery is delayed, treatment can be extended to 14 days.

** In the setting of ileus, we favor FMT over rectal vancomycin. However, such procedures are associated with risk of colonic perforation; therefore, they should be restricted to patients who are not responsive to standard therapy, and the procedure should be performed by personnel with appropriate expertise. Refer to the UpToDate topic on FMT for discussion of safety, efficacy, and delivery protocols.

¶¶ Rectal vancomycin may be administered as a retention enema, either in addition to oral vancomycin (if the ileus is partial) or in place of oral vancomycin (if the ileus is complete). Given potential risk of colonic perforation in setting of CDI, rectal vancomycin instillation should be performed by personnel with appropriate expertise.

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*Reference:*

1. *Kelly CR, Fischer M, Allegretti JR, et al. ACG Clinical Guidelines: Prevention, Diagnosis, and Treatment of Clostridioides difficile Infections. Am J Gastroenterol 2021; 116:1124.*

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Graphic 53273 Version 44.0

## Indications for operative management in patients with CDI

| **A diagnosis of CDI as determined by one of the following:** |
| --- |
| 1. Positive laboratory assay for *C. difficile*<br>2. Colonoscopic findings consistent with *C. difficile* colitis<br>3. CT scan findings consistent with *C. difficile* colitis (pancolitis with or without ascites) |
| **Plus any one of the following criteria:** |
| 1. Peritonitis<br>2. Colonic perforation or full-thickness ischemia<br>3. Sepsis<br>4. Respiratory failure requiring intubation and mechanical ventilation<br>5. Vasopressor requirement after resuscitation<br>6. Mental status changes attributable to *C. difficile* colitis<br>7. Clinical deterioration despite adequate medical management<br>8. Acute renal failure (or other worsening end-organ failure)<br>9. Serum lactate level >5 mmol/L<br>10. White blood cell count greater than or equal to 50,000 cells/mL<br>11. Abdominal compartment syndrome or intra-abdominal hypertension |

CDI: *Clostridioides* (formerly *Clostridium*) *difficile* infection; CT: computed tomography.

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*Original table modified for this publication. From: Hrebinko K, Zuckerbraun BS. Clostridium difficile: What the surgeon needs to know. Semin Colon Rectal Surg 2018; 29:28. Table used with the permission of Elsevier Inc. All rights reserved.*

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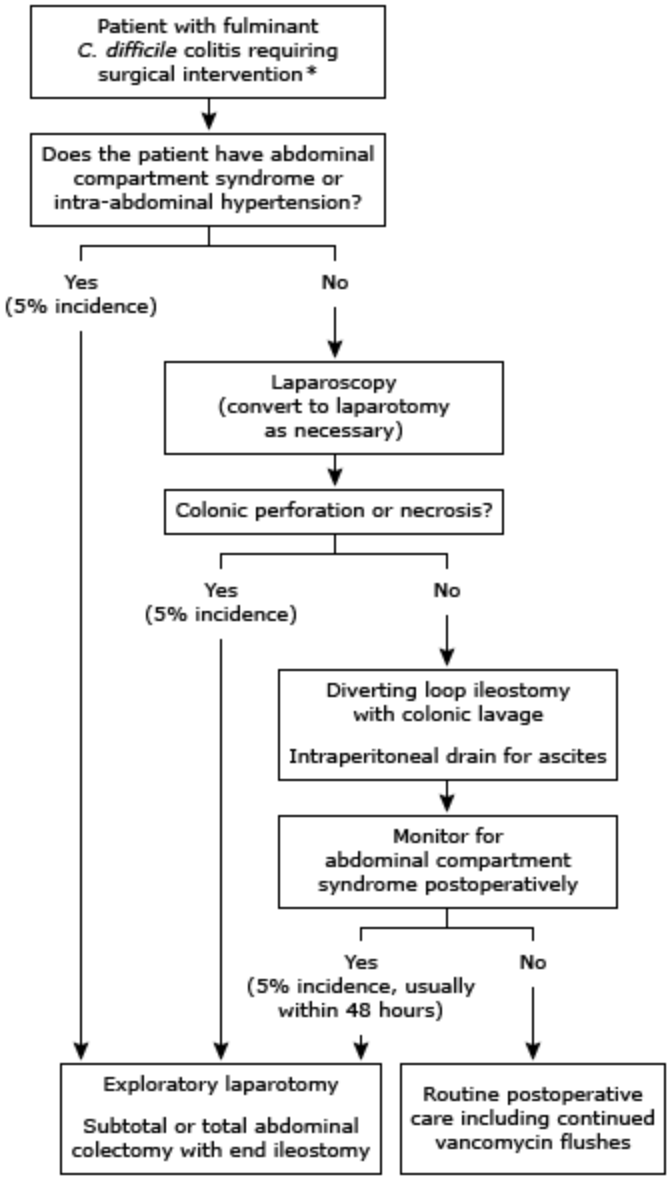
Graphic 119208 Version 2.0

## Diverting loop ileostomy/colonic lavage in managing fulminant *Clostridioides* (formerly *Clostridium*) *difficile* colitis in adults




This algorithm is intended for choosing between total abdominal colectomy and diverting loop ileostomy/colonic lavage as the initial surgical treatment for fulminant *C. difficile* colitis. Surgeons who do not perform the latter procedure can use total abdominal colectomy for all such patients. Limited studies have associated diverting loop ileostomy/colonic lavage with lower mortality, but those studies were not randomized trials.

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* Refer to UpToDate topic for a list of indications for surgical intervention in patients with fulminant *C. difficile* colitis.

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Graphic 119206 Version 2.0

## Contributor Disclosures

**Sunil G Sheth, MD** No relevant financial relationship(s) with ineligible companies to disclose. **J Thomas Lamont, MD** Equity Ownership/Stock Options: Allurion [Weight loss]. Consultant/Advisory Boards: Teledoc [Gastrointestinal diseases]. All of the relevant financial relationships listed have been mitigated. **Martin Weiser, MD** Consultant/Advisory Boards: PrecisCa [Gastrointestinal surgical oncology]. All of the relevant financial relationships listed have been mitigated. **Wenliang Chen, MD, PhD** No relevant financial relationship(s) with ineligible companies to disclose.

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