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# Investigation and management of ischemic colitis

## ABSTRACT

The colon is the most common site of gastrointestinal ischemia. The condition resolves completely with conservative treatment in most cases, but late diagnosis or severe ischemia can be associated with high rates of complications and death. Once ischemic colitis is diagnosed, serial physical examinations and colonoscopies are helpful to follow the condition. Prompt surgery is required for severe episodes, when conservative measures fail, and for patients with chronic symptoms.

## KEY POINTS

Colonic ischemia is associated with many precipitating factors and may be due to single-vessel occlusion or global hypoperfusion.

The clinical manifestations are varied and often subtle, and a high level of awareness is needed. Special consideration should be given to the condition in patients who have recently undergone cardiac or aortic surgery.

Clinical patterns vary from transient colitis to fulminant ischemia with gangrene.

Routine biochemical tests are helpful but nonspecific. The diagnosis is usually made by history, examination, and endoscopy.

**I**SCHEMIA OF THE COLON probably happens more often than we think, as the signs may be subtle and highly variable. Although most cases resolve spontaneously, chronic colonic ischemia is increasingly being recognized, and in a sizable minority of acute cases it progresses to infarction and requires immediate surgery.

In this article we review the causes, signs, and management of ischemic colitis.

## RECOGNITION INCREASING

Colonic ischemia and infarction have long been recognized. In 1953, Shaw and Green reported an episode of infarction after inferior mesenteric artery ligation for colon cancer.<sup>1</sup> A decade later, Boley et al<sup>2</sup> were the first to describe nongangrenous ischemia when they reported reversible vascular occlusion of the colon. Since then, the condition has been recognized with increasing frequency.

## CAUSES ARE MANY

Many medical conditions and medications can cause ischemia by reducing blood flow to the colon (TABLE 1).<sup>3,4</sup> The causes have been variously classified as systemic or local, occlusive or nonocclusive, and iatrogenic or noniatrogenic. An idiopathic or “spontaneous” form is generally thought to be related to localized nonocclusive ischemia of the bowel.

Some of the more common causes of ischemia in hospitalized patients include ligation of the inferior mesenteric artery during aortic surgery, low flow after cardiopulmonary bypass surgery, myocardial ischemia, and sepsis. In these situations it is difficult for the patient to compensate because the collateral



pathways to increase colonic blood flow have already been compromised.

Ischemia is now known to be most common in the elderly, although it can occur at almost any age. Approximately 90% of cases of colonic ischemia occur in patients over 60 years of age, who may be predisposed to ischemia due to age-related lengthening of the colic vessels.<sup>5</sup>

## ■ ANATOMY AND AREAS OF THE COLON AT RISK

The colon is protected from ischemia to a great extent by an abundant collateral blood supply (FIGURE 1). However, certain areas are more vulnerable in some people.

Two major arteries supply most of the blood to the colon: the superior mesenteric artery (which supplies the ascending and transverse colon) and the inferior mesenteric artery (which supplies the descending and sigmoid colon).

The marginal artery of Drummond, which runs along the mesentery within 1 to 8 cm of the colon, is composed of the terminal portions of the branches from the major vascular arcades. This artery can keep the left colon viable when the inferior mesenteric artery is ligated during rectosigmoidectomy.

But the anatomy is highly variable. For example, the marginal artery of Drummond is occasionally tenuous at the splenic flexure, as described by Griffiths, and indeed is absent at this point in up to 5% of patients.<sup>6</sup> It is poorly developed in the right colon in 50% of the population, explaining the occurrence of right-sided colitis.<sup>7</sup> One or more of the three branches of the superior mesenteric artery may be absent in up to 20% of people. Branches of the inferior mesenteric artery may similarly be absent.

On the other hand, 60% of people have an additional vessel, called the arch of Riolo or meandering mesenteric vessel, which communicates between the left colic and superior mesenteric arteries.

The splenic flexure is a “watershed” area between the areas supplied by the two main arteries. Sierocinski found that a 1.2-cm to 2.8-cm area of the splenic flexure was devoid of vasa recta, thereby predisposing this area to

**TABLE 1**

### **Etiologic factors in colonic ischemia**

**Idiopathic (spontaneous)**

**Colonic obstruction**

**Shock**

**Medications**

Digitalis, diuretics, nonsteroidal anti-inflammatory drugs, catecholamines, estrogens, danazol, gold, neuroleptics

**Major vascular occlusion**

Mesenteric arterial thrombosis or embolization

Mesenteric venous thrombosis

Trauma

**Small vessel disease**

Diabetes mellitus, vasculitis, amyloidosis, rheumatoid arthritis, radiation injury

**Hematologic disorders**

Protein C deficiency, protein S deficiency, antithrombin III deficiency, sickle cell disease

**Cocaine abuse**

**Long-distance running**

ischemia.<sup>8</sup> There is also a watershed area at Sudek's point between the sigmoid colon and the rectum where the lowest sigmoid branches usually join branches of the superior rectal artery. A third potential watershed area is the right colon, where the marginal vessel is poorly developed in up to 50% of people.

Therefore, any portion of the bowel may be affected, but the sites most often affected are the sigmoid colon, ascending colon, and splenic flexure. In systemic low-flow states the right colon is most often involved, while localized nonocclusive ischemia involves watershed areas such as the splenic flexure and the junction of the sigmoid and rectum.

Ligation or occlusion of the inferior mesenteric artery produces changes in the sigmoid colon, although changes may be more widespread if other vessels are previously occluded.

Colonic ischemia isolated to the right colon is often a manifestation of acute ischemia, which may have a more fulminant course. Right-sided ischemic colitis accounts for 8% to 46% of cases.<sup>9–11</sup>

**Colonic ischemia is most common in patients over age 60**

## ■ Why some areas of the colon are prone to ischemia

The colon is protected from ischemia by a collateral blood supply via the marginal artery of Drummond, a system of arcades connecting the major arteries. The anatomy is highly variable, however, and certain areas are more vulnerable in some people.

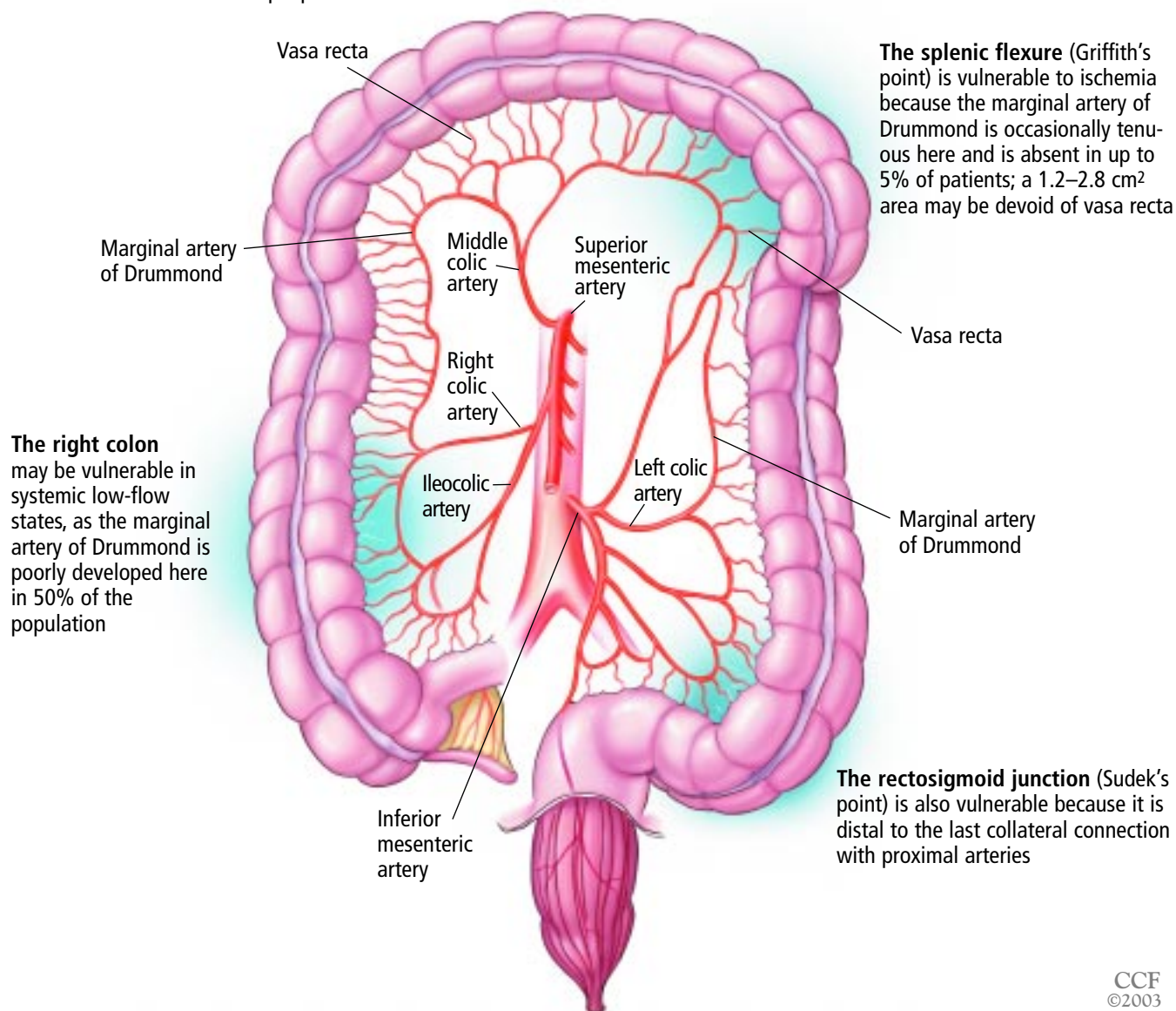


FIGURE 1

### ■ CLINICAL PRESENTATION

Once blood flow drops below a critical threshold, ischemia occurs, with consequences dependent on the individual's ability to respond by increasing flow. Ischemia is then manifested as a spectrum of findings varying from transient intramural and submucosal hemorrhage and edema to gangrene.

Ischemic colitis may present in two major clinical patterns: gangrenous (15%–20% of cases) and nongangrenous (80%–85%). In the nongangrenous form, lesions may develop that

are transient and reversible, or that progress to chronic and irreversible strictures (10%–15%) or chronic segmental colitis (20%–25%).<sup>4</sup>

The pattern of clinical presentation (TABLE 2) depends on the cause, the extent of vascular obstruction, the speed of ischemic insult, the degree of collateralization, and comorbid conditions. In most cases there is no identifiable initiating factor, but a recent history of cardiac or vascular surgery, major systemic illness, or myocardial event may be present.<sup>12–16</sup> Up to 20% of patients may have associated colonic pathology such as cancer.

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**FIGURE 2.** Contrast study in a patient with colonic ischemia, demonstrating irregularity and mucosal edema in the descending colon, with mucosal edema causing thumbprinting most noticeable on the inferior border of the distal transverse colon (arrows).

**Bleeding in colonic ischemia is mild—profuse bleeding suggests another diagnosis**

### Signs and symptoms

Mild to moderate abdominal pain is present in about 60% of cases, is generally abrupt in onset, and is usually crampy. Patients often have an urgent desire to defecate. The pain may be associated with diarrhea, frequently followed within 12 to 24 hours by mild bleeding. The blood may be bright red or maroon and is mixed with the stool. The bleeding is not copious—profuse bleeding should suggest another diagnosis.

Clinical examination may reveal mild to moderate tenderness over the ischemic segment. If peritoneal signs develop, they develop late in the course of the condition and are often very subtle.

The white cell count is generally raised, but significant ischemic injury can occur without leukocytosis.<sup>17,18</sup>

If acute ischemia leads to infarction, then fever, neutrophilia, and a metabolic acidosis may be present. Severe ischemia may lead to elevated levels of lactate, inorganic phosphate, and alkaline phosphatase. Unfortunately, these are all unreliable as tests and are poor predictors of the presence of colonic ischemia.<sup>19</sup>

**TABLE 2**

### Colonic ischemia: Classification based on clinical course

#### Nongangrenous form

Reversible (50%)

Transient

Persistent/recurrent

Irreversible

Chronic segmental colitis

Strictures

#### Gangrenous form

### ■ DIAGNOSTIC TESTS FOR COLONIC ISCHEMIA

The diagnosis of colonic ischemia depends on early and repeated evaluation of the patient in conjunction with biochemical, radiological, and endoscopic assessment.

#### Serum markers

Various markers have been investigated as tests for colonic ischemia, but none—including the leukocyte count, acid-base status, electrolytes, or enzymes—has been found specific. Others (TABLE 3) are under investigation, although usually in populations that include patients with ischemia of the small bowel.<sup>19</sup> None has yet passed into routine clinical practice.

#### Radiographic imaging

**Plain radiography**, when performed to investigate abdominal symptoms and signs, reveals signs suggestive of ischemia such as “thumbprinting” (which appears as if a thumb has been pressed against the side of the colon, caused by submucosal hemorrhage and edema), loss of haustration, and dilation of colonic loops in up to 20% of cases. Pneumoperitoneum, pneumatosis coli, and portal venous pneumatosis are late signs and suggest infarction.

**Barium enema** has a sensitivity approaching 80%.<sup>20</sup> The most common finding is thumbprinting (FIGURE 2); ulcers, ridges, edema, and strictures may also be seen. Many of these findings are transient because the mucosa heals rapidly in mild acute ischemia.

Although barium evaluation was formerly

TABLE 3

## Reported experimental biochemical tests for intestinal ischemia

TEST	AUTHORS	YEAR	NO. OF PATIENTS	DISEASE	SENSITIVITY	SPECIFICITY
Creatine kinase-BB	Fried et al <sup>32</sup>	1991	8	Infarction	63%	100%
Lactic dehydrogenase	Calman et al <sup>33</sup>	1958	11	Infarction	73%	NA
Inorganic phosphate	Feretis et al <sup>34</sup>	1985	18	Infarction	94%	NA
Intestinal fatty acid-binding protein	Kanda et al <sup>35</sup>	1996	13	Strangulation or infarction	54%	NA
			5	Infarction	100%	NA
Serum D-lactate	Poeze et al <sup>31</sup>	1998	11	Ischemia	82%	77%
Alpha-glutathione S-transferase	Delaney et al <sup>36</sup>	1999	13	Ischemia	100%	86%

NA = not available

### Colonoscopy is the most sensitive test for colonic ischemia

used in conjunction with flexible sigmoidoscopy, it has been largely replaced by colonoscopy. Barium studies should not be performed in any patient with a suspicion of gangrene, perforation, or peritonitis; bowel preparation is best avoided in the acute stage.

**Computed tomography.** Colonic ischemia has been documented by computed tomography (CT) for many years.<sup>21</sup> Findings reflect those seen on barium studies and include mural thickening, luminal narrowing, and polypoid defects (equivalent to thumbprinting). CT may also show the double halo sign, in which the outer mural layer enhances with intravenous contrast, while there is inner mucosal hypoperfusion (FIGURE 3). Pneumatosis and pneumoperitoneum may also be seen.<sup>22</sup>

**Ultrasonography** or CT may reveal a lack of patency of the mesenteric veins, and venous filling is not seen on arteriography. Color flow duplex imaging may be useful in distinguishing inflammatory from ischemic causes of bowel wall thickening.<sup>23</sup>

### Colonoscopy

Colonoscopy, although invasive, is the most sensitive test for colonic ischemia. Significant mucosal changes can be seen, and biopsies can be taken when necessary, especially when investigating chronic patterns of colonic ischemia.

Extreme care is needed during colonoscopy, particularly in patients with acute colonic ischemia. Only a small amount of air is insufflated to minimize the risk of further reduction in intestinal perfusion caused by high intraluminal pressures (FIGURE 4). Some authors suggest insufflation with CO<sub>2</sub> to minimize these risks, as the CO<sub>2</sub> is rapidly absorbed and avoids prolonged high intraluminal pressures. Furthermore, CO<sub>2</sub> may directly improve colonic perfusion.

Frank necrosis manifests as a black bowel wall, and this is an indication to stop the colonoscopy procedure and proceed with laparotomy. Hemorrhagic nodules suggest less severe ischemia and are seen early in the course, as they are transient.

Nonspecific findings include superficial ulceration, mucosal friability, edema, erythema, and luminal narrowing.<sup>24</sup> Endoscopic findings that suggest a diagnosis of ischemia rather than inflammatory bowel disease include a normal rectum, sharply defined segments of involvement, and rapid resolution on serial examinations. Biopsy specimens of nodules or bullae show nonspecific inflammatory changes. Isolated involvement of the right side of the colon with hemorrhagic nodules on colonoscopy suggests superior mesenteric artery occlusion, and angiography may be indicated.





**FIGURE 3.** Computed tomographic scan of a patient with colonic ischemia. The colonic wall is thickened secondary to mucosal edema (arrow).

As changes in the color of the mucosa may reflect the severity of the ischemia, the viability of the colon, and the prognosis, Church<sup>25</sup> has proposed a management algorithm based on findings at colonoscopy.

### Experimental tests for colonic ischemia

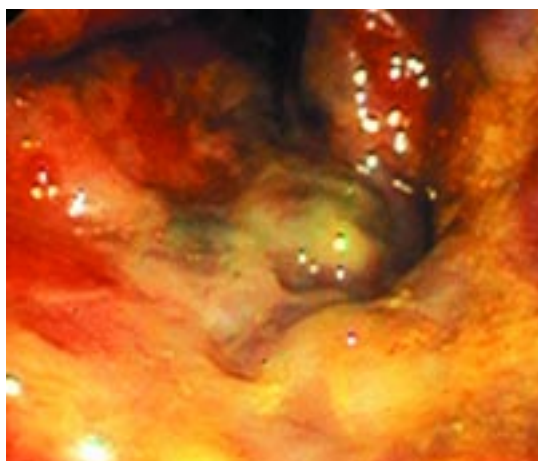
The difficulty diagnosing ischemic colitis without colonoscopy and the hope of identifying patients who might develop colonic ischemia after aortic surgery have spurred several studies (TABLE 3).<sup>26–36</sup>

**Intraoperative tests.** Bowel ischemia has always been difficult to evaluate accurately during surgery<sup>26</sup>; hence, new intraoperative tests and ways of using currently available tests are under investigation. These include intraoperative photoplethysmography,<sup>27</sup> tonometry,<sup>28</sup> and sampling of inferior mesenteric blood.<sup>29</sup> None of these, however, is established in clinical practice at this time.

**Serum D-lactate,** a bacterial product that translocates across the ischemic intestinal wall, appears to be significantly elevated in patients with acute mesenteric ischemia,<sup>30</sup> and has been used to help predict colonic ischemia after repair of a ruptured abdominal aortic aneurysm.<sup>31</sup>

**Intestinal fatty acid-binding protein** has also been shown to be elevated in patients with mesenteric infarction.<sup>32</sup>

**Alpha-glutathione S-transferase (alpha-GST)** belongs to a family of enzymes involved in the detoxification of a range of toxic and foreign compounds within the cell. It has been



**FIGURE 4.** Endoscopy performed to make a diagnosis of ischemic colitis must be performed with great care and minimal insufflation of air. Classic changes include patchy erythema with mucosal friability and edema, and ulceration with sloughing and ulceration of the mucosa. Areas of dark grey or black suggest full-thickness ischemia.

reported as a marker for ischemia<sup>36</sup>; an isolated rise in alpha-GST indicated segmental ischemia, while massive elevation with coincident elevation of transaminase levels suggested a global, hypoperfused, nonocclusive type of ischemia.

### MANAGEMENT OF ACUTE COLONIC ISCHEMIA

Most cases of colonic ischemia do not have any identifiable cause. However, one should suspect it in patients with abdominal pain, diarrhea, rectal bleeding, and abdominal tenderness who have a possible precipitating cause. Serial physical examinations and repeat endoscopy may be required for the diagnosis and ongoing management.<sup>25</sup>

If the physical examination does not suggest gangrene or perforation, the patient is treated expectantly. Very mild cases can be managed on an outpatient basis with liquid diet, close observation, and antibiotics.

For inpatients, a combination of intravenous fluids and bowel rest is recommended to reduce intestinal oxygen requirements. Parenteral nutrition should be considered for patients who do not respond immediately and

**Suspect acute ischemic colitis if there is abdominal pain, diarrhea, rectal bleeding, abdominal tenderness, a possible cause**

TABLE 4

**Indications for surgery in ischemic colitis****Acute ischemia**

Peritonitis  
 Pneumoperitoneum  
 Endoscopic marks of gangrene  
 Otherwise unexplained sepsis not responding to medical treatment  
 Persistent diarrhea, rectal bleeding, or protein-losing colopathy for more than 14 days

**Chronic ischemia**

Chronic segmental colitis with clinically recurrent sepsis  
 Symptomatic colonic strictures  
 Asymptomatic strictures with any suspicion of neoplasia



**FIGURE 5.** Operative colectomy specimen showing patchy ischemia, with full-thickness ischemia at the watershed area in the ascending colon and at Griffith's point. The proximal resection was at healthy, viable small bowel. Note the normal viable mucosa at the distal margin.

for those who are poor candidates for surgery,<sup>37</sup> as they may need prolonged bowel rest.

Broad-spectrum antibiotics have been recommended by many authors, as there is experimental evidence that this reduces the length and severity of bowel damage.<sup>3</sup>

It is critically important to maximize

intestinal perfusion. Therefore, digitalis and other vasopressors are withdrawn or minimized, if possible, and cardiac output is maximized by adequate fluid resuscitation.<sup>12,38</sup>

Steroids have no role in the treatment of acute ischemia, and they serve only to mask the development of peritoneal signs and delay a necessary laparotomy. Likewise, oral cathartics and bowel preparations should not be given because of the risk of precipitating colonic perforation or toxic dilation of the colon.<sup>4</sup>

Persistent unexplained sepsis or pyrexia increases concern about infarction of the bowel. Assuming there is no full-thickness ischemia on the initial endoscopy, repeat endoscopy is performed regularly until the ischemic changes improve or until there is a change in the clinical condition which mandates other investigations or laparotomy.

**Surgery**

About 20% of patients with acute ischemic colitis require surgery. Indications include ongoing sepsis refractory to medical management, signs of peritoneal irritation, diarrhea and bleeding lasting more than 10 to 14 days, evidence of pneumoperitoneum on imaging, endoscopic evidence of full-thickness ischemia, or protein-losing enteropathy that goes on longer than 2 weeks (TABLE 4).<sup>39</sup> Without surgery, the risk of perforation is high.

At laparotomy, the diagnosis is confirmed and the involved segment of colon resected.

It is crucial to check for the viability of the mucosal margins of the resected specimen, as the serosal surface of the bowel may look surprisingly well-perfused (FIGURE 5). Some authors have reported the use of intraoperative techniques to exclude colonic ischemia, such as Doppler ultrasonography, intraoperative colonoscopy with laser Doppler, intraoperative photoplethysmography, oxygen electrodes, pulse oximetry of transcolonic oxygen saturation, and intravenous fluorescein for determination of viability.<sup>40,41</sup> Many of these studies were evaluated at the time of aortic surgery in an effort to predict the development of ischemia.<sup>26-29</sup>

Generally, surgery involves colectomy



with end colostomy or ileostomy, leaving the distal bowel as a Hartmann stump or a mucous fistula if poor perfusion of the distal bowel end precludes oversewing.

Depending on how much of the colon is involved, the stoma may have to be permanent. In one series,<sup>42</sup> 75% of patients who underwent resection and stoma formation for segmental involvement of the colon were able to have their stomas closed, vs only a third of patients with total colonic involvement.

As a group, patients who require surgery are more critically ill, and the associated mortality rate is 30% to 60%.<sup>3,12</sup>

### Total parenteral nutrition

If a patient who would otherwise require surgery has a concurrent or recent myocardial infarction or major medical contraindications to surgery, a trial of long-term parenteral nutrition and intravenous antibiotics may be considered as an alternative, but less-than-ideal, form of treatment.

### ■ CLINICAL PROGRESSION OF ACUTE ISCHEMIC COLITIS

The disease is reversible in about half of cases. In about two thirds of patients with a reversible injury, the symptoms resolve in 24 to 48 hours, and endoscopic and radiographic investigations confirm healing within 2 weeks. In severe but reversible injury (eg, in segmental ulcerating colitis), the colon may take 1 to 6 months to heal.<sup>3</sup>

In the other one third of cases, however, the damage is too severe to heal, leading to chronic segmental colitis or strictures. In such cases, the patient may have persistent diarrhea, rectal bleeding, protein-losing enteropathy, or repeated episodes of sepsis, which may lead to perforation.

Gangrene occurs in about 15% of patients and requires laparotomy within hours. Others (20%–25%) develop chronic segmental ulcerating colitis, while about 10% subsequently develop strictures. Fulminant pancolitis due to ischemia is rare, occurring in only 1%. Total

colonic ischemia without rectal involvement occurs in up to 18%, and this requires surgery in all cases; the mortality rate is 75%, even with surgery.<sup>42</sup>

### ■ MANAGEMENT OF CHRONIC COLONIC ISCHEMIA

Chronic colonic ischemia is increasingly being recognized in the population at large. The patients are older and describe a history of bloody diarrhea associated with crampy or constant episodes of abdominal pain. Endoscopy may suggest segmental colitis. Biopsy specimens of bullae show submucosal hemorrhage and edema, while intervening areas reveal nonspecific inflammation. Venous congestion, mucus depletion, and injury to the crypt architecture and surface epithelial cells are also common.

The diagnosis is not always easy, however, and chronic ischemic colitis can easily be mistaken for inflammatory bowel disease. Compounding the difficulty, pseudopolyps may be present in patients with ischemic colitis. Patients may also develop ischemic strictures, which are classically smoother than neoplastic strictures; however, differentiation is not always easy and resection may be required, both for treatment of symptoms and to obtain a definitive histopathologic diagnosis.

Mildly symptomatic chronic disease frequently responds to supportive management. In contrast to acute ischemia, chronic ischemia may respond to topical steroid preparations.

Resectional surgery is generally reserved for patients for whom conservative supportive therapy fails and for those with recurrent episodes of colitis or with symptomatic strictures. As in surgery for acute ischemia, the resected specimen must be examined to confirm that the mucosa is normal at the resection margins, and pulsatile bleeding must be noted from the bowel ends. Surgery in patients with chronic ischemia usually is curative, and development of further ischemic disease is rare.

**Chronic ischemic colitis is easily mistaken for inflammatory bowel disease**

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