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GASTROINTESTINAL DISORDERS IN THE ELDERLY

ISCHEMIC BOWEL DISEASE IN THE ELDERLY

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Ischemic bowel diseases are caused by acute or chronic insufficiency of blood flow to all or part of the gastrointestinal tract and include acute and chronic mesenteric ischemia and colonic ischemia. Reduction in blood flow to the intestine may reflect inadequate systemic perfusion, as in cardiogenic shock, or local structural or functional changes in the mesenteric vascular bed. Whatever the cause of the ischemic insult, the end result is a spectrum of damage to the bowel, ranging from completely reversible functional alterations to total hemorrhagic necrosis.

Colonic ischemia is the commonest manifestation of ischemic injury to the gastrointestinal tract, and most patients with colonic ischemia are older than age 60 years. Similarly, acute mesenteric ischemia typically is seen in elderly patients and often in association with other common disorders of the aged, including congestive heart failure, cardiac arrhythmias, myocardial infarction, and hypotension.

MESENTERIC CIRCULATION

The intestines are protected from ischemia by an abundant collateral circulation. Collateral blood flow around occlusions of the smaller splanchnic arterial branches is

made possible by the primary, secondary, and tertiary arcades in the small bowel and by the marginal arterial complex of Drummond, central anastomotic artery, and arc of Riolan in the colon. Within the bowel wall, there is a network of communicating submucosal vessels that maintain the viability of short segments of the intestine when the extramural arterial blood supply has been compromised. Collateral pathways open immediately on occlusion of a major vessel in response to arterial hypotension distal to the occlusion.[12] Increased blood flow through collateral pathways maintains adequate perfusion for a variable, but brief, period of time. If blood flow is diminished for a prolonged period, vasoconstriction develops in the affected bed and may persist after the primary cause of mesenteric ischemia has been corrected.[8] Such vasoconstriction increases vascular resistance, producing a rise in arterial pressure in the dependent segment that, in turn, impairs collateral blood flow. Mesenteric ischemia is a complex condition that depends on the (1) state of the systemic circulation, (2) degree of functional or anatomic vascular compromise, (3) number and caliber of vessels affected, (4) response of the vascular bed to diminished perfusion, (5) nature and capacity of the collateral circulation, (6) duration of the ischemic insult, and (7) metabolic needs of the involved segment of bowel.[21]

Disorders of the Mesenteric Circulation

Intestinal ischemia can be classified into 3 broadly defined types[16] :

Acute mesenteric ischemia (AMI)

Superior mesenteric artery embolus

Superior mesenteric artery thrombosis

Nonocclusive mesenteric ischemia

Superior mesenteric vein thrombosis

Focal segmental ischemia

Chronic mesenteric ischemia (CMI) (intestinal angina)

Colonic ischemia (CI)

Reversible ischemic colonopathy

Transient ulcerating ischemic colitis

Chronic ulcerating ischemic colitis

Colonic stricture

Colonic gangrene

Fulminant universal ischemic colitis

CI is the commonest vascular disorder, followed in frequency by AMI. In AMI, there is a reduction of blood flow in the distribution of the superior mesenteric artery affecting all, or portions of, the small intestine and possibly the right half of the colon. In CMI, the circulation is unable to meet the increased functional demands of the intestine, but there is no loss of tissue viability. Each of these disorders has distinct clinical manifestations and is managed differently.

ACUTE MESENTERIC ISCHEMIA

Because of a growing awareness of the varied clinical syndromes produced by interference with blood flow to the intestine and because of an absolute rise in the number of patients with these disorders, AMI has been diagnosed with increasing frequency. The rising incidence of this disorder has been attributed to the aging of the population; it is especially common in elderly patients with serious cardiovascular, degenerative, or systemic diseases. Similarly, advances in medical technology, particularly the widespread use of intensive care units, have extended the lives of patients with conditions that previously were fatal, allowing mesenteric ischemia to develop as a late consequence of the primary disease.

AMI may be caused by a superior mesenteric artery embolus or thrombus; nonocclusive mesenteric ischemia, with a resulting low-flow state and associated vasoconstriction; or mesenteric venous thrombosis.[16] [54] Superior mesenteric artery embolus is the commonest cause of AMI and accounts for approximately 50% of cases (Fig. 1) (Figure Not Available) . Nonocclusive mesenteric ischemia is being reported less often now than in the past. This reduction in frequency is probably the result of better monitoring of patients in intensive care units, with correction of hemodynamic abnormalities before hypotension and consequent mesenteric vasoconstriction occur. The widespread use of vasodilating agents in the management of congestive heart failure and myocardial ischemia also may contribute to this decrease.

Figure 1. (Figure Not Available) Incidence and causes of acute mesenteric ischemia. In 1926, the absence of arterial occlusion in the presence of infarction was interpreted as the result of venous thrombosis, because vasospasm, the commonest cause of nonocclusive mesenteric ischemia, was unrecognized. Today, superior mesenteric artery embolus is even commoner than nonocclusive disease as a cause of acute mesenteric ischemia. *(From Reinus JF, Brandt LJ, Boley SJ: Ischemic diseases of the bowel. Gastroenterol Clin N Am 19:319-343, 1990.)*

Regardless of its cause, AMI is an intra-abdominal catastrophe almost as lethal today as it was 50 years ago, with an average mortality rate of 71%, ranging from 59% to 93% in various series (Fig. 2) (Figure Not Available) .[16] [38] Making a diagnosis before intestinal infarction ensues is the most important factor in improving outcome. Early diagnosis of AMI depends on the identification of persons at risk and the recognition that the disparity

between the severity of the abdominal pain and the absence of significant abdominal findings is characteristic of early AMI.[10] [11] Patients at risk usually are older than age 50 and have congestive heart failure, cardiac arrhythmias, recent myocardial infarction, hypovolemia, hypotension, or sepsis. Intestinal ischemia, especially nonocclusive mesenteric ischemia, has been recognized increasingly after cardiac surgery[30] and dialysis.[27] [35] Other risk factors for AMI include a history of a hypercoagulable state, previous arterial emboli, vasculitis, or deep vein thrombosis. Therapy with potent splanchnic vasoconstrictors, such as digitalis or its derivatives, may play an adjunctive role in the development of mesenteric ischemia.[29] [36]

Figure 2. (Figure Not Available) Mortality rates for acute mesenteric ischemia. The aggressive approach of Boley and his colleagues, using prompt angiography and vasodilator (papaverine) infusion, dramatically improved survival in patients with acute mesenteric ischemia. *(From Reinus JF, Brandt LJ, Boley SJ: Ischemic diseases of the bowel. Gastroenterol Clin N Am 19:319-343, 1990.)*

Patients with AMI usually complain of severe abdominal pain, which may be localized or diffuse. The severity of the pain helps to differentiate AMI from CI, in which pain is less prominent.[15] Although abdominal pain typically is severe, the abdomen usually is soft, flat, and nontender early in the course of AMI. The combination of severe abdominal pain and a paucity of significant abdominal findings in a patient *at risk* demands that AMI be excluded if another cause for the pain is not discovered on plain film or computed tomography (CT) of the abdomen. Reluctance to undertake early diagnostic angiography in patients who often are critically ill is a primary cause of the continuing high mortality rate for AMI. An improvement in survival can be achieved only when it is recognized that waiting for definite physical signs (i.e., the development of an acute abdomen) or radiologic signs (i.e., ileus, thumbprinting, or intramural air) is equivalent to waiting for the ischemic, but viable, bowel to infarct. The dangers of delay outweigh the risk of early invasive studies in patients who are suspected of having ischemic bowel.

Abdominal pain may be absent in 15% to 25% of patients with AMI, especially those who have the nonocclusive variety of this disorder. Unexplained abdominal distention or gastrointestinal bleeding may be the only manifestation of ischemia, and distention may be the first sign of impending infarction. As intestinal necrosis develops, abdominal tenderness, rebound tenderness, and muscle guarding become prominent. The presence of significant abdominal findings is strong evidence for bowel necrosis; nausea, vomiting, fever, rectal bleeding, hematemesis, intestinal obstruction, back pain, shock, and increasing abdominal distention are other late signs. Mental confusion has been reported to develop in 30% of elderly patients with AMI.[28]

A leukocytosis of more than 15,000 cells/mm^3 occurs in approximately 75% of patients with AMI, and a metabolic acidosis is present in approximately 50% of patients. Elevations of serum and peritoneal fluid amylase, alkaline phosphatase, and inorganic phosphate values have been reported, but the consistency and specificity of these findings have not been established.[43] Leukocytosis (especially if out of proportion to the physical findings), an elevated hematocrit value, and blood-tinged peritoneal fluid (often with a high amylase content) are late signs, seen with intestinal necrosis.

Plain radiographs of the abdomen usually are obtained and show no abnormalities early in the course of AMI. Positive findings on plain films typically are nonspecific but portend a poor prognosis. In one study by Ritz et al,[60] patients with AMI and normal abdominal radiographs had a mortality rate of 29%, whereas patients with AMI and an abnormal plain radiograph, indicating later stage disease, had a mortality rate of 78%. CT scanning yields information similar to that of plain radiographs, especially when AMI is caused by superior mesenteric artery embolus or nonocclusive mesenteric ischemia.[66] [69] By contrast, CT is valuable in the detection of superior mesenteric vein thrombosis.[7] Duplex ultrasonography is highly specific (92% to 100%) for the identification of occlusion or severe stenoses of the splanchnic vasculature but has a lower sensitivity (70% to 89%) and cannot be used to detect distal emboli or for diagnosing nonocclusive mesenteric ischemia.[13] [53] [72] Magnetic resonance angiography, with and without gadolinium, appears to be useful in detecting severe narrowing or occlusion of the celiac axis and superior mesenteric artery but is inferior in detecting more distal occlusions and nonocclusive mesenteric ischemia.[49]

In 1973, Boley et al[11] proposed an aggressive plan of management employing early angiography and the intra-arterial infusion of the vasodilator papaverine to interrupt splanchnic vasoconstriction. This approach resulted in the salvage of compromised bowel and improved survival. When AMI is suspected, treatment begins with resuscitation of the patient and correction, as far as possible, of predisposing or precipitating causes (Fig. 3 (Figure Not Available) *A*).[16] Therapy of congestive heart failure, control of cardiac arrhythmias, and replacement of blood volume should precede any diagnostic studies. Efforts to increase intestinal blood flow would be futile if low cardiac output, hypotension, or hypovolemia persists. Persons who are hypotensive or hypovolemic should not undergo angiography because mesenteric vasoconstriction always is present in this setting, even in the absence of intestinal ischemia. Such patients should not receive intra-arterial vasodilators (e.g., papaverine) because these agents increase the size of the vascular bed and precipitate a drop in the blood pressure.

Figure 3. (Figure Not Available) Algorithm for the diagnosis and treatment of patients with suspected intestinal ischemia *(A)* and the management of chronic mesenteric ischemia *(B)* and colon ischemia *(C).* Solid lines indicate accepted management plan; dashed lines indicate alternate management plan. DVT = Deep vein thrombosis; SMA = superior mesenteric artery; MRA = magnetic resonance angiography; CT = computerized tomography; BE = barium enema; NPO = nothing by mouth; IV = intravenous; PLC = protein-losing colopathy; IBD = inflammatory bowel disease. *(A, From American Gastroenterological Association Medical Position Statement: Guidelines on Intestinal **Ischemia** [erratum]. Gastroenterology [erratum] 119:281, 2000 [original published Gastroenterology 118:951, 2000]; B-C, From American Gastroenterology Association Medical Position Statement: Guidelines on Intestinal **Ischemia**. Gastroenterology 118:951, 2000; with permission.)*

In the management of critically ill patients, it is important to remember that digitalis preparations have a direct splanchnic vasoconstrictor action on superior mesenteric artery smooth muscle and should be avoided, if possible.[29] [36] Vasopressors are contraindicated in the treatment of shock when mesenteric ischemia is suspected. Systemic vasodilators may improve cardiac output and theoretically are ideal agents to treat the low mesenteric blood flow associated with heart disease.

When intestinal ischemia has progressed to the point that systemic signs are present, correction of plasma volume deficits, decompression of the gastrointestinal tract, and parenteral antibiotics are essential before any radiologic studies are obtained. Broad-spectrum antibiotics usually are administered, although there is little evidence that such therapy is beneficial. Antibiotics have been shown to prolong survival after intestinal ischemia in rats and offer theoretic protection against bacterial translocation, which has been shown to occur with loss of mucosal integrity.[4] [57] [58] No randomized prospective clinical studies have proved the efficacy of broad-spectrum antibiotics in AMI, however, and it is not likely that such studies will be done in the future.

At this stage of the evaluation, plain radiographs of the abdomen are obtained, not only to identify signs of intestinal ischemia, which occur late and usually indicate bowel infarction, but also to exclude other causes of abdominal pain, such as a perforated abdominal viscus or intestinal obstruction. A normal plain film of the abdomen does not exclude a diagnosis of AMI. In patients suspected of having AMI, the combination of severe abdominal pain lasting several hours, a relatively unimpressive abdominal examination, and a normal plain film of the abdomen identifies the patient who is the best candidate for angiography (i.e., the individual with AMI who does not yet have an infarcted bowel and who probably will survive). After other causes of abdominal pain have been excluded by plain films, angiography is performed.

Early selective mesenteric angiography is the key to the successful management of AMI (Fig. 4) (Figure Not Available) .[11] [16] [39] Although the need for angiography in a patient with suspected AMI and signs of an acute abdomen (i.e., a patient who requires surgery) is more controversial, many investigators still believe that angiography is crucial to the management of these patients. Angiography can show the presence and site of emboli and thromboses and mesenteric vasoconstriction as well as the adequacy of the splanchnic circulation.

Figure 4. (Figure Not Available) Patient with nonocclusive mesenteric ischemia managed with papaverine infusion for 3 days. *A,* Initial angiogram showing spasm of main superior mesenteric artery, origins of branches, and intestinal arcades. *B,* Angiogram after 36 hours of papaverine infusion. Study was obtained 30 minutes after papaverine was replaced with saline. At this time the patient's abdominal symptoms and signs had resolved. *(From Boley SJ, Brandt LJ, Veith FJ: Ischemic disorders of the intestines. In Current Problems in Surgery, vol XV, no 4. April 1978. Chicago, Year Book Medical; with permission.)*

The angiographic catheter also provides a route for the administration of intra-arterial vasodilators, such as papaverine, which relieves the mesenteric vasoconstriction of nonocclusive and occlusive mesenteric ischemia (Figs. 4 (Figure Not Available) and 5) (Figure Not Available) . Infusion of papaverine has been used as sole therapy--without surgery--in highly selected patients with major superior mesenteric artery emboli (those that occur in the superior mesenteric artery above the origin of the ileocolic artery).[6] Intra-arterial papaverine is used as an integral part of the preoperative, intraoperative, and postoperative management of selected patients with AMI and to improve mesenteric perfusion in the nonoperative management of other patients. Intra-arterial infusions have been maintained for 5 days without complication. The standard treatment of superior

mesenteric artery embolus is surgical embolectomy, but intra-arterial vasodilators as well as intra-arterial thrombolytic agents, such as streptokinase, urokinase, and recombinant tissue plasminogen activator, have been used in selected cases.[14] [44] [63] Thrombolytic therapy is most likely to be successful when the thrombus is partially occluding or is in one of the branches of the superior mesenteric artery or in the main superior mesenteric artery distal to the origin of the ileocolic artery, and when the study is performed within 12 hours of the onset of symptoms. Depending on the angiographic findings and the presence or absence of peritoneal signs, the patient can be managed according to a therapeutic algorithm incorporating surgery, intra-arterial infusions of vasodilators, and serial angiographic studies (see Fig. 3 (Figure Not Available) *A*). [1] In patients without peritoneal findings, minor superior mesenteric artery emboli (occurring in the superior mesenteric artery distal to the origin of the ileocolic artery or in one of its branches) have been treated with thrombolytic agents, anticoagulants, and intra-arterial papaverine.[16]

Figure 5. (Figure Not Available) Superior mesenteric angiogram. *A,* An embolus is evident *(arrow)* and is associated with mesenteric vasoconstriction. *B,* Papaverine is being infused, relieving the vasoconstriction while clot lysis occurs. Incidental gallstones are noted. *(From Boley SJ, Brandt LJ, Veith FJ: Ischemic disorders of the intestines. In Current Problems in Surgery, Vol. XV, No. 4. April 1978, Chicago, Year Book Medical; with permission.)*

Laparotomy is performed to restore intestinal blood flow obstructed by an embolus or thrombus or to resect necrotic bowel. Intestinal viability at the time of surgery may be assessed clinically or by certain common techniques, including Doppler ultrasonography[55] and perfusion fluorometry.[24] Early in the course of an intestinal ischemic insult, serosal blood flow is preserved despite injury to the mucosa and the submucosa, and inspection of the external surface of the bowel is unreliable. Nonetheless, assessments of bowel color and the presence of pulsations, bleeding, and peristalsis are the criteria for assessing tissue viability. Bowel that is clearly necrotic is resected at the time of surgery, and a primary anastomosis is performed. If there is any question regarding the viability of unresected intestine, a planned reexploration, or *second-look* operation, may be performed within 12 to 24 hours.[64] The intervening time is used to improve perfusion of the ischemic bowel.

The use of anticoagulants in the management of AMI of arterial origin is controversial. There is general agreement that anticoagulation is indicated to prevent the occurrence of progressive or recurrent thrombosis late in the postoperative period. There is debate, however, about the best time to initiate such therapy, ranging from immediately on diagnosis (and possibly incurring an increased risk of early gastrointestinal or intraoperative bleeding) to 48 hours after diagnosis.[3] [6]

Early diagnosis of AMI, combined with an aggressive approach to therapy, has improved outcomes.[10] The importance of rapid diagnosis is highlighted by a report from Madrid of 21 patients with superior mesenteric artery embolus. In this report, 100% of patients had continued intestinal viability if the duration of symptoms was less than 12 hours, in contrast to only 18% if symptoms were present for greater than 24 hours before a diagnosis was established.[46] In early studies using an aggressive diagnostic and

therapeutic strategy employing angiography and infusion of papaverine, 35 of the first 50 patients (70%) proved to have AMI, and 19 (54%) survived.[10] Of the survivors, 85% did not lose any bowel or had excision of less than 3 feet of small intestine, permitting the preservation of relatively normal bowel function. Similar results with this method have been reported from the University of Cincinnati.[26] In this study of 47 patients with intestinal ischemia caused by superior mesenteric artery emboli, the survival rate was 55% in patients managed according to the aggressive protocol of Boley et al,[26] but only 20% of those treated in a traditional fashion (see Fig. 2) (Figure Not Available) . Complications of mesenteric angiography and infusions of vasodilator drugs are uncommon but may include transient acute tubular necrosis and local hematomas. Problems with prolonged papaverine infusion are rare.

Acute Mesenteric Venous Thrombosis

Mesenteric venous thrombosis (MVT) is an infrequent condition, representing 5% to 10% of patients with AMI. A review of the English language literature since 1950 yielded 191 cases of this entity.[7] [33] MVT may be secondary to a variety of conditions or idiopathic (primary):

Primary

Secondary

Hematologic and hypercoagulable states

Sickle cell anemia

Polycythemia vera

Thrombocytosis

Antithrombin III deficiency

Protein C or S deficiency

Factor V Leiden mutation (activated protein C resistance)

Lupus anticoagulant

Factor II 20210A mutation (in combination with oral contraceptive use)

Carcinomatosis (especially intra-abdominal)

Pregnancy

Migratory thrombophlebitis

Peripheral deep vein thrombosis

Local venous congestion and stasis

Hepatic cirrhosis

Congestive splenomegaly

Compression of the portal venous radicals by tumor

Intra-abdominal inflammation and sepsis

Cholangitis

Appendicitis

Diverticulitis

Inflammatory bowel disease

Peritonitis

Pancreatitis

Pelvic or intra-abdominal abscess

Parasitic infestation

Ascaris lumbricoides

Low-flow states

Abdominal trauma

Decompression sickness

Iatrogenic

Abdominal operations (especially splenectomy and pancreatectomy)

Infusion of vasopressin into the superior mesenteric artery after sclerotherapy of esophageal varices

Estrogens (oral contraceptives)

No cause is identified in only 20% to 35% of cases. Many cases were described as idiopathic before conditions such as protein S deficiency and protein C deficiency were recognized, and as knowledge of hematologic and other predisposing disorders increases, the percentage of cases of MVT without an apparent cause probably will decrease further.[59]

MVT long has been known as an imitator of other abdominal disorders, in part because symptoms are nonspecific. The difficulty in diagnosing MVT was described best by Anane-Sefah et al,[2] who stated in 1975, "Perhaps the best overall finding was an uneasy feeling on the part of the examining physician that his patient looks sick but that he could not say why or from what." In one study, the mean duration of pain before hospital admission was 5 to 14 days; some patients had pain for more than a month before a diagnosis was made.[62] Abdominal pain is present in approximately 90% of patients and varies in nature, severity, and location. Other prominent symptoms include nausea and vomiting in 60% to 75% of patients and diarrhea and constipation each in approximately 30% of affected persons. Bloody diarrhea and hematemesis, which occur in 15% of cases, indicate bowel infarction. Occult blood is present in the stool of more than half of patients with MVT.

The presentation of patients ultimately diagnosed as having MVT is less acute and more variable than that of patients with AMI secondary to superior mesenteric artery embolus. Almost all patients present with fever and abdominal tenderness. Most patients have decreased bowel sounds and abdominal distention, but only two thirds manifest signs of peritonitis. Laboratory studies have not proved to be of value in the early diagnosis of MVT and may suggest, but neither confirm nor exclude, the diagnosis.

The absence of reliable specific symptoms, signs, or laboratory studies in patients with MVT makes diagnosis difficult. The variability of the disease (some patients have an indolent course of days to weeks, and others have a relatively acute onset) further obscures the diagnosis. Plain films of the abdomen either are normal or reveal a pattern of nonspecific ileus. The diagnosis of some form of AMI is suggested in less than 25% of cases; when a radiologic abnormality is apparent, infarcted bowel usually is present. Barium enema is of little value, and radiologic study of the upper gastrointestinal tract may show submucosal hemorrhage and thumbprinting. Contrast-enhanced CT may show a thrombus within the superior mesenteric vein, thickening of the bowel wall, collateralization, or ascites and is useful in making the diagnosis of MVT in more than 90% of cases.[25] [37] Angiography may reveal a thrombus within the superior mesenteric vein or failure of the arterial arcades to empty, even into the venous phase of the study.[71]

Because most patients with MVT are suspected initially to have some form of AMI, the same management protocol used for other forms of AMI is recommended (see Fig. 3) (Figure Not Available) .[1] Some asymptomatic patients may have MVT diagnosed on a CT scan of the abdomen obtained for other reasons. In such cases, either no therapy or a short course of anticoagulation is appropriate.

In symptomatic patients in whom the diagnosis of MVT has been made by CT or angiography, treatment depends on the presence or absence of peritoneal signs. In the absence of peritoneal signs, some patients may be treated adequately with anticoagulation (typically heparin followed by warfarin), followed by careful clinical observation.[34] [59] In patients with signs of peritonitis, laparotomy is indicated, and short segments of nonviable bowel are resected; surgery is followed by prompt anticoagulation. If long segments or the entire small bowel are infarcted, resection produces a short-bowel

syndrome and a commitment to life-long parenteral nutrition. If it is not clear whether a segment of bowel is viable, and angiography shows that the major vein allows some return of blood flow, a second-look operation may be performed 12 to 24 hours after the first operation. The intervening time is used to improve the circulation by infusing vasodilators, such as papaverine, into the superior mesenteric artery to relieve any associated arterial spasm that may be contributing to the ischemic injury. Relief of arterial vasoconstriction may improve the blood supply enough to preserve bowel viability. Mesenteric venous thrombectomy may have a role in selected cases.

MVT is the form of ischemic bowel disease in which anticoagulants should be used routinely postoperatively, after resection or thrombectomy. Heparin, then warfarin are administered to prevent the recurrence of venous thromboses.[56] Although the question of the optimal duration of therapy has not been answered by prospective studies, anticoagulation typically is continued for 3 to 6 months. If thrombosis recurs on heparin, protein C, protein S, antithrombin III, or another factor deficiency leading to coagulopathy is likely.

The mortality rate of MVT is lower than that encountered in other forms of AMI, varying from 2% to 50%.[40] Of patients who receive heparin, 13% have recurrent or progressive disease, with a mortality rate of approximately 13%. In patients who do not receive postoperative anticoagulation, the recurrence and mortality rates are 20% to 25% and 50%.

Focal Segmental Ischemia

Ischemic insults to short segments of the small intestine produce a broad spectrum of clinical features without the life-threatening systemic consequences associated with ischemia of more extensive portions of the gut. There are many causes of focal segmental ischemia (FSI). The commonest are collagen-vascular diseases, vasculitis, degenerative vascular disorders, radiation therapy, and oral contraceptive use. In FSI, there usually is adequate collateral circulation to prevent transmural hemorrhagic infarction; however, damaged areas of the bowel often become secondarily infected. Limited tissue necrosis may result in complete healing, chronic enteritis, or stricture formation with partial or complete intestinal obstruction. Transmural infarction with perforation or localized peritonitis may follow a severe local insult.

The clinical presentation of persons with FSI depends on the severity of the infarct. With transmural necrosis, the sudden onset of abdominal pain often simulates acute appendicitis. Patients develop the clinical signs associated with peritonitis and sepsis. Another common presentation, often closely resembling that of Crohn's disease, is with crampy abdominal pain, diarrhea, weight loss, and occasionally fever. The commonest presentation is that of small bowel obstruction, with or without a history of an antecedent episode of trauma, pain, or herniation. Intermittent abdominal pain, distention, and vomiting are the direct results of the obstruction, and bacterial overgrowth in the dilated bowel proximal to the obstruction may lead to derangements usually associated with the blind-loop syndrome. The preoperative diagnosis of FSI is difficult to make; a previous

episode of transient pain, trauma, herniation, or a known systemic illness may suggest the diagnosis.

The treatment of acute FSI usually is surgical. Some patients without signs of peritonitis can be managed expectantly, and in these cases serial small bowel radiographs should show a resolving pattern. The nonoperative approach should be abandoned if the clinical findings fail to resolve. Limited resection is the procedure of choice for focal enteritis and obstructing lesions.

CHRONIC MESENTERIC ISCHEMIA

Elderly individuals with CMI, also known as *intestinal angina*, experience recurrent acute episodes of insufficient blood flow to the bowel during periods of increased metabolic demand associated with digestion.[23] [51] Intestinal angina almost always is caused by atherosclerosis of the splanchnic blood vessels. The circulation is inadequate to satisfy the metabolic demands arising from the increased motility, secretion, and absorption that occur after meals, and ischemia is manifested by visceral pain, disordered gastrointestinal absorption, or abnormal motility. The abdominal pain in this condition is analogous to the chest pain associated with angina pectoris or calf muscle pain associated with intermittent claudication.

Most commonly in patients with CMI, abdominal pain occurs 10 to 15 minutes after eating, gradually increases in severity, reaches a plateau, then slowly abates during 1 to 3 hours. The pain is crampy, located in the upper abdomen, and may radiate from the epigastrium through to the back. Some patients find that squatting or assuming a prone position can relieve the pain. Initially, pain occurs only after a large meal, but as the disease progresses, patients reduce the size of meals and eventually become reluctant to eat. Weight loss is characteristic and often severe. Bloating, flatulence, and constipation or diarrhea are seen, and steatorrhea develops in approximately half of affected persons. Intermittent episodes of vomiting occur less commonly. Patients usually present in their 50s or 60s, and there is a 3:1 female predominance. There frequently are symptoms and signs of generalized atherosclerotic disease, such as carotid, coronary, or peripheral vascular disease. Physical findings are limited and nonspecific; a systolic bruit is heard in the upper abdomen of approximately half of patients, but similar bruits have been reported in 15% of healthy patients and are not diagnostic of CMI.

The failure to identify the cause of postprandial abdominal pain associated with weight loss in an elderly patient should suggest the possibility of CMI (see Fig. 3 (Figure Not Available) *B*). There is no specific or reliable test to confirm this diagnosis; the diagnosis is based on the typical clinical symptoms and arteriographic demonstration of an occlusive process of the splanchnic vessels as well as exclusion of other gastrointestinal diseases. Conventional radiologic examination of the gastrointestinal tract is usually unremarkable.

In CMI, angiography shows stenosis or occlusion of at least 2 of the major vessels but, by itself, does not establish the diagnosis of arterial insufficiency or intestinal angina (Figs. 6 (Figure Not Available) and 7) (Figure Not Available) . In one review of patients with CMI, 91% had occlusion of 2 vessels, and 55% had involvement of all 3 vessels.[51] A marked decrease in, or total absence of, blood flow in the major mesenteric arteries may be shown by duplex ultrasonography.[72] [73] Doppler ultrasonography has been used to show that in subjects with CMI the splanchnic blood flow fails to increase normally after a meal, but does increase after successful arterial reconstruction. Magnetic resonance angiography,[22] [49] magnetic resonance oximetry,[45] and intestinal oxygen consumption all have been studied as diagnostic tools for this disease. All are indirect measures of intestinal blood flow and alone cannot establish the presence or absence of CMI.

Figure 6. (Figure Not Available) Angiogram from patient with no abdominal symptoms. Flush aortogram in lateral position shows occlusion of celiac axis, superior mesenteric artery, and inferior mesenteric artery. *(From Boley SJ, Brandt LJ, Veith FJ: Ischemic disorders of the intestines. In Current Problems in Surgery, Vol. XV, No. 4. April 1978, Chicago, Year Book Medical; with permission.)*

Figure 7. (Figure Not Available) Lateral view of a flush aortogram in a patient suspected of having abdominal angina. *A,* There is occlusion of the celiac and superior mesenteric arteries. *B,* Balloon angioplasty has been performed on the superior mesenteric artery, thereby resulting in improved flow and resolution of symptoms. *(From Reinus JF, Brandt LJ, Boley SJ: Ischemic diseases of the bowel. Gastroenterol Clin N Am 19:319-343, 1990.)*

Surgical revascularization has been the mainstay of therapy for patients with CMI.[42] [48] The difficulty in establishing a diagnosis of CMI, the fragility of elderly patients with this condition, and the risks of a major operation to revascularize the gut have made the selection of patients for surgery difficult, however.[52] There is general agreement that a patient with the typical pain of intestinal angina and unexplained weight loss in whom diagnostic evaluation has excluded other gastrointestinal diseases and angiography shows occlusive involvement of at least 2 of the 3 major arteries may benefit from revascularization. Several procedures, including aortic reimplantation of the superior mesenteric artery, transarterial and transaortic mesenteric endarterectomy, and antegrade and retrograde bypass, have been advocated for restoring normal blood flow distal to an occlusion of the superior mesenteric or celiac arteries.[67] The issue is much less clear if only one major vessel is involved or if the clinical presentation is atypical. Reported surgical outcomes have varied depending on the nature of the operation employed and the number of vessels revascularized, but in general success rates are greater than 90%, with low operative mortality and recurrence rates of less than 10%. Current studies suggest that 5-year survival rates for patients who undergo surgical revascularization are 71% to 86%. [16] [41] [42]

In selected patients, percutaneous transluminal mesenteric angioplasty, alone or in combination with insertion of a stent, is an option. Although experience is limited, success rates have been similar to those of conventional surgery, but with higher recurrence rates.[16] [47] [61] Current recommendations suggest that patients with CMI who are good surgical candidates should have an attempt at surgical revascularization; patients at

higher surgical risk may be appropriate candidates for percutaneous transluminal mesenteric angioplasty with or without stenting.[16]

COLONIC ISCHEMIA

CI is recognized to be the commonest vascular disorder of the intestines in the elderly. Until the 1950s, the only well-described form of CI was gangrene. During the 1950s, however, a variety of ischemic manifestations other than gangrene were noted after high ligation of the inferior mesenteric artery during abdominal aortic aneurysmectomy or colectomy. Careful review of these cases revealed a spectrum of diseases, in addition to infarction, that included healed ulcers, strictures, pseudotumors, and ischemic ulcerative colitis.

In 1963, based on retrospective and experimental studies, Boley et al[9] described the clinical, radiologic, and pathologic features of reversible vascular occlusion of the colon, now recognized to be the commonest form of CI. Their animal research, reported in 1965, confirmed that spontaneous CI could result in irreversible pathologic colonic injury, specifically, stricture, gangrene, and chronic colitis.

CI encompasses a spectrum of injury.[32] The specific conditions resulting from ischemic injury to the colon are classified as reversible or irreversible, and then can be categorized further as (1) reversible ischemic colonopathy (submucosal or intramural hemorrhage), (2) reversible or transient ischemic colitis, (3) chronic ulcerative ischemic colitis, (4) ischemic colonic stricture, (5) colonic gangrene, and (6) fulminant universal ischemic colitis. Despite a growing understanding of the pathophysiology of colonic ischemia and its disparate clinical presentations, many cases of transient or reversible ischemia still are missed because diagnostic studies are not performed early enough in the course of the disease or patients do not seek medical advice because the disease is self-limited and often confused with other diseases such as inflammatory bowel disease.

The most important clinical problem in evaluating a patient with suspected CI is to differentiate it from AMI (Table 1) . As discussed previously, patients with AMI usually present with severe abdominal pain in the context of a predisposing illness, such as congestive heart failure, cardiac arrhythmia, or hypovolemia. In contrast, patients with CI usually are not critically ill at the time of diagnosis, and their abdominal pain typically is mild. Mesenteric angiography plays little role in the diagnosis and management of this condition; because colonic blood flow usually has normalized by the time of presentation, the prognosis typically is excellent.

TABLE 1 -- DIFFERENTIATING ACUTE MESENTERIC ISCHEMIA FROM COLONIC ISCHEMIA

Acute Mesenteric Ischemia	Colonic Ischemia

TABLE 1 -- DIFFERENTIATING ACUTE MESENTERIC ISCHEMIA FROM COLONIC ISCHEMIA	
Acute Mesenteric Ischemia	**Colonic Ischemia**
Most patients >50 y old	90% of patients >60 y old
Acute precipitating cause is usual (e.g.,myocardial infarction, congestive heart failure, cardiac arrhythmias, hypotensive episodes)	Acute precipitating cause is rare
Predisposing lesion is uncommon (excluding atherosclerosis)	Associated predisposing lesion in 10% (e.g., colon carcinoma, stricture, diverticulosis, fecal impaction)
Patients usually appear seriously ill	Patients do not appear ill
Pain more severe; abdominal findings minimal early in course but become pronounced later	Mild abdominal pain with tenderness and guarding usual
Rectal bleeding and diarrhea uncommon	Moderate rectal bleeding or bloody diarrhea
First diagnostic procedure should be plain film or CT followed, if negative, by angiography	First diagnostic procedure should be gentle barium enema or colonoscopy
CT = computed tomography.	

In most cases, the cause of an episode of CI cannot be established with certainty, and no vascular occlusion can be identified. Causes of colonic ischemia include:

Inferior mesenteric artery thrombosis

Arterial embolus

Cholesterol emboli

Cardiac arrhythmia

Congestive heart failure

Shock

Volvulus

Strangulated hernia

Vasculitis

Hematologic disorders

Sickle cell anemia

Protein C and S deficiencies

Antithrombin III deficiency

Factor V Leiden mutation (activated protein C resistance)

Factor II 20210A mutation (in combination with oral contraceptive use)

Polycythemia vera

Infections

Parasites

Angiostrongylus costaricensis

Entamoeba histolytica

Viruses

Cytomegalovirus

Bacteria

Escherichia coli O157:H7

Trauma

Long-distance running

Pregnancy

Surgical

Aneurysmectomy

Aortoiliac reconstruction

Gynecologic operations

Exchange transfusion

Colonic bypass

Lumbar aortography

Colectomy with inferior mesenteric artery ligation

Colonoscopy and barium enema

Medications

Related to vasoconstriction or vasculitis

Digitalis

Vasopressin

Gold

Pseudoephedrine

Sumatriptan

Cocaine

Methamphetamine

Nonsteroidal anti-inflammatory drugs

Imipramine

Related to hypovolemia or constipation

Interferon-alpha

Saline laxatives

Estrogens

Progestins

Danazol

Psychotropic medications

Alosetron (?)

That the incidence of CI is greater in the elderly than the young does suggest a relationship between this process and degenerative changes of the vascular tree, however.[17] Approximately 90% of persons with CI are older than age 60 and have evidence of widespread atherosclerosis. Up to 10% of patients may have a potentially obstructing lesion of the colon, including carcinoma, benign stricture, and diverticulitis (Figs. 8 (Figure Not Available) and 9) (Figure Not Available) .

Figure 8. (Figure Not Available) *A,* Barium enema showing area of ischemic colitis and stricture (S) in descending colon and a nonobstructing carcinoma (C) in the sigmoid colon. *B,* Gross specimen from same patient demonstrating typical segmental ischemic ulcerative colitis *(between large arrows).* The *small arrows* point to the neoplasm. *(From Reinus JF, Brandt LJ, Boley SJ: Ischemic diseases of the bowel. Gastroenterol Clin N Am 19:319-343, 1990.)*

Figure 9. (Figure Not Available) Barium enema demonstrating a narrowed segment of colon owing to diverticulitis (D). There is an area of ischemic colitis (C) proximal to the stricture. *(From Reinus JF, Brandt LJ, Boley SJ: Ischemic diseases of the bowel. Gastroenterol Clin N Am 19:319-343, 1990.)*

Factors that may predispose to ischemic injury of the colon are an inherently low colonic blood flow, which is less than that of the small intestine, and an additional decline in perfusion associated with functional motor activity of the colon. Constipation may exacerbate colonic circulatory inadequacy through the effects of straining at stool on systemic arterial and venous pressure. The ultimate cause of an ischemic episode is conjectural in most instances; whether increased demand by colonic tissue is superimposed on an already marginal blood flow or whether blood flow itself is diminished acutely by some as yet undiscovered cause remains to be determined.

The differential diagnosis of CI includes infectious colitis, inflammatory bowel disease, pseudomembranous colitis, diverticulitis, and colon carcinoma.[19] In all patients suspected of having colonic ischemia, a stool culture for *Salmonella, Shigella, Campylobacter,* and *E. coli* O157:H7 should be sent. That last-mentioned organism induces a colitis that mimics or may cause CI.[68] Parasites such as *Angiostrongylus costaricensis* and *Entamoeba histolytica* as well as viruses such as cytomegalovirus also may cause CI. Many medications are associated with CI; many are used commonly and include digitalis, nonsteroidal anti-inflammatory drugs, imipramine, danazol, sumatriptin, and alosetron. In the United States, alosetron was removed from the market in 2000 because of its association with CI.

Typically, CI presents with the sudden onset of mild crampy left lower quadrant abdominal pain. The pain frequently is accompanied, or followed within 24 hours, by bloody diarrhea or bright red blood per rectum. With irreversible transmural necrosis or accompanying small bowel involvement, the pain may be quite severe. In most cases, blood loss is minimal; hemodynamically significant bleeding should prompt consideration of other diagnoses, such as diverticular bleeding.

On physical examination, mild to severe abdominal tenderness may be elicited in the location of the involved segment of bowel. Although any part of the colon may be affected, the splenic flexure, descending colon, and sigmoid are the commonest sites of ischemic injury (Fig. 10) (Figure Not Available) . Although the prognosis cannot be derived from the pattern and distribution of the disease, some causes tend to result in injury to specific areas of the colon. Nonocclusive ischemic injury usually involves the watershed areas of the colon, such as the splenic flexure and the junction of the sigmoid colon and rectum. Similarly the length of the involved segment varies depending on the cause of the injury; atheromatous emboli, which are an unusual cause of CI, result in

damage to short segments, whereas nonocclusive injury usually involves much larger portions of the colon. Signs of peritoneal irritation have been noted with lesions that are reversible ultimately, but if peritoneal signs persist for more than a few hours, they should be considered as evidence of transmural necrosis and infarction, prompting surgical exploration.

Figure 10. (Figure Not Available) Distribution and length of involvement in colon ischemia in 250 cases. *(From Reinus JF, Brandt LJ, Boley SJ: Ischemic diseases of the bowel. Gastroenterol Clin N Am 19:319-343, 1990.)*

If AMI is thought not to be present, an elderly patient with the sudden onset of abdominal pain and rectal bleeding or bloody diarrhea should have a *gentle* barium enema or colonoscopy within 48 hours of presentation (see Fig. 3 (Figure Not Available) *C*). [18] Colonoscopy is preferable because it is more sensitive in showing mucosal abnormalities and permits biopsy.[65] Conventional sigmoidoscopy is of value only if the segment of involved bowel is within reach of the sigmoidoscope; CI involves the sigmoid in approximately 50% to 60% of patients and the rectum in less than 10% of cases. Findings vary greatly depending on the stage at which sigmoidoscopy or colonoscopy is performed. At the outset, purplish blebs representing mucosal and submucosal hemorrhage may be seen. As the hemorrhage is resorbed, varying degrees of necrosis, inflammation, ulceration, and mucosal sloughing occur, resembling ulcerative colitis or Crohn's disease (Fig. 11) (Figure Not Available) . Nonspecific inflammatory changes neither confirm nor exclude an antecedent ischemic episode, but sequential changes, from submucosal hemorrhage to colitis and finally to normal mucosa evolving during 10 to 14 days, are characteristic of CI.

Figure 11. (Figure Not Available) Two barium enemas performed 10 years apart in an elderly woman with recurrent bloody diarrhea. The clinical course suggested colonic ischemia. *A*, The study was interpreted as ulcerative colitis; *B*, the segmental nature of the colitis and deep ulcers are more consistent with Crohn's disease. *(From Reinus JF, Brandt LJ, Boley SJ: Ischemic diseases of the bowel. Gastroenterol Clin N Am 19:319-343, 1990.)*

Care must be taken during barium enema or colonoscopy to avoid overdistending the colon because increasing intraluminal pressure beyond 30 mm Hg diminishes intestinal blood flow, especially to the mucosa. At pressures greater than 30 mm Hg, which can be generated routinely during barium enema examination and colonoscopy, there also is shunting of blood from the mucosa to the serosa, with a resulting progressive reduction in the arterial-venous oxygen difference; these changes increase the risk of ischemic damage. Using carbon dioxide rather than room air to inflate the colon during a diagnostic procedure may minimize this risk.[20] Carbon dioxide is a potent vasodilator and is absorbed rapidly from the colon, leading to a shorter period of distention, less compromise of colonic blood flow, and a more comfortable examination. Because of its vasodilating effects, carbon dioxide increases colonic blood flow at the lower range of intracolonic pressures (Fig. 12) (Figure Not Available) and is probably a safer agent than room air with which to inflate the colon, especially in elderly patients with CI.

Figure 12. (Figure Not Available) Representative experiment showing inferior mesenteric artery blood flow at a constant intraluminal pressure of 65 mm Hg maintained with CO_2 and room air. Blood flow is 179% of control values with CO_2 and 68% of control values with room air. *(From Brandt LJ, Boley SJ, Sammartano R: CO_2 and room air insufflation of the colon: Effects on colonic blood flow and intraluminal pressure in the dog. From Gastrointest Endosc 32:324, 1986; with permission.)*

Thumbprints, or pseudotumors, are the major radiologic finding in the acute presentation of CI. Thumbprints represent submucosal and mucosal hemorrhage and edema (Fig. 13 (Figure Not Available) *A*). A barium enema repeated 1 week after an initial study should reflect evolution of the injury (Fig. 13 (Figure Not Available) *B*); either the areas of hemorrhage resorb and the study returns to normal, or the thumbprints are replaced by a segmental pattern of colitis as the mucosa ulcerates. Magnetic resonance imaging may be useful in differentiating ischemic from nonischemic tissue,[70] and indium-111 white blood cell scans have been used in the early diagnosis of CI.[50]

Figure 13. (Figure Not Available) Ischemic changes in transverse colon and splenic flexure. *A,* Initial study shows dramatic thumbprints throughout area of involvement. *B,* Eleven days later, thumbprints are gone, and involved colon has typical appearance of segmental colitis including ulcerations. *C,* Five months after onset, there is complete return to normal. Patient was asymptomatic 3 weeks after her illness. *(From Boley SJ, Schwartz SS: Colonic **ischemia**: Reversible ischemic lesions. In Boley SJ, Schwartz SS, Williams LF (eds): Vascular disorders of the intestine. New York, Appelton-Century-Crofts, 1971; with permission.)*

In most patients, CI is a single event; only 5% of affected persons experience recurrent episodes (Fig. 13 (Figure Not Available) *C*). Damage resolves spontaneously and completely in most cases; the balance can be divided into 3 roughly equal groups: (1) patients who present with gangrene and perforation, (2) patients who present with chronic ischemic colitis, and (3) patients who present weeks to months later with a colonic stricture. In mild disease, symptoms and signs usually subside in 24 to 48 hours, and complete clinical and radiologic healing occurs within 1 to 2 weeks. Patients with a prolonged course may be clinically well, even in the presence of persistent mucosal abnormalities that may persist 6 months. Severe ischemia may become obvious within hours of presentation when gangrene or perforation occurs or may follow a protracted course, with the development of chronic colitis or a stricture (Fig. 14) (Figure Not Available) . The diagnosis of colonic infarction is made on the basis of abdominal guarding, rebound tenderness, fever, leukocytosis, and evidence of a paralytic ileus. These signs, although nonspecific for infarction, dictate a need for emergency laparotomy.

Figure 14. (Figure Not Available) Barium enema demonstrating a smoothly tapering, tight ischemic stricture in the descending colon. Patient had a history of rectal bleeding. *(From Reinus JF, Brandt LJ, Boley SJ: Ischemic diseases of the bowel. Gastroenterol Clin N Am 19:319-343, 1990.)*

The treatment of CI is based on early diagnosis and continued monitoring, with special attention to the radiologic or colonoscopic appearance of the colon. This form of surveillance is essential in that it establishes the diagnosis and verifies its reversibility or shows progression to chronic ischemic colitis or stricture. Management includes

stabilization of the patient, optimization of cardiac function, and bowel rest. Systemic antibiotics are administered routinely in most cases. Systemic glucocorticoids are of no proven value and may increase the chance of perforation.[31] If the abdominal examination, fever, and leukocytosis suggests deterioration or if the patient experiences diarrhea or bleeding for more than 2 weeks, irreversible damage is likely, and surgical resection usually is indicated.

SUMMARY

The ischemic bowel diseases are a heterogeneous group of disorders usually seen in elderly individuals. They represent ischemic damage to different portions of the bowel and produce a variety of clinical syndromes and outcomes. Colonic ischemia is the commonest of these disorders and has a favorable prognosis in most cases. In contrast, acute mesenteric ischemia, most commonly caused by a superior mesenteric artery embolus, is a disease with a poor prognosis. Acute mesenteric ischemia secondary to nonocclusive mesenteric ischemia usually is a catastrophic complication of other severe medical illnesses, most notably atherosclerosis. Proper diagnosis and management of patients with ischemic bowel disease requires vigilance on the part of the physician and a willingness to embark on an aggressive plan of diagnosis and management in the appropriate setting.

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