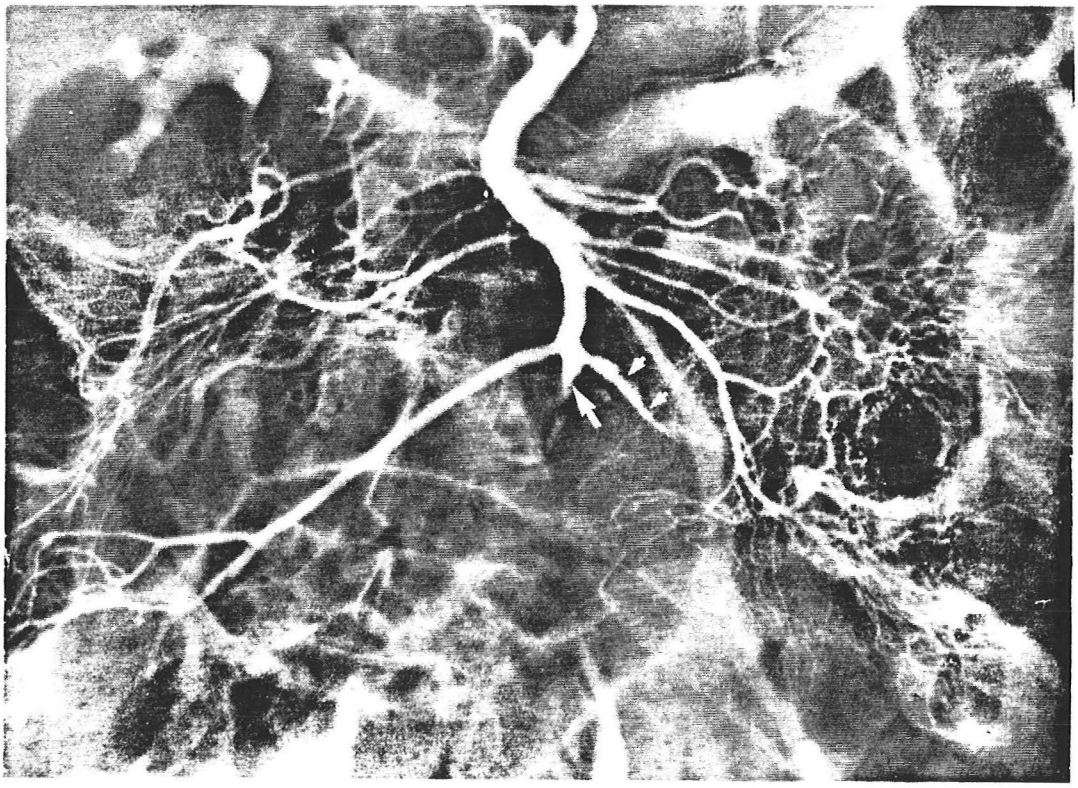
INTESTINAL ISCHEMIA



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INTESTINAL ISCHEMIA

INTRODUCTION

Mesenteric vascular insufficiency is an uncommon, but important problem because it leads to disastrous consequences, particularly if not recognized early. Delays in diagnosis, and misdiagnosis, are frequent because it is uncommon, and because symptoms and signs are non-specific. In recent years, there have been improvements in diagnostic studies and treatment which, although not dramatic, should lead to improved outcomes for those patients in whom the diagnosis is suspected early. The purpose of this presentation is to review aspects of normal mesenteric anatomy and physiology, the pathophysiology of intestinal ischemia, and the syndromes of intestinal angina, acute mesenteric ischemia, ischemic colitis, and mesenteric venous thrombosis.

INTESTINAL ARTERIES AND VEINS

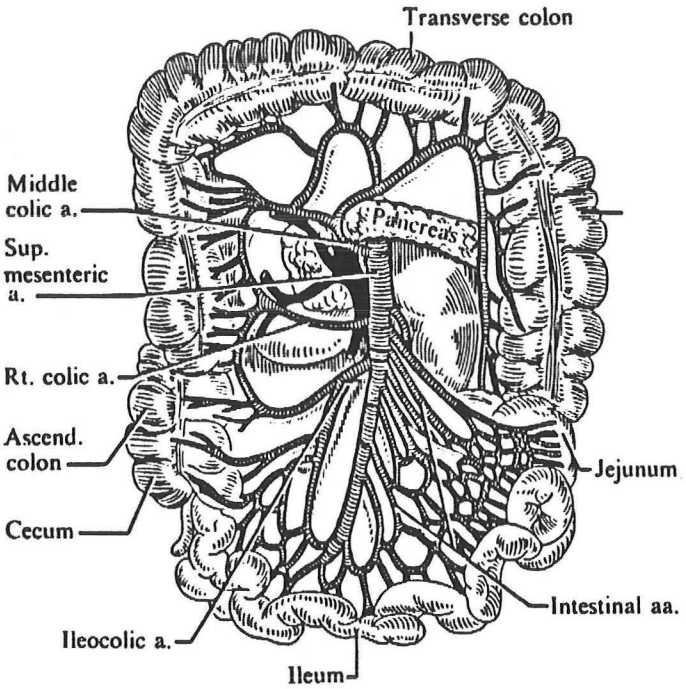
Arteries

The stomach, small bowel, and colon are supplied by the celiac, superior mesenteric, and inferior mesenteric arteries.

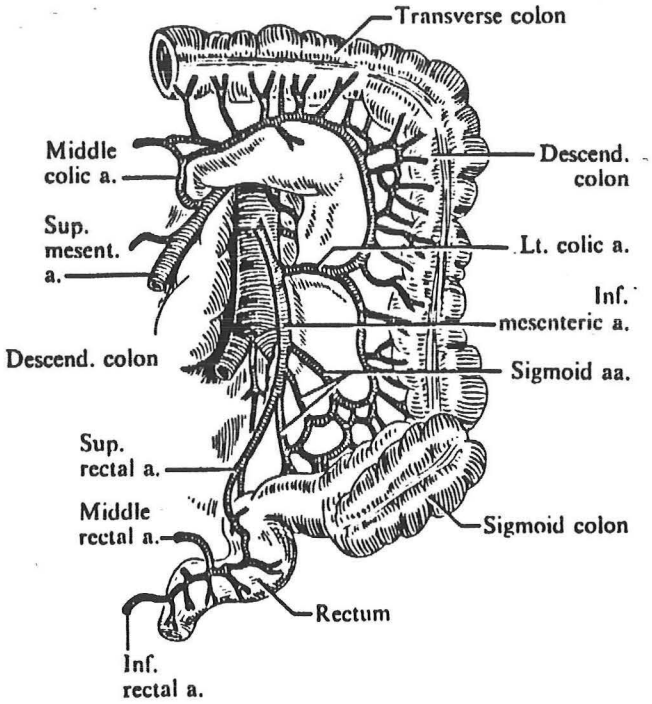
The celiac artery arises from the aorta immediately below the diaphragmatic hiatus. The hepatic, splenic, and left gastric branches supply the liver, spleen, stomach, duodenum, and pancreas. There are many collateral connections between the major branches of the celiac system.

The superior mesenteric artery (SMA) arises about 1 cm. distal to the celiac. A large number of intestinal branches from the main SMA trunk supply the jejunum and ileum. The cecum, ascending colon, and transverse colon are supplied by the ileocolic, right, and middle colic arteries. Branches of the SMA form a pattern of anastomosing arcades. The terminal arcades of the colic branches form a continuous artery coursing along the mesenteric wall of the colon, called the marginal artery, or artery of Drummond. From the terminal arcades the end arteries, or vasa recta, enter the intestinal wall.

The inferior mesenteric artery (IMA) originates at the level of L4. The superior hemorrhoidal and sigmoid branches supply the rectosigmoid. The left colic artery supplies the left colon proximally as far as the splenic flexure. The distal IMA arcades form a marginal artery along the left colon.



INTESTINAL AND COLIC ARTERIES



INFERIOR MESENTERIC ARTERY

Collateral circulation

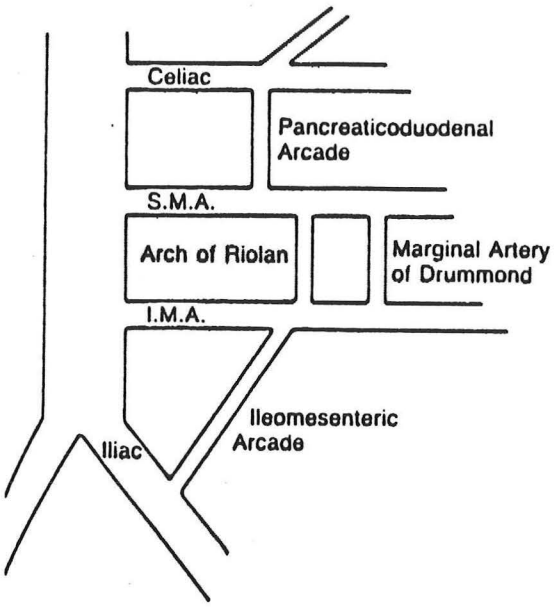
The intestines are protected from ischemia by a rich collateral circulation. There are several important areas of collateral flow between the major arterial systems.

The celiac and SMA connect through the superior and inferior pancreaticoduodenal arcades.

The SMA and IMA connect through the marginal artery of Drummond at the splenic flexure, or Griffith's point, in about 50% of individuals. This connection is absent in the other 50%, leaving the splenic flexure particularly vulnerable to ischemia. The middle colic branch of the SMA may also connect with the left colic branch of the IMA through the "arc of Rolan", or "meandering mesenteric artery".

The IMA connects with the internal iliac artery through the superior and inferior hemorrhoidal arcades.

Collateral blood flow around occlusion of smaller arterial branches occurs through the arcades. In addition, within the bowel wall there is a network of communicating submucosal vessels. These can maintain the viability of short segments of the intestine when the extramural arteries have been compromised.



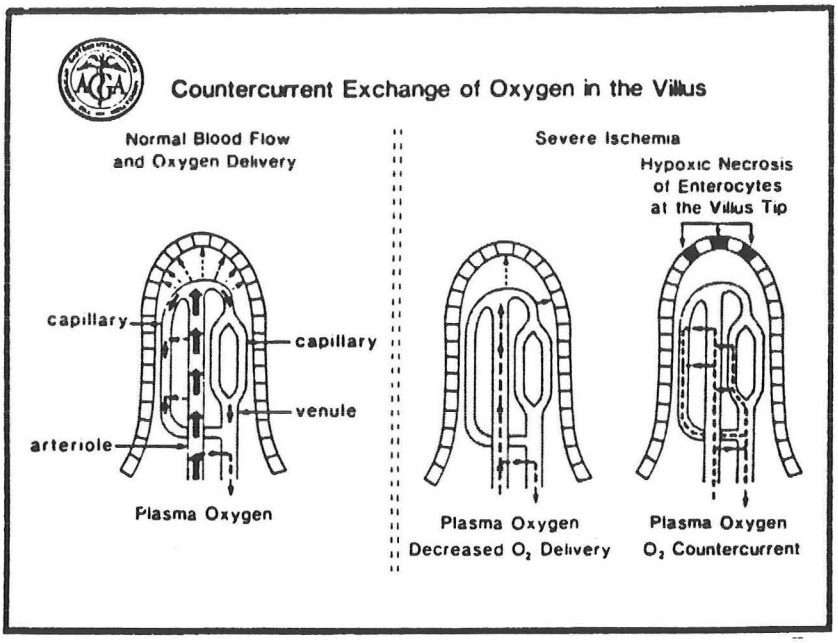
Veins

The inferior mesenteric vein drains into the splenic vein, which joins the superior mesenteric vein (SMV) to form the portal vein. Like the arterial system, the venous drainage is also arranged in anastomosing arcades.

INTESTINAL MICROCIRCULATION

From the mesentery, arterioles penetrate the wall of the intestine and give off parallel branches to the serosa, muscle layers, and submucosa. This arrangement of parallel arterial supplies allows independent regulation of blood flow to the mucosal and muscular layers.

From the submucosa, arterioles ascend into each villus and empty into the capillary network. Blood returns through central venules which run in close proximity to the arterioles, within 20 microns. This arrangement creates a countercurrent system like that of the renal medulla. The countercurrent multiplier is important in sodium and water absorption in the gut, and also plays a role during intestinal ischemia(1,2).



NORMAL PHYSIOLOGY OF THE MESENTERIC CIRCULATION

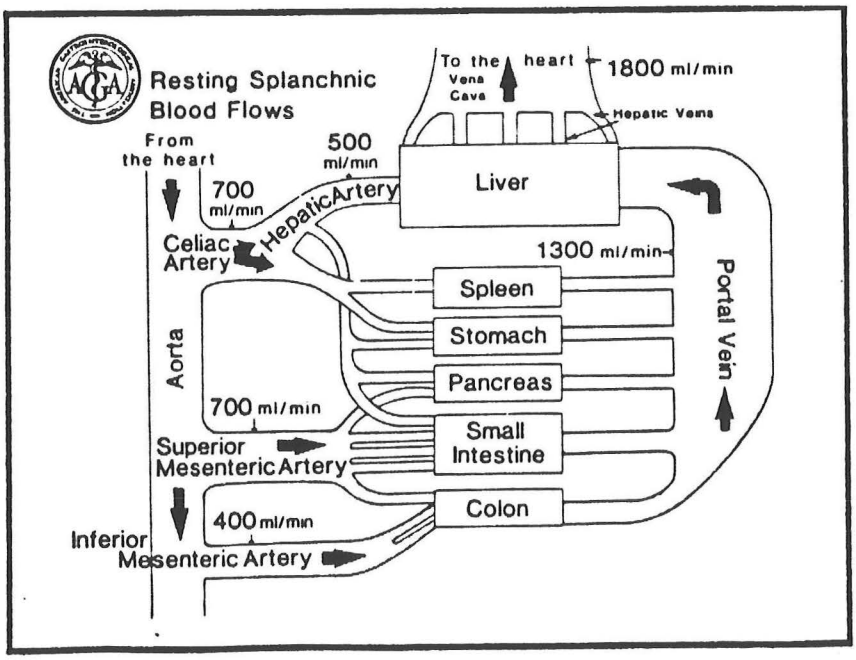
The intestine is richly perfused compared to other body tissues.

Resting Blood Flow
ml/min/100 gm

Stomach	Small Bowel	Colon	Skeletal Muscle
11	29-70	8-35	2-5

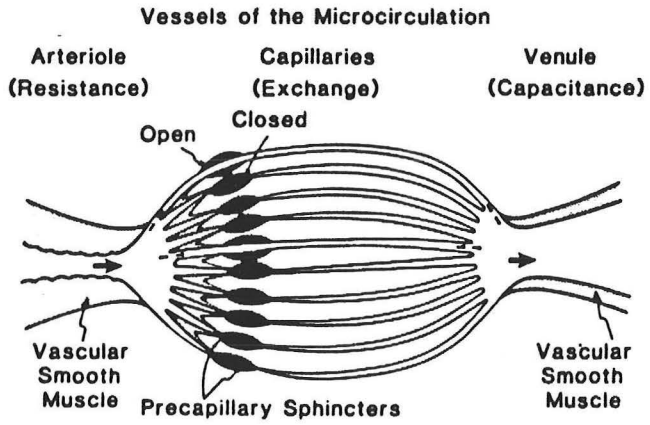
(3)

At rest, about 1800 ml/min, or 25% of the cardiac output, go to the splanchnic circulation. About 700 ml per min go to the celiac artery, 700 to the SMA, and 400 to the IMA. The mucosa receives 75% of the intestinal blood flow, and the muscular layers 25%.



Regulation of intestinal perfusion

Regulation of intestinal perfusion occurs at two distinct control points: the arteriole and the precapillary sphincter. Arterioles are the primary resistance vessels of the intestinal circulation and thus control flow. Precapillary sphincters do not alter blood flow significantly. By opening more capillary units to perfusion, they increase perfused surface area and improve oxygen extraction.



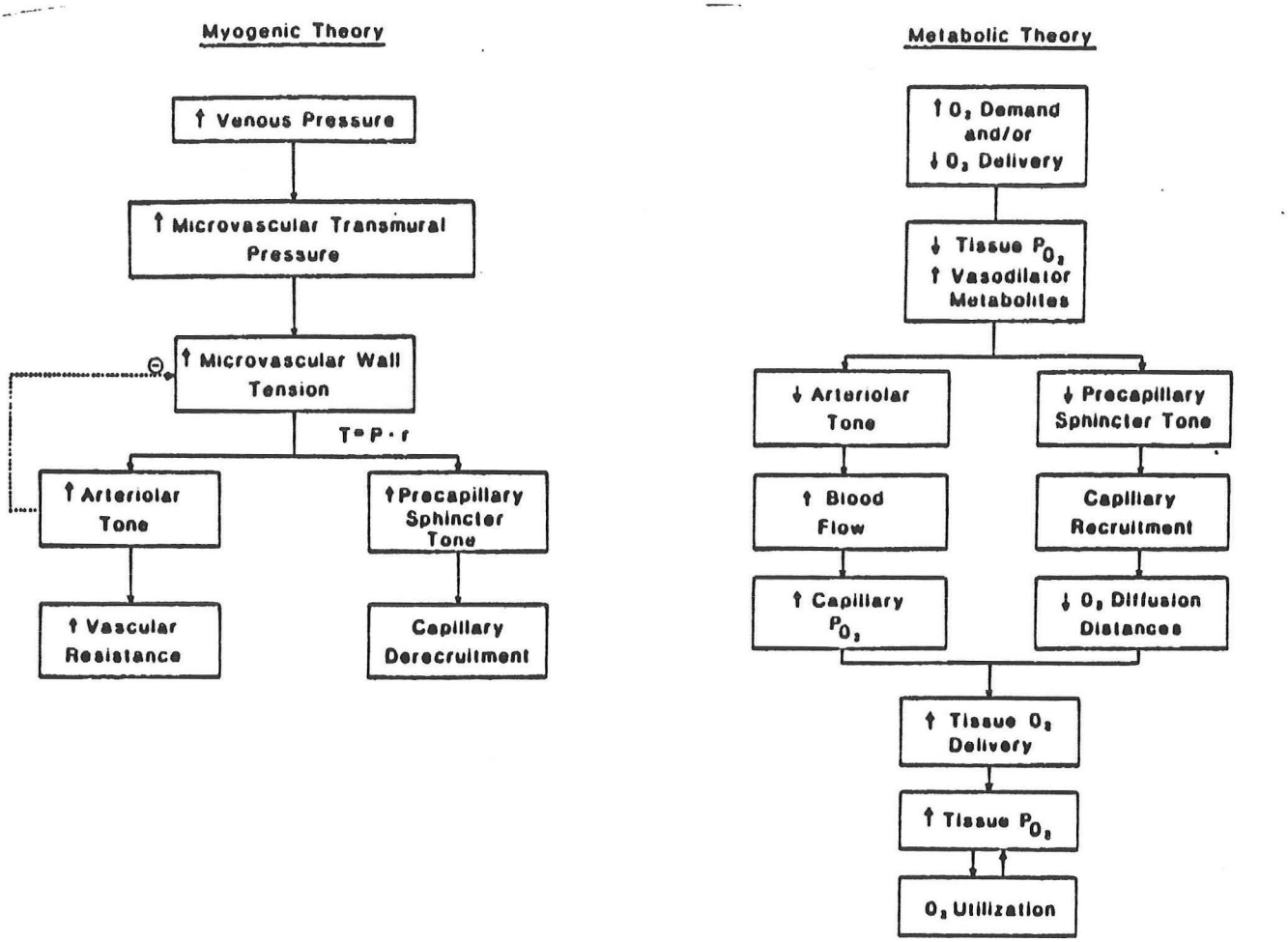
Intestinal perfusion is controlled by several mechanisms, either intrinsic or extrinsic.

Intrinsic regulation

Myogenic and metabolic mechanisms control intestinal perfusion in response to changes in arterial pressure or tissue oxygenation.

Myogenic control involves changes in vessel wall tension with changes in pressure. When pressure falls, the smooth muscle of the mesenteric vessels relaxes, and the vessels dilate (4).

Metabolic control is mediated through accumulation of vasodilators. Conditions that increase oxygen demand, such as digestion, or decrease oxygen delivery, will lead to accumulation of substrates such as adenosine, which cause arteriolar dilatation and relaxation of precapillary sphincters, resulting in increased perfusion (5).



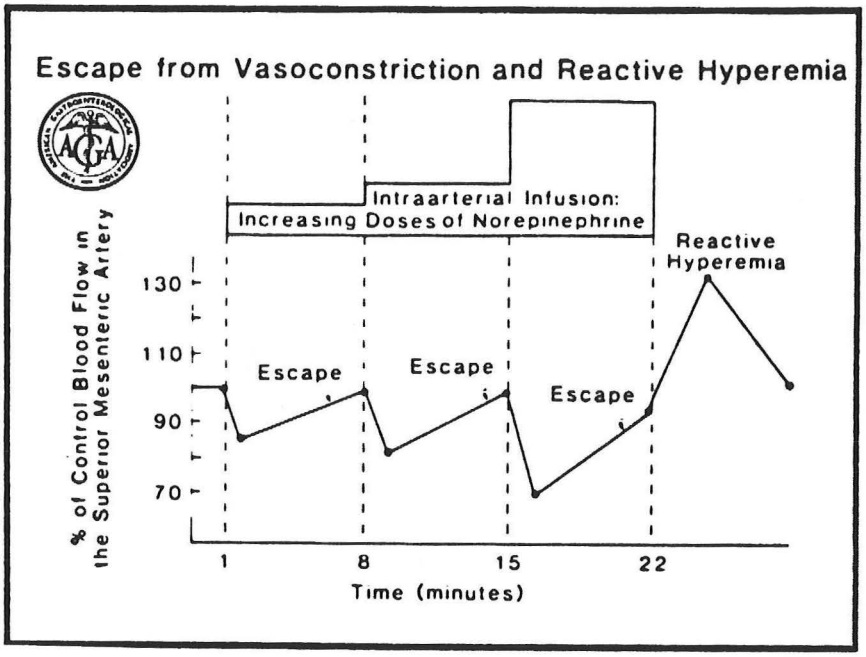
The enteric nervous system may participate in intrinsic control of intestinal perfusion. A large number of neurotransmitters, including vasoactive intestinal peptide (VIP), have been found in neurons of the intrinsic nervous system of the intestine. The release of VIP, which is known to be a vasodilator, coincides with meal-induced increased blood flow.

Gastrointestinal hormones such as gastrin, cholecystokinin, and glucagon, among others, have been shown to increase intestinal blood flow. However, studies have been done with pharmacologic levels of these hormones, and it is not clear whether they have a physiological role in the control of intestinal perfusion (1,6).

Extrinsic regulation

The sympathetic nervous system participates in extrinsic control of intestinal perfusion. Alpha adrenergic stimulation causes arteriolar vasoconstriction and reduction in mesenteric blood flow. However, blood flow returns to normal with time despite continued sympathetic stimulation, a phenomenon called

"autoregulatory escape." Thus, the role of the sympathetic nervous system in mesenteric vasoconstriction during shock, for example, is not clear (7).



Other circulating vasoactive substances, particularly vasopressin and angiotensin II, also cause mesenteric vasoconstriction, and may play a role during such conditions as volume depletion and congestive heart failure (1).

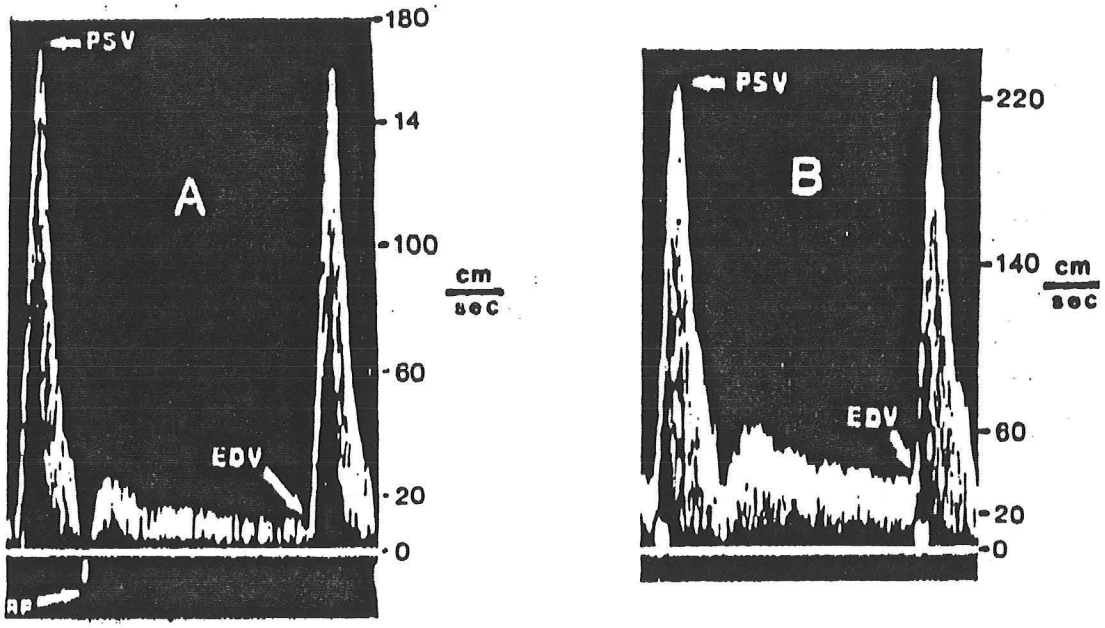
Response to a meal

Dye dilution studies: Information regarding mesenteric blood flow in human has been difficult to obtain. A Swedish group studied changes in mesenteric blood flow after a 700 cal. meal in 5 adults by indocyanine green infusion into the SMA. Sampling was done through a catheter placed into the SMV through a reopened umbilical vein. Basal SMA flow was 700 ml/min. SMA flow rose by 60% over baseline after 5 min and by 100% after 30 min. SMA resistance fell 55% (8).

Doppler ultrasound studies: Recently it has possible to study intestinal blood flow non-invasively by using Doppler ultrasound. The artery is first imaged with the B mode ultrasound. The Doppler beam is then placed in the artery and flow velocity

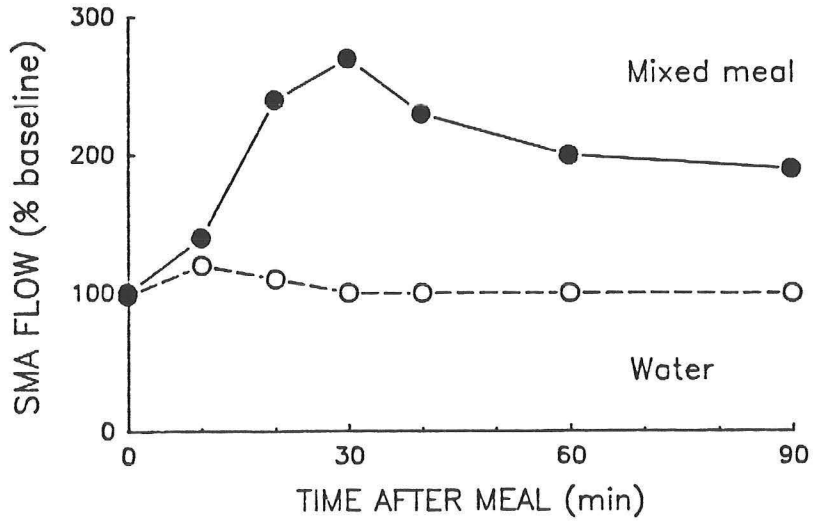
wave forms are obtained. The flow velocity wave form of the SMA is characteristic of a high resistance system. There is a sharp velocity peak in systole and a low velocity in diastole. Flow reversal occurs in early diastole.

After a meal, SMA resistance falls, and flow velocity increases, particularly in diastole. The early diastolic flow reversal disappears.



Superior mesenteric artery waveform before (*A*) and 30 min after (*B*) ingestion of the mixed meal. Note loss of reverse flow (*RF*) and increases in peak systolic velocity (*PSV*) and end-diastolic velocity (*EDV*) after feeding.

Using measured SMA diameter and mean flow velocity, SMA flow can be calculated. In one study using Doppler ultrasound, calculated SMA flow rose to 270% of baseline within 30 min after a meal, and 200% after 90 min.



Doppler ultrasound studies of the celiac have shown no significant increase in flow after meals, in contrast to the SMA (9).

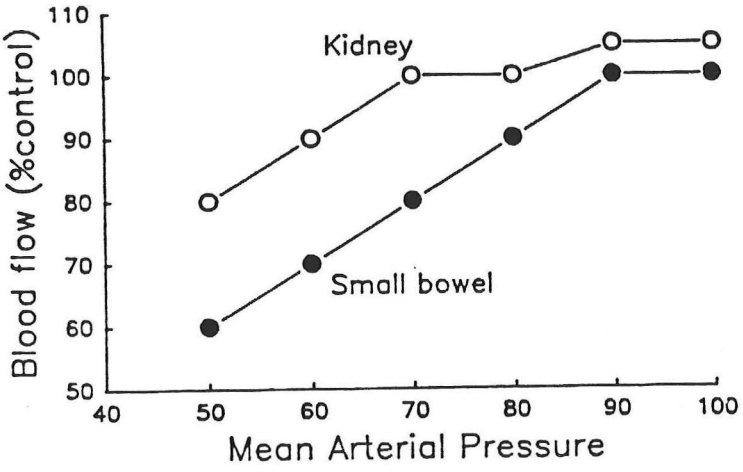
Response to exercise

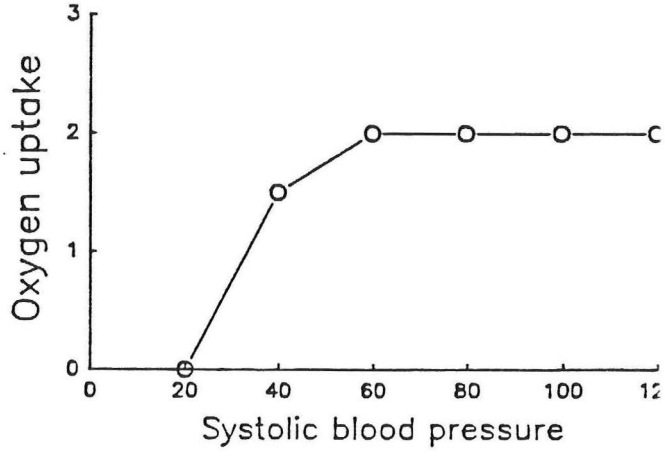
At rest, the splanchnic circulation receives 25% of the cardiac output, and contains 20% of the total blood volume. Thus it represents an important reserve for the increased demands of the systemic circulation during exercise. Mesenteric flow may fall to 30% of resting value during exercise, and splanchnic blood volume may decrease by 30-40% (10).

PATHOPHYSIOLOGY OF THE MESENTERIC CIRCULATION

Mesenteric defenses against systemic hypotension

When systemic arterial pressure drops, mesenteric vascular resistance falls, at least initially. This helps to maintain mesenteric flow. However, this mechanism is not as effective in maintaining blood flow in the intestine as it is in the kidney or the brain. When blood flow falls, oxygen uptake can be maintained through dilatation of precapillary sphincters, capillary recruitment, and improved oxygen extraction.

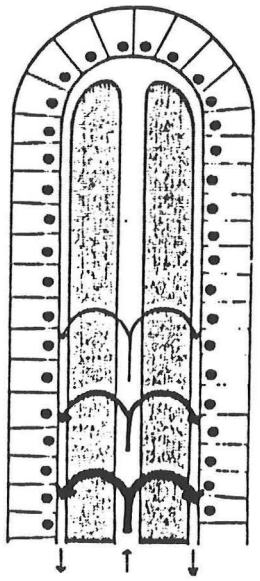




With continued systemic hypotension, intestinal counter-regulatory defenses fail, and intestinal hypoxia occurs. Because of high mucosal metabolic demands, the intestinal mucosa is injured before the intestinal muscle.

Countercurrent hypoxia

Within the mucosa, the tips of the villi are most affected by hypoxia. Under normal circumstances there is a gradient of oxygen tension in the villi, with the tips being relatively hypoxic. This is due to shunting of oxygen from arterioles to venules because of countercurrent flow. During ischemia, blood flow slows markedly, and countercurrent shunting is increased, increasing the oxygen gradient and producing hypoxic injury (1).



Counter Current Gradient
in the Intestinal Villus

Tissue injury during ischemia

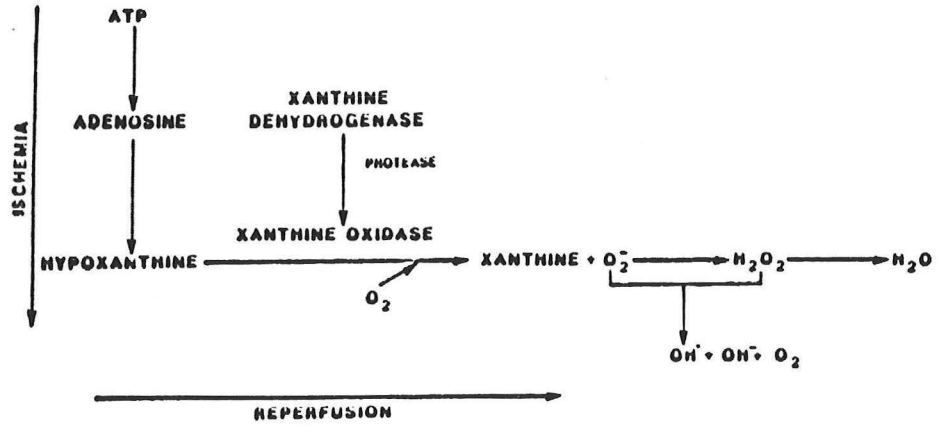
The first histologic change in intestinal ischemia is separation cells of the tips of the villi from the basement membrane. As ischemia progresses, the entire mucosa is sloughed, exposing the submucosa to invasion by bacteria. Bacterial endotoxins and other vasoactive compounds gain access to the circulation. In addition to mucosal damage, there is loss of vascular integrity. As much as 30% of the circulatory volume may be lost through edema and fluid loss into the lumen, in acute animal experiments. As ischemia progresses, hemorrhage into the intestinal wall and lumen occur. These processes aggravate circulatory collapse,

which in turn worsens the mesenteric ischemia. Experimental animals often die of vascular collapse before transmural infarction occurs.

The initial motor response of the intestinal muscle to ischemia is increased peristalsis. With progressive ischemia, peristalsis ceases, muscle tone is lost, and intestinal dilatation occurs. The dilatation further aggravates ischemia by increasing wall tension and thus decreasing blood flow.

Reperfusion injury

Mucosal injury in mesenteric ischemia is due in large part to hypoxia. However, in animal experiments, when a ligature is placed to produce ischemia, the animals die earlier if the ligature is released after several hours than if it is not removed. During the ischemic period, anaerobic metabolism leads to the breakdown of ATP and accumulation of hypoxanthine. In addition, xanthine dehydrogenase is converted to xanthine oxidase. When oxygen is available once more during reperfusion, xanthine oxidase reacts with hypoxanthine to produce xanthine and oxygen free radicals and hydroxyl ions. These cause lipid peroxidation and membrane damage (11). Whether reperfusion injury is relevant to human mesenteric ischemia is open to question. Although allopurinol, superoxide dismutase, and other agents limit ischemic bowel injury in animal studies, there are no such studies in humans.

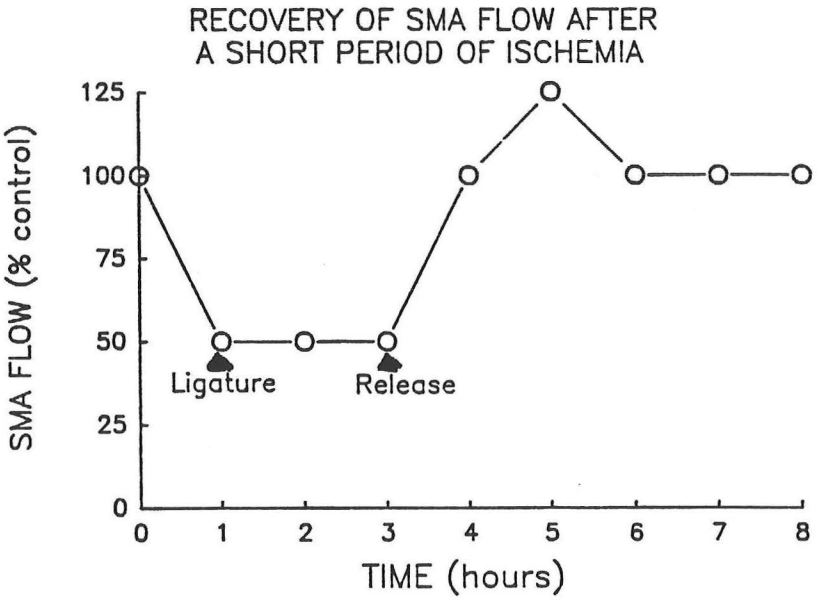


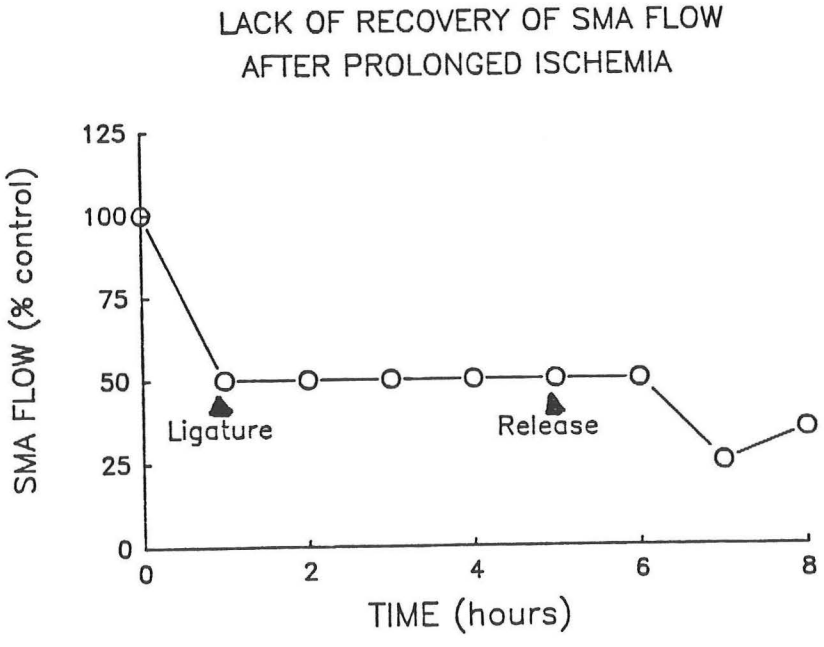
Ischemia and Reperfusion Injury

Arterial spasm

Arterial spasm often complicates acute mesenteric ischemia. Mesenteric arterial spasm may develop during intestinal ischemia of any cause, and may persist for hours after the initial event has resolved. After a mesenteric embolus, for example, the development of arterial spasm may lead to intestinal infarction even if the embolus is promptly removed.

Arterial spasm was studied by Boley in a classical series of animal experiments. Ligatures were placed on the superior mesenteric arteries of dogs and blood flow was reduced acutely by 50%. Arterial resistance distal to the ligature fell. Celiac artery blood flow increased. Both of these changes helped to maintain SMA perfusion. Within a few hours, the SMA resistance returned to normal. If the ligature was removed before the return of arterial resistance, SMA blood flow returned to normal. However, if the ligature was kept on longer, beyond the point at which resistance had increased, SMA flow did not recover when the ligature was removed. Persistent arterial spasm had developed.





The mechanism for this persistent arterial spasm is not clear. Boley showed that it could be prevented or reversed by intra-arterial infusion of papaverine. This forms the basis for intra-arterial papaverine therapy for mesenteric ischemia in humans, and will be discussed later (12).

INTESTINAL ANGINA

Case presentation: A 55 year old man presented with 6 months of vague abdominal discomfort beginning soon after meals, lasting about 1 hour, associated with occasional nausea and vomiting, and loose stools. His pain progressed. He developed a fear of eating. His weight fell from 150 to 115 lbs. Cimetidine did not help.

Past history included hypertension, a myocardial infarct, and claudication, with an aortofemoral (AF) bypass 3 years before this admission.

His examination was normal except for evidence of weight loss and peripheral vascular disease. Routine laboratory studies were normal.

Upper endoscopy showed 2 antral ulcers and duodenitis. Barium enema was normal.

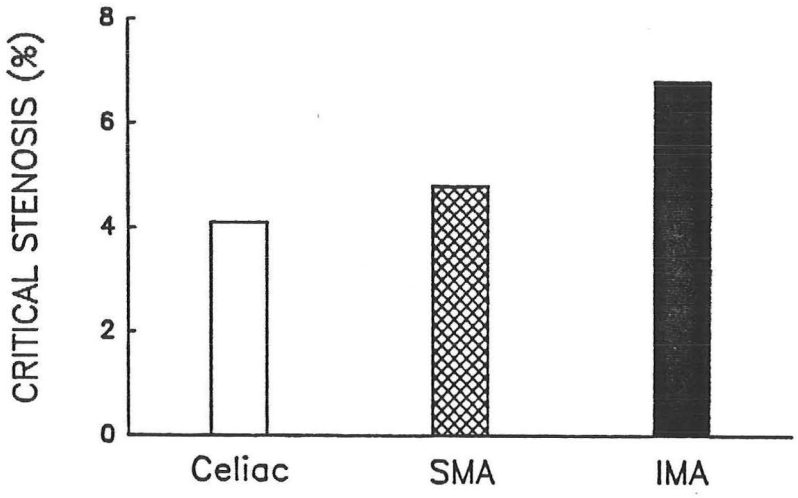
His pain improved with cimetidine in the hospital, and he was discharged with a diagnosis of gastric ulcer.

He was readmitted 2 weeks later with worsening abdominal pain. His examination and laboratory studies were unchanged. KUB and abdominal ultrasound were normal. On the third hospital day he had an upper gi bleed. Upper endoscopy showed antral ulcers, and severe diffuse erosive gastritis and duodenitis. The mucosa of the duodenum was dusky. At surgery he was found to have necrosis of the entire small intestine and the colon to the splenic flexure. Resection was felt to be incompatible with life. He died the next day. Autopsy showed a 50% stenosis of the celiac artery and an 80% stenosis of the superior mesenteric artery. The inferior mesenteric artery had been resected at the time of the AF bypass.

Prevalence of intestinal angina: Intestinal angina is rare. A medical records search disclosed only one case at PMH and one at the DVAMC during 1990. At the Middlesex Hospital in London, which is a referral center for mesenteric vascular disease, 100 patients were evaluated for intestinal angina over a period of 30 years. Of these, 47 were felt to have this diagnosis after investigation, and 41 had surgical revascularization (13). However, although intestinal angina is rare, it is important to identify, not only because it causes pain and disability, but because it may portend catastrophic intestinal infarction.

Physiology of intestinal angina: Gradual obstruction of the mesenteric arteries leads to the development of collateral flow. Because of this, although older people

have a substantial incidence of visceral artery stenosis, most are not symptomatic (14).



Incidence of Critical Stenosis of Visceral Vessels, Age > 60 (Croft, Br J Surg, 1981)

Collaterals may compensate for severe occlusive disease. Intestinal ischemia does not develop unless 2 of the 3 mesenteric vessels are compromised, and some individuals may be asymptomatic with even severe 3 vessel disease. Individuals who develop intestinal angina have inadequate collaterals, with fixed mesenteric blood flow. This flow may be adequate at rest, but is insufficient to meet the physiological demands of digesting a meal. In addition, individuals with intestinal angina are at risk of developing intestinal infarction with a superimposed stress, such as a fall in systemic arterial pressure, or a thrombus in a stenotic vessel.

Clinical presentation

History: The pain of intestinal angina is may be vague and mild initially. It is usually epigastric or periumbilical. Patients soon recognize the association between eating and pain, and although they do not lose their appetite, they develop a characteristic fear of eating. FEAR OF EATING IS THE HALLMARK OF INTESTINAL ANGINA. They eat small meals, or avoid eating altogether, so weight loss is the rule. Nausea or vomiting are less common. Constipation is due to decreased intake. Symptoms may be present for weeks to months.

Patients with intestinal angina are usually older, with generalized arteriosclerotic vascular disease. However, the last patient with intestinal angina at PMH was a 29 year old woman.

Physical examination: Physical examination will show signs of weight loss and

Physical examination: Physical examination will show signs of weight loss and vascular disease. The presence of an abdominal bruit is not helpful, because bruits may be absent in advanced mesenteric vascular disease, and may be heard in normals.

Laboratory studies: Routine laboratory studies are normal. Barium and endoscopic studies seldom show any characteristic changes. Ischemic gastric ulceration, as was seen in the case presented, has been reported (15), but is rare.

No study will positively establish the diagnosis of intestinal angina. Angiography should be done if intestinal angina is suspected and will support the diagnosis if at least 2 of the 3 mesenteric vessels are significantly obstructed. However, patients with advanced mesenteric vascular disease on angiography may be asymptomatic, as discussed. Therefore, other potential causes of abdominal pain, such as peptic ulcer disease, chronic pancreatitis, or inflammatory bowel disease, must also be considered.

Screening for intestinal angina with Doppler ultrasound

Doppler ultrasound studies are done by our vascular surgery department to screen patients suspected of having intestinal angina. Mesenteric vascular insufficiency is felt to be unlikely if a Doppler study is normal, that is, with normal velocities and no turbulent flow. Studies with turbulent flow are more difficult to interpret, and, when the clinical history warrants, are followed up with arteriography. There is a substantial experience in using Doppler to evaluate carotid and peripheral vessels, but little in using it for mesenteric vessels. There are a number of potential sources of error with this technique. First of all, velocities, and not flows, are measured. In stenotic vessels, turbulent flow may cause increased velocities without an increase in flow. Flow can be calculated, but the diameter of the SMA, which is about 6 mm, is difficult to measure accurately, and small changes in this measurement or in the angle of the Doppler beam may introduce large errors into flow measurements. The ideal physiological study would be measurement of flow before and after a test meal. In a patient with intestinal angina we would expect a fixed mesenteric flow, which would not increase after the meal. Doppler ultrasound has been used to follow patients after surgical revascularization (16)

Treatment

Surgical revascularization: The standard treatment for intestinal angina is mesenteric revascularization. Antegrade autologous vein or Dacron grafts or transaortic endarterectomy are the most commonly used techniques. Good symptom relief has been reported in more than 90% of patients, with postoperative mortality rates of 3- 17% (17-20).

Revascularization of multiple vessels reduces the rate of recurrent intestinal angina compared to single vessel reconstruction (19).

Angioplasty: Many patients with intestinal angina have high operative risk. Percutaneous transluminal angioplasty is well established as treatment for coronary and renal artery stenosis, and has been applied to patients with intestinal angina as an alternative to surgery. (21-25). In the largest series, 8 of 9 patients with arteriosclerotic lesions had at least temporary relief of symptoms. Symptoms recurred in 5 patients, 3 of whom responded to repeat angioplasty (25). PTA of celiac and SMA stenosis may be a reasonable alternative to surgery in selected patients.

Review of case presentation: A history of pain after meals with weight loss in a patient with extensive vascular disease should have lead to a strong suspicion of intestinal angina. We were mislead by finding an alternative explanation for the abdominal pain, that is, gastric ulcers. In this case the gastric ulcers were ischemic, not peptic. Had our level of suspicion been higher, a screening Doppler ultrasound study would have been requested, and followed by an arteriogram.

ACUTE MESENTERIC ISCHEMIA

Definition

In a strict sense, all mesenteric ischemia is acute. However, intestinal angina is considered a separate syndrome in the medical literature, and the term acute mesenteric ischemia is used to refer to ischemia in the distribution of the SMA, usually leading to bowel injury. Acute ischemia in the distribution of the celiac artery is rare, probably because of the many collateral connections in that system. Acute ischemia in the distribution of the IMA leads to ischemic colitis, which, like intestinal angina, is considered a distinct clinical syndrome. Ischemic colitis, as well as mesenteric venous thrombosis, will be considered separately.

Prevalence

Acute mesenteric ischemia is unusual, but more common than intestinal angina. A medical records search disclosed 7 cases at PMH and DVAMC during 1990. This is probably an underestimate, because in many series about 50% of the cases are found at autopsy.

Physiology

Ischemia in the distribution of the superior mesenteric artery may be occlusive or non-occlusive. Occlusive ischemia may be due to thrombus or embolus. Non-occlusive ischemia occurs in low flow states, such as cardiogenic shock. In non-occlusive ischemia the SMA may be completely patent, or partially occluded by previous arteriosclerotic disease. Both occlusive and non-occlusive ischemia are often complicated by arterial spasm.

In recent series superior mesenteric embolus was the most common cause of acute mesenteric ischemia, followed by thrombus and non-occlusive ischemia(26).

Acute Mesenteric Ischemia (N=81)

Cause	Frequency (%)
Embolus	41
Thrombus	19
Non-occlusive	19
Venous thrombosis	11
Arteritis	2
Not determined	8

(Clavien, Br. J. Surg., 1987)

Clinical presentation

History: The pain of acute mesenteric ischemia may occur suddenly in embolus, or more gradually in non-occlusive ischemia. It is poorly localized until frank bowel infarction occurs. The initial response of the bowel to ischemia is hyperperistalsis, so the pain is often cramping. Pain may be mild at first, but becomes severe. PAIN OUT OF PROPORTION TO PHYSICAL FINDINGS IN A PATIENT AT RISK IS A HALLMARK OF ACUTE MESENTERIC ISCHEMIA. About one third of patients with acute mesenteric thrombosis will report a history of intestinal angina during the preceding weeks or months. Patients with mesenteric embolus may have a history of previous emboli to other organs.

Nausea and vomiting occur in about 50% of cases. Diarrhea is not uncommon. Gastrointestinal bleeding occurs with mucosal infarction.

Examination: Physical findings in early acute mesenteric ischemia are mild and non-specific. They include abdominal distention, mild diffuse tenderness, and hyperactive bowel sounds. Fever, tachycardia, and hypotension, localized tenderness with rebound, and hypoactive bowel sounds occur late, and are signs of bowel infarction.

Laboratory studies: There are no specific laboratory markers which distinguish intestinal ischemia from other causes of abdominal pain.

The WBC count is elevated in about 75% of patients, and lactic acidosis may be present initially in 50%. Elevations of inorganic phosphorus and distinctive patterns of CPK and LDH isoenzymes have been described, but have not gained wide acceptance (27,28).

X-rays: Plain x-rays should be done not to make a positive diagnosis of bowel infarction, but to exclude some other cause.

Abdominal x-rays are usually either normal or show generalized dilatation of small and large bowel loops. Edema and hemorrhage of the bowel wall may cause "thumbprinting", and separation of bowel loops. After bowel infarction, air may be seen free in the peritoneum, in the wall of the bowel, or in the portal venous system.

Serendipity - Clues to acute mesenteric ischemia

It should be apparent that in most cases of mesenteric ischemia the history, examination, and laboratory studies are not diagnostic. The differential will include a number of other conditions, such as peptic ulcer, pancreatitis, cholecystitis, and diverticulitis. In the course of evaluation for one of these conditions, other studies may lead to clues to the diagnosis of acute mesenteric ischemia.

Sonography and CT scanning: Both sonography and CT may show edema of segments of bowel and a small amount of ascites. This combination should raise the suspicion of ischemic bowel. In addition, CT is sensitive for the detection of gas in the bowel wall or portal venous system (29-31)

Endoscopy and laparoscopy: Mesenteric ischemia has been diagnosed by endoscopy and laparoscopy (32,33). At endoscopy, ischemic bowel may show edema, diffuse superficial ulceration, and submucosal hemorrhage.

Clinical suspicion

THE KEY TO THE EARLY DIAGNOSIS OF ACUTE MESENTERIC ISCHEMIA IS CLINICAL SUSPICION. Acute mesenteric ischemia should be considered in patients over the age of 50 with the acute onset of abdominal pain lasting morethan 2- 3 hours, particularly if the pain is out of proportion to physical and laboratory findings, and if the patient has risk factors for mesenteric ischemia. These include:

Risk Factors for
Acute Mesenteric Ischemia

Arteriosclerotic or valvular heart disease
Cardiac arrhythmias
Recent myocardial infarction
Decompensated congestive heart failure
Treatment with digitalis, vasopressors
Previous embolic disease
Burns, bleeding, sepsis, dialysis

Unfortunately, the diagnosis of mesenteric ischemia is often unsuspected, and many cases are diagnosed at autopsy or at surgery. When the diagnosis is made at surgery, options are limited. Necrotic bowel can be resected. Mesenteric arteries can be palpated for pulses, and if an occlusion is suspected, a bypass graft can be constructed, but this can be difficult without the information which would be provided by an arteriogram.

Arteriography in the diagnosis and treatment of acute mesenteric ischemia

Surgical therapy alone results in mortality rates of 80% or more in acute mesenteric ischemia (34-36). Dissatisfied with these results, Scott Boley and his associates at Montefiore Hospital initiated an approach combining the aggressive use of arteriography with surgery. Physicians were encouraged to refer patients with suspected acute mesenteric ischemia for arteriography immediately after resuscitation. Of the fifty patients referred 35 were found to have either non-occlusive ischemia, an embolus, or thrombosis, and 15 had no abnormality on arteriogram. In patients with an non-occlusive ischemia or an embolus, papaverine, a vasodilator, was infused. Patients with persistent peritoneal signs were taken to surgery. Nineteen of 35 (54%) patients survived. Of the 19 survivors, 17 had resection of less than 3 feet of bowel (37). There was no control group in Boley's study, but others have reported similar results(38).

Arteriography contributes to the management of acute mesenteric ischemia in 2 ways. First, a specific diagnosis is usually possible. Treatments of embolus, thrombosis, and non-occlusive disease differ, and a normal angiogram can exclude mesenteric ischemia. Secondly, infusion of vasodilators can prevent or reverse the persistent arterial spasm which complicates mesenteric ischemia.

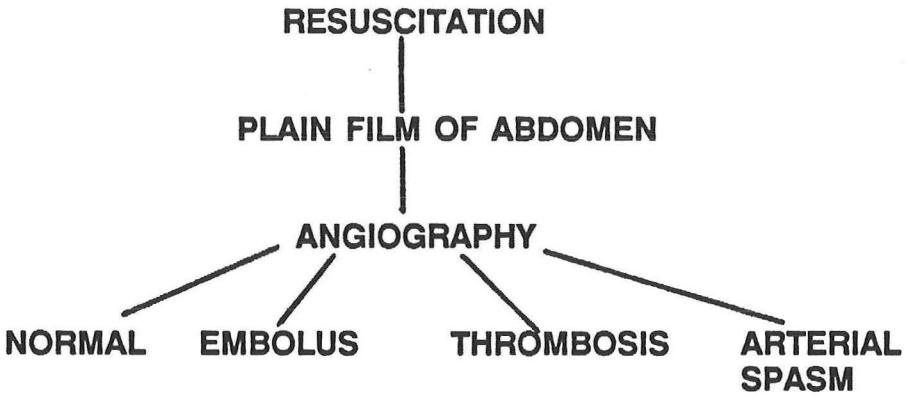
Approach to the patient with acute mesenteric ischemia.

Resuscitation: Resuscitation of patients with acute mesenteric ischemia should include intravenous fluids, antibiotics, nasogastric suction, and, as far as possible, correction of any precipitating conditions, such as heart failure or hypotension. However, digitalis and vasopressors, which produce splanchnic vasoconstriction, should be used cautiously or withdrawn if possible. Correction of hypotension before arteriography is important, since hypotensive patients will show changes on arteriography indistinguishable from non-occlusive ischemia.

Plain film of the abdomen: A plain film of the abdomen is done, as mentioned, not to make a diagnosis of mesenteric ischemia, but to rule out other obvious causes.

Arteriography: A flush aortogram is done in the lateral position to evaluate the origins of the celiac and SMA. If these are not occluded at their origins, selective injections are done. The arteriogram will either be normal, or show embolus, thrombosis, or arterial spasm. If vasoconstriction is seen, an bolus of tolazoline, 25 mg., a rapidly acting vasodilator, is given and the arteriogram repeated. Papaverine a longer acting vasodilator, is given as an infusion at 60 mg./min. if

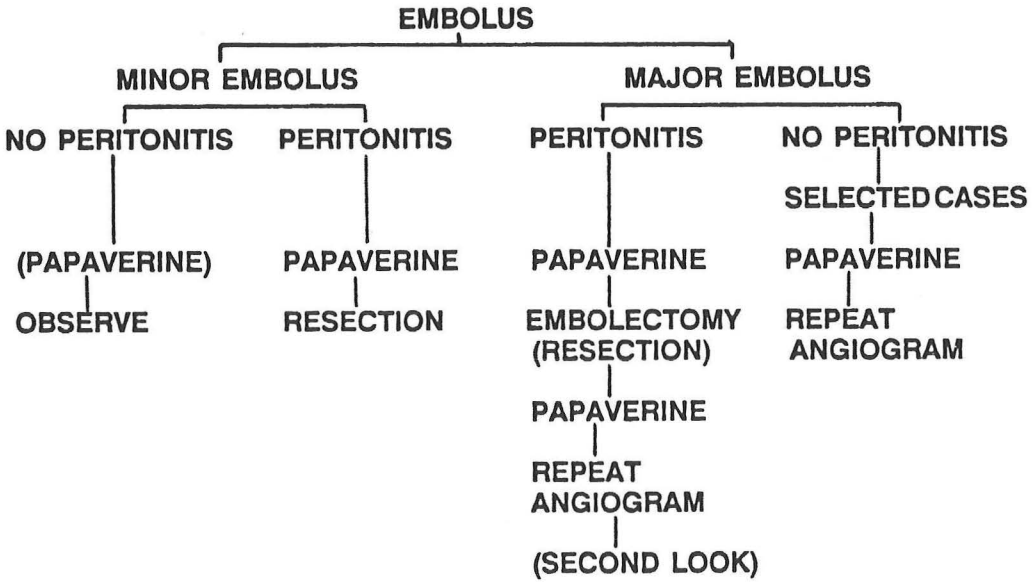
thrombosis or arterial spasm is found. The infusion is continued during and after surgery.



Approach to the Patient with Acute Mesenteric Ischemia

Treatment of specific syndromes

Embolus: Patients with persistent peritoneal signs after arteriography and papaverine infusion are likely to have bowel infarction and should be taken to surgery. Embolectomy is done, and frankly ischemic bowel is resected. The papaverine infusion is continued after surgery, and anticoagulation is started within 48 hours. In the minority of patients without initial peritoneal signs or whose peritoneal signs improve with papaverine, particularly those with a distal embolus, surgery can be deferred. The papaverine infusion is continued, and the arteriogram is repeated the next day.



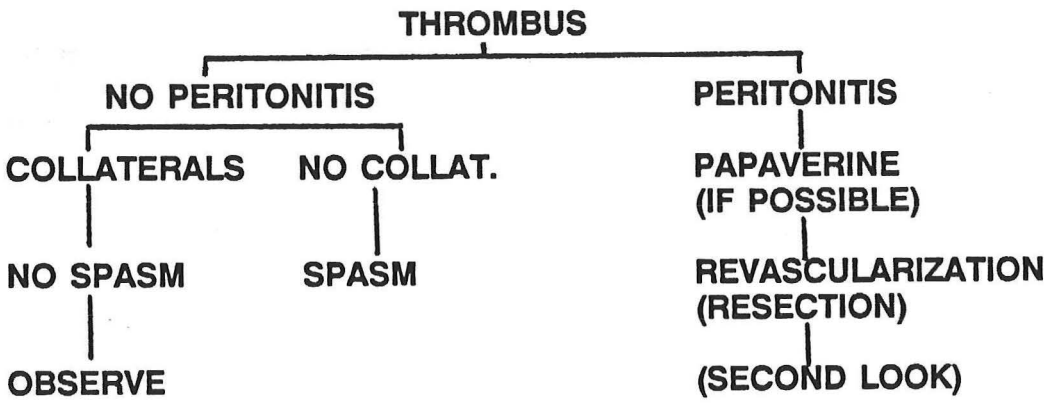
Streptokinase infusion -

Streptokinase infusion has been used for the treatment of acute SMA embolus. Several days of treatment were necessary for clot lysis. Streptokinase may be an alternative to papaverine infusion and embolectomy, but clot lysis may occur slowly (39,40).

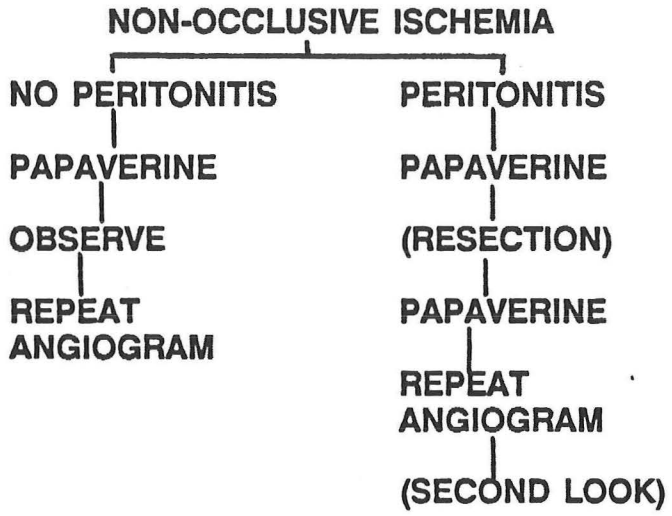
Thrombosis: When thrombosis is found at arteriography, the collateral circulation should be assessed. If there is good collateral flow, and no vasoconstriction, the patient can be followed. When no collateral flow is found, the patient should be taken to surgery. Papaverine infusion is started if possible, but often the SMA is completely occluded at its origin. At surgery, revascularization is done and the viability of the bowel is assessed. Frankly infarcted bowel is resected. If papaverine was started before surgery, it is continued during and after surgery. Anticoagulation is started within 48 hours.

Angioplasty-

Angioplasty has been used in a patient with acute mesenteric ischemia who had signs of peritoneal irritation. After dilatation of a high grade SMA stenosis, the patient recovered, and required no further treatment (41).



Non-occlusive ischemia: The primary treatment of non-occlusive mesenteric ischemia is correction of the precipitating condition. Arteriography plays an important part in establishing the diagnosis and in treatment. Patients without peritoneal signs treated with papaverine infusion may not require need surgery. Patients in whom peritoneal signs progress should be taken to surgery for resection of infarcted bowel. The prognosis of non-occlusive ischemia is very poor, with fatality rates of close to 100% in some series, but, using arteriography, one author reported survival of 5 of 11 patients (38).



Surgical considerations

Vascular reconstruction -

At surgery, vascular reconstruction is done if the bowel appears ischemic but not frankly necrotic, or if the area of necrosis is limited. Both bypass and endarterectomy have been used for revascularization. An antegrade bypass, from the proximal aorta to an artery distal to the obstruction, using either a saphenous vein or Dacron graft is preferable. As many mesenteric arteries as possible are bypassed, since the rate of recurrent stenosis after multiple bypasses is lower than with a single bypass. Endarterectomy is an alternative procedure, but is not used as often as bypass.

Assessment of bowel viability at surgery -

Assessment of bowel viability is important when the segment of ischemic bowel is long. Resection of a few feet more of bowel can make the difference between a patient who is a short bowel cripple, and a patient who can live a relatively normal life. Bowel viability is assessed after revascularization, when that is done. Clinical assessment includes observation of color, motility, arterial pulsations, and capillary bleeding, but generally results in a tendency to resect more bowel than necessary. Doppler ultrasound and fluorescein dye injection can also be used to assess bowel viability. A Doppler ultrasound probe can assess flow in the small vessels of short segments of intestine. This is useful in checking the margins of resection, and can be done repeatedly. Fluorescein dye is injected intravenously. When an Woods light is used, areas of ischemic or necrotic bowel will show abnormal fluorescence. Fluorescein may be used to check large areas of bowel, but can be used only once. Doppler ultrasound and fluorescein injection are complementary, and may both be used in the same case (42,43).

"Second look"-

Sometimes the viability of a section of bowel is in doubt even after Doppler and fluorescein have been used. Under these circumstances a "second look operation" may be planned after 12 to 36 hours. In the interval, papaverine infusion is continued, and other attempts are made to improve the patient's general condition. Sometimes primary reanastomosis is avoided. The loop of bowel is brought out as an ostomy, so it may be observed.

ISCHEMIC COLITIS

Case presentation: A 75 year old woman presented with 1 day of cramping lower abdominal pain, and passed about 1 cup of bright red blood. There was a history of irritable bowel syndrome. A colonoscopy had been normal several years before. She had hypertension, but was otherwise in good health. On examination her vital signs were normal. She had left lower quadrant tenderness, but no rebound. Her laboratory studies, including WBC count and hematocrit, were normal. A colonoscopy done the day after admission showed edema and submucosal hemorrhage in the area of the splenic flexure. She recovered without further therapy, and had no recurrences.

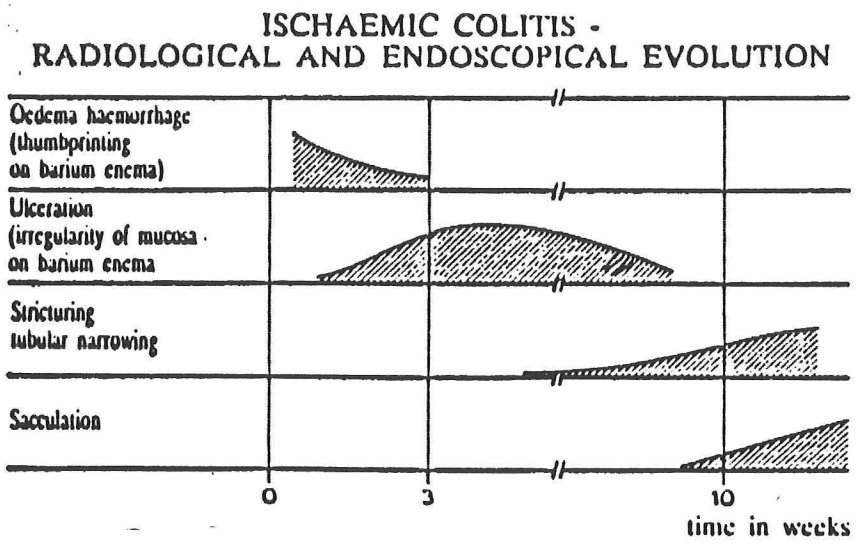
Prevalence

Ischemic colitis may be the most common form of intestinal ischemia. A medical records search at PMH and DVAMC showed 7 cases. However, some cases of ischemic colitis are mild, and do not require hospitalization.

Pathophysiology

The pathophysiology of ischemic colitis is similar to that of acute mesenteric ischemia. Arteriosclerotic disease and low flow states also cause ischemic colitis. Embolus is a less common cause. Ischemic colitis is also associated with obstructing colon cancer, and abdominal aortic aneurysm (AAA) repair (39,44). In many cases, however, the cause of an episode of ischemic colitis is not established.

A characteristic pattern of injury occurs in ischemic colitis. Mucosal edema and hemorrhage occur first, and often resolve within 10 days, although they occasionally persist up to several months. As edema and hemorrhage resolve, most patients develop mucosal ulcerations. In the majority of patients the mucosa heals after several weeks, leaving minimal or no scarring. In a minority the ischemic injury is more severe. Acute transmural infarction may occur. If the injury is not transmural, but involves the muscular layers, scarring with stricture formation may result. In a few patients the mucosal injury does not resolve, leading to persistent colitis.



Reeders, Acta Endoscopica, 1985

In his experience with 250 cases of ischemic colitis, one author noted that 51% had transient mucosal damage, 12% developed a stricture, 21% developed persistent colitis, and 18% presented with transmural infarction or perforation (45).

Ischemic colitis may involve any area of the colon, but the splenic flexure and the sigmoid colon are most often affected, because the blood supply is most tenuous there. The rectum is rarely involved because of good collateral flow, except in patients with disease of the internal iliacs (46).

Clinical presentation

Ischemic colitis is considered a distinct clinical syndrome largely because it does not usually have the disastrous consequences of acute mesenteric ischemia.

History: The typical case of ischemic colitis begins with the sudden onset of mild to moderate cramping lower abdominal pain. This is followed by several loose stools, with a moderate amount of blood. Patient are usually over 50 years old, and often have generalized arteriosclerosis. There is usually no identifiable precipitating event.

Examination: Mild to moderate localized tenderness is often present. Fever, hypotension, and peritonitis occur with transmural infarction. Blood will be found on rectal examination, but proctoscopy is usually normal.

Laboratory: Laboratory studies are usually normal.

X-ray: Plain abdominal x-rays may show nonspecific bowel dilatation. Occasionally edema of the wall of the colon, or "thumbprinting", may be seen.

Barium enema and colonoscopy in ischemic colitis

The characteristic evolution of ischemic colitis may be seen by barium enema or colonoscopy.

With barium enema, "thumbprinting" is the earliest change, and corresponds to edema and submucosal hemorrhage. As thumbprinting resolves, ulceration is seen in 40-50% of cases. After several weeks, the barium enema may be normal, or show scarring in the form of stricture or eccentric sacculation(47,48).

With colonoscopy the earliest changes are areas of red, edematous, friable mucosa alternating with areas of blanching. Large dark blebs, representing submucosal hemorrhage, are typical. Ulceration is appreciated more often with colonoscopy than with barium enema. In one series, 70% of patients had ulceration after 2 weeks. The ulcers may be large and irregular. Healing may leave normal mucosa, fine granularity, or strictures. Colonoscopy is more sensitive than barium enema for the diagnosis of ischemic colitis. In patients who do not have clinical signs of gangrene or perforation, colonoscopy with no prep, or after a minimal prep, is well tolerated and may be the best way to make the diagnosis(49,50). Arteriography is rarely indicated.

Differential diagnosis: The differential diagnosis of ischemic colitis includes acute infectious colitis (including pseudomembranous colitis), diverticulitis, colon cancer, and inflammatory bowel disease (51,52).

Infectious colitis usually involves the rectum, and stool cultures or assays for clostridia toxin will be positive. Diverticulitis is rarely associated with bleeding. Ischemic colitis has been associated with obstructing colon cancers, so the two may coexist.

Distinguishing ischemic colitis from inflammatory bowel disease (IBD) may be difficult. Mucosal inflammation, ulceration, pseudopolyps, pseudomembranes, and toxic megacolon are seen in ischemic colitis, as well as IBD. Biopsies in ischemic colitis may show inflammation and crypt abscesses. In one study, one half of patients older than 50 originally thought to have Crohns disease, ulcerative colitis, or non-specific colitis were reclassified as having ischemic colitis, making it the most common cause of colitis in that age group (53).

Abdominal aortic aneurysm repair and ischemic colitis

Ischemic colitis is common following repair of AAA. In a prospective series, 19/71 patients developed ischemic colitis after AAA surgery. Most presented with diarrhea in the postoperative period. Some had only signs of sepsis. Diagnosis

was made by fiberoptic sigmoidoscopy. Eleven of the 19 died (44). Preoperative angiography for elective AAA repair should include assessment of the mesenteric vessels. If the IMA is occluded, it may be sacrificed, but if it is not, the SMA and marginal artery must be checked. If collateral flow is poor, the IMA must be reimplanted.

Treatment and prognosis: Most patients require no specific therapy. Most strictures, when they develop, are not symptomatic. Patients with acute peritonitis and those with non-healing ulceration require surgery.

Review of case presentation: This patient illustrated the most typical clinical presentation of ischemic colitis: transient colitis without complications. Follow-up colonoscopy or barium enema would be advisable to document the resolution of the ischemic changes and to exclude the formation of a stricture.

MESENTERIC VENOUS THROMBOSIS

Case report: A 39 year old man was admitted with abdominal pain, nausea, and hematochezia. Two weeks before admission he had watery diarrhea associated with rectal bleeding, diffuse abdominal pain, vomiting, and subjective fever.
He had diabetes controlled with diet. One year before admission he suffered a nail wound to his left foot, which did not heal, and required amputation. At that time, a preoperative angiogram showed severe peripheral vascular disease.
On examination he was afebrile. Pulse was 120 and blood pressure 170/100. His abdomen was distended, but not tender. Bowel sounds were normal. He had black Hemoccult positive stool. Proctoscopy was normal. Nasogastric aspirate revealed 800 cc. of coffee-ground material.

Initial WBC count was 38000. Hematocrit was 51, BUN 30, glucose 350, AST 67, LDH 328, and CPK 1500. Amylase was normal. Distended loops of small bowel were seen on KUB.

He was treated with nasogastric suction, intravenous fluids, and antibiotics. His pain improved by the next day, but during the next several days, he complained of recurrent intermittent abdominal pain. Abdominal distention persisted, but bowel sounds were normal. He developed no tenderness.

EGD showed mild esophagitis. Colonoscopy was normal. Abdominal CT showed a moderate amount of ascites, edematous, dilated small bowel, and thickened mesentery.

Ascitic fluid had a RBC count of 50000, and WBC count of 4300, of which 97% were PMNs. Ascitic fluid albumin was 1.8, and amylase was 10.

When an attempt was made to discontinue his nasogastric suction, his abdominal pain worsened, and he developed a low grade fever. Surgery was scheduled, but

he died suddenly.

At autopsy he was found to have thrombosis of the SMV and its tributaries, with segmental infarction of the ileum. There was also thrombosis of the femoral and external iliac veins. The immediate cause of death was a pulmonary embolus.

Prevalence: Mesenteric venous thrombosis (MVT) with intestinal infarction is rare. At Montefiore Hospital, approximately 1 case per year is seen (54). In a series of 98 cases of intestinal infarction, only 15% were due to MVT (55). In addition, MVT does not always lead to intestinal ischemia. In an autopsy study from the Mayo clinic only 50% of patients with MVT had intestinal infarction (56). In 2 reports in which MVT was diagnosed by CT scan, intestinal ischemia was present in only 1 of 15 cases (57,58).

Pathophysiology: The mesenteric venous system has extensive collaterals in both the bowel wall and mesenteric arcades. Bowel infarction does not occur unless the arcades and vasa recta are clotted. Occlusion of the portal vein, superior mesenteric vein, or the larger tributaries often does not compromise the bowel. However, a small area of thrombus in the bowel wall and arcades can cause intestinal ischemia without involvement of the central veins. Clot may begin in the central veins and propagate toward the bowel, or begin at the bowel and propagate centrally.

Mesenteric venous thrombosis causes congestion, edema, and mucosal hemorrhage. Like other forms of mesenteric vascular disease, it can be complicated by arterial spasm.

Predisposing conditions

Conditions which predispose to MVT include:

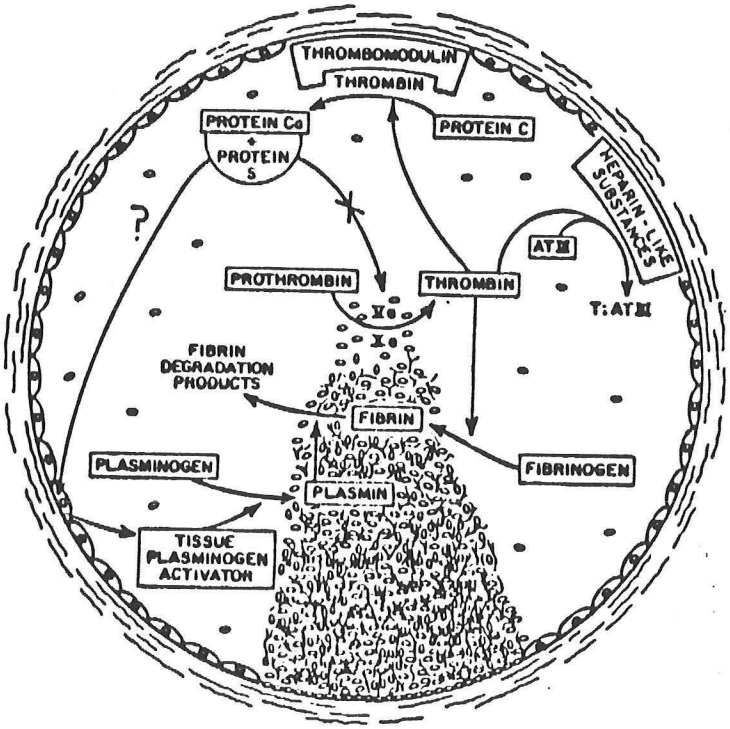
- Abdominal infections
- Inflammatory bowel disease
- Surgery, particularly splenectomy
- Abdominal malignancy
- Portal hypertension
- Sclerotherapy esoph. varices
- Hypercoagulable states

Abdominal malignancies, particularly tumors of the pancreas and colon may compress or invade the venous system, or lead to a hypercoagulable state. Mesenteric venous thrombosis has been reported as a complication of sclerotherapy for esophageal varices. Studies have shown that sclerosant may flow retrograde into the portal vein, initiating clotting there (59-62). In one fatal case, the entire portal, splenic, and mesenteric venous system was found to be thrombosed(59). Vasopressin, which slows splanchnic blood flow, may contribute.

Hypercoagulable states: A number of cases of MVT occur in hypercoagulable states. In addition to its association with tumors, MVT has been associated with sickle cell disease, thrombocytosis, polycythemia vera, pregnancy, and the use of birth control pills (63).

In older series, 15-30% of cases of MVT were associated with recurrent deep venous thrombosis (DVT) of unknown cause (63). Since the 1980s we have been able to define several of the primary hypercoagulable states.

In normal circumstances several anticoagulant mechanisms operate to prevent clot formation. These include antithrombin III, protein C, and protein S. Antithrombin III inactivates thrombin, especially in the presence of heparin. Protein C and protein S degrade activated factor V and VIII after exposure to thrombin and a cofactor on vascular intimal surfaces (64).



Formation of the hemostatic plug at the site of vascular injury. Three major physiologic anticoagulant mechanisms—antithrombin III (*AT III*) protein C, and the fibrinolytic system—are activated to limit clot formation to the site of damage and to prevent generalized thrombosis. T = thrombin.

(Schafer, Ann Int Med, 1985)

The primary hypercoagulable disorders are listed in the table below.

Primary Hypercoagulable States

Antithrombin III deficiency
Protein C deficiency
Protein S deficiency
Hypoplasminogenemia
Abnormal plasminogen
Plasminogen activator deficiency
Dysfibrinogenemia
Factor XII deficiency
Lupus anticoagulant

MVT has been reported with deficiency of AT III, protein C, and protein S, so MVT should be considered in patients with abdominal pain and a history of previous DVT (65-68).

Clinical presentation

History: Symptoms of MVT are non-specific. The pain of MVT usually begins insidiously, with gradual worsening over a period of days or even weeks. In one series of 20 patients, 12 had symptoms for more than 5 days, and 6 had pain for more than one month before seeking medical care (69). As in other forms of intestinal ischemia, the pain is often out of proportion to the physical findings. In contrast with intestinal angina, fear of eating is uncommon. Nausea and vomiting occur in about one half of patients, and changes in bowel habits or gastrointestinal bleeding are less common.

Physical examination: Physical examination is also nonspecific. Abdominal tenderness and distention are common. Bowel sounds are usually hypoactive. Guarding, rebound tenderness, and low grade fever are present in about half the patients.

Laboratory: WBC count is often elevated, but there are no other consistent laboratory abnormalities.

X-ray: As in other forms of intestinal ischemia, plain abdominal x-rays usually show only dilatation, but may show edema and thumbprinting, which may also be seen on barium studies (70).

Arteriography: If arteriography is done, intense and prolonged opacification of the capillary phase is seen, with poor or no venous return. As discussed, arterial spasm is common.

Sonography and CT: Sonography may demonstrate edema of intestinal loops, and a small amount of ascites, which when tapped will be bloody. Abdominal gas may

make evaluation of mesenteric veins difficult (71).

CT scan may be the best single diagnostic study for making the diagnosis of MVT. Contrast enhanced CT scanning will disclose not only bowel edema and ascites, but clot can be visualized in the superior mesenteric vein (57,58,71,72).

The diagnosis of MVT is difficult because of its insidious and non-specific presentation. The key to the diagnosis, is a high level of suspicion in patients with abdominal pain and a condition predisposing to MVT. As in acute mesenteric ischemia, most cases are diagnosed at laparotomy or in the course of investigating some other possibility.

Treatment:

Many patients will have surgery for diagnosis or because they have peritonitis. If a short segment of necrotic bowel is found, it is resected with generous margins, and anticoagulation is started promptly. When a long segment is found, frankly necrotic bowel is resected, but marginal bowel is not. Thrombectomy may be attempted. Anticoagulation and intraarterial papaverine are started, and a second look surgery is planned (54).

When the diagnosis is made before the development of peritonitis, it may be possible to start anticoagulation and follow the patient closely. A number of cases have been managed successfully with anticoagulation alone (57,71,72).

Prognosis

The prognosis of MVT is considerably better than that of arterial thrombosis. Smaller segments of bowel are usually involved. With heparinization, survival rates are approximately 80%, although they depend on age and associated conditions.

Review of case presentation: The clinical presentation and CT findings were suggestive, but were not appreciated at the time. Edematous bowel loops with a small amount of bloody ascites made mesenteric ischemia likely. Anticoagulation early in the course might have prevented the progression to bowel infarction and the pulmonary embolism. This patient may have had a primary hypercoagulable condition, since he was found to have both mesenteric and systemic venous thrombosis.

MESENTERIC ARTERITIS

Various forms of arteritis may involve the gastrointestinal tract. These include polyarteritis nodosa, SLE, and rheumatoid arthritis.

Arteritis causes ischemia of short segments of bowel, rather than generalized ischemia. Systemic symptoms usually are related to the arteritis.

There are several patterns of clinical presentation in mesenteric arteritis. Mucosal ulceration may cause acute bleeding. Stricture may form, causing symptoms of small bowel obstruction. The combination of mucosal disease and partial obstruction may be difficult to distinguish from Crohns disease.

A local area of transmural infarction, with perforation presents as the sudden onset of pain with localized peritoneal signs, like appendicitis, cholecystitis, or diverticulitis.

COCAINE AND INTESTINAL ISCHEMIA

Cocaine abuse causes myocardial ischemia and infarction (Lange, R.A., Cardiovascular Complications of Cocaine Use, Medical Grand Rounds, U.T. Southwestern Medical School, 1990). There have also been reports of intestinal ischemia associated with cocaine (73-76). In one report, a patient gave a history of recurrent right sided abdominal pain and diarrhea within 15 minutes of using cocaine. A more severe episode lead to hospitalization and surgery, at which time an ischemic right colon was resected. Other cases have involved the small bowel. In all the reports the patients were young, and none had stenosis of the major vessels. Cocaine causes mesenteric vasoconstriction. This may be the mechanism of intestinal ischemia, but members of our cardiology section have noted that cocaine may also cause fibrointimal injury, with hyper-reactivity and a proliferative response, in the coronary arteries. (Eichorn, E.,et al, unpublished data).

EXERCISE AND INTESTINAL ISCHEMIA

Many runners are familiar with "runners trots", or symptoms of abdominal cramping and diarrhea which may occur during exercise. Occult gastrointestinal blood loss is common in marathon runners (77). Occasionally, overt hematemesis or rectal bleeding occur. After his world record marathon in 1979, Derek Clayton related that he was "vomiting black mucus and had a lot of black diarrhea." A number of reports have documented ischemic colitis in runners (78-81). In one report, 34 year old Swiss woman was hospitalized with abdominal pain and bleeding after a 15 km. mountain race, and found to have hemorrhagic gastritis and extensive ischemic colitis. Using duplex scanning, the same authors found a 70% fall in mesenteric blood flow in another symptomatic runner (79). "Runners trots" are probably due to mild intestinal ischemia. Runners who become volume depleted, or have unfavorable mesenteric arterial anatomy, may develop more severe mesenteric ischemia and mucosal damage.

BIBLIOGRAPHY

1. Parks DA, Jacobson ED. Mesenteric Circulation. In: Johnson LR, Christensen J, Jackson MJ, Jacobson ED, Walsh JH, eds. Physiology of the Gastrointestinal Tract. New York: Raven Press, 1987:1649-1670.

2. Jodal M, Haglund U, Lundgren O. Countercurrent Exchange Mechanisms in the Small Intestine. In: Shepherd AP, Granger DN, eds. Physiology of the Intestinal Circulation. New York: Raven Press, 1984:83-97.

3. Perry MA, Ardell JL, Barrowman JA, Kvietys PR. Physiology of the Splanchnic Circulation. In: Kvietys PR, Barrowman JA, Granger DN, eds. Pathophysiology of the Splanchnic Circulation. Boca Raton, Florida: CRC Press, 1987:1-56.

4. Johnson PC. Myogenic and Venous-Arteriolar Responses in Intestinal Circulation. In: Shepherd AP, Granger DN, eds. Physiology of the Intestinal Circulation. New York: Raven Press, 1984:49-60.

5. Shepherd AP, Granger DN. Metabolic Regulation of the Intestinal Circulation. In: Shepherd AP, Granger DN, eds. Physiology of the Intestinal Circulation. New York: Raven Press, 1984:3-47.

6. Chou CC, Mangino MJ, Sawmiller DR. Gastrointestinal Hormones and Intestinal Blood Flow. In: Shepherd AP, Granger DN, eds. Physiology of the Intestinal Circulation. New York: Raven Press, 1984:121-130.

7. Greenway CV. Neural Control and Autoregulatory Escape. In: Shepherd AP, Granger DN, eds. Physiology of the Intestinal Circulation. New York: Raven Press, 1984:61-71.

8. Norryd C, Dencker H, Lunderquist A, Olin T, Tylen U. Superior mesenteric blood flow during digestion in man. Acta Chir Scand 1975; 141:197-202.

9. Moneta GL, Taylor DC, Helton S, Mulholland MW, Strandness DE. Duplex ultrasound measurement of postprandial intestinal blood flow: Effect of meal composition. Gastroenterology 1988; 95:1294-301.

10. Rowell LB, Johnson JM. Role of the Splanchnic Circulation in Reflex Control of the Cardiovascular System. In: Shepherd AP, Granger DN, eds. Physiology of the Intestinal Circulation. New York: Raven Press, 1984:153-163.

11. Parks D, Granger DN. Contributions of ischemia and reperfusion to mucosal lesion formation. Am J Physiol 1986; 250:G749-G753.

12. Boley SJ, Regan JA, Turnick PA. Persistent vasoconstriction - a major factor in nonocclusive mesenteric ischemia. Curr Top Surg Res 1971; 3:425-433.

13. Marston A. Chronic Intestinal Ischaemia. Acta Chir Scand Suppl 1990; 555:237-243.

14. Croft RJ, Menon GP, Marston A. Does intestinal angina exist? A critical study of obstructed visceral arteries. British Journal of Surgery 1981; 68:316-318.

15. Cherry RD, Jabbari M, Goresky C, Herba M, Reich D, Blundell PE. Chronic mesenteric vascular insufficiency with gastric ulceration. Gastroenterology 1986; 91:1548-1552.

16. Flinn WR, Rizzo RJ, Park JS, Sandager GP. Duplex scanning for assessment of mesenteric ischemia. Surgical Clinics of North America 1990; 70:99-107.

17. McCollum CH, Graham JM, DeBakey ME. Chronic mesenteric arterial insufficiency: results of revascularization in 33 cases. Southern Medical Journal 1976; 69:1266-1268.

18. Rapp JH, Reilly LM, Qvarfordt PG, Goldstone J. Durability of endarterectomy and antegrade grafts in the treatment of chronic visceral ischemia. Journal of Vascular Surgery 1986; 3:799-806.

19. Hollier LH, Bernatz PE, Pairolero PC, Payne WS, Osmundson PJ. Surgical management of chronic intestinal ischemia: a reappraisal. Surg 1981; 90:940-946.

20. Zelenock GB, Graham LM, Whitehouse WM, Erlandson EE. Splanchnic arteriosclerotic disease and intestinal angina. Arch Surg 1980; 115:497-501.

21. Uflacker R, Goldany MA, Constant S. Resolution of mesenteric angina with percutaneous transluminal angioplasty of a superior mesenteric artery stenosis using a balloon catheter. Gastrointest Radiol 1980; 5:367-369.

22. Castaneda-Zuniga WR, Gomes A, Weens C, Ketchum D, Amplatz K. Transluminal angioplasty in the management of mesenteric angina. ROFO 1982; 137:330-332.

23. Golden DA, Ring EJ, McLean GK, Freiman DB. Percutaneous transluminal angioplasty in the treatment of abdominal angina. Am J Roentgenol 1982; 139:247-249.

24. Roberts L, Wertman DA, Mills SR, Moore AV, Heaston DK. Transluminal angioplasty of the superior mesenteric artery: an alternative to surgical revascularization. Am J Roentgenol 1983; 141:1039-1042.

25. Odurny A, Sniderman KW, Colapinto RF. Intestinal angina: Percutaneous transluminal angioplasty of the celiac and superior mesenteric arteries. Radiology 1988; 167:59-62.

26. Clavien PA, Muller C, Harder F. Treatment of mesenteric Infarction. Br J Surg 1987; 74:500-503.

27. Thompson JS, Bragg LE, West WW. Serum enzyme levels during intestinal ischemia. Ann Surg 1990; 211:369-373.

28. Graeber GM, Clagett GP, Wolf RE, Cafferty PJ. Alterations in serum creatine kinase and lactate dehydrogenase. Association with abdominal aortic surgery, myocardial infarction, and bowel necrosis. Chest 1990; 97:519-520.

29. Smerud MJ, Johnson CD, Stephens DH. Diagnosis of bowel infarction: a comparison of plain films and CT scans in 23 cases. Am J Roentgenol 1990; 154:99-103.

30. Alpern MB, Glazer GM, Francis IR. Ischemic or infarcted bowel: CT findings. Radiology 1988; 166:149-152.

31. Balthazar EJ, Chako AC. Computerized tomography in acute gastrointestinal disorders. Am J Gastroenterol 1990; 85:1445-1452.

32. Jabbari M, Cherry R, Goresky CA. The endoscopic diagnosis of mesenteric venous thrombosis. Gastrointest Endosc 1985; 31:405-406.

33. Serreyn RF, Schoofs PR, Baetens PR, Vandekerckhove D. Laparoscopic diagnosis of mesenteric venous thrombosis. Endoscopy 1986; 18:249-250.

34. Ottinger LW. The surgical management of acute occlusion of the superior mesenteric artery. Ann Surg 1978; 188:721-731.

35. Wilson C, Gupta R, Gilmour DG, Imrie CW. Acute superior mesenteric ischaemia. Br J Surg 1987; 74:279-281.

36. Levy PJ, Krausz MM, Manny J. Acute mesenteric ischemia: improved results-a retrospective analysis of ninety-two patients. Surg 1990; 107:372-380.

37. Boley SJ, Sprayregen S, Siegelman SS, Veith FJ. Initial results from an aggressive roentgenological and surgical approach to acute mesenteric ischemia. Surg 1977; 82:848-855.

38. Clark RA, Gallant TE. Acute mesenteric ischemia: angiographic spectrum. Am J Roentgenol 1984; 142:555-562.

39. Hillers TK, Ginsberg JS, Panju A, Gately J, Gill G, Waterfall WE. Intra-arterial low-dose streptokinase infusion for superior mesenteric artery embolus. Can Med Assoc J 1990; 142:1087-1088.

40. Flickinger EG, Johnsrude IS, Ogburn NL, Weaver MD, Pories WJ. Local streptokinase infusion for superior mesenteric artery thromboembolism. Am J Roentgenol 1983; 140:771-772.

41. VanDeinse WH, Zawacki JK, Phillips D. Treatment of acute mesenteric ischemia by percutaneous transluminal angioplasty. Gastroenterology 1986; 91:475-478.

42. Carter MS, Fantini GA, Sammartana RJ, Mitsuda S, Silverman DG, Boley SJ. Qualitative and quantitative fluorescein fluorescence in determining intestinal viability. Am J Surg 1984; 147:117-122.

43. Bulkley GB, Zuidema GD, Hamilton SR, O'mara CO, Klacsmann PG, Horn SD. Intraoperative determination of small intestinal viability following ischemic injury. Ann Surg 1981; 193:628-637.

44. Maupin GE, Rimar SD, Villalba M. Ischemic colitis following abdominal aortic reconstruction for ruptured aneurysm. A 10-year experience. American Surgeon 1989; 55:378-380.

45. Boley SJ. Colonic ischemic - 25 years later. Am J Gastroenterol 1990; 85:931-934.

46. Nelson RL, Schuler JJ. Ischemic proctitis. Surg Gynecol Obstet 1982; 154:27-33.

47. Reeders JWAJ, Tytgat GNJ. Ischemic colitis: Serial changes in double-contrast barium enema examination. Radiology 1987; 162:583.

48. Lida M, Matsui T, Fuchigami T, Iwashita A, Yao T, Fujishima M. Ischemic colitis: Serial changes in double-contrast barium enema examination. Radiology 1986; 159:337-341.

49. Scowcroft CW, Sanowski RA, Kozarek RA. Colonoscopy in ischemic colitis. Gastro Endosc 1981; 27:156-161.

50. Reeders JWAJ, Tytgat GNJ, Rosenbusch G, Gratama S. Colonoscopy in diagnosis of ischaemic colitis: a survey of 39 patients. Acta Endoscopica 1985; 15:201-212.

51. Reeders JWAJ, Rosenbusch G, Tytgat GNJ. Ischaemic colitis associated with carcinoma of the colon. Europ J Radiol 1982; 2:41-47.

52. Eisenberg RL, Montgomery CK, Margulis AR. Colitis in the elderly: Ischemic colitis mimiking ulcerative and granulomatous colitis. Am J Roentgenol 1979; 133:1113-1118.

53. Brandt L, Boley S, Goldberg L, Mitsudo S, Berman A. Colitis in the elderly. A reappraisal. Am J Gastro 1981; 76:239-245.

54. Kaleya RN, Boley SJ. Mesenteric Venous Thrombosis. In: Najarian JF, Delaney J, eds. Progress in Gastrointestinal Sugery. Chicago: Year Book Medical Publishers, 1989:417-424.

55. Clavien PA, Durig M, Harder F. Venous mesenteric infarction: a particular entity. Br J Surg 1988; 75:252-255.

56. Johnson CC, Baggenstoss AH. Mesenteric vascular occlusion I. Study of 99 cases of occlusion of veins. Mayo Clinic Proceedings 1949; 24:628-636.

57. Rosen A, Korobkin M, Silverman PM, Dunnick NR, Kelvin FM. Mesenteric vein thrombosis: CT identification. Am J Roentgenol 1984; 143:83-86.

58. Vogelzang RL, Gore RM, Anschuetz SL, Blei AT. Thrombosis of the splanchnic veins: CT diagnosis. Am J Roentgenol 1988; 150:93-96.

59. Ashida H, Kotoura Y, Nishioka A, Takagi K, Yoshikawa H, Ishikawa Y, Utsunomiya J. Portal and mesenteric venous thrombosis as a complication of endoscopic sclerotherapy. Am J Gastroenterol 1989; 84:306-310.

60. Thatcher BS, Sivak MV, Ferguson DR, Petras RE. Mesenteric venous thrombosis as a possible complication of endoscopic sclerotherapy: a report of two cases. Am J Gastro 1986; 81:126-129.

61. Stoltenberg PH, Goodale RL, Silvis SE. Portal vein thrombosis following combined endoscopic variceal sclerosis and vasopressin therapy for bleeding varices. Am J Gastro 1987; 82:1297-1300.

62. Sukigara M, Omoto R, Miyamae T. Systemic dissemination of ethanolamine oleate after injection sclerotherapy for esophageal varices. Arch Surg 1985; 120:833-836.

63. Grendell JH, Ockner RK. Mesenteric venous thrombosis. Gastroenterology 1982; 82:358-372.

64. Schafer AI. The hypercoagulable states. Ann Int Med 1985; 102:814-828.

65. Pokorney BH, Eyster ME, Jeffries GH. Antithrombin III deficiency appearing as mesenteric vein thrombosis. Am J Gastroenterol 1981; 76:534-537.

66. Maung R, Kelly JK, Schneider MP, Poon MC. Mesenteric venous thrombosis due to antithrombin III deficiency. Arch Pathol Lab Med 1988; 112:37-39.

67. Broekmans AW, Rooyen W, Westerveld BD, Briet E, Bertina RM. Mesenteric vein thrombosis as presenting manifestation of hereditary protein S deficiency. Gastroenterology 1987; 92:240-242.

68. Harward TRS, Green D, Bergan JJ, Rizzo RJ, Yao JST. Mesenteric venous thrombosis. Journal of Vascular Surgery 1989; 9:328-333.

69. Matthews JE, White RR. Primary mesenteric venous occlusive disease. Am J Surg 1970; 122:579-583.

70. Clemett AR, Chang J. The radiologic diagnosis of spontaneous mesenteric venous thrombosis. Am J Gastro 1975; 63:209-215.

71. Matos C, Gansbeke DV, Zalcman M, Ansay J, Delcour C, Engelholm L, Struyven J. Mesenteric vein thrombosis: early CT and US diagnosis and conservative management. Gastrointest Radiol 1986; 11:322-325.

72. Clavien PA, Huber O, Mirescu D, Rohner A. Contrast enhanced CT scan as a diagnostic procedure in mesenteric ischaemia due to mesenteric venous thrombosis. Br J Surg 1989; 76:93-94.

73. Freudenberger R, Cappell M, Hutt D. Intestinal infarction after intravenous cocaine administration. Ann Int Med 1990; 113:715-716.

74. Nalbandian H, Sheth N, Dietrich R, Georgiou J. Intestinal ischemia caused by cocaine ingestion: report of two cases. Surg 1985; 97:374-376.

75. Garfia A, Valverde JL, Borondo JC, Candenas I, Lucena J. Vascular lesions in intestinal ischemia induced by cocaine-alcohol abuse: report of a fatal case due to overdose. Journal of Forensic Sciences 1990; 35:740-745.

76. Fishel R, Hamamoto G, Barbul A, Jiji V, Efron G. Cocaine colitis. Dis Colon Rectum 1985; 28:264-266.

77. Baska RS, Moses FM, Graeber G, Kearney G. Gastrointestinal bleeding during an ultramarathon. Dig Dis Sci 1990; 35:276-279.

78. Cooper BT, Douglas SA, Firth LA, Hannagan JA, Chadwick VS. Erosive gastritis and gastrointestinal bleeding in a female runner. Gastroenterology 1987; 92:2019-2023.

79. Heer M, Repond F, Hany A, Sulser H, Kehl O, Jager K. Acute ischaemic colitis in a female long distance runner. Gut 1987; 28:896-899.

80. Moses FM, Brewer TG, Peura D. Running-associated proximal hemorrhagic colitis. Ann Int Med 1991; 108:385-386.

81. Schwartz AE, Vanagunas A, Kamel PL. Endoscopy to evaluate gastrointestinal bleeding in marathon runners. Ann Int Med 1990; 113:632-633.

General Reviews

1. Reinus JF, Brandt LJ, Boley SJ. Ischemic diseases of the bowel. Gastroenterology Clinics of North America 1990; 19:319-343.

2. Williams LF. Mesenteric ischemia. Surgical Clinics of North America 1988; 68:331-380.

3. Westergaard H. Intestinal ischemia. Medical Grand Rounds, University of Texas Southwestern Medical School, 1983.