

Intestinal Ischemia

Chronic Mesenteric Ischemia

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Board Question:

An 80 year old woman with CAD complains to PCC that she has had abdominal pain for the past 4-6 months. Typically, it occurs 30 minutes postprandially and usually resolves in 1-3 hours. The severity of the pain has increased, and she is losing weight. Exam reveals a cachectic woman, but no abnormality is found on abdominal exam. The additional symptom that would be most suggestive of chronic mesenteric ischemia is:

- a. Intermittent nausea and vomiting
- b. Bloating
- c. Fear of eating resulting in weight loss
- d. Diarrhea

Intestinal Ischemia

■ Objectives:

- Review vascular anatomy of GI tract
- Pathophysiology of intestinal ischemia
- Review types of intestinal ischemia
- Diagnosis of intestinal ischemia
- Management of intestinal ischemia
- Board-style questions



Who cares?



■ MORTALITY

- Acute Mesenteric Ischemia
 - Early diagnosis and intervention: 10%
 - Infarction: 60%-93%
- Colon Ischemia: 50%
- Mesenteric Venous Thrombosis: 20-50%
- "Occlusion of the mesenteric vessels is apt to be regarded as one of those conditions of which the diagnosis is impossible, the prognosis hopeless, and the treatment almost useless" (Cokkinis, 1926).

Intestinal Ischemia

- Spectrum of disorders
 - Acute vs. Chronic
 - Arterial vs. Venous disturbance
 - Small Intestine vs. Large Intestine vs. Both
- Acute is more common than Chronic
- Arterial disease is more common than Venous

Types and Approximate Frequencies of Intestinal Ischemia

Type	Frequency, %
Colon ischemia	70-75
Acute mesenteric ischemia	20-25
Focal segmental ischemia	5
Chronic mesenteric ischemia	5
Mesenteric venous thrombosis	Included in above ^[*]

* Mesenteric venous thrombosis may manifest as colon ischemia, acute mesenteric ischemia, or as focal segmental ischemia. The frequency of mesenteric venous thrombosis is rising as computed tomography is performed more commonly.

Celiac Axis

- 3 major branches: left gastric, common hepatic, and splenic arteries
- Provides arterial blood supply to:
 - STOMACH
 - DUODENUM
 - PANCREAS
 - LIVER

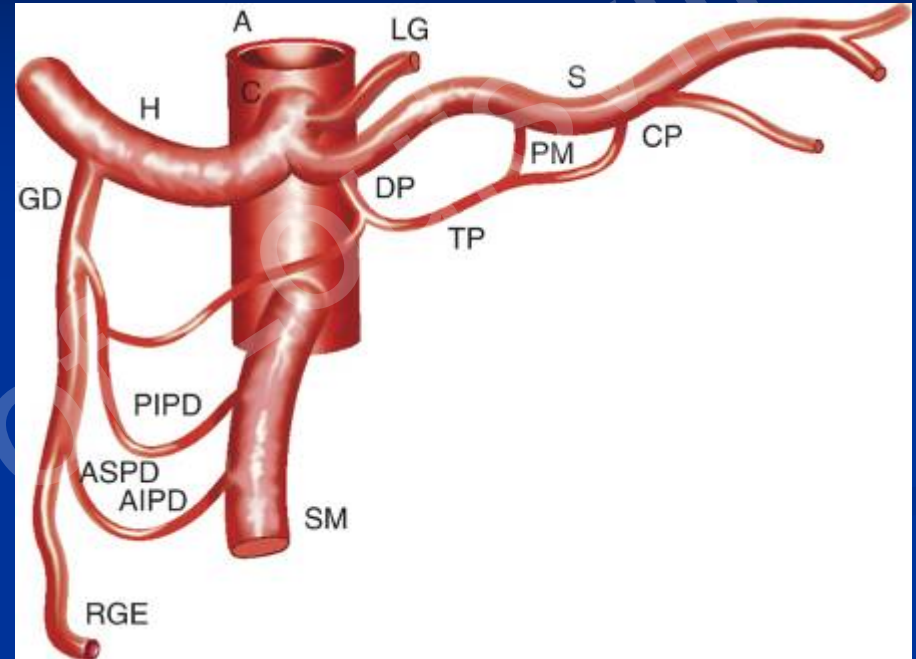


Figure 111-1 Diagram of typical celiac axis anatomy. A, aorta; AIPD, anterior inferior pancreaticoduodenal artery; ASPD, anterior superior pancreaticoduodenal artery; C, celiac axis; CP, caudal pancreatic artery; DP, dorsal pancreatic artery; GD, gastroduodenal artery; H, common hepatic artery; LG, left gastric artery; PIPD, posterior inferior pancreaticoduodenal artery; PM, pancreata magna; RGE, right gastroepiploic artery; S, splenic artery; SM, superior mesenteric artery; TP, transverse pancreatic artery. (From Nebesar RA, Kornblith PL, Pollard JJ, Michels NA: *Celiac and Superior Mesenteric Arteries: A Correlation of Angiograms and Dissections*. Boston, Little, Brown, 1969.)

Superior Mesenteric Artery

- 4 major branches: inferior pancreaticoduodenal, middle colic, right colic, and ileocolic arteries
- Series of jejunal and ileal branches – form ARCADES
 - From the terminal arcade, straight vessels enter the intestinal wall
- Supplies:
 - JEJUNUM AND ILEUM
 - RIGHT HALF OF LARGE BOWEL

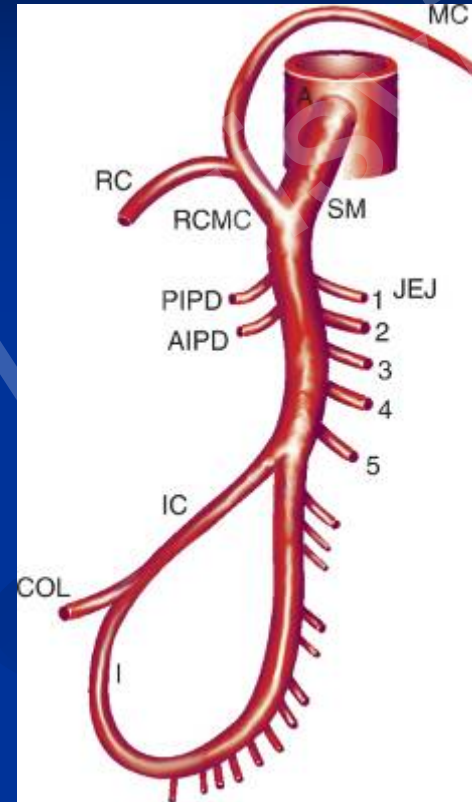


Figure 111-2 Diagram of typical superior mesenteric artery anatomy. A, aorta; AIPD, anterior inferior pancreaticoduodenal artery; COL, colic branches; I, ileal branches; IC, ileocolic artery; JEJ, jejunal branches; MC, middle colic artery; PIPD, posterior inferior pancreaticoduodenal artery; RC, right colic artery; SM, superior mesenteric artery. (From Nebesar RA, Kornblith PL, Pollard JJ, Michels NA: *Celiac and Superior Mesenteric Arteries: A Correlation of Angiograms and Dissections*. Boston, Little, Brown, 1969.)

Inferior Mesenteric Artery

- Branches include left colic artery, multiple sigmoid branches, and terminates as the superior rectal artery
- Supplies:
 - LARGE INTESTINE FROM DISTAL TRANSVERSE COLON TO PROXIMAL RECTUM
- **The distal rectum is supplied by the internal iliac artery and its hypogastric artery branch

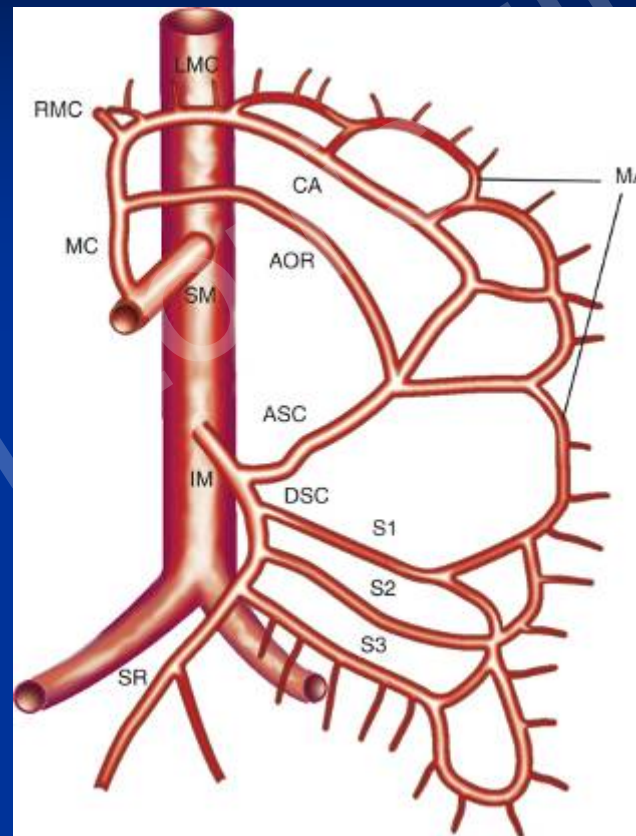


Figure 111-3 Diagram of typical inferior mesenteric artery anatomy. AOR, arc of Riolo; ASC, ascending branch of the left colic artery; CA, central artery; DSC, descending branch of the left colic artery; IM, inferior mesenteric artery; LMC, left branch of middle colic artery; MA, marginal artery; MC, middle colic artery; RMC, right branch of middle colic artery; S1, S2, S3, sigmoid branches; SM, superior mesenteric artery; SR, superior rectal artery. (From Nebesar RA, Kornblith PL, Pollard JJ, Michels NA: *Celiac and Superior Mesenteric Arteries: A Correlation of Angiograms and Dissections*. Boston, Little, Brown, 1969.)

Intestinal Ischemia - Pathophysiology

- Innate preventative measures
 - Collateral circulation – particularly to stomach, duodenum, and rectum, so less likely to have ischemia to these organs
 - Splenic flexure and sigmoid colon have fewer collateral vessels, so higher risk for ischemia
 - Compensatory mechanisms – 1/5 mesenteric capillaries are open at a time.
- The bowel can tolerate a 75% reduction of mesenteric blood flow and oxygen consumption for 12 hours with no microscopic changes of ischemia.

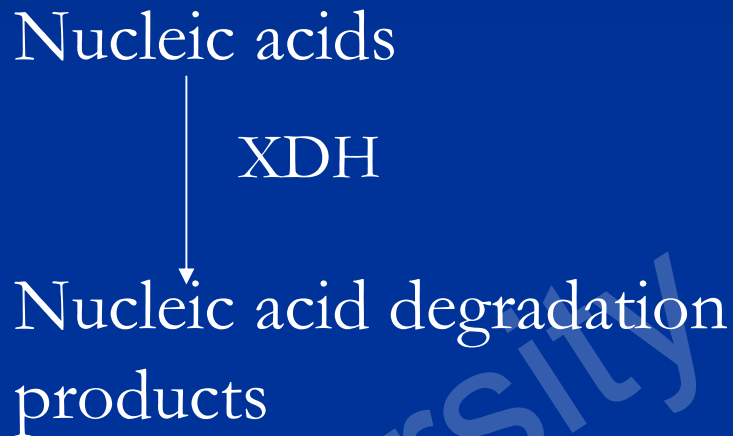
Intestinal Ischemia - Pathophysiology

- Occlusive vs nonocclusive (NOMI)
- Reversible ischemia to transmural infarction and perforation
- Vascular occlusion —→ collaterals open distally initially
- Hours of ischemia —→ vasoconstriction which reduces collateral flow
 - Vasoconstriction is irreversible after a certain period of time
- Tissue hypoxia leads to bowel wall spasm which leads to gut emptying
- Mucosal sloughing leads to GI bleeding
 - Occlusive: Hemorrhagic infarction is final common pathway
- Disruption of the mucosal barrier becomes allows bacteria, toxins, and vasoactive substances to be released into the systemic circulation

Intestinal Ischemia - Pathophysiology

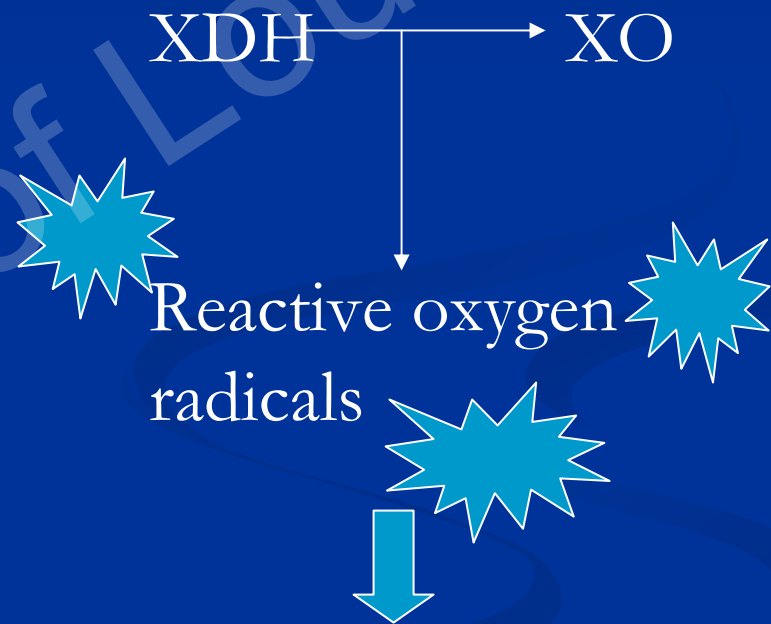
- Ischemic damage from hypoxia and reperfusion
 - Brief insult: more damage during reperfusion
 - Long insult: more damage from hypoxia
- Reperfusion injury due to reactive oxygen radicals
 - Oxygen radicals cause cell lysis and necrosis on reperfusion of ischemic tissue
 - Xanthine Dehydrogenase – enzyme in nucleic acid degrad.
 - Converted to Xanthine Oxidase in ischemia
 - Xanthine oxidase (XO) – source of oxygen radicals

Non-ischemic Tissue



**Allopurinol inhibits XO =
decreased epithelial cell necrosis
during reperfusion

Ischemic Tissue

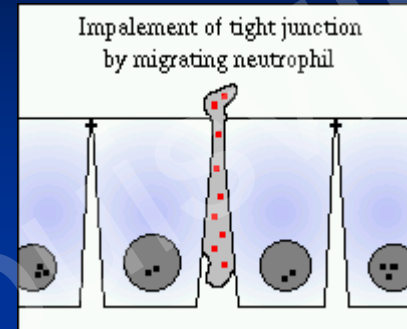


Reperfusion Injury

Intestinal Ischemia - Pathophysiology

■ Role of Neutrophils

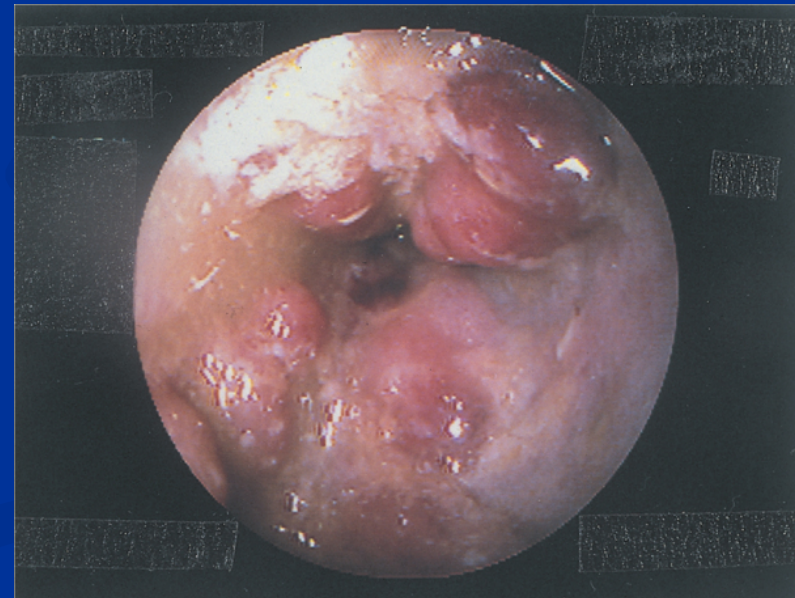
- Source of reactive oxygen metabolites
- In reperfusion, XO \longrightarrow increased production of leukotriene B4 and platelet-activating factor = neutrophil adherence and migration
- Increased microvascular injury by neutrophils causing release of proteases which disrupt endothelial barrier and tight junctions
- In vitro, XO inhibitors and agents that inhibit leukocyte adherence and migration protect organs against reperfusion injury. In vivo, agents must be given before ischemic insult



Board Question:

A 71 year old woman comes to the ER with severe nausea, vomiting, and diarrhea determined to be secondary to viral gastroenteritis. Her BP is 70/50mmHg. She is given IVF. One day later, she returns to the ER complaining of sudden onset of crampy LLQ pain and passage of bloody diarrhea. Sigmoidoscopy findings indicate her symptoms are due to:

- a. Recurrence of viral GE
- b. Superimposed bacterial infection
- c. Ulcerative proctitis
- d. Colon ischemia



Types of Intestinal Ischemia

■ **Acute Mesenteric Ischemia**

- Arterial – thrombus, embolus (cardiac), nonocclusive
- Mesenteric Venous Thrombosis
- Focal Segmental Ischemia - Venous

■ Colon Ischemia

■ Chronic Mesenteric Ischemia

■ Vasculitis and Angiopathy of Splanchnic Circulation

Acute Mesenteric Ischemia

- Insufficient blood flow to all or part of the small bowel and may involve the right half of the colon (SMA)
- **SMA** most often site of embolic AMI due to straighter take-off from Aorta

Causes and Approximate Frequencies of Acute Mesenteric Ischemia

Cause	Frequency, %
SMA embolus	50
Nonocclusive mesenteric ischemia	25
SMA thrombosis	10
Mesenteric venous thrombosis	10
Focal segmental ischemia	5

Acute Mesenteric Ischemia

■ Thrombotic AMI

- Final cause of ischemia may be sudden drop in cardiac output or ruptured plaque
- Often 2/3 vessels must be occluded for symptoms

■ Nonocclusive Mesenteric Ischemia

- “low flow state” – hypovolemia, cardiogenic or septic shock
- Failure of autoregulation
- No thrombus or embolus
- Cocaine, digitalis, vasopressin can cause local vasoconstriction

Acute Mesenteric Ischemia

■ Risk Factors:

- ≥ 50 y/o: CHF, cardiac arrhythmia, recent MI, hypotension
- Young: amphetamines, cocaine, triptans, phenylephrine, thrombophilic d/o

■ Signs and Symptoms:

- Early: Abdominal pain
- Late: Abdominal distention
 - First sign of intestinal infarction
- If rebound tenderness or guarding = think infarction
- GI bleeding
- Recurrent bacteremia s/p cardiopulmonary arrest (gut translocation of bacteria)
- Critically ill patient: intolerance to tube feeds
- Confusion (especially in elderly)

Acute Mesenteric Ischemia

- Abdominal pain:
 - Acute
 - SMAT: postprandial pain in the weeks to months preceding the acute onset of severe pain
 - Late complication of severe atherosclerotic disease when usually 2/3 vessels occluded.
 - SMAE: sudden, severe pain accompanied by rapid, forceful bowel evacuation
 - MVT: indolent
 - NOMI: no pain in 25%



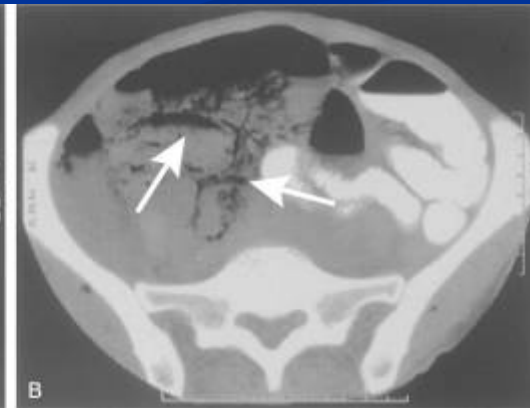
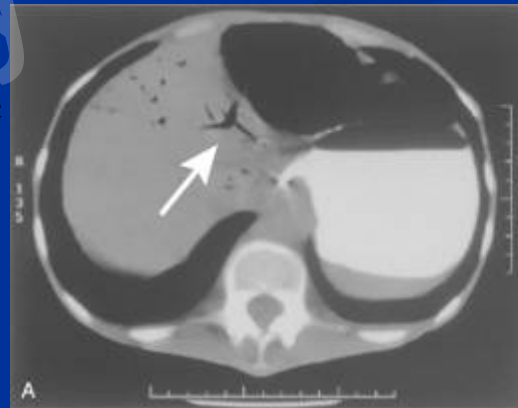
Acute Mesenteric Ischemia

■ Diagnosis:

- Labs – nonspecific; late-stage
- Plain films – normal 70%
 - Formless fixed loops of SB, ileus, “thumbprinting” or pneumatosis
- CT –arterial occlusion or venous thrombosis, intramural gas or portal venous gas, focal lack of bowel wall enhancement (sens 64%, spec 92%)
- Dopplers – limited in clinical value
 - Visualize proximal portion of vessel, occlusion nondiagnostic, variable blood flow through SMA
 - Spec 92%, sensitivity 70-89%



Ileus and
formless
SB loop
due to
SMAE



Acute Mesenteric Ischemia

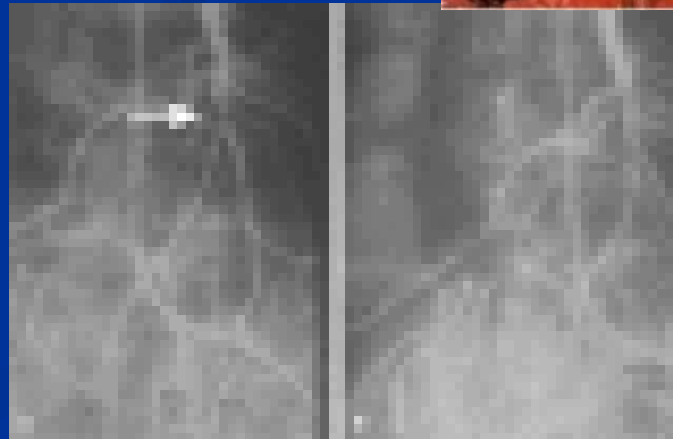
Diagnosis . . .

- CTA – sens 71-96% and a spec of 92-94%, rapid
- MRA – sens 100%, spec 91%, but time-consuming
- Laparoscopy – less helpful b/c serosa may look normal when mucosa necrotic and SMA flow decreases with incr pressure
- Laparotomy – use when angiography not available or if signs of peritonitis
- Mesenteric Angiography – diagnostic and therapeutic, gold standard
 - Sens: 90-100%, spec 100%
 - Drawbacks: delays surgery, difficult in critically ill
 - Decreased mortality
 - Only way to dx NOMI



Infarcted
loop of
bowel.

SMV
thrombus



SMA embolus,
s/p embole-
ctomy

Acute Mesenteric Ischemia - Management

- STAT surgical consult
- SMAE:
 - Acute abdomen: Laparotomy, embolectomy and/or resection
 - Re-exploration often – may leave abdomen open.
 - No peritonitis: Angiography
 - “Road map” for revascularization
 - Papaverine infusion
 - Given through angio catheter directly into SMA
 - VASODILATOR: Relieves mesenteric vasoconstriction
- SMAT:
 - Emergency surgical revascularization

Acute Mesenteric Ischemia - Management

- NOMI:
 - Papaverine infusion into SMA
 - Decreased mortality in small case series
- Broad spectrum antibiotics (no RCTs)
- No anticoagulants for first 48 hours, except in MVT

Mesenteric Venous Thrombosis

- 10% of Acute Mesenteric Ischemia
- Risk Factors:
 - Hypercoagulable States
 - Estrogen – OCP, HRT, pregnancy
 - Malignancy
 - DVT – 60% MVT have h/o peripheral DVT
 - Portal Hypertension
 - Inflammatory States – diverticulitis, pancreatitis, peritonitis, IBD
 - Trauma
 - Decompression Sickness

Mesenteric Venous Thrombosis

- Location, Location, Location
 - Initial thrombus location varies with etiology
 - Cirrhosis, Neoplasm: Start proximal, extend peripherally
 - Hypercoag state: Start peripherally and extend proximally
- Rare intestinal infarction
- Pathophysiology:
 - Impaired venous drainage leads to congestion and cyanosis of bowel and thickened bowel wall with intramural hemorrhage
- Clinical: acute, subacute, or chronic. Abdominal pain, GI bleed.
- Diagnosis:
 - SB wall thickening, thumbprinting
 - **CT – test of choice**
 - Angiography
 - Laparotomy – serosanguinous peritoneal fluid, blue-black bowel, thrombi

Mesenteric Venous Thrombosis

■ Treatment

- Asymptomatic – 3-6 mos anticoagulation or no therapy
- Peritoneal signs – laparotomy
 - Papaverine infusion if viable bowel
 - Thrombectomy if possible
 - Immediate heparinization for 7-10 days (improves survival)
- No peritoneal signs – 3-6 mos anticoagulation
- Lifelong anticoagulation if hypercoagulable state
- EGD for esophageal varices if chronic MVT

Focal Segmental Ischemia

- Ischemia to a short segment of small intestine
- Causes: Atheromatous emboli, strangulated hernia, immune complex disorders/vasculitis, blunt abdominal trauma, segmental venous thrombosis, radiation therapy, OCP's.
- Clinical: acute abdomen or chronic enteritis with chronic SBO from stricture with intermittent abdominal pain and vomiting
- Xray:
 - “blind loop” syndrome – bacterial overgrowth of the dilated loop proximal to the SBO.
 - Smooth tapered stricture with abrupt change to normal mucosa
- Treatment: surgical resection of involved bowel

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- **Colon Ischemia**
- Chronic Mesenteric Ischemia
- Vasculitis and Angiopathy of Splanchnic Circulation

Colon Ischemia

- The Most Common form of Intestinal Ischemia
- Causes: Vast and often idiopathic
 - Emboli
 - Hematologic d/o – vasculitis, hypercoagulable states
 - Infectious – E.coli 0157:H7, HBV, CMV, parasites
 - Surgical – includes colonoscopy; more often Aortic, Cardiac
 - Drugs, Drugs, Drugs – GoLYTELY among many
 - NSAIDs, PCN, saline laxatives, cocaine, estrogens, IFN- α , Lotronex
 - Shock, Trauma
 - Obstructing colon lesions
 - Pancreatitis
 - Strangulated Hernia
 - Long distance running



Colon Ischemia

- Causes and affected segments:
 - Systemic low-flow states = Right colon
 - Local nonocclusive ischemic injury – the watershed area = splenic flexure and rectosigmoid
 - Ligation of IMA – sigmoid colon
 - Atheromatous emboli - short segments of injury
 - Nonocclusive injury – longer portions of colon
- In most cases, no specific cause is identified

Colon Ischemia

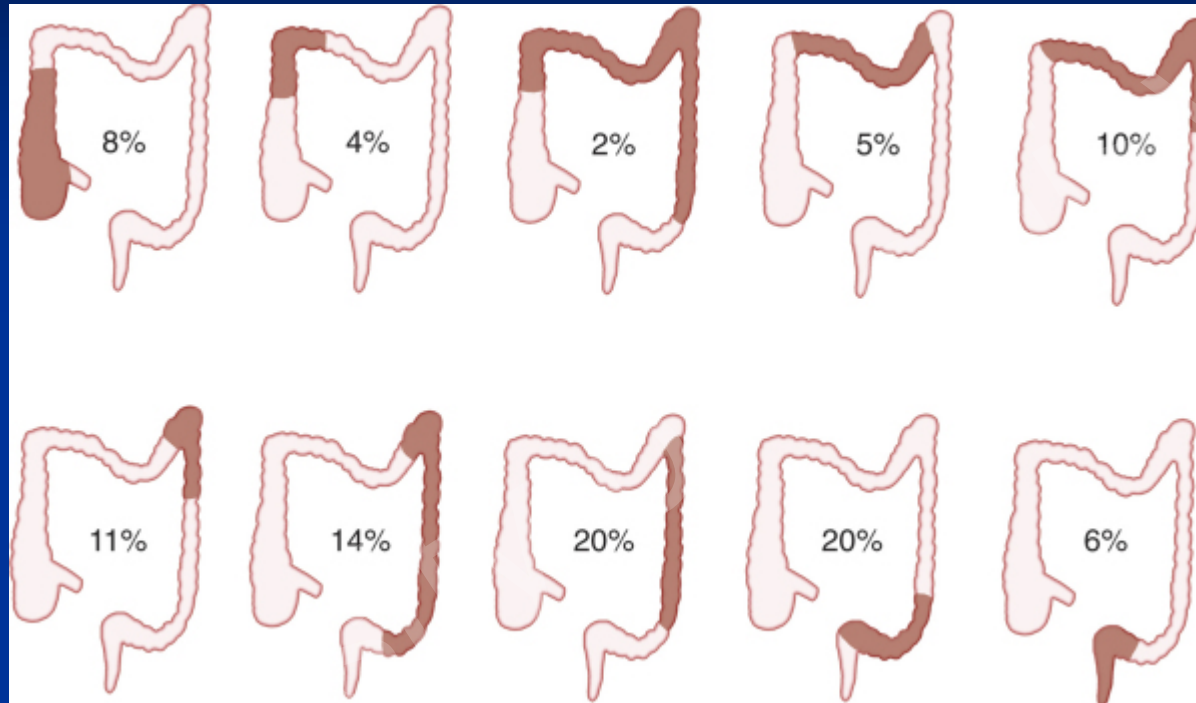


Figure 111-12 Schematic of patterns of colon ischemia showing the percentage of involvement of each pattern in a total of 250 cases

Colon Ischemia

■ Pathology

- Varies with duration and severity of ischemia
- Mild: mucosal and submucosal hemorrhage and edema +/- partial necrosis and mucosal ulceration
- Moderate: chronic ulcerations, crypt abscesses, pseudopolyps (**MIMICKS IBD)
- Severe: MP replaced by fibrous tissue (stricture formation)
- Very Severe: transmural infarction

Colon Ischemia

■ Clinical

- Sudden, cramping pain, can be mild intensity
- LLQ
- Urgent need to defecate
- Hematochezia within 24 hours (small volume)

Colon Ischemia - Diagnosis

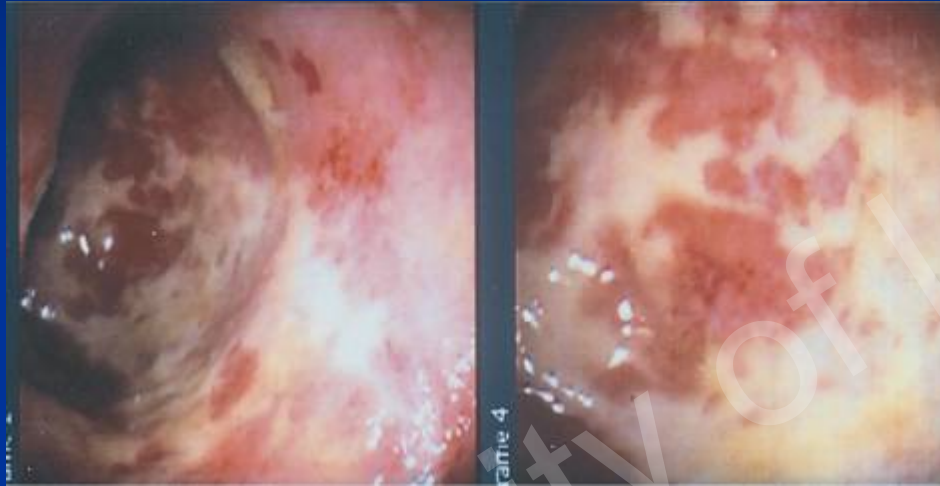
- Unprepped colonoscopy w/in 48 hrs if no signs of peritonitis
 - Do not overdistend the colon –can worsen ischemia
 - “**Hemorrhagic nodules**” = submucosal bleeding
 - “thumbprints” on barium enema study
 - “**Colon single-stripe sign**” – single erythematous line with ulceration oriented along longitudinal axis of colon. 75% sensitive.
 - Indicates milder dz than if circumferential ulcer
 - Rectal sparing
 - Segmental disease
 - Mucosal gangrene
 - More sensitive than barium enema



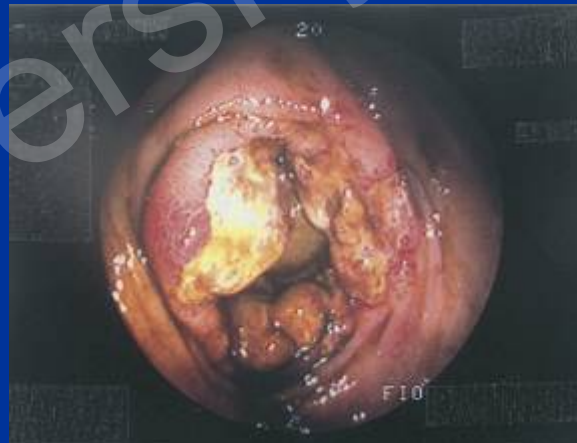
Colon Ischemia - Diagnosis

- No Mesenteric Angiography unless cannot distinguish btw CI and AMI (Right colon involvement or severity of pain) b/c colon blood flow returns to normal by the time of presentation
- If unclear CI vs AMI, first order air enema
 - Will show presence of submucosal edema and hemorrhage of CI
 - If no thumbprinting seen or only in the right colon, then order mesenteric angiography

Colon Ischemia : Differential Diagnosis at Endoscopy



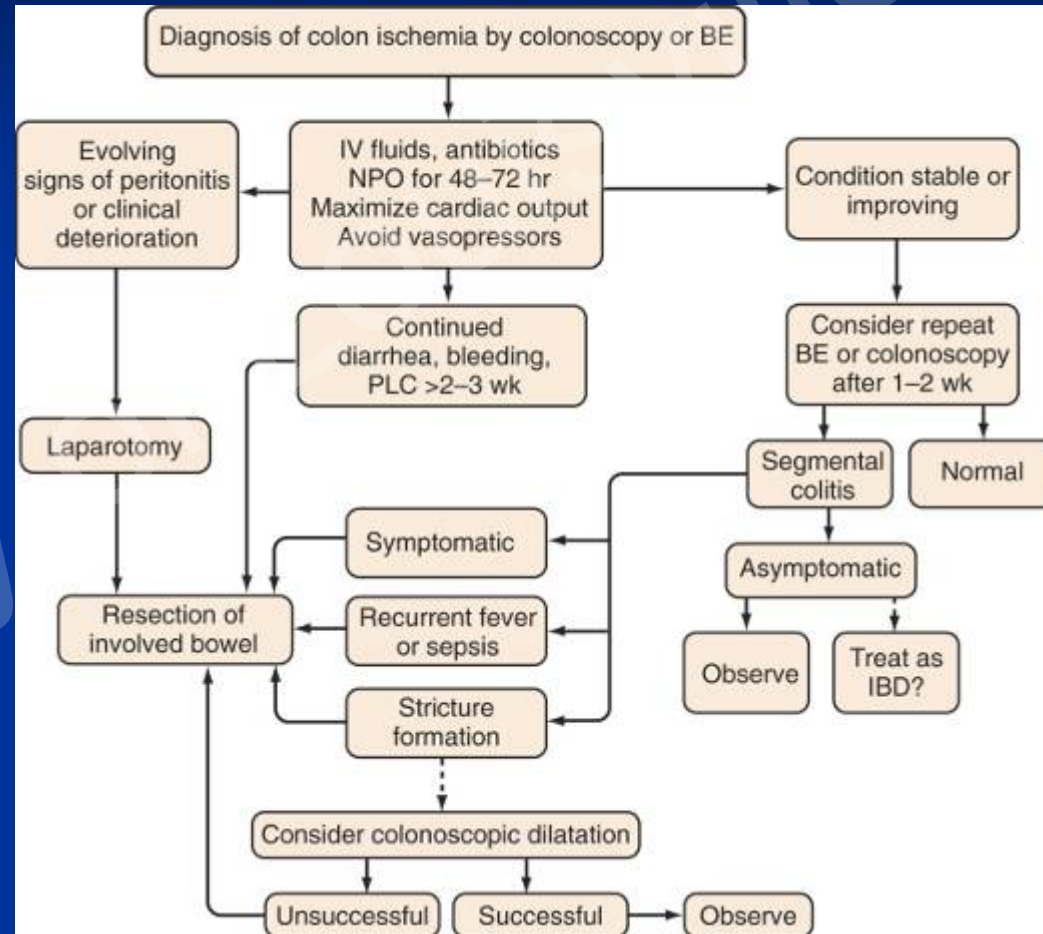
Ischemia or Crohn's?



Ischemia or Neoplasm?

Colon Ischemia - Management

- If no peritonitis, conservative
 - Bowel rest, IVF, ABx
 - Rectal tube prn colon distention
 - Monitor labs, xrays
- Signs of infarction = to OR
 - Worsening abdominal tenderness or rebound, guarding, fever



PLC: protein-losing colopathy

Types of Intestinal Ischemia

- Acute Mesenteric Ischemia
 - Arterial – thrombus, embolus, nonocclusive
 - Mesenteric Venous Thrombosis
 - Focal Segmental Ischemia - Venous
- Colon Ischemia
- **Chronic Mesenteric Ischemia**
- Vasculitis and Angiopathy of Splanchnic Circulation

Chronic Mesenteric Ischemia

- “Intestinal Angina”
- Prevalence: less than 5% of intestinal ischemia
- Risk factors:
 - coronary or peripheral vascular disease
 - 75% of pts with CMI have h/o smoking

Chronic Mesenteric Ischemia

■ Pathophysiology:

- Almost always caused by mesenteric atherosclerosis
- New Theory: Ischemia of the small bowel due to preferential blood supply to stomach upon food ingestion
- Old Theory: Limited blood supply to the small intestine during digestion

Chronic Mesenteric Ischemia

- Symptoms: ABDOMINAL PAIN & WEIGHT LOSS
- Abdominal Pain:
 - Starts within 30 minutes of food ingestion
 - Increases in severity
 - Resolves over 1-3 hours acutely
 - Progressively increases in severity over time and may become continuous, unassociated with food intake
 - BAD SIGN = INFARCTION IMINENT
- Fear of eating, resulting in weight loss
 - “sitophobia”

Chronic Mesenteric Ischemia

■ Other Symptoms:

- Nausea, bloating
- Episodic diarrhea
- Constipation
- Malabsorption

Chronic Mesenteric Ischemia

- Uncommon presentations:
 - Antral ulcers that do not heal with PPI
 - Gastroparesis (reversible with revascularization!!)
 - Acalculous cholecystitis



Chronic Mesenteric Ischemia

■ Physical Exam:

- Overall benign
- Cachexia if significant weight loss
- Abdomen is NON-TENDER even if having pain
 - Pain out of proportion to physical exam
- Could have abdominal distention
- Abdominal bruit may be present

Chronic Mesenteric Ischemia

■ Diagnosis

- No specific diagnostic test – dx of exclusion
- X-Ray and CT – normal or vascular calcifications
- Endoscopy – may have antral ulcers not assoc with H.pylori
- Barium – normal or motility d/o or malabsorption
- Gastric Emptying Test – may be delayed
- Provocative balloon tonometry – evaluates the physiological adequacy of intestinal blood flow

Chronic Mesenteric Ischemia

■ Diagnosis

- Duplex USN – elevated peak systolic velocity in SMA of 275 cm/sec and CA of 200 cm/sec suggests 70% stenosis of these vessels, but does not establish diagnosis of CMI
- MRA or mesenteric angiography – show anatomic limitations of splanchnic blood flow but cannot diagnose intestinal ischemia
 - Angiography –at least 2 of 3 splanchnic vessels should be severely stenosed or occluded

Chronic Mesenteric Ischemia

- Surgical Revascularization vs PTMA (percutaneous transluminal mesenteric angioplasty)
 - Literature with varied criteria to define outcomes
 - Initial success at revascularization similar
 - Surgical approach – bypass grafts, aortic reimplantation of SMA, and endarterectomy
 - improved duration of graft patency but increased perioperative mortality
 - PTMA with decreased perioperative mortality but increased recurrence of symptoms and stenosis. Stenting improves these outcomes.
- Management based on surgical risk

Chronic Mesenteric Ischemia: Management

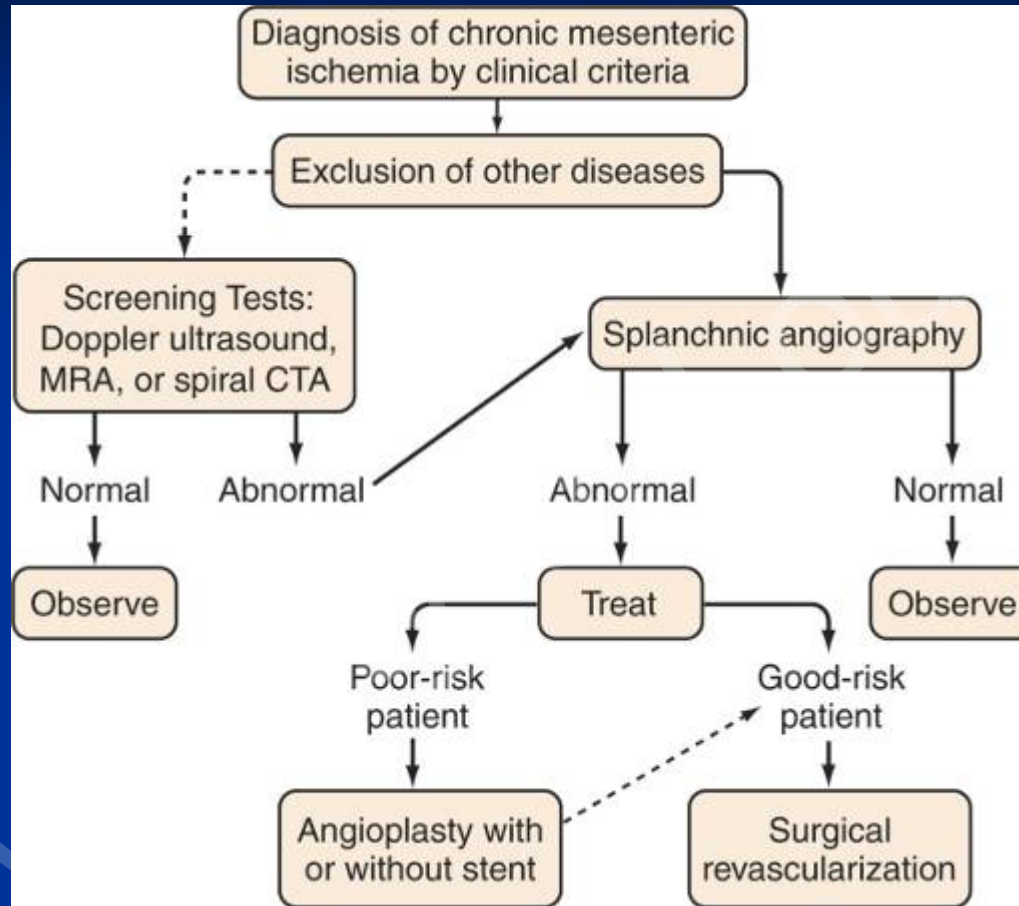


Figure 111-19 Algorithm for the management of chronic mesenteric ischemia. *Solid lines* indicate accepted management plan; *dashed line* indicates alternative management plan. CTA, computed tomographic angiogram; MRA, magnetic resonance angiography. (From Brandt LJ, Boley SJ: AGA technical review on intestinal ischemia: American Gastrointestinal Association. *Gastroenterology* 118:954, 2000.)

Types of Intestinal Ischemia

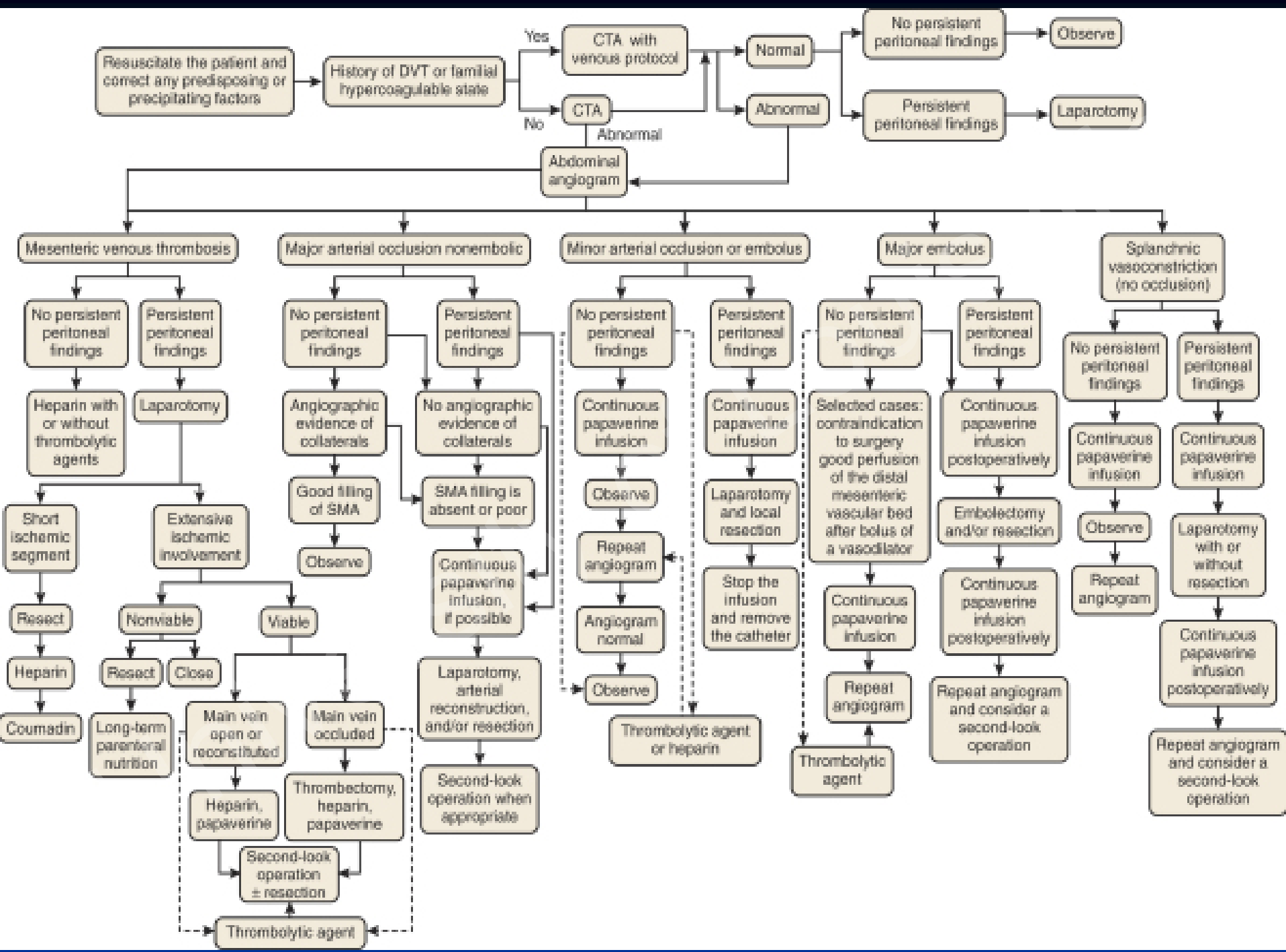
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- Chronic Mesenteric Ischemia
- **Vasculitis and Angiopathy of Splanchnic Circulation**

Vasculitis

- Many types
- Segmental ischemia
- Clinical symptoms similar to other causes of ischemia
 - Abdominal pain, fever, bloody diarrhea, intestinal obstruction
 - Ulceration and strictures common; perforation uncommon
- Pathophysiology:
 - Immune complex deposition in the vascular walls leads to complement activation, inflammatory reaction; then aneurysms form which can rupture. Vascular occlusion, thrombosis, and fibrosis ensue.
- Treatment: steroids, immunosuppressants

Intestinal Ischemia

- A very basic algorithm from the 2000 AGA technical review on intestinal ischemia for the diagnosis and treatment of intestinal ischemia. . .



References

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- Mesenteric vein thrombectomy associated with intestinal resection in extended venous mesenteric infarction – case report. AVRAM J., MOCANU N., TOMA DIDINA, SĂNDESCU
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