GI Bleeding and Peptic Ulcer Disease

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Disclosure

Advisory Board: Ethicon Endosurgery; Medtronic; Phathom; Sandhill/Diversatek

Consultant: Ethicon Endosurgery; Laborie; Medtronic; Phathom; Sandhill/Diversatek

Patent Royalties: Laborie

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Speaker's Bureau: Ethicon Endosurgery; Phathom

Stocks: Medtronic

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Learning Objectives

To be able to:

1. be more careful with NSAIDs in patients with GI bleeding
2. focus on treating the underlying cause, as opposed to placing patients on indefinite PPI therapy
3. be more comfortable with outpatient work ups for GI bleeding

Focus on Dyspepsia: Common Outpatient Complaint

- Dyspepsia: Pain or discomfort in the upper abdomen
- Differentiating Dyspepsia
  - Non-urgent Abdominal Pain versus Acute Abdomen
  - GERD versus Dyspepsia
- Common Causes of Dyspepsia
  - *Peptic Ulcer Disease*
  - *Medications*
  - *H. Pylori Infection*
  - Gallbladder
  - Pancreas
  - **Idiopathic/Functional**

Urgent versus Non-urgent

- Abdominal pain is difficult to evaluate and manage.
  - Acute versus Chronic
  - History has low sensitivity/specificity- especially for chronic pain
- Any patient with acute abdominal pain with:
  - Unstable vital signs
  - Peritoneal signs
  - Concern for infection
  - Unable to maintain hydration

Is best managed in the ER or an Acute Care Clinic or Immediate Care Clinic as they will likely need imaging and an urgent surgical consultation.

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Chronic Abdominal Pain

Dyspepsia

- Means bad digestion or disordered digestion
  - Associated with food
  - Nausea/Vomiting, Bloating, Fullness
- Implies chronicity and recurrent pain
- Sometimes mistakenly called gastritis

- ***Common complaint with 1% incidence***
  - about 5% of PCP visits and 20% of GI consults.
  - Investigated versus uninvestigated
  - 70% have no organic explanation

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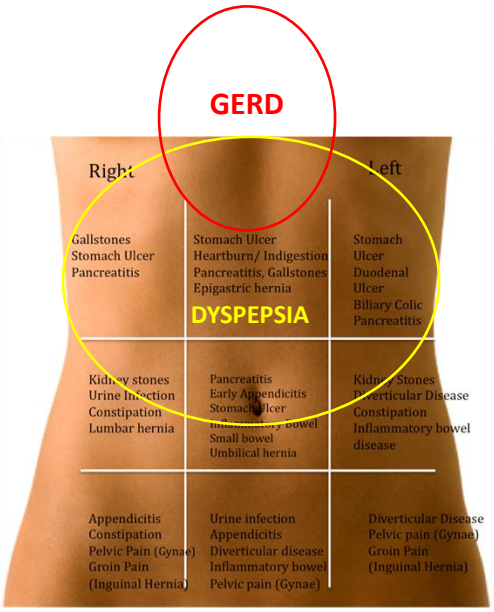
Location of Abdominal Pain



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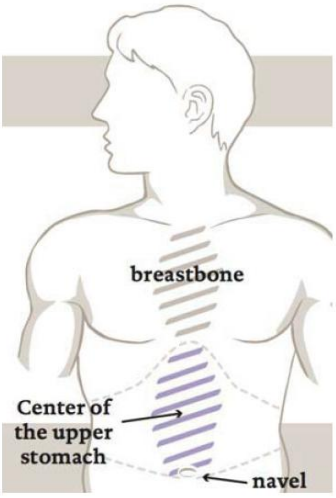
Differentiating GERD from Dyspepsia- GERDQ



Thinking about your symptoms over the past 7 days.....

	0 Never	1 One Day	2 2-3 Days	3 4-7 days
How often did you have a burning feeling behind your breastbone (heartburn)?	O	O	O	O
How often did you have stomach contents (liquid or food) moving upwards to your throat or mouth (regurgitation)?	O	O	O	O
How often did you have a pain in the center of your upper stomach?	O	O	O	O
How often did you have nausea?	O	O	O	O
How often did you have difficulty getting a good night's sleep because of your heartburn and/or regurgitation?	O	O	O	O
How often did you take additional medication for your heartburn and/or regurgitation other than what the physician told you to take (such as Tums, Rolaids, Maalox)?	O	O	O	O

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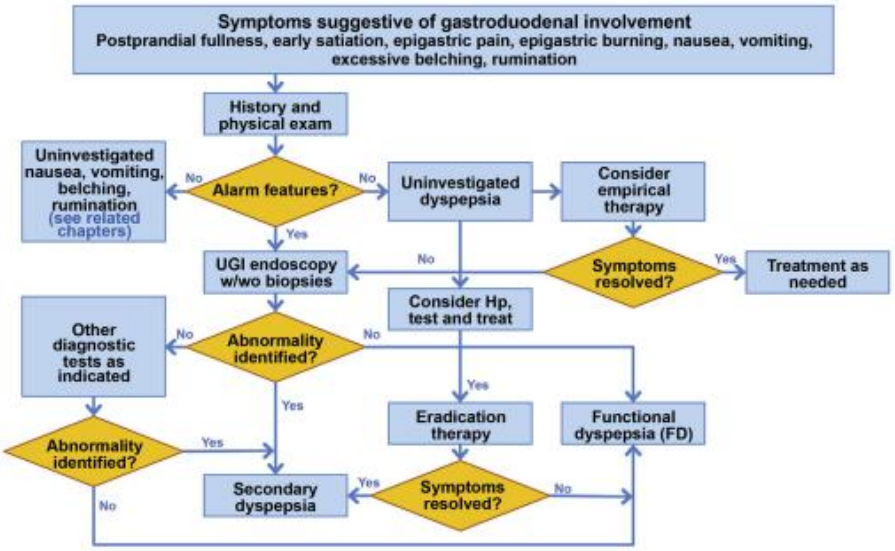
Dyspepsia Work UP



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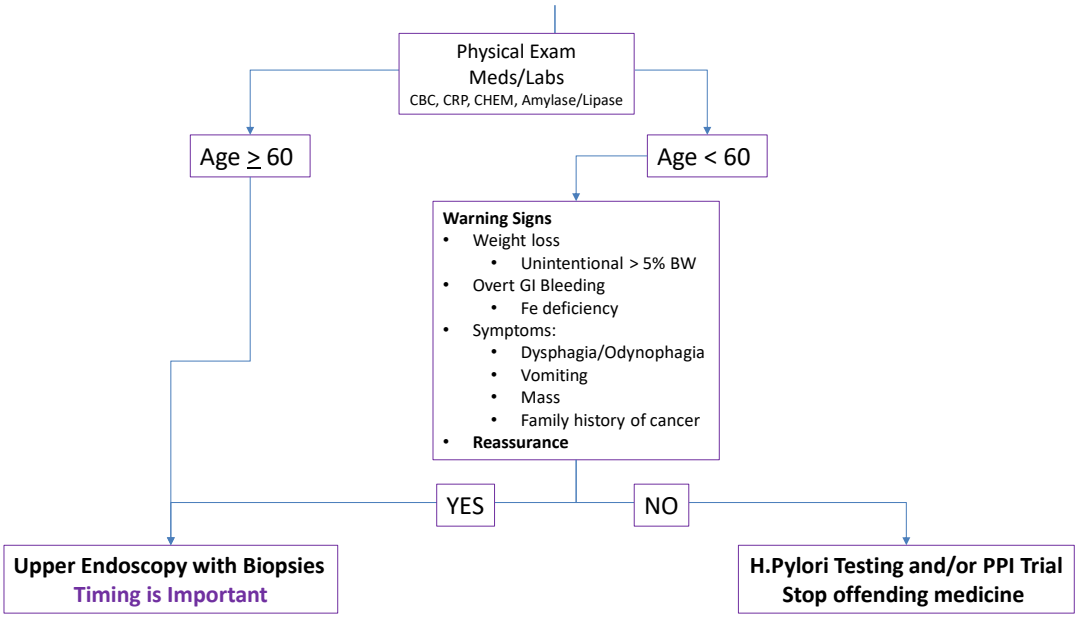
Patient with Dyspepsia Symptoms



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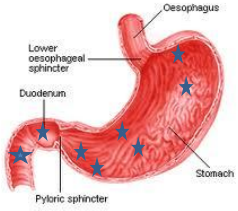
Patient with Dyspepsia Symptoms

Upper Endoscopy with Biopsies



Most patients will have a negative endoscopy and negative biopsies for H. Pylori
- OFF PPI Therapy
- Gastritis is a pathologic diagnosis

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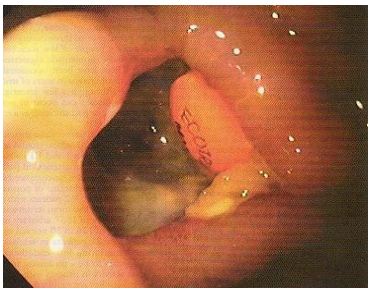
Medications

- NSAIDs and COX-2 selective inhibitors can cause dyspepsia even in the absence of peptic ulcer disease.
- Other drugs:
  - calcium channel blockers, methylxanthines, alendronate, orlistat
  - potassium supplements, iron, vitamin D, selective
  - serotonin reuptake inhibitors, sulfonylureas, and certain antibiotics (erythromycin)
  - acarbose, dabigatran



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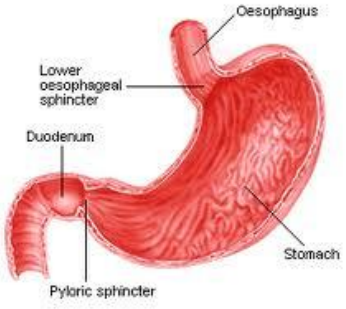
Presentation and Causes of PUD

Patients with DU usually present with increased appetite or nocturnal abdominal pain

Patients with GU present with abdominal pain after food ingestion, nausea, vomiting, and weight loss[1]

Elderly patients with PUD are usually asymptomatic or have only mild symptoms



- Positive for *Helicobacter pylori* infection
- Drug (ie, non-steroidal anti-inflammatory drug [NSAID])-induced
- *H pylori* and NSAIDs positive
- *H pylori* and NSAIDs negative*
- Acid hypersecretory state (ie, Zollinger-Ellison syndrome)
- Anastomosis ulcer after subtotal gastric resection
- Tumours (ie, cancer, lymphoma)
- Rare specific causes
  - Crohn's disease of the stomach or duodenum
  - Eosinophilic gastroduodenitis
  - Systemic mastocytosis
  - Radiation damage
  - Viral infections (eg, cytomegalovirus or herpes simplex infection, in particular in immunocompromised patients)
  - Colonisation of stomach with *H heilmanii*
  - Severe systemic disease
- Cameron ulcer (gastric ulcer where a hiatus hernia passes through the diaphragmatic hiatus)
- True idiopathic ulcer

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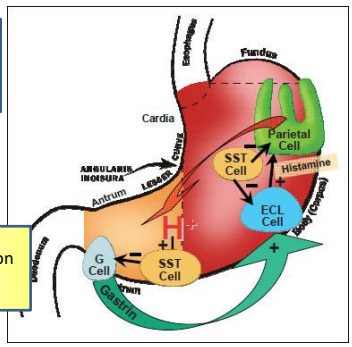
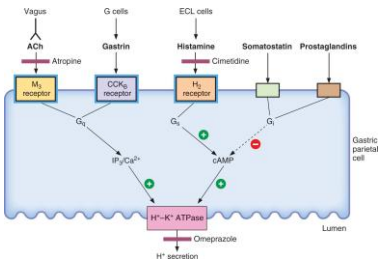
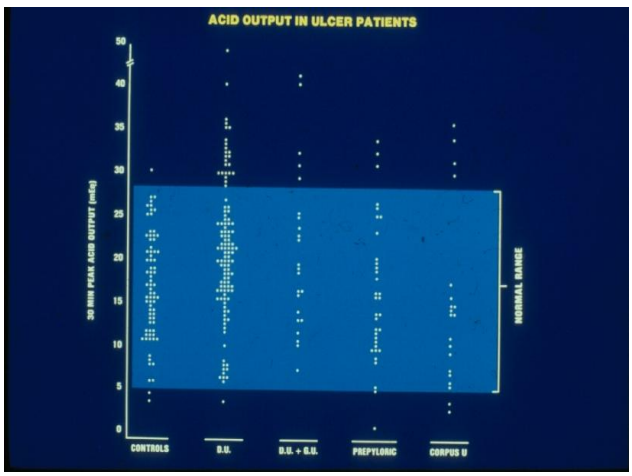
Gastric Acid Secretion

Cephalic phase Vagus Ach

Antral distension Ach, gastrin







Courtesy of Basil Hirschowitz

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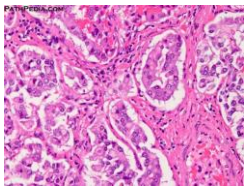
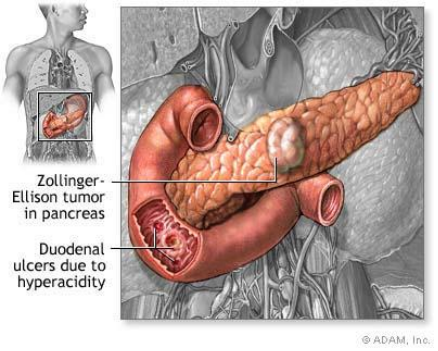
Zollinger-Ellison Syndrome



- Incidence 0.1-1%
- MEN Type I
  - Primary hyperparathyroidism (90%)
  - Pituitary tumors (10-20%)
  - Enteropancreatic tumors (60-70%)
- Intractable or multiple ulcers, diarrhea, enlarged gastric folds



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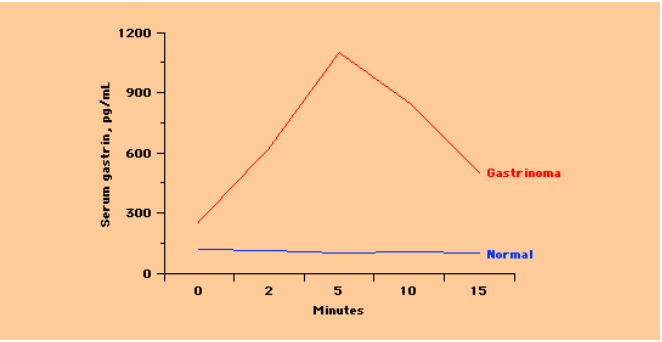
Elevated Serum Gastrin

- >1000 pg/mL diagnostic
  - Rule out pernicious anemia
  - Most ZES have lower levels
- <1000 pg/mL
  Small bowel resection
  Renal insufficiency
  Use of PPI's
  Gastric outlet obstruction
  Retained gastric antrum



Secretin test in gastrinoma Marked hypersecretion of gastrin occurs after the administration of secretin in a patient with a gastrinoma (Zollinger-Ellison syndrome) compared to the lack of response in normal subjects.

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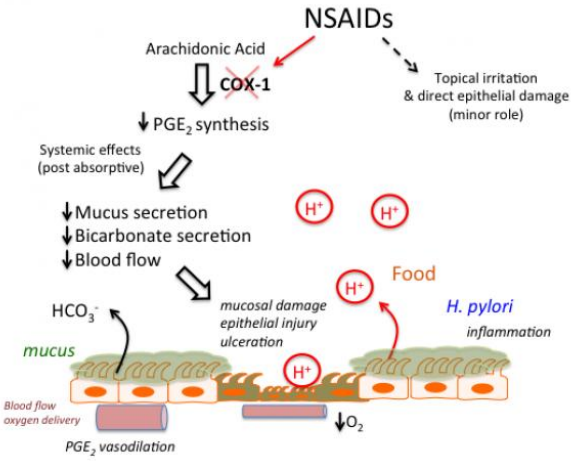
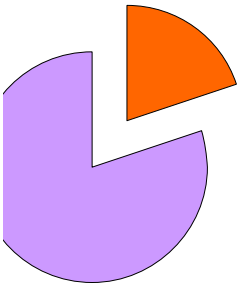
IMPACT: NSAID's and the Gut





20% ulcers

↓

2-4% symptomatic

107,000 hospitalizations

16,500 deaths

$1 billion expenditure

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NSAID Associated PUD

- NSAIDs are the most important etiological factor for recurrent PUD
- *H. pylori* infection positively increases the risk of NSAID-related GI complications

High risk	
1.	History of a previously complicated ulcer, especially recent
2.	Multiple (>2) risk factors
Moderate risk (1–2 risk factors)	
1.	Age >65 years
2.	High dose NSAID therapy
3.	A previous history of uncomplicated ulcer
4.	Concurrent use of aspirin (including low dose) corticosteroids or anticoagulants
Low risk	
1.	No risk factors

Am J Gastroenterol. 2009;104(3):728-738.

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NSAID Associated PUD

Risk for NSAID-Induced GI Toxicity	Preventive Measures
Very–high-risk group	• Treatment with NSAIDs should be avoided or must be administered with extreme caution and maximal protective measures • COX-2 inhibitor plus misoprostol or a PPI therapy is indicated if anti-inflammatory treatment is required
High-risk group	COX-2 inhibitor plus misoprostol or PPI
Moderate-risk group	COX-2 inhibitor alone or NSAID plus misoprostol or PPI
Low-risk group	No protective measures

Am J Gastroenterol. 2009;104(3):728-738.

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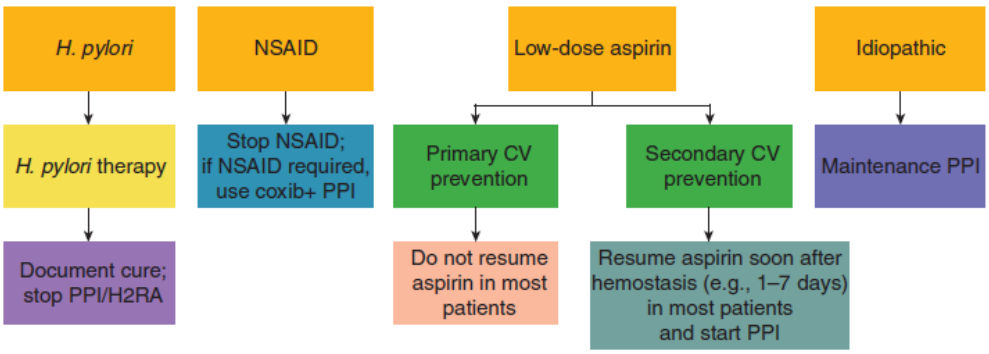
Management of PUD



- Complicated history- consider maintenance therapy based on risk factors.
- Document healing in Gastric Ulcers

Am J Gastroenterol. 2012;107(3):345-360

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Patient with Dyspepsia Symptoms

Upper Endoscopy with Biopsies

When to Test for *H. pylori*

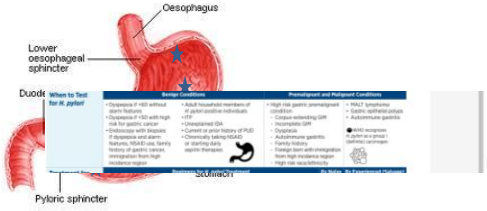
Benign Conditions

- Dyspepsia if <60 without alarm features
- Dyspepsia if <50 with high risk for gastric cancer
- Endoscopy with biopsies if dyspepsia and alarm features, NSAID use, family history of gastric cancer, immigration from high incidence region
- Adult household members of *H. pylori* positive individuals
- ITP
- Unexplained IDA
- Current or prior history of PUD
- Chronically taking NSAID or starting daily aspirin therapies

Premalignant and Malignant Conditions

- High risk gastric premalignant condition
  - Corpus-extending GIM
  - Incomplete GIM
  - Dysplasia
  - Autoimmune gastritis
  - Family history
  - Foreign born with immigration from high incidence region
  - High risk race/ethnicity
- MALT lymphoma
- Gastric epithelial polyps
- Autoimmune gastritis

WHO recognizes *H. pylori* as a group I (definite) carcinogen



The American Journal of Gastroenterology 119(9):p 1730-1753, September 2024
DOI: 10.14309/ajg.0000000000002968

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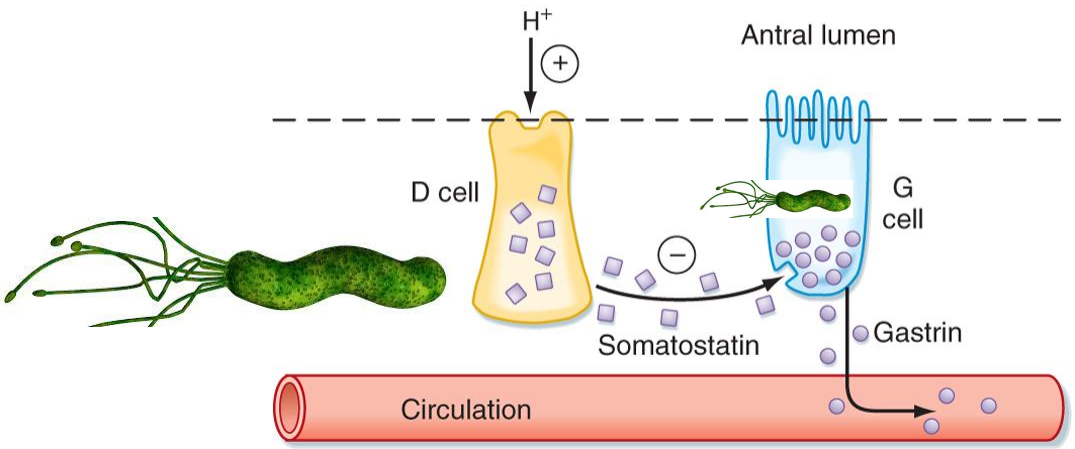
ACID IN THE ANTRUM STIMULATES SOMATOSTATIN RELEASE TO INHIBIT MEAL-STIMULATED GASTRIN SECRETION



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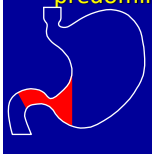
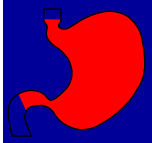
Two Major Patterns of *H. pylori* Gastritis

Pattern	Pathology	Acid	Duodenal path	Ulcer risk
Antrum-predominant 	• Chronic inflammation • Polymorph activity	Increased	• Gastric metaplasia • Active chronic inflammation	Duodenal ulcer
Pan-gastritis 	• Chronic inflammation • Polymorph activity • Atrophy • Intestinal metaplasia	Reduced	Normal	Gastric ulcer

Dixon 1994

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Worldwide Prevalence of *H. pylori* Infection

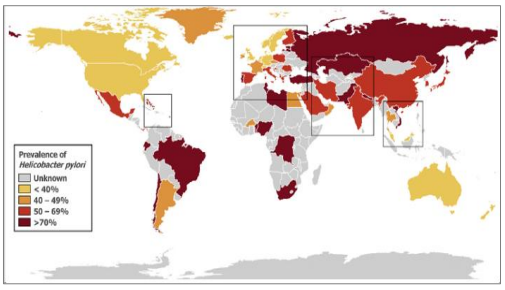
Early childhood is a period of transmission of *H. pylori* infection and the presence of an infected sibling was an important risk factor for transmission of the disease.[1]

An oral-oral or oral-fecal route has been identified to be responsible for spread of *H. pylori* infection.[1]

The presence of *H. pylori* in drinking water, poor living conditions, and lack of sanitation are important risk factors in *H. pylori* infection.[1]

H. pylori eradication decreased the burden of dyspepsia and peptic ulcer disease.[1]

More than half of the world's population was found to be infected with *H. pylori*.



1Hooi JKY, et al. Global prevalence of *Helicobacter pylori* infection: Systematic review and meta-analysis. *Gastroenterology*. 2017;153:420-429.

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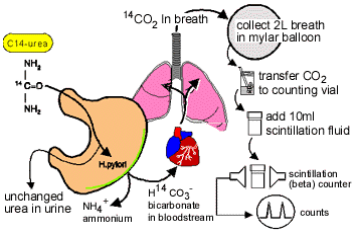
Patient with Dyspepsia Symptoms



Testing for H. Pylori

Pretest probability of *H. pylori* infection

- Higher
  - IgG *H. pylori* antibody test
    - **Urea breath test**
- Lower
  - Other *H. pylori* tests
    - **Fecal antigen test**
    - **Mucosal biopsy-based test, if endoscopy is performed**

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ACG Guidelines: Therapies

Overall resistance rates:	
Clarithromycin	22.2%
Amoxicillin	1.2%
Metronidazole	69.2%

1st-Line Regimens for Treatment-Naive Patients with *H. pylori* infection Without Antibiotic Susceptibility Testing

No Penicillin Allergy

- Optimized BQT*
- Rifabutin Triple
- PCAB Dual
- PCAB-Clarithromycin Triple**

Penicillin Allergy*

- Optimized BQT*

BQT, bismuth quadruple therapy, PCAB, potassium-competitive acid blocker
*Includes appropriately dosed PPI, bismuth, nitroimidazole, and tetracycline (not doxycycline)
** Avoid in those with previous macrolide exposure
*** May require formal allergy testing

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ACG Guidelines: Salvage Therapies

Table 6. Recommended salvage regimens for treatment-experienced patients with persistent *H. pylori* infection

Regimen	Drugs (doses)	Dosing frequency	AST required?	Recommendation
Optimized bismuth quadruple[a]	PPI (standard dose)[b] Bismuth subcitrate (120–300 mg) or subsalicylate (300 mg) Tetracycline (500 mg) Metronidazole (500 mg)	b.i.d. q.i.d. q.i.d. t.i.d. or q.i.d.	No	Conditional (very low quality of evidence)
Rifabutin triple	PPI (standard to double dose)[b] Amoxicillin (1,000 mg) Rifabutin (50–300 mg)[c]	b.i.d. b.i.d. or t.i.d. q.d., b.i.d., or (Talicia which contains 50 mg t.i.d.)[c]	No	Conditional (low quality of evidence)
Levofloxacin triple[d]	PPI (standard dose)[b] Levofloxacin (500 mg)[d] Amoxicillin (1,000 mg) or metronidazole[e] (500 mg)	b.i.d. q.d. b.i.d.	Yes	Conditional (low quality of evidence)
P-CAB triple (Voquezna TriplePak)[f]	Vonoprazan (20 mg) Clarithromycin (500 mg) Amoxicillin (1,000 mg)	b.i.d	Yes	No recommendation (evidence gap)
High-dose dual therapy[g]	Vonoprazan (20 mg)[h] or PPI (double dose) Amoxicillin (1,000 mg)	b.i.d. or t.i.d. t.i.d	No	No recommendation (evidence gap)

AMOX, amoxicillin; CAM, clarithromycin; FDA, Food and Drug Administration; LV, levofloxacin; MNZ, metronidazole; PPI, proton pump inhibitor.

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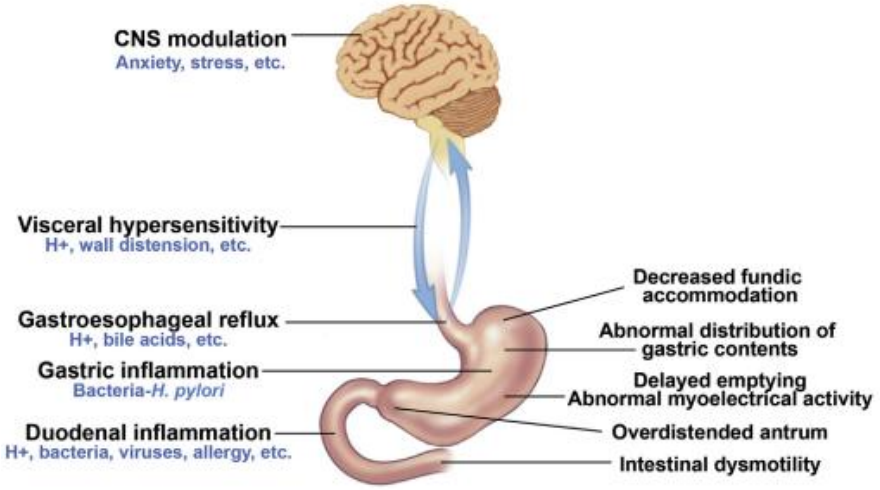
Dyspepsia Work UP



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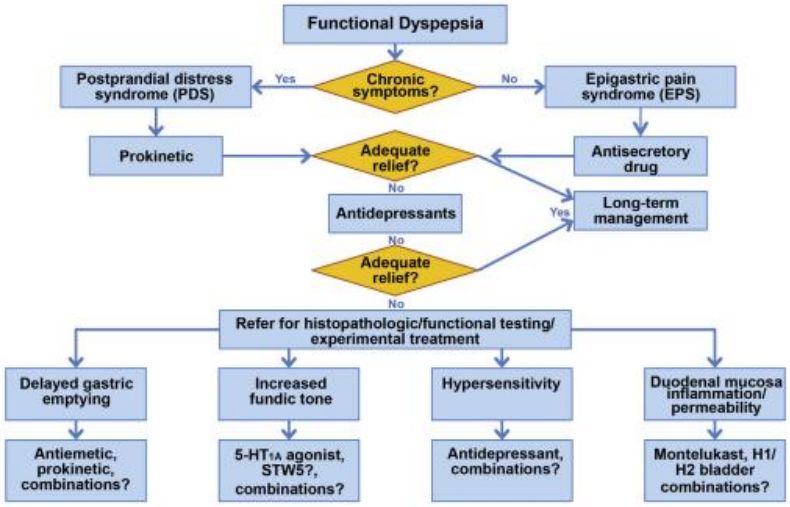
Dyspepsia Work UP



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Functional Dyspepsia: Epigastric Pain Syndrome

Primarily Pain- Epigastric Burning

- TCA [low dose]
  - Amitriptyline 10 mg
  - Desipramine 25 mg.
  - The dose is started at night and may be increased at 1-2 week intervals.
    - Max dose is around 75 mg
    - Continue for 6 months- try to wean off.
    - Trazadone is another alternative

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Functional Dyspepsia: Dysmotility Overlap/ Post-prandial Distress Syndrome

Prokinetic agents

- Metoclopramide 5 to 10 mg three times daily one-half an hour before meals and at night for four weeks) for 4 week intervals.
- I prefer for patients to have evidence of dysmotility with objective testing and/or nausea or vomiting.
- Systematic review and meta-analysis that included 29 trials of six individual agents in patients with functional dyspepsia, overall, global symptom improvement was greater with individual agents than placebo (40 versus 26 percent).

Fundic relaxant drugs – There is limited evidence that relaxing the gastric fundus may improve early satiation and postprandial fullness.

- Buspirone 10 mg, three times daily for four weeks increased gastric accommodation and reduced the overall severity of symptoms of dyspepsia, despite inducing mild gastroparesis

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Functional Dyspepsia: Epigastric Pain Syndrome

- **Psychotherapy**
  - My first line therapy.
  - A systematic review of four trials (relaxation therapy and hypnosis, psychodrama, psychotherapy, and cognitive-behavioral therapy) suggested therapy could be beneficial for one year.
  - some question regarding durability- but can repeat and train patients in self management.

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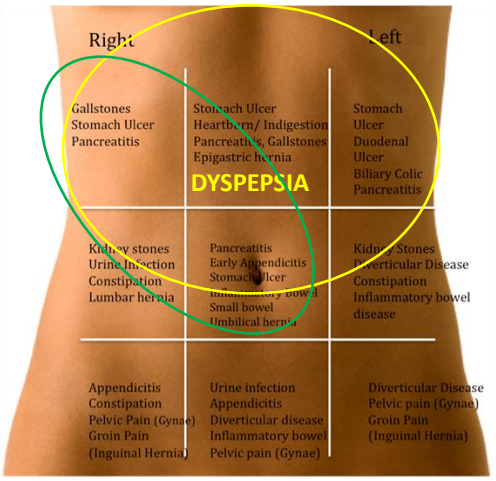
Location of Abdominal Pain



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Functional Dyspepsia: Pain Clusters

- **RUQ Pain** – Gallbladder/Pancreas
  - Classic biliary pain is characterized by episodic intense dull pain located in the right upper quadrant, epigastrium, or (less often) substernal area that may radiate to the back.
    - often constant and associated with diaphoresis, nausea, and vomiting. The pain typically lasts at least 30 minutes and can occur at night.
  - Chronic Pancreatitis pain is in the epigastric region associated with N/V and radiating to the back and worse in the recumbent position.
  - LFTs, Amylase/Lipase and RUQ US- CS Imaging may be needed.
  - EPI- bloating/diarrhea
    - Fecal elastase < 200 mcg/g is abnormal.
    - Pancreatic enzymes

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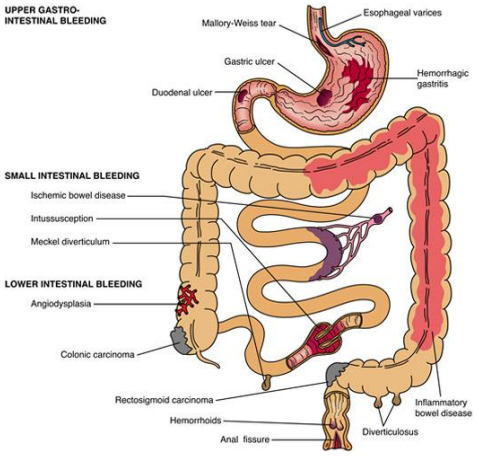
GI Bleeding: Approach

- **Confirmation and Location**
  - Factors that are predictive of bleeding coming from an upper GI source:
    - Melenic stool on examination (LR 25)
    - a ratio of BUN to serum creatinine greater than 30 (LR 7.5)
  - The majority of melena (black, tarry stool) originates proximal to the ligament of Treitz (90 percent),
    - may also originate from the oro/nasopharynx, small bowel, or colon.
    - Melena may be seen with as little as 50 mL of blood.
  - Hematochezia (red or maroon blood in the stool) is usually due to lower GI bleeding. However, it can occur with massive upper GI bleeding that is hemodynamically unstable.
  - *The presence of blood clots in the stool made an upper GI source less likely (LR 0.05).*



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GI Bleeding: Approach

- **Resuscitate/Stabilize**
- Hemodynamics
  - Access/ Labs/ Type and Cross
  - Fluids- Based on hemodynamics
    - Mild to moderate hypovolemia (less than 15 percent of blood volume lost) – Resting tachycardia.
    - Blood volume loss of at least 15 percent – Orthostatic hypotension
    - Blood volume loss of at least 40 percent – Supine hypotension
  - Bleeding risk
    - Bleeding Disorder
    - Anticoagulants, Antiplatelet agents
  - Triage
    - Scores: Rockall, GBS, AIMS 65
    - All patients with hemodynamic instability or active bleeding (manifested by ongoing hematemesis, bright red blood per nasogastric tube, or hematochezia) should be admitted to an intensive care unit for resuscitation and close observation with automated blood pressure monitoring, electrocardiographic monitoring, and pulse oximetry.
  - Consultants
  - Medications

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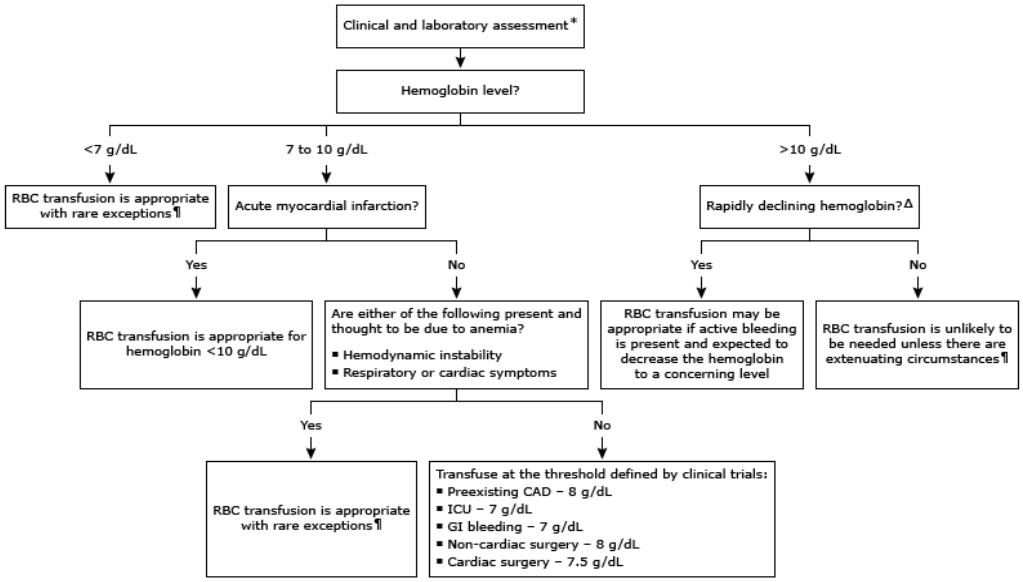
GI Bleeding: Transfusion



Modified from Up to Date: approach-to-lower-gastrointestinal-bleeding/ approach-to-upper-gastrointestinal-bleeding (uptodate.com).

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GI Bleeding: Approach

- **Medications:**

Pharmacotherapy for all patients with suspected or known severe bleeding:
Give a proton pump inhibitor: **Esomeprazole or pantoprazole, 80 mg IV**
If endoscopy delayed beyond 12 hours, give second dose of esomeprazole or pantoprazole, 40 mg IV
Pharmacotherapy for known or suspected esophagogastric variceal bleeding and/or cirrhosis:
Give somatostatin or an analogue (eg, octreotide 50 mcg IV bolus followed by 50 mcg/hour continuous IV infusion)
Give an IV antibiotic (eg, ceftriaxone or fluoroquinolone)

- **Coagulopathy/Anticoagulants**
  - For most patients, endoscopy should not be delayed because of anticoagulant or antiplatelet agent use
    - For patients undergoing upper endoscopy, wait until the INR is <2.5 to perform the endoscopy, if possible.
      - endoscopy is safe and endoscopic therapy effective in patients who are mildly to moderately anticoagulated.
  - If a patient is taking antiplatelet monotherapy such as aspirin for secondary cardiovascular prevention (prior acute coronary syndrome, coronary artery stent), the agent may be continued.
  - If the patient is taking dual antiplatelet therapy, then one of the antiplatelet agents is generally discontinued

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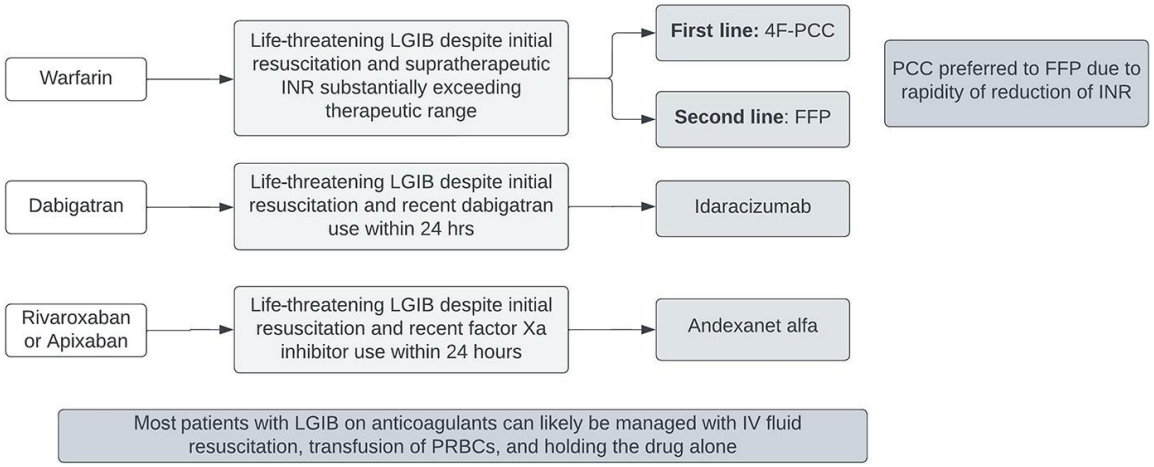
GI Bleeding: Reversal

Anticoagulant Reversal Strategy in Life-Threatening LGIB



Sengupta, N. The American Journal of Gastroenterology 118(2):p 208-231, February 2023.

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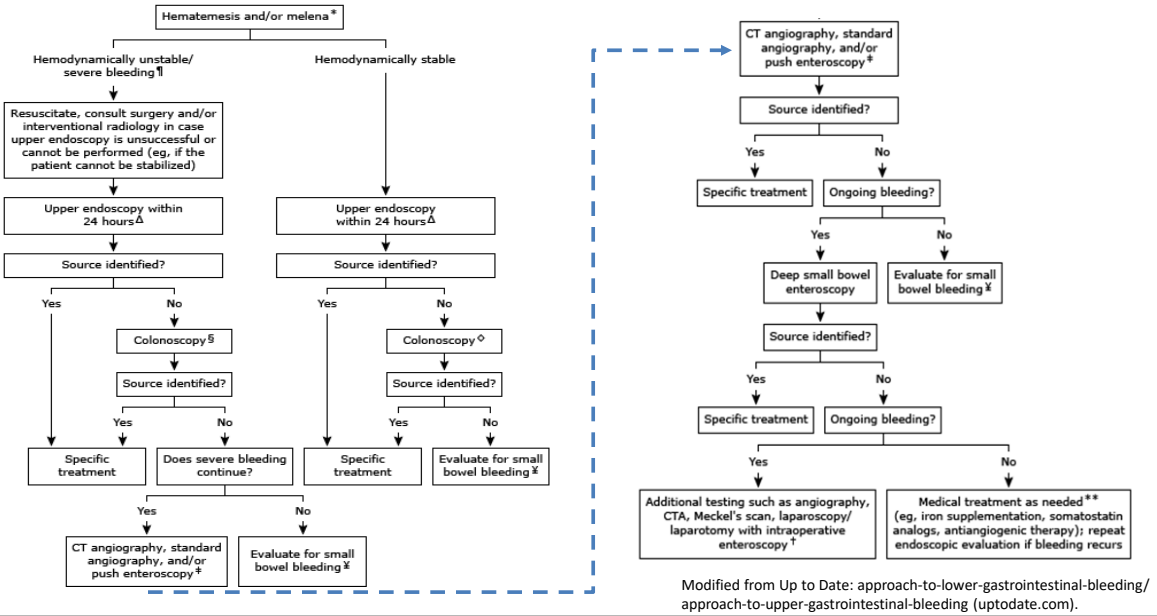
GI Bleeding: Approach



Modified from Up to Date: approach-to-lower-gastrointestinal-bleeding/ approach-to-upper-gastrointestinal-bleeding (uptodate.com).

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GI Bleeding: Endoscopy

Forrest Classification

- First described in 1974 by J.A. Forrest et al. in The Lancet
- Standardized classification system for endoscopists to describe peptic ulcers
- Helps prognosticate and risk stratify patients based on stigmata of recent hemorrhage and decide on discharge versus close inpatient monitoring

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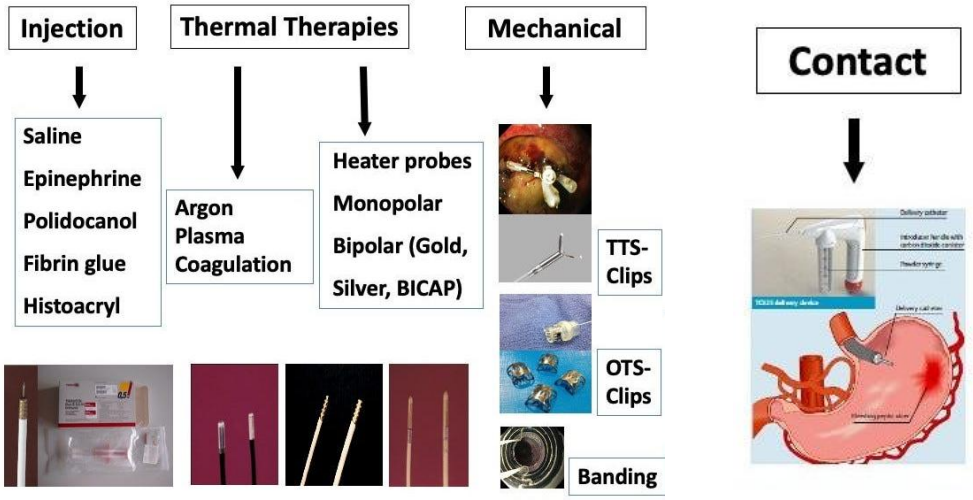
GI Bleeding: Endoscopy



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https://endocollab.com/blogs/gi-endoscopy-tips-tricks/treating-upper-gastrointestinal-bleeding-an-update-on-endoscopic-techniques/

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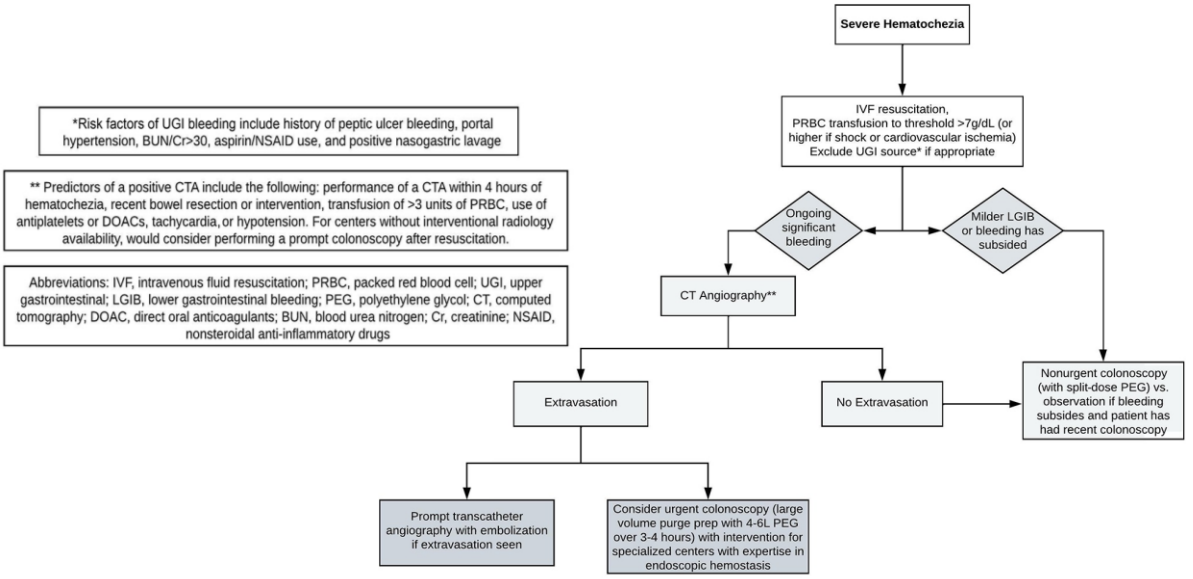
GI Bleeding: Lower GI Bleeding



Sengupta, N. The American Journal of Gastroenterology 118(2):p 208-231, February 2023.

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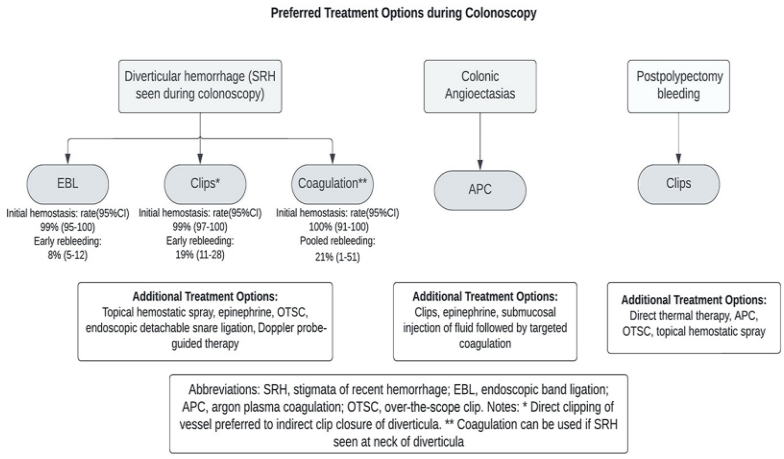
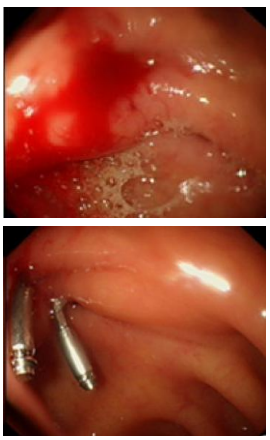
GI Bleeding: Lower GI Bleeding





Sengupta, N. The American Journal of Gastroenterology 118(2):p 208-231, February 2023.

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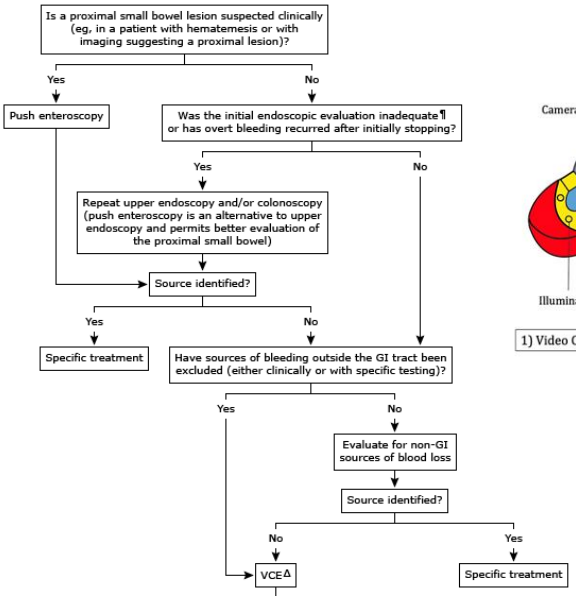
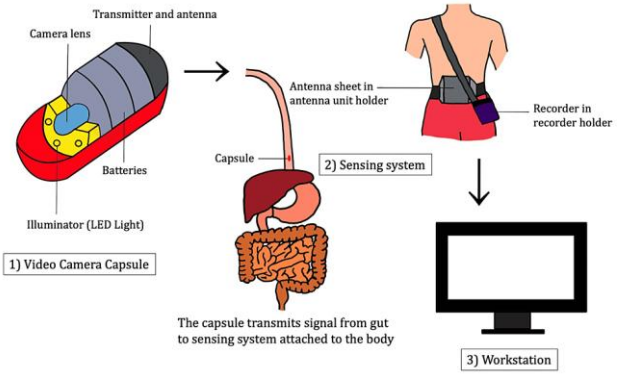
GI Bleeding: Suspected Small Bowel Bleeding





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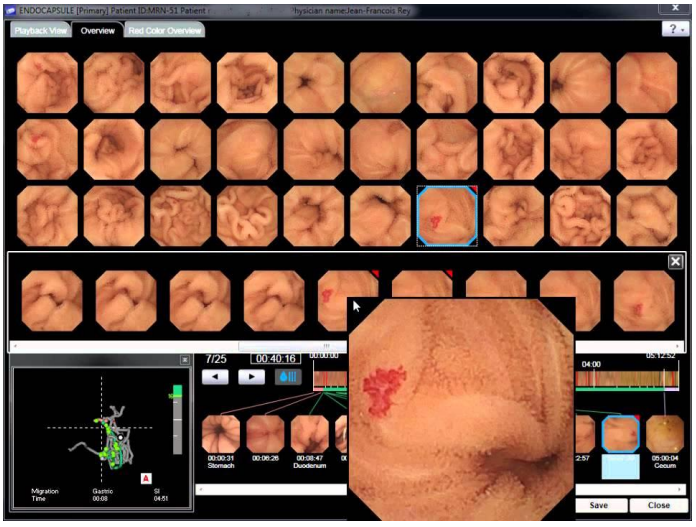
GI Bleeding: Suspected Small Bowel Bleeding



WEO Video Capsule Endoscopy (VCE) Library: clinical case 51

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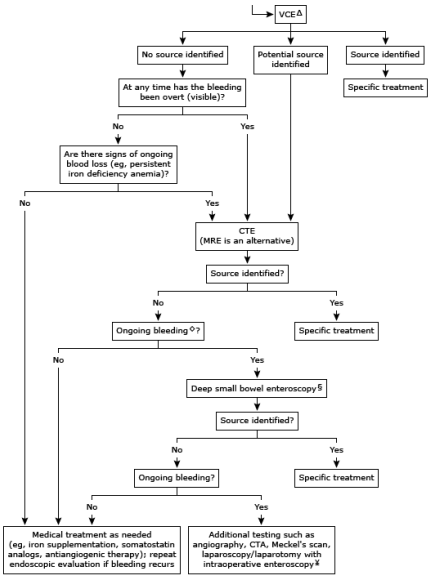
Capsule Endoscopy (VCE) in SBB

- **What is Capsule Endoscopy (VCE)?**
  - A non-invasive method to visualize the small bowel.
- Involves swallowing a capsule with a camera that takes images as it moves through the gastrointestinal tract.
- **Indications for VCE**
  - When other diagnostic tests are negative or inconclusive.
  - Recurrent or obscure bleeding with suspected small bowel origin.
- **Visual Findings on VCE**
  - Vascular malformations
  - Tumors (e.g., lymphoma, adenocarcinoma)
  - Inflammatory lesions (e.g., Crohn's disease)



Modified from Up to Date: approach-to-lower-gastrointestinal-bleeding/ approach-to-upper-gastrointestinal-bleeding (uptodate.com).

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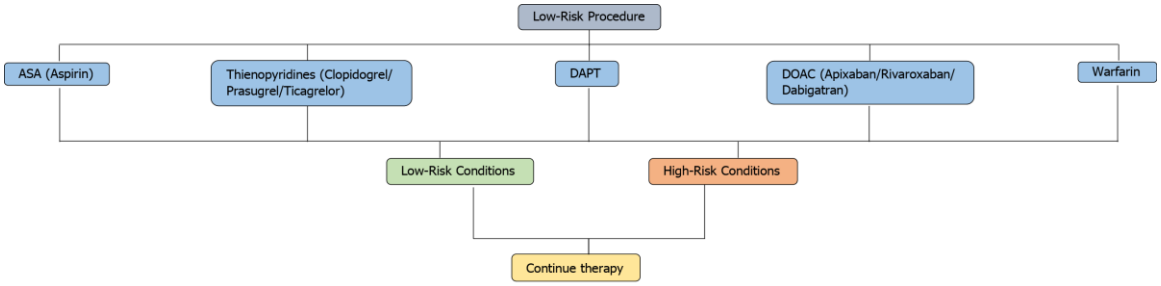
Anticoagulants/APA and Endoscopy



Low-Risk Procedures

- Diagnostic endoscopy with biopsy
- ERCP with stenting without sphincterotomy
- EUS without FNA
- Diagnostic push or device assisted enteroscopy
- Capsule endoscopy
- Oesophageal, enteral, and colonic stenting
- Argon plasma coagulation
- Barrett's ablation

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Anticoagulants/APA and Endoscopy

High-Risk Procedures	
- Polypectomy - ESD - EMR of polyps ≥ 2 cm - ERCP with sphincterotomy +/- balloon sphincteroplasty - Ampullectomy	- Therapy of varices - PEG / PEJ insertion - EUS with FNA - Dilatation of strictures - Cystgastrostomy - Tumour ablation - Balloon enteroscopy

Low-Risk Conditions	High-Risk Conditions[4]
- Mechanical aortic valve (without any risk factors[1]) - All bioprosthetic heart valves - VTE > 12 mo (with no other risk factors[1]) - Stable CAD - AF without valvular disease and CHA_2DS_2-VASc[2] < 2	- AF with mitral stenosis - Mechanical mitral valve - Mechanical aortic valve with one or more risk factors[1] - VTE < 3-12 mo - Thrombophilia - AF with CHA_2DS_2-VASc[2]≥2 - PCI – DES ≤ 12 mo or BMS ≤ 3 mo (with no other history of stent occlusion)[3] - Active malignancy
[1]AF, prior CVA or TIA, HTN, DM, CCF, age > 75	
[2]CHA_2DS_2-VASc = CCF, HTN, age ≥ 75 (2 pts), DM, stroke (2 pts), vascular disease, age 65–74, female	
[3]If ACS or PCI < 6 wk, ideally defer the procedure unless emergency procedure	
[4]Medium-risk conditions (indicated in the APAGE-APSDE guideline only) have been considered as high-risk procedures	

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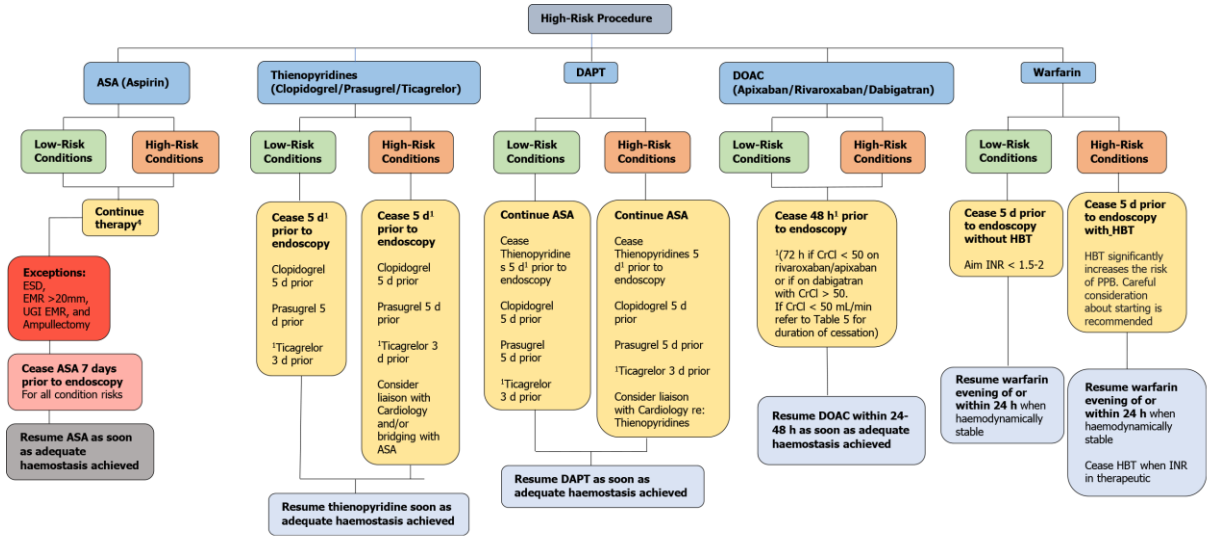
Anticoagulants/APA and Endoscopy



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Which of These Is Not Considered a Warning Sign for Urgent Endoscopy in Dyspepsia?

A. Anemia- GI Bleeding
B. Unintentional weight loss
C. Age > 45
D. Early satiety
E. Dysphagia