Review of Acute GI Bleeds

Endoscopy Skills Day for Practicing Endoscopists

The Rimrock Resort Hotel
Banff, Alberta
January 18, 2020

Rajveer Hundal, MD, FRCPC

ASEP

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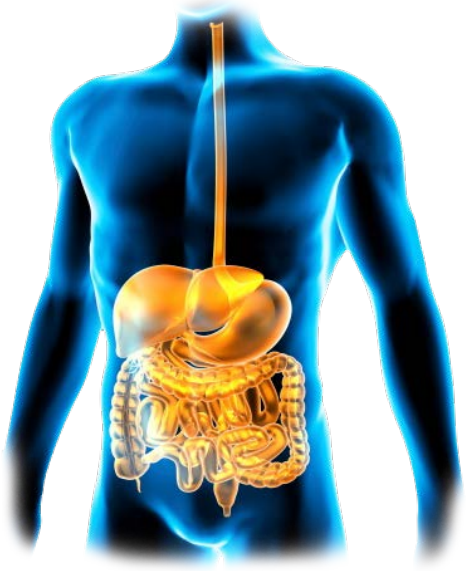
The Gastrointestinal Tract



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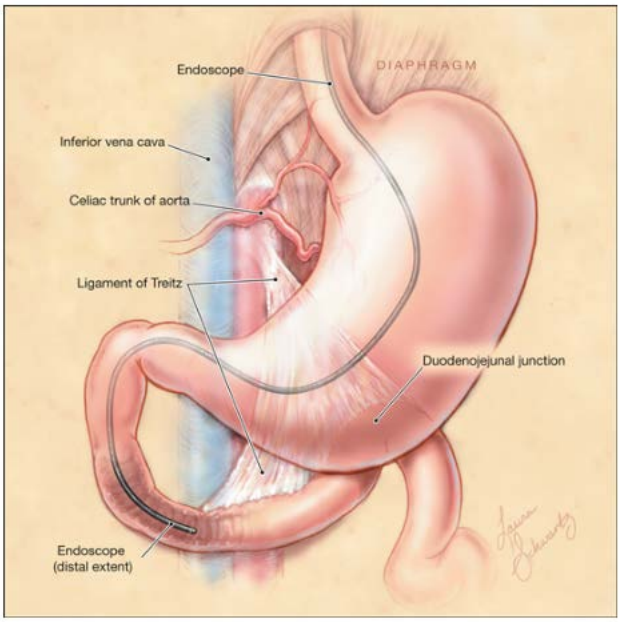

JAMA

JAMA, March 14, 2012—Vol 307, No. 10

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Objectives

- Review common causes of upper gastrointestinal bleeds.
- Understand clinical features associated with GI bleeds.
- Discuss management principles for GI bleeds.

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Causes of Upper GI Bleeds

Diagnosis	Distinguishing features	Frequency (%)
Peptic ulcer bleeding	History of aspirin or nonsteroidal anti-inflammatory drug use associated with abdominal pain, food consumption reduces pain, nocturnal symptoms, history of peptic ulcer bleeding or *Helicobacter pylori* infection	62
Gastritis and duodenitis	Same as peptic ulcer bleeding	8
Esophageal varices	History of cirrhosis and portal hypertension	6
Mallory-Weiss tear	History of repeated retching or vomiting	4
Gastrointestinal malignancy	History of weight loss, smoking, or alcohol consumption; more common in Asians	2
Arteriovenous malformations	Painless bleeding in older patients (older than 70 years), history of iron deficiency anemia	10
Esophagitis or esophageal ulcer	Heartburn, indigestion, or dysphagia	
Dieulafoy ulcer	Painless bleeding, more common in men	
No identifiable source	—	8

American Family Physician
Volume 85, Number 5 • March 1, 2012

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Approach to acute upper GI bleeds

- **History:** Hematemesis, coffee-ground emesis, melena, hematochezia
- **PMHx:** Previous GI bleed, Liver disease/EtOH, A-E fistula, Angiodysplasia (aortic/renal disease), PUD, NSAIDs, H. pylori, Malignancy
- **Medications:** NSAIDs, pill esophagitis, Plavix/anticoagulants, iron/bismuth
- **Physical Exam:** Hemodynamic stability (hypovolemia)
  - Mild to moderate: resting tachycardia
  - ≥ 15%: orthostatic hypotension
  - ≥ 40%: supine hypotension

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Does This Patient Have a Severe Upper Gastrointestinal Bleed?

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Clinical Factors	Sensitivity, % (95% CI)	Specificity, % (95% CI)	Positive LR (95% CI)	Negative LR (95% CI)
Demographic and historical features				
Prior history of UGIB[8]	22 (18-25)	96 (94-98)	6.2 (2.8-14.0)	0.81 (0.74-0.89)
Age <50 y[8]	27 (22-31)	92 (89-95)	3.5 (2.0-6.1)	0.80 (0.71-0.89)
Cirrhosis[8]	5 (3-6)	99 (97-99.4)	3.1 (0.78-12.0)	0.97 (0.93-1.00)
Warfarin use[8]	12 (8-15)	95 (93-97)	2.3 (1.1-5.0)	0.93 (0.87-1.00)
Iron use[8]	6 (3-8)	98 (96-99)	2.2 (0.7-6.6)	0.97 (0.93-1.00)
History of LGIB[8]	6 (3-11)	64 (62-67)	0.17 (0.09-0.35)	1.5 (1.3-1.6)
Symptoms				
Black stool history (melena)[8,27,a]	77-95	81-87	5.1-5.9	0.06-0.27
Epigastric pain[8]	17 (12-21)	93 (90-95)	2.3 (1.2-4.4)	0.90 (0.82-0.98)
Signs				
Melenic stool on examination[27]	49 (45-50)	98 (91-99.6)	25 (4-174)	0.52 (0.42-0.64)
Nasogastric lavage with blood or coffee grounds[28]	44 (39-48)	95 (90-98)	9.6 (4.0-23.0)	0.58 (0.49-0.70)
Clots in stool[8]	15 (14-15)	99.2 (96.0-99.9)	0.05 (0.01-0.38)	1.2 (1.1-1.2)
Laboratory findings				
Serum urea nitrogen: creatinine ratio >30[8,29-33,b]	51 (26 to 75)	93 (87 to 99)	7.5 (2.8-12.0)	0.53 (0.28-0.78)
Hematocrit, %[8,c]				
≤20	NA	NA	2.6 (1.4-4.6)	
21-29	NA	NA	1.9 (1.4-2.5)	
30-39	NA	NA	0.46 (0.32-0.65)	
≥40	NA	NA	0.26 (0.10-0.67)	

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Does This Patient Have a Severe Upper Gastrointestinal Bleed?

JAMA THE RATIONAL CLINICAL EXAMINATION

Clinical Factors	Sensitivity, % (95% CI)	Specificity, % (95% CI)	Positive LR (95% CI)	Negative LR (95% CI)
Demographic and historical features				
History of malignancy or cirrhosis[34]	22 (14-28)	94 (92-96)	3.7 (1.6-8.8)	0.83 (0.72-0.97)
Cirrhosis[35]	15 (12-18)	95 (94-97)	3.2 (2.1-4.9)	0.89 (0.85-0.94)
Syncope[35]	8 (6-10)	98 (97-98)	3.0 (1.7-5.4)	0.95 (0.91-0.98)
Analgesic use[36]	13 (8-19)	95 (94-96)	2.6 (1.3-5.2)	0.92 (0.84-0.99)
Coffee ground vomiting[35]	7 (4-10)	83 (82-84)	0.41 (0.26-0.64)	1.1 (1.1-1.2)
Hematochezia[35]	2 (1-4)	92 (91-93)	0.22 (0.09-0.53)	1.1 (1.0-1.1)
Signs				
Pulse rate >100/min[34]	71 (60-79)	86 (82-89)	4.9 (3.2-7.6)	0.34 (0.22-0.53)
Nasogastric lavage, red blood[16,17,21,34,b]	77 (57-90)	76 (32-95)	3.1 (1.2-14.0)	0.32 (0.17-0.57)
Shock[17,34,c,d]	78 (56-90)	71 (46-88)	2.8 (1.1-7.2)	0.32 (0.10-0.96)
Nasogastric lavage, red blood or coffee grounds[17,21,28,c]	81 (67-89)	55 (19-87)	2.0 (1.0-4.0)	0.40 (0.20-0.81)
Hypotension[34,36,e]	55-59	53-89	1.2-4.8	0.51-0.78
Laboratory findings				
Hemoglobin level <8 g/dL[34,e]	65-68	86-89	4.5-6.2	0.36-0.41
Serum urea nitrogen level >90 mg/dL[34]	63 (52-72)	83 (79-86)	3.6 (2.4-5.5)	0.45 (0.31-0.65)
White blood cell count >12 x10^9/L[34]	61 (50-71)	82 (78-86)	3.4 (2.2-5.1)	0.48 (0.34-0.68)

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Management of UGIB

- Resuscitation, risk assessment, and pre-endoscopy management
- Endoscopic management
- Pharmacologic management
- Non-endoscopic and nonpharmacologic in-hospital management
- Secondary prophylaxis

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Resuscitation, Risk Assessment, and Pre-endoscopy Management

- Fluid resuscitation should be initiated in acute UGIB/hemodynamic instability.
- Uncertainty remains regarding the type of fluid (colloid vs. crystalloid) and the rate and timing of resuscitation (aggressive vs. restrictive).

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Scoring Systems

- Glasgow Blatchford
- Rockall Score
- AIMS65 Score

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Risk Scores: Blatchford

Blood urea nitrogen

- ○ <18.2 mg/dL (<6.5 mmol/L) (0 points)
- ○ >=18.2 and <22.4 mg/dL (>=6.5 and <8 mmol/L) (2 points)
- ○ >=22.4 and <28 mg/dL (>=8 and <10 mmol/L) (3 points)
- ○ >=28 and <70 mg/dL (>=10 and <25 mmol/L) (4 points)
- ○ >=70 mg/dL (>=25 mmol/L) (6 points)

Hemoglobin

- ○ Male >=13 g/dL (>130 g/L) (0 points)
- ○ Male >=12 and <13 g/dL (>=120 and <130 g/L) (1 point)
- ○ Male >=10 and <12 g/dL (>=100 and <120 g/L) (3 points)
- ○ Female >=12 g/dL (>120 g/L) (0 points)
- ○ Female >=10 and <12 g/dL (>=100 and <120 g/L) (1 point)
- ○ Male or female <10 g/dL (<100 g/L) (6 points)

Systolic blood pressure

- ○ >=110 mmHg (0 points)
- ○ 100 to 109 mmHg (1 point)
- ○ 90 to 99 mmHg (2 points)
- ○ <90 mmHg (3 points)

Other markers

- ☐ Heart rate >=100 per minute (1 point)
- ☐ Melena at presentation (1 point)
- ☐ Syncope at presentation (2 points)
- ☐ Hepatic disease present (2 points)
- ☐ Cardiac failure present (2 points)

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Risk Stratification Scores: Rockall

Age

- ◯ <60 years old (0 points)
- ◯ 60-79 years old (1 point)
- ◯ >=80 years old (2 points)

Hemodynamic Shock

- ◯ None with systolic BP >=100 mmHg and pulse <100/min (0 points)
- ◯ Tachcardic with pulse >=100/min but systolic BP >=100 mmHg (1 point)
- ◯ Hypotension with systolic BP <100 mmHg (2 points)

Major Comorbidities

- ◯ None (0 points)
- ◯ Cardiac failure, ischemic heart disease or similar major comorbidity (2 points)
- ◯ Renal failure, hepatic failure or disseminated cancer (3 points)

Diagnosis

- ◯ Mallory-Weiss tear, but no major lesions and no stigmata of recent bleed (0 points)
- ◯ Other nonmalignant gastrointestinal diagnoses (1 point)
- ◯ Upper gastrointestinal tract malignancy (2 points)

Recent hemorrhage

- ◯ None (or dark area only) (0 points)
- ◯ Blood found in upper gastrointestinal tract (clot adherence, spurting or visible vessel) (2 points)

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Risk Scores: AIMS65

- **A**lbumin less than 30 g/L
- **I**NR greater than 1.5
- Altered **M**ental status (Glasgow coma score less than 14, disorientation, lethargy, stupor, or coma)
- **S**ystolic blood pressure of 90 mmHg or less
- Age older than **65** years

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- Consider placement of a nasogastric tube in selected patients because the findings may have prognostic value.
- In patients with acute UGIB without underlying cardiovascular disease, we suggest giving blood transfusions for those with a hemoglobin level <80 g/L.
- In patients with acute UGIB with underlying cardiovascular disease, we suggest giving blood transfusions at a higher hemoglobin threshold than for those without cardiovascular disease.

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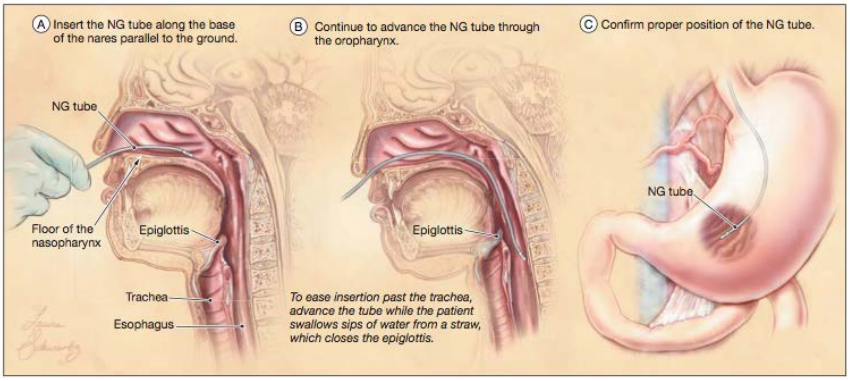
THE RATIONAL CLINICAL EXAMINATION

CLINICIAN'S CORNER

Does This Patient Have a Severe Upper Gastrointestinal Bleed?



JAMA, March 14, 2012—Vol 307, No. 10

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The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 JANUARY 3, 2013 VOL. 368 NO. 1

Transfusion Strategies for Acute Upper Gastrointestinal Bleeding

RESULTS

A total of 225 patients assigned to the restrictive strategy (51%), as compared with 61 assigned to the liberal strategy (14%), did not receive transfusions (P<0.001). The probability of survival at 6 weeks was higher in the restrictive-strategy group than in the liberal-strategy group (95% vs. 91%; hazard ratio for death with restrictive strategy, 0.55; 95% confidence interval [CI], 0.33 to 0.92; P=0.02). Further bleeding occurred in 10% of the patients in the restrictive-strategy group as compared with 16% of the patients in the liberal-strategy group (P=0.01), and adverse events occurred in 40% as compared with 48% (P=0.02). The probability of survival was slightly higher with the restrictive strategy than with the liberal strategy in the subgroup of patients who had bleeding associated with a peptic ulcer (hazard ratio, 0.70; 95% CI, 0.26 to 1.25) and was significantly higher in the subgroup of patients with cirrhosis and Child–Pugh class A or B disease (hazard ratio, 0.30; 95% CI, 0.11 to 0.85), but not in those with cirrhosis and Child–Pugh class C disease (hazard ratio, 1.04; 95% CI, 0.45 to 2.37). Within the first 5 days, the portal-pressure gradient increased significantly in patients assigned to the liberal strategy (P=0.03) but not in those assigned to the restrictive strategy.

CONCLUSIONS

As compared with a liberal transfusion strategy, a restrictive strategy significantly improved outcomes in patients with acute upper gastrointestinal bleeding. (Funded by Fundació Investigació Sant Pau; ClinicalTrials.gov number, NCT00414713.)

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- In patients with acute UGIB receiving anticoagulants (vitamin K antagonists, DOACs), we suggest not delaying endoscopy (with or without endoscopic hemostatic therapy).
- Promotility agents should not be used routinely before endoscopy to increase the diagnostic yield.
- Selected patients with acute ulcer bleeding who are at low risk for rebleeding on the basis of clinical and endoscopic criteria may be discharged promptly after endoscopy.
- Pre-endoscopic PPI therapy may be considered to downstage the endoscopic lesion and decrease the need for endoscopic intervention but should not delay endoscopy.

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ORIGINAL ARTICLE

Omeprazole before Endoscopy in Patients with Gastrointestinal Bleeding

METHODS

Consecutive patients admitted with upper gastrointestinal bleeding underwent stabilization and were then randomly assigned to receive either omeprazole or placebo (each as an 80-mg intravenous bolus followed by an 8-mg infusion per hour) before endoscopy the next morning.

RESULTS

Over a 17-month period, 638 patients were enrolled and randomly assigned to omeprazole or placebo (319 in each group). The need for endoscopic treatment was lower in the omeprazole group than in the placebo group (60 of the 314 patients included in the analysis [19.1%] vs. 90 of 317 patients [28.4%], P=0.007). There were no significant differences between the omeprazole group and the placebo group in the mean amount of blood transfused (1.54 and 1.88 units, respectively; P=0.12) or the number of patients who had recurrent bleeding (11 and 8, P=0.49), who underwent emergency surgery (3 and 4, P=1.00), or who died within 30 days (8 and 7, P=0.78). The hospital stay was less than 3 days in 60.5% of patients in the omeprazole group, as compared with 49.2% in the placebo group (P=0.005). On endoscopy, fewer patients in the omeprazole group had actively bleeding ulcers (12 of 187, vs. 28 of 190 in the placebo group; P=0.01) and more omeprazole-treated patients had ulcers with clean bases (120 vs. 90, P=0.001).

CONCLUSIONS

Infusion of high-dose omeprazole before endoscopy accelerated the resolution of signs of bleeding in ulcers and reduced the need for endoscopic therapy. (ClinicalTrials.gov number, NCT00164866.)

The NEW ENGLAND JOURNAL of MEDICINE

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Proton pump inhibitor treatment initiated prior to endoscopic diagnosis in upper gastrointestinal bleeding

- There is conflicting evidence regarding the clinical efficacy of proton pump inhibitors (PPI) initiated before endoscopy for upper gastrointestinal bleeding.

Main results

- 6 RCTs with n = 2223
- PPI treatment significantly reduced endoscopic therapy at index endoscopy (OR 0.68; 95% CI 0.50 to 0.93)
- No differences in mortality, re-bleeding or surgery between groups

Conclusions

- PPI treatment initiated before endoscopy for upper gastrointestinal bleeding might reduce the proportion of participants with treatment at index endoscopy and significantly reduces requirement for endoscopic therapy during index endoscopy.
  - there is no evidence that PPI treatment affects clinically important outcomes, namely mortality, rebleeding or need for surgery.

Cochrane Library

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Medications

- **Acid suppression:** IV PPI bolus followed by oral PPI daily if no recurrent bleeding after 72-hrs.
- **Prokinetics** (erythromycin and metoclopramide) can aid in gastric visualization before endoscopy.
- **Octreotide** can aid in the treatment if variceal bleeding
- Abx for patients with cirrhosis to reduce infectious complications and potential mortality.
- **Tranexamic acid** is an antifibrinolytic agent found a benefit with mortality but not bleeding, surgery or transfusion requirements → usually not given.
- Anticoagulant reversal: vitamin K, FFP, octaplex.

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Endoscopic Management

- Develop institution-specific protocols for multidisciplinary management. Include access to an endoscopist trained in endoscopic hemostasis.
- Have support staff trained to assist in endoscopy available on an urgent basis.
- For patients admitted with acute UGIB, we suggest performing early endoscopy (within 24 hours of presentation).

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Alberta Health Services

Gastrointestinal Bleed, Adult – Inpatient Order Set

For Suspected or known ulcer bleed

Intermittent proton-pump inhibitors IV (PPI) is equivalent to IV PPI infusions for patients with known ulcer bleeds. Furthermore, IV dosing has failed to show superiority to PO dosing. IV infusions are generally not indicated; suggest PO dosing in stable patients not actively vomiting.

- ☐ pantoprazole 40 mg IV/PO BID for 72 hours post endoscopy
  OR
- ☐ pantoprazole 40 mg PO every 12 hours

For Suspected or known variceal bleed

- ☐ octreotide IV loading dose: 50 microgram IV x 1

Antibacterial

If cirrhosis

For antibiotics, if UGIB in the setting of cirrhosis, decreases mortality, rebleeding and sepsis

Choose ONE while NPO:
For cefTRIAXone IV, recommended duration of 5-10 days. 10 days recommended if bacteremic. 5 days if repeat paracentesis (at 48 hours) shows less than 0.25 x 10exp9/L PMNs and culture negative.

- ☐ cefTRIAXone 1 g IV daily for _____ days

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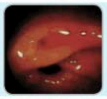
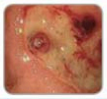
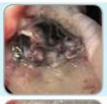
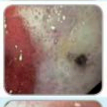
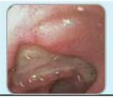
FORREST CLASSIFICATION OF ULCERS			REBLEED RISK (WITHOUT THERAPY)
I: BLEEDING	Ia Spurting		85-100%
	Ib Oozing		10-30%
II: STIGMATA OF RECENT HAEMORRHAGE	IIa "Visible Vessel"		50-60%
	IIb Adherent Clot		25-35%
	IIc Pigmented Spot		<8%
III: CLEAN BASE			<5%

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- Endoscopic hemostatic therapy is not indicated for patients with low-risk stigmata (a clean-based ulcer).
- A finding of a clot in an ulcer bed warrants targeted irrigation in an attempt at dislodgement, with appropriate treatment of the underlying lesion.
- The role of endoscopic therapy for ulcers with adherent clots is controversial. Endoscopic therapy may be considered, although intensive PPI therapy alone may be sufficient.

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- Endoscopic hemostatic therapy is indicated for patients with high-risk stigmata (active bleeding or a visible vessel in an ulcer bed).
- Epinephrine injection alone provides suboptimal efficacy and should be used in combination with another method.
- No single method of endoscopic thermal coaptive therapy is superior to another.

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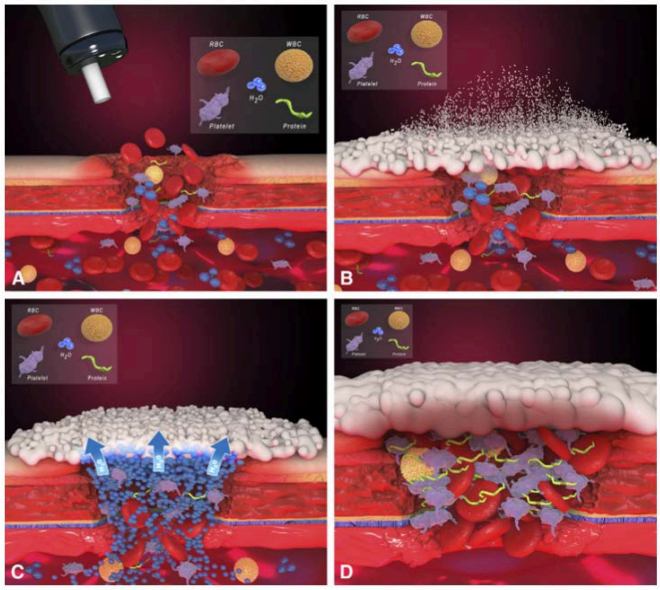
Hemospray



Volume 77, No. 5 : 2013 GASTROINTESTINAL ENDOSCOPY

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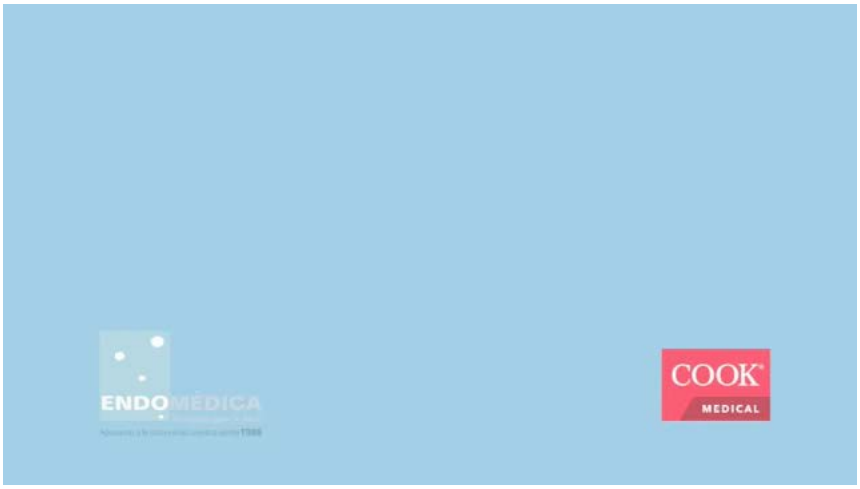

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- For patients with acutely bleeding ulcers with high-risk stigmata, we recommend endoscopic therapy with thermocoagulation or sclerosant injection.
- For patients with acutely bleeding ulcers with high-risk stigmata, we suggest endoscopic therapy with (through-the-scope) clips.
- In patients with actively bleeding ulcers, we suggest using TC-325 as a temporizing therapy to stop bleeding when conventional endoscopic therapies are not available or fail.
- In patients with actively bleeding ulcers, we suggest *against* using TC-325 as a single therapeutic strategy vs. conventional endoscopic therapy (clips alone, thermocoagulation alone, or combination therapy).

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- Routine second-look endoscopy is not recommended.
- A second attempt at endoscopic therapy is generally recommended in cases of rebleeding.

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Pharmacologic management

- H2RAs are not recommended for patients with acute ulcer bleeding.
- Somatostatin and octreotide are not routinely recommended for patients with acute ulcer bleeding.
- For patients with bleeding ulcers with high-risk stigmata who have undergone successful endoscopic therapy, we recommend using PPI therapy via intravenous loading dose followed by continuous intravenous infusion (as opposed to no treatment or H2RAs).

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- For patients who present with ulcer bleeding at high risk for rebleeding (that is, an ulcer requiring endoscopic therapy followed by 3 days of high-dose PPI therapy), we suggest using twice-daily oral PPIs (vs. once-daily) through 14 days, followed by once daily.
- Patients should be discharged with a prescription for a single daily-dose oral PPI for a duration as dictated by the underlying cause.

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Non-endoscopic and non-pharmacologic in-hospital management

- Patients at low risk after endoscopy can be fed within 24 hours.
- Most patients who have undergone endoscopic hemostasis for high-risk stigmata should be hospitalized for at least 72 hours thereafter.
- Seek surgical consultation for patients for whom endoscopic therapy has failed.

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- Where available, percutaneous embolization can be considered as an alternative to surgery for patients for whom endoscopic therapy has failed.
- Patients with bleeding peptic ulcers should be tested for *Helicobacter pylori* and receive eradication therapy if it is present, with confirmation of eradication.
- Negative *H pylori* diagnostic tests obtained in the acute setting should be repeated.

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Secondary Prophylaxis

- In patients with previous ulcer bleeding who require an NSAID, treatment with a traditional NSAID plus a PPI or COX-2 inhibitor alone is still associated with a clinically important risk for recurrent ulcer bleeding.
- In patients with previous ulcer bleeding who require an NSAID, the combination of a PPI and a COX-2 inhibitor is recommended to reduce the risk for recurrent bleeding from that of COX-2 inhibitors alone.
- In patients who receive low-dose ASA and develop acute ulcer bleeding, ASA therapy should be restarted as soon as the risk for cardiovascular complication is thought to outweigh the risk for bleeding.

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- In patients with previous ulcer bleeding receiving cardiovascular prophylaxis with single- or dual-antiplatelet therapy, we suggest using PPI therapy vs. no PPI therapy.
- In patients with previous ulcer bleeding requiring continued cardiovascular prophylaxis with anticoagulant therapy (vitamin K antagonists, DOACs), we suggest using PPI therapy vs. no PPI therapy.

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Push Enteroscopy

- Extended upper endoscopy performed with a long endoscope (typically 250 cm in length).
  - Pediatric colonoscope, commercial push enteroscope
- An ideal second-look procedure as examination of distal duodenum and proximal jejunum is possible.
- Allows for a limited view of the proximal small bowel (~ 70 cm distal to ligament of treitz).
- Looping and patient discomfort are disadvantages which may be prevented with an overtube.

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Video Capsule Endoscopy (VCE)

- Introduced in the US in 2001.
- The VCE measures 26x11 mm^2 and has the capacity to take images at the rate of 2 frames/s, over an 8–12 h period.
- Findings on VCE leading to endoscopic or surgical intervention or a change in medical management have been reported in 37-87% of patients.
- Up to 66% of patients remain transfusion free after VCE-directed interventions.
- Re-bleeding rates range from 6-27% in patients with a negative capsule study.

Gastroenterology 2004;126:643–53.
Gastroenterol 2006;101:1224–8.

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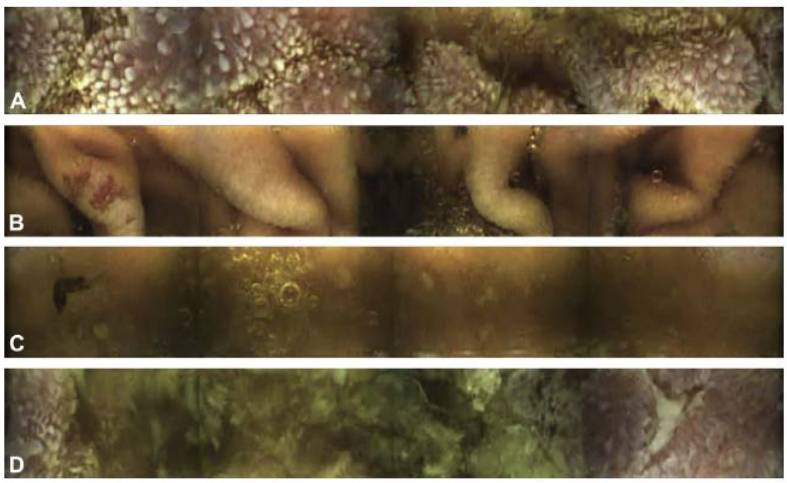
VCE continued…



GASTROINTESTINAL ENDOSCOPY Volume 85, No. 2 : 2017

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VCE continued…

Increased Yield	Limitations
Hemoglobin < 100 g/L	Lack of therapeutic capabilities
Longer duration of bleeding (> 6 mos)	Inability to control movement through GI tract
> 1 episode of bleeding	Difficulty in localizing lesions
Within 2 weeks of bleeding episode	Fails to identify major papilla in a majority of cases
Male gender, age > 60 are also independent predictors	Up to 36% false negative rate
Cardiac comorbidity	Capsule retention in ~ 1.5% of patients
Renal comorbidity	Perforation – exceedingly rare

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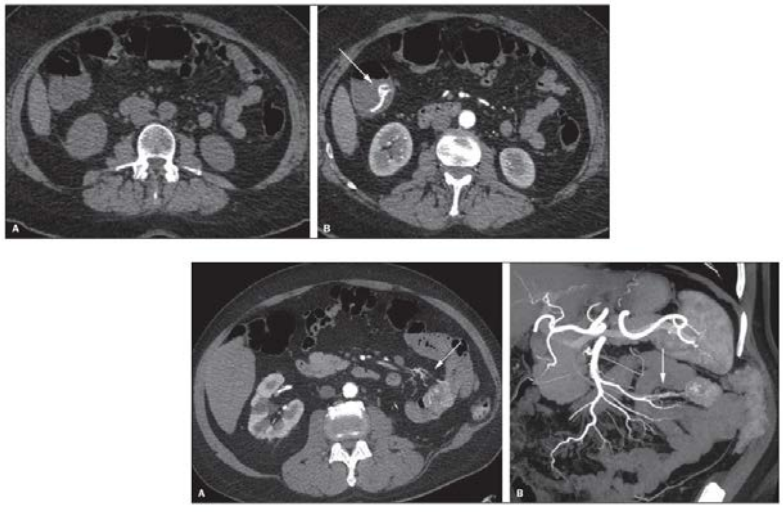
CT Angiography

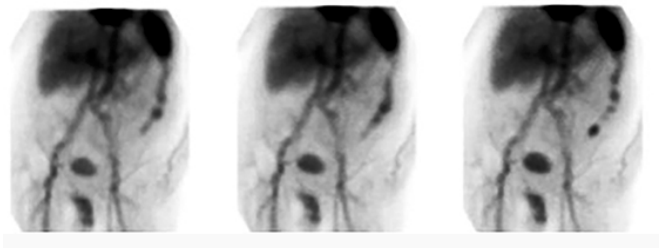


Reis FRS et al. / **CT angiography in active gastrointestinal bleeding**

42

Scintigraphy

- ^{99m}Tc-labeled RBC scintigraphy can detect lower rates of bleeding (0.2 mL/min).
- Radioisotope which can bind to RBCs and thus detect gastrointestinal bleeding.
- Some variability in localization of bleeding and inability to characterize source of bleeding.



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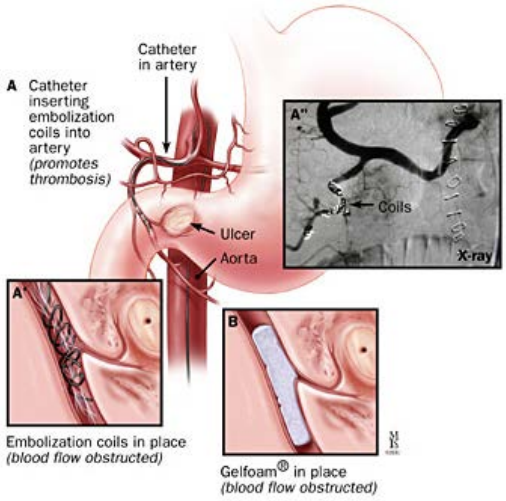
Angiography

- Offers diagnostic and therapeutic interventions for patients with transarterial embolization.
- For small vascular abnormalities that require surgical intervention, placement of a catheter in the vessel supplying the vascular abnormality and dye staining can assist with intraoperative localization.
- Requires higher rates of bleeding for detection (0.5-1.0 mL/min).
- Potential complications include:
  - Renal failure
  - Infections
  - Thromboembolic events

44

Angiography



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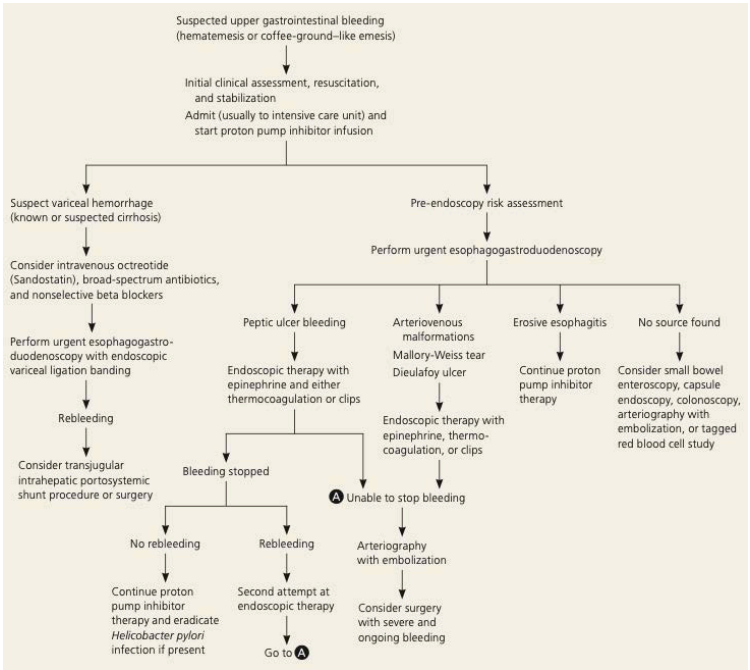

American Family Physician Volume 85, Number 5 • March 1, 2012

46

Conclusions

- Peptic ulcer bleeds are a common cause of upper GI bleeds.
- NGT insertion, Ur:Cr ratio > 30, tachycardia offer the highest positive likelihood rations for an upper GI bleed.
- The Glasgow Blatchford Score should be used to assess patient's need for endoscopy.
- Many treatments exist to aid in management before, during and after endoscopy.
- Plans are under way to develop a user-friendly clinical algorithm for UGIB management.

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Endoscopic Approach to Anemia

Endoscopy Skills Day for Practicing Endoscopists

The Rimrock Resort Hotel
Banff, Alberta
January 18, 2020

Rajveer Hundal, MD, FRCPC

ASEP

49

Iron Deficiency Anemia

- Iron deficiency affects more than 2 billion people worldwide.
- Iron is crucial to biologic functions, including respiration, energy production, DNA synthesis, and cell proliferation.
- Iron-deficiency anemia is a more severe condition in which low levels of iron are associated with anemia and the presence of microcytic hypochromic red cells.

50

Pathophysiology

- The mechanisms of iron acquisition are tightly regulated by hepcidin-based homeostatic controls.
- Hepcidin is a peptide hormone that is synthesized primarily in the liver.
- Hepcidin expression increases in response to high circulating and tissue levels of iron and in persons with systemic inflammation or infection.
- Its production is inhibited by the expansion of erythropoiesis, iron deficiency, and tissue hypoxia in response to signals originating in the bone marrow, the liver, and probably muscle tissue and adipocytes.
- Increases in hepcidin levels ← inflammatory cytokines (interleukin-6)
  - → iron sequestration and reduced supply of erythropoietic iron that occurs in the anemia of chronic disease

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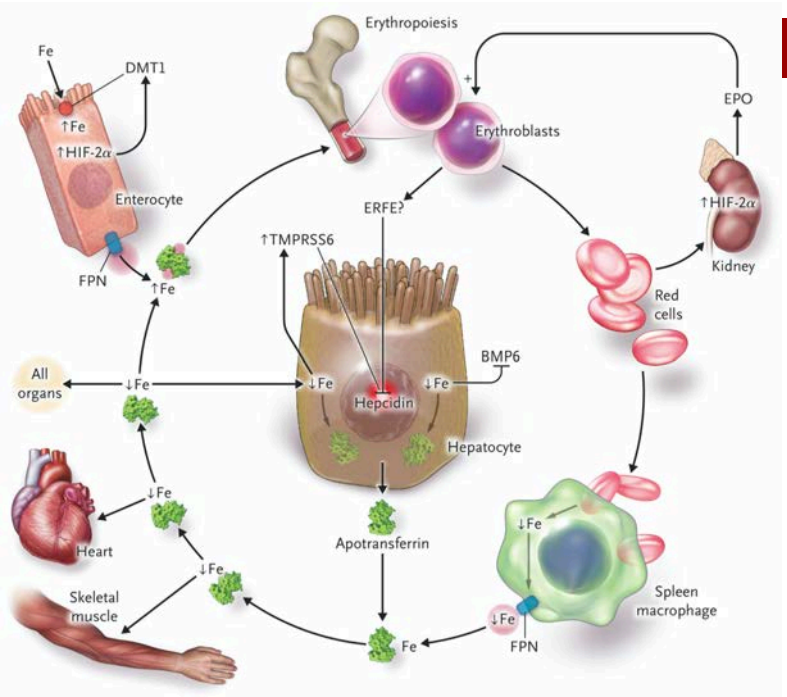

52

Table 1. Causes of Iron Deficiency.

Cause	Example
Physiologic	
Increased demand	Infancy, rapid growth (adolescence), menstrual blood loss, pregnancy (second and third trimesters), blood donation
Environmental	Insufficient intake, resulting from poverty, malnutrition, diet (e.g., vegetarian, vegan, iron-poor)
Pathologic	
Decreased absorption	Gastrectomy, duodenal bypass, bariatric surgery, *Helicobacter pylori* infection, celiac sprue, atrophic gastritis, inflammatory bowel diseases (e.g., ulcerative colitis, Crohn's disease)*
Chronic blood loss	Gastrointestinal tract, including esophagitis, erosive gastritis, peptic ulcer, diverticulitis, benign tumors, intestinal cancer, inflammatory bowel diseases, angiodysplasia, hemorrhoids, hookworm infestation, obscure source Genitourinary system, including heavy menses, menorrhagia, intravascular hemolysis (e.g., paroxysmal nocturnal hemoglobinuria, autoimmune hemolytic anemia with cold antibodies, march hemoglobinuria, damaged heart valves, microangiopathic hemolysis) Systemic bleeding, including hemorrhagic telangiectasia, chronic schistosomiasis, Munchausen's syndrome (e.g, self-induced hemorrhages)
Drug-related	Glucocorticoids, salicylates, NSAIDs, proton-pump inhibitors
Genetic	Iron-refractory iron-deficiency anemia
Iron-restricted erythropoietic	Treatment with erythropoiesis-stimulating agents, anemia of chronic disease, chronic kidney disease*

* Inflammatory conditions may be associated with iron deficiency. NSAIDs denotes nonsteroidal antiinflammatory drugs.

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Table 3. Indications for Parenteral Iron Therapy.

Established indication
Failure of oral therapy
Iron intolerance or with low iron levels that are refractory to treatment (e.g., after gastrectomy or duodenal bypass, with *Helicobacter pylori* infection, or with celiac disease, atrophic gastritis, inflammatory bowel disease, or genetically induced IRIDA*)
Need for quick recovery (e.g., with severe iron deficiency in the second or third trimester of pregnancy or with chronic bleeding that is not manageable with oral iron, as may occur in patients with congenital coagulation disorders)
Substitution for blood transfusions when not accepted by patient for religious reasons
Use of erythropoiesis-stimulating agents in chronic kidney disease
Potential indication
Anemia of chronic kidney disease (without treatment of erythropoiesis-stimulating agents)
Persistent anemia after use of erythropoiesis-stimulating agents in patients with cancer who are receiving chemotherapy
Anemia of chronic disease unresponsive to treatment with erythropoiesis-stimulating agents alone
Potential indication with insufficient supporting data
Iron deficiency in heart failure
Transfusion-sparing strategy in surgical patients

* Celiac disease or *H. pylori* infection should be considered if the anemia remains refractory to treatment. IRIDA denotes iron-refractory iron-deficiency anemia.

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Decreased absorption

- Gastrectomy – decreased intrinsic factor leads to pernicious anemia. Decreased gastric acid limits conversion of dietary iron to absorbable form.
- Duodenal Bypass
- H. pylori infection – Gastritis related to an autoimmune mechanism (eg, anti-parietal cell antibodies) or *H. pylori* has also been implicated in causing iron deficiency.
- Celiac disease - Celiac disease can contribute to anemia by several mechanisms, including iron deficiency, reduced absorption of supplemental iron, and malabsorption of other nutrients required for red blood cell (RBC) production(vitamin B12, folic acid, and copper).
- IBD – UC or Crohn's disease can contribute to malabsorption and bleeding.

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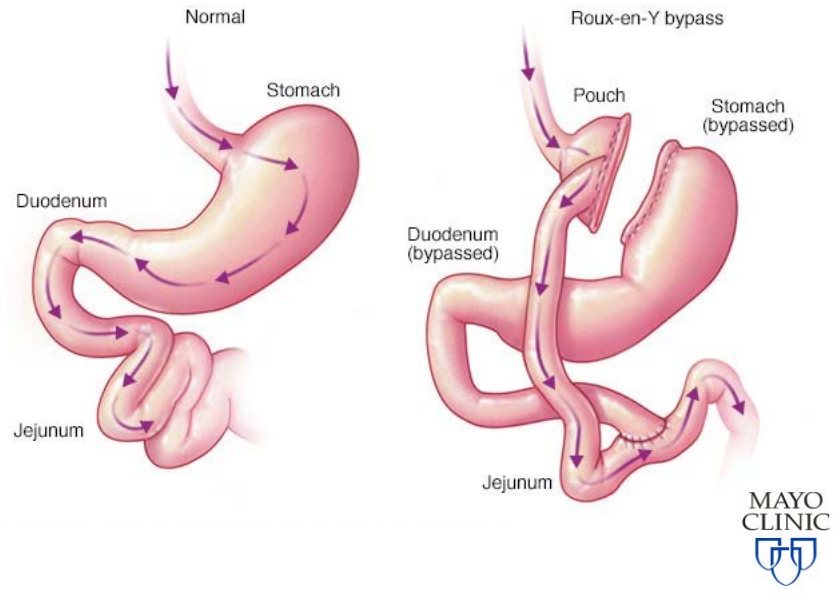


56

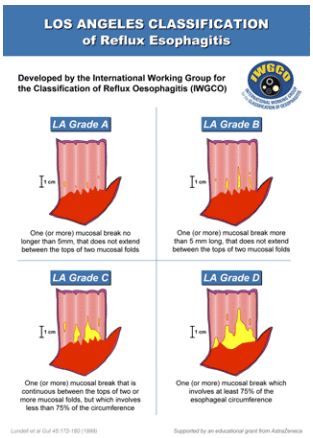
Chronic Blood Loss

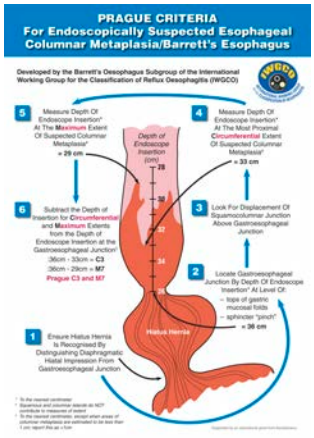
- Esophagitis
- Erosive Gastritis
- Peptic Ulcer Disease
- Diverticulosis/Diverticulitis
- Angiodysplasia
- Hemorrhoids
- Parasitic infection (hookworm)
- Obscure bleeds

57

Esophagitis

- Can be medication induced, related to acid-reflux, eosinophilic esophagitis, related to candida infection etc.





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Drug-related

- Glucocorticoids
- Salicylates
- NSAIDs

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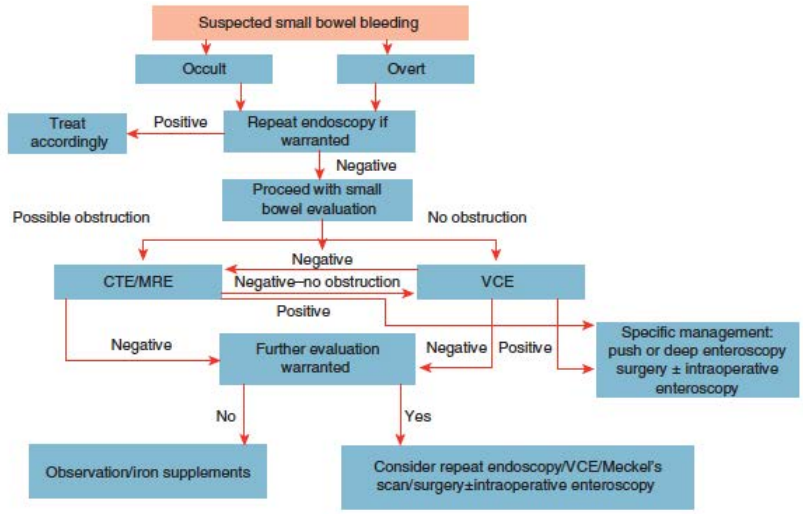

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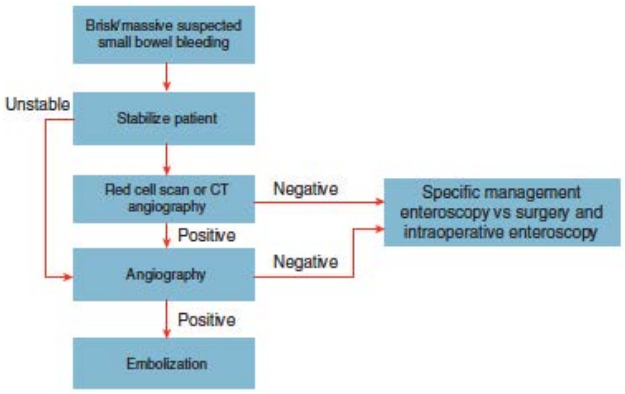
Unstable?



61

Common causes		Rare causes
Under age 40 years	**Over age 40 years**	**Henoch–Schoenlein purpura**
Inflammatory bowel disease	Angioectasia	Small bowel varices and/or portal hypertensive enteropathy
Dieulafoy's lesions	Dieulafoy's lesions	Amyloidosis
Neoplasia	Neoplasia	Blue rubber bleb nevus syndrome
Meckel's diverticulum	NSAID ulcers	Pseudoxanthoma elasticum
Polyposis syndromes		Osler–Weber–Rendu syndrome
		Kaposi's sarcoma with AIDS
		Plummer–Vinson syndrome
		Ehlers–Danlos syndrome
		Inherited polyposis syndromes (FAP, Peutz–Jeghers)
		Malignant atrophic papulosis
		Hematobilia
		Aorto-enteric fistula
		Hemosuccus entericus

FAP, familial adenomatous polyposis; NSAID, nonsteroidal anti-inflammatory drug.

62

Meckel's Diverticulum

- Most common congenital anomaly of the GI tract.
- True diverticulum arising from the antimesenteric surface of the mid-to-distal ileum.
- 'Rule of twos.'
- Often clinically silent, can present as GI bleed, abdominal pain (bowel obstruction).
- Diverticulectomy can be considered for symptomatic patients.

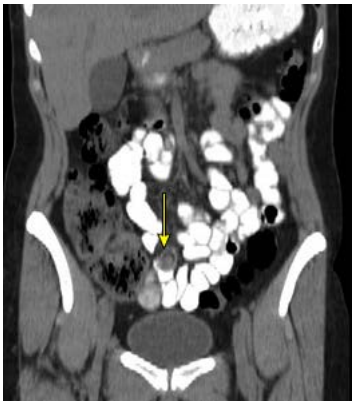


Figure 1: *Incidental Meckel's diverticulum on CT scan*

63

Blue Rubber Bleb Nevus Syndrome

- Rare congenital disorder with numerous, diffuse, cutaneous and internal venous malformations (VM).
- Patients often born with a 'dominant' lesion and can develop VMs of the skin, soft tissue and GI tract.
- Lesions can sometimes affect the liver, spleen, bladder, kidney, lung, and brain.

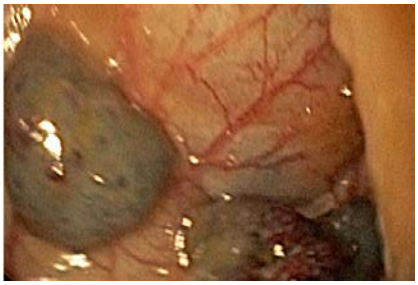
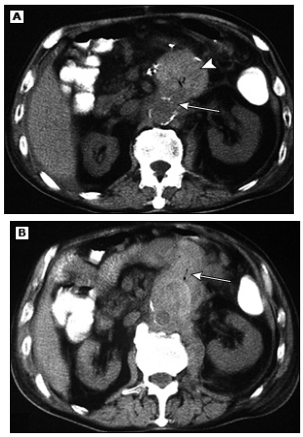


Figure 1: *Venous malformation involving the small bowel in a six-year-old child with blue rubber bleb nevus syndrome*

64

Aorto-enteric fistula

- Abnormal connection between the aorta and the gastrointestinal tract.
- Primary aortoenteric fistulae arise de novo between the aorta and the bowel.
- Secondary aortoenteric fistulae (SAEF) can occur following virtually any aortic reconstruction.
  - Commonly SAEF involve a surgically-placed aortic graft.
  - Can also present after other aortic interventions, including endovascular aneurysm use of bare metal aortic stents.



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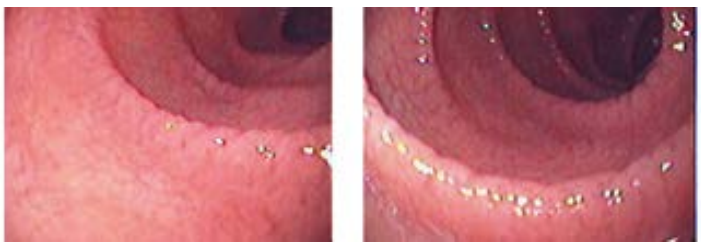
Uncommon causes

- Non-small bowel sources: hematobilia, hemosuccus pancreatitis, aortoenteric fistulae.
- Celiac disease? Now deemed to be a malabsorptive disorder without presence of occult GI bleeding.
  - Ulcerative jejunitis
  - Lymphoma
  - Adenocarcinoma



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Second-look Endoscopy

- Most small intestinal bleeding presents as stable overt or occult bleeding.
- A high percentage of patients designated as having "potential small bowel bleeding" were found to have missed bleeding sources.
  - Up to 25% of patients undergoing repeat EGD.
  - Up to 23% of patients undergoing repeat colonoscopy.
  - Studies utilizing DBE and capsule endoscopy have confirmed these findings.

Canad J Gastroenterol 2004;18:559–65.
Gastrointest Liver Dis 2010;19:141–5.

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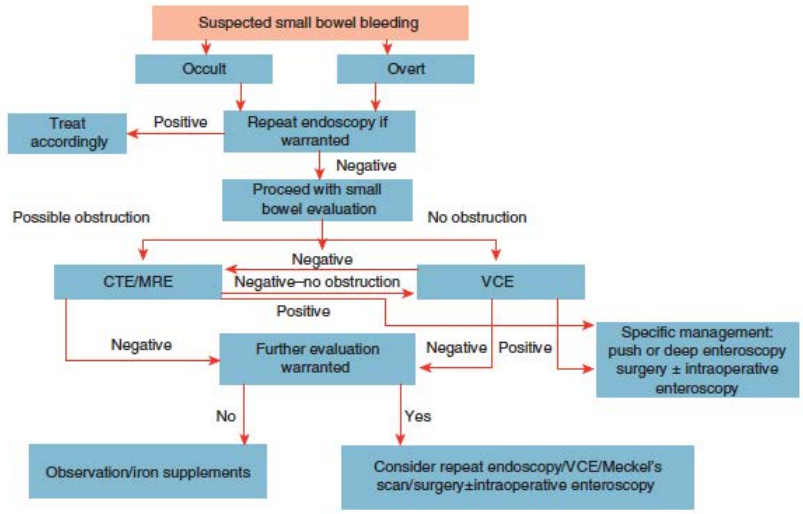

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Push Enteroscopy

- Extended upper endoscopy performed with a long endoscope (typically 250 cm in length).
  - Pediatric colonoscope, commercial push enteroscope
- An ideal second-look procedure as examination of distal duodenum and proximal jejunum is possible.
- Allows for a limited view of the proximal small bowel (~ 70 cm distal to ligament of treitz).
- Looping and patient discomfort are disadvantages which may be prevented with an overtube.

69

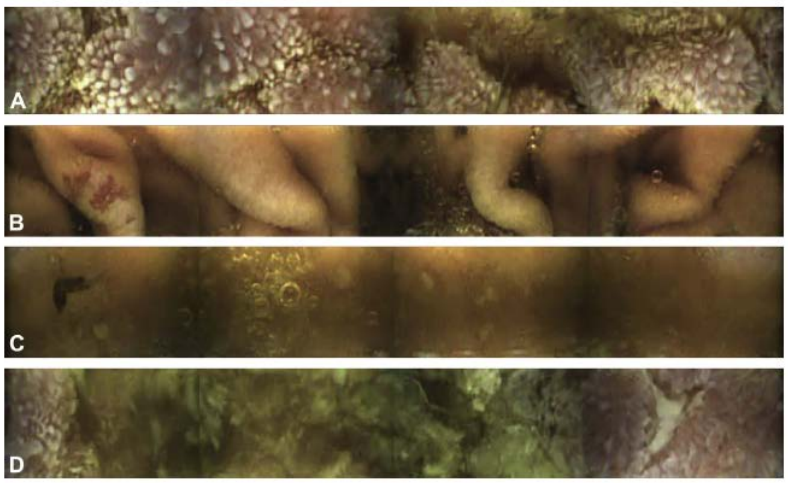
Video Capsule Endoscopy (VCE)

- Introduced in the US in 2001.
- The VCE measures 26x11 mm^2 and has the capacity to take images at the rate of 2 frames/s, over an 8–12 h period.
- Findings on VCE leading to endoscopic or surgical intervention or a change in medical management have been reported in 37-87% of patients.
- Up to 66% of patients remain transfusion free after VCE-directed interventions.
- Re-bleeding rates range from 6-27% in patients with a negative capsule study.

Gastroenterology 2004;126:643–53.
Gastroenterol 2006;101:1224–8.

70

VCE continued…



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VCE continued…

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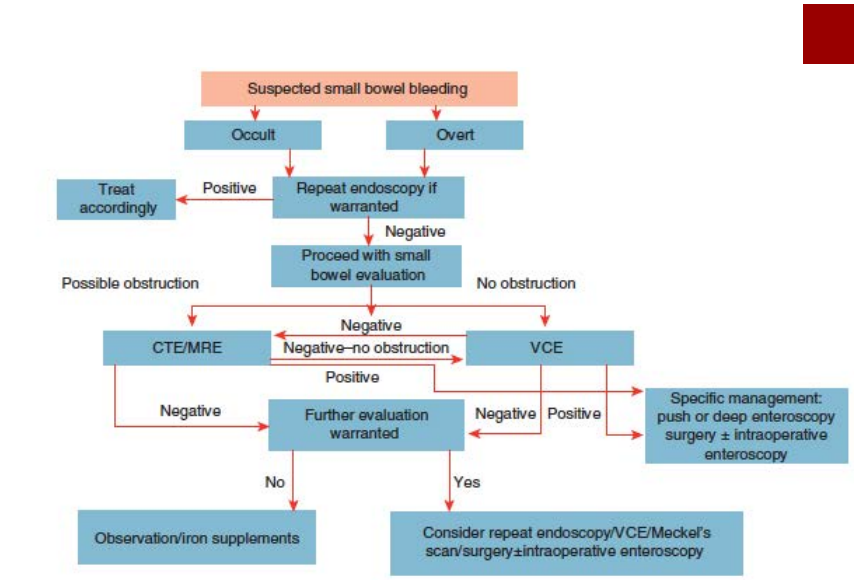

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Deep Enteroscopy

- Principle of push and pull enteroscopy.
  - Single balloon and double balloon enteroscope (DBE)
- Both scopes include an overtube with balloons at the distal end.
  - Can be performed via the oral and rectal approach.
- DBE can be advanced a distance of ~ 240-360 cm distal to the pylorus.
- Ability to perform total enteroscopy.
- Limitations: prolonged procedure time, anaesthesia support, pancreatitis (0.3% of patients).

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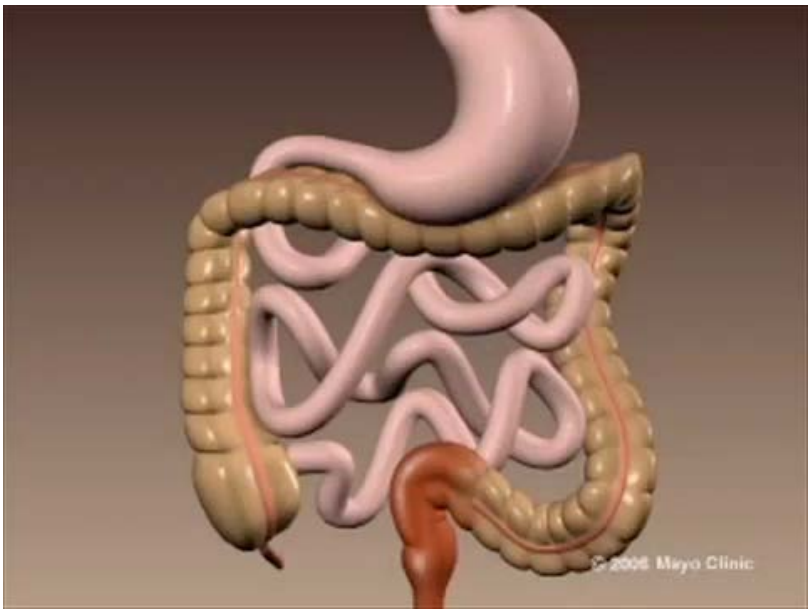

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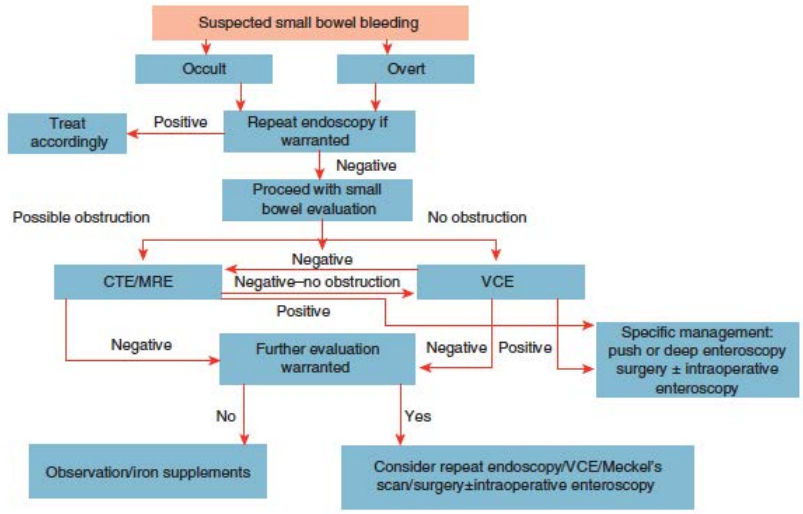
Enteroscopy continued…

- Spiral enteroscopes have a unique overtube with an outer raised spiral ridge at the distal end.
- Utilizes clockwork rotation of the ridged overtube to draw the enteroscope forward.
- Intraoperative enteroscopy involves SB evaluation at laparotomy.
  - Orally, rectally or via enterotomy.
- Should be reserved for patients with recurrent bleeds requiring multiple transfusions after negative comprehensive evaluation.
  - Risk of serosal tears, avulsion of mesenteric vessels, prolonged ileus, mortality rate as high as 17%.

Am J Surg 1992;163:94–8.

77



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Abdominal Imaging

- Cross-sectional imaging techniques (CT, CTE, MRE, Angiography).
  - Can see all bowel loops without superimposition.
  - Can visualize extraluminal structures.
  - Enterography: ingesting large volumes of contrast medium.
  - Enteroclysis: administration of enteric fluid by NG tube (superior small bowel distension but not as well tolerated).
- CT offers better temporal and spatial resolution than MR.
- CTE can offer higher detection rates of small bowel mural-based masses than VCE.

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Recommendations

1. Barium studies should not be performed in the evaluation of small bowel bleeding (strong recommendation, high level evidence).
2. CTE should be performed in patients with suspected small bowel bleeding and negative capsule endoscopy because of higher sensitivity for the detection of mural-based small bowel masses, superior capability to locate small bowel masses, and ability to guide subsequent deep enteroscopy. (strong recommendation, low level of evidence).
3. CT is preferred over MR imaging for the evaluation of suspected small bowel bleeding. MR can be considered in patients with contraindications for CT or to avoid radiation exposure in younger patients (conditional recommendation, very low level of evidence).
4. CTE could be considered before VCE in the setting of established inflammatory bowel disease, prior radiation therapy, previous small bowel surgery, and/or suspected small bowel stenosis (strong recommendation, very low level of evidence).
5. In patients with suspected small bowel bleeding and negative VCE examination, CTE should be performed if there is high clinical suspicion for a small bowel source despite the performance of a prior standard CT of the abdomen (conditional recommendation, very low level of evidence).

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Acute overt GI Bleeding

- Is the patient hemodynamically unstable?
- CT Angiography multiple phases of contrast enhancement including arterial phase.
  - With oral contrast – multiphasic CTE.
  - Without oral contrast – multiphasic CT.
- CTA can detect bleeding rates as slow as 0.3 mL/min.
- Limitations:
  - To detect contrast extravasation, patient must be actively bleeding.
  - Renal function can be adversely affected by IV contrast administration (especially if angiography is required).

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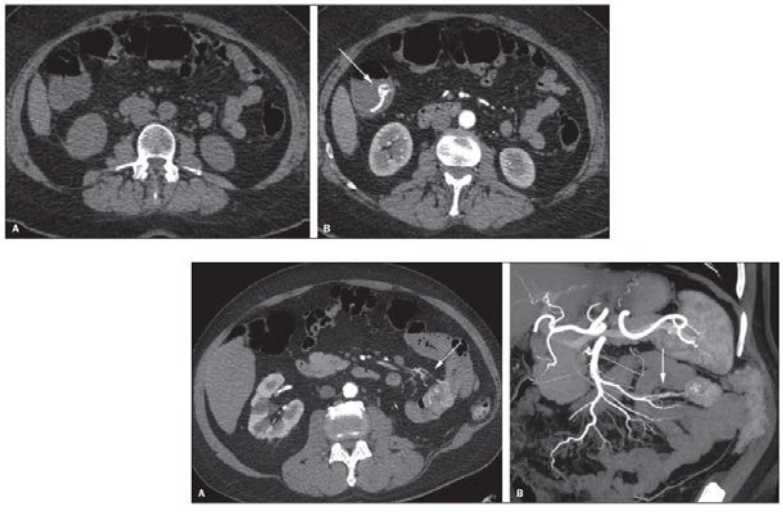
CT Angiography



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82

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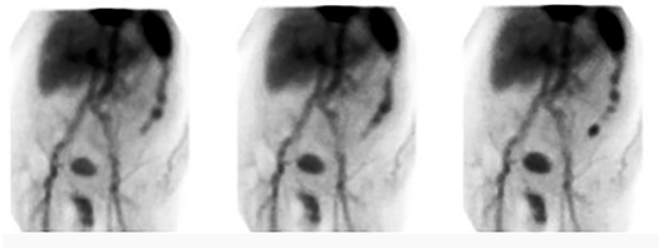

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83

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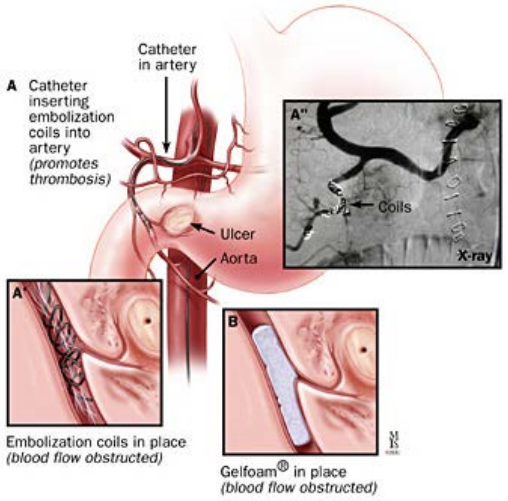
84

Angiography



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Medical treatments

- Supportive care with oral or intravenous iron .
- Hormonal therapy (estrogen based) → ineffective.
- Somatostatin analogs (octreotide) → inhibit angiogenesis, decrease splanchnic flow, increase vascular resistance and platelet aggregation.
- Thalidomide – antiangiogenic agent which inhibits vascular endothelial growth factor.
  - RCT available demonstrating efficacy.
    - 75% (9/12 patients) with small bowel angioectasia failing endoscopic therapy had resolution of bleeding.

Ge ZZ, Chen HM, Gao YJ *et al.* Efficacy of thalidomide for refractory gastrointestinal bleeding from vascular malformation. Gastroenterology 2011;141:1629–37.

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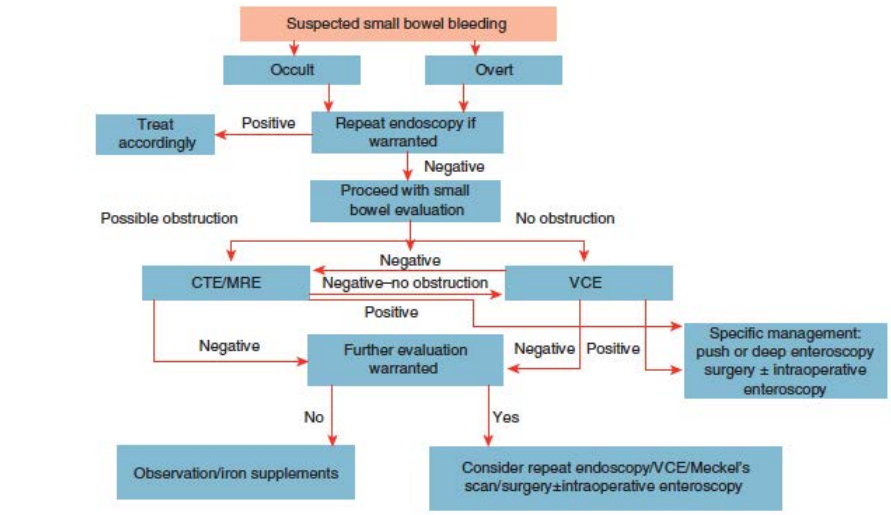

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Conclusion

- Small bowel bleeding is a relatively uncommon event.
- Repeat endoscopic examination can help identify previously undetected sources of bleeding.
- Sources of bleeding can likely be identified with VCE, deep enteroscopy or CTE studies.
- Small bowel angiodysplastic lesions are the most common cause of bleeds and demonstrate high recurrence rates despite endoscopic therapy.
- Medical therapy may be an option for refractory patients but is not in widespread use.
- Surgical intervention is usually reserved as a last option.

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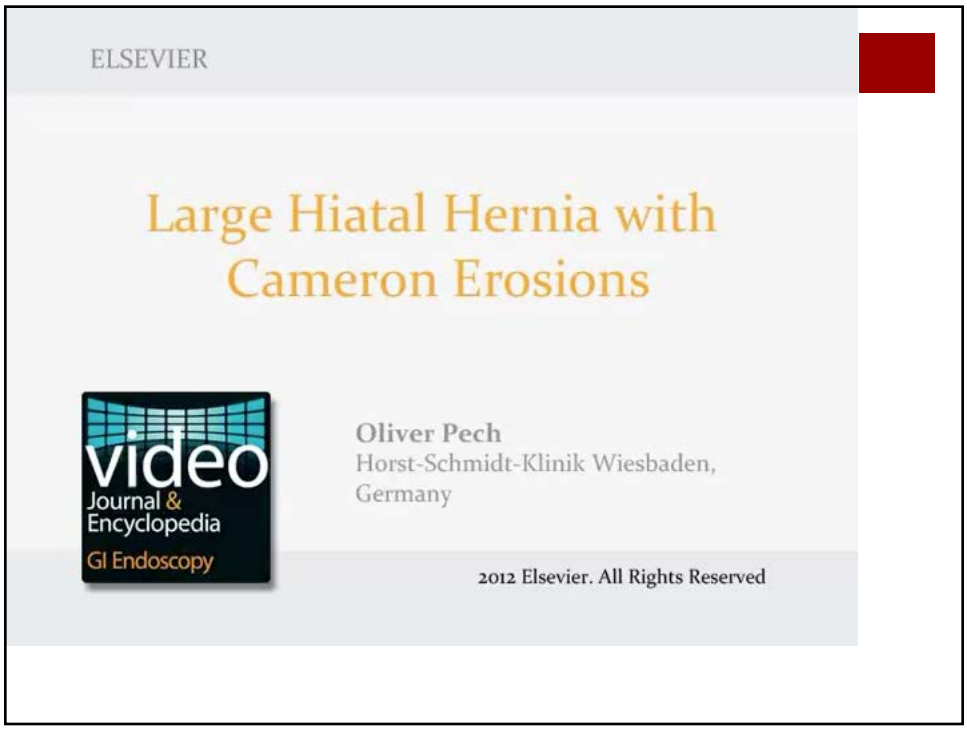
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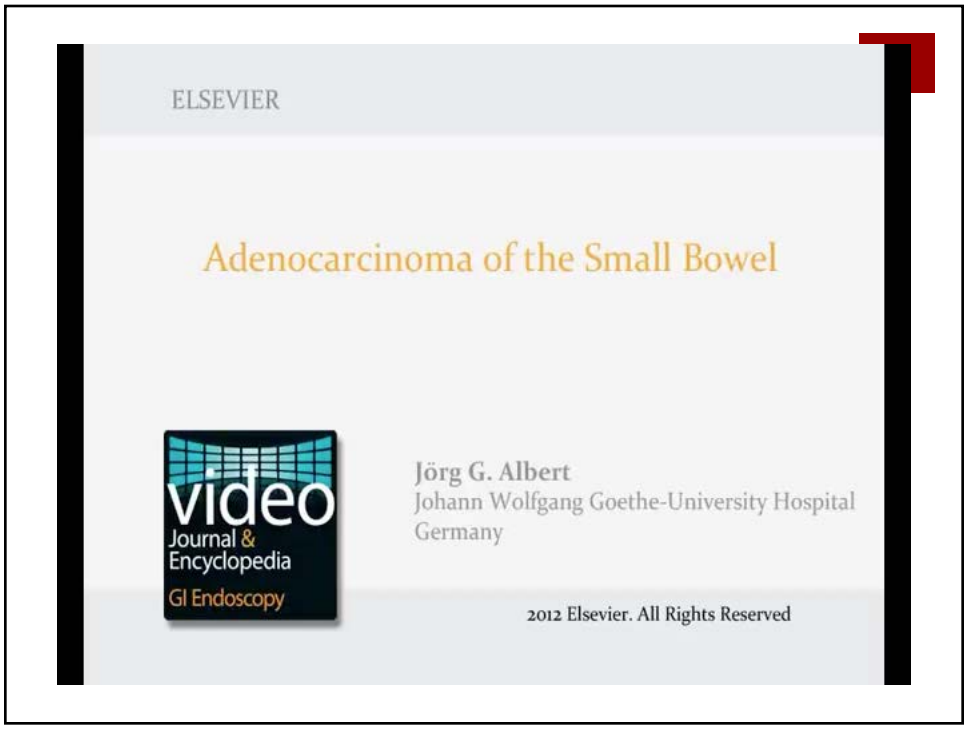
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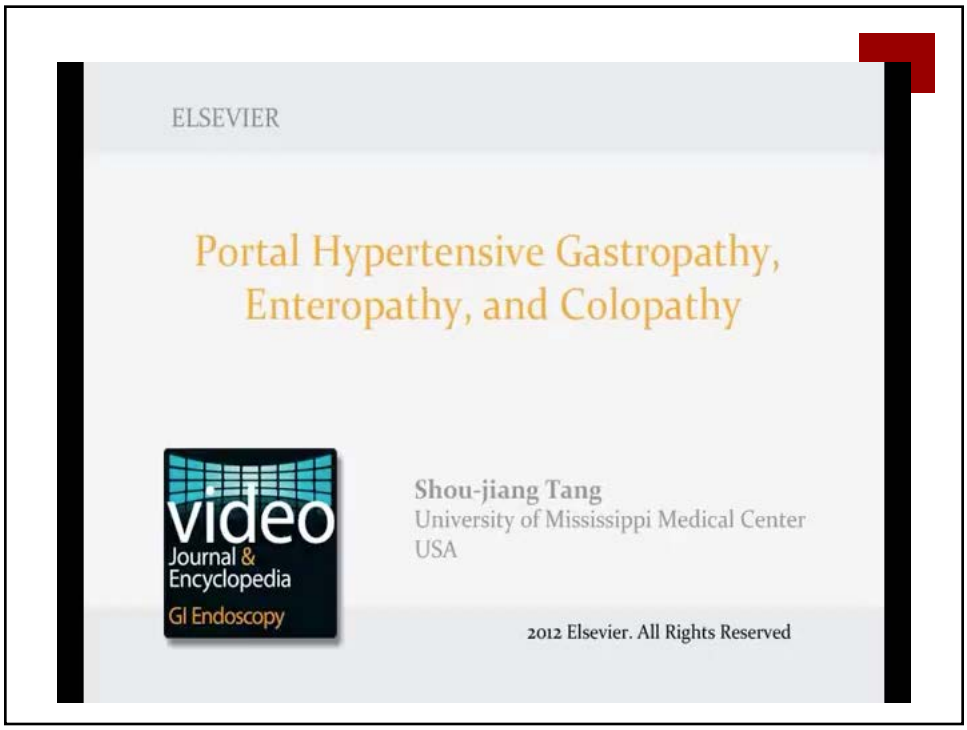
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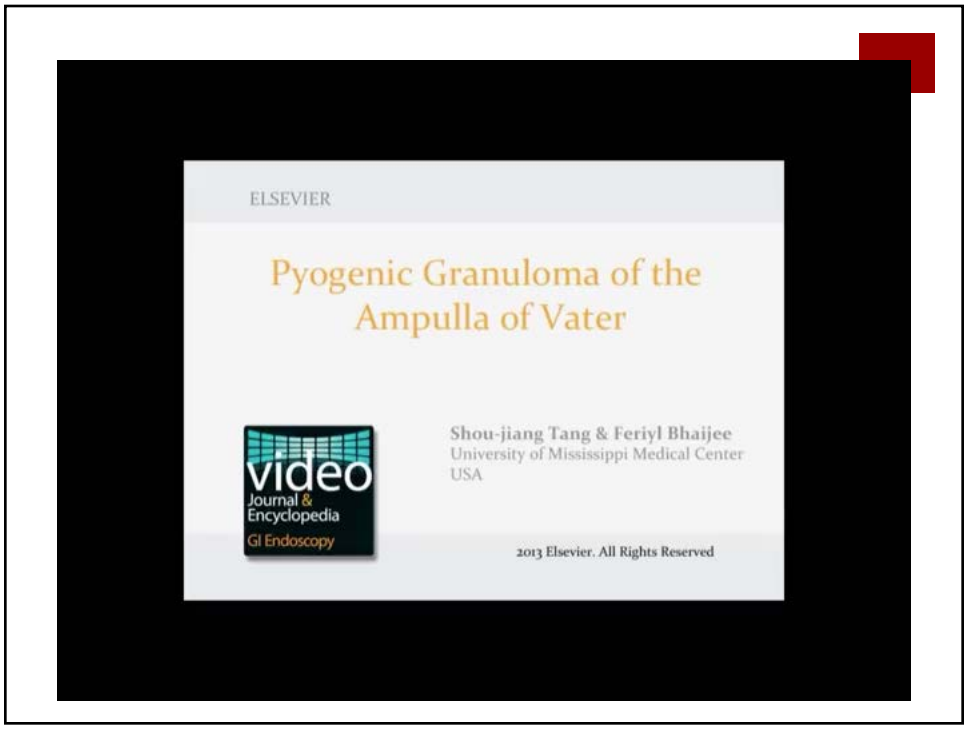
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