Non-Emergent GI Bleeding

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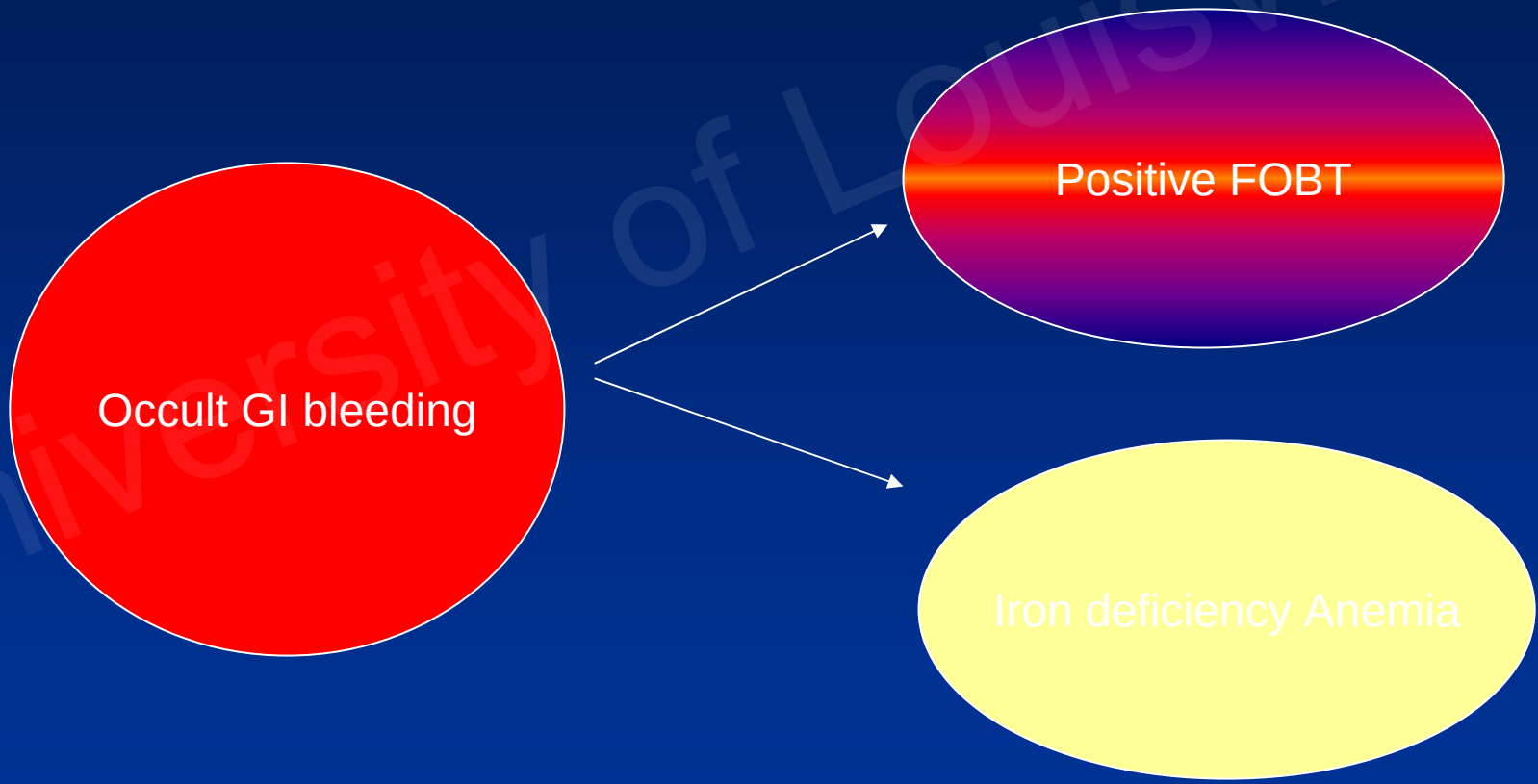
Non-Emergent GI Bleeding

- **Objectives**
  - Occult and Obscure GI bleed
  - How to evaluate Occult GI bleed
    - FOBT and different types of FOBT
  - How to Evaluate Obscure GI bleed
  - Advances in Endoscopy
    - Capsule endoscopy
    - Double balloon enteroscopy

Non-Emergent GI Bleeding

- **Classification**
  - Occult GI bleed
    - GI bleed that Initially presents as FOBT and/or iron deficient anemia without any visible blood in the stool
  - Obscure GI bleed
    - GI bleed that persist or recurs without any obvious etiology after standard endoscopic examination

Occult Bleeding



Occult GI Bleeding

- Sub-classified
  - Acute
  - chronic
  - Intermittent
  - continuous

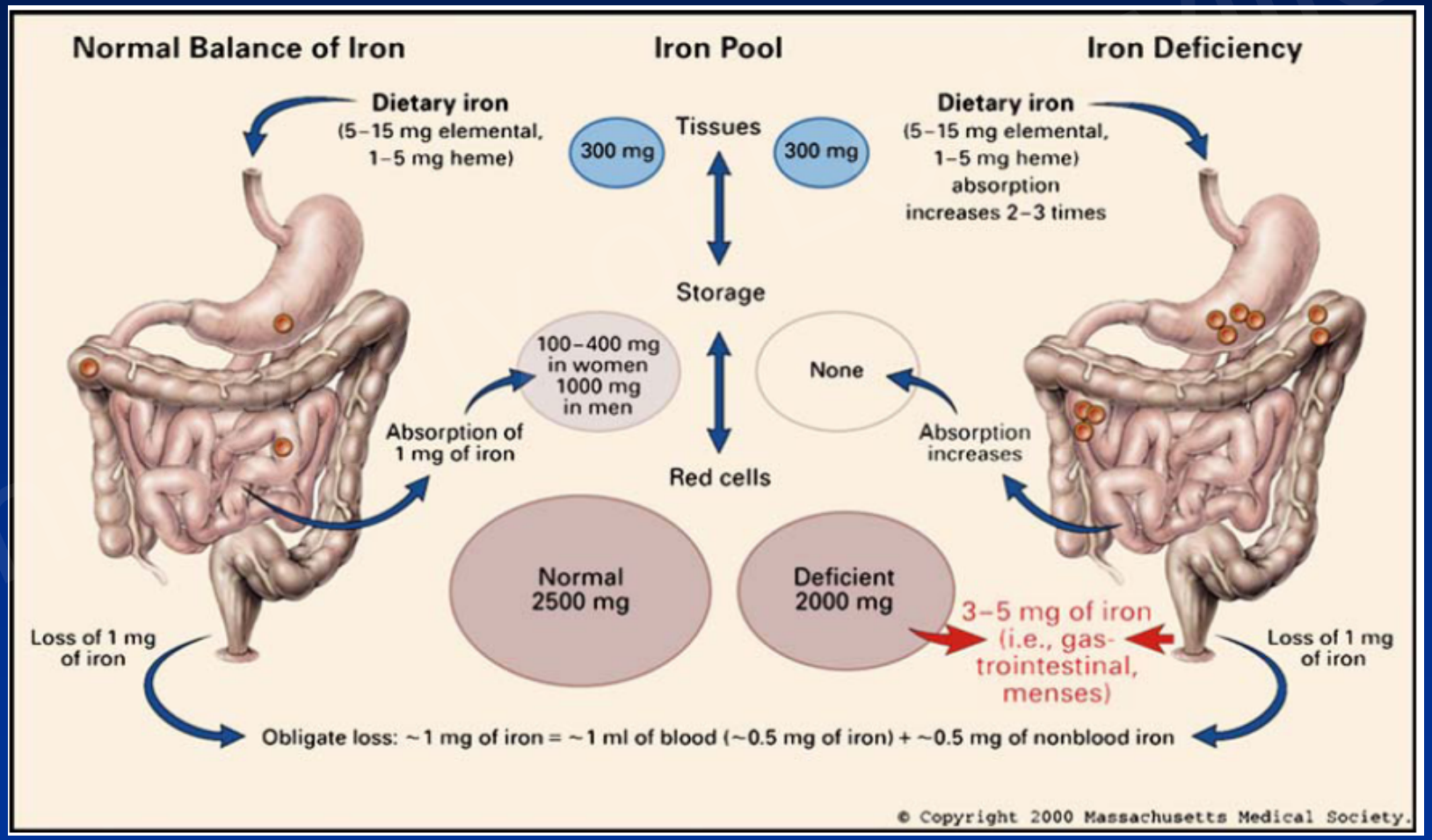
Occult GI Bleeding

- Iron deficiency anemia
  - 20 Million have iron deficiency anemia in the Uinted States.
  - Affects 6-10% of general population
    - 5-11% women
    - 1-4% Men
- Worldwide
  - 15-20% have iron deficiency anemia

Iron Deficiency Anemia

- Obligate daily GI blood loss
  - 0.5 to 1.5ml per day
  - Typically we lose 1mg of iron per day through stool
  - Iron deficiency results when the absorptive capacity of small bowel is exceeded by iron loss over prolonged period of time.

Iron Deficiency Anemia



Iron Deficiency Anemia

- Gastrointestinal blood loss is the most common cause of IDA in developed countries
- Poor absorption like celiac disease

Occult GI Bleeding

- Blood loss in the GI tract can be detected by chemical testing of the stool
- Fecal occult blood testing

Occult GI Bleeding

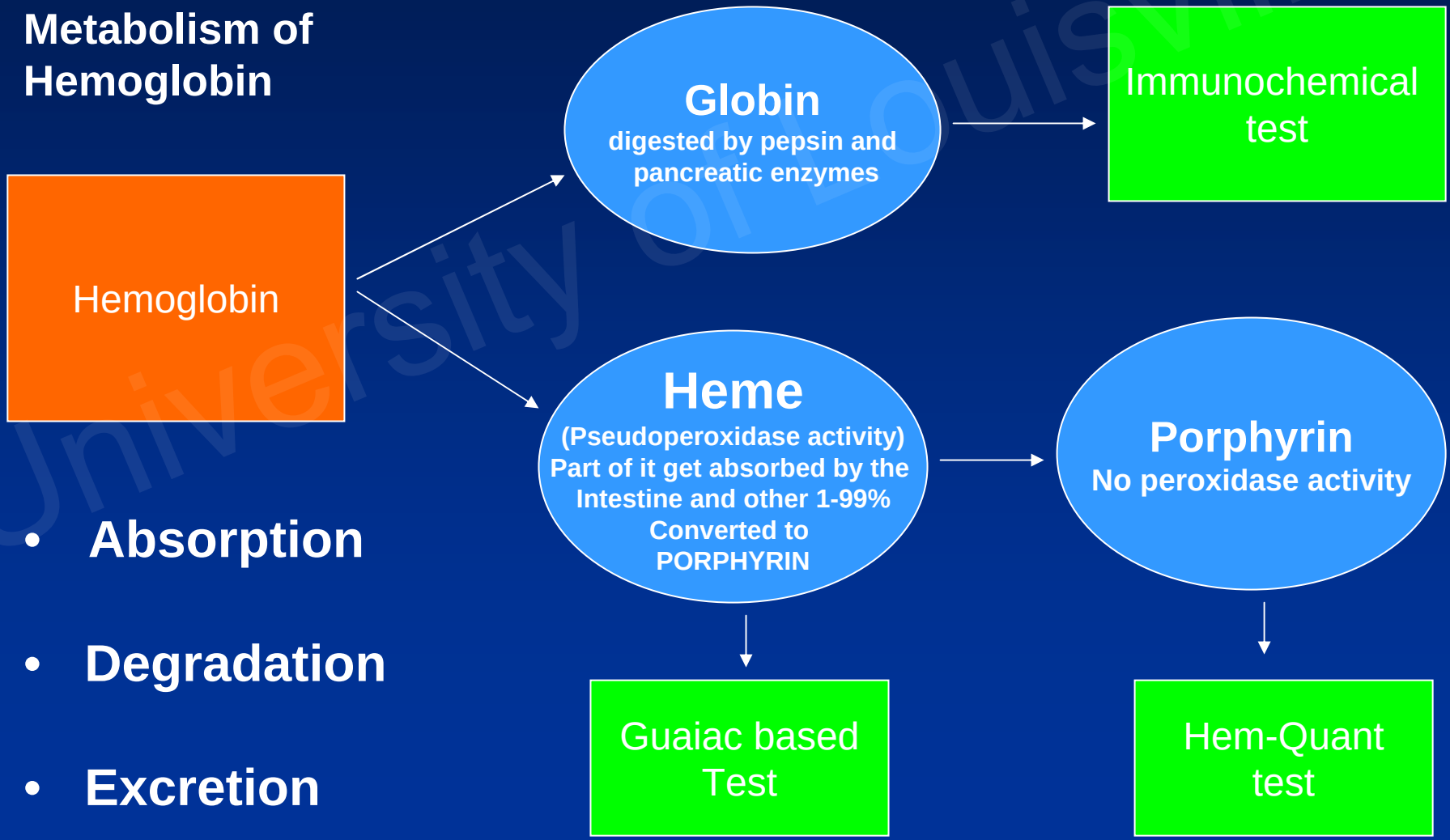
- **Fecal occult blood test**
  - Based on detection of Hemoglobin and its derivatives in the stool
  - Blood loss in normal individual varies o.5 ml to 1.5ml/day
  - FOBT positive when loss >2ml/day
  - Loss of 10ml/day leads to 50% positive FOBT

Occult GI Bleeding

- **Fecal Occult Blood Test**
  - Three types of FOBT
    - Guaiac test
    - Heme-porphyrin test
    - Immnuochemical test

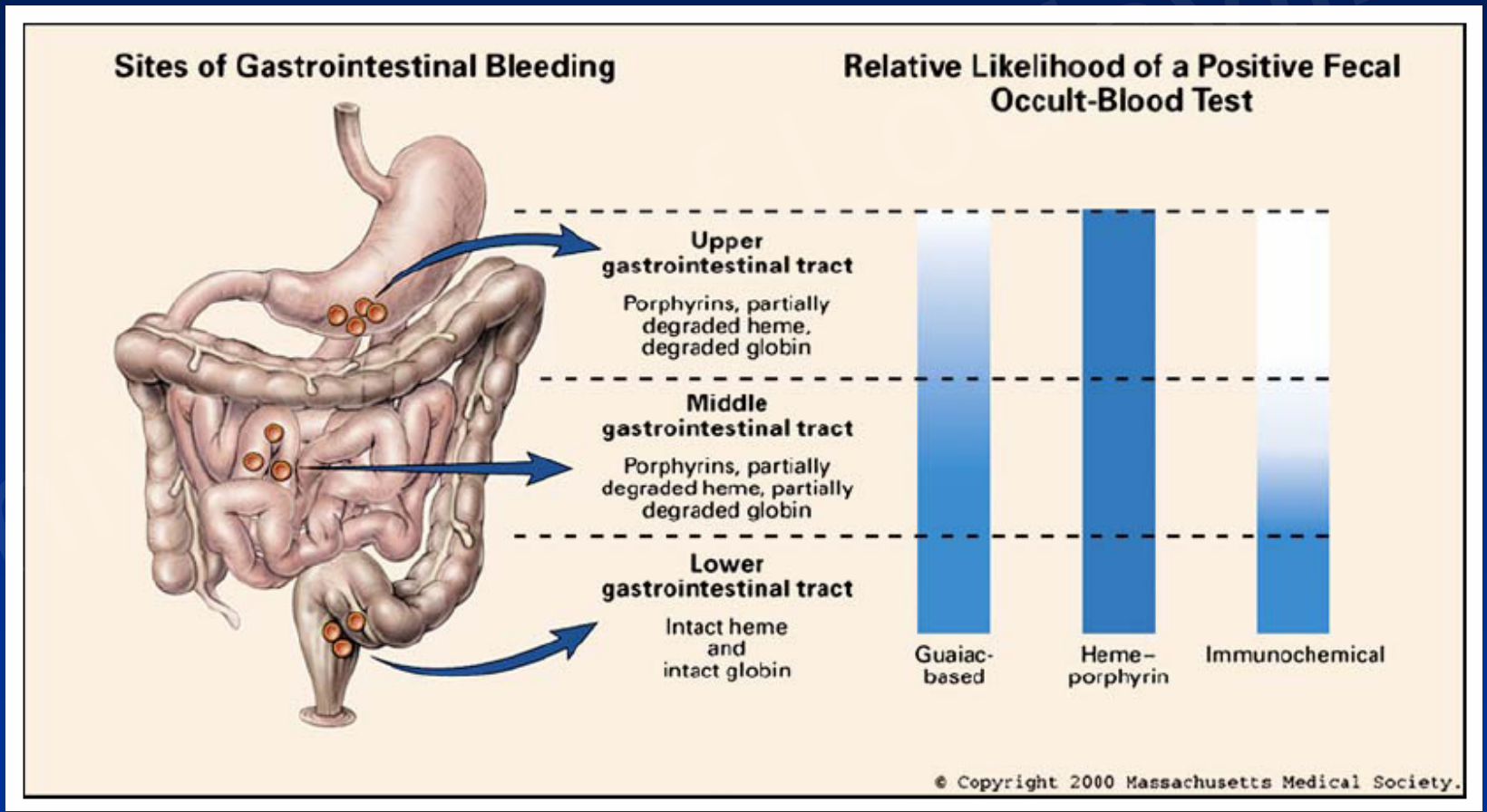
Occult GI Bleeding

Metabolism of Hemoglobin



- **Absorption**
- **Degradation**
- **Excretion**

Occult GI Bleeding



Occult GI Bleeding

- **Guaiac based test**
  - Being used for more than a century
  - Gum like coloreless compound that becomes colored in the presence of adequate peroxidases
  - Hem part of Hb turns guaiac compound blue in the presence of hydrogen peroxide.
  - Two types
    - Hemoccult
    - Hemoccult II SENSA

Occult GI Bleeding

- **Guaiac test**
  - May be positive with as little as 1mg Hb/gm of stool or remain negative in those with more than 80mg Hb/gm of stool
  - Sensitivity is enhanced by wetting the fecal smear, but lowers the specificity. Not recommended

Occult GI Bleeding

- **False positive FOBT**
  - Medications
    - Aspirin/NSAIDS
  - Exogenous peroxidase activity
    - Red meat consumption
    - Fruit consumption(cantaloupe,grapefruit, figs)
    - Uncooked vegetables (radish, cauliflower, broccoli,turnip
  - Extraintestinal blood loss
    - Epistaxis/gingival bleeding/hemoptysis

Occult GI Bleeding

- **False negative FOBT**
  - Dry stool specimen
  - Hem degtadation to porphyrin
  - Ascorbic acid/vitamin C
  - Heat
  - Defective regents

Occult GI Bleeding

- Guaiac test not indicated
  - Person who don’t follow the diet
    - In hospital patients
    - Naso-gastric aspirate or vomit
    - Apparent melena or hematochezia

Occult GI Bleeding

- **Immunochemical FOBT**
  - Based upon immunological recognition of intact human globin
  - Anti globulin or anti-albumin antibody are used
  - These antibody don’t react with diet/peroxidases or medications so less false -/+
  - Detects as little as 0.3mg of blood added to stool but fail to detect if 100-200ml of blood ingested
  - Detects only lower GI tract bleeding not upper as globulin is digested by pepsin and pancreatic enzymes

Occult GI Bleeding

- Hem-porphyrin assay FOBT
  - HemoQuant
  - Involves hem and hem derived porphyrin
  - Quatification of blood loss
  - Sensitive for both upper and lower GI bleed
  - Higher sensitivity for upper bleed compared to guaiac and immunichemical testing
  - Takes 2-4 days for the result
  - Not affected by medications/dietry peroxidases except red meet

What Test to Select?

Characteristics of fecal occult blood tests

Variable	Guaiac	Heme-Porphyrin	Immunochemical
Detection characteristics			
Upper gastrointestinal	+	++++	0
Small bowel	++	++++	+
Right colonic	+++	++++	+++
Left colonic	++++	++++	++++
Test factors			
Bedside availability	++++	0	+
Time to develop	1 minute	1 hour	5 min to 24
False positives			
Animal hemoglobin	++++	++++	0
Dietary peroxidases	+++	0	0
False negatives			
Hemoglobin degradation	++	0	++
Storage	++	++++	++
Vitamin C	++	0	0

Relative comparisons are shown on a scale of 0 to ++++, with 0 being the negative and ++++ being highly positive.

What Test to Select

- Guaiac and immunochemical best for
  - colorectal cancer screening
- Hem-porphyrin assay best for
  - iron deficincy anemia because it accurately quantify the luminal blood loss.

Causes of Occult GI Bleeding

Differential diagnosis of occult gastrointestinal bleeding (iron deficiency anemia or fecal occult blood)

Mass lesions
- [1]Carcinoma (any site)
- Large (>1.5 cm) adenoma (any site)

Inflammation
- [1]Erosive esophagitis
- [1]Ulcer (any site)
- [2]Cameron lesions
- Erosive gastritis
- Celiac sprue
- Ulcerative colitis
- Crohn's disease
- Colitis (nonspecific)
- Idiopathic cecal ulcer

Miscellaneous
- Long-distance running
- Factitious
- Pancreaticobiliary

Vascular
- [1]Vascular ectasia (any site)
- Portal hypertensive gastropathy/colopathy
- Watermelon stomach
- Hemangioma
- [3]Dieulafoy's ulcer

Infectious
- Hookworm
- Whipworm
- Stronglyoidiasis
- Ascariasis
- Tuberculous enterocolitis
- Amebiasis

Surreptitious
- Hemoptysis
- Oropharyngeal (including epistaxis)

Approach to Evaluate Occult Bleeding

- History
  - Medication like NSAIDS/alendronate/KCL and anticoagulants
  - F/H of GI blood loss
    - Hereditary hemorrhagic telengectasia
    - Blue rubber bleb nevus syndrome
- Physical Examination
  - Dermatitis herpetiformis for celiac sprue
  - Kaposi sarcoma with skin lesions
  - Plummer vinsen syndrome (brittle, spoon shaped nails, atrophied tongue)

Evaluation of Occult Bleeding

- Endoscopic
  - Conventional
    - EGD/Colon
  - Advanced
    - Enteroscopy/ileoscopy
    - Endo capsule
- Radilogical
  - ACBE/ upper GI series
  - SBFT /enteroclysis
  - CT/CT colonography

Evaluation of Occult GI Bleed

- What test should be done first to order first ?
  - EGD
  - Colonoscopy
  - SBFT
  - CT
  - Endo-capsule

Approach to Evaluate Occult Bleeding

- In asymptomatic pts. >50 or <50 with F/H or risk for colon ca should under go Colonoscopy first if negative then EGD or further work up.

Rockey et al; Gastro Clinic of N. Am 34 (2005)

Approach to Evaluate Occult Bleeding

- In symptomatic pt. age <50, if upper symptoms predominant, start with EGD and then colonoscopy if upper negative

- In symptomatic pt. age >50, if upper symptoms predominates, can do EGD but also perform colonoscopy due to higher risk for colon cancer and possibility of synchronous lesions (2-17% IDA or FOBT have colon ca)

Rockey et al Gastroent Clin of N. Am; 2005 :34)

Approach to evaluate Occult GI Bleed

- In older pts. If upper and lower scope negative, before proceeding expensive w/u
  - Trial of iron supplements for 6-8 wks
  - If no response, evaluate small bowel
- Younger pts Evaluate SB sooner

What are Evidences?

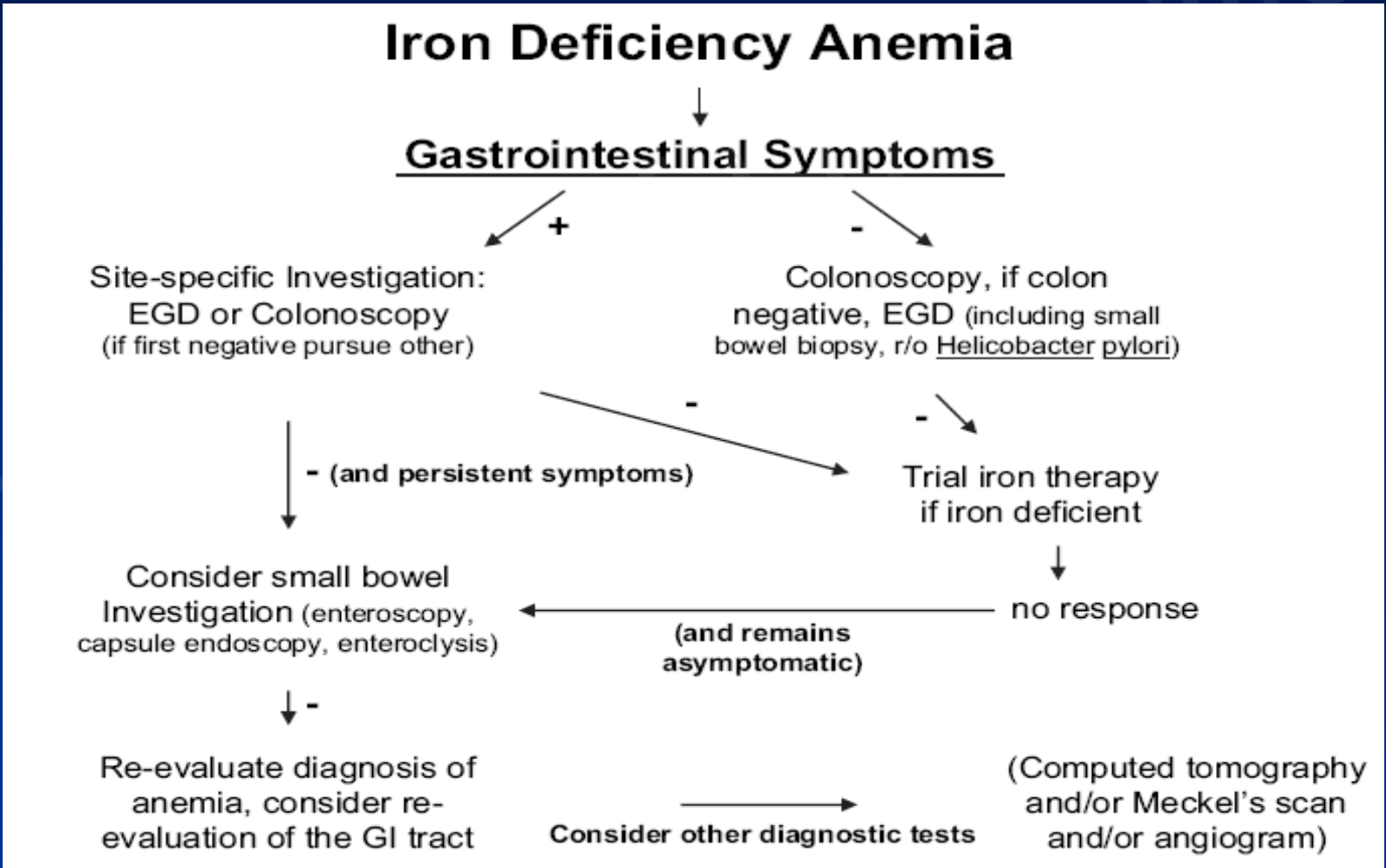
Table 2
Major gastrointestinal lesions identified in studies of patients with iron deficiency anemia

Lesion	Author (total # of patients evaluable) [1]Cook (100)	[1]McIntyre (111)	Rockey (100)	Kepczyk (70)	Total (381)
Esophagus (%)					47
Esophagitis	14	15	6	10	
Cancer	1	na	0	1	
Stomach					98
Ulcer	7	13	8	3	
Gastritis	[2]14	7	6	11	
Cancer	5	8	1	3	
Vascular ectasia	5	0	3	4	
Duodenal ulcer	1	10	11	3	25
Other upper small intestine	0	2	2	3	7
					10
[3]Celiac dis.	0	3	0	4	
Vascular ectasia	1	1	0	0	
Large intestine					85
Cancer	14	5	11	4	
Vascular ectasia	2	1	5	6	
Adenoma	6	4	5	6	
Colitis	1	2	2	1	
Other	0	3	3	4	
[4]Upper lesion	40 (47)	42 (51)	37	39 (43)	158 (41%)
Lower lesion	23	15	26	21	85 (22%)
Small intestine	2	4	0	4	10 (3%)
Upper and lower	7	0	1	12	20 (5%)
No gastrointestinal lesion	35	50	37	6	128 (34%)

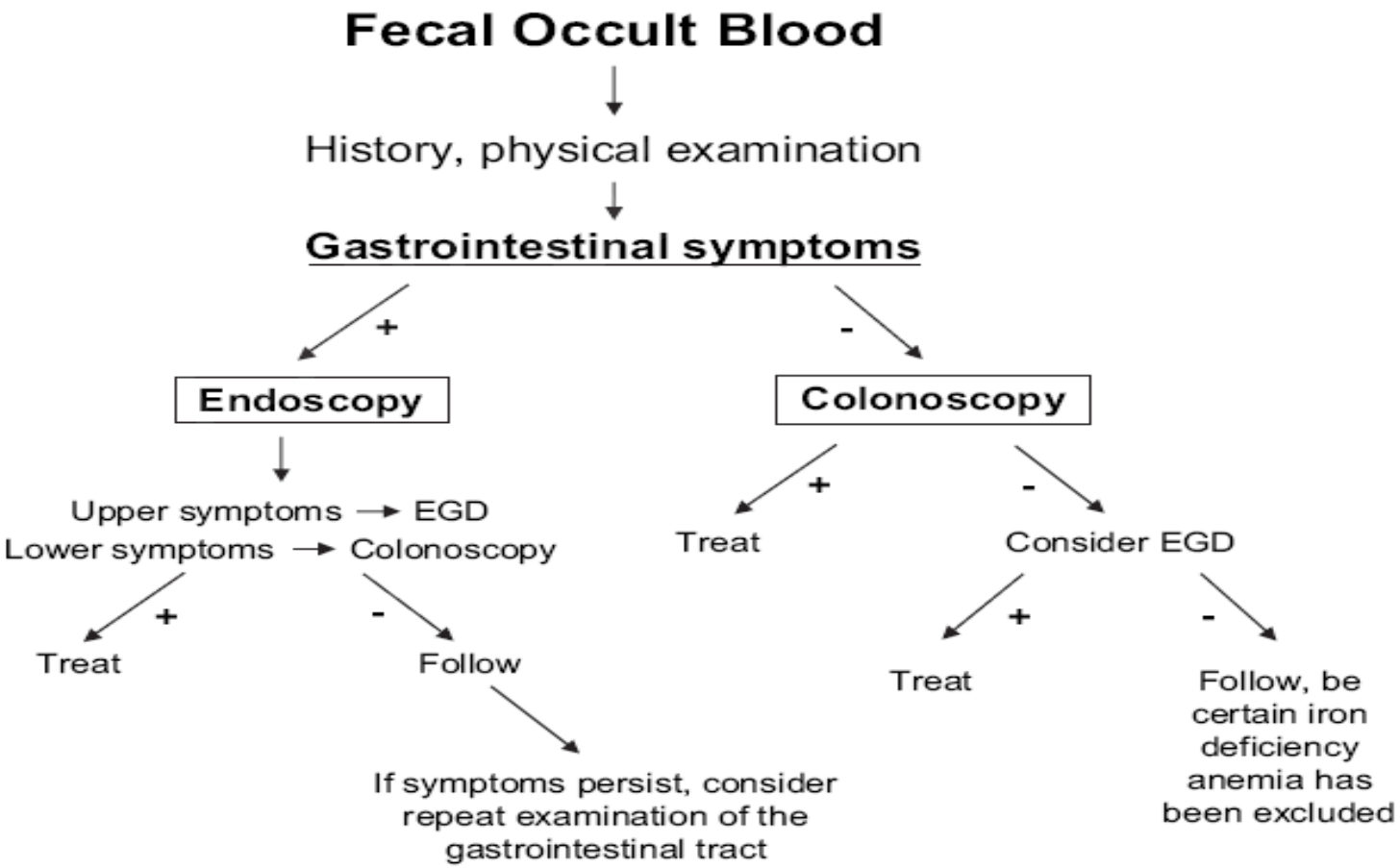
Evaluation of Occult Bleeding

- 2/3rd of pt with IDA has identifiable GI cause for bleeding and only ½ in case of positive FOBT.
- Upper 29-56%
- Lower 20-30%
- Simultaneous 1-17%(6%)

Approach to Evaluate Occult Bleeding



Approach to Evaluate Occult Bleeding



Obscure GI Bleeding

- Two types
  - Obscure occult GI bleeding
    - Persistently positive FOBT with or without iron deficiency anemia with initial negative endoscopic work up and no visible blood in the stool to patient or physician
  - Obscure overt GI bleeding
    - Clinically evident bleeding that persists or recurs after negative endoscopic examinations

Obscure GI Bleeding

- GI bleeding leads to 300,000 hospitalization per year
- 10-20% of these don't have identifiable cause for bleeding
- Only 5% of these pt have recurrent bleeding of unknown etiology leading to extensive work up

Obscure GI Bleeding

- **THREE Main reasons**

- Missed lesion on previous endoscopy
- Lesions in the small bowel
- Uncommon/difficult to identify causes
  - Hemosuccus pancraeticus
  - Hemobilia
  - Aortoenteric fistula
  - Dielafoy's lesions
  - Meckel's diverticulum
  - Extra-esophageal varices (gastric, SB, colonic)

Obscure GI Bleeding

- Obscure Overt
  - Brisk or active bleeding
    - Hematemasis/hematochazia/active melena
    - Orthostatic sign
    - Repeat EGD/Colonoscopy, if negative arrange for RBC scan or angiography, if massive bleed surgical consult
  - Subacute or intermitant
    - Coffee ground emesis/BRBPR
    - Repeat EGD/Colonoscopy, If negative evaluate small bowel

Obscure GI Bleeding

- Evaluation of OGIB
  - Endoscopy
  - Radiology
  - Surgery

Obscure GI Bleeding

- Endoscopic modalities
  - Routine endoscopy (repeating EGD/Colon)
  - Enteroscopy (examination of small bowel)
    - Push enteroscopy
    - Double balloon enteroscopy
    - Sonde enteroscopy
    - Retrograde enteroscopy
    - Intra-operative enteroscopy
  - Capsule endoscopy

Obscure GI Bleeding

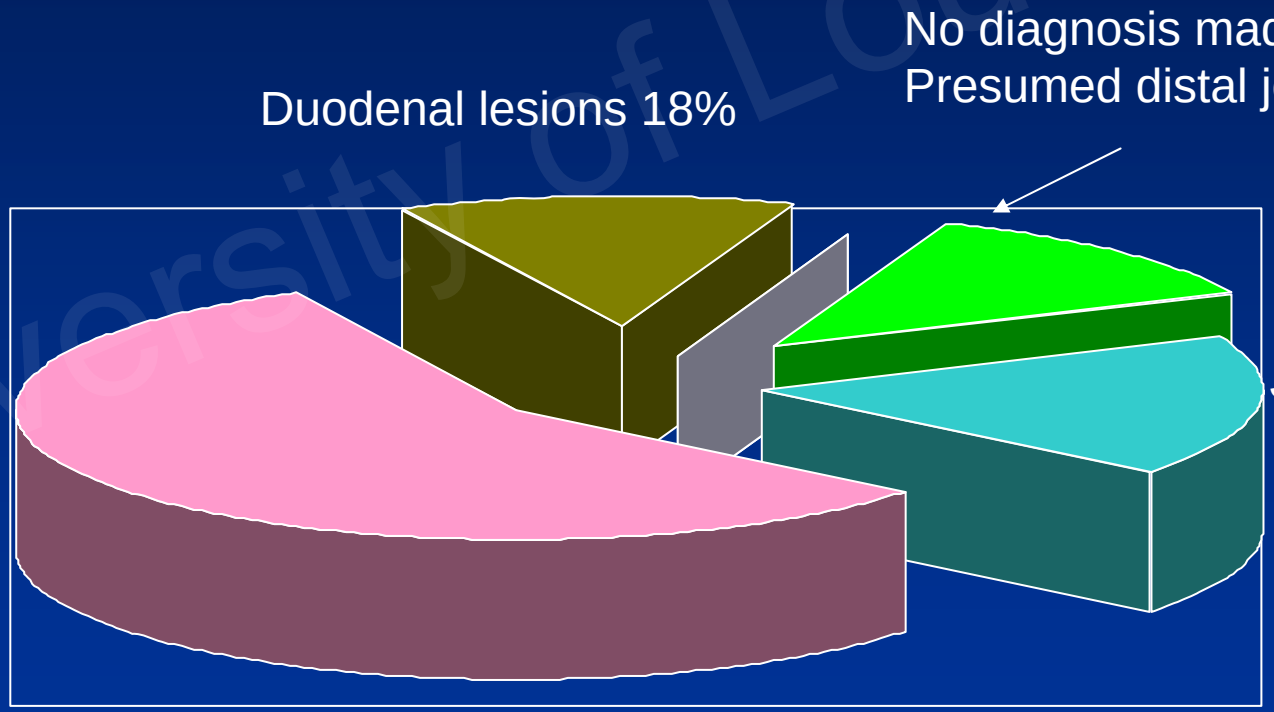
- Repeat Upper Endoscopy
  - High yield for diagnosis up to 25-64% (34%)
  - Commonly missed lesions are
    - Vascular ectasia (AVMs)
    - Polyps
    - Cameron's ulcers
    - Peptic ulcers
- Repeat colonoscopy
  - Less useful only 6% diagnostic yield
    - Angiodysplasia and neoplasia

Evaluation of Obscure GI Bleeding

- **Enteroscopy**
  - Push Enterosocopy
    - 220-250cm endoscope or pediatric colonoscope
    - Should be the first test after negative EGD/colon
    - Scope advanced15-150 cm beyond ligament treitz
    - Diagnostic yield 13-75%
    - Thearpeutic advantage
      - treating bleeding vascular lesions decrease hospitalization and transfusion requirement up to 13%
    - Safe and with fewer complications
    - Disadvantage
      - Entire small bowel can not be visualized

Evaluation of Obscure GI Bleeding

206 Pts referred for PUSH enteroscopy to evaluate Obscure GI bleeding



Evaluation of Obscure GI Bleeding

- **Enteroscopy**
  - Sonde enteroscopy
    - Can visualize the entire small bowel
    - Not performed any more due to lengthy procedure and pt. discomfort
    - With newer technology, its role extremely limited

Evaluation of Obscure GI Bleeding

- Double balloon Entrososcopy
  - Newer technology
  - Approved in 2004
  - Entire small bowel can be visualized
  - Sequential inflation of two balloon, it pleats the SB over endoscope
  - Therapeutic advantage
  - Role being evalaluated

Evaluation of Obscure GI Bleeding

- Capsule Endosocpy
  - novel noninvasive technology
  - Primarily to access the small bowel pathology
  - Developed by Given imaging
  - FDA approved in August 2000
  - Subsequentlt replaced M2A plus capsule
  - Now renamed PilCam
    - Pilcam SB
    - Pilcam ESO

Capsule Endoscopy

- Disposable M2A capsule
- 26x11mm
- 8hr battery
- Flash, camera, transmitter
- 2 pictures per second
- Allows detection of red color

Capsule Endoscopy

- The Patient
  - 8hr fast
  - No bowel prep
  - 8 sensors on abdomen
  - Walkman-size data recorder
  - Outpatient

Capsule Endoscopy

- Downloaded to workstation
- Capsule retrieval not needed
- Images viewed as video 1-50 per sec
- Review time based on experience

Capsule Endoscopy

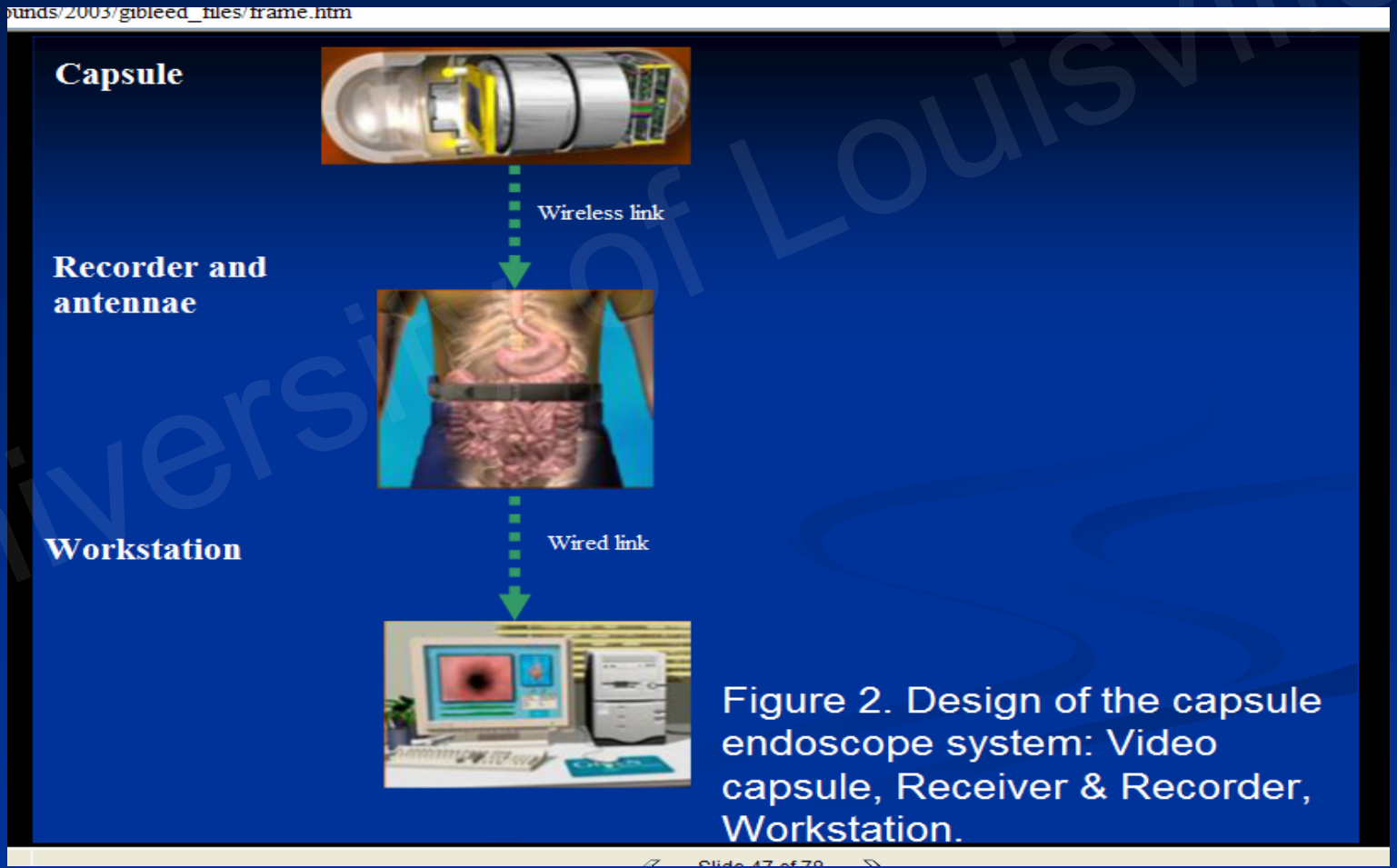


Figure 2. Design of the capsule endoscope system: Video capsule, Receiver & Recorder, Workstation.

Capsule Endoscopy

– Diagnostic yield for small bowel bleeding

- Overall 70%
- Ongoing obscure overt 92%
- Ongoing obscure occult 44%

Pennazio et al Gastro 2004; 126

Capsule Endoscopy

- Indications
  - Evolving
  - Primarily for diagnosis of Obscure GIB
  - Crohn's disease diagnosis, extent and severity.
  - Small bowel tumors
  - Detection of small bowel injury associated with the use of NSAIDs,
  - Assessment of celiac disease
  - Esophageal Varices surveillance
  - Abdominal pain work up functional or organic

Capsule Endoscopy

- Contraindications
  - Suspected small bowel obstruction or stricture
  - Swallowing problems
  - Pacemaker
  - Gastropresis
  - Advance dementia

Capsule Endoscopy

- **Ell et al.**
  Endoscopy 2002
  - Capsule vs.. push enteroscopy
  - 65 patients referred for chronic GI bleeding
  - After data review and workup 33 excluded
  - 32 pts enrolled, had CE and PE for “severe” bleeding

Capsule Endoscopy

- Ell et al
  - Examiners blinded
  - 21 diagnosed by CE, 9 by PE
  - Bleeding source identified
    - 66% with CE vs. 28% PE $p<0.001$
  - Conclusion
    - **Capsule endoscopy better than push entersocopy in diagnosis for OGIB**

Capsule Endoscopy

- **Mylonaki et al.**
  Gut 2003
  - Capsule vs. push enteroscopy
  - 52 pts with OGIB enrolled, 2 dropped out
  - Multiple failed diagnostic procedures
  - 38 diagnosed by CE vs. 16 by push enteroscopy
  - 1 lesion missed by CE identified

Capsule Endoscopy

- Bleeding site identified
  - 76% CE vs. 38% PE $p<0.05$
- 1 false negative

- Conclusion
  - **Capsule endoscopy superior in diagnosis**
  - **Better tolerated and preferred by pts. than push enterosocopy**

Mylonaki et al GUT 2003; 97

Evaluation of Obscure GI Bleeding

- **Radiological**
  - Small bowel follow through
    - Diagnostic yield very poor 0 - 5.6%
    - Only use if suspecting small bowel tumor or Crohn's disease
    - Minimal Role in occult and obscure GI bleed

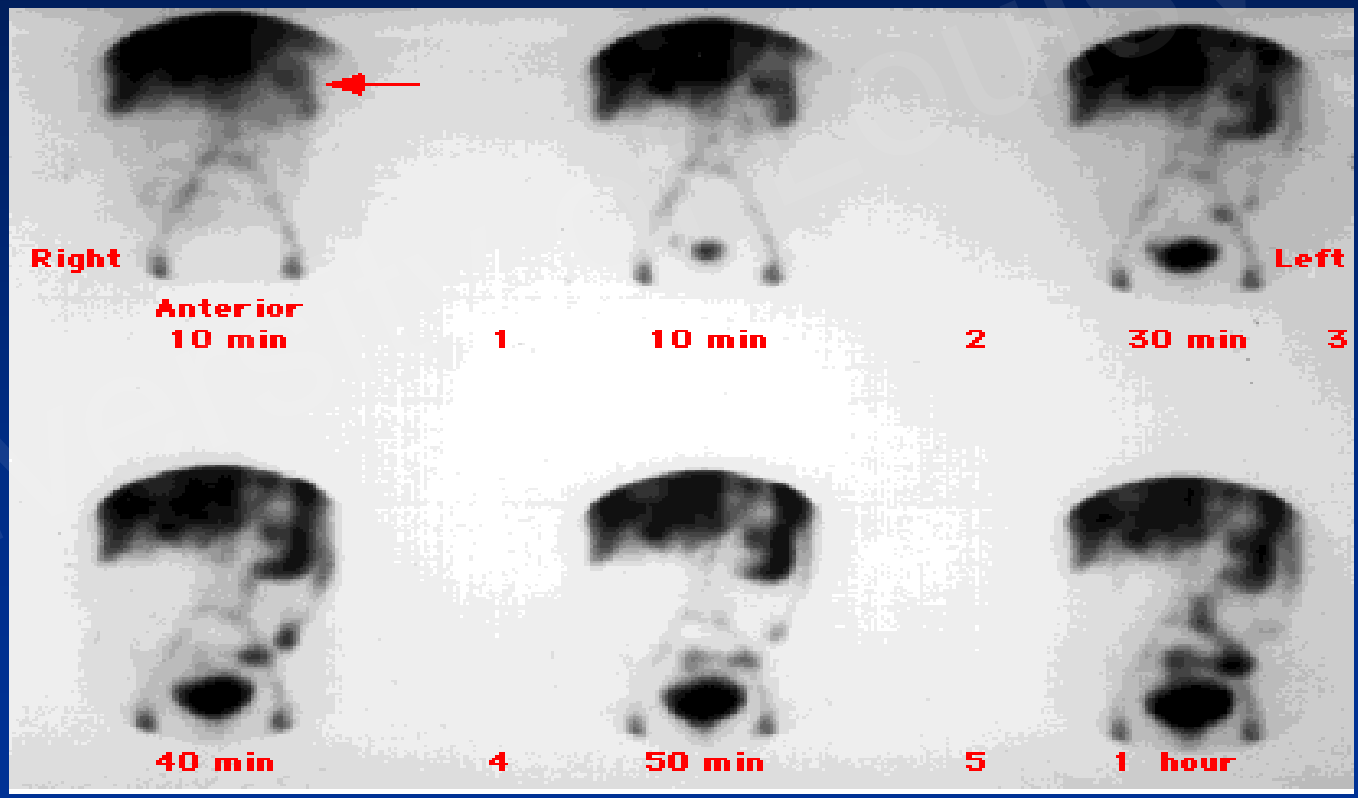
Evaluation of Obscure GI Bleeding

- **Radiological**
  - Enterolclysis
    - Modified form of SBFT
    - Barium and air infused in SB under higher pressure to better distend and visualize SB
    - Diagnostic yield better than SBFT 10-21% for obscure GIB
    - Excellent for Crohn's disease diagnosis

Evaluation of Obscure GI Bleeding

- **Radiological**
  - Technetium labeled nuclear scan
    - Two types
      - RBC labeled detects bleeding at 0.1ml/min
      - Sulfur colloid labeled detects bleeding at 0.05%ml/min
    - 20ml blood/sulfur tagged with technetium and injected into the pt.
    - Diagnostic yield for
      - obscure occult GIB 15 % and obscure overt GIB for 70%
    - RBC labeled more commonly used
    - Poor localization for bleeding

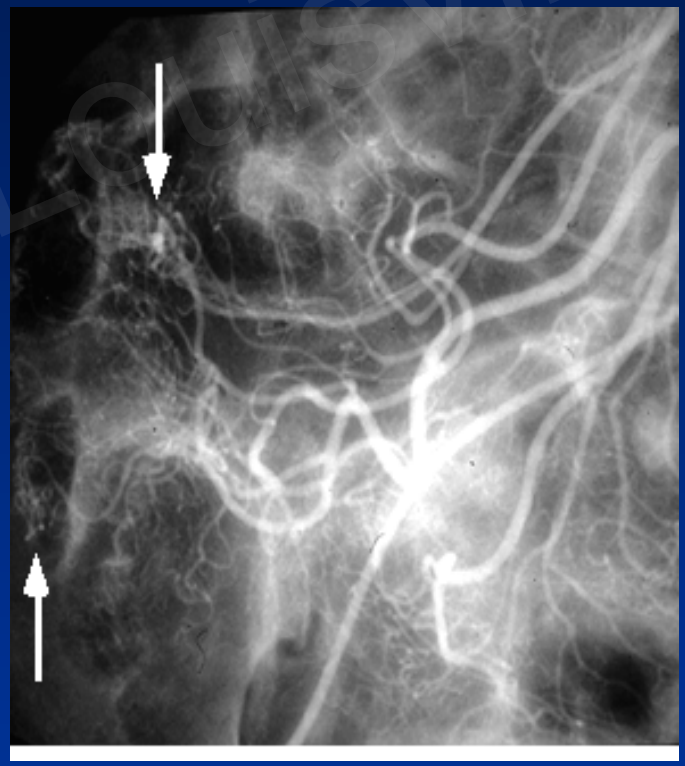
Evaluation of Obscure GI Bleeding



Evaluation of Obscure GI Bleeding

- **Radiological**
  - Angiography
    - Useful for pt. actively bleeding at 1ml/min
    - Provides both diagnostic and therapeutic options
    - Invasive and less sensitive than nuclear scan
    - Often performed after positive nuclear scan
    - Diagnostic yield for OGIB (overt) is 40%
    - Excellent in localization of bleeding
  - Provocative Angiography
    - Anticoagulants/vasodilators and thrombolytics

Evaluation of Obscure GI Bleeding



Evaluation of Obscure GI Bleeding

- **Radiological**
  - CT angio
    - Comparable with angiography in some study
    - 24 pts. with OGIB were studied, 15 were positive compared to angiography, 11+
  - MRI
    - No Role

Ernst et al; Eur Radiol 2003:114

Evaluation of Obscure GI Bleeding

- **Radiological**
  - Meckel's scan
    - Detects abnormal gastric mucosa in Meckel's diverticulum
    - Meckel's diverticulum congenital anomaly
    - Rule of 2
      - Present in 2%
      - Above 2 feet from TI
      - Bleeds in 2%
    - Cause 50% GIB in pt younger than 3 year
    - Less common in adults

Evaluation of Obscure GI Bleeding

- **Surgical**
  - Last option in overt obscure GIB
  - Includes
    - Exploratory laprotomy
    - Intraoperative enterosocopy
      - Entire SB examined in >90%
      - Diagnostic yield 50-90%

Evaluation of Obscure GI Bleeding

- **Surgical**
  - Specific diagnosis in 83%
    - 34% AVMS
    - 24% SB mass
    - 4% with Meckel's diverticulum
  - 31% re-bleed on long tern follow up
  - Invasive
  - Complications up to 12% and mortality 8%

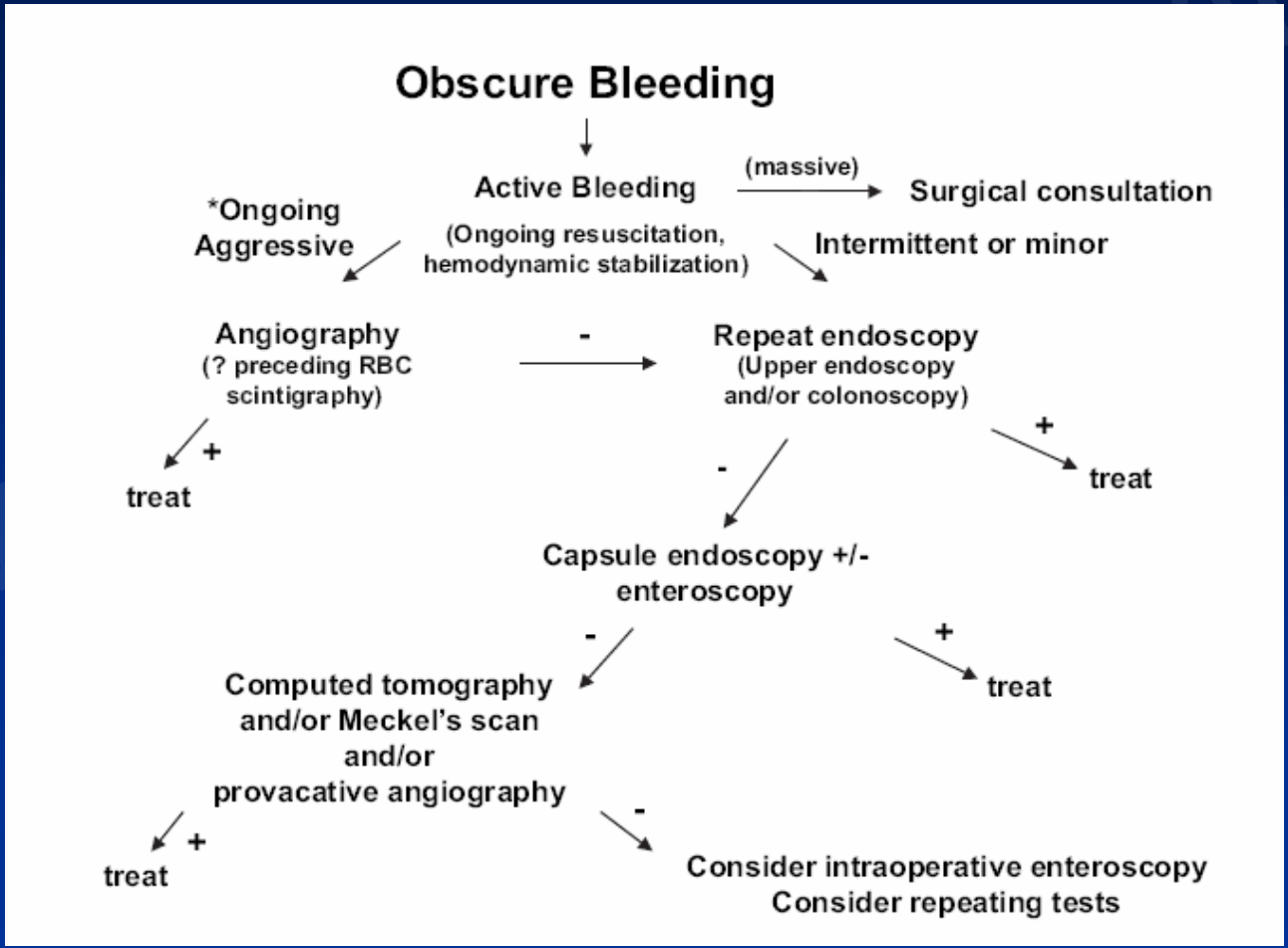
Baille et al; Gastro Endos 1997: 219

Evaluation of Obscure GI Bleeding

Studies in obscure gastrointestinal bleeding

Study	Therapy (Y/N)	Advantages	Disadvantages
SBFT	N	Safe	Insensitive
Enteroclysis	N	Safe	Poor for mucosal lesions
Scintigraphy	N	Safe	Localization only
Angiography	Y	Often helpful in active bleeding	Unable to identify lesion, invasive
CT	N	Safe	Little experience
Enteroscopy	Y	Wide experience	Unclear outcome data
Capsule endoscopy	N	Safe	Unclear outcome data
Surgery	Y	Great potential for therapeutic efficacy	Highly invasive

Evaluation of Obscure GI Bleeding



Treatment for Obscure GIB

- Conservative
  - Iron supplements
  - Blood transfusion
- Treat underlying etiology
  - Endoscopic
  - Rdiological
  - Surgical

Treatment for Obscure GIB

- Most common etiology for OGIB
  - Vascular ectasia
    - Telengectasia
    - Hemangiomas
    - AVMS
  - Treatment not very satisfactory

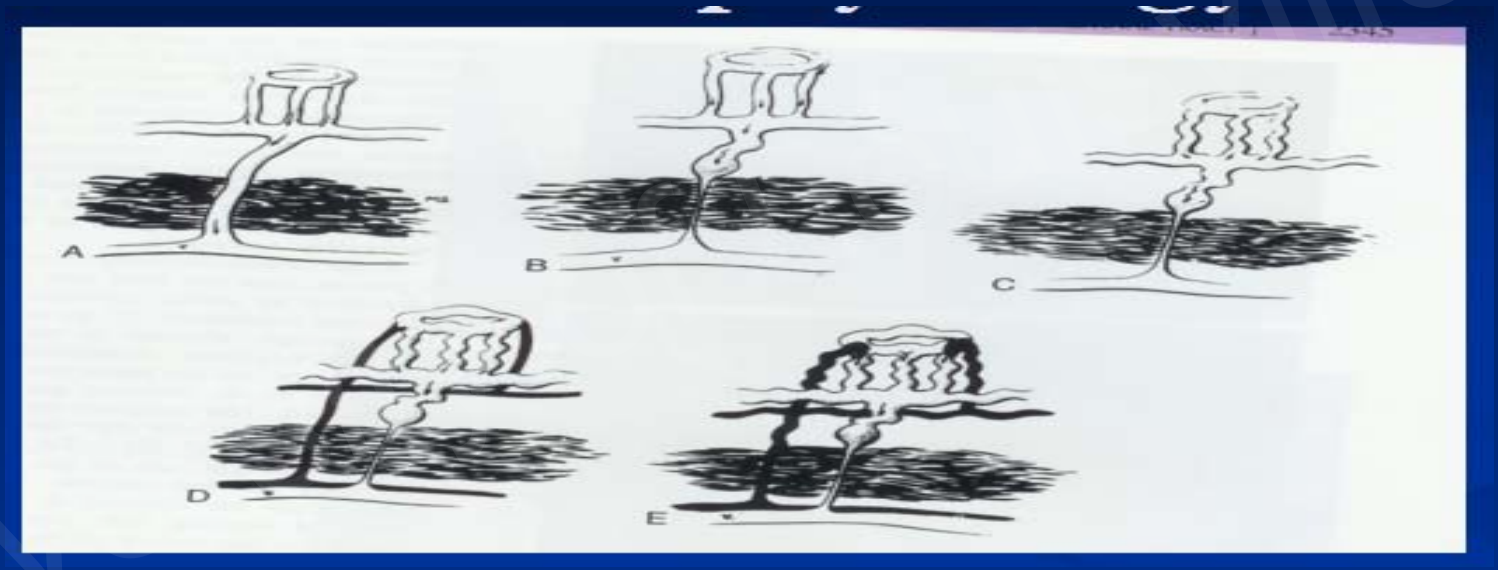
Treatment for Obscure GIB

- vascular ectasias
  - Common to right colon
  - Increased incidence with age
  - 2/3 patients over 70
  - Bleeding painless, occult or brisk
  - Natural history unknown

Treatment for Obscure GIB

- Vascular ecstasias are associated with
  - Chronic renal failure
  - Scleroderma
  - CREST
  - Cirrhosis
  - Aortic valve disease

Pathophysiology of Vascular ectasias



- Poorly understood
- Increase bowel wall stress
- Congestion of submucosal vein
- Dilation of arteriole- capillary-veins
- Creates AVM

Treatment for Obscure GIB

- Vascular ectasiasa
  - Hereditary like Osler-Weber-Rendu syndrome
    - Hormone therapy with Estrogen-progesterone
      - Decrease transfusion requirement and hospitalization
  - Sporadic lesions
    - No benefit with hormone treatment
    - Octreotide may be better
      - Decrease transfusion requirement

•Cutsem et al Lancet; 1990
•Junquera et al Gastro; 2002

Treatment for Obscure GIB

- Endoscopic therapy of vascular ectasias
  - Mixed result
  - APC and Electrocautery
    - Highly effective in acutely bleeding lesions
    - Decrease transfusion requirement when compared to no treatment
- Surgical therapy
  - Mixed result

Askin et al Gastrointes Endos 1996

Treatment for Obscure GIB

- Rebleed common
  - Medical — 26% at one yr and 46% 3 yr
  - Endoscopic — 20-30%
  - Surgical — 16% at one yr and 24% 3 yr

Obscure and Occult GI Bleed

- A diagnostic challenge
- Need better test to evaluate IDA and FOBT
- Newer technology evolving
- No promising treatment available

Occult and Obscure GI Bleed

QUESTIONS?

Evaluation of occult bleeding