

ای که با نامت جهان آغاز شد
دقتر ما هم به نامت باز شد

رویکرد بالینی به دفع خون مخفی در مدفوع



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Occult GI bleeding  GI bleed that Initially presents as FOBT and/or iron deficient anemia without any visible blood in the stool

Obscure GI bleeding  GI bleed that persist or recurs without any obvious etiology after standard endoscopic examination

The healthy person passes roughly 2 ml of blood in 150 grams of stool.

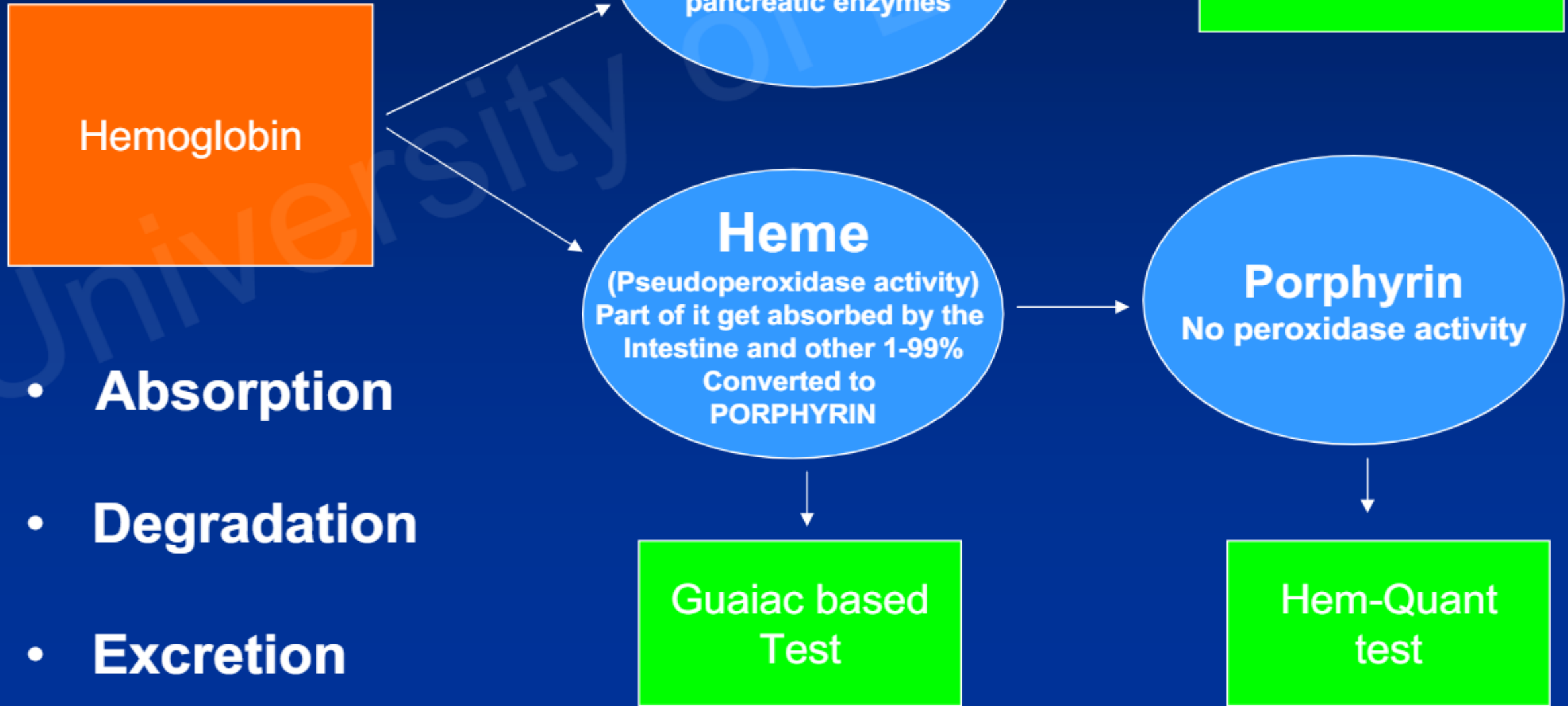


TYPES

- Guaiac test
- Heme-porphyrin test
- Immunochemical test

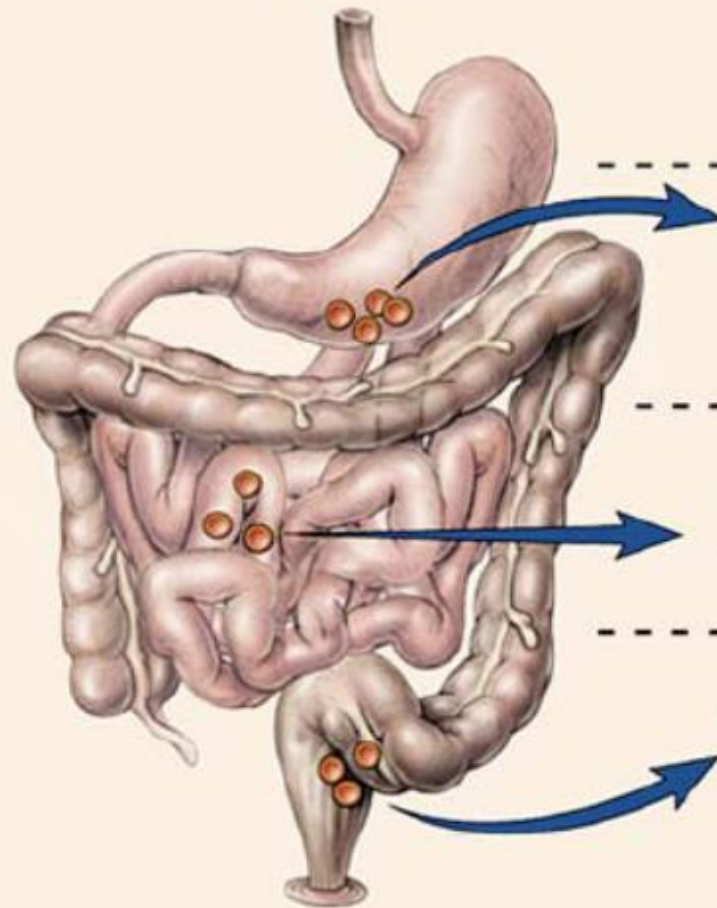


Metabolism of Hemoglobin



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

Sites of Gastrointestinal Bleeding



Relative Likelihood of a Positive Fecal Occult-Blood Test

Upper gastrointestinal tract

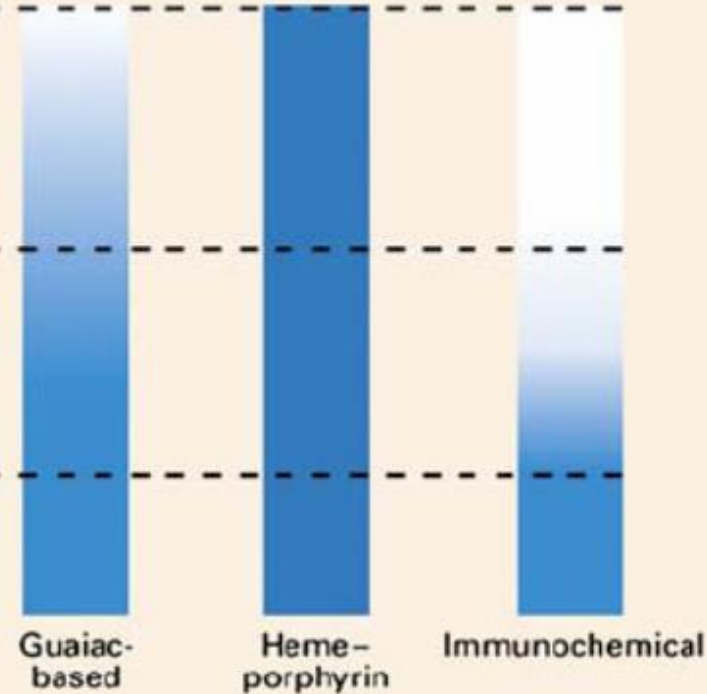
Porphyrins, partially degraded heme, degraded globin

Middle gastrointestinal tract

Porphyrins, partially degraded heme, partially degraded globin

Lower gastrointestinal tract

Intact heme and intact globin



Guaiac based test

- Being used for more than a century

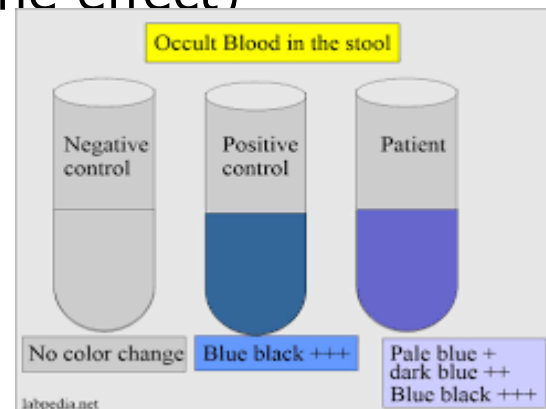
The test involves placing a fecal sample on guaiac paper (containing a phenolic compound, alpha-guaiaconic acid, extracted from the wood resin of Guaiacum trees) and applying hydrogen peroxide which, in the presence of blood, yields a blue reaction product within seconds.

- 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 (prozone effect)

- Two types

1- Hemoccult

2- Hemoccult II SENSA



False positive FOBT (Guaiac)

Medications

- Aspirin/NSAIDS , anticoagulants and steroids/ boric acid, colchicine, bromides, and iodine.

Iron supplements(In vivo vs in vitro)

Exogenous peroxidase activity

- Red meat consumption
- Fruit consumption(cantaloupe , grapefruit, figs ,bananas ,grapes...)
- Uncooked vegetables (radish, cauliflower, broccoli , turnip ,mushroom)

Extraintestinal blood loss

- Epistaxis/gingival bleeding/hemoptysis
 - Hemorrhoid and women on menstrual flow
 - White cells and bacteria also cause a false positive test.



False negative FOBT

- Dry stool specimen
 - Hem (Fe^{2+} {ferrous ion}) degradation to porphyrin(heme oxygenase's catabolize heme's porphyrin ring and iron atom within it to carbon monoxide and ferrous, $\text{Fe}(\text{II})$)
 - Ascorbic acid/vitamin C (more than 250 mg/day)
 - Heat



Guaiac test not indicated

- Person who don't follow the diet
- In hospital patients
- Naso-gastric aspirate or vomit
- Apparent melena or hematochezia



Immunochemical FOB(T)(FIT)

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(prozone effect)
- Detects only lower GI tract bleeding not upper as globulin is digested by pepsin and pancreatic enzymes



Hem-porphyrin assay FOBT

HemoQuant – Involves hem and hem derived porphyrin

- Quantification of blood loss
 - Sensitive for both upper and lower GI bleed
 - Higher sensitivity for upper bleed compared to guaiac and immunochemical testing
- Takes 2-4 days for the result
- Not affected by medications/dietary peroxidases except red meat



- **The most common indications for FOBT are anemia, and colon cancer screening.**
- It can also be used to help discriminate irritable bowel syndrome (IBS) from inflammatory bowel disease (IBD), which is more likely to yield a positive test result





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College of Surgeons

Southern surgical association article

Colon Cancer in Patients Under 25 Years Old: A Different Disease?



Clinical features of pediatric CRC patients.

Case No.	Age (years)	Gender	Presenting symptoms with duration	Site	Modified Duke's Stage	Histopathology	Management	Outcome
1	10.2	Male	Abdominal pain, vomiting, fever (15 day)	Right	C	Mucinous	Laprotomy with ileostomy with biopsy, neo-adjuvant chemotherapy, R1 resection, adjuvant chemotherapy	Disease free at 1.8 year follow up
2	9	Male	Intestinal obstruction (7 day)	Left	C	Signet cell	Laprotomy with biopsy, adjuvant chemotherapy. Re-exploration with ileostomy	Expired after 2 month
3	9.9	Male	Abdominal lump, lower limb swelling (4 month)	Right	-	NOS	Guided biopsy, neoadjuvant chemotherapy	On treatment
4	9.4	Female	Multiple perineal abscess (3 month)	Rectum	-	Mucinous	Per rectal biopsy	Expired after 5 days
5	8.6	Male	Per rectal bleeding (7 month)	Rectum	-	Mucinous	Per rectal biopsy, chemotherapy	Expired after 3.5 month
6	9	Male	Abdominal pain, low grade fever (8 month)	Right	-	Signet cell	Biopsy, refused surgery	Expired after 1 month
7	11.8	Female	Intestinal obstruction (5	Right	-	Mucinous	Open laparotomy with biopsy, ileostomy,	Lost to follow up





- CRC can present in the first decade of life. Its different biology is responsible for its atypical presentation, advanced stage at diagnosis, aggressive histological subtypes and poorer survival.
- Increasing awareness of this entity at such young age amongst pediatricians and family practitioners would aid early diagnosis, prompt management, and **also prevent side effects of wrong treatments such as antituberculosis treatment(ATT)or steroids.**
- **Poorer outcome** in children warrants a need for pediatric CRC trials both to establish etiology and for refining treatment recommendations in these children.



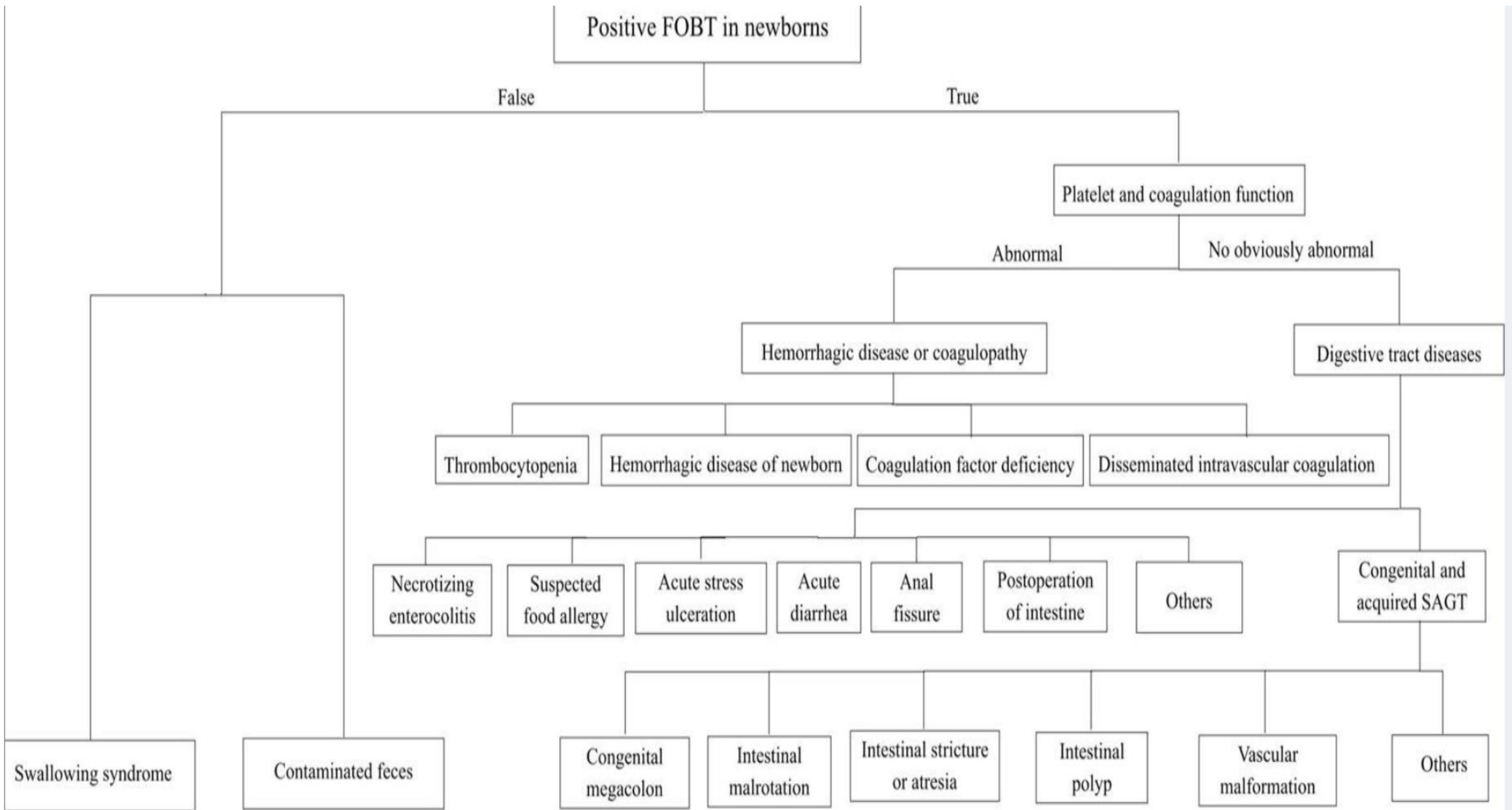
- The majority of CRCs occur sporadically. A mere 10%–30% of the reported childhood CRCs has been found to arise in the setting of hereditary cancer syndromes, more commonly FAP and HNPCC.
- Other associated polyposis syndromes include: Peutz-Jegher's and Juvenile Polyposis coli. The most important genetic mutation observed in childhood CRC if any is high MSI (MSI-H).
- Tumor that shows mutations of two or more of the five microsatellite sequences (enlisted by the National Cancer Institute) is labeled as MSI-H, which is the hallmark of early-onset CRC.



Note

- GIST(hemorrhagic)
- GI neuroblastoma
- Gastrointestinal metastasis:
 - Non Hodgkin lymphoma
 - MALT lymphoma





Positive FOBT in newborns

False

True

Platelet and coagulation function

Abnormal

No obviously abnormal

Hemorrhagic disease or coagulopathy

Digestive tract diseases

Thrombocytopenia

Hemorrhagic disease of newborn

Coagulation factor deficiency

Disseminated intravascular coagulation

Necrotizing enterocolitis

Suspected food allergy

Acute stress ulceration

Acute diarrhea

Anal fissure

Postoperation of intestine

Others

Congenital and acquired SAGT

Swallowing syndrome

Contaminated feces

Congenital megacolon

Intestinal malrotation

Intestinal stricture or atresia

Intestinal polyp

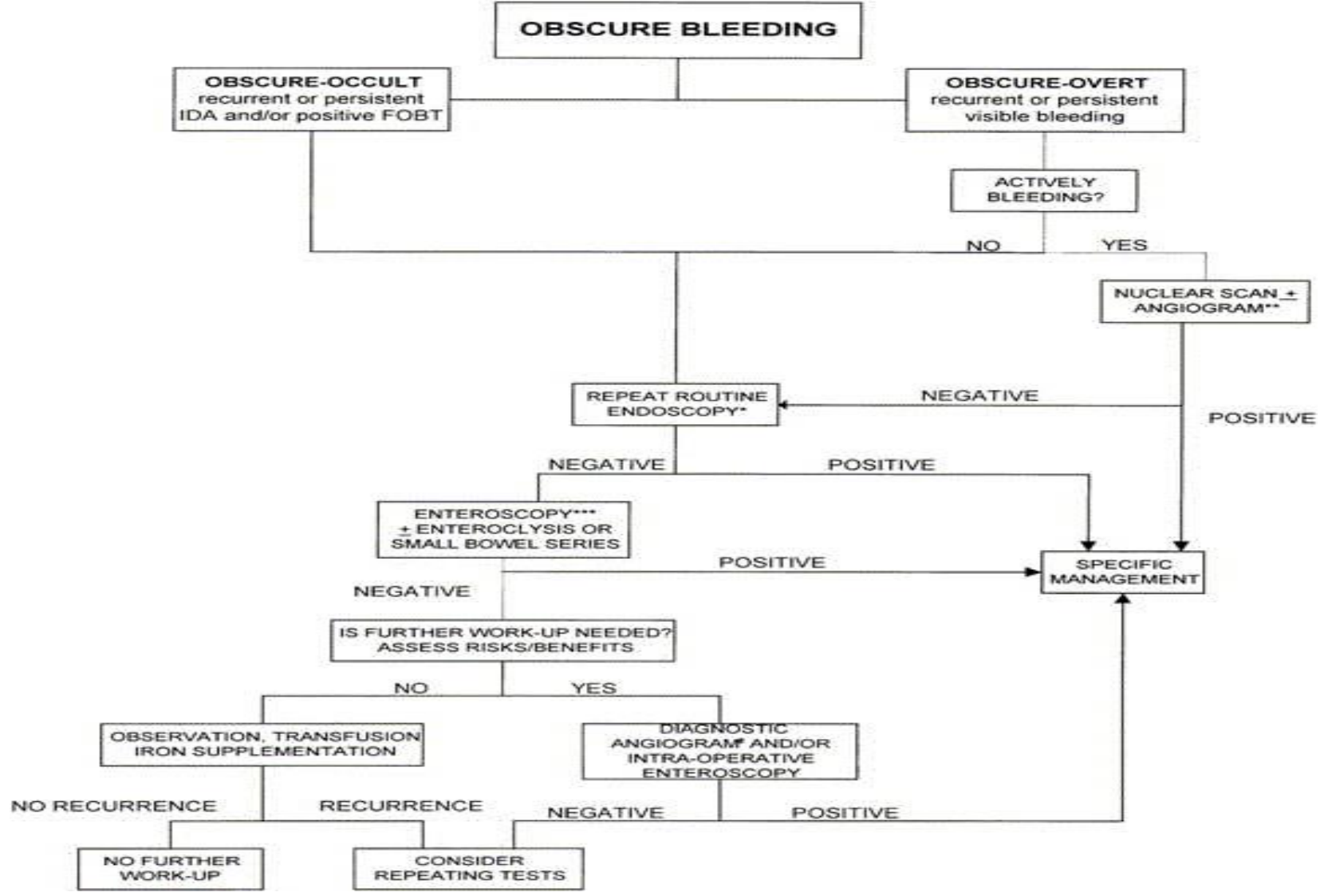
Vascular malformation

Others

NEC

- Stool tests: **Generally not useful**
- — Bedside stool tests (examination for occult blood and reducing substances, and measurement of alpha-1 antitrypsin) have not been clinically helpful as they are nonspecific findings .
- For example, occult blood in the stool is commonly found in preterm infants. In a survey of infants <1800 g, 58 percent of infants had at least one positive occult blood in stool test over a six-week period.
- OGT/NGT





Constipation

Recommendations	Quality of evidence ^a
General recommendations	
A thorough history and physical examination are an important part of the complete evaluation of the infant or child with constipation.	III
Performing a thorough history and physical examination is sufficient to diagnose functional constipation in most cases.	III
A stool test for occult blood is recommended in all constipated infants and in those children who also have abdominal pain, failure to thrive, diarrhea, or a family history of colon cancer or polyps.	III
In selected patients, an abdominal radiograph, when interpreted correctly, can be useful to diagnose fecal impaction.	II-2
Rectal biopsy with histopathological examination and rectal manometry are the only tests that can reliably exclude Hirschsprung disease.	II-1
In selected patients, measurement of transit time using radiopaque markers can determine whether constipation is present.	II-2
Recommendations for infants	
In infants, rectal disimpaction can be achieved with glycerin suppositories. Enemas are to be avoided.	II-3
In infants, juices that contain sorbitol, such as prune, pear, and apple juices can decrease constipation.	II-3
Barley malt extract, corn syrup, lactulose, or sorbitol (osmotic laxatives) can be used as stool softeners.	III
Mineral oil and stimulant laxatives are not recommended for infants.	III
Recommendations for children	
In children, disimpaction can be achieved with either oral or rectal medication, including enemas.	II-3
In children, a balanced diet, containing whole grains, fruits, and vegetables, is recommended as part of the treatment for constipation.	III
The use of medications in combination with behavioral management can decrease the time to remission in children with functional constipation.	I
Mineral oil (a lubricant) and magnesium hydroxide, lactulose, and sorbitol (osmotic laxatives) are safe and effective medications.	I
Rescue therapy with short-term administration of stimulant laxatives can be useful in selected patients.	II-3
Senna and bisacodyl (stimulant laxatives) can be useful in selected patients who are more difficult to treat.	II-1
Polyethylene glycol electrolyte solution, given in low dosage, may be an effective long-term treatment for constipation that is difficult to manage.	III
Biofeedback therapy can be an effective short-term treatment of intractable constipation.	II-2
^a Categories of the quality of evidence (95):	
I: Evidence obtained from at least one properly designed randomized controlled study. II-1: Evidence obtained from well-designed cohort or case-control trials without randomization. II-2: Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than 1 center or research group. II-3: Evidence obtained from multiple time series with or without intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence. III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.	





AMERICAN ACADEMY OF
FAMILY PHYSICIANS

STRONG MEDICINE FOR AMERICA

- A stool test for occult blood is recommended in all constipated infants (greater likelihood of an organic etiology) and in those children who also have abdominal pain ; failure to thrive ; diarrhea or a family history of colon cancer or polyp.
- (Fissure/Hemorrhoid...)

Occult blood in stool

Hirschsprung disease, food
allergy, necrotizing enterocolitis



Food allergy

- Although the FOBT has an adequate sensitivity to diagnose **Food protein-induced allergic proctocolitis (FPIAP)** in infants with rectal bleeding, this test had abnormal results in more than a third of healthy infants. Therefore, the routine use of FOBT is not recommended for the diagnosis of FPIAP.
- Diagnostic validity of fecal occult blood test (FOBT) was assessed in infants with rectal bleeding secondary to allergic proctocolitis compared to healthy infants. The results of this study showed that, although FOBT has adequate sensitivity (84%; negative predictive value 83%), it has inadequate specificity (66%; positive predictive value 68%) since more than one-third of healthy infants had positive FOBT
- **Nodular lymphoid hyperplasia(NLH)** occasionally presents as anemia and positive FOBT



Screening for fecal occult blood loss in severely malnourished children

- A positive fecal occult blood test (FOBT) is strongly associated with moderate to severe anemia in severe PEM patients.
- So all patients having a positive FOBT should have a hemogram profile done and then appropriately treated for anemia.



Fecal Occult Blood Test and Gastrointestinal Parasitic Infection(Saudi Arabia)

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Parasite (n)	(Single infection)		(Mixed infection)		P-value
	+Ve FOB	-Ve FOB	+Ve FOB	-Ve FOB	
Hookworm (184)	32	67	35	50	0.213
<i>T. trichiura</i> (123)	14	37	19	53	0.896
<i>A. lumbricoides</i> (11)	2	4	1	4	0.621
<i>H. nana</i> (10)	0	4	0	6	*
<i>S. mansoni</i> (14)	2	1	4	7	0.347
<i>S. stercoralis</i> (20)	1	4	3	12	1.0
<i>E. vermicularis</i> (2)	0	0	0	2	*
<i>T. saginata</i> (2)	0	1	0	1	*
<i>E. histolytica</i> (43)	1	0	14	28	0.167
<i>G. lamblia</i> (39)	4	17	3	15	0.847
<i>B. hominis</i> (245)	16	109	17	103	0.754
Nonpathogenic protozoa (156)	12	33	19	92	0.176



India

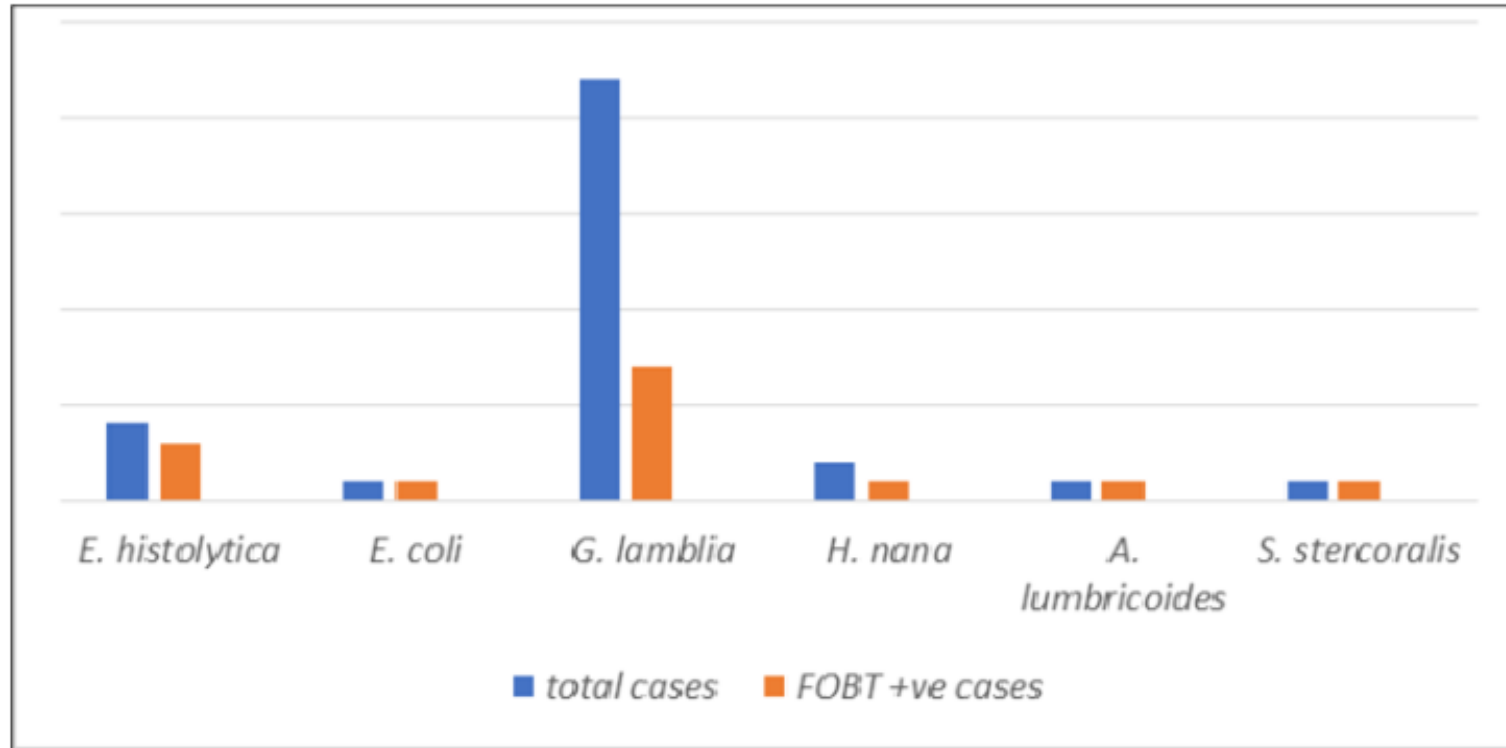


Figure 2 Comparison between total cases and FOBT positive cases of respective parasitic infections



Giardia

- Vitamin k malabsorption?
- Electrolyte transport abnormalities?
- Enterocyte apoptosis and loss of epithelial barrier function?
- Role of parasite virulence factors?



TB

- From the obtaining results and after comparing the results of FOB with the results of PCR. Obviously, the FOB strips used as screening test for the GI tuberculosis patients. If the test is positive need confirm by a well-established methods like PCR techniques.

Table-2: Shows the result of FOB test of 67 patients

The result	No. of patients	percentage
Positive	53	79.1%
negative	14	20.9%



H. Pylori



- H.pylori consumption of iron by the organism itself
- Gastrointestinal blood loss due to *H. pylori*-induced gastrointestinal lesions and gastritis increased levels of neutrophil-derived lactoferrin, and since *H. pylori* has a lactoferrin-binding protein receptor, the infection may result in increased iron losses related to bacterial turnover.
- Since these bacteria have a high turnover rate, a large amount of iron may be lost in stools in the form of dead bacteria



- **Intussusception** : a negative fecal occult blood test cannot reliably rule out the diagnosis of intussusception .
- **Meckel diverticulum** : Anemia- positive fecal occult blood
- **Mesenteric ischemia** : While a positive fecal occult blood test further points towards the diagnosis, it is likely to be positive only after mucosal infarction sets in.



Celiac disease

- Occult gastrointestinal bleeding occurs in a small number of symptomatic celiac disease patients before diagnosis, but is no more frequent in treated and undetected celiac disease patients than in the general population.
- Abnormal activation of the immune system following the release of inflammatory cytokines----- Inflammation ?Macrophages?
- The results suggest that bleeding is uncommon in celiac disease, and that positive results with colorimetric tests might be due to excess loss of intestinal cells and/or malabsorption of peroxidase-containing foods. Our results suggest that bleeding is not an important contributor to the iron deficiency often found in these subjects.



IBD

	Sensitivity (95% CI)	Specificity (95% CI)
FOBT and perianal examination	65.9% (54.8–75.8)	72.0% (66.0–77.5)
Hematocrit	59.0% (47.7–69.7)	60.4% (53.8–66.8)
Platelet count	33.8% (23.6–45.2)	95.5% (91.9–97.8)
Albumin	18.4% (10.5–29.0)	97.4% (94.0–99.2)
CRP	50.7% (38.4–63.0)	89.2% (82.8–93.8)
ESR	54.4% (42.8–65.6)	90.8% (85.9–94.5)

CI = confidence interval; CRP = C-reactive protein; ESR = erythrocyte sedimentation rate; FOBT = fecal occult blood testing.



	Odds ratio (95% CI)	<i>P</i>	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)
CRP	8.85 (2.79–27.78)	0.0002	51.2 (35.9–66.5)	91.0 (84.7–97.4)	75.0 (59.0–91.0)	78.0 (69.5–86.5)
Platelet count	6.13 (1.26–29.41)	0.0247	36.6 (21.9–51.3)	93.6 (88.2–99.0)	75.0 (56.0–94.0)	73.7 (65.0–82.4)
FOBT and perianal examination	6.10 (2.08–17.86)	0.001	82.9 (71.4–94.4)	56.4 (45.4–67.4)	50.0 (38.1–61.9)	86.3 (76.9–95.7)

CI = confidence interval; CRP = C-reactive protein; FOBT = fecal occult blood testing.

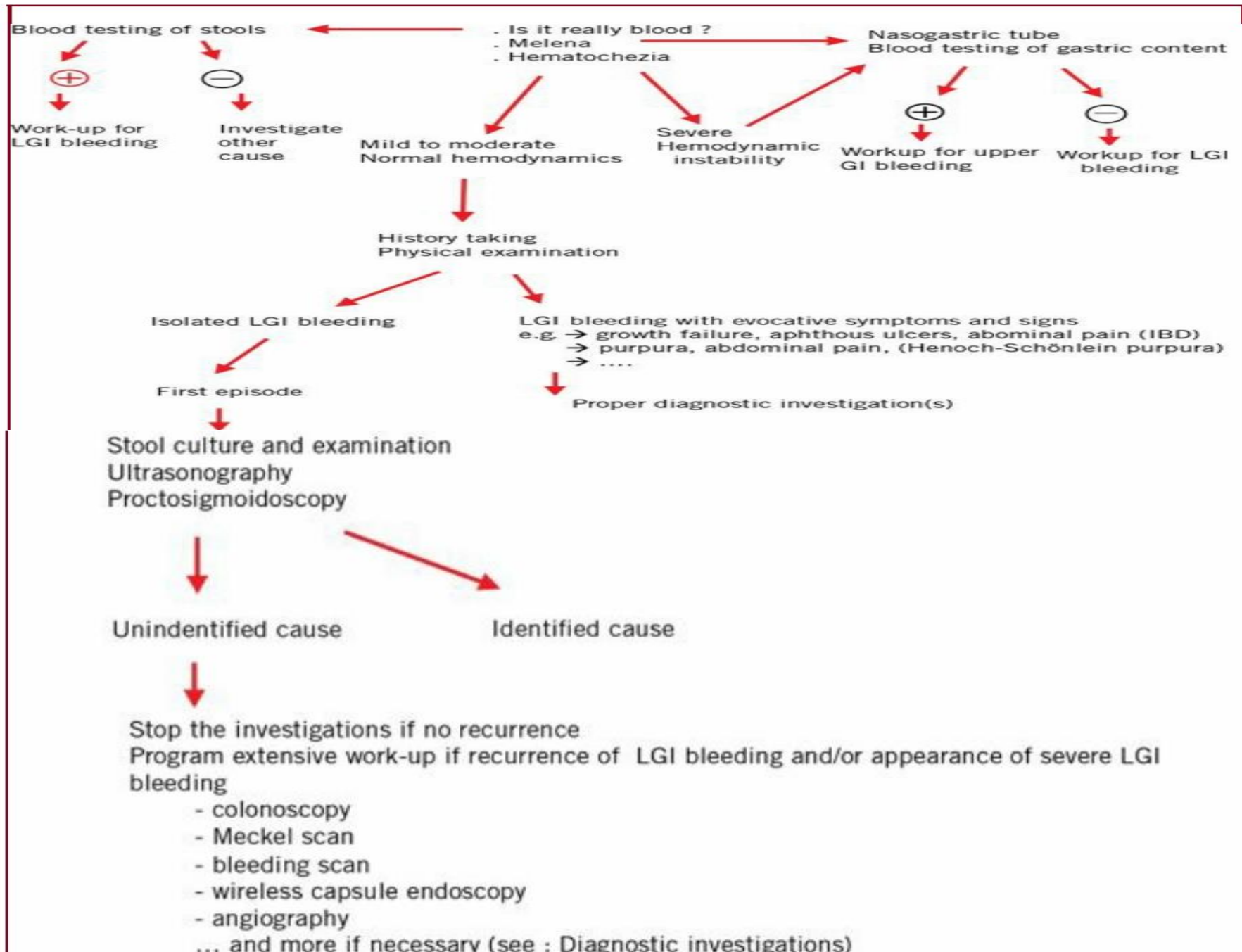
JOURNAL OF PEDIATRIC GASTROENTEROLOGY AND NUTRITION

Addition of FOBT and perianal examination to a laboratory-based testing strategy improves the screening process of children for IBD



- **Sexual abuse** & Sexually transmitted infection (STI). STIs such as gonorrhoea, chlamydia, **syp**hilis, and herpes can cause inflammation and bleeding. Bleeding can also be a result of damage from anal sex.
- Solitary rectal ulcer
- Polyps
- OB&pica





- Diagnostic approaches for OGIB in **anemia**, after negative endoscopy and colonoscopy, can require small bowel endoscopic investigation by video capsule endoscopy (VCE).
- Balloon-assisted enteroscopy (BAE), with single or double-balloon enteroscopy (DBE), is the second-line technique, having the advantage of therapeutic as well as diagnostic properties.



Causes of occult gastrointestinal bleeding

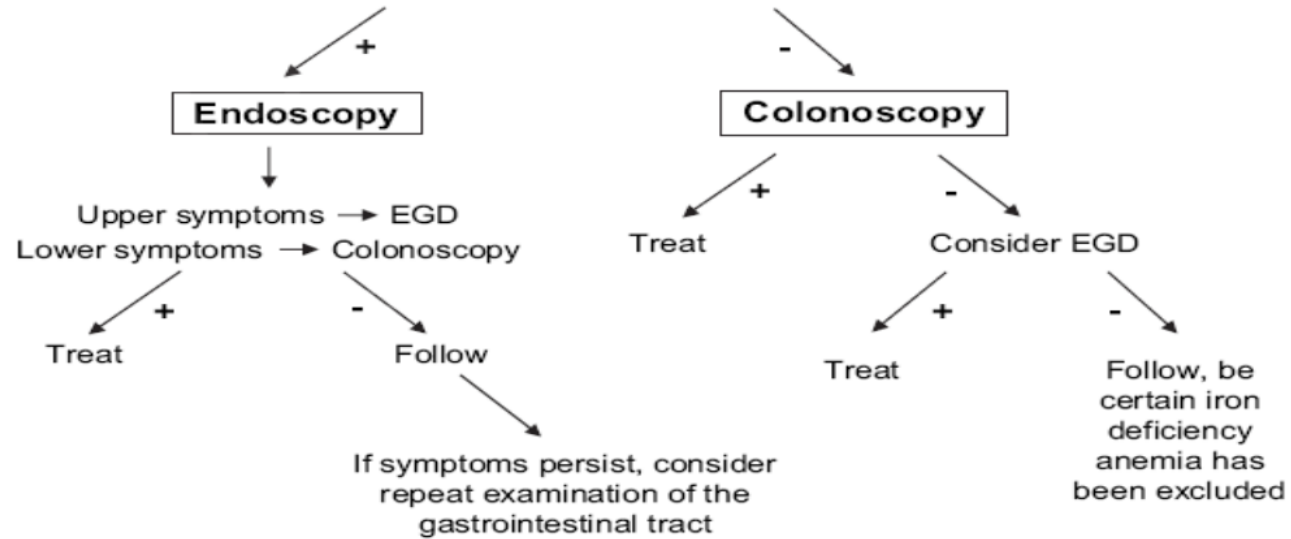
Inflammatory/mechanical trauma	Mass lesions	Vascular	Infectious	Miscellaneous
		Vascular ectasia(s)	Hookworm	Long-distance running
Reflux esophagitis	Carcinoma (any site)	Portal hypertensive gastropathy	Strongyloidiasis	Factitious
Cameron lesions	Large polyps (any site)	Portal hypertensive enteropathy and colonopathy	Ascariasis	Hemoptysis
Erosive gastritis		Gastric antral vascular ectasia	Tuberculous enterocolitis	Epistaxis
Gastric ulcer		Hemangiomas	Amebiasis	Oropharyngeal
Duodenal ulcer		Blue rubber bleb nevus syndrome		
Celiac sprue				
Whipple disease				
Meckel diverticulum with ulceration				
Idiopathic cecal ulcer				
Crohn disease				
Ulcerative colitis				



Fecal Occult Blood

↓
History, physical examination

↓
Gastrointestinal symptoms



CRC screening

- The U.S. Preventive Services Task Force (USPSTF) recommends initiating screening at age 45 (Grade B) while maintaining its strongest recommendation (Grade A) for initiating at age 50 .
- The American College of Gastroenterology (ACG) 2021 guidelines also recommend initiating screening at age 45 in all adults at average risk .
- Initiating screening at age 45 years is a “qualified” recommendation from the American Cancer Society (ACS); this accompanies its strong recommendation to screen at age 50 or older. The ACS noted that data to support starting at age 45 years are limited; the rationale is supported from some but not all modeling analyses .
- Initiating screening at age 50 years for average-risk adults is recommended by the Canadian Task Force on Preventive Health Care (CTFPHC), the European Council, the American Academy of Family Physicians (AAFP), and the American College of Physicians (ACP)



- **Fecal immunochemical testing** – We advise screening with FIT for occult blood annually on a single sample as an option for screening.
- We recommend FIT for screening for patients unable or unwilling to have a colonoscopy as initial screening, or when access to colonoscopy is limited, with the understanding that if the FIT result is positive, colonoscopy needs to be performed promptly.
- Compared with colonoscopy, FIT has similar detection rates for CRC but lower detection rates for advanced adenomas.
- However, compared with fecal occult blood testing (FOBT), FIT has greater sensitivity without loss of specificity as well as better detection of advanced adenomas



