**الكلية : الطب**

**القسم او الفرع : الباطنية**

**المرحلة: الثالثة**

**أستاذ المادة : م.د احمد عبدالسلام رشيد**

**اسم المادة باللغة العربية : الباطنية**

**اسم المادة باللغة الإنكليزية : internal medicine**

**اسم المحاضرة الثامنة باللغة العربية: اليرقان و نزف الجهاز الهضمي**

**اسم المحاضرة الثامنة باللغة الإنكليزية : Jaundice and GIT bleeding**

# PRESENTING PROBLEMS IN INTERNAL MEDICINE

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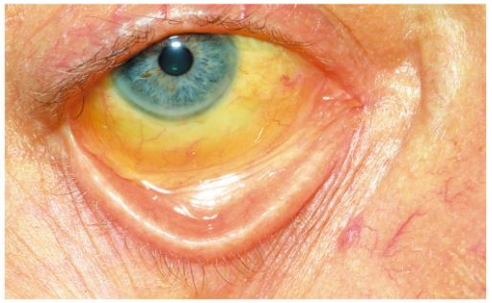
# Presenting problems in Gastrointestinal system

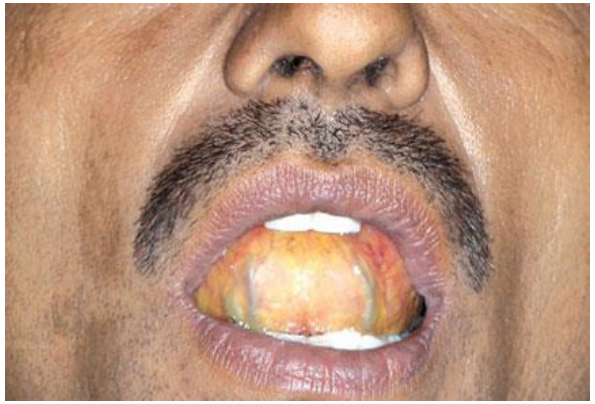
- ✓Dysphagia
- ✓Dyspepsia
- ✓Heartburn and regurgitation ( GERD )
- ✓Vomiting
- ✓Diarrhea
- ✓Constipation
- ✓Abdominal pain
- ✓Weight loss
- ✓Jaundice
- ✓Gastrointestinal bleeding

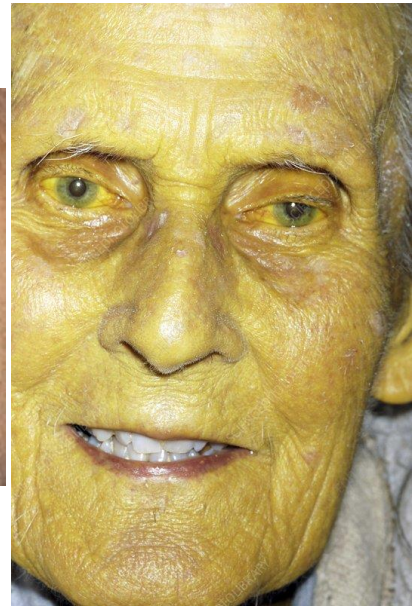
# Jaundice

# Definition

- **Jaundice** is a yellowish discoloration of the skin, sclerae and mucous membranes caused by hyperbilirubinemia .
- Jaundice is clinically detected, in good light, when bilirubin levels exceed 50 mmol/L (**3 mg/dL**).
- Sclerae have a particular affinity for bilirubin due to their high elastin content .
- Sites to detect jaundice during examination :
  - ✓sclera , first site
  - ✓under the tongue
  - ✓and when severe , the skin





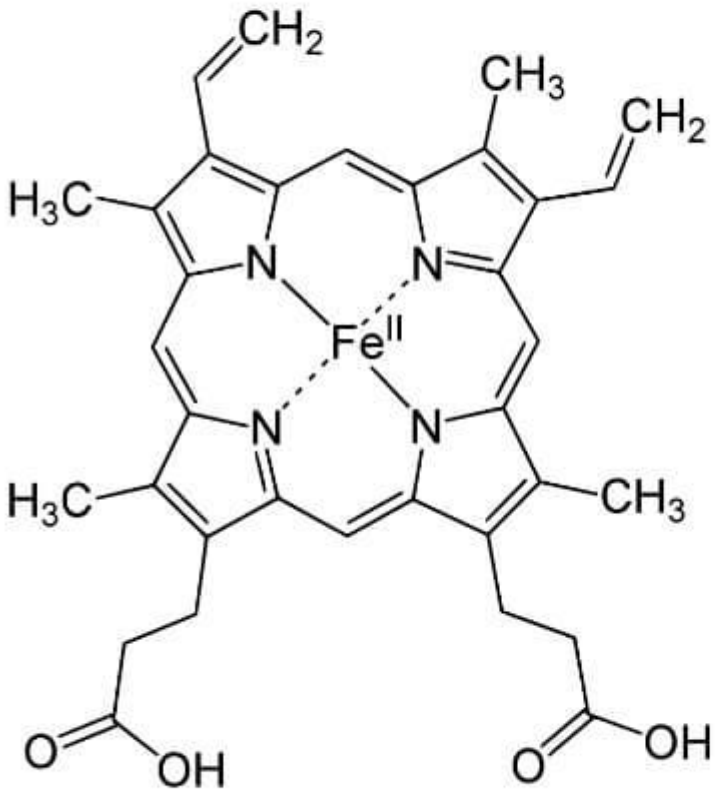


**Define Carotenoderma**

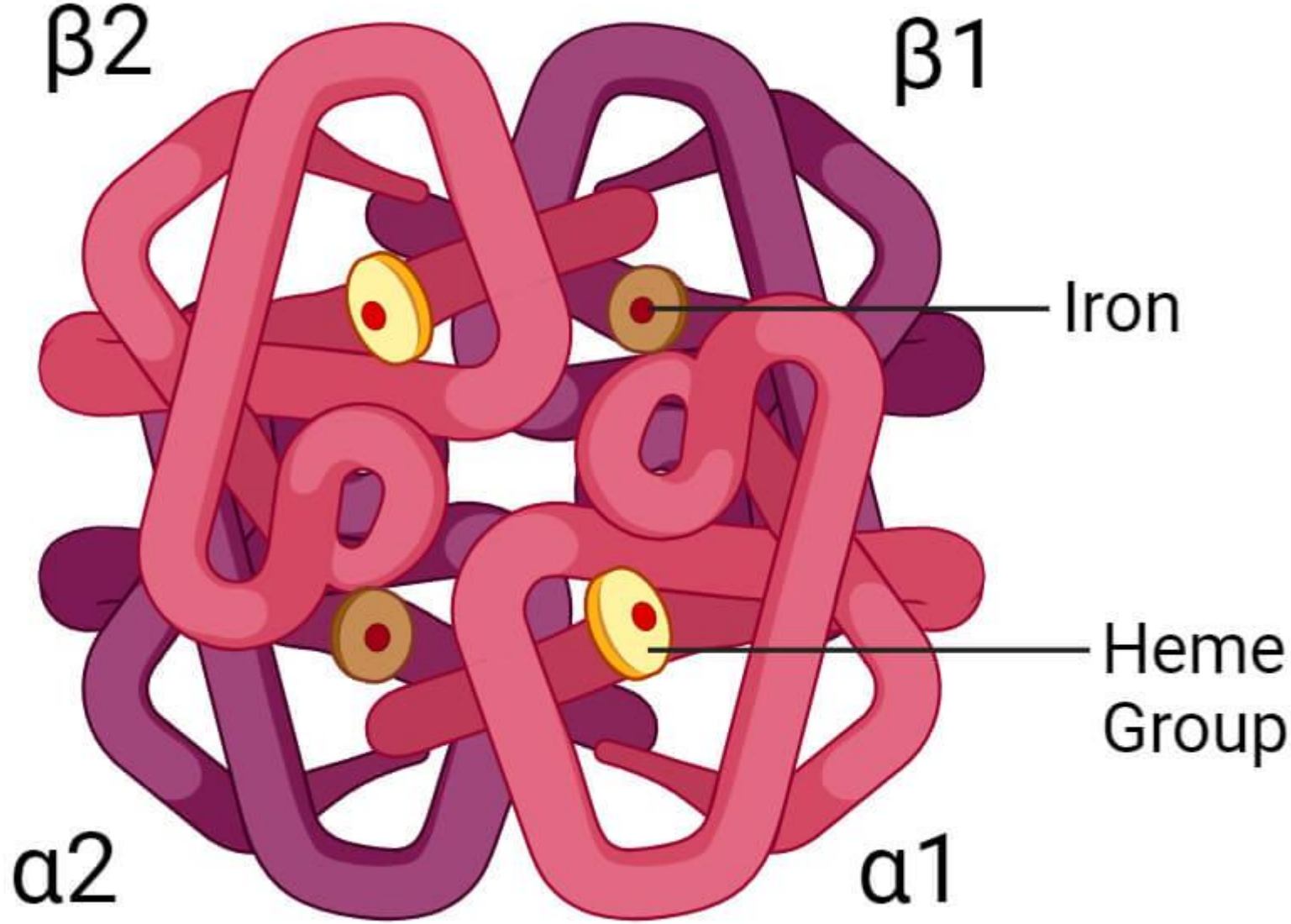
How to differentiate clinically between Carotenoderma and Jaundice ?

What are the causes of Carotenoderma

# Hemoglobin

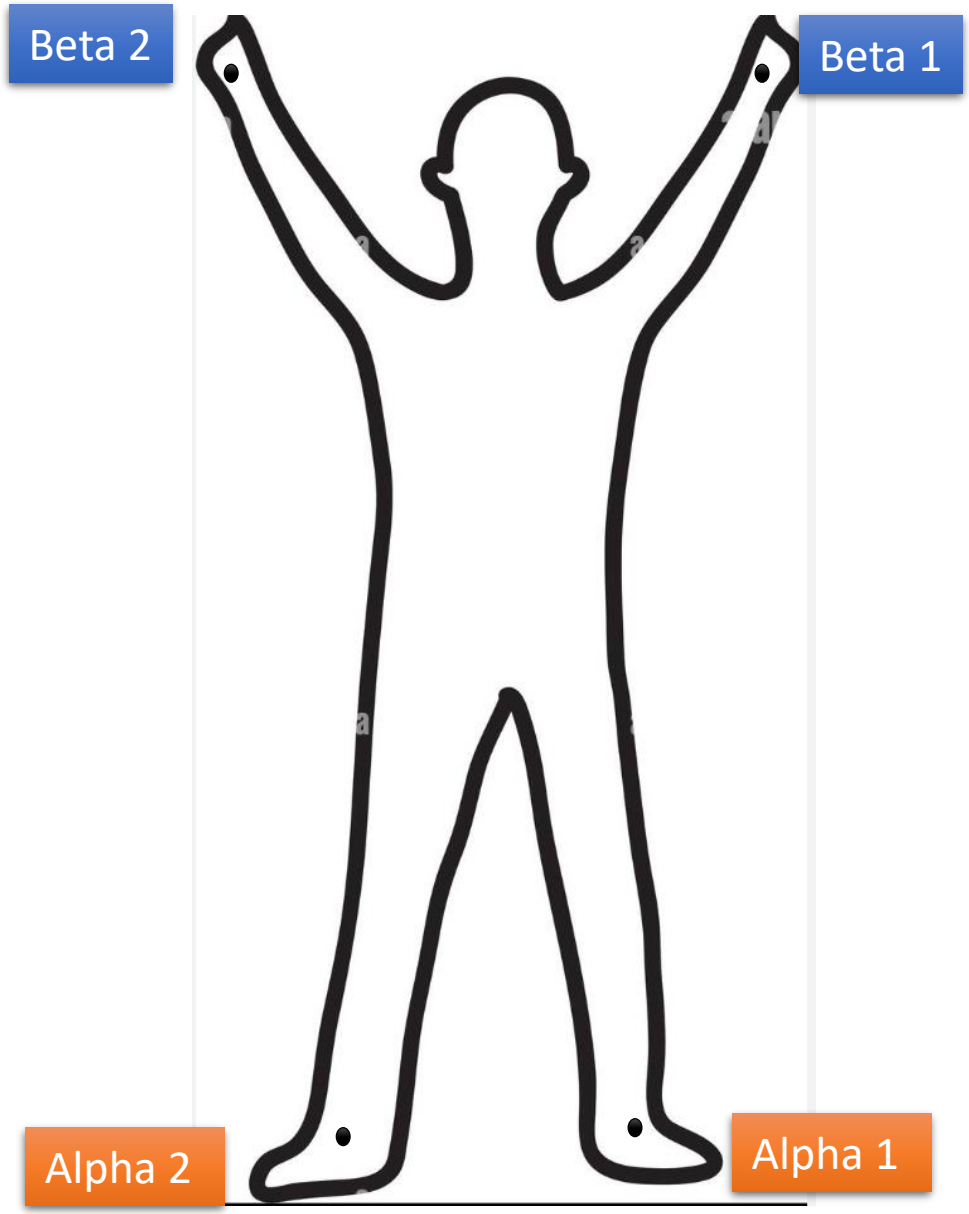


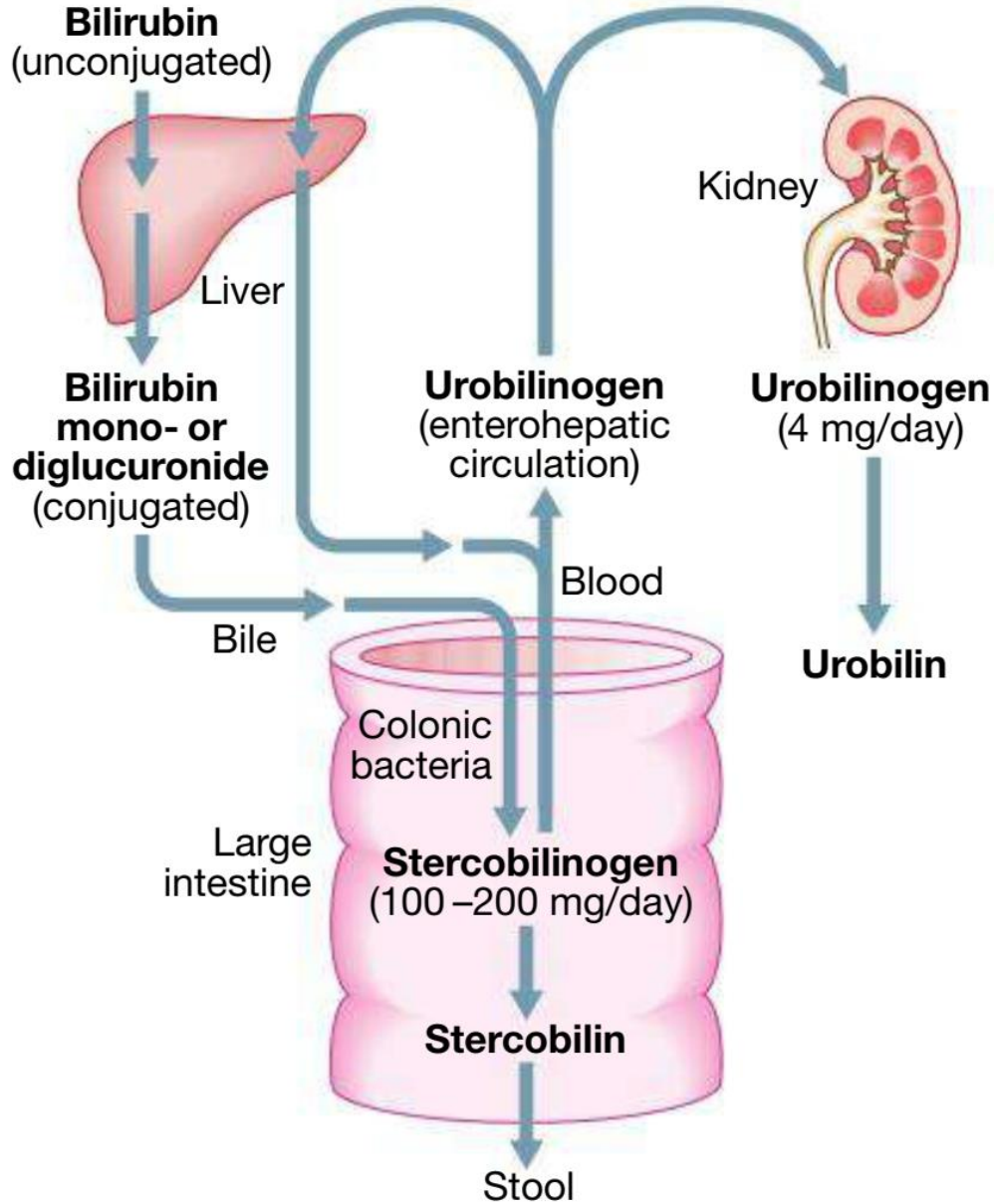

heme *b*



Heme

iron




Bilirubin
(unconjugated)
Liver
Bilirubin
mono- or
diglucuronide
(conjugated)
Bile
Urobilinogen
(enterohepatic
circulation)
Blood
Kidney
Urobilinogen
(4 mg/day)
Urobilin
Colonic
bacteria
Large
intestine
Stercobilinogen
(100 –200 mg/day)
Stercobilin
Stool

# Bilirubin metabolism and bile

- The liver plays a central role in the metabolism of bilirubin and is responsible for the production of bile , Between 425 and 510mmol (250–300mg) of unconjugated bilirubin is produced from the catabolism of haem daily.
- **Bilirubin in the blood is normally almost all unconjugated and, because it is not water-soluble, is bound to albumin and does not pass into the urine**.
- Unconjugated bilirubin is taken up by hepatocytes at the sinusoidal membrane, where it is conjugated in the endoplasmic reticulum by **UDP-glucuronyl transferase** , producing bilirubin mono- and diglucuronide. Impaired conjugation by this enzyme is a cause of inherited hyperbilirubinaemias
- These **bilirubin conjugates are water-soluble** and are exported into the bile canaliculi by specific carriers on the hepatocyte membranes. The conjugated bilirubin is excreted in the bile and passes into the duodenal lumen.
- Once in the intestine, conjugated bilirubin is metabolised by colonic bacteria to form stercobilinogen, which may be further oxidised to stercobilin. Both stercobilinogen and stercobilin are then excreted in the stool, contributing to its brown colour.
- Biliary obstruction results in reduced stercobilinogen in the stool, and **the stools become pale**. A small amount of stercobilinogen (4mg/day) is absorbed from the bowel, passes through the liver and is excreted in the urine, where it is known as urobilinogen or, following further oxidisation, urobilin.
- The liver secretes 1–2L of bile daily. Bile contains bile acids (formed from cholesterol), phospholipids, bilirubin and cholesterol.

**Jaundice causes are classified as**
Prehepatic
Hepatic
Post hepatic


Hyperbilirubinemia may result from (1) overproduction of bilirubin; (2) impaired uptake, conjugation, or excretion of bilirubin; or (3) regurgitation of unconjugated or conjugated bilirubin from damaged hepatocytes or bile ducts. An increase in unconjugated bilirubin in serum results from overproduction, impaired uptake, or conjugation of bilirubin. An increase in conjugated bilirubin is due to decreased excretion into the bile ductules or backward leakage of the pigment.

# Pre-hepatic jaundice (Unconjugated/indirect )

- **Haemolysis**, destruction of red blood cells or their marrow precursors causes increased bilirubin production. Jaundice due to haemolysis is usually mild because a healthy liver can excrete a bilirubin load six times greater than normal before unconjugated bilirubin accumulates in the plasma.
  - **Inherited disorders** include spherocytosis, sickle cell anemia, thalassemia, and deficiency of red cell enzymes such as pyruvate kinase and glucose-6- phosphate dehydrogenase (G6PD) , In these conditions, the serum bilirubin level rarely exceeds (5 mg/dL)
  - **Acquired hemolytic disorders** include microangiopathic hemolytic anemia (e.g. hemolytic-uremic syndrome), paroxysmal nocturnal hemoglobinuria, spur cell anemia, autoimmune hemolysis, and parasitic infections (e.g., malaria ) . Ineffective erythropoiesis occurs in B12 , folate, and iron deficiencies.

- **diminished hepatic uptake of bilirubin** : drugs like rifampin and probenecid
- **Impaired conjugation of bilirubin (genetic conditions) :** due to reduced bilirubin UDPGT activity : Gilbert syndrome (serum levels almost always <6 mg/dL) , Crigler-Najjar syndrome types I and II

# Hepatocellular jaundice (conjugated/direct )

- This is characterised by jaundice due to hepatic dysfunction (usually indicated by abnormal liver enzymes : ALT , AST ) but normal biliary imaging. This can be due to
  - acute hepatocellular injury
  - decompensation of cirrhosis.
  - intrahepatic cholestasis

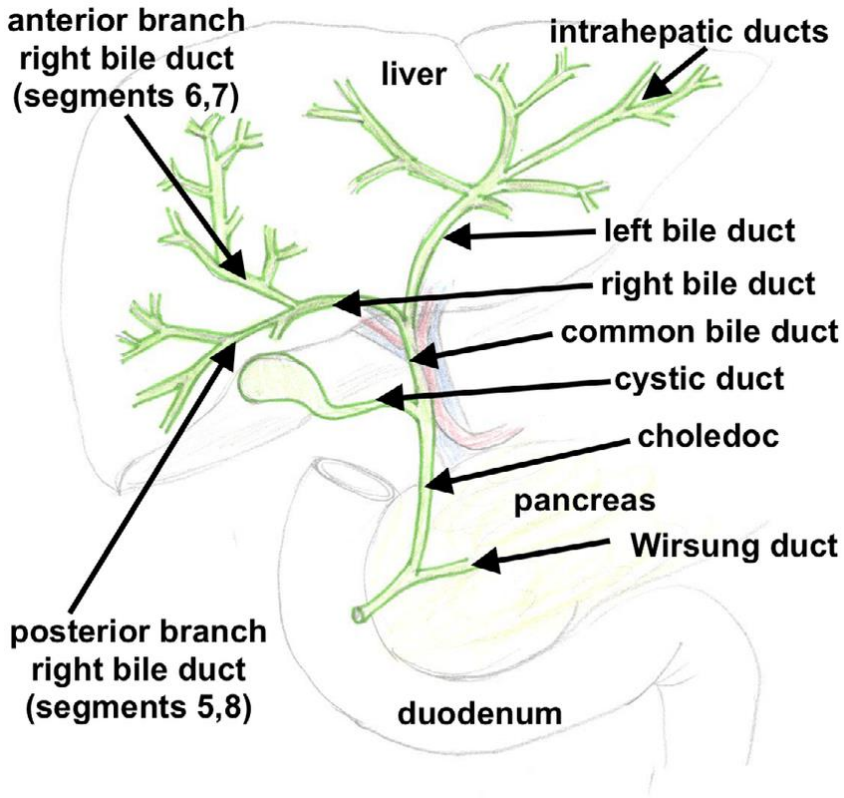
# Hepatocellular jaundice

- Viral hepatitis
  - Hepatitis A, B, C, D, and E
  - Epstein-Barr virus
  - Cytomegalovirus
  - Herpes simplex virus
- Alcoholic hepatitis
- Chronic liver disease and cirrhosis
- Drug toxicity
  - Predictable, dose-dependent (e.g., acetaminophen)
  - Unpredictable, idiosyncratic (e.g., isoniazid)
- Environmental toxins
  - Vinyl chloride
  - Jamaica bush tea—pyrrolizidine alkaloids
  - Kava kava
  - Wild mushrooms—*Amanita phalloides, A. verna*
- Wilson's disease
- Autoimmune hepatitis

# *Cholestatic jaundice* (Intrahepatic or extrahepatic )

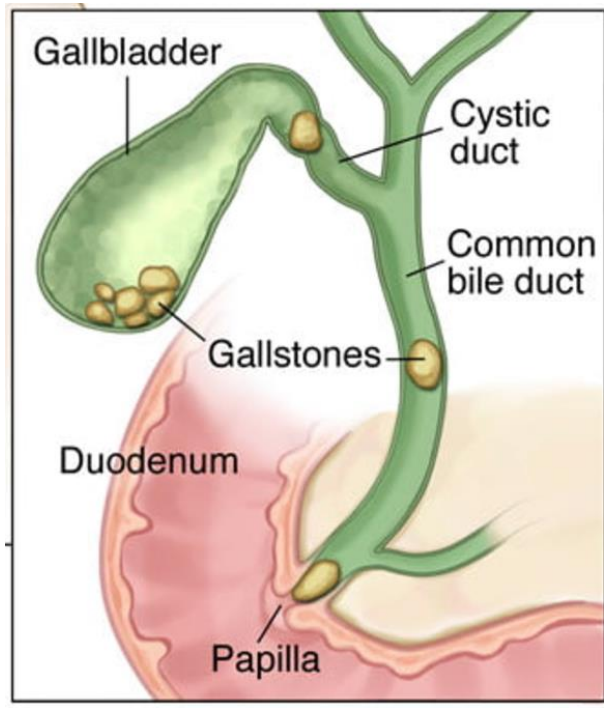
- **Intrahepatic cholestatic jaundice**

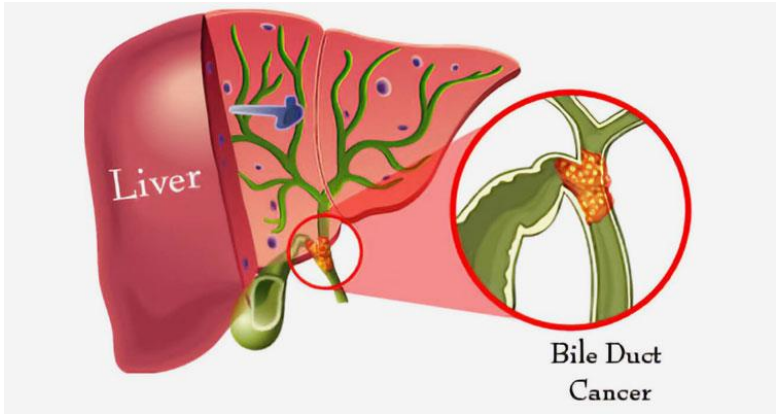
- Primary biliary cholangitis
- Primary sclerosing cholangitis
- Alcohol
- Drugs
- Hepatic infiltrations (lymphoma, granuloma, amyloid, metastases)
- Cystic fibrosis
- Sepsis
- Pregnancy
- Inherited cholestatic liver disease (e.g. benign recurrent intrahepatic cholestasis)
- Right heart failure

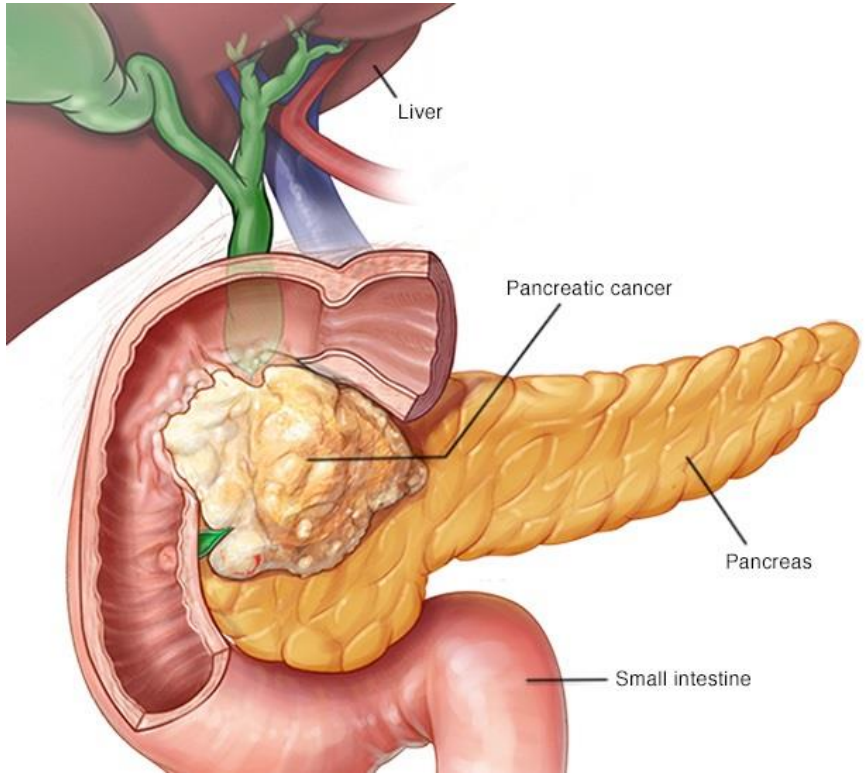


# Extrahepatic cholestasis jaundice ( obstructive )

- May be caused by obstruction of the larger bile ducts, usually between the hilum and the ampulla of Vater, resulting in biliary dilatation can be seen on ultrasound



## Clinical features and complications of cholestatic jaundice

### Cholestasis

#### Early features

- Jaundice
- Dark urine
- Pale stools
- Pruritus

#### Late features

- Malabsorption (vitamins A, D, E and K): weight loss, steatorrhoea, osteomalacia, bleeding tendency
- Xanthelasma and xanthomas

### Cholangitis

- Fever
- Rigors
- Pain (if gallstones present)

# Important points in history

- **Describe jaundice :**
  - Noticed by the patient or someone else ?
  - Site of yellowish discoloration : eyes , skin
  - onset : sudden or gradual
  - Intermittent( example : gilbert ) or continuous
  - Progressive , improved or stayed the same

- **Try to know the type / cause of jaundice**
  - Symptoms of Anemia or family history of hemolytic anemia may suggest hemolysis ( prehepatic )
  - Cholestatic jaundice : skin itching , pale stool , dark urine
  - Fever ,rigor and right hypochondrial pain may suggest cholangitis
  - Abdominal distention may suggest ascites due to liver cirrhosis .
  - Nausea and vomiting may suggest acute hepatitis
  - Past medical history of gallbladder stones may suggest biliary stone .
  - Weight loss and loss of appetite may suggest malignancy ( hepatic , biliary or pancreatic head )
  - History of previous blood transfusion , intravenous drug abuse , tattoos and sexual history : these are risk factors for viral hepatitis B , C which may lead to hepatocellular jaundice
  - History of Alcohol intake
  - Drug history
  - travel history and immunisations

# Points in Examination

- **Stigmata of chronic liver disease**, including spider nevi, palmar erythema, gynecomastia, caput medusae, Dupuytren's contractures, parotid gland enlargement, and testicular atrophy, are commonly seen in advanced alcoholrelated cirrhosis and occasionally in other types of cirrhosis
- The abdominal examination should focus on the size and consistency of the liver, on whether the spleen is palpable and hence enlarged, and on whether ascites is present

# What is Courvoisier’s Law ?

# Investigations

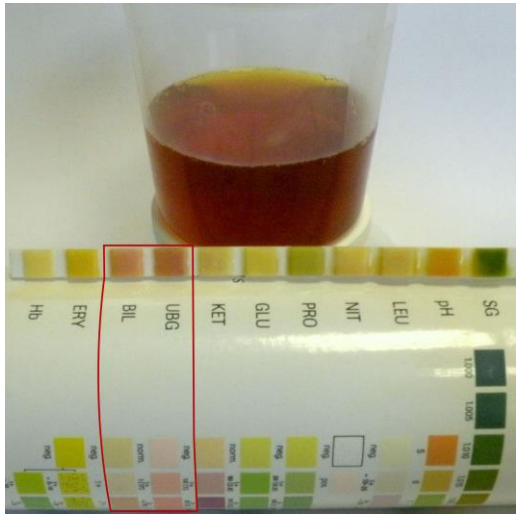
- **High bilirubin ( TSB ) with normal liver enzymes ( ALT , AST , ALP )**
  - Indirect bilirubin with low hemoglobin : hemolysis
  - Indirect bilirubin with normal Hb : Gilbert , drugs ..
  - Direct bilirubin : *Dubin Johnson syndrome* and *Rotor syndrome*

- **High TSB ( direct ) with elevated ALT , AST > ALP**
  - Hepatocellurar jaundice

- **High TSB ( direct ) with elevated ALP > ALT , AST**
  - Cholestasis
  - Do abdominal US to see if extrahepatic bile duct is dilated or not

- Another sensitive indicator of increased serum bilirubin is darkening of the urine, which is due to the renal excretion of conjugated bilirubin. Patients often describe their urine as tea- or cola-colored. Bilirubinuria indicates an elevation of the direct serum bilirubin fraction and, therefore, the presence of liver or biliary disease

A false negative result is possible in patients with prolonged cholestasis due to the predominance of delta bilirubin, which is covalently bound to albumin and therefore not filtered by the renal glomeruli.



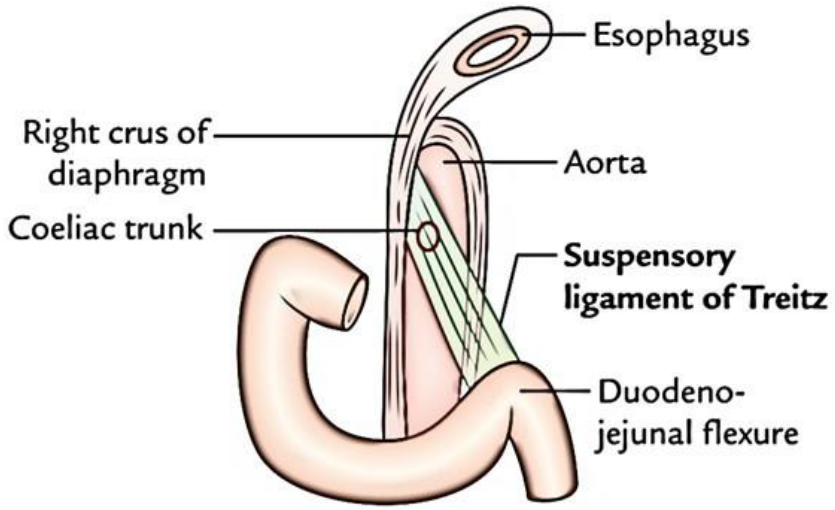
## 6.8 Urine and stool analysis in jaundice

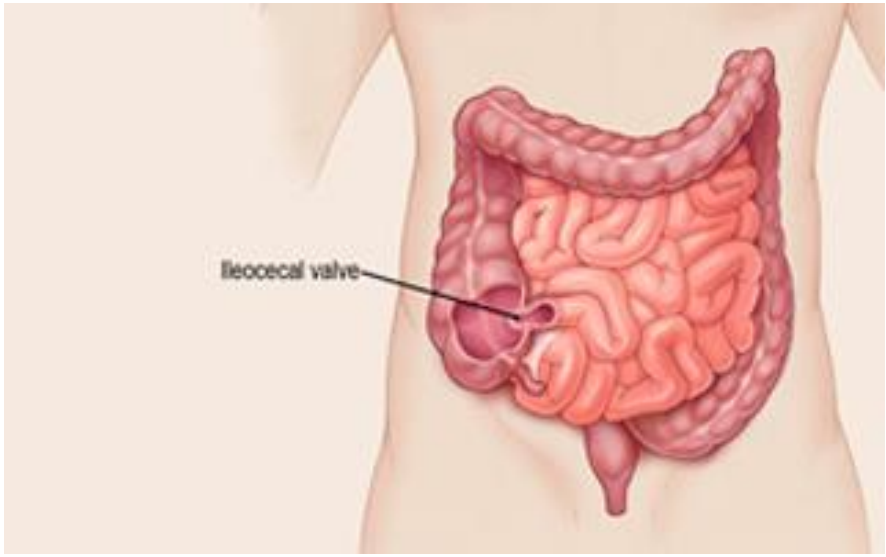
| | Urine | | | Stools |
|---|---|---|---|---|
| | Colour | Bilirubin | Urobilinogen | Colour |
| Unconjugated | Normal | – | ++++ | Normal |
| Hepatocellular | Dark | ++ | ++ | Normal |
| Obstructive | Dark | ++++ | – | Pale |

- conjugated hyperbilirubinemia is present when the direct fraction is >15% of the total serum bilirubin.
- conjugated hyperbilirubinemia is always associated with bilirubinuria (except in the presence of delta bilirubin in prolonged cholestasis when jaundice is overt), detection of bilirubin in urine via dipstick test is extremely helpful to confirm the presence of conjugated hyperbilirubinemia in a patient with mildly elevated direct fraction.

# GIT bleeding

- **Gastrointestinal (GI) bleeding can originate from**
  - The upper GI tract (proximal to the ligament of Treitz )
  - Small bowel
  - Lower GI tract (distal to the ileocecal valve) , typically colon, rectum or anus

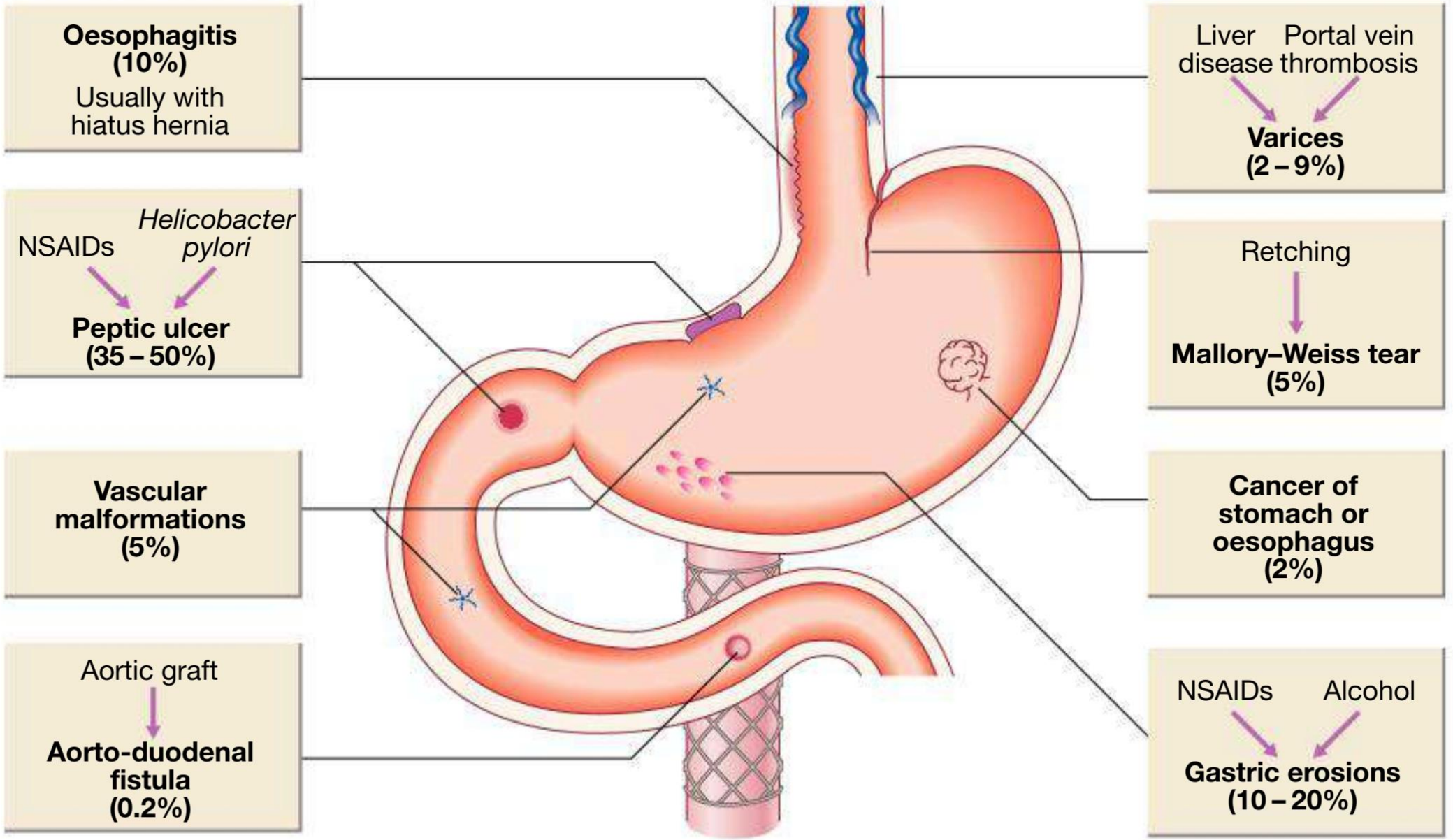


- Gastrointestinal bleeding can be classified as:
  - **Overt:** visible signs of blood loss from the gastrointestinal tract as hematemesis, hematochezia, or melena
  - **Obscure:** bleeding not found on an upper endoscopy, colonoscopy, or small bowel radiography
  - **Occult:** subacute bleeding which is not clinically visible

# Acute upper gastrointestinal bleeding

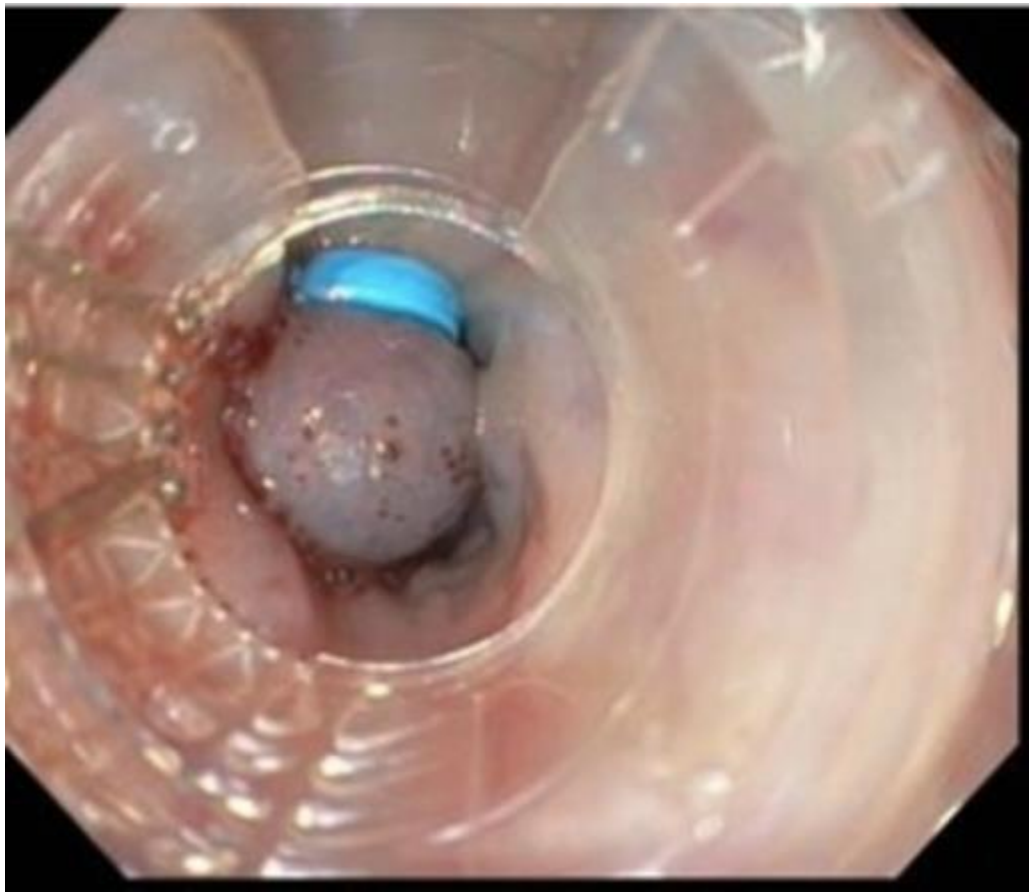
- **Haematemesis** : vomiting of blood ; Haematemesis is red with clots when bleeding is rapid and profuse, or black (‘coffee grounds’) when less severe.
- **Melaena** is the passage of black, shiny, tarry stools containing altered blood; it is usually caused by bleeding from the upper gastrointestinal tract, although haemorrhage from the right side of the colon is occasionally responsible. The characteristic colour and smell are the result of the action of digestive enzymes and of bacteria on haemoglobin.
- Distinguish this from the matt black stools associated with oral iron or bismuth therapy.
- **Hematochezia** usually represents a lower GI source of bleeding, although an upper GI lesion may bleed so briskly that blood transits the bowel before melena develops. **When hematochezia is the presenting symptom of UGIB, it is associated with hemodynamic instability and dropping hemoglobin**

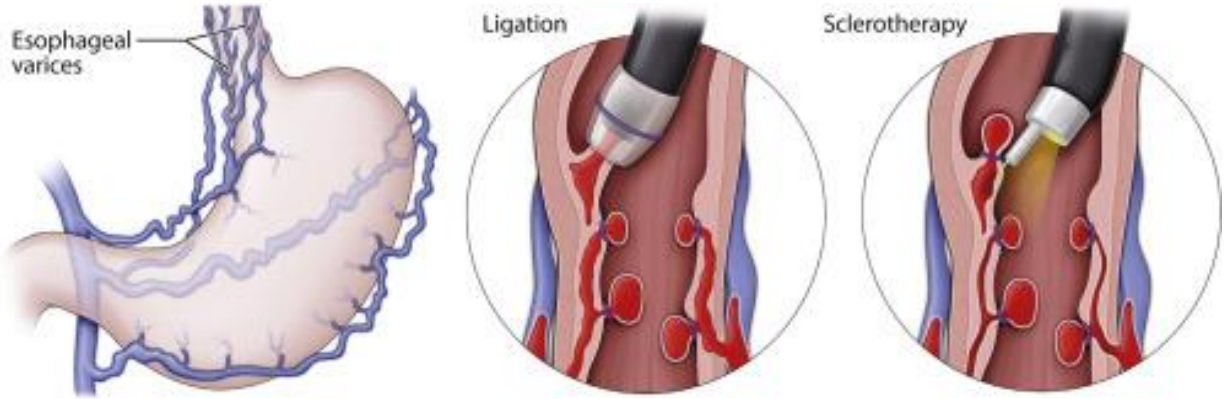



**Causes of acute upper gastrointestinal haemorrhage.** Frequency is given in parentheses. (NSAIDs = non-steroidal anti-inflammatory drugs)

# Summary of the management of acute upper GIT bleeding

- **Intravenous access**, ideally using two large-bore cannulae
- **Check the vitals** : give oxygen if hypoxia ,check for hypotension and postural hypotension ; give fluid (Intravenous crystalloid ) to raise the blood pressure
- **Draw blood for investigations** ( cross match of at least 2 units of blood , check CBC , RFT and electrolytes , LFT , PT ,PTT ) and assess the patient by taking rapid history and examination
- **Give blood when indicated :** haemoglobin is less than 7g/dL, although transfusion should be considered at higher levels in those with haemodynamic instability or ischaemic heart disease.
- **Medical management :**
  - PPI in non-variceal bleeding ;
  - prophylactic antibiotics, and vasoactive medications (e.g. terlipressin or octreotide ) in variceal bleeding for 2–5 days
- **Endoscopy**
  - Epinephrine injection , thermal coagulation , application of clips or band ligation for PUD
  - Band ligation or sclerotherapy for esophageal varices
- **Monitoring**
- **Surgery** for Patients who have recurrent bleeding, where endoscopic attempts at haemostasis have failed
- **Eradication** of H.pylori and avoid NSAIDs if possible




Esophageal varices
Ligation
Sclerotherapy

# Management of acute upper GIT bleeding

- **1. Intravenous access :** The First step is to gain intravenous access, ideally using two large-bore cannulae.

  **2. Initial clinical assessment**
  - Define circulatory status. Severe bleeding causes tachycardia, hypotension or postural hypotension and oliguria. The patient is cold and sweating, and may be agitated.
  - Seek evidence of liver disease .Jaundice, cutaneous stigmata, hepatosplenomegaly and ascites may be present in decompensated cirrhosis.
  - Identify comorbidity. The presence of cardiorespiratory, cerebrovascular or renal disease is important, both because these may be worsened by acute bleeding and because they increase the hazards of endoscopy and surgical operations. These comorbidities are, therefore, a common cause of death following acute gastrointestinal haemorrhage, even after successful haemostasis.
  - The **Rockall and Glasgow-Blatchford score (GBS)** scores are used to assess the risk of gastrointestinal bleeding

- 3. **Basic investigations**
  - **Full blood count**. Chronic or subacute bleeding leads to anaemia, but the haemoglobin concentration may be normal after sudden, major bleeding until haemodilution occurs. Thrombocytopenia may be a clue to the presence of hypersplenism in chronic liver disease.
  - **Urea and electrolytes**. This test may show evidence of renal failure. The blood urea rises as the absorbed products of luminal blood are metabolised by the liver; an elevated blood urea with normal creatinine concentration implies severe bleeding.
  - **Liver function tests.** These may show evidence of chronic liver disease.
  - **Prothrombin time.** Check when there is a clinical suggestion of liver disease or patients are anticoagulated.
  - **Cross-matching. At least 2 units of blood** should be cross-matched if a significant bleed is suspected

- 4. **Resuscitation**
  - Intravenous crystalloid Fluids should be given to raise the blood pressure, with a 500ml bolus recommended over less than 15minutes in haemodynamically unstable patients.
  - In most patients, blood should be transfused when haemoglobin is less than 7g/dL, although transfusion should be considered at higher levels in those with haemodynamic instability or ischaemic heart disease.
- 5. **Oxygen**
  - Oxygen saturations should be monitored with pulse oximetry, with a target saturation of 94%–98% and oxygen prescribed as required.

- 6**. Antithrombotic drugs**
  - Aspirin can be continued during an upper gastrointestinal bleed.
  - P2Y12-receptor antagonists (e.g. clopidogrel) should be temporarily stopped (unless prescribed following coronary artery stenting), as well as warfarin and direct oral anticoagulant therapy.
  - However, early reintroduction of these medications should occur after haemostasis has been achieved to reduce thrombotic events and death.
- **7. Specific therapy**
  - **Proton pump inhibitor (PPI) therapy**
  - Intravenous PPI infusion should be given in non-variceal bleeding ; intermittent intravenous PPI and oral high-dose PPI can be considered as alternatives .
  - **All patients with cirrhosis and gastrointestinal bleeding** should receive :
  - prophylactic broad-spectrum antibiotics, such as intravenous cephalosporin or piperacillin/tazobactam, because sepsis is common and treatment with antibiotics improves survival.
  - The measures used to control acute variceal bleeding include vasoactive medications (e.g. terlipressin)

- 8. **Endoscopy :** This should be carried out after adequate resuscitation, ideally within 24 hours
- **9. Monitoring**
  - Patients should be closely observed, with hourly measurements of pulse, blood pressure, oxygen saturations and urine output.
- **10. Radiology and surgery**
  - Patients who have recurrent bleeding, where endoscopic attempts at haemostasis have failed, should be considered for radiological or surgical intervention.
- **11. Eradication**
  - Following treatment for ulcer bleeding, all patients should avoid non-steroidal anti-inflammatory drugs (NSAIDs) and those who test positive for H. pylori infection should receive eradication therapy . Successful eradication should be confirmed by urea breath or faecal antigen testing.

# lower gastrointestinal bleeding

- A patient with lower gastrointestinal (GI) bleeding typically reports **hematochezia (passage of maroon or bright red blood or blood clots per rectum).**
- Blood originating from the left colon tends to be bright red in color, whereas bleeding from the right side of the colon usually appears dark or maroon colored and may be mixed with stool.
- Rarely, bleeding from the right side of the colon will present with malena.
- In practice, however, patients with UGIB and right-sided colonic bleeding may also present with bright red blood per rectum if the bleeding is brisk and massive.
- Bleeding lesions of the **small bowel** may present as melena or hematochezia

# DIFFERENTIATION OF UGIB FROM LGIB

- Hematemesis indicates an UGIB source.
- Melena indicates blood has been present in the gastrointestinal (GI) tract for ≥14 h and as long as 3–5 days. The more proximal the bleeding site, the more likely melena will occur.
- Hematochezia usually represents a lower GI source of bleeding, although an upper GI lesion may bleed so briskly that blood transits the bowel before melena develops. When hematochezia is the presenting symptom of UGIB, it is associated with hemodynamic instability and dropping hemoglobin.
- Bleeding lesions of the **small bowel** may present as melena or hematochezia.
- Other clues to UGIB include hyperactive bowel sounds and an elevated blood urea nitrogen (due to volume depletion and blood proteins absorbed in the small intestine .

## 23.18 Causes of lower gastrointestinal bleeding

### Severe acute

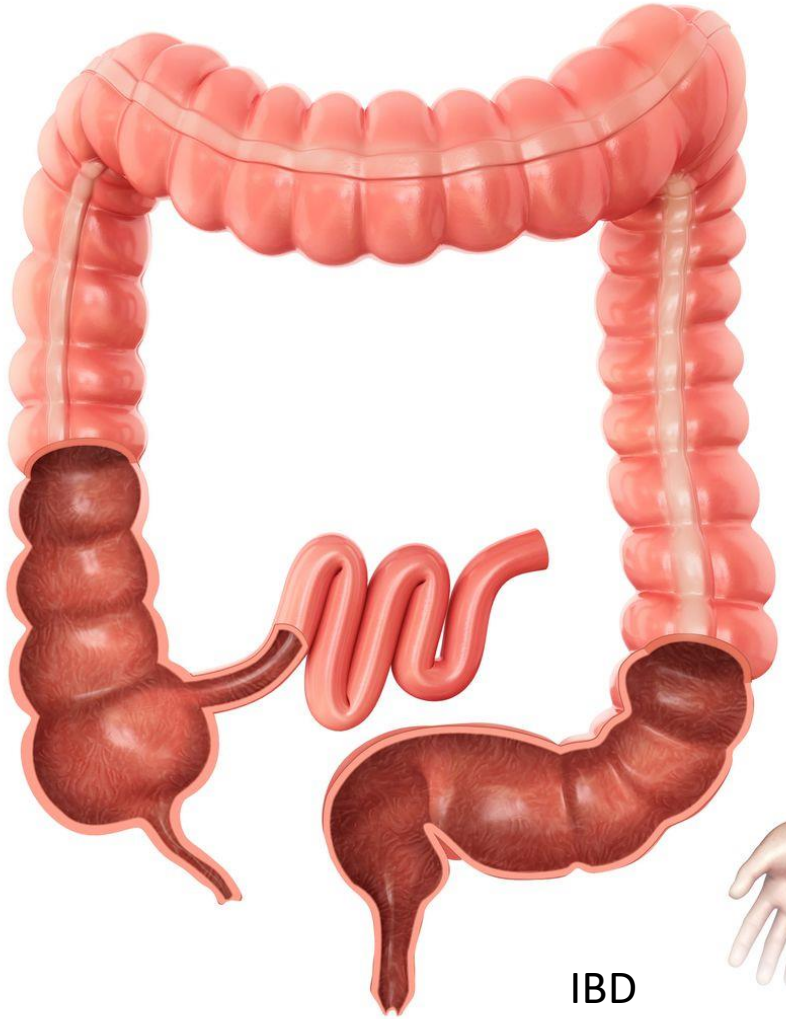
- Diverticular disease
- Angiodysplasia
- Ischaemia
- Meckel's diverticulum
- Inflammatory bowel disease (rarely)

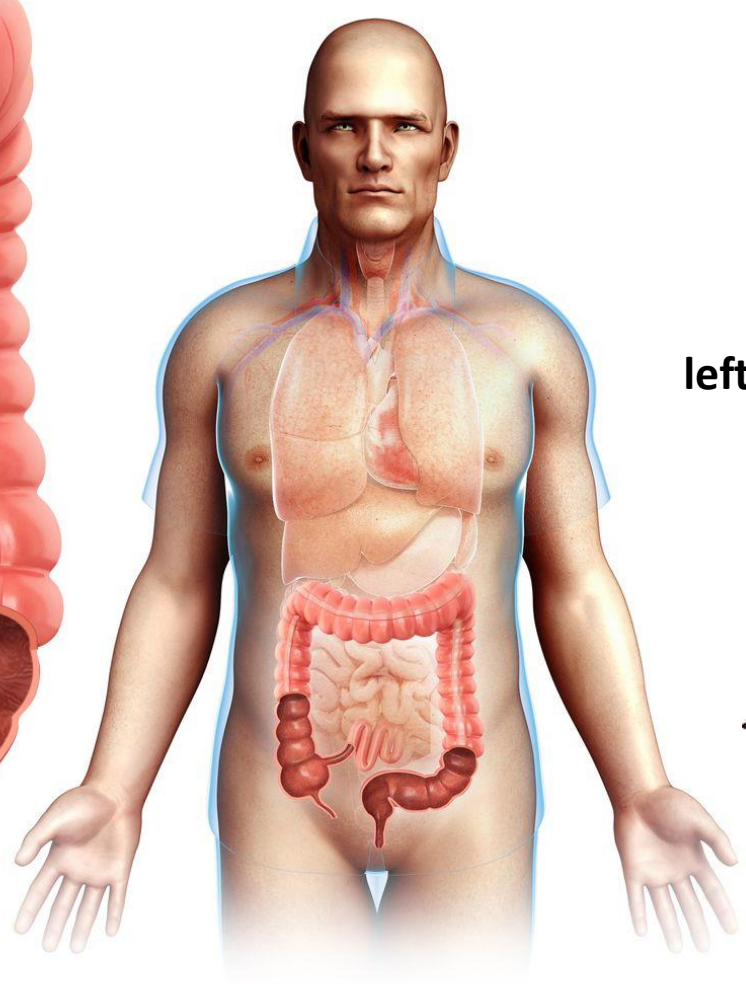
### Moderate, chronic/subacute

- Fissure
- Haemorrhoids
- Inflammatory bowel disease
- Carcinoma
- Large polyps
- Angiodysplasia
- Radiation enteritis
- Solitary rectal ulcer

**North** : ice
Ischemic colitits

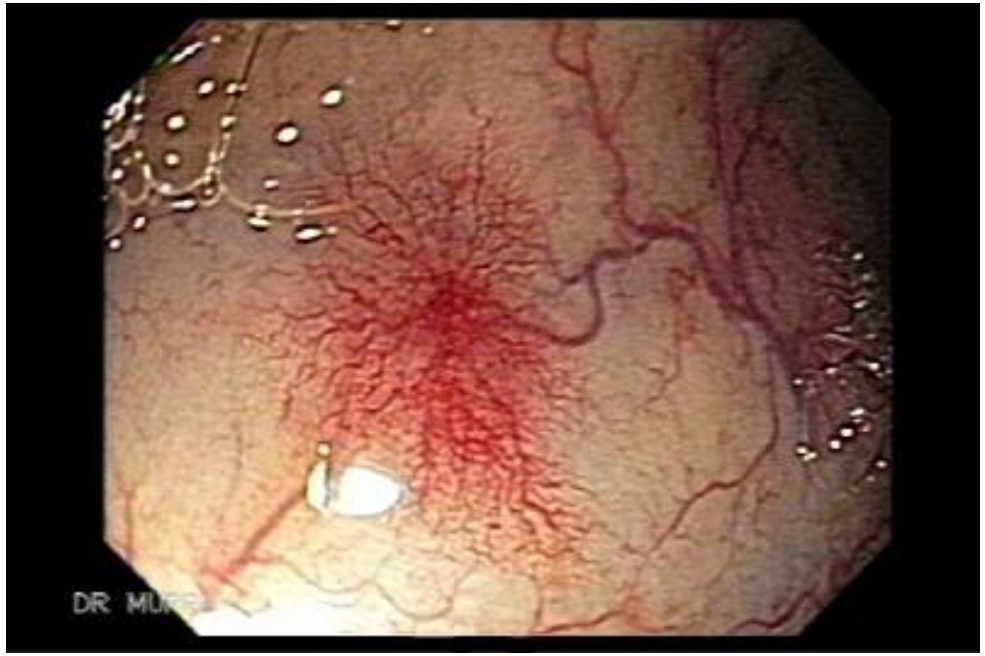
**Right**
Angels
Meckle’s

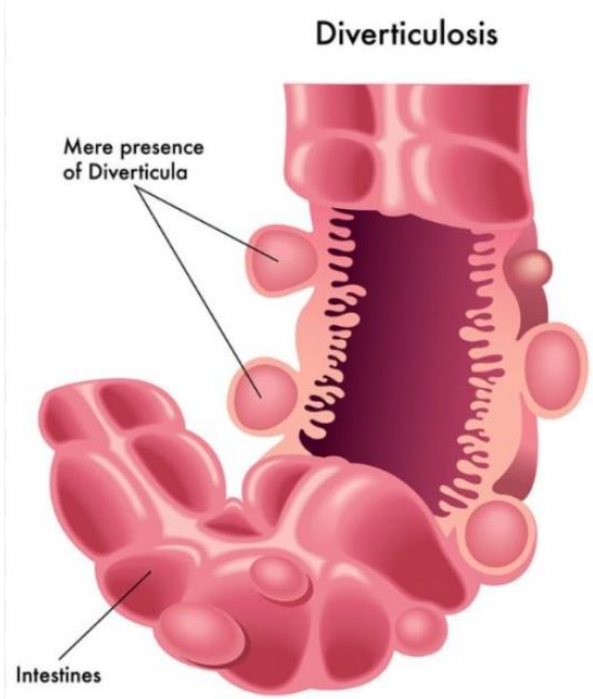


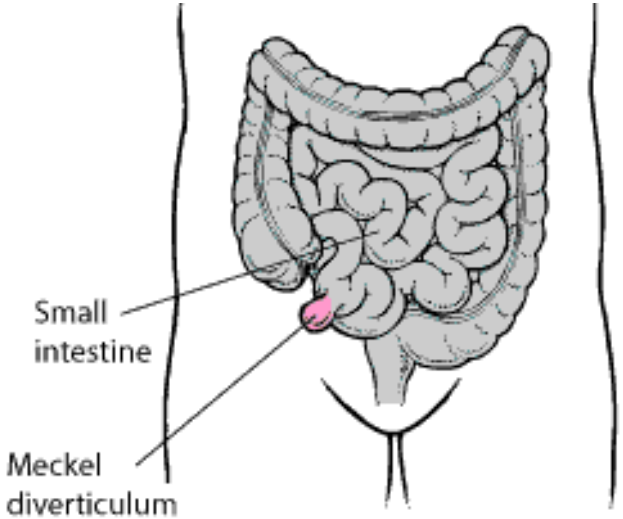


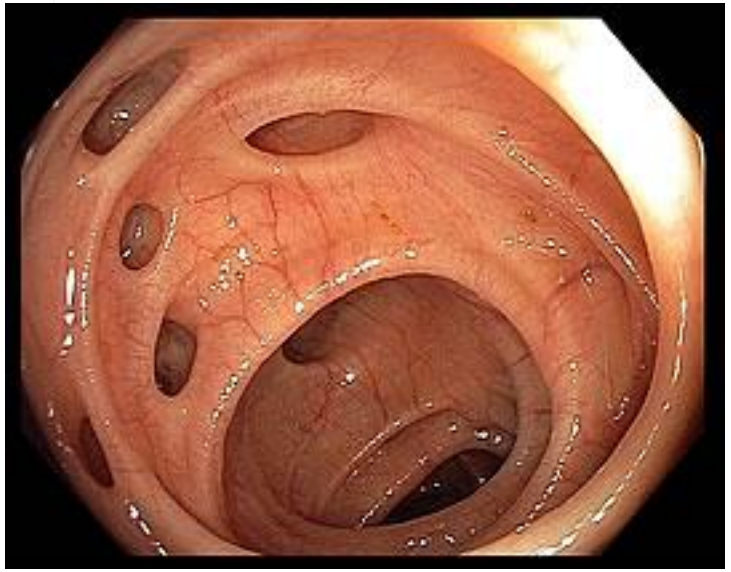
**left** :Devil

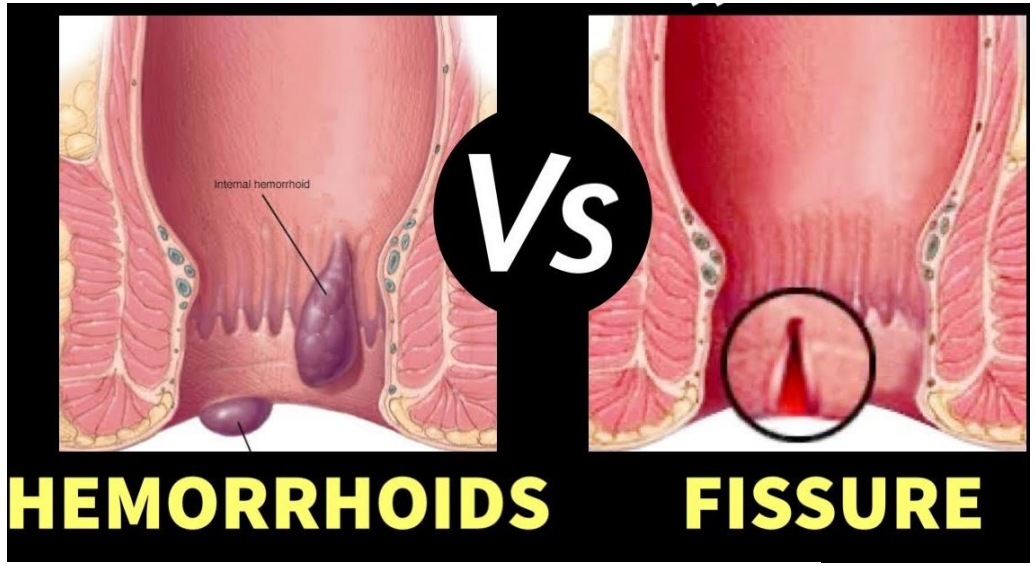
IBD

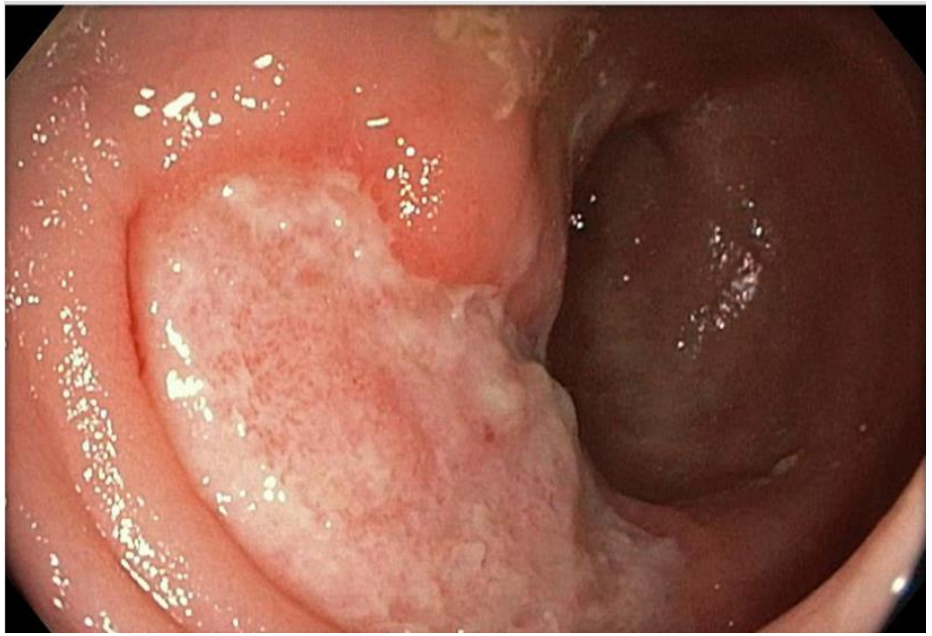


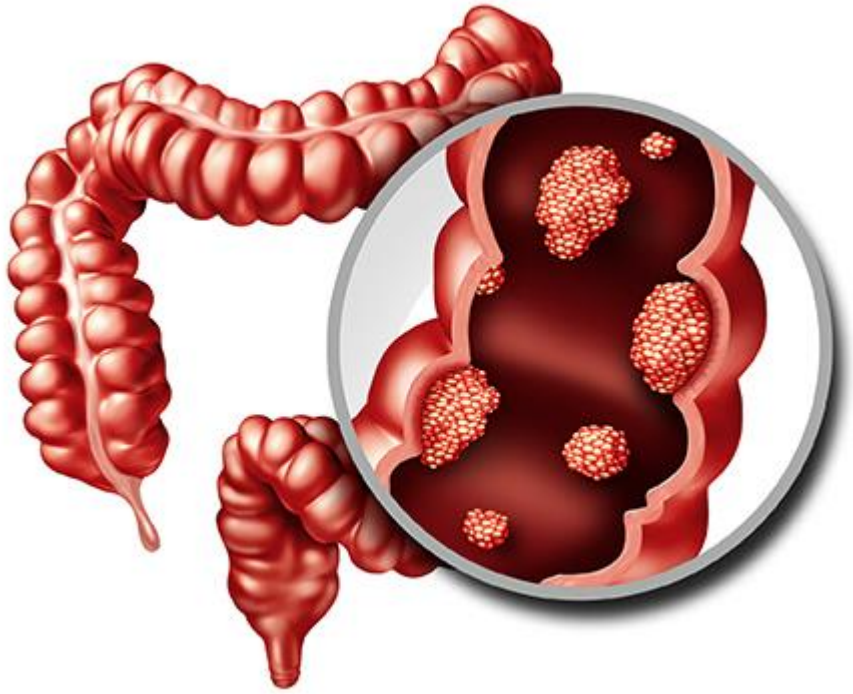

Diverticulosis
Mere presence
of Diverticula
Intestines

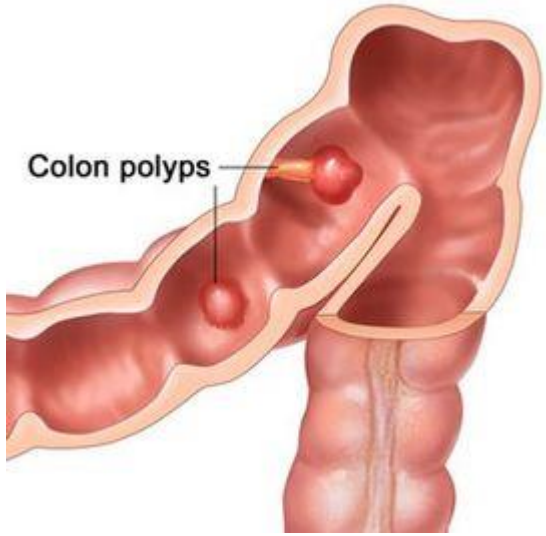

Small
intestine
Meckel
diverticulum

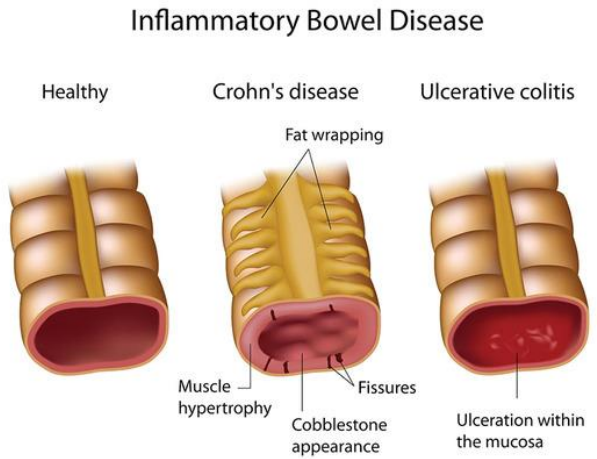



Internal hemorrhoid
Vs
HEMORRHOIDS
FISSURE






Colon polyps


Inflammatory Bowel Disease
Healthy
Crohn's disease
Ulcerative colitis
Fat wrapping
Muscle hypertrophy
Fissures
Cobblestone appearance
Ulceration within the mucosa

# Severe acute lower gastrointestinal bleeding

- This presents with profuse red or maroon bleeding per rectum and with hypovolaemic shock. If available, CT angiography should be performed initially to localise the site of blood loss. If the bleeding source is identified, then catheter angiography with embolisation should be performed.
- If no source of bleeding is found then a colonoscopy should be performed.
- Some patients presenting with an apparent severe lower GI bleed are ultimately found to have a significant upper GI bleed.

# Severe acute lower gastrointestinal bleeding

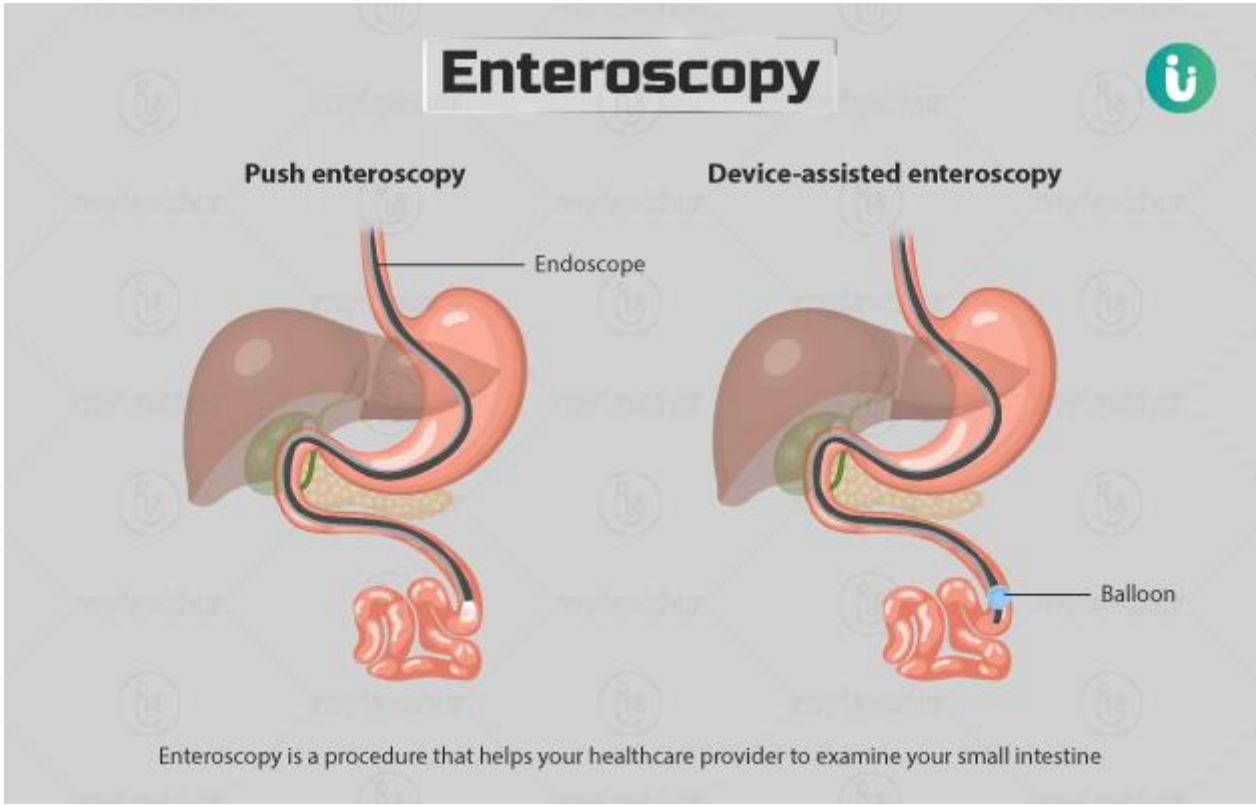
- **The commonest cause of lower GI bleeding is diverticular disease**, with up to two-thirds of cases being classiffied as severe. Bleeding from diverticular disease is often due to erosion of an artery within the mouth of a diverticulum. The bleeding is usually painless. Multiple endoscopic options are available, with endoscopic clipping either alone or after the injection of dilute adrenaline (epinephrine) considered as first-line treatment in the UK.
- **Angiodysplasia** is a disease of older adults, in which vascular malformations develop within the GI tract, commonly in the caecum. Bleeding can be acute and profuse; it usually stops spontaneously, but commonly recurs. The bleeding is usually painless . Diagnosis is often difficult. Colonoscopy may reveal characteristic vascular spots and, in the acute phase, angiography can show bleeding into the intestinal lumen and an abnormal large, draining vein. The treatment of choice is endoscopic thermal ablation, but resection of the affected bowel may be required if bleeding continues.
- **Bowel ischaemia** due to occlusion of the inferior mesenteric artery can present with abdominal colic and rectal bleeding. It should be considered in patients (particularly older patients) who have evidence of generalised atherosclerosis. The diagnosis is made at colonoscopy. Bleeding is self-limited, and most cases (85 to 90 percent) resolve with correction of the underlying cause and volume repletion
- Meckel's diverticulum with ectopic gastric epithelium may ulcerate and erode into a major artery. The diagnosis should be considered in children or adolescents who present with profuse or recurrent lower gastrointestinal bleeding. A Meckel's 99mTc-pertechnetate scan is sometimes positive, but the diagnosis is commonly made only by laparotomy, at which time the diverticulum is excised.

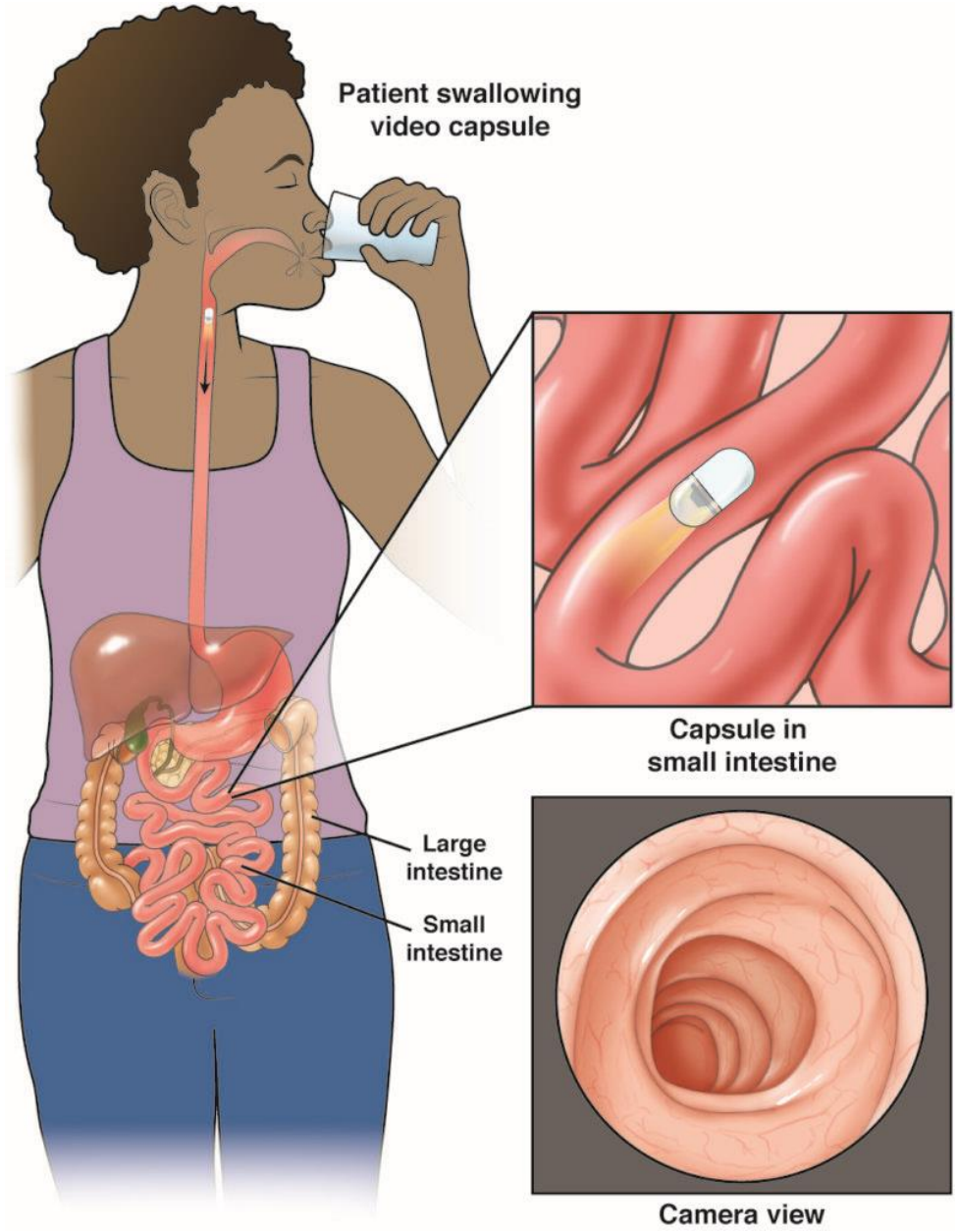
# subacute or chronic lower gastrointestinal bleeding

- This can occur at all ages and is usually due to haemorrhoids or anal fissure.
- **Haemorrhoidal bleeding** is bright red and occurs during or after defecation. Hemorrhoidal bleeding is almost always painless. Bright red blood typically coats the stool at the end of defecation. Blood may also drip into the toilet or stain toilet paper.  Proctoscopy can be used to make the diagnosis, but individuals who have altered bowel habit and those who present over the age of 40 years should undergo colonoscopy to exclude coexisting colorectal cancer.
- **Anal fissure** should be suspected when fresh rectal bleeding and anal pain occur during defecation.

# Major gastrointestinal bleeding of unknown cause ( Obscure )

- In some patients who present with major gastrointestinal bleeding, upper endoscopy, colonoscopy and CT angiography may fail to reveal a diagnosis.
- **Wireless capsule endoscopy** is increasingly used in such patients. The diagnostic yield is highest when performed as close as possible to the bleeding episode, particularly within the First 48 hours of presenting with bleeding.
- Wireless capsule endoscopy is often used to define a source of bleeding prior to enteroscopy ,with push or double balloon enteroscopy being used to visualise the small intestine and treat the bleeding source.
- When all else fails, laparotomy with on-table endoscopy is indicated.


Enteroscopy
Push enteroscopy
Device-assisted enteroscopy
Endoscope
Balloon
Enteroscopy is a procedure that helps your healthcare provider to examine your small intestine


Patient swallowing video capsule
Capsule in small intestine
Large intestine
Small intestine
Camera view

# Chronic occult gastrointestinal bleeding

- In this context, occult means that blood or its breakdown products are present in the stool but cannot be seen by the naked eye.
- Occult bleeding may reach 200mL per day and cause iron deficiency anaemia.
- Any cause of gastrointestinal bleeding may be responsible, but the most important is colorectal cancer, particularly carcinoma of the caecum, which may produce no gastrointestinal symptoms.
- **In clinical practice, investigation of the upper and lower gastrointestinal tract should be considered whenever a patient presents with unexplained iron deficiency anemia .**