GI medicine

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Hepatitis

- When you take history suspecting hepatitis, ask about previous blood transfusions.
- All hepatitis viruses are RNA viruses except for hepatitis B, which is a DNA virus
- Hepatitis A and E are transmitted feco-orally. Hepatitis B, C, and D are transmitted in a different fashion
- Hepatitis E was discovered to cause chronic infection
- 30-40% of hepatitis E is associated with neurological disorders such as neuropathy, dementia, and other neurological problems
- Presentation:
    - Fatigue(feeling unwell)
    - Jaundice
    - Abnormal liver function test
    - Elevated liver enzymes (ALT, AST, alkaline phosphatase, GGT)
    - Elevated bilirubin
    - Our main concern is ALT and AST (normal levels 30-40)
    - If alkaline phosphatatase and GGT are not raised, this does not rule out hepatitis
    - A disease in liver parenchyma will mainly elevate ALT and AST
- Risk factors for hepatitis:
    - Blood transfusion
    - Needles
    - Circumcision
    - Injection
- It is important to ask about maternal history and family history of hepatitis. Ask about other disease like common bile duct stones (in acute bile stone impaction, ALT, AST, GGT, and alkaline phosphatase might be elevated)
- CMV, EBV, and herpes can cause hepatitis in immunocompromised patients.

- **Hepatitis A:**
    - It is a disease related to the socioeconomic class. If you get the disease at a young age, you will be immune as an adult. If you get infected as an adult, it is a problem.
    - Severe hepatitis A can occur in 1% of adult patients
    - No chronic infection from hepatitis A
    - Slide 6:
        - First, you get the symptoms: usually patients come to you complaining of fatigue, decreased smoking habits lack of appetite, and then they start to have symptoms. At the time of the onset symptoms, the virus is in the feces (we rarely test for that) then the ALT and AST go up. Then, you will

develop IgM antibodies. After a while IgM levels decrease, and IgG levels start to rise.

- We test for hepatitis A using IgM antibodies
- You can infect others up to two weeks after the onset of jaundice (after than you are not contagious)
- The older you are the more significant the type of infection you will get
- The patient may develop a case of cholestasis, which is an on and out state of abnormal liver function (raised ALT, AST, GGT alkaline phosphatase, and bilirubin). This is not a chronic form of the infection; it is an autoimmune phenomenon created by the virus and can be settled by itself and can last for a few months.
- Hepatitis A has extrahepatic manifestations:
  - Nephritis
  - GN
  - Rash
  - Arthalgia
  - Carditis
- You should have the vaccine if you are traveling or if you don't have the antibodies
- You give immunoglobulins but not routinely after exposures. Only administered if the patient is immunocompromised
- Hepatitis A is a common virus you will see with hospital admissions.

- **<u>Hepatitis B:</u>**
  - Causes chronic infection
  - The commonest viral hepatitis
  - Transmitted by sexual contacts, needles, or blood transfusions
  - In Asia, transmission is mainly vertical (from the mother to her child). But in the west, it is mainly sexual or related to needle use.
  - The virus is mainly concentrated in blood and serum
  - Shedding the virus by sexual contact from male to female is rare. However, a new term, MSM (men having sex with men), is the highest rate of transmission
  - Perinatal transmission is commonest form of transmission, this is why we give babies vaccines and immunoglobulins at the time of birth.
  - We test the mother for B28 to see if she has a high viral load and we give her treatment to prevent transmission of the virus to the baby
  - Unlike hepatitis A, if you get hepatitis B as a child there is a 90% chance of having a chronic infection. However, if you get it as an adult, the chance of having a chronic infection is 5%.

- Your chance of having a chronic infection from hepatitis B decreases with age
- Antigens:
  - Viral shedding starts, and the patient becomes HBeAg (hepatitis B e antigen)
  - Then, you start developing anti-(e) antibody (IgM) and anticore antibody
- How do you test for hepatitis B?
  - Surface antigen
  - If the patient has hepatitis band, then the patient definitely has the disease. But, if the surface antigen is negative we look for anti-core antibody and this period is called the window period which is the period between the time when HBsAg disappears and HBsAb appears and it takes weeks to months
- The definition of cure from hepatitis B is the development of anti HBsAg (the presence of antibodies against HbsAg means that you are either cured or vaccinated.)
- When the patient has HBeAg positive, this means that the virus is active
- We treat the patients until they develop the antibody against the "e" antigen; this is called sero-conversion. This is not a complete cure, but in this condition the virus is suppressed.
- Within 20-30 years of the onset of the disease, patients lose the HBeAg and develop the antibody. They are not cured, but the disease is inactive
- Can you be cured from hepatitis B?
  - Mainly, 5% will have chronic disease and 95% will clear the virus. Technically, that is not true because we have what is called covalently bound surface DNA. The virus itself is integrated in the patient's DNA, so it will hide away. The patient appears completely asymptomatic and HBsAb is positive; if the patient get lymphoma, for example, and we administer chemotherapy the virus will activate itself again so the best we can get in getting rid of the virus is the HBsAb so you can be cured by definition but you can reactivate the virus.
- If you are vaccinated, and you get the virus you are not supposed to get infected
- Let us suppose that a baby received the virus from his mother. The first phase of his infection is called immune tolerant phase (the body tolerates the virus) so the viral load is very high but since the body is tolerating the virus ALT levels are normal. This immune-tolerant phase can last 10 or 20 years. The child is born with very high viral load and a normal liver function test (no damage to the liver). This means that the body is in harmony with the virus. The damage from hepatitis B is not related to the virus, it is related to the body and how it reacts to the virus
- Can babies infect other babies in nurseries?
  - Horizontal infection has been reported, but it is very uncommon.

- When the child becomes 20 or 25 years of age, the body starts acting against the virus to clear it (immune clearance). During this phase, ALT rises indicating liver inflammation. Viral DNA decreases; so, during the clearance phase, you either clear the virus or enter the control stage in which both viral DNA and ALT are low. Patients live in the control phase for years. After a while, the body will react again in an immune escape attempt, which causes elevation in both viral DNA and ALT.
- HBeAg is positive in tolerance and clearance phases
- HBeAg is negative in control phase
- If the patient is HBsAg positive, the next thing we ask about is HBeAg to see if the patient is infectious or not. Then, we ask for HB-DNA to see the burden of the disease (how much virus there is)
- Chronic infection develops in 5-10% of patients and those develop hepatocellular carcinoma or cirrhosis.
- Important: can you develop HCC in hepatitis B in the absence of cirrhosis? Yes, unlike hepatitis C, because hepatitis B is oncogenic
- Who to treat with hepatitis B? (2 of the following criteria)
  - Abnormal LFT
  - High viral load
  - Liver damage or fibrous cap
- The goal of treatment:
  - Decrease viral load (decrease HB-DNA)
  - Stop viral replication
  - Seroconversion (convert HBeAg to HBeAb)
- Treatment:
  - Interferon-alpha-2b
  - Oral antiviral treatment such as tenofovir (nucleoside inhibitor) and entecavir (reverse transciptase inhibitor). Very long duration of treatment.
  - Interferons are used when the viral load is low and liver enzymes are high. The way it acts is that it stimulates your immune response to get rid of the virus. Interferon treatment is one year long.
  - Lamivudine: within 5 years of the start of treatment, 40% of patients develop resistance

- **<u>Hepatitis C:</u>**
  - Transmitted like hepatitis B, but the mother to child transmission is less than 1-2%.
  - It is rare to have acute hepattits C
  - How to diagnose?

        - Anti hepatitis C antibodies.
        - If antibodies are positive, confirm with PCR
    - It takes a long time to develop complications of hepatitis C (20-30 years)
    - Rule of thirds:
        - 1/3 will have cirrhosis
        - 1/3 of those who develop cirrhosis, will develop liver cancer (a patient with cirrhosis has 1% chance per year to develop liver cancer so if he has cirrhosis for 20 years the chance is 20% to develop liver cancer
        - 1/3 of those with cirrhosis will have liver failure
    - The more liver injury you have, the more problems you have in your liver.
    - You can be treated (cured) from hepatitis C 100%
    - treatment:
        - Sofosbuvir
        - Harmony
        - Dasabuvir (exviera)
        - Pataralt
        - pegylated interferons are rarely used

- **Hepatitis D**
    - It cannot infect you on its own. It needs hepatitis B
    - If you treat a patient for hepatitis B and you see no improvement, suspect hepatitis D infection
    - Diagnosis:
        - IgM against hepatitis D
        - Confirm with HD-RNA
    - Co-infection: infection with both viruses at the same time
    - Superinfection: you get B then you get D

- **Hepatitis E:**
    - Can cause chronic infection and neurological symptoms
    - Incubation period is 60 days
    - Serious in pregnant ladies
    - The commonest virus

Inflammatory bowel disease

- Ulcerative colitis is limited to the colon. It can affect the terminal ileum causing ileitis, but it is mild
- Crohn's disease can affect any part of the GIT from the mouth to the anus. Skip lesions. Crohn's is a granumolatous disease. When the disease penetrates the bottom layer, it will cause a normal inflammatory response with formation of granulomas. However, this is not a definitive way to diagnose Crohn's because if a patient underwent a colon biopsy and granuloma was not found, this doesn't rule out CD. Only 30-40% of patients with Crohn's will have granulomas in their biopsy
- Undetermined colitis: undifferentiated form; cannot determine whether the disease is CD or UC
- IBD has a bimodal onset; before 20 and at the age of 50
- Smoking worsens CD
- We don't advise people with UC to smoke
- Why do patients develop IBD?
    - Increased hygiene during childhood is associated with an increased risk for developing IBD. If you had a very clean childhood, when you are older and exposed to antigens, your immune system will respond in a more aggressive way so you might develop IBD.
    - NOD2 gene: encodes for a barrier in the small bowel; if you have a mutation in this gene, the barrier (the gates) in your small bowel are basically ineffective
    - The genetic background is not very strong, so if the patient has CD or UC the chances of his brother having the disease is 10-15%.But, it is different in twins
- Differentiation between CD and UC is based on type of T-cell activation. People don't switch classes (no one with UC will develop CD)
- The extent and the severity may vary during the course of the disease

- **Ulcerative colitis:**

    - Only affects the colon
    - This disease always starts at the rectum, then it spreads.
    - Classes:
        - Rectum only → proctitis
        - The disease extends beyond the splenic flexure → pancolitis
        - Rectum + sigmoid →Distal colitis
        - Left side up to the splenic flexure → left sided colitis

- The first thing you do when you diagnose UC and give treatment is to do colonoscopy at a later stage to check the extent of the disease
- 30-40% of patients have left sided colitis and of those, 30-40% will develop pancolitis
- In pancolitis, patients have continuous inflammation of the colon so they develop pseupolyps. Normal polyps have adenomas which will undergo dysplasia and become cancerous; pseudopolyps will not change.
- The inflammation is related to the mucosa and submucosa
- Crypt abscesses are small neutrophic aggregations in the crypts of the mucosa
- UC is limited to the mucosa and submucosa; this is why patients with UC don't develop fistulas or strictures.
- If you have the choice to have UC or CD what would you choose?
  - UC because you get cured
- Symptoms:
  - Proctitis: tenesmus, rectal bleeding, occasional diarrhea
  - More extension → diarrhea, and more rectal bleeding
  - Patients with UC rarely complain of abdominal pain because it is a superficial inflammation that you don't feel.
  - Advanced colitis: may have fever endocytosis
- Why do people with distal colitis develop constipation?
  - Due to a mechanical obstruction
  - Distal disease causes inflammation of the mucosa leading to swelling of the intestinal wall. This narrows the lumen causing constipation.
- Leukocytosis is not very common in UC
- In acute UC patients have high platelets, low hemoglobin, and low albumin. Low hemoglobin is due to bleeding (rectal or diarrhea) and anemia of chronic disease
- Barium enema is rarely used to diagnose UC
- CT scan is used when we suspect perforation
- The gold standard for diagnosis is colonoscopy
- In acute fulminant colitis, you don't want to put a scope inside the patient. This increases the risk of perforation; a limited sigmoidoscopy is enough
- In the first presentation of UC (acute severely inflamed), we perform a 5 minute sigmoidoscopy to see an inflamed rectum and we start the patient on steroids. We initially see the rectum, because this is where the disease starts. When the patient is stable, we complete the colonoscopy.

- **<u>Crohn's disease:</u>**
  - To diagnose it we do colonoscopy, upper endoscopy, and MRI of the small bowel all together

- If the disease is in the small bowel it is more aggressive so your treatment must be aggressive. Patients are started on Imuran, anti-TNF agents.
- If you have it only in the colon you may only give mesalamine only (doesn't work for upper GI Crohn's because mesalamines don't work on small bowel
- It is a transmural ulceration. That is why it causes strictures, fibrosis, fistulas, etc…
- CD is divided into:
    - Inflammatory
    - Obstructive: chronic inflammation, the most common is seen in the terminal ileum
    - Fistulating: perianal fistula is the most common. You can develop an entercutaneous fistula, as well.
- Before rectal examination, we ask the patients about perianal discharge as they might have a leaking fistula
- Ultrasound is better than CT because it looks at the mucosa and the bowel; however, it is not used in Jordan
- PSC: a chronic inflammation of the bile duct. so any patient with IBD and abnormal liver function test either in a cholestatic or parenchymal pattern (GGT, alkaline phosphatase, bilirubin). We do MRCP to diagnose
- All patients with IBD are at high risk of thrombosis, so when a patient with a flare of UC or CD comes to the hospital we give him low molecular weight heparin even if they are bleeding as a prophylactic dose. We give the heparin when they come to the hospital because if they are mobile outside the hospital it is fine. Thrombosis can occur anywhere recurrently at any age.
- If you have IBD, you are at a higher risk of developing colon cancer especially in UC due to ongoing inflammation and dysplasia of the colon
- The risk of colon CA develops after 10 years of onset of the disease; and you screen after 10 years of the onset
- The more severe the disease is, the more inflammation you have, the more extent of the disease you have, and if you have family history of CA this leads to higher risks.
- Patients with severe pancolitis have more risk of developing CA compared to those with mild pancolitis
- If the patient is stable with family history of CA, we screen every 5 years. But, if he has a severe disease, we screen every 2 years
- Pancolitis patients must have annual colonoscopy because the risk is very high
- **Treatment:**
    - In treating IBD, it is important to know whether it is CD or UC and to evaluate the severity and the extent of the disease

- If the patient has IBD and abscesses, don't give anti TNF because you will kill him
- When you treat IBD, you either target immunity by giving immune-suppressants (Imuran, 6-mercatopurine, methotrexate, nitrophinulin), or with anti-TNF agents which are more expensive more potent immune-suppressants
- If the patient suffers from a severe disease, start with top-down approach (use of most aggressive drugs first). However, if the disease is mild, start with a bottom-up approach (use of mild drugs first, mesalasines)
- The most commonly used drug is mesalamine. It is used in treatment of UC and mild Crohn's colitis. It is effective in induction of remission, but it is not used for severe disease.
- The effect of mesalamine is local on the mucosa; that is why they don't work in CD because CD is not limited to the mucosa, it is deep
- Side effects of sulfasalzine are related to sulfapyridine
- Dual treatment is the administration of both local and systemic agents for treatment of UC.
- Steroids are not used for maintenance in the treatment of IBD. The only exception is patients with Crohn's terminal ileitis; these are kept on budesonide as a maintenance treatment.
- Most of the time, we give steroids as induction of remission. When a patient comes with severe colitis you administer 40mg of IV steroids. Then you taper the dose 5mg every week over 6 weeks. Then, you start another treatment (mesalamin or infliximab)
- If the patient has proctitis, you give steroids enema as maintenance
- Ulcerative colitis: approach is usually bottom up
    - Proctitis: enema or suppositories
    - Distal colitis: enema if this doesn't work systemic treatment
    - Pancolitis: start with mesalamine and then we go up to the maximum dose (4g). If this doesn't work, the second line of treatment immune-suppressants such as azathioprine, 6-mercatopurine, methotrexate, or infliximab\
- Immuno-modulators work after 3-4 months; patients won't improve after 1-2 months
- The main drugs in treating CD are immunomo-dulators not mesalamine except if the patient has very mild CD. If a patient has small bowel CD, we use immune-modulators (azathioprine)
- Immuno-modulators are very aggressive drugs so they are used for fistulating CD and with patients with inflammatory structuring disease

- In acute colitis, whether it is UC or CD, you first administer IV steroids and mesalamine. Then, you wait for 3 days. If, at day 3, the patient does not improve and is not yet a candidate for surgery, you have to rule out infection. If this happens, you have two choices; either transfer the patient for surgery or give a more aggressive treatment (anti-TNF (infliximab)or cyclosporine)
- Infliximab is used for induction of remission and maintenance
- In UC you may still have proctitis even after surgery. Other lower Gi symptoms may still persist (tenesmus and irritation)

Miscellaneous diseases

- **Malabsorption disease:**
  - Symptoms:
    - Weight loss
    - Anemia
    - Deficiencies (iron B12)
    - Steatorrhea
    - Diarrhea
    - Muscle wasting
    - Failure to thrive in children
  - If you have a problem in the lumen (inside or outside), like bacterial overgrowth this will cause malabsorption. Celiac disease will cause malabsorption. Any cause of pancreatic insufficiency like pancreatitis or cystic fibrosis can cause malabsorption. Any bile problem may cause malabsorption. Any patient who underwent resection of his bowel will not have enough bowel to absorb food especially in patients with IBD. Ask about how much bowel is left in surgery patients.
  - How much is the length of the bowel needed to left in order not to be dependant completely on supplement? (small bowel)
    - One meter or more. If you have 80 cm or less, then you are dependent on TPN
  - Other causes of malabsorption:
    - Mucosal abnormalities
    - Tropical sprue
    - Lactase deficiency: enzyme deficiency
    - Infections: TB Giardia
    - Sclerosing diseases: systemic sclerosis
    - DM → causes bacterial overgrowth and this will lead to a problem in the absorption itself
- **Celiac disease:**
  - Can present at any age or stage of life
  - Severe form of celiac doesn't occur at late of life
  - If the patient presented at a late stage of life, this means it is latent or mild
  - It is gluten hypersensitivity (formation of antibodies against gluten; anti tissue transglutaminase). This leads to obstruction of the mucosa of the small bowel
  - There is a genetic relationship with HLA-DQ2 and DQ8. If you don't have this gene it is unlikely that you have celiac. 98% of cases have this gene
  - Diagnosis:

        - Biopsy, endoscopy, histopathology, IgA → not conclusive. If we are not sure whether the patient has celiac or not, we order a genetic test to be sure.
    - Classical celiac:
        - Diarrhea
        - Weight loss
        - Vitamin deficiency
        - Failure to thrive
    - Latent: present at old age (mild or silent)
    - Potential: you are not sure whether the patient has celiac or not
    - Most common presentation of celiac is asymptomatic, then iron deficiency anemia
    - Celiac affects the liver, so patients may present with abnormal liver tests and when you put them on a gluten free diet the liver function will improve
    - It is rare to develop neuro-psychotic disorders with celiac (seizures, epilepsy, ataxia)
    - Arthritis and osteoporosis are common
    - Approach to patient:
        - History and
        - Blood count
        - IgA transglutaminase (97% sensitivity and specificity); if it is positive, need for endoscopy (and biopsy to confirm diagnosis). But, if it was low this could be a false negative because celiac could be caused by other immunoglobulins, so we do total immunoglobulin assay. If IgA was positive we do duodenal biopsy (d2 biopsy). We find villus atrophy, mucosal inflammation, crypt hyperplasia
    - Management: gluten free diet

- **PSC (primary sclerosing cholangitis):**
    - Appears with IBD
    - Abnormal liver test
    - Diagnosed by MRCP, rarely ERCP
    - We find stricturing and peeling of the bile duct
    - 20% of patients with PSC develop cholangiocarcinoma
    - Colon cancer and gallbladder cancer are not uncommon
    - Treatment: ballooning, stenting, or liver transplant. There is no medical treatment for PSC

- **PBC (primary biliary cholangitis):**
    - Autoimmune disease of the bile ducts
    - positive N2 antibody
    - Common in females
    - The patient is in her 30's with increased ALT and AST. But, mainly, GGT is high
    - On ERCP, onion ring appearance
    - Treatment for PBC: deoxycolic acid 15mg/kg is the only effective treatment. This will delay the onset of cirrhosis.
    - Biopsy to confirm diagnosis

- **Autoimmune hepatitis:**
    - Mainly females
    - Disease that mainly affects kids → ANA +ve
    - Disease that mainly affects adults→ anti smooth muscle antibody, anti-liver kidney antibody
    - Mainly AST elevated (parnchymal injury)
    - Criteria for diagnosis:
        - Raised immunoglobulins
        - Female
        - Rule out hepatitis Band C
        - Positive antibody
        - High titer of autoantibodies
    - Livery biopsy to confirm diagnosis
    - Treatment: immune-suppressants; start with steroids then add Imuran

Esophagus

- Anatomy of the esophagus:
    - Upper esophageal sphincter
    - The esophageal body
    - Lower esophageal sphincter
- The upper esophagus is voluntary; if you swallow something, you can hold it in for a few minutes. However, the lower esophageal sphincter is involuntary. You have no control over it.
- Innervation of the esophagus and the pharynx along with the skeletal muscles of the esophagus comes from nerves in the brain and in the spinal cord
- If someone comes with an upper esophageal problem, think about esophageal problems, bulbar palsies, CVA's, or myasthenia gravis. Patients usually present with:
    - Choking with food
    - Once they start eating the food gets stuck
- Common esophageal presentations:
    - Dysphagia:
        - Difficulty in swallowing.
        - It is important to clarify what the patient means by dysphagia.
        - It means that the patients cannot get the food down, and they might need water to ease the process of swallowing.
        - Some patients might confuse dysphagia with odynophagya or difficulty swallowing from reflux.
    - Odynoophagea:
        - Pain on swallowing mainly
        - Can be caused by esophagitis, herepes esophagitis, or chemical esophagitis (ingestion of chemicals)
    - Heartburn
    - Chest pain:
        - The first differential of chest pain is a cardiac problem. Never think of GI problems as the first cause of chest pain.
        - Esophageal spasm or regurgitation can cause chest pain
    - How to diagnose esophageal problems?
        - Barium swallow:
            - Old fashion method, still used
            - Gives you an idea about the anatomy, contraction, and diameter of the esophagus
            - Usually preferred over endoscopy if the patient is at a high risk of perforation due to endoscopy (pharyngeal pouch patients). In endoscopy, the first 10 cm of intubation are blind; if the patient has

a pouch, there is a high chance for perforation. If you suspect a pouch, ask for a barium swallow before proceeding for endoscopy. Patients usually complain of problems in swallowing along with regurgitation of undigested food particles.

- You always follow a barium swallow with an endoscopy. If there is a pathology, a barium swallow will not reveal the cause. A narrowing in the esophagus on barium swallow can be due to strictures, inflammations, or any other cause.

- Endoscopy:
  - Esophagus is made of squamous epithelium
  - Some columnar cells can found at the gastroesophageal junction.
  - Migration of the columnar cells upwards is called Barrett esophagus
- Motility studies
- Esophageal pH monitoring:
  - 24 hours monitoring
  - A probe is installed in the patient's lower esophagus.
  - Whenever the patients have symptoms, they press a button.
  - The probe is taken out after 24 hours, and data analysis is performed
  - Used for patients who have recurrent reflux symptoms, but have normal endoscopy. Many patients come with symptoms of reflux but are negative on endoscopy. In these patients, you can correlate between their symptoms (reflux) and the acidity of the esophagus.
  - If you want to send the patient for surgery you need to make sure that the symptoms are caused by acidity. The idea is to correlate between the acidity and symptoms. If there is a direct correlation, it means that the acidity is what causes the symptoms.
  - If the symptoms are caused by reflux, maximum treatment is given. If patients do not respond, they are sent for fandoplication (anti-reflux surgery)
- Pressure studies

- **<u>Motility disorders:</u>**
  - Patients present with dysphagia
  - If the patient is elderly, you think of a tumor
    - Squamous (mid-esophageal)
    - adenocarcinoma (lower esophageal)
    - Pill esophagatis
    - Motility disorders.
  - **Achalasia:**

- Failure of relaxation of the lower esophageal sphincter with lack of peristalsis that cannot be attributed to other causes like cancer or fibrosis.
- Peristalsis is a coordinated sequential movement of contraction and relaxation that helps move food down the esophagus. If the esophagus as a whole contracted at the same time, nothing moves.
- In achalasia, peristalsis is impaired.
- It is caused by failure of distal esophageal inhibitory neurons.
- If the manometric appearance or X-ray appearance are atypical, think about pseudoachalasia (gastric carcinoma, lymphoma, gastroenteritis, neurodegenerative diseases)
- Clinical presentation
    - Difficulty swallowing
    - Chest pain: due to failure of relaxation of the lower sphincter
    - Regurgitation
    - Difficulty breathing air out: the stomach is bloated
- Findings:
    - Absence of fluid/air level (we rarely depend on the X-ray for diagnosis)
    - Beading in the lower esophageal sphincter
    - Bird peak sign
    - Dilatation of the upper body of the esophagus: due to the lack of contraction.
- Diagnosis criteria :
    - Failure of relaxation
    - No peristalsis
    - Manometry (or high resolution manometry): normally, the waves measured by manometry occur at different times. However, with achalasia, the contraction is absent
    - Endoscopy of achalasia:
        - Dilated esophagus
        - Full of food
        - Difficulty to go through sphincter due to failure of relaxation
    - Treatment:
        - Drugs don’t work (CCB’s and nitrates)
        - Botulinum toxins (botox) to relax the muscles: injected in the esophagus. The problem is that these injections induce fibrosis or ulcerations. Usually done for patients who are not fit for surgery
        - Surgery: dissection of the muscle to relax the esophagus:

        - Heller's myotomy: deep cut in the muscles
        - POEM (peroral endoscopic myotomy): it is a very invasive procedure
    - Dilation by ballooning:
        - Some authorities recommend ballooning; if patients do not recommend, move to surgery
        - British guidelines do not recommend ballooning as it might cause fibrosis making later surgeries complicated.
- Achalasia can be divided according to the motility of the upper esophagus.

- **Hypertensive lower esophagus:**
    - Increased resting pressure at the lower esophagus >45 mmHg
    - Peristalsis is normal.
    - The difference between this disease and achalasia is the presence of peristalsis…
- **Esophageal spasms:**
    - Simultaneous raise in pressure of smooth muscles in more than 30% of swallows.
    - When we do manometry, we ask patients to drink 10 swallows of water. Abnormality in 3 swallows diagnoses the disease
    - Patients have normal function, the dysfunction is intermittent.
    - Here, the amplitude of the contraction is normal. However, it is uncoordinated.
- **Nutcracker esophagus:**
    - Very high pressure raise in the esophagus (might reach up to 220 mmHg)
    - High pressure wave that causes severe spasm of the esophagus.
    - It is related to neurological disorders; imbalance between inhibitory and stimulatory waves….
    - Here, the contractions are normal; however, their amplitude is very high. An extreme case of nutcracker esophagus is referred to as a jackhammer esophagus.
- **CREST:**
    - Calcinosis in fingers
    - Esophageal problems: mainly in the lower smooth muscles. The upper esophagus is normal. Absent contraction in the lower esophagus.
    - Raynaud's phenomenon, mainly the lower esophagus is affected (smooth muscle)

- **Eosenophilic esophagatis:**
  - Ring like appearance on endoscopy
  - Infiltration of the esophagus with eosenophils
  - Patients present with dysphagia
  - Biopsy is taken during endoscopy for confirmation
  - Reflux disease can cause the same endoscopic appearance
  - Put the patient on PPI's for 4 weeks. If there is improvement, the patient has reflux. If the patient does not improve, the patient has eosenophilic esophagitis.
  - Treatment:
    - Inhaled and swallowed steroids
    - The idea is to provide steroid topical treatment for the abnormality (topical steroids, oral don't work)
    - When the patients stop treatment, most have recurrence of symptoms
- **GERD:**
  - The commonest esophageal disorder
  - Acid reflux from the stomach to the esophagus
  - Caused by:
    - Hiatus hernia
    - Muscle weakness
    - Pregnancy
    - Scleroderma
    - Drugs
    - Pyloric stenosis
    - Tumor in the antrum
    - Increased stomach acidity
    - Ingestion of fizzy drinks
    - Previous surgeries
    - Failure of the anti-reflux mechanism.
    - Obesity: causes increased abdominal pressure, which pushes on the stomach and encourages acid reflux
  - The diaphragm, the muscles, and the sphincter prevent you from having reflux. The gradient of pressure between stomach and esophagus causes reflux Causes of reflux:
  - Correlation between pH and reflux disease:
  - GERD might lead to ulcerations
  - 70% of patients with GERD have normal endoscopy
  - Give PPI's; if patients don't improve, monitor pH

- Patients who have erosive esophagaits have positive endoscopic findings, and respond better to PPI's.
- Symptoms:
    - Heartburn
    - Regurgitation
    - Acidity
    - Difficulty in swallowing
    - Hoarseness
    - Asthma patients can have exacerbation of symptoms with GERD; acid causes bronchospasm.
- Diagnosis:
    - History
    - Barium swallow: we see acid going up and down
    - Manometry
    - Bernstein test: put acid in esophagus and see if there is recurrence of symptoms; rarely done
    - High resolution manometry
- Treatment:
    - Lifestyle modification: weight loss, decrease fizzy drinks, change bed angle, stay away from food that trigger reflux
    - H_2 blockers
    - PPI's
    - If medical treatment fails, fandoplication is recommended (wrapping the fundus around the lower esophagus)

- **Barrett esophagus:**
    - The stomach has columnar epithelium; due to reflux, part of the esophagus becomes stomach-like.
    - This leads to metaplasia, dysplasia, and cancer
    - Less than 0.3% of the population
    - Diagnosis: biopsy of the lower esophagus to confirm metaplasia or dysplasia of squamous cells
    - Treatment:
        - Treat acidity
        - Surveillance and continuous biopsies
        - If the patient has dysplasia, treat with laser surgery
        - If patients have a tumor
        - Low grade dysplasia: follow up…
        - High grade dysplasia: laser therapy
- **Corrosive esophegitis:**
    - Chemical cause

- Ingestion of corrosive agents

- **Hiatus hernia:**
  - Part of the stomach goes up the esophageal sphincter due to weakness or relaxation of the diaphragm.
  - This predisposes patients to reflux..

Peptic ulcer disease and H. pylori

- One of the most important topics to discuss is H.pylori infection as it is one of the most common infections
- Peptic ulcer:
    - Defect in the mucosa and submucosa of the intestines or stomach extending to the vascularity; regardless of the cause.
    - Erosion is superficial. Just like abrasions, erosions don't break through the wall of the stomach
    - Ulcers are diagnosed by endoscopy or barium swallow, but most importantly, history.
- Perforating ulcers: perforate all the way through the peritoneal cavity
- Penetrating ulcer: penetration to adjacent or far organs e.g. aortogastric ulcer
- Fistulating ulcers: perforating ulcer to the colon
- Ulcers affect men more than women.
- Related to smoking and polymorphism
- Ulcers develop due to an imbalance between what protects your mucosa and what damages it. Some of the protective factors include: bicarbonate, blood flow, mucosa, and prostaglandins
- Patients with a hypovolemic shock develop what is caused stress or ischemic ulcer due to diversion of the blood away from the stomach. This happens in total body burns, road traffic accidents, major surgeries, septic shock, and patients in critical care, as well. These are treated with a combination of Gaviscon and PPI'.
- The commonest cause of duodenal ulcers is H. pylori infection
- Causes of ulcer:
    - NSAIDs (aspirin); common in critical care patients. Mostly duodenal
    - Herpes and CMV (immune-compromised)
    - Tumors
    - Vasculitis: has to do with the blood supply of the stomach
    - Crohn's disease: can cause upper GI ulceration stomach or duodenal ulcerations
    - Gastrinomas
    - Tumor cell secreting hormones
    - Increased stomach acidity causing self digestion
- Although atypical, sometimes, patients might present with GI bleeding
- Presentation depends on the location of the ulcer:
    - Esophagus: dysphagia or odynophagia
    - Gastric ulcer:
        - Dyspepsia
        - Abdominal pain: epigastric pain, localized. Ulcer doesn't give you severe pain unless it is complicated.

        - Severe epigastric pain is usually associated with a perforating ulcer
        - Tenderness and guarding
        - Anemia
        - Hematemesis (vomiting blood)
        - Asymptomatic: dyspepsia is the only complaint
- Hunger pain and non-hunger pain is not a reliable sign for the location of the ulcer.
- Complications: (the following are signs of gastric outlet obstruction. This can be caused due to edema in the pylorus which leads to gastric outlet obstruction. Treated with high dose PPI's; if treatment doesn't work refer to surgery
    - Dyspepsia for a long time
    - Continuous epigastric pain
    - Vomit all food
- NSAIDs can give rise to multiple ulcerations
- Zollinger-Ellison syndrome: deep ulcerations covering the stomach and first part of the duodenum
- Examination is normal except for mild tenderness
- Blood tests are not usually done unless we suspect H. pylori
- Endoscopy is very important:
    - Duodenal ulcer rarely associated with malignancy (rarely biopsied), unless the patient is high risk: aka has bleeding, you need to administer
    - Do not repeat endoscopy for duodenal ulcer unless there is an indication.
    - In gastric ulcers, you must repeat the endoscopy until the ulcer is healed due to high risk of malignancy. Treat for 8 weeks, biopsy, and then repeat the cycle
- Many patients have chronic non-healing gastric ulcers; however, their biopsies are benign. In this case increase the PPI dose, and treat for H. pylori; if pain persists, refer to surgery.
- H. pylori:
    - A bacteria that colonizes our stomach.
    - Acquired in the first years of life.
    - Usually, does not cause symptoms; however, in some patients, it causes ulcerations
    - Gram negative
    - Attaches to the mucosa of the stomach
    - The hallmark of H. pylori is breaking up urea via urease enzyme releasing ammonia and CO_2. We depend on this reaction to detect for the bacteria (breath test or gel-test)
    - A common cause of ulceration in Jordan (70% of people with ulcers have H. pylori)
    - It causes ulceration in the distal part of the stomach, usually at the antrum. This is the preferred location as the acidity in the antrum is less than the rest of the

stomach. When you give PPI's, the microorganism will migrate more proximally. If we cannot stop PPI's, we usually take biopsies from the proximal parts of the stomach (fundus).

- Acute infection is rarely associated with symptoms. Patients might only complain of gastroenteritis-like symptoms (abdominal pain, nausea, and flatulus)
- After a few weeks of the acute infection, the chronic stage begins. It can be divided into:
  - Alpha predominant gastritis in the antrum: leading to duodenal ulcer..
  - non-atrophic pangastritis: leads to lymphoma
  - Corpus predominant gastric ulcer and tumors: proximal
- What will happen to the ulcer?
  - Depends on your genes (polymorphisms), ability of your body to get rid of the bacteria, the virulence of the subtype of H. pylori, and environmental factors (alcohol and tobacco)
- Peptic ulcer develops in 3% of those who have H. pylori
- Risk of carcinoma: 0.1%. If we treat H. pylori, we cannot be sure that we will prevent cancer
- In Japan, they had an eradication program. H. pylori was eradicated from every citizen who tested positive for the bacteria. Since Japan has a high incidence of gastric cancers, after 20 years of the eradication, studies showed a significant decrease in the incidence of carcinoma.
- Non-ulcerative dyspepsia:
  - Atypical presentation of H. pylori infection
  - Symptoms of dyspepsia without ulceration on endoscopy
  - Patients were treated for H. pylori; their symptoms improved. However, these patients had increase in their reflux symptoms. This is why this case is not an indication for treatment.
- Diagnosis:
  - Serology is useless: due to the high prevalence of this bacterium, many people test positive for the antibody)
  - Decal antigen of H. pylori: time consuming test; we don't use it in Jordan
  - Endoscopic biopsy from the mucosa: sample is placed in a gel that detects for urease activity. A positive test is a change in the color of the gel from yellow to red. Can be done in an hour
  - Culture: only done when patients are resistant to antibiotic treatment
- Indications for treatment:
  - Duodenal ulcer
  - Gastric ulcer
  - MALToma
  - Atrophic gastritis: can lead to gastric cancer..

        - Recent recession of gastric cancer
        - Functional dyspepsia and GERD: treatment can be initiated, but not strongly recommended
    - Treatment:
        - Two antibiotics and a PPI
        - PPI's are used to decrease the acidity of the stomach. When the acidity decreases, H. pylori will increase in number. A high colony count will make antibiotics more effective. Moreover, changing the pH will increase the delivery of the drug.
        - Resistance can develop to:
            - Clarithromycin
            - Levofloxacin
            - Erythromycin
    - Types of treatment:
        - First line treatment (triple or quadriple therapy): PPI (2x1), amoxicillin (2x1) and erythromycin (2x1) with or without bismuth therapy. If you have a high resistance area, use bismuth and sequential treatment. In areas of high resistance, we don't use erythromycin, we use levofloxacin instead. Bismuth is a bacteriostatic agent.
        - Alternative first line treatment: Bismuth, metronidazole, tetracycline, PPI
        - Second line treatment: replace erythromycin with levofloxacin; called levofloxacin based treatment.
        - Third line treatment: if second line treatment fails, do an endoscopy and take a biopsy. Culture the biopsy. Choose 2 susceptible antibiotics and give them with a PPI.
        - Sequential treatment: PPI + amoxicillin for 5 days. Then, PPI and metronidazole for 5 more days. concomitant treatment 4 antibiotics together)
        - Concomitant treatment: same drugs used in sequential treatment but given together. Either for 7 days (according to the British guidelines) or for 10 days (according to the American guidelines)
        - If the patient has amoxicillin allergy, replace it with flagyl (metronidazole)
    - Confirmation of eradication: stop antibiotics for 4 weeks, stop PPI's for 14 days, stop H_2 blockers for 7 days. There is no need to stop antacids.
        - Breath test
        - Stool antigen
        - Endoscopy
    - Before you treat with NSAID's, test for H. pylori. If the patient is positive, stop NSAID's, especially in patients with RA.

GI bleeding

- A massive GI bleeding is a medical emergency that usually requires surgical intervention.
- In cases of emergency, the most important thing to look for in physical examination is hemodynamic stability: tachycardia, bradycardia, blood pressure changes, orthostatic blood pressure changes.
- If the patient has any hemodynamic compromise, this indicates a massive bleeding
- The most common etiology of upper GI bleeding is PUD. PUD's most common causes are H. pylori and NSAID's respectively.
- It is important to differentiate between a bleeding varix and non-varicelle bleeding. Examples of non-varicelle bleeding include: Mallory-Weiss tear, gastric erosions, PUD, and malignancies.
- The most common cause of lower GI bleeding in OPD: hemorrhoids
- The most common cause of lower GI bleeding in hospitalized patients: diverticulosis
- Patients with lower GI bleeding present with blood per rectum (hematochezia). The blood can be mixed with stool or separate from it. Fresh blood or blood separated from stool indicates rectal or anorectal bleeding. Blood mixed with stool usually indicated bleeding from a more proximal area in the GI.
- Other etiologies of lower GI bleeding:
    - IBD
    - Ischemic colitis
    - Tumors…
- The difference between upper and lower GI bleeding from a GI perspective is the need for surgical intervention. Most cases of upper GI bleeding do not require surgeries, while the opposite is true for lower GI bleeding. In upper GI bleeding, surgeons are required when there is hemodynamic instability; however, this rarely happens. In lower GI bleeding it is different because most of the time internists cannot treat the problem
- Upper GI bleeding:
    - In 90-95% of cases melena is an indicator of upper GI bleeding. To produce melena you need 50cc of blood; any less will produce a positive hemoccult stool test.
    - In 10% of cases, melena can be due to lower GI bleeding with slow transient time.
    - How to assess for upper GI bleeding: history and physical assessing hemodynamic status
    - In cases of emergency: quick history, assess stability, put IV access, draw blood for: CBC, PT, PTT, KFT, and specify blood group and class in case transfusion is needed.
    - There is no role for fecal occult blood testing in GI emergencies. It is a colon cancer screening. A fecal occult testing is indicated if you are not sure of the stool content. Usually, a rectal exam suffices.
    - How to assess for upper GI bleeding using a bedside tool?

        - NG tube is a useful tool to test for upper GI bleeding. Putting an NG tube can help in diagnosis and does have prognostic value.
        - Coffee ground material in tube: 6% mortality rate
        - Clear NG tube: mortality 3%
        - Fresh blood: 20% mortality
        - You can have massive GI bleeding with a clear NG tube. This happens in cases of a bleeding duodenal ulcer. The bleeding ulcer will cause an inflamed area around the pylorus preventing blood reflux to the stomach giving a negative NG tube test. There is a 15-16% chance of having a massive GI bleed with a negative NG tube test.
        - If you are an expert, you don't call an NG tube test a negative test simply by seeing a yellow secretion. It is truly negative when there is negative PCI. If there is bile in you NG tube; this means that there is no active bleeding
    - Rectal tube: if you get fresh blood when you insert a rectal tube, it indicates a massive bleeding. Mortality rate is 30%
    - Management:
        - Determine degree of severity to determine place of admission (ICU vs. floor). Patients with a bleeding varix are administered to the ICU (mortality rate up to 20%)
        - Perform an endoscopy:
            - Bleeding varix: with signs of chronic liver disease and portal hypertension
            - Other causes (non-varocele bleeding)
        - In case of a bleeding varix, do not administer any hypotensive agents. Give vasopressors (cardiopressin; improves mortality), GTN, and other vasopressors. The administration of vasopressors will decrease bleeding time, decrease hospitalization, and decrease need for transfusions. Continue treatment for 5 days.
        - In case of non-varocele bleeding, administer PPI's to stop the bleeding. This will decrease hospitalization, decrease requirement for transfusion, and has the added benefit of decreasing stomach acidity.
        - Third decision: time of endoscopy. Non-varocele endoscopy done in 24 hours… varocele: expedite pathway 6-12 hours of admission… the bleeding here can be massive… catch the varix when it is not actively bleeding!
    - Prognostic factors:
        - Age
        - Hemodynamic status

        - Comorbidities: having comorbidities increases the chances of having end organ damage due to lack of perfusion caused by bleeding.
        - Etiology: malignancies tend to have a worse prognosis.
        - Use of medications (NSAID;s and anticoagulants)
    - Mortality rate due to non-varocele bleeding has not changed dramatically. In the past, bleeders used to be younger and their bleeding was a complication of H. pylori. However, nowadays, most bleeders are elderly patients who are chronic NSAID users. This is why mortality has not changed significantly. Most of those who die are above the age of 60. Mortality below age of 60 is less than 1%.
    - Why do we need endoscopy?
        - Treatment: banding of a varix
        - Localization of the site of bleeding
        - Diagnosis of the etiology: PUD, varocele
        - Prognosis…
    - Prognostic endoscopic criteria: (stigmata of recent bleeding)
        - Clean based ulcer: An ulcer with a white base; no visible vessels, clots, or pigmentation. Chance of re-bleeding is less than 5%. Discharge the patient right after endoscopy.
        - Pigmented spot: the base is white with a red spot or black spot. 10% chance of re-bleeding. Observe overnight
        - Adherent clot: the presence of an irremovable clot that is adherent to the ulcer's base. 15-20% chance of re-bleeding… When it comes to treatment, some people would mechanically remove the clot to see what is under it. Others would simply leave the clot. These patients benefit from continuous PPI infusions. If we keep pH above 6, we inhibit fibrinolysis of the clot. This will stop the bleeding, which will allow the vessel underneath to heal. This class of patients gets the best benefit of pharmacological treatment
        - Visible vessel: obliterate the vessel. 40-50% chance of re-bleeding. Target group of endoscopic treatment
        - Spurting vessel: obliterate that vessel, 50-70% chance of re-bleeding. Target group for endoscopic treatment
    - In case of Varices, the location is very important. Esophageal varices are easily treated while gastric and duodenal varices are difficult to treat. In terms of prognosis, a smaller varix is less likely to re-bleed. Moreover, the presence of red dots along the vessel is a sign of weakness and an indicator of likely re-bleeding.
    - Esophageal varices can be treated with banding orsclerobanding. Gastroesophagealvarices can be treated endoscopically. Other varices require TIPS procedure (shunting of the blood to reduce pressure on the affected vessel)

    - Pharmacological therapy is usually continued for 5 days as bleeding most commonly happens 48-72 hours after endoscopy.
    - In cases of esophageal varices, band the vessels and repeat if necessary. Sometimes, banding is done over two sessions. When the banding is complete, patients review the clinic every 6 months for surveillance.
- Lower GI bleeding:
    - In case of an emergency, perform the same aforementioned steps (history, physical, IV line, and blood tests)
    - When taking history focus on: previous endoscopies showing diverticulosis, previous bleeding, predisposing factor for ischemic colitis (elderly, CAD, CHF, on digoxin, atrial fibrillation)
    - Try to perform a colonoscopy 6-12 hours after admission. That is not possible in all patients.
    - Endoscopy is important for:
        - Localization
        - Treatment: in cases of lower GI bleeding, we rarely find any causes that can be treated endoscopically. An exception is AV malformations which can be treated endoscopically. Malignancies are not treated endoscopically. Diverticulosis cannot be treated endoscopically (it is very hard to localize which diverticulus bleeds). What endoscopy does is locate the approximate site of bleeding, which assesses surgeons in their job.
    - Localization tools:
        - Bleeding scan: Tc label RBC scan. Used to locate the site of bleeding (we trace the blood and see where it leaks.) In theory, it works. However, it is of an intermediate clinical value.
        - Angiography: can be used if bleeding rate is more than 0.5cc/min. The bleeding must be active during time of angiography. You can obliterate the affected vessel.
        - In cases of mild to moderate bleeding, you can perform double balloon endoscopy (take a scope to the stomach all the way to the proximal half of the bowel… and from the rectum to the other half of the bowel)
        - If the bleeding is very severe, the patient is taken to the operation room. There, we perform an intraoperative enteroscopy (The surgeon makes a hole in the intestines and inserts a scope to locate the site of bleeding).
        - . CT angiogram: used when bleeding is active and at a high rate. Intervention cannot be done.
    - The main treatment of lower GI bleeding is surgery. You can treat AV malformations. However, if the patient has a hemorrhoid, you diagnose it and the surgeon operates on it.
    - Prognosis depends on the same factors as upper GI bleeding

- Melena caused by lower GI bleeding is due to oxidation of the blood through the bacterial pathway. However, melena caused by upper GI bleeding is due to oxidation of the blood through the acidic pathway.

Inborn liver disorders

- Genetic diseases
- Hemochromatosis: iron overload
    - The body needs iron for:
        - Oxygen transport
        - Oxygen production
        - Cell growth
        - Cell proliferation
    - Body's iron content: 3.5 grams
    - Iron is excreted to keep the balance in our body.
    - Any person normally ingests 10-20mg of iron daily. What is absorbed is 1-2 mg.
    - IDA is rarely caused by nutritional deficiencies as we can easily meet our iron needs through nutrition. In fact, on average, people ingest 10 times of their daily need.
    - The body gets rid of 2mg of iron daily. Iron is excreted through the skin (shedding of the cells) or through the GI tract (sloughing of the mucosa). Females can excrete iron through menses; they lose 30mg every month. Because females have menses, men tend to have more iron overload problems.
    - If a person has a deficiency in iron, the body will automatically absorb more iron to compensate for the loss.
    - Iron enters our body through specialized transporters called transferrins. Transferrins can import two iron particles at a time.
    - Uses of iron:
        - Erythropoiesis
        - Storage: in the form of ferretin. A protein that can store thousands of iron particles at a time.
    - Hemochromatosis:
        - Iron over-absorption.
        - The body absorbs 20-30% of the iron in food.
        - Ironaccumulates in different places of the body.
        - Symptoms appear at the age of 30 when enough iron has accumulated in the patient's body.
        - Most of the excess iron is stored in the liver. In fact, it is the organ first affected (liver cirrhosis)
        - Iron levels in hemochromatosis patients:
            - Normal: 3.5 grams
            - Age 10 : 5.5 grams
            - Age 20: 16 grams
            - Age 30: 33 grams.

- Autosomal recessive
- People develop liver cirrhosis by the age of 40. Develop heart failure between the age of 50-60.
- Organs affected:
    - Pituitary gland: hypogonadism
    - Heart: cardiomyopathy
    - Liver: HCC (100 fold increase in risk) or cirrhosis (liver becomes iron colored)
    - Pancreas: DM (bronze diabetes)
    - Recurrent infections
    - Skin: bronze color (color change not easy to spot in non-Europeans). An alarming sign is appearance of sunburned skin in people who are not exposed to the sun.
    - Testicular atrophy
    - Chronic arthritis
    - Pseudogout
- The symptoms are non-specific. In fact, 40% of the patients present with weight loss, fatigue and other non-specific symptoms. It is usually discovered incidentally
- Many people die undiagnosed. 90% of people who have hemochromatosis die undiagnosed
- Diagnosis:
    - Incidental finding
    - NL of serum iron 50-150. These individuals have higher serum iron, low iron binding capacity, high transferrin saturation (more than 50%), elevated ferritin.
    - Transferring saturation is calculated by dividing iron concentration over TIBC (total iron binding capacity)
    - The best way to screen for hemochromatosis is to calculate transferring saturation.
    - Biopsy is the gold standard for diagnosis
    - CT scan: compare liver color to other organs… the liver is darker compared to other organs…
- Treatment:
    - Before treating patients, you need to make sure that there are no other causes for increased iron in their body (iron injections, recurrent blood transfusions)
    - Iron chelation therapy is ineffective (drug's name Deferroxamine)

        - Phlebotomy: removal of blood on regular basis (like donating blood). Blood is removed weekly or bimonthly for a period of two years. Patients are allowed to become anemic.
        - If we discover the disease early, most of the changes in the body are reversible
        - If the patient has cirrhosis or arthritis, those are irreversible. Patient's risk for developing HCC does not decrease
    - People cannot get overloaded or deficient in iron with food!!

- Wilson's disease:
    - One of the most common causes of mental retardation in 1970's.
    - Wilson's disease is very common in Jordan; we have a specialized clinic for Wilson's.
    - Genetic defect causing decreased copper excretion.
    - Copper accumulates in different parts of the body causing several symptoms.
    - Some organs affected:
        - CNS: neuropsychiatric disorders
        - Eyes: early cataracts, KF ring (rarely seen on physical examination)
        - Heart: cardiomyopathies
        - Kidneys: renal failure, Fanconi's syndrome
        - Hemolysis
        - Liver: cirrhosis
        - Skin: bronze color
    - In advanced cases, people become completely physically and mentally retarded. In fact, many of those diagnosed with physical or mental retardation turn out to have Wilson's disease.
    - It is a gradual disease; however, it has an earlier age of onset compared to hemochromatosis. People are diagnosed between the ages of 18-30. Sometimes, diagnosis can be made earlier.
    - When to think of Wilson's?
        - Hemolysis with abnormal liver enzymes
        - Neurological problems in children (seizures)
        - Abnormal liver enzymes + Fanconi's syndrome
        - KF rings + early cataracts
        - Abnormal liver enzymes + hyperurecemia
    - Typical presentation: the patients are in their usual state of health, and suddenly get a psychological deterioration (acute psychosis or depression).
    - Diagnosis:
        - No definitive diagnostic test except for liver biopsy

        - Ceruloplasmin (decreased levels)
        - 24-hour urine copper (increased)
    - Treatment:
        - Copper chelating agents: penicillamine, Zinc, Trientene…
        - Low copper diet: decrease seafood (especially shells), avoid pistachios and peanuts.
    - If discovered early, the disease's progression can be stopped.
    - Wilson's disease is usually discovered early; when you discover a case of Wilson's disease screen the rest of the family, and start treating accordingly.
    - Most people die because they stop medications not because of the disease itself.

Fatty liver diseases

- Fatty liver disease is defined as the transformation of normal liver tissue into fatty tissue. It can be either steatosis or steatohepatitis (with inflammation).
- Classified into:
    - ASH: alcoholic steatohepatitis
    - NASH: non-alcoholic steatohepatitis
- ASH and NASH have become the most important cause for chronic liver disease in the world. In the past, it used to be hepatitis. However, it is currently decreasing.
- ASH:
    - Alcohol is highly associated with chronic liver disease
    - Alcohol was described as a causative agent for liver disease in 1793
    - In the developed world, alcohol consumption is decreasing. However, in the developing world, it is increasing. The global trend is a decrease in alcohol consumption.
    - Alcohol can cause many problems in the liver:
        - Acute hepatitis
        - ASH
        - Dependency
        - Liver cirrhosis
        - Cancer of the liver
    - Alcoholism: defined as a psychological dependence on alcohol. In the social history part of history, it is more correct to say that the patient doesn't consume alcohol rather than saying non-alcoholic. Females tend to be more alcoholic than males; they are easily intoxicated.
    - Factors predisposing to alcoholism:
        - Drinking pattern: weekly drinking is different than daily drinking. Drinking large amounts (binge drinking) is different than moderate drinking.
        - Female gender: males have faster alcohol metabolism. They are more predisposed to cirrhosis
        - Genetic differences: some people might drink daily, but never become alcoholic. Others might become alcoholic if they drink a little.
        - Type of alcohol: beer has the lowest alcohol concentration with 5% of its content made of alcohol. Wine has 10-12%. While spirits (vodka, tequila, etc..) have 40% or more.
        - Malnutrition: due to easier intoxication.
    - When taking alcohol consumption history, make sure to take it in a detailed manner. Ask about amount, pattern of drinking, type of drink, surrounding social circumstances, and dependency.
    - Alcoholic hepatitis:

- People who get alcohol hepatitis have a history of drinking.
- Alcoholic hepatitis cannot happen in patients without a history of drinking.
- Every time you drink alcohol, the liver is damaged. The body can tolerate a certain level of damage. At one point, the balance tips off; this is when you get signs of alcoholic hepatitis.
- Alcoholic hepatitis happens in chronic drinkers: 10-20 years of drinking. Consumption of 100 grams of alcohol per day.
- Typically, people who suffer from acute alcoholic hepatitis are in their 40's-50's
- Presentation:
    - Jaundice
    - Fever
    - Confusion
    - Tender hepatomegaly: characteristic finding.
    - Increase in liver enzymes (AST and ALT): AST is typically more elevated than ALT (characteristic). The increase is moderate; does not exceed 300 (NL: 30). In acute viral hepatitis, the increase is much higher. The elevation is not high due to previous liver injury. The increase in the enzymes comes from healthy cells; these patients don't have many healthy cells left.
    - Elevated serum bilirubin
    - Elevated WBC
    - Elevated INR
- Treatment:
    - No definitive treatment
    - Supportive care
    - Abstinence: people usually get withdrawal symptoms. In fact, most patients don't die of hepatitis. They die of withdrawal symptoms.
    - Administer anti-abuse drugs e.g. antabuse.
    - Prevention of alcohol withdrawal symptoms
    - Nutritional support to prevent infections. These patients are usually malnourished which increases their risk of infection. Alcohol becomes the patient's only source of energy. Fatty acids accumulate on the liver causing fatty liver. Common infections include tuberculosis and meningitis.
- Most alcoholics are admitted to hospital due to withdrawal symptoms not due to hepatitis
- Alcohol history is important. Sometimes, you admit a patient for pneumonia, but the patient is alcoholic. While you are treating the patient

for pneumonia, he might develop signs of withdrawal. This is why it is important to take a careful alcohol consumption history.
        - Any patient who is admitted with alcoholic hepatitis should be given protection for the stomach mucosa.
        - In patients with severe hepatitis, we use the DF (discriminant function) formula to determine the mortality rate:
            - Formula: 4.6 x increase in PT+ total bilirubin
            - If the number is more than 32, mortality rate is 33%
            - If the number is greater than 32, steroids are started right away

- NASH:
    - ASH is less common than NASH
    - NASH is an increasing problem; it is considered the top cause of mildly elevated liver enzymes
    - New disease described in 1980
    - The liver looks like the alcoholic hepatitis liver, but the patient does not drink alcohol (less than 20 grams per day or less than 40 grams per week)
    - These patients have fatty changes in their liver followed by fibrosis and inflammation
    - Our liver normally has 2-5% fat tissue. In some people this can go up to 20% without any significant symptoms. In others an increase to 10% causes significant symptoms.
    - The transition from a fatty liver (Steatosis) to an inflamed fatty liver(steatohepatitis)is a multifactorial process that is still poorly understood. However, insulin resistance is speculated to be one contributing factor.
    - People can have NASH without any symptoms. In fact, 20-30% of the population has fatty liver. Only 7-9% develop hepatitis
    - Fatty liver is the earliest sign of metabolic syndrome: any person with a fatty liver in their 20's will develop diabetes in their 40's
    - People with NASH do have metabolic syndrome, but it is not fulminant, yet. These people usually have diabetes, are overweight, or have dylipedemias.
    - Causes:
        - Drugs: tamoxifen, amiodarone
        - Rapid weight loss: patients who lose weight quickly whether surgically or using a diet (Atkin's, for example), will develop a fatty liver. Any decrease in the weight should be gradual; rapid fat loss can cause fatty liver. If the patient is overweight, we advise the patient to drop 10% of their weight. A 10% drop in the weight will cause 30% reduction in liver size and this should be enough to avoid further complications. Further weight loss is recommended; but it should be done over a prolonged period of time (1-2 kilos drop per week). Examples of bad diets include:

grapefruit juice diet (carbohydrates only) and Atkin's diet (high protein, low carbohydrates), starvation based diet (people regain weight as soon as the diet stops)

- Refeeding syndrome: When starved people eat large amounts of food after a period of starvations. These people develop fatty liver within hours and usually die of complications of fatty liver. In these patients, severe electrolyte imbalances cause most of the symptoms (Potassium and phosophorus)
- NASH is a silent disease; diagnostic tools are still somehow lacking.
- Clinical picture:
    - Hepatomegaly
    - Splenomegaly in advanced cases
    - Abnormal liver enzymes
- Diagnosis:
    - Liver biopsy is the gold standard diagnostic test. However, it is not practical. The procedure is invasive and carries 5-10% complication rate. Moreover, it has a low acceptance rate among patients. It is only done in severe cases or when patients do not respond to treatment .
    - Ultrasound: effective when fat comprises 30% or more of liver tissue. Fatty regions look hyperechoic.
    - CT scan: The spleen, liver, and stomach are usually the same density on a CT. However, in cases of fatty liver disease, the liver looks lighter.
- Treatment:
    - No established treatment
    - Lifestyle modification: mainly weight loss
    - Exercise: exercise is more important than diet. It helps get rid of the fatty cells in the liver. Medically speaking, it is better to be overweight and exercise than be skinny and not exercise
    - Control diabetes
    - Bile salts: Increased ingestion of bile salts will help replace the body's toxic bile salts with healthy bile.
    - Drug of choice for NASH: vitamin E

Acute pancreatitis

- The pancreas is located in the upper area of the abdomen.
- It is made of three major types of cells:
    - Ductal cells: line the pancreatic ducts; serve the purpose of carrying the excretions of the pancreas to the small bowel in order to digest food.
    - Acinar cells: secrete the pancreatic excretions which are carried by the ductal cells.
    - Islet cells: endocrine secretory cells of the pancreas. Divided into four types:
        - Beta cells: insulin
        - Alpha cells: glucagon
        - Gamma cells: pancreatic polypeptides
        - Delta cells: somatostatin
- Feedback loop for the exocrine function of the pancreas:
    - Upon eating, food is delivered to the small bowel (mainly fats and proteins)
    - The acidic medium of the small bowel stimulates secretion of **secretin,** a hormone produced by the duodenal cells.
    - Secretin stimulates secretions of the acinar cells, which produce bicarbonate and digestive enzymes.
    - Bicarbonate neutralizes the acidic medium of the pancreas activating the digestive enzymes.
    - The enzymes start digesting food along with secretin which inhibits further excretion of digestive enzymes.
- Functions of the pancreas:
    - Bicarbonate secretion to neutralize acids: The stomach is layered with a thick layer of mucin. This protects the stomach against high acidity; however, the duodenum is not protected due to the lack of the mucin layer. If the duodenal medium continues to be acidic, damage will ensue. In fact, this is what happens in the Zollinger-Ellison syndrome where the high acidity of the duodenum forms ulcers in its walls.
    - Synthesis of digestive enzymes
    - Control of metabolism through hormones
- Acute pancreatitis
    - Etiology:
        - Alcohol: most common cause of acute and chronic pancreatitis in the west
        - Gallstones: most common cause of pancreatitis in our part of the world
        - Other etiologies (1%):
            - Idiopathic
            - Drugs: most of the culprits are OTC medications, which makes their control difficult. However, one of the classes of drugs that

can be controlled is the hydrochlorothiazides; high doses of which are causative of pancreatitis.
- Hyperlipedemia
- Ductal obstructions (rarely due to tumors, because tumors expand progressively letting the duct adapt to the growing size of the tumor)
- Infectious agents
- Trauma
- Hypotension
- Ischemia

- Pathophysiology:
  - Ductal obstruction
  - Back flow of pancreatic secretions to the acini
  - Activation of acinar cells and release of digestive enzymes.
  - Alcohol, drugs, and infections cause destruction of the acini. This leads to the diffusion of the digestive enzymes to the surrounding area causing digestion of the adjacent tissues.
  - Hypotension: In the case of hypotension, perfusion to the pancreas will decrease, which might lead to ischemia. This leads to destruction of the membrane of these cells and subsequently the release of the digestive enzymes to the surroundings.
- Classification:
  - Interstitial pancreatitis: inflammation of the pancreas that does not cause loss of tissue
  - Necrotizing pancreatitis: severe form of acute pancreatitis where part of the pancreatic tissue is lost
- Presentation:
  - Severe epigastric abdominal pain radiating through the back (not around the back). The pain is severe because the pancreas is a retroperitoneal organ
  - Gastroperisis: due to severe inflammation
  - Low grade fever without infection: inflammation of the pancreas is severe enough to assure the development of fever
  - Tachycardia
  - Third spacing: sequestration of large amounts of fluid into the abdomen. Due to this, aggressive rehydration is considered one of the main modalities of treatment. Severe inflammation of the pancreas causes hypoxia to certain parts of the organ; if hypoxia continues, more damage will ensue. Severe rehydration assures avoiding this possibly fatal complication.

- Grey-Turner's sign: sign of hemorrhagic pancreatitis. Bluish discoloration over the flanks
- Cullen's sign: sign of hemorrhagic pancreatitis. Bluish discoloration over the periumbilical area.
- Leukocytosis
- Elevation of amylase and lipase levels:
    - The increase is at least three fold. One to two fold increase is non-specific and can be caused by different entities including: ectopic pregnancy, enteritis, salpingitis, or cholecystitis
    - Lipase is more specific than amylase as lipase is secreted in the pancreas, only. Amylase is secreted by salivary glands (parotitis can produce very high amylase)
    - Amylase and lipase levels in different pathologies:
        - Pancreatitis: both elevated
        - Parotitis: elevation of amylase only
        - Billiary stones: both are elevated (less than threefold). Common bile duct stones are the most common.
        - Intestinal injury: both elevated (less than threefold)
        - Reticulo-ovarian pathologies: both elevated, but amylase more than lipase.
        - Renal failure: both elevated
    - Once the initial insulting agent of acute pancreatitis subsides, amylase and lipase levels decrease. Amylase will be cleared in three to four days, and lipase will be cleared in a week.
- Differential diagnosis of abdominal pain vomiting:
    - Choledocolithiasis
    - Perforated or penetrating duodenal ulcer
    - Salpingitis
    - Ectopic pregnancy
    - Intestinal obstruction
    - Acute mesenteric ischemia
    - Lower chest pathology: inferior MI
- Factors predictive of gallstone pancreatitis: (the less these factors, the higher the chances of alcoholic pancreatitis)
    - Age: above 50
    - Female gender
    - Amylase: more than 4000
    - AST: more than 100
    - Alkaline phosphatase: more than 300

- Classification of pancreatitis according to severity (Ranson's criteria): severe cases are admitted to the ICU for close monitoring. These patients are at a higher risk for infection, hypotenstion, ARDS, and multi-organ failure. A score of 6 or above on the Ranson's criteria warrants an ICU admission.
    - White cell count: above 16,000
    - Age: above 55
    - Blood glucose: above 200
    - Serum LDH: above 350
    - Serum AST: more than 250

    On admission

    - Decrease in hematocrit: more than 10%
    - BUN: increase more than 5
    - Arterial pO_2: below 60
    - Serum calcium: below 8
    - Base deficit: above 4
    - Sequestration of more than 6 liters of fluid

    48h post admission

- Other investigations and imaging:
    - CT scan: useful tool to evaluate severity of pancreatitis. Used for Ranson's score above 3. Useful to rule in or rule out certain complications. CT staging:
        - Normal CT: good prognosis, moderate disease
        - Diffuse edematous pancreas
        - Peri-pancreatic inflammation
        - Fluid collection: pancreatic necrosis
        - Multiple ductal collections
    - Indications for CT:
        - Ranson's score above 3
        - Refractory hypoxemia
        - Refractory hypotension
        - Resistant fever
        - Tender abdominal mass
        - Hemodynamic instability
        - Signs of hemorrhagic pancreatitis
- Phlegmon: Severe diffuse inflammatory reaction of the pancreas with or without necrosis.

- Interstitial pancreatitis: in interstitial pancreatitis there are no signs of fluid collection, necrosis, or an abscess. It is a mild or moderate form of the disease.
- In acute pancreatitis patients, the risk of infection and death depends on the amount of necrosis. If the necrotic part of the pancreas becomes infected, the prognosis is very bad.
- Based on CT scan findings, ¾ of the patients are admitted with interstitial pancreatitis. Only ¼ are admitted with necrotizing pancreatitis
- Infection and mortality in interstitial pancreatitis are low. The course is benign, and patients can be managed conservatively.
- Necrotizing pancreatitis patients have a 30-50% chance for developing an infection with a mortality rate of 30% (significantly increases with infection)
- Signs of severity:
    - Echymcosis in the flanks: Grey-Turner's sign
    - Echomycosis in the periumbilical area: Cullen's sign
    - Suggestion of hemorrhage
- Management and treatment:
    - Supportive care: IV fluids. If a previously healthy person presents to the ER with normal blood pressure, a bolus of 1-2 liters is administered within an hour. Then, 250mL per hour for maintenance. If the patient is hypotensive, a 6 liters bolus is given with a maintenance of 250mL per hour.
    - Reduce the inflammation
    - Keep the patient NPO: to avoid pancreatic secretions. To decrease stomach upset (these patients with gastroperesis). Retrieval of appetite is a good sign of recovery. If the patient is kept NPO for more than 5 days, insertion of a naso-jejunal tube is indicated. The tube is introduced endoscopically to the jejunum or the 2^{nd} or 3^{rd} part of the duodenum. This mode of feeding is better than TPN as it prevents GI tract disuse atrophy. GI tract disuse atrophy increases the risk for bacterial translocation, which can cause a septic reaction.
    - Observe for complications and treat accordingly: ARDS, hypotension, renal failure, multi-organ failure, hypocalcemia, and sepsis.
    - Nutritional support
    - Pain control: use strong narcotics.
    - Antibiotics: only given when there is high suspicion of infection.
    - NG suction

- Glucophage
- Somatostatin

- Biliary pancreatitis:
  - If it is associated with cholangitis: immediate ERCP
  - If it is not associated with cholangitis: leave the patient for24-48 hours; if there is no improvement, proceed with ERCP.
- The difference between acute fluid sequestration (in acute pancreatitis) and chronic fluid sequestration (in ascites) is the degree of adaptation of the abdomen. In the chronic cases, the abdominal wall muscles are weakened, allowing for more fluid to accumulate without a change in the intra-abdominal pressure. However, in cases of acute sequestration, compartment syndrome might become a problematic consequence. Monitor for hypocalcemia…
- Local complications:
  - Abscess
  - Pseudocyst
  - Infected pseudocyst
- Pseudocyst:
  - In cases of continuing pain two weeks after treatment, suspect the formation of a pseudocyst
  - A pseudocyst is a cyst that lacks epithelial lining. Instead of the normal epithelial lining, its borders are made of the surrounding inflamed tissue. It is classically formed due to rupture of pancreatic ducts.
  - Surgical intervention is not indicated unless it becomes symptomatic.
  - If antibiotic are indicated, use antibiotics with high penetration to the pancreatic tissue like: fluoroquinolones. Aminoglycosides, third generation cephalosporines, and penicillins have low pancreatic penetration, so they are not used.
  - The most common organisms that affect the pancreas are gram negative bacteria.

  - Complications of a pseudocyst:
    - Dissection to the abdomen
    - Erosion of splenic artery leading to aneurysm
    - Infection and leakage to different organs

        - Rupture
    - Indications for treatment of a pseudocyst:
        - Size (obsolete criterion): more than 5 cm
        - Persistence for more than 4-6 weeks; any surgical intervention prior to this period can lead to rupture of the cyst (due to an immature wall)
        - Symptoms: regardless of size
        - Infection: regardless of size; infection is a fatal complication, if left untreated.
        - Rapid expansion
        - Acute worsening of the clinical condition
    - Pseudocysts can be treated surgically, endoscopically, or percutaneously.
    - Treatment is by drainage of the fluid into the jejunum. This will cause regression of the cyst.
- In many patients, non-ionized calcium is low; however, they are asymptomatic. Do not treat patients unless they become symptomatic.
- ARDS is a progressive respiratory failure with hypoxemia not responsive to oxygenation. It is one of the complications of acute pancreatitis; it carries a dismal prognosis.

- Other etiologies of acute pancreatitis:
    - Pancreatic divisum:
        - Congenital anomaly of the pancreas
        - Affects 5-10% of population.
        - During embryological development, the dorsum of the pancreas opens into a minor ampulla. The ventral part of the pancreas although smaller, opens into the major ampulla. During development, these two parts usually fuse. If this fusion fails, the increased flow from the dorsal part of the pancreas will cause recurrent pancreatitis (due to high resistance due to the smaller size of the ampulla)
    - Hereditary pancreatitis:
        - Uncommon etiology
        - Positive family history (autosomal dominant)
        - Childhood onset
        - High risk of carcinomas
    - Recurrent unexplained pancreatitis:
        - One of the common causes of acute pancreatitis
        - Idiopathic

- If you work-up the patient (with ERCP), and the results turn out to be normal, observe the patient.
- In the rare case of Sphincter of Oddi dysfunction, Sphincterotomy is performed.
- If the workup is abnormal, treat the patient accordingly.

Liver cirrhosis

- Liver cirrhosis is the end stage of liver disease, in which the cells become surrounded by fibrous tissue that pressures the hepatocytes preventing normal function and ability for regeneration.
- Liver has the ability to regenerate itself quickly. In fact, it is the fastest healing organ in the body.
- Fibrosis prevents liver cells from regenerating themselves. So, in theory, anti-fibrotic medication can solve the issue of liver cirrhosis. Remove the fibrous tissue around the cells; the liver can take care of the rest.
- Liver cirrhosis causes distortion of the hepatic architecture along with reduced regeneration of diseased liver tissue.
- The only way to treat liver cirrhosis is by liver transplants.
- Liver is divided into different lobes. The liver is an organ supplied by copious amounts of blood. All the intestinal circulation from the superior mesenteric, inferior mesenteric, and left gastric veins has to pass through the liver in what is called the portal circulation. These veins enter the liver and branch to form a mesh of vessels that act as a filter for the blood. Once this process is done, blood emerges from the other side of the liver. Any bypass to this circulation will cause encephalopathy. This happens because the toxic material will bypass the filtration process. Thus, toxins will accumulate in the blood which produces encephalopathy.
- Functions of the liver:
    - Detoxification (body's filter)
    - Protein synthesis
    - Hormone synthesis
    - Immunological function (synthesis of immunoglobulins)
    - Hormone synthesis.
- Liver cirrhosis is one of the most undiagnosed diseases in the world. Most people with liver cirrhosis die without knowing they have had this condition. Autopsies revealed that 30%of the population has cirrhosis. Symptoms of liver cirrhosis occur in the setting of co-morbid conditionions.
- Under normal conditions, any ingested toxins will induce and inflammatory reaction in the liver. This inflammation will be followed by fibrosis. However, if ingestion of the insulting agent continues, the process of inflammation and fibrosis will continue uncontrolled, which causes permanent dysfunction of the liver.
- Physical manifestations of liver disease:
    - Spider nevi
    - Palmar erythema
    - Clubbing
    - Gynecomastia and testicular atrophy
    - Hepatosplenomegaly: due to shunting of the blood towards the spleen.

    - Jaundice: Although jaundice is a common presentation of chronic liver disease, its absence does not rule this condition out. The presentation of jaundice depends on many factors including: bilirubin levels, skin color, and skin texture. Many people can have severe liver disease without having signs of jaundice. On the other hand, the opposite is true.
    - High portal pressure: In liver cirrhosis, portal circulation is increased. The blood tries to pass through the liver (a broken filter), but it can't. Increased portal flow will cause ascites. Vasoconstriction in the liver, and peripheral vasodilation. This is called a hyperdynamic circulation.
    - Caput medusa: distended periumbilical veins
- Patients with liver cirrhosis cannot develop hypotension. Hypertensive patients on their medications are compensated. If these patients stop needing their medications, this indicates decompensation.
- Lab investigations: people with liver cirrhosis can have normal liver function test (LFT) and normal liver enzymes. There is no definite laboratory finding in patients with liver cirrhosis; however, there are certain clues that this patient might have a liver disease:
    - Reversal of AST/ALT ratio: Normally, ALT is higher than AST. A reversal of this ratio, even in the presence of normal levels, indicates a liver disease.
    - Impaired LFT: PT, PTT, albumin, and bilirubin
    - Impairment in liver enzymes: ALT, AST, GGT, Alkaline phosphatase
    - Low platelets count: this happens due to portal hypertension. Blood cannot pass through the liver, so it is shunted to the spleen. The spleen enlarges to accommodate the size of the blood; however, it fails. Then, it starts sequestering the platelets.
- Impairment of LFT signifies a damaging process in the liver. However, impaired liver enzymes indicate a temporary impairment in the liver function: acute hepatitis, drug-induced, and alcohol.
- In advanced cases of liver cirrhosis anemia can happen
- Imaging studies:
    - CT, MRI, ultrasound: these modalities cannot give a definite diagnosis. However, they can reveal what is called a "coarse liver appearance". Under normal conditions, the liver has a smooth surface. A change in the smoothness of this surface, due to fibrosis, is reflected as a coarse appearance.
    - Fibro-scan: a new technique that employs ultrasound waves to detect liver fibrosis. It does not give a definite diagnosis; however, it can tell you that the liver is stiff. Liver stiffness is highly indicative of cirrhosis.
- The gold standard for diagnosing liver cirrhosis is a liver biopsy. However, it is rarely performed due to the high rate of complications (10%). Complications include: bleeding, pain, discomfort, and death.

- Staging of liver cirrhosis: The most commonly used classification is the Child classification. This depends on many factors including: LFT, encephalopathy, and ascites:
    - Stage A: Child score below 7; compensated disease
    - Stage B: Child score 7-10; intermediate stage
    - Stage C: Child score more than 10; liver transplant is the only option
- In liver cirrhosis, the liver is trying to work properly. However, the presence of fibrotic tissue prevents it from carrying out its function, which leads to decompensation. Complications of liver cirrhosis include:
    - Ascites: due to leakage of fluids which is caused by decreased amounts of proteins (albumin is low because the liver synthesizes albumin). Moreover, it happens due to the backflow of blood.
    - Esophageal varices: blood vessels are congested; to relieve the pressure, blood is shunted to the lower part of the esophagus creating a varix. In many patients, a bleeding esophageal varix is the first presentation of liver cirrhosis. A bleeding varix carries a mortality rate of 70%.
    - Hepato-renal syndrome
    - Hepatic encephalopathy: When the portal circulation is bypassed, toxins leak into the blood stream (mainly ammonia), which causes an alteration in the mental state.
- Measuring portal pressure is a challenging non-practical process. To measure it, a catheter must be introduced into the portal circulation. Since this is not practical, a clinical method has been devised to estimate portal pressure. Through endoscopy, a clinician can appreciate an increase in the portal blood pressure through the appearance of the esophageal veins.
- Types of portal HTN:
    - Pre-hepatic:
    - Post-hepatic
    - Intra-hepatic:
        - Pre-sinusoidal
        - Sinusoidal
        - Post-sinusoidal
- Pump failure in the case of heart failure causes backflow of the blood to the liver. This increases portal pressure leading to ascites. In this case, patients do not have cirrhosis, but have portal hypertension.
- 50% of cirrhotic patients become decompensated or develop varices. Out of these, 50% will develop a bleeding varix.
- Approach to a patient with ascites:

    - For any patient with ascites, the first step to do is to take a sample of the ascetic fluid. The sample is a 5cc tube of fluid taken by a simple needle puncture through the abdominal wall. This procedure has a very low rate of complications.
    - Analyze the fluid (SAAG): Serum Ascites Albumin Gradient is a simple calculation through which we can determine the cause of ascites.
    - A high SAAG value (more than 1.1) indicates high portal hypertension. If the fluid contains low amounts of protein, the problem is hepatic. If the fluid contains high amounts of protein, the problem is cardiac.
    - A low SAAG value (less than 1.1) indicates a problem other than portal hypertension. The causes include: TB, carcinoma, nephrotic syndrome, or any other abdominal cavity problem.
    - Treatment of ascites:
        - A combination of Potassium losing and Potassium sparing diuretics (furosamide, spironlactone).
        - If diuretics fail, an abdominal tap is indicated.
        - Peritoneal venous shunt: a rarely done procedure where a connection is established between the veins and peritoneum. Complications are due to the presence of high amounts of protein; mainly DIC.
        - TIPS (Trans-jugular Intra-hepatic, Porto-systemic Shunt): here, you open pores in the "diseased filter (liver)". Problems with this procedure are due to the leakage of toxic materials through the shunt. These patients will suffer from repeated episodes of hepatic encephalopathy.
        - Liver transplant
    - Liver transplant is a procedure with low mortality rate, 5-year survival over 85%, transplants are either cadaveric or from live donors. The liver can be taken out of the body and remain viable for up to 12 hours. The most important complication of this procedure is due to miscalculation of the transplanted liver volume; a low-volume transplant will progress to hepatic failure in the recipient
- Hepatic hydrothorax: it is complication of ascites. When ascites is under a high pressure in the abdomen, it can pass through a weak point in the diaphragm. This will lead to pleural effusion.
- Encephalopathy: encephalopathy is a common complication of liver cirrhosis. It happens due to increased amounts of toxins in the blood stream. The symptoms are mainly neurological and psychiatric. Patients might have an altered state of consciousness along with changes in their personality. In many cases, hepatic encephalopathy is subclinical. In these patients, EEG is normal, other functions are normal; however, through the use of special testing techniques, encephalopathy can be demonstrated. A sudden change in the handwriting of a chronic liver disease patient can be a sign of encephalopathy. The earliest sign of liver encephalopathy is reversal of sleep pattern (inability to sleep at night, and excessive daytime sleepiness). Laboratory testing for encephalopathy is of no

clinical value because ammonia values are not correlated with the degree of encephalopathy. However, if a patient presents with loss of consciousness for an unknown reason, and test results show an increase in ammonia levels, this indicates encephalopathy.

- Stages of encephalopathy:
    - Subclinical: Normal level of consciousness, cannot be detected easily
    - Stage 1: sleep reversal, restlessness
    - Stage 2: lethargy, slowed responses
    - Stage 3: somnolence, confusion
    - Stage 4: coma

- Predisposing factors:
    - Increased protein intake
    - TIPS
    - GI bleeding
    - Cancer
    - Drug toxicity: those patients, due to liver failure, cannot metabolize drugs properly. This leads to accumulation of drugs in their system, which leads to toxicity.