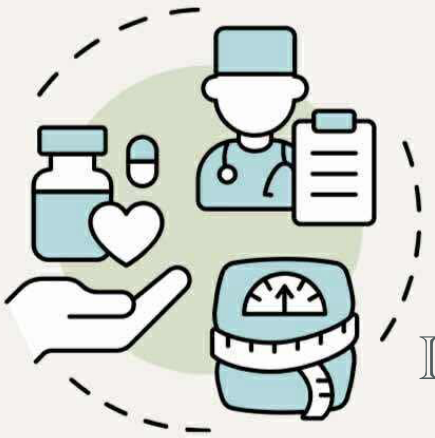
تفريغ كلينكال



المحاضرة: Liver diseases p2

الصيدلاني/ة: ياسمين خليل

Soul Academy

لجان الدُّفعات

Disorders of the liver

jaundice

- Jaundice, or icterus: is the yellowish discoloration of the skin and sclerae resulting from hyperbilirubinemia
- Although the upper limit of normal for total serum bilirubin is 1 mg/dL, jaundice is not clinically apparent until the bilirubin level exceeds 2-3 mg/dL
- In African American or Asian patients, yellowing of the sclerae may be the only clinical evidence of jaundice
- Except in infants, hyperbilirubinemia is generally well tolerated.
- In infants, hyperbilirubinemia (>15-20 mg/dL) may be associated with kernicterus (serious disorder of the CNS resulting from increased bilirubin levels) it only occurs in infants because the immature CNS does not have a well-developed blood-brain barrier

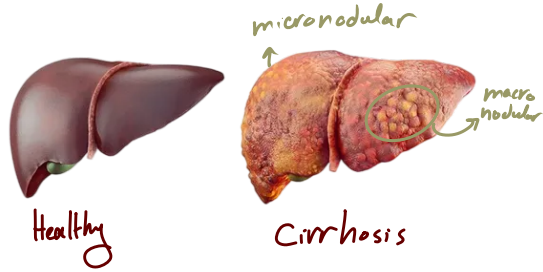
Jaundice

- Although all cases of jaundice result from hyperbilirubinemia, not all are caused by hepatic dysfunction.
- hyperbilirubinemia may also result from **erythrocyte destruction**, or hemolysis in patients with normal liver function
- Hypercarotenemia (excessive ingestion of vitamin A) may produce skin discoloration indistinguishable from that of hyperbilirubinemia. In hypercarotenemia, the sclerae are usually not discolored.

Cirrhosis

تليفق الكبد
ممكن أسبابه السرطان
عافانا الله تكوينه سببه منه

← هو موت خلايا الكبد وتبطل تشتغل بشكل طبيعي



- Cirrhosis refers to the irreversible scarring process by which normal liver architecture is transformed into abnormal nodular architecture

شكل الكبد من الخارج مش طبيعي زي الصورة عافانا الله

- One way to classify cirrhosis is by the appearance of the liver (by the size of the nodules). These conditions are referred to as **macronodular** and **micronodular** cirrhosis, although **mixed** forms occur

macro + micro

التقاعيد أو الملمس هيك
خشن ومش سطح أملس وناعم

- In the USA, Canada, and Western Europe, the leading cause of cirrhosis is alcohol abuse, which leads to a micronodular type of cirrhosis

① أول و أكبر سبب لهالمشكلة هو الكحول وبكونه micro nodule

- Other causes of cirrhosis include hemochromatosis, postnecrotic cirrhosis (occurs as a late consequence of hepatitis), and primary biliary cirrhosis (an autoimmune disorder).

وهو خلل بخلي الجسم يمتص حديد من الأكل بشكل كبير فبتجمع الحديد براحتو خلايا الكبد

② وثاني أكبر مسبب كمان

③ المقصود إنو بصير على الكبد بعد التهاب الكبد

④ (cirrhosis إلى (الخلايا الميتة ممكن تتبدل) necrosis من) hepatitis

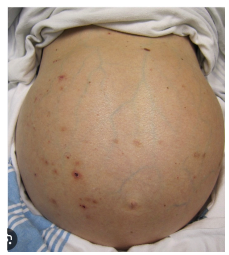
liver cells و bile duct جهاز الصفراء بيها جسم

cirrhosis وبيها جسم الجسم عالة وبصير

اللهم اغفر لي ولوالدي و للمسلمين والمسلمات الأحياء و الأموات

Cirrhosis

- Cirrhosis is a serious disorder and one of the ten leading causes of death in the United States. It causes many complications:
  - **Portal hypertension** results when blood flow through the portal vein is obstructed by the cirrhotic liver. This may result in splenomegaly and esophageal varices (may rupture and lead to fatal hemorrhage)
    - The synthetic ability of the liver is reduced, causing **hypoalbuminemia** and deficiency of the clotting factors, which may lead to hemorrhage
    - **Ascitic fluid** may accumulate in the abdomen due to hypoalbuminemia



    - Although some patients with cirrhosis are capable of prolonged survival, generally this diagnosis is an ominous one

Tumors

سرطانات الكبد
الحمد لله الذي عافانا

صار الورم في خلايا الكبد نفسها

- On a worldwide basis, primary malignant tumors of the liver, known as hepatocellular carcinoma are an important cause of cancer mortality

أشهر سبب هو فايروسات الكبد، ويمكننا منه بتقنيات الحماية

- In the United States, these tumors are relatively uncommon. Most cases of hepatocellular carcinoma can be related to previous infection with a hepatitis virus.

- Liver is frequently involved secondarily by tumors arising in other organs. Metastatic tumors to the liver from primary sites, such as the lung, pancreas, gastrointestinal tract, or ovary, are common. Benign tumors of the liver are relatively uncommon

الورم المنتقل من مكانه الأصلي

غالبًا أورام الكبد خبيثة ونادرًا ما تكون حميدة

ورم في خلايا الكبد
ورم خارج الكبد وانتقل للكبد (درجة ثانية)

- Whether primary or secondary any malignant tumor in the liver is a serious finding with a poor prognosis

في الوقت الحاضر يكفي المريض (سرطان) سيء (عافانا الله)

صعب عمل عملية استئصال للورم والخلايا

- The only hope For cure relies on surgical resection, which is usually impossible. Patients with malignancies of the liver usually have a survival measured in months

الشخص المصاب بسرطان كبد ما بكون معه كثير وقت يضل عايش والأعمار بيد الله

لما يأخذ الطفل اسبرين ممكن
يصير عنده Reye's syndrome
بالذات لما يكون عنده إلتهاب فايروسي

Reye's Syndrome

- Reye's syndrome is a disorder of unknown cause, involving the liver and arising primarily in children,
- It is a form of hepatic destruction that usually occurs following recovery from a viral infection, such as varicella (chickenpox) or influenza.

جدري — انفلونزا

- It has been related to aspirin therapy. Shortly after the infection, the patient develops neurologic abnormalities, which may include seizures or coma

مع يصير ارتفاع في انزيمات الكبدي الدم كاينها متضررة

- Liver functions are always abnormal, but the bilirubin level is not usually elevated
- Without treatment, rapid clinical deterioration, leading to death, may occur

تتراجع الحالة للاسوء ثم الموت
لو ما لحقنا المريض

كابه ربي أنت سبحانك إني كنت من الظالمين

Drug- and Alcohol-Related Disorders

ethanol → acetaldehyde → acetate

- Many drugs and chemicals are toxic to the liver. This toxicity may take the form of overwhelming hepatic necrosis, leading to coma and death, or it may be subclinical and pass entirely unnoticed

ممكن يكون التأثير حاد ويؤدي إلى ... أو خفيف وما بيوصل لمرحلة الغيبوبة

تؤثر بشكل حاد لو الكمية كبيرة أما لو الكمية صغيرة فتسبب damage أو injury

- In small amounts, **alcohol** may cause mild, inapparent injury. Heavier consumption leads to more serious damage, and prolonged, heavy use may lead to cirrhosis (exact amount is unknown)

مهدئات

- Certain **drugs**, including tranquilizers (phenothiazines), certain antibiotics, antineoplastic agents, and anti-inflammatory drugs, may cause liver injury

هاي الأدوية ترفع من إنزيمات الكبد في الدم، وظائف الكبد في الدم، مؤثر على الكبد

- Usually this is mild and manifested only by elevation of liver function tests, which return to normal when the drug is discontinued. This may lead to massive hepatic failure or cirrhosis

راح يرجع الوضع طبيعي لما يوقفهم

+ Retinol

بتسبب

حسب قديش تناول المريض الأدوية المذكورة أو كحول وكم المدة راح يكون حجم الضرر

- The most common drug associated with serious hepatic injury is **acetaminophen**. When taken in massive overdose, it produces fatal hepatic necrosis unless rapid treatment is initiated

Paracetamol

الشكل الناتج من السيتامول جواتي بعمل ضرر لبتجمع بشكل من radicles وبتهاجم خلايا الكبد) لو أخذ شخص 25 ترا حاد بيوت، بس راح يعوش بلا كبده

Assessment Of Liver Function
Analysis of Bilirubin (Method Selection)

تقييم وظائف الكبد

- Unfortunately, no single method for the determination of bilirubin will meet all the requirements of the clinical laboratory

صعب على حالة في إنها طريقة تخصص
ما في طريقة واحدة معقدة لكل الطرق

  - For the evaluation of jaundice in newborns (no lipochromes), the direct spectrophotometric method is satisfactory

الموجود إلي لونها مائل للأحمر مثل carotene
إلي غير الجزيرة في الطفل إلي لسا بادوب مولود الكبد
مساعده طريقة المادة في طريقة مناسبة إنهم أما الأكبرين ما يتميز بط إنهم (إلي أكبرين شهر)

  - The sources of error in this technique are turbidity, hemolysis, and yellow lipochrome pigments

الأخطاء في هاي العينة تكون ب

  - Hemolysis and turbidity can be blanked out by measuring a second wavelength, but the yellow lipochromes cannot be blanked out.

2nd wavelength بستخدم
طول مركزي
بنقدر نتخلص منهم وفحصنا يكون صحيح
هدول ما في إنهم حل وإنما يعملوا errors

  - In patients older than 1 month, a diazo-colorimetric procedure is necessary

مكنا الأكبرين شهر ما بنستخدم هاي التكنيك لأنه
عنهم بل بستخدم التقنية في السلايد الجاية hipochromes

هاي الطريقة فيها توجيه λ_{max} على العينة مباشرة

jendrassik-Grof Method for Total and Conjugated Billirubin Determination

- Serum or plasma is added to a solution of sodium acetate and caffeine-sodium benzoate, which is then added to diazotized sulfanilic acid to form **purple azobilirubin**
- The **sodium acetate** buffers the pH of the diazotization reaction, whereas the **caffeine-sodium benzoate** accelerates the coupling of bilirubin with diazotized sulfanilic acid
- This reaction is terminated by the addition of **ascorbic acid**, which destroys the excess diazo reagent
- A **strongly alkaline tartrate** solution is then added to convert the purple azobilirubin to blue azo-bilirubin, and the intensity of the color is read at 600 nm
- A **fasting** serum specimen, which is **neither hemolyzed** nor **lipemic**, is preferred.
- The specimen should be **kept in dark** after collection, analyzed within 3hrs, kept for 1 week in the refrigarator or 3 months in -20

Reference range

- Normal blood contains no conjugated bilirubin.
- Some conjugated bilirubin is reported as normal because current available methodology picks up some of the total bilirubin as a false positive
- For **adults**
  - Conjugated: 0-0.2 mg/dL (0-3 µmol/L)
  - Unconjugated: 0.2-0.8 mg/dL (3-14 µmol/L)
  - Total: 0.2-1.0 mg/dL (3-17 µmol/L)
- For **infants**

INFANTS	PREMATURE, TOTAL	FULL TERM, TOTAL
24 hours	1–6 mg/dL	2–6 mg/dL
48 hours	6–8 mg/dL	6–7 mg/dL
3–5 days	10–12 mg/dL	4–6 mg/dL

Direct Spectrophotometric Method for Determination of Total Bilirubin in Serum

- The absorbance of bilirubin in serum at 455 nm is proportional to its concentration

- The serum of newborns does not contain lipochromes, such as carotene, that would increase the absorbance at **455 nm**. The absorbance of hemoglobin at 455 nm is corrected by subtracting the absorbance at **575 nm**.

- Error will be introduced if the buffer is turbid. Because the method depends on the extinction coefficient of bilirubin, **all volumes must be accurate** and **cuvettes must be flat-surfaced**, with a path length of exactly 1 cm

- This method is relatively insensitive to hemolysis, which is often present in specimens obtained from infants, due to difficulty in skin puncture technique

- it is significantly affected by the presence of lipochromes and so cannot be used in infants older than a few months of age

Urobilinogen in Urine and Feces

bilirubin —oxidation→ urobilinogen (urine, colorless) —oxidation→ urobilin (feces, brown)

- Urobilinogin is a colorless end product of bilirubin metabolism that is oxidized by intestinal bacteria to the brown pigment urobilin

- In the normal individual, part of the urobilinogen is excreted in the **feces**, and the remainder is reabsorbed into the portal blood and returned to the **liver.** A small portion that is not taken up by the hepatocytes is excreted by the **kidney** as urobilinogen

- Increased levels of urinary urobilinogen are found in hemolytic disease and in defective liver-cell function, such as hepatitis

- **Absence of urobilinogen** from the urine and stool is most often seen with complete **biliary obstruction.** Fecal urobilinogen is also decreased in biliary obstruction and in hepatocellular disease

Urobilinogen in Urine and Feces

- Most quantitative methods for urobilinogen are based on the reaction of this substance with **p-dimethylaminobenzaldehyde** to form a red color.
- Major improvements were made by using **alkaline ferrous hydroxide** to reduce urobilin to urobilinogen and added **sodium acetate** to eliminate interference from such compounds as indole
- The use of **petroleum ether** rather than diethyl ether for the extraction of urobilinogen was introduced to help in the removal of other interfering substances

Determination of Urine Urobilinogen (Semiquantitative)

- Principle.
  - Urobilinogen reacts with p-dimethyl aminobenzaldehyde (Ehrlich's reagent) to form a red color, which is then measured spectrophotometrically.
  - Ascorbic acid is added as a reducing agent to maintain urobilinogen in the reduced state.
  - The use of saturated sodium acetate stops the reaction and minimizes the combination of other chromogens with the Ehrlich's reagent.
- Specimen
  - A fresh 2-hour urine is collected which should be kept cool and protected from light.

Sources of Error

- The results of this test are reported in **Ehrlich units** rather than in milligrams of urobilinogen because of interfering substances
- Compounds, other than urobilinogen, that may be present in the urine and react with Ehrlich's reagent include porphobilinogen, sulfonamides, procaine, and 5-hydroxyindoleacetic acid. Bilirubin will form a green color and, therefore, must be removed, as previously described
- Fresh urine is necessary and the test must be performed without delay to prevent oxidation of urobilinogen to urobilin. Similarly the spectrophotometric readings should be made within 5 minutes after color production because the urobilinogen-aldehyde color slowly decreases in intensity.

Reference Range: Urine urobilinogen, 0.1-1.0 Ehrlich units/2 hr or 0.5-4.0 Ehrlich units/day (0.8 - 6.8 mmol/day); 1 Ehrlich unit is equivalent to approximately 1 mg of urobilinogen

Fecal Urobilinogen

- Visual inspection of the feces usually suffices to detect decreased urobilinogen.
- The semiquantitative determination of fecal urobilinogen is available It is carried out in an aqueous extract of fresh feces, and any urobilin present is reduced to urobilinogen by treatment with alkaline ferrous hydroxide before Ehrlich's reagent is added
- A range of 75-275 Ehrlich units/100 g of fresh feces or 75-400 Ehrlich units per 24-hour specimen is considered a normal reference range.

Measurement of Serum Bile Acids

ماني فايدة من قياسه

- Unfortunately; complex methods are required for the analysis of bile acids in serum

نستخدم عينة serum

- they involve extraction with organic solvents, partition chromatography; gas chromatography-mass spectroscopy spectrophotometry ultraviolet light absorption, fluorescence, radioimmunoassay and enzyme immunoassay methods

- Although serum bile acid levels are elevated in liver disease, the total concentration is extremely variable and adds no diagnostic value to other tests of liver function.

في نستخدم liver enzymes

كاين ارتفاعهم في مكان معين فيها يكون عارفة في مشكلة

أما bile يكون مختلف في اليوم الواحد حتى ، فما بقدر أميز إذا في مشكلة عندي ولا