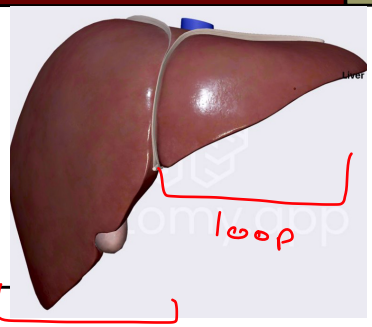
تفريغ كلينكال

المحاضرة: Liver diseas

الصيدلاني/ة: Rahaf Ziyad

Liver disease

Liver



- The liver is the largest, most versatile organ in the body

- It consists of two main lobes that, together, weigh from 1400-1600 g in the normal adult

- It has an abundant blood supply receiving about 15 ml/minute from two major vessels: the hepatic artery and the portal vein

- The hepatic artery a branch of the aorta, contributes 20% of the blood supply and provides most of the oxygen requirement

- The portal vein, which drains the gastrointestinal tract, transports the most recently absorbed material from the intestine to the liver

20% ⟶ hepatic artery

80% ⟶ Portal Vein

شو وظائف ال Liver ؟؟

1- excretion of bile

اول اشي الجسم مشو بحتاج ال bile ؟؟ ال bile مسؤول عن امتصاص ال fat [وجبه دسمة]

excretion in intestin ↑

T كلت T كلا دسم ← ال bile المخزن بال gallbladder بروح للـ intestin (مصنعه ال Liver)

→ absorption for fat

ال Liver بنتج 3L من ال bile باليوم بس الجسم ما بستهلك كتير

1L اي رح يصير اله excretion بال intestine

> ال Conjugated يعني امسك مادة واربطها على مادة ثانيه لاخليها More Water soluble

bile acid:

- Primary bile acid ← ① Cholic acid ② chenodeoxy cholic acid ← رح يصنعه ال Cholesterol
  - رح تتكون ال bile salt ← رح يصير عليهم Conjugated بـ glycin / turin
- لما يكون الواحد صايم ال bile acid رح يصير concentrated للـ 10 اضعاف

> خيب ليش ال Conjugation ؟؟
> لانه ال Primary bile رح تروح للـ gall bladder وتتخزن فيها بس ال gall bladder حواليها membran وهاي ال membran تكون hydrophobic اذا ال Primary bile كانت hydrophobic رح تتسرب من ال gall bladder فلما اعمل الها Conjugation رح تصير water soluble وما رح تتسرب منه ، وبس ناكل fat رح يروحوا ال bile salt للـ intestin ورح يفكوا ال Conjug- وبعدها برجعوا Lipid-soluble و بعملوا ال absorption

- ال bacteria اللي بال Colon وال terminal ileum رح يفكو ال Conjugation [taurin , glycin] ويعملو ..... ← Secondary bile acid

> وهاي هي ال enterohepatic circulation

2- ال bilirubin

ال bilirubin مادة بنتجها ال Liver (unconjugated for) ويخلطها مع ال bile acid وبخزنها بال gallbladder مع ال bile وبصير اله excretion مع ال bile بال intestin

وهو المسؤول عن اللون الاصفر للـ bile ، طيب من وين رح تكون ؟؟ بس تموت ال RBC وتتحلل رح تروح للـ liver وهناك رح تتكون ال bilirubin ، وال Liver مسؤول كمان عن التخلص منه ، بعض الاطفال اول ما ينولدوا بكون عندهم Jaundice [صفار] ليش ؟ لانه ال Liver عندهم غير مكتمل عشان هيك ما تقدر تتخلص من ال bilirubin وعشان هيك رح يتراكم بالجلد والعيون ويخلي لونهم اصفر ، حتى لو واحد كبير بالعمر وصار عنده مشكل بال excretion للـ bilirubin من الجسم رح يصير عنده Jaundice

خلينا نحكي بشكل اكثر عن تكون ال bilirubin

RBC
↓ تتكسر
hemoglobi
- globin [بروتين ، الجسم بقدر يكسره لـ a.a ويستفيد منه] → a.a → a.a Pool
- heme
  - Fe^{+}
  - Porphyrin → bilirubin

ال heme بدون ال Fe^{+2} عبارة عن Porphyrin ← excreted من الـ (spleen, Liver, bone marrow) وبيروح للدم ورح ينتج منه bilirubin

* بما انه الـ bilirubin ← Lipid soluble رح يحتاج للـ albumin عشان ينتقل بالدم ويروح للـ Liver ويتعامل معه وهناك بصير اله Conjugation مع ال diclucuronid وبعدها رح يصير اله excretion بال feces وهو المسؤول عن اللون البني للـ feces

Liver function

- **The excretion of bile**: Total bile production averages about 3 L per day, although only 1 L is excreted.

1 L [excreted to intestin] 2 L [Faecal output]

- The primary bile acids, cholic acid and chenodeoxycholic acid, are formed in the liver from cholesterol. The bile acids are conjugated with the amino acids glycine or taurine, forming bile salts.

- During fasting and between meals, bile acid pool is concentrated up to 10-fold in the gallbladder

- When the conjugated bile acids (salts) come into contact with bacteria in the terminal ileum and colon, dehydration to secondary bile acids occurs, and these secondary bile acids are subsequently absorbed

- The absorbed bile acids enter the portal circulation and return to the liver, where they are reconjugated and reexcreted. The enterohepatic circulation of bile occurs 2-5 times daily

Bilirubin

- The principal pigment in bile is derived from the breakdown of hemoglobin when aged red blood cells are phagocytized by the reticuloendothelial system, primarily in the spleen, liver, and bone marrow

- When hemoglobin is destroyed, the protein portion- globin-is reused by the body, The iron enters the body's iron stores and is also reused. The **porphyrin** is broken down as a waste product and excreted

- Bilirubin is transported to the liver in the bloodstream bound to albumin where it is conjugated with diglucuronide on it two carboxylic acids and excreted to the intestine

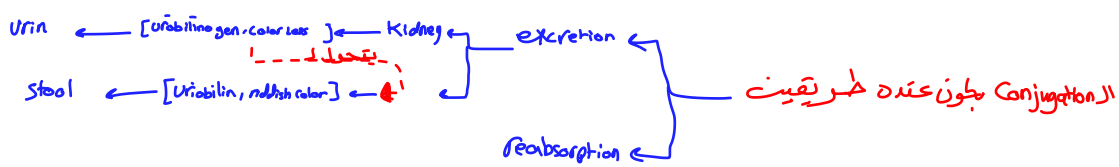
2 Carboxylic acid على ال

bilirubin diglucuronid اسمه يصير Conjugation بعد ال

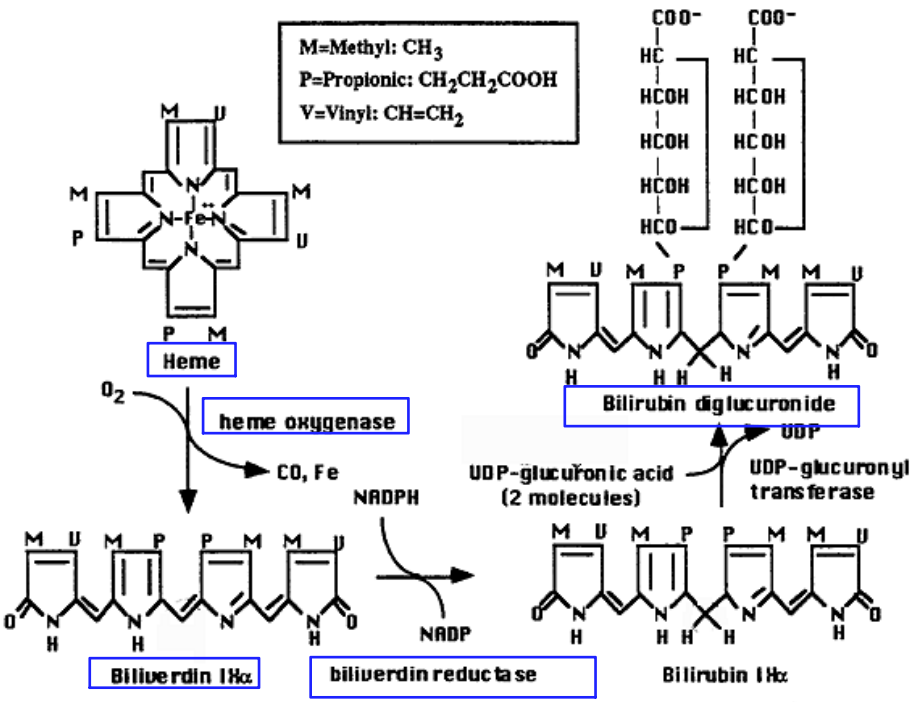
- The normal flora in the colon oxidize it further where it is reabsorbed, excreted to the stool (urobilin, reddish brown) or excreted in kidney (urobilinogen, colourless)

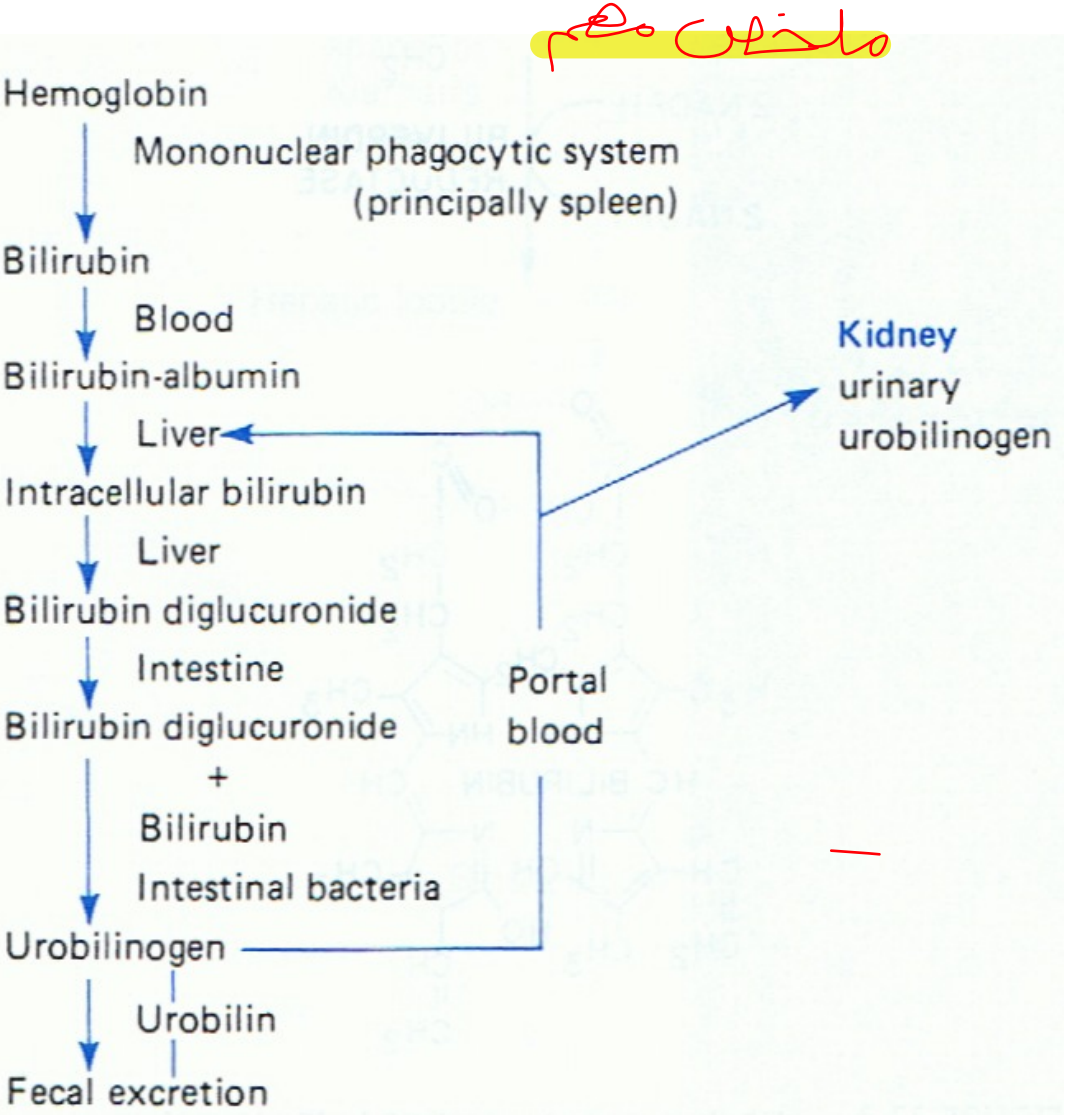
بين يطلع الـ bilirubin مع الـ bile لـ intestin و يفلح

Urobilinogen ممكن تتحول لـ Urobilin و بعدها يصير إله excretion بالـ stool



Bilirubin


M=Methyl: CH_3
P=Propionic: CH_2CH_2COOH
V=Vinyl: $CH=CH_2$
Heme
O_2
heme oxygenase
CO, Fe
Biliverdin IXα
NADPH
NADP
biliverdin reductase
Bilirubin IXα
Bilirubin diglucuronide
UDP-glucuronic acid
(2 molecules)
UDP
UDP-glucuronyl
transferase


Hemoglobin
Mononuclear phagocytic system
(principally spleen)
Bilirubin
Blood
Bilirubin-albumin
Liver
Intracellular bilirubin
Liver
Bilirubin diglucuronide
Intestine
Bilirubin diglucuronide
+
Bilirubin
Intestinal bacteria
Urobilinogen
Urobilin
Fecal excretion
Kidney
urinary
urobilinogen
Portal
blood

Bilirubin

- When the bilirubin concentration in the blood rises, the pigment begins to be deposited in the sclera of the eyes and in the skin. This yellowish pigmentation in the skin or sclera is known as jaundice, or icterus
- The cause can be:

  - **Prehepatic**: results when an excessive amount of bilirubin is presented to the liver for metabolism, such as in hemolytic anemia. This type of jaundice is characterized by unconjugated hyperbilirubinemia

  - The serum bilirubin levels rarely exceed 5 mg/dL because the normal liver is capable of handling most of the overload. bilirubin will not appear in the urine in this type of jaundice.

هي حسب شكل الـ bilirubin المتراكم رح نعرف المشكلة

وفي unconjugated ← → conjugated

نبلش بأول سبب :-

الـ Prehepatic : بيكون الـ Liver شغال تمام بس في كميات كبيرة من الـ bilirubin وهو مش ملحق يعمل الها كلها Conjugation [بسبب اي مرض يؤدي لتكسر الـ RBC زي الـ Anemia/الانيميا]

طيب شو شكل الـ bilirubin الناتج؟ UnCojugation ، بس مع هيك ارتفاع الـ serum bilirubin

ما رح يتعدى الـ 5mg/dl لأنه الـ Liver شغال فبعد كم يوم الـ Liver رح يتخلص منه

وكمان الـ hyberbilirubinemia [ارتفاع الـ bilirubin] رح يبين بالـ serum وما رح يبين بالـ Urin

لأنه مرتبط مع الـ albumin والـ albumin ما رح يطلع بالـ Urin Unconjugated + albumin

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السبب الثاني

الـ hepatic ← بيكون عنده مشاكل بتخص الـ Liver

(a) Impaired cellular uptake

(b) defective conjugation

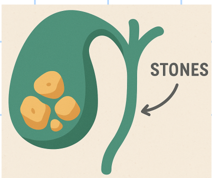
(c) abnormal secretion of bilirubin by Liver

ثالث سبب

الـ Post hepatic : بيكون الـ bilirubin وصل الـ Liver وصار الـ Conjugation بس لما طلع منه واجه مشكلة خلته يتراكم

طيب شو شكل الـ bilirubin المتراكم؟ Conjugated [مش مرتبط بالـ albumin]

شو ممكن تكون الأسباب



(1) obstruction of flow of bile into intestin. بسبب
→ gallston [حصوة]
→ tumor

لما الـ bilirubin يبطل يطلع للـ intestin ← رح يلاحظوا انه الـ stool فقد لونه الطبيعي وصار Clay-colored ← لون فاتح

والـ Conjugation رح يتراكم بالدم و يصير يروح للـ Kidney فقط [مش قادر يروح للـ intestin] و يطلع بالـ Urin عشان هيك رح نلاقي الـ Conjugation في الـ Urin .

• الـ Urobilinogen رح يقل مستواه

Bilirubin

- **Hepatic**: Impaired cellular uptake, defective conjugation, or abnormal secretion of bilirubin by the liver cell are the main causes of this kind of jaundice

- **Posthepatic**: results from the impaired excretion of bilirubin caused by mechanical obstruction of the flow of bile into the intestine. This may be due to gallstones or a tumor

- When bile ceases to flow into the intestine, there is a rise in the serum level of conjugated bilirubin and the stool loses its source of normal pigmentation and becomes clay-colored

- Conjugated bilirubin appears in the urine, and urine urobilinogen levels decrease

Major Synthetic Activity

albumin
α,β-globulin
بصنع بروتينات تشتغل بالدم

- The liver plays an important role in **plasma protein production**, synthesizing albumin and the majority of the α and β-globulins. All the blood-clotting factors (except VIII) are synthesized in the liver

ما عدا الثامن دا

- المصدر الأساسي للأمونيا في الجسم هو عملية نزع مجموعة الأمين (Deamination) من الحمض الأميني جلوتامات، والتي تحدث في الكبد.
- يتم بعد ذلك تحويل الأمونيا إلى يوريا (Urea) في الكبد للتخلص منها بأمان عبر الكلى.

- The deamination of glutamate in the liver is the primary source of ammonia, which is then converted to **urea**

glycogen انتاج الـ
انتاج الـ glucose من
انتاج الـ lipid

- Glycogenesis and gluconeogenesis, lipogenesis, metabolism of cholesterol into bile acids, Very-low-density lipoproteins (transport TG into the tissues), High-density lipoproteins, phospholipids are all made in the liver

- The formation of **ketone bodies** → keto diet او في حاله الصيام / نقص الـ

- The liver is the storage site for all fat-soluble vitamins **(A, D, E, and K)** and several water-soluble vitamins, such as **B12** and is responsible for the conversion of carotene into **vitamin A**

صارة موجودة بالجزر
بتعطي اللون البرتقالي

3. Synthesis of liver enzymes

Many enzymes are synthesized by liver cells, but not all of them have been found useful in the diagnosis of hepatobiliary disorders, this includes:

Aspartate aminotransferase (AST) and **alanine aminotransferase (ALT)** which escape into the plasma from **damaged liver** cells

Alkaline phosphatase (ALP) and **5'-nucleotidase (5NT):** induced or released when the canalicular membrane is damaged and **biliary obstruction** occurs

γ-glutamyltransferase (GGT): increased in both **hepatocellular** and **obstructive disorders**

4- Detoxification and Drug Metabolism

الـ liver هو المسؤول عن تخليص الجسم من الـ toxic compound

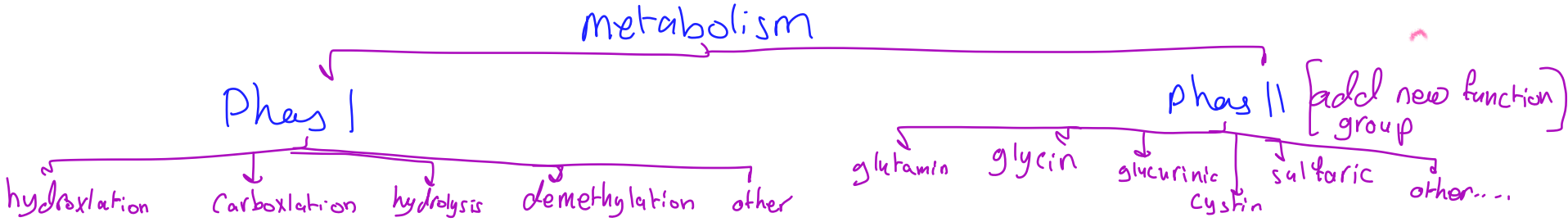
- The liver protects the body from **potentially injurious substances** (ضار) absorbed from the intestinal tract and toxic by-products of metabolism.

- The most important mechanism in this detoxification activity is the **microsomal drug-metabolizing system** of the liver. It is responsible for many detoxification mechanisms, including oxidation, reduction, hydrolysis, hydroxylation, carboxylation, and demethylation that convert many insoluble compounds into other forms that are less toxic or more water-soluble and, so excretable by the kidney.

مجموعة الـ enzyme المسؤولة عن الـ metabolism

- Conjugation with moieties, such as glycine, glucuronic acid, sulfuric acid, glutamine, acetate, cysteine, and glutathione, occurs mainly in the cytosol or smooth ER. This mechanism is the mode of bilirubin and bile acid excretion.

هدف الـ metabolism الأساسي هو تحويل الـ drugs لـ more water soluble



Disorders of the liver
jaundice

- Jaundice, or icterus: is the yellowish discoloration of the skin and sclerae resulting from hyperbilirubinemia

1 mg/dl ← bilirubin الـ upper limit الـ
(2-3)mg/dl ← بين الـ Jaundic ح يظهر لما يتعدى

- 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

الـ black people ← ح يبين اللون على الجلد
أحدّ بشرتهم لونها مائل للاصفر
عشان المميز بالـ Jaundic هو : اصفر ابياض العين

- 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.

الـ Jaundic عند الكبار عادي مش مشكلة
كبيرة ، بس بالـ Infant تعتبر مشكلة كبيرة كانه

- 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

ارتفاع الـ bilirubin ح يخليه يروح الـ brain و يتجاوز الـ BBB
كانه مش مكتمل ح يعمل مشاكل بالـ CNS و يحمل مرض
Kernicterus ← اسمه

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

تليف الكبد

شكل الـ liver

لما الشخص الـ cirrhosis بالغي الـ architecture ← module [حبيبات]

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

- 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

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

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

رح نصنف الـ Liver cirrhosis حسب حجم الـ nodule بكون في:
- macronodular ← كبيرة
- micronodular ← صغيرة
- Mixed ← كبير + صغير

① الـ micronodular ← inc alchole abus [بشرب alchole كثير ولفترات طويلة]

② سبب ثاني للـ Cirrhosis هو الـ hemochromatosis [خلل بالجسم بخلي الـ Liver يمتص الحديد بزيادة وهو يعمل تأثير ضار]

③ Postnecrotic cirrhosis ← ضرر بصير بالـ Liver بعد الـ hepatitis

④ Primary biliary cirrhosis ← مرض مناعي جهاز المناعة بهاجم خلايا الـ liver bile duct

الـ Complication للـ Liver chirrhosis

① Portal-hypertension ← الـ Chirrosis يعني انه الخلايا رح تموت ، والخلايا الي رح تموت رح تتجمع بالـ Portal vein ورح تعمله obstruction فالدم الي المفروض يدخل للـ Liver رح يصير يروح للـ spleen ويصير في speelenomegaly [تضخم بالـ spleen] ويرفضه يرجع للـ esophagus ويعمل esophagel varices [دوالي بالمريء] بكون في شعيرات دموية ضعيفة قريبة لسطح المريء وممكن بأي وقت تنفجر وتعمل نزيف فالواحد ممكن ينخنق ويموت Fetal hemorrha

② Synthtic ability of Liver is reduced ← لأنه الخلايا رح تموت ، عشان هيك بيبطل يعمل albumin كفاية ويعمل hypoalbumin وبرجع بعمل deficiency of clotting factor ← حيث انه اذا انجرح رح يصير عنده نزيف ← hemorrhage

③ accumulation of Ascitic fluid in abdomin (بسبب hypoalbumin)

الـ albumin مسؤول عن الـ osmotic pressur بالبطن

الـ Liver tumor

بنصنف لقسمين:
- Primary tumor ← بكون الـ Cancer بخلايا الـ Liver نفسها
- الـ secondary tumor ← بكون الـ Cancer منتقل من اعضاء اخرى للـ Liver زي الـ kidney, Lung

الـ hepatocellular Carcinoma ← Primary tumor [اختصارها PT]

أكثر سبب شائع للـ PT هو الـ hepatitis virus ← أي نوع ؟ ① hepatitis B ② hepatitis C

الـ Metastatic tumor ← Secondary tumor (الـ Cancer الي رح يتحرك)

نادراً ما الاقي bergin tumor [ورم حميد] بالـ Liver ، بالغالب بكون خبيث

حاولوا يشيلو الجزء المصاب بالـ Cancer بشكل جراحي بس Surgical resection هاد اشي مستحيل لانه لسه بحرفني انه هذا الجزء مصاب وهنا لأ للاسف الي بصير معه tumor بالـ Liver بكون قدامه 6 أشهر عشان يعيش فقط

لا تنسوا زميلنا ابرهيم الله
يرحمه من دعائكم

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

كل الواحد ممكن يعيش وهو معه Liver Cirrhosis بس هو تشخيص مشؤوم

Tumors

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

- 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

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

- 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

Reye's Syndrome

يتصير لما الطفل يكون عنده viral infection والطبيب يعطيه Aspirin والـ Reye's syndrom
تصير مشاكل بالـ liver لأسباب غير معروفه

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

برضه الـ Syndrom رح تعمل هاي المشاكل غير مشاكل الـ liver

- Liver functions are always abnormal, but the bilirubin level is not usually elevated

رح يصير مشاكل بالـ liver function بس الـ bilirubin مارح يرتفع فالمريض مارح يكون عنده Jaundic

- Without treatment, rapid clinical deterioration, leading to death, may occur

Drug- and Alcohol-Related Disorders

- 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

- 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)

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

- 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

Necrosis من اشهر الأدوية اي رح تسبب injury بحال اخذ overdose ← اذا كانت عالية كتير ب تعمل

- 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

Assessment of Liver function فحوصات لتقييم وظائف الـ Liver

شرح السلايد الحالي

1) Analysis of Billirubin

بدي احرف شو سبب الـ Jaundic عند الـ newborn، بما انهم مواليد جداد فصعب يعرف انه ما عندهم Lipochromes وهي مادة لونها شبه الـ billirubin وممكن تعمل error (زي الـ Carotin اي بالجزر) كيف بدهم ياكلوها اصلاً عشان هيك نقدر استخدم Direct-spectrophoton method بس لو صار عمره شهر ما رح اقدر استخدمها

طيب بالطريقة الـ direct هاي ممكن يطلع error طيب شو الاسباب

1. turbidity
2. hemolysis
3. yellow lipochrom pigment

بس الـ hemolysis والـ turbidity ممكن Can blancked out يعني نقدر احل مشكلة هذا الـ error عن طريق اني استخدم wavelength ثاني

بس الـ yellow lipochrom pigment مالها حل ← not blanked out

عشان هيك ما نقدر استعمل الـ direct للي عمرهم اكبر من شهر

* اي اكبر من شهر بستخدم diazo-colormetric Procedure.

في مواد كيميائيه وادويه رح تسبب ضرر لخلايا الـ Liver و التأثيرات مختلفه

بدرجة حدتها فممكن تعمل hepatic nacrosis
- شديد يموت وممكن يأدي لـ coma و الواحد ممكن
- خفيف والحريف يمكن ما يحس باشي

مثلاً الـ alchol
- small amount → mild and inapparent Injury {خفيفه وغير ملحوظة}
- prolong, heavy amount → chirrhosis
  - هو حكينا انه موت الخلايا، و المشكلة انه الكميه اي رح تعمل cirrhosis غير معروفة

ادويه بيعمل hepatic injury
- antiinflammatory
- antieoplasti agent
- antibioti
- tranquilizers (مهدئات) [phenothiazin]

هاي الادويه قادرة على رفع انزيمات الكبد ← ارتفاع وظائف الكبد ← اذا وقفت الدوا بعد فترة قصيرة → وظائف الكبد رح ترجع طبيعية

طيب لو ما وقفها [chronic] ← ممكن تعمل
- Chirrhosis
- hepatic failure

{يعني استخدام مش Chronic}

Assessment Of Liver Function
Analysis of Bilirubin (Method Selection)

- Unfortunately, no single method for the determination of bilirubin will meet all the requirements of the clinical laboratory صاني فحص محدد اقدر استخدمه لقياس ال bilirubin عند كل الاشخاص
- For the evaluation of jaundice in newborns (no lipochromes), the direct spectrophotometric method is satisfactory
- The sources of error in this technique are turbidity, hemolysis, and yellow lipochrome pigments
- Hemolysis and turbidity can be blanked out by measuring a second wavelength, but the yellow lipochromes cannot be blanked out.
- In patients older than 1 month, a diazo-colorimetric procedure is necessary

Conjugated billirubin بالوضع الطبيعي ما في

و بالوضع الطبيعي تكون في unconjugation billirubin مرتبط مع الAlbumin

وهيك احنا اصلاً بنميز بين الـ Conjugated والـ Unconjugated بس مرات لما اخذ العينة

الـ albumin بيحل مرتبط بالـ albumin فلما اشوفه free بالعينة بعتقد انه Conjugated بينما

هو unconjugated ، فبيبين عندي انه False-Positive ، عشان هيك مسموح يبين شوي Conjugated

كاني حسبت حساب هذا الـ error ، عشان هيك بالـ Refrenc Rang بلاقي انه في Conjugated [0-0.2]

وطبيعي الاقي الـ unconjugation بالدم لانه لا يتصنع بالـ spleen

او الـ bone marrow ومنه ينتقل بواسطة الـ albumin بالدم للـ Liver

عشان هيك بلاقيه

> لما تسميه بسيطة لأنه حسبت حساب القمة الي حكيت عنها فوق بس اكثر من هيك بكون الوضع مش normal

الـ diazo-Colormetric Procedure ← Jendrassik-Grof Method

بجيب العينة (plasm / serum) الي فيها billirubin وبضيف عليها ① Sodium acetate

و بجيب هاي الخلطة بجيبها وبحط عليها ② Caffeien-Sodium benzoate

الـ sulfanilic acid diazotid ③ ورح نيفاعل العينة ويعطي

azobillirubin [purple لونه] طيب ليش ضفت ① و ② اذا كان ③

هو اللي رح يتفاعل مع العينة؟؟ لانه الهم وظائف ثانية زي الـ Sodium acetate اي رح يشتغل

buffer حيث يخلي التفاعل يصير بالـ PH الي بدك اياها ، طيب الـ Caffeien-Sodium benzoate

رح يعمل Accelerate (تسريع التفاعل) لإرتباط الـ billirubin مع الـ diazotized sulfanilic acid .

طيب كيف انهي التفاعل بحيث اتخلص من excess diazo reagent عن طريق

إضافة الـ Ascorbic acid ، طيب هيك العينة جاهزة عشان اشوفها بالـ UV ؟؟

لا ، لسا لازم اضيف strongly alkalin tartrate عشان تحول الـ

purple-azobillirubin لـ blue azobillirubin عشان اقدر اقرأه

at [600nm] wavelenght واقدر اعرف الـ abrorbance ومنها اعرف الـ conc

الـ conc ↑ يعني الـ billirubin ↑

* العينة لما اخذها تكون صائم (fasting) وخلايا الدم الحمراء ما بتتكسر (no hemolysis [بسبب الانيميا او جرح او نزيف]) و ما تكون مالها Lipid (no Lipid)

العينة لازم تكون بمنطقة dark لانه الـ billirubin ← sensitive to light

إذا حطيناها بمكان في ضوء رح يتكسر الـ bilirubin ورح ← underestimated يعطي قيمة اقل من الموجود

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

إذا بدي احللها مباشرة بعد 3 hrs
بال refrigarator بعد 1 week و بحرارة 20- ← 3months

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

ال jendrassik-crof method تقيس ال total billirubin وال conjugated فبالوضع الطبيعي رح اعرف انه ال total هو ال unconjugated لانه برضه بالوضع الطبيعي مافي conjugated
ال direct method تقيس فقط ال total ما بتميز ال conjugated وال unconjugated

- For **adults**
  - Conjugated: 0-0.2 mg/dL (0-3 µmoI/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

إي يولد قبل ٩ اشهر ← الحل
ولد عند ٩ اشهر ←
كانه هي الـ Jaundice عندهم خطير حاسبين إنهم بالأيام
ممكن نقل ويصير طبيعي و ممكن يظل يرتفع و يعني فيه مشكله
آخر اشي رح خطه المستويات .

Direct Spectrophotometric Method for Determination of Total Bilirubin in Serum

هاي حكينا عنها قبل

λmax

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

لأنه لونها بشبه لون الـ bilirubin رح تزيد من امتصاص الـ λmax

وهيك رح يبين انه الـ absorbance ذاك وبالتالي الـ conc بالي بدير error ← hyperbillirubin

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**.

عنطرح اختيار Can blanked out بس النتيجه رح بأثر ع الـ hemoglobin الـ

(455) billirubin الـ λmax الـ abs صحتن بدير الله hemoglobin الـ انه 575 / ذاتي ← Wavelength

- 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

لـ عرض الـ Cuvette

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

بما انه حديث ولاده بكون الجلد طري وضعيف احتمال كبير يصير عنده hemolysis بس مارح بكون insensitive to hemolysis مشكله لانه هاي الطريقه

- 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

- 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

* حطينا انه

ال Urobilinogin ← Color less ← excreted in urin

ال Urobilin ← give brown pigment of stool ← excretion in stool

Urobilinogen

- Oxidative to Urobilin → excreted in stool
- excreted as Urobilinogen in urin
- reabsorption by Portal Vein → يرجع لل liver ع ال bile

اذا كان في زيادة لل Urobilinogen بتكون لعدة اسباب بال urin

- hemolytic diseas زي الانيميا ← pre hepatic
- hepatitis ← hepatic

طيب مافي Urobilinogen in urin and stool

- biliray obstruction ← Post hepatic
- hepatocellular ← hepatic

* حسب نوع مشكله ال Liver رح يكون في زيادة او ما في اصلاً

كيف احسب كم ال Urobilinogen ؟!

نخليه يتفاعل مع ال P-dimethyl amino benzyl aldehyd ليعطي Red color
وبعدين بقيسه كله بال UV
مرات بكون في Urobilinogen صار اله oxidation وتحول ل Urobilin
عشان هيك بضيف alkiline ferrous hydroxid ليعمل reduction لل Urobilin ويرجع لل Urobilinogen، وبضيف ال Sodium acetate عشان يشيل [eliminate] ال indol & ايضا رح تأثر على التفاعل
وبستخدمه عشان يوقف ال rxn [termination]
زمان كنا نستعمل ال diethyl ether ليعمل extration لل lipid & مادة تكون ، بس هسا نستعمل ال Petrloeum ether لانه ح
يشيل اي مادة غير ال Urobilinogen بدون اي اشي يتداخل معه
بدون intertering substanc

ممكن اضيف ال Ascorbic acid ← ليعمل reduction لل Urobilin عشان يرجع لل Urobilinoge

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. → حسابيًا قيل انه الـ Urobilinogen ممكن تتحول لـ Urobilin إلي رح يعطي اللون البني لـ stool ، فإذا قل الـ Urobilinogen رح تقل الـ Urobilin واللون رح يصير اخف

- 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.

* إذا كانت العينة stool يكون صعب اعرف الـ conc لـ Urobilin
عشان بضيف reduction agent [alkalin ferrous hydroxid] كل العينة لتحول
الـ Urobilin لـ Urobilinogen وهيك بقدر اعرف قيمته.

Measurement of Serum Bile Acids

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

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

كل هاي الطرق بستعملها عشان اوزن الـ conc الـ bile acid بالـ serum

- 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.

ال bile acid كميتها ممكن تختلف قيمها خلال اليوم ٥ وحسب المرض ممكن يرتفعوا وممكن يقلوا

Enzyme Tests in Liver Disease

- Any injury to the liver that results in cytolysis and necrosis causes the liberation of various enzymes.

- The most common enzymes assayed in hepatobiliary disease include ALP and the aminotransferases.

- Used less often are γ-glutamyltransferase, lactate dehydrogenase (LD) and its isoenzymes, 5'-nucleotidase, ornithine carbamoyltransferase, and leucine aminopeptidase

Enzyme Tests in Liver Disease

لخدهم تحت كلهم

Alkaline Phosphatase: in the clinical diagnosis of **bone** and **liver** disease.

- The most striking elevations occur in extrahepatic biliary obstruction, such as a stone in the common bile duct, or in intrahepatic cholestasis, such as drug cholestasis or primary biliary cirrhosis. This enzyme is almost always increased in metastatic liver disease and may be the only abnormality on routine liver function tests.
- The enzyme is found in **placenta**, and **pregnant** women also have elevated levels

Phosphatase enzyme

① ALP

② 5- Nucleotidase (5 NT)

Aminotransferases (Transaminases)

- AST and ALT are two enzymes widely used to assess hepatocellular damage. AST is found in all tissue, especially heart, liver, and skeletal muscle.
- ALT is more “liver specific”

Enzyme Tests in Liver Disease

5'-Nucleotidase: is another phosphatase in the liver and used clinically to determine whether an ALP elevation is caused by liver or bone disease

- This enzyme is much more sensitive to metastatic liver disease than is ALP because, unlike ALP, its level is **not** significantly elevated in other conditions, such as **pregnancy** or **childhood**

- Some increase in its activity may occur after **abdominal surgery**

Enzyme Tests in Liver Disease

- **γ-Glutamyltransferase (GGT)**: high in kidney and the liver and is elevated in the serum of almost all patients with hepatobiliary disorders
  - It is not specific for any type of liver disease but is frequently the first abnormal liver function test demonstrated in the serum of persons who consume large amounts of alcohol
  - The highest levels are seen in biliary obstruction
  - Sensitive test for alcoholic liver disease
  - Measurement of this enzyme is also useful if jaundice is absent for the confirmation of hepatic neoplasms and to confirm hepatic disease in patients with elevated ALP

- **Leucine Aminopeptidase**: widely distributed in human tissue, is found in the pancreas, gastric mucosa, liver, spleen, brain, large and small intestine, and kidney.
  - The serum activity of leucine aminopeptidase cannot be used to differentiate hepatocellular from obstructive jaundice.
  - The measurement of this enzyme does not provide any useful information

Enzyme Tests in Liver Disease

- **Lactate Dehydrogenase**: Measurement of total serum LD is usually not helpful diagnostically because LD is present in all organs and released into the serum from various tissue injuries
- Fractionation of LD into its five tissue-specific isoenzymes may give useful information about the site of origin of the LD elevation
- LD-5 is mostly present in liver and skeletal muscle. elevated LD-5 is noted in a patient with jaundice
- Moderate elevations of total serum LD levels are common in acute viral hepatitis and in cirrhosis, whereas biliary tract disease may produce only slight elevations
- High serum levels may be found in metastatic carcinoma of the liver.

Tests Measuring Hepatic Synthetic Ability

- The measurement of the end products of hepatic synthetic activity can be used to assess liver disease. Although these tests are not sensitive to minimal liver damage, they are useful in quantitating the severity of hepatic dysfunction

- Most serum proteins are produced by the liver. A decreased serum **albumin** may be a result of decreased liver protein synthesis. The albumin level correlates well with the severity of functional impairment and is found more often in chronic rather than acute liver disease. The serum **α-globulins** (α1-antitrypsin) tend to decrease with chronic liver disease

- Serum **γ-globulin** levels are transiently increased in acute liver disease and remain **elevated in chronic liver disease**. The highest elevations are found in **chronic active hepatitis** and postnecrotic cirrhosis.

- lgG and IgM levels are more consistently elevated in chronic active hepatitis, IgM in primary biliary cirrhosis, and IgA in alcoholic cirrhosis.

نبلش بالـ enzyme

1- ALP (Alkalin phospate)

بكون مرتفع بحالتين ① مشكله بالـ Liver ② مشكله بالـ bone

- Liver ↓ مرتفع ارتفاع بسيط عن الـ normal rang اضعاف (3-4) مثلاً
- bone ↓ مرتفع ارتفاع كبير (6-7) اضعاف مثلاً

وفي اشي ثاني بخليني اميز شو سبب الارتفاع وهو الـ 5NT

اذا كان inc (5NT + ALP) ← المشكله Liver ① biliary obstruction

← وأ موجودة اسبابها بالسلايد.

② metastatic Liver disease

inc (ALP) ← ① مشكله بالـ bone

② pregnant + in placenta

③ child during growth

عادي ممكن حتى الـ ALP لحاله هو المرتفع

② الـ AST + الـ ALT

ALT → Liver

AST → skeletal muscle, heart, Liver

بالعاده نفيسو الـ 2 مع بعض اذا كانوا الـ 2 مرتفعات بحكي المشكله بالـ Liver

③ الـ 5NT

الـ 5NT ارتفاعه بعطيني دقه اعلى من الـ ALP لما تكون المشكله metastatic Liver diseas ، لانه مارح الا فيه بالـ Pregnant او بالـ Childr

اذا الواحد كان عامل عمليه بالبطن (abdomin surgary) ممكن يرتفع ارتفاع بسيط وموقت.

④ الـ GGT

بكون مرتفع بمشاكل الـ Liver والـ Kidney واكثر سبب لارتفاع الـ GGT هو الـ hepato cellular disorder ، وارتفاعه مش sensitive للمشكله معطيني بالـ Liver بحكي مارح اعرف عن طريقه شو المشكله بالتحديد

بس الاشي المميز فيه انه رح يكون اول enzym يكون مرتفع لما الواحد يشرب alchole كثير ، فاذا كان يشرب كحول كثير وبدي اعرف الـ Liver تضرر ولا لا بعمل فحص للـ GGT ← Alcholic liver disease

و اذا الواحد عنده biliray obstruction رح يكون مرتفع كثير كثير

واذا الواحد ما كان عنده Jaundic ممكن استخدم هذا الـ enzyme لحتى اكشف عن الـ hepatic neoplasma

وزي ما حكينا قبل عشان نأكد انه ← cancer

في Liver disease اذا كان الـ ALP مرتفع.

Test Measurment [hepatic synthatic ability] HSA

يشوف ال Liver قديه رح يطلع protien ويرح اقارنها مع شدة ال disease بال Liver

Acute Liver diseas → ال ASH رح تكون normal

Chronic liver diseas → ال ASH رح تكون منخفضة

مش اي ضرر رح يصيب على ال Liver رح يادي لانخفاض ال ASH لازم يطول في فترة الضرر ف كلما كانت ال ASH منخفضه كان الضرر اعلى

ال albumin + α-globulin → انخفاضهم موجود بال Chronic

ال γ-globulin → مرتفع بحالة ال Acut بس اذا عالجته رح يرجع لوضعه الطبيعي طيب ال acute اذا تحول لل Chronic رح تظل قيمه مرتفعه

وفي حالتين لل γ-globulin رح يكونوا مرتفعين كثير
① Chronic active hepatitis ② Postnecrotic cirrhosis

وبروتينات المناعة [IgG , IgM] بتكون مرتفعين مع بعض
Chronic active hepatitis, اذا كان ↑IgM لحالة → Primary biliary cirrhosis
اذا كان ال ↑IgG لحالة → alcholic cirrhosis

5- ال Leucine Aminopeptidase

هذا ال enzyme موجود بعده اماكن بعدة مستوى بأماكن كثيرة وحتى لو عملت test لهذا ال enzyme رح يعطيني معلومات مفيدة وبوقته ما بقدر استخدمه عشان اميز بين اسباب ال Jaundic

- Pancereas
- gastric mucose
- spleen / Liver
- brain
- small and large intestin
- Kidney

Jaundic → hepatocellular / obstruction

6- ال Laetat dehydrogenase [LD]

اذا رح اقيس ال total serum LD مارح استفيد لانه ال LD موجود بكل ال organ واي injury رح تصير باي tissue رح تكون افرازه طيب كيف رح استفيد منه؟؟ عن طريق ال isoenzyme حيث ال 5 isoenzyme

5, 4, 3, 2, 1

ال isoenzym اللي رقمه 5 هو اللي يدل على مشاكل ال Liver ورح اسميه 5IE

ارتفاع ال 5IE بكون لسببين → skeletal / Liver → Jaundic

skeletal vs حسب الامراض

اذا كان ال Total serum LD:
- modarat elevatation → cirrhosis + acut viral hepatitis
- sligh elevation → Biliary tract diseas
- high elevation → metastatic carcinoma of the liver

Tests Measuring Hepatic Synthetic Ability

platlet aggregation

بما انه ال liver مسؤوله عن تصنيع ال clotting factor فاذا صار مشكله في رح يقل تصنيعهم وهيك الزمن اللي بحتاجه الدم حتى يعقد تختثر رح يزيد

- **Prothrombin time** is commonly increased in liver disease because the liver is unable to manufacture adequate amounts of clotting factor or because the disruption of bile flow results in inadequate absorption of vitamin K from the intestine

زمن تختثر الدم

اذا gallbladder كان فيها obstruction و bile صارح يقدر يعمل absorption لل Lipid soluble vit وضمنهم vit K المسؤول عن ال clotting factor وشغلهم وهيك ال Prothrombin time رح يزيد

- Response of the prothrombin time to the administration of vitamin K is of some value in differentiating intrahepatic disease with decreased synthesizing capacity from extrahepatic obstruction with decreased absorption of fat-soluble vitamins.

اذا المريض كان عنده Prolong prothrombin time وهيك ما رق السبب هو obstruction و مشكلة بال Liver و بعطيه اله vit K اذا تحسن المشكله obstruction

اذا ما رح تكون مشكلة بال Liver

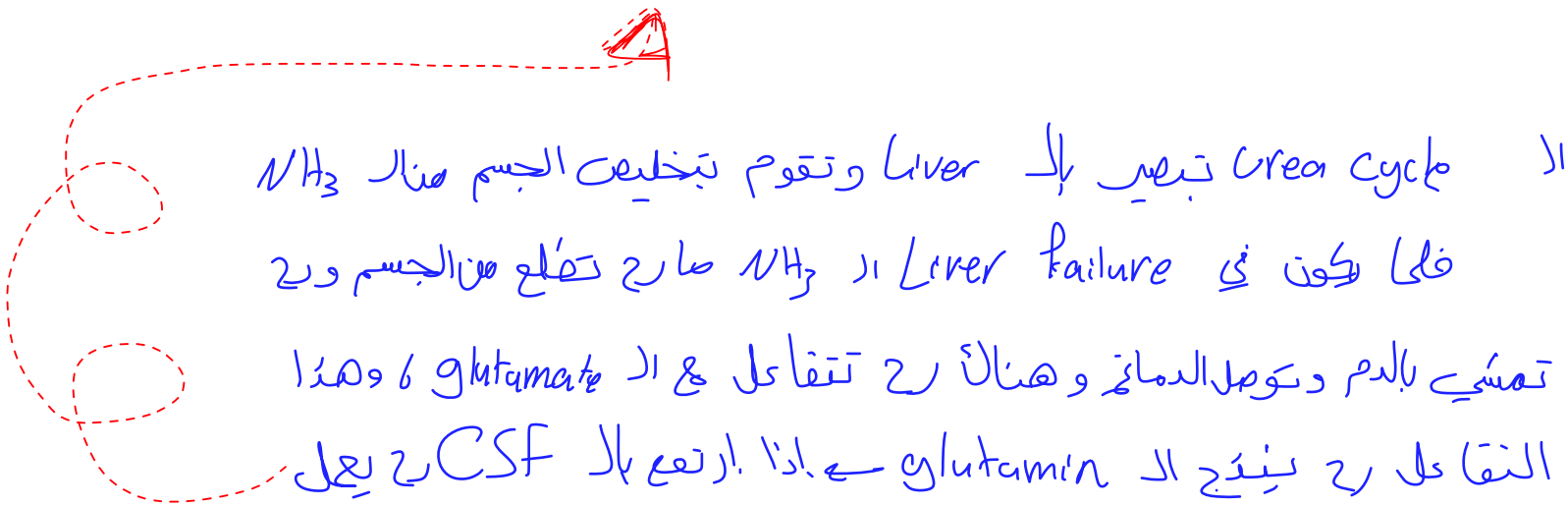
- A marked prolongation of the prothrombin time indicates severe diffuse liver disease and a poor prognosis

العبارة تشير إلى أن **اختبار زمن البروثرومبين هو مؤشر هام لشدة مرض الكبد**. عندما يكون هذا الزمن طويلاً بشكل ملحوظ، فإنه يخبر الطبيب أن الكبد يعاني من تلف واسع النطاق وأنه لم يعد قادراً على أداء وظيفته الحيوية في تصنيع بروتينات التجلط، وهذا يرتبط باحتمالية ضعيفة للتعافي.

Tests Measuring Nitrogen Metabolism

- The liver plays a major role in removing ammonia from the bloodstream and converting it to urea so in liver failure ammonia will increase leading to coma

- In brain, glutamate react with ammonia to give glutamine which increases in CSF to cause encephalopathy



Hepatitis

هدول السلايدين محسين ابحطوهم لحالهم

- inflammation of the liver, may be caused by viruses, bacteria, parasites, radiation, drugs, chemicals, or toxins.
- Among the viruses causing hepatitis are hepatitis types A, B, C, D (or delta), and E, **cytomegalovirus**, **Epstein-Barr** virus, and probably several others.
- Hepatitis A is usually transmitted by the **fecal/oral** route and causes a mild or inapparent infection with no tendency to chronic disease.
- Hepatitis B and C are primarily transmitted **parenterally**. Hepatitis B causes a serious illness in a minority of patients, however, in many patients, the infection is mild or even inapparent

Hepatitis

- Acute infection with hepatitis C is usually mild to inapparent
- Hepatitis B has a slight tendency to chronic disease, while most patients with hepatitis C infection develop chronic infection.
- Delta hepatitis is a unique satellite virus that causes a superinfection in patients already infected with hepatitis B.
- Hepatitis E is primarily transmitted by the **fecal/oral** route and causes serious disease **only** in **pregnant** women
- Chronic hepatitis is a major cause of morbidity and mortality worldwide
- Chronic hepatitis is a major risk factor for the development of hepatocellular carcinoma

Case study

ادخل وقت دخلهم وبنزلهم بملف

CASE STUDY 22-1

The following laboratory test results were obtained in a patient with severe jaundice, right upper quadrant abdominal pain, fever, and chills (Case Study Table 22-1.1).

Question

1. What is the most likely cause of jaundice in this patient?

CASE STUDY TABLE 22-1.1. LABORATORY RESULTS

Serum alkaline phosphatase	4 times normal
Serum cholesterol	Increased
AST (SGOT)	Normal or slightly increased
5′-Nucleotidase	Increased
Total serum bilirubin	25 mg/dL
Conjugated bilirubin	19 mg/dL
Prothrombin time	Prolonged but improves with a vitamin K injection

Case study

CASE STUDY 22-2

The following laboratory test results were found in a patient with mild weight loss and nausea and vomiting, who later developed jaundice and an enlarged liver (Case Study Table 22-2.1).

Question

1. What disease process is most likely in this patient?

CASE STUDY TABLE 22-2.1. LABORATORY RESULTS

Total serum bilirubin	20 mg/dL
Conjugated bilirubin	10 mg/dL
Alkaline phosphatase	Mildly elevated
AST (SGOT)	Significantly elevated
ALT (SGPT)	Moderately elevated
Albumin	Decreased
γ-Globulin	Increased