

تغريغ كلينكال

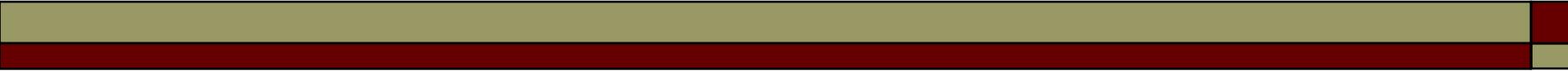


المحاشرة: Liver disease

الصيدلاني لة: Alaa' Otoum



لجان الدفاع



Liver disease

Liver

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

Liver function

- **The excretion of bile:** Total bile production averages about 3 L per day, although only 1 L is excreted.
- 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.
مثلاً ما ذكرنا سابقاً بفضلها يتذكرها
gallbladder by hydroxylase enzyme.
- 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.
taurine → glycine
normal flora
deoxycholic acid.
dubdium. Bile salt || Carrier → باخر الـ ileum
. Bile acid . اذاب في بعده بـ ادخله على Liver, مع بـربطه مع
- 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

Spleen, BM, liver → reticuloendothelial system → Bilirubin →胆红素

Bilirubin
liver uptake
to RBC cell.
glucuronylation
gallbladder
bile acid
phospholipid
cholesterol
excretion
once we eat.

Bilirubin

↑ تفرز في البول

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gallbladder →
Bile → Bilirubin
Cholesterol → phospholipid.

Heme → porphyrin
toxicity: cytochrome b5 → iron
iron → iron storage
Hemoglobin or globin → amino acid
Hemochromatosis → iron → iron storage

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

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bilirubin go from spleen
and bone marrow to the liver.

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 (feces) → 2 glucuronide → become polar

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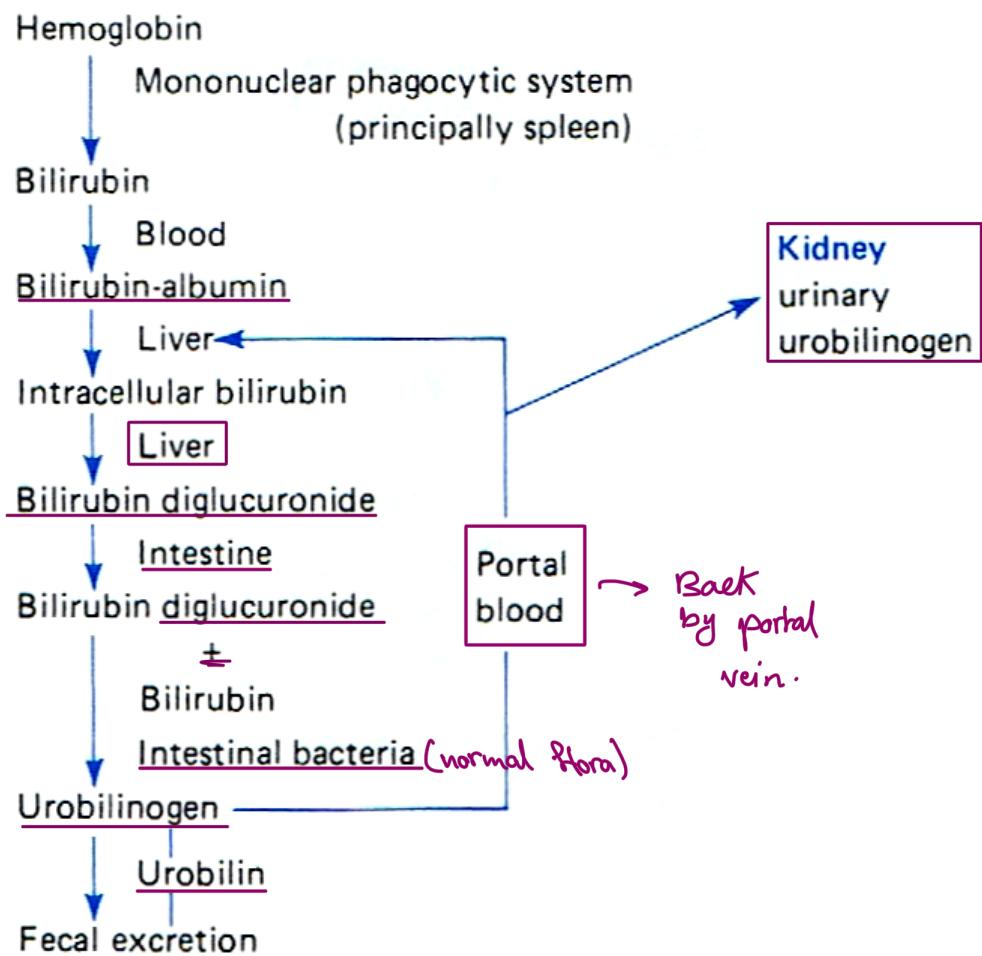
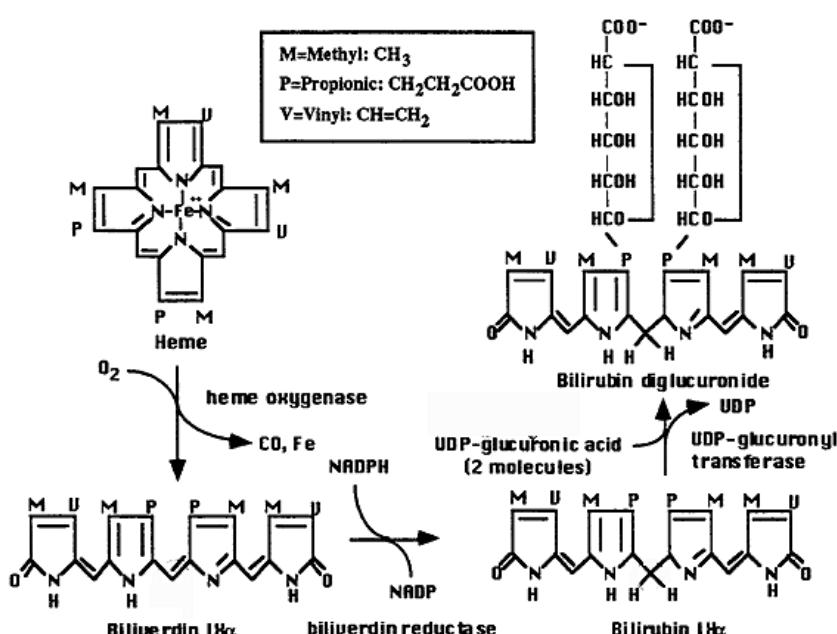
The normal flora in the colon oxidize it further where it is reabsorbed, excreted to the stool (urobilin, reddish brown) or excreted in kidney (urobilinogen, colourless)

Reabsorption
to blood and
back to liver and
then excretion.

bilirubin →
obstruction of gallbladder
feces → liver → kidney → urine
liver → kidney → urine

liver → intestine → Bilirubine →
normal flora →
Bilirubin metabolism
Bacterium → liver → kidney → urine
Kidney → liver → kidney → urine
colorless → reddish brown

Bilirubin



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

• $1 \text{ mg/dL} \equiv 5 \text{ المليمoles/لتر}$ • لا تتجاوز 115

➤ 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. وَيَكُونُ الْجَلْدُ بَلَّوِي prehepatic jaundice

عند الطلق في البول \rightarrow urine \rightarrow bilirubin
حالما يمر مرتين \rightarrow ؟

لذتْ طالع كبارتْ مائدةَ مالكَ بـ *Bilirubin* .

- صریح عکس \Rightarrow unconjugated

لذته طالع كليرات هائلة من **Bilirubin** .
بالذكى الى **Urobilin** كثیر .

Bilirubin

prehepatic	↑ unconjugated	no bilirubin → سریع
Hepatic	↑ unconjugated + Conjugated	✓ conjugated
post hepatic	↑ conjugated	✓ conjugated.

- **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 → "hepatobiliary obstruction".

➤ 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 لونه خاتم حُمَّاً.

- Conjugated bilirubin appears in the urine, and urine urobilinogen levels decrease
 - in urine موجع في البول.
 - very polar & Bilirubine
 - or absence

Major Synthetic Activity

- 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
 - except gamma → in WBC's
 - ammonia → urea cycle.
- The **deamination of glutamate** in the liver is the primary source of **ammonia**, which is then converted to **urea**
- **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**
 - الوجين التي يقدرون مستدعوا
 - RBC's & liver
- 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**

Synthesis of liver enzymes

↳ من الأدوية التي يترافق معها
Statin, iornic acid
Rifampicin, paracetamol.

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

↳ موجود في أماكن ثانية غير liver. مثل: Kidney, muscle.

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

↳ لازم يكون AST, ALT مرتتفعين معاً في حالة liver.

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

↳ gallbladder.

↳ موجود أحياناً
أماكن أخرى من body، إذا كانت فيه ارتفاع بسيط
بعي من (130, 140, 150) في نقص تكسير وينتهي، مما يزيد إلى عن المعدل الطبيعي
(ALP) يحدث فيه ارتفاع بسيط
in growing child or pregnant woman، إذا كانت فيه ارتفاع بسيط
بعي من (130, 140, 150) في نقص تكسير وينتهي، مما يزيد إلى عن المعدل الطبيعي
normal → (44-122)

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

↳ biliary obstruction
or

↳ hepatic
↳ السبب الكولي.

→ the Best indicator to
Alcoholic patient is -
increased in level of GGT.

* في حالة تكون مرتتفع عالي -

albumin & conjugated & ALP & 5NT & GGT
Bilirubin

↳ مرتتفع عالي
الصلة بالرئتين
أعلى من شهرها يعني
أمثلة: Chronic disease in the liver
acute liver
Neither high nor low (normal)
لأنه من بالرئتين مادي يعني

Detoxification and Drug Metabolism

* ما يمتص الأمعىء toxic لا can بعد يمتص liver
لا can قادر liver على metabolize بالنتي به يمتص

phase 1 metabolism polar مساواة اذامر مخلوط بعد ما يمتص بـ oxidation reduction hydrolysis carboxylation demethylation
The liver protects the body from **potentially injurious substances** absorbed from the intestinal tract and toxic by-products of metabolism.

(conjugation) polar بعد ما يمتص بـ conjugation highly polar بعد ما يمتص بـ excreted
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 excreted by the kidney.

حولت لـ highly polar بعد ما يمتص بـ excreted
مخلوط بعد ما يمتص بـ conjugation highly polar بعد ما يمتص بـ excreted

- **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.

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 ($>15-20 \text{ mg/dL}$) 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

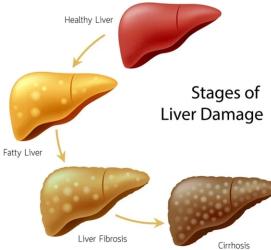
- Although all cases of jaundice result from hyperbilirubinemia, not all are caused by hepatic dysfunction.
→ unconjugated bilirubin.
- hyperbilirubinemia may also result from erythrocyte destruction, or hemolysis in patients with normal liver function

أكل كيتو جوز بغير مجهك (أيضاً بين
لعدة المعيتة لا

Hypercarotenemia (excessive ingestion of vitamin A) may produce skin discoloration indistinguishable from that of hyperbilirubinemia. In hypercarotenemia, the sclerae are usually not discolored.

2 Cirrhosis

The biggest cause of liver cirrhosis is alcohol consumption



Synthetic "Chronic" liver disease
 ملک الفیبرو-لیپیڈیٹ ڈنے
 drug metabolism liver
 معناہ ایڈا بیدے
 اٹھیں اسکو بیدے
 اٹھلے ॥ بیدے
 liver disease

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 جمعها كبير
- 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). Viral hepatitis mainly HCV (5-10%)
 - **hemochromatosis**: *Accumulation of the iron in the liver* Iron store < recycle mode
 - **postnecrotic cirrhosis**: Auto immune disease
 - **primary biliary cirrhosis**: Auto immune disease

- الإنسان الثاني فهو سُخّلَتُ polymorphism التي هي تلك الأمهات من كل الإنزيمات التي يُعَنِّي بالثالثي الأمهات القليلة بالسبة إلى غيرها من تلك مثل الإنزيمات التي مني قادرة تحرأ العكن إنزيماتٍ سُبْعِيَّة.

Cirrhosis

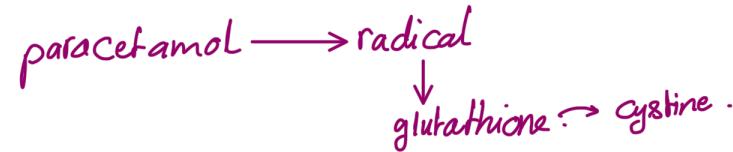
- Cirrhosis is a serious disorder and one of the ten leading causes of death in the United States. **It causes many complications:**
- **Portal hypertension** results when blood flow through the portal vein is obstructed by the cirrhotic liver. This may result in **splenomegaly** and **esophageal varices** (may rupture and lead to fatal hemorrhage)
الشعاير الدموية المحيطة بهذه مج تتفجر ودخلت ترني
دمانع علوي هراري "كوي".
- The synthetic ability of the liver is reduced, causing **hypoalbuminemia** and **deficiency of the clotting factors**, which may lead to hemorrhage
بالناتي مج يلين ←
يتفق لذن كلن ←
albumin ←
مساير فن ←
osmolarity ←
تعت الم ، فرح نلاق ←
منطقة الربط ←
edema ←
"accumulation of" ←
ascitic fluid ←
فرقة دن يغير عاليه.
* دن لو أتعبي Vitamin K ما مج يسكن.
- **Ascitic fluid** may accumulate in the abdomen
- Although some patients with cirrhosis are capable of prolonged survival, generally this diagnosis is an ominous one
مشؤون

3. Tumors

- primary → originated from the liver (chronic hepatitis → Cirrhosis → cancer)
- Secondary → Cancer in the other site (Colorectal, stomach, pancreatic)

- 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
- 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



- 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.
 → give him aspirin → damage to the liver (Reye's syndrome).
- It has been related to aspirin therapy. Shortly after the infection, the patient develops neurologic abnormalities, which may include seizures or coma.
- Liver functions are always abnormal, but the bilirubin level is not usually elevated.
- Without treatment, rapid clinical deterioration, leading to death, may occur.

الكلمات المائية بدل كل حارض (mild injury) ← **الكلمات المائية بدل كل حارض (mild injury)**

Die accumulation of
injury from it is

$$\begin{array}{c}
 \text{ethanol} \\
 \downarrow \\
 \text{acetate} \\
 \downarrow \\
 \text{acetyldehyde}
 \end{array}$$

metabolism of ethanol (أثيل) ، حيث تسبب السُّيُّولَةُ العَادِمُ بِالْجَانِبِ الْأَكْبَرِ damage ॥

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
- 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

Analysis of Bilirubin (Method Selection)

direct bilirubin \neq total
conjugated bilirubin
 \neq total.

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

◀ الـطـفـلـ يـسـجـمـواـ الـدـمـ
مـنـ كـعـبـ الرـجـلـ وـبـالـنـاـكـ
لـقـلـبـ الـعـنـاـنـةـ تـتـحـكـمـ

ناتئ على امتصاص 455 nm

hemolysis & bilirubin
575nm \rightarrow ابْلَقَ

ذبح يقيس الـ hemolysis بالـ ACh من
عند بالـ ACh يطلع عندي Bilirubin .

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

١/ $\frac{1}{2}$ من مجرى الماء فيها الحبر = Serum or plasma blood . (مجرى الماء يحتوي على سائل).
يرجح نفس ال absorbance .

الخلايا الجديدة التي تولدت في المخيخة تكتسب القدرة على امتصاص الضوء (absorbance) في الماء الوردي. بيليروبين (bilirubin) هو الماء الوردي الذي يمتص الضوء الأحمر (red light) في الماء الوردي.

jendrassik-Grof Method for Total and Conjugated Bilirubin Determination⁶

(10-15) \leftarrow obstruction \leftarrow sine \leftarrow total left range (0.2-0.9) \leftarrow normal \leftarrow

$$\begin{aligned} \text{Tot bilirubine} &= 0.8 \text{ mg/dl} \\ \text{direct bil} &= 0.1 \text{ mg/dl} \\ \text{unc conjugated} &= 0.8 - 0.1 \\ &= 0.7. \\ (0.2 - 0.9) &\text{ normal} \end{aligned}$$

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
 - direct bilirubin \leq 0.2 mg/dL (0-3 μ mol/L)
 - unconjugated bilirubin \leq 0.8 mg/dL (3-14 μ mol/L)
 - total bilirubin \leq 1.0 mg/dL (3-17 μ mol/L)
- For adults
 - Conjugated: 0-0.2 mg/dL (0-3 μ mol/L)
 - Unconjugated: 0.2-0.8 mg/dL (3-14 μ mol/L)
 - Total: 0.2-1.0 mg/dL (3-17 μ mol/L)

INFANTS	PREMATURE, TOTAL	<i>See also Growth</i>	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.
↳ not sensitive to hemolysis.
- 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

↳ this method ideal newborn less than one month.

$$A = \frac{abc}{l}$$

Absorbivity ←
C = Conc
l = path length

* so no standardised
and must be accurate.

ارتفاع
الختام
ارتفاع
أ. اختمام
liver disease

Urobilinogen in Urine and Feces

"mesurment"

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

الآن هنا
العلم
استرج
صلبرات
سابق
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

conjugated

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

المستخدم حالياً، لا ينتمي إلى تجربة أختنل.

ـ عـانـى

Determination of Urine Urobilinogen (Semi-quantitative)

- 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.


like amber glass.

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.

• لازم ما أستن يليها منزة طبلة
• كي تفتخ على الـ oxidation الميخت
• تجيئي ذات أشكال متعددة الـ الـ
• تصرى ملئ بقى في أعلى من 5 min

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

By dilution

- Visual inspection of the feces usually suffices to detect decreased urobilinogen.
عند العادة يستحسن هنا لأنها حتى الخامسة تعرف بالعين المجردة
بالناتي إذا كانت العلبة فاتحة وبالتالي obstruction air وإذا كانت لامنة
urobilin & urobilinogen موجود في feces أكثر ناصع معندهما يكتسب مظهر
- 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

→ not important test and very expensive.

- 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
- 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.

Enzyme Tests in Liver Disease

لـ blockage of enzymes \Rightarrow cellular obstruction

کائنات حیاتی میں اسکا
فیکٹر میکر
مسنونہ
Any injury to the liver that results in cytolysis and necrosis causes the liberation of various enzymes.
damage continuous.

- 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 *↳ urea cycle*.

* كل ما كانت enzyme قادر على تحفيز كل ما كان تختلف في test
الآن أعلم ، بالذاتي من مخبر دليله .

Enzyme Tests in Liver Disease

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

لے ارتقائے بھونتے ہیں اہمیات و طالع۔

- 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. مُرتفع بالتالي هذا الأنزيم مرتفع .
- The enzyme is found in **placenta**, and **pregnant** women also have elevated levels مُرتفع عن كثير . الارتفاع العالى جداً لهذا الأنزيم عده في حالة Bone Cancer .

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”

لے ما بر تفعِ الاِدا
کانت مشکلۃ
بلا حسنا .

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

→ Best indication to alcohol consumption.

- **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.

بالنسبة مني طبيه اعلمه بما ينفعه زهد موجود في كفر آمانت
 - 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

* يقدر اثربت دين ميكنانه بناء
على الأعراض التي ميكنه.
- 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

→ We have acute or a chronic liver disease?

- 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
عَنْ كِيدْنَى مُسْكَلَةٍ فَيَنْتَهِي لِكِيدْنَى مُسْكَلَةٍ فَيَنْتَهِي Kidney مُسْكَلَةٍ فَيَنْتَهِي (chronic). liver عَنْ كِيدْنَى مُسْكَلَةٍ فَيَنْتَهِي
- 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** (α 1-antitrypsin) tend to decrease with chronic liver disease
وَعَنْ تَرْفَعِ وَبَسِ immuno-globulin (IgG's)
- 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.
- IgG and IgM levels are more consistently elevated in chronic active hepatitis, IgM in primary biliary cirrhosis, and IgA in alcoholic cirrhosis.

Tests Measuring Hepatic Synthetic Ability

Chronic liver disease \rightarrow Biliary obstruction \rightarrow Carboxylation \rightarrow prothrombin

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

can be solved by
vitamin K injection

prothrombin
time

ورفع الماء
معنادل الماء
بiliary

like Vitamin K

clotting II in the liver
 factor

؟ \rightarrow chronic liver II
 gives to chronic liver II
 injection of V K \rightarrow prolongation of prothrombin time
 stones (in) clotting factor II \rightarrow chronic liver II
 \rightarrow chronic liver II
 poor prognosis

gallbladder

stones (in)

clotting factor II

poor prognosis

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

. ammonia & glutamate \rightarrow glutamine \leftarrow liver \rightarrow CSF

Hepatitis

- 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.

↳ يعنى الها في المختبر
- **Hepatitis A** is usually transmitted by the fecal/oral route and causes a mild or inapparent infection with no tendency to chronic disease.

↳ يعنى نقله من الماء
- **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.
 - ↑ تتحول إلى مرض مزمن (5-10) % chronic
 - ↑ مرض مزمن (5-10) % chronic
 - ↑ ≥ 90% chronic → cirrhosis → carcinoma → death
- 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
 - ↑ B ≥ C
- Chronic hepatitis is a major risk factor for the development of hepatocellular carcinoma

Case study

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