

Enterohepatic circulation

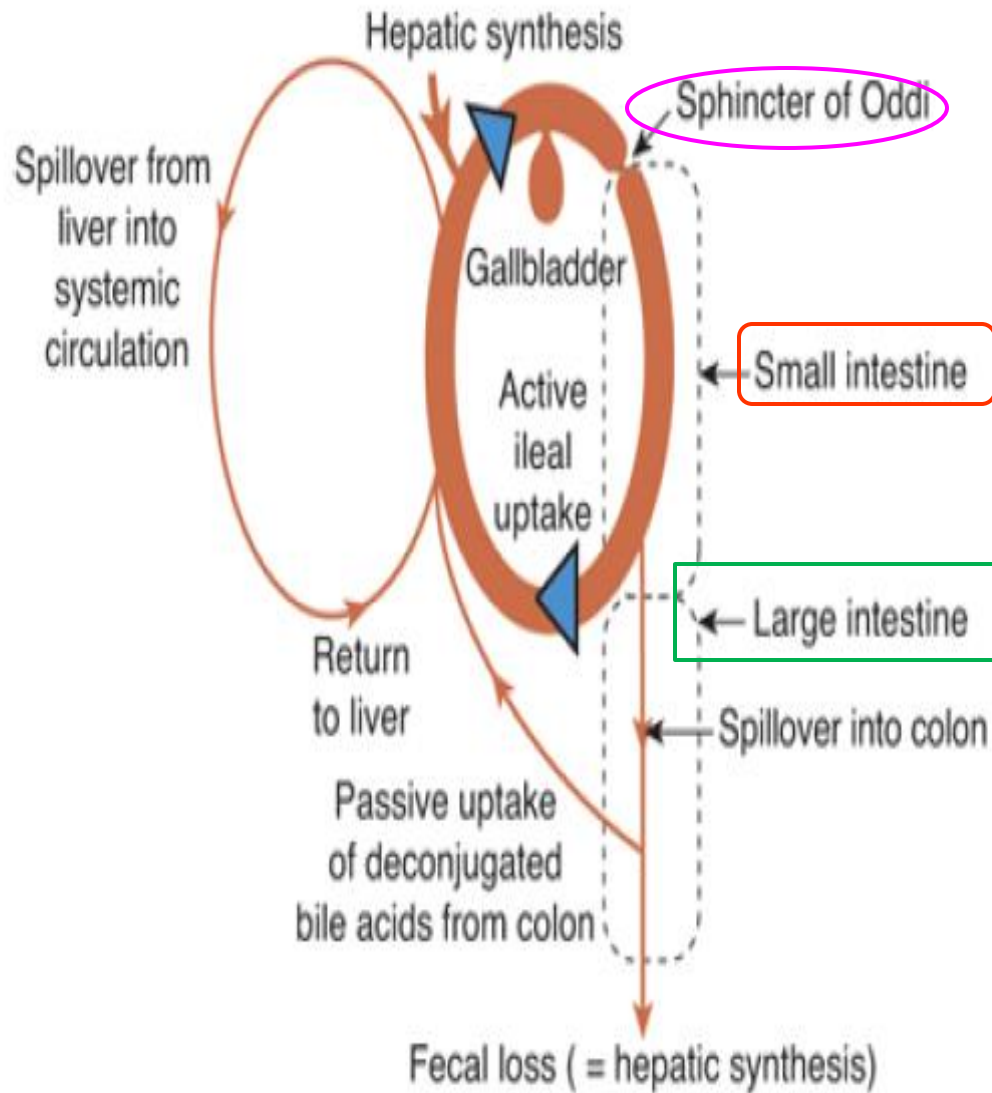
- **94%** of bile salts are reabsorbed, about **one half** of this by Diffusion through the mucosa in the early portions of the small intestine and the remainder by an Active transport process from the Terminal ileum and returned to the liver to be secreted. المعظم من هان بصيرله reabsorption، بعدين بروح على ال Superior mesentific vein ومئه لل liver

- **5-10%** enter the colon → salts of deoxy (reabsorbed) and lithocholic acid (insoluble and excreted in the stool). 2nd bile salts.

- The total bile salt pool in the body is **3.5 gm** (recycles **6-8 times**), and the amount lost in stools (**0.2-0.4 gm/day**) is replaced by new synthesis in the liver.

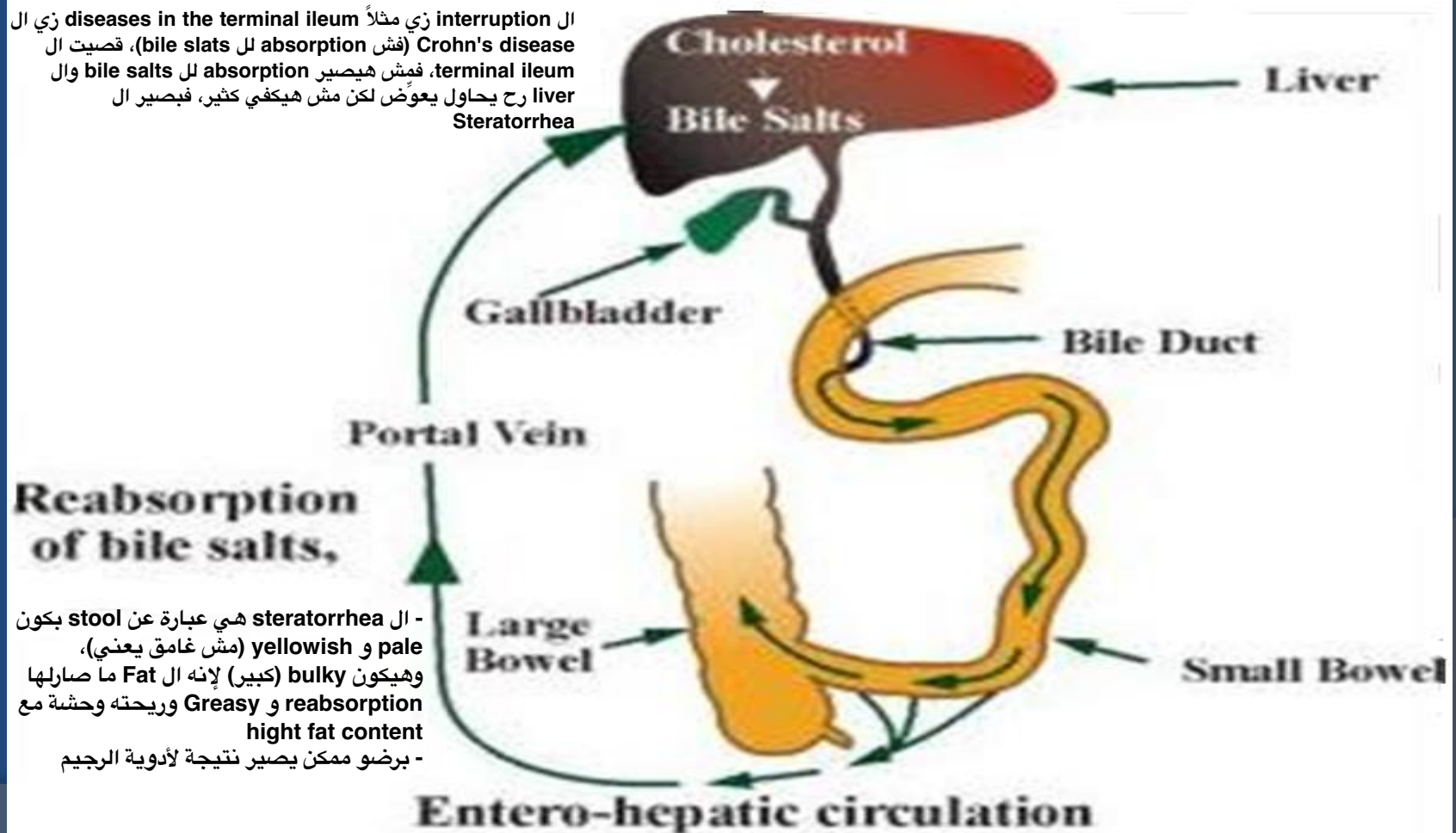
6-8 time/day

أو مرتين مع كل وجبة



- If the enterohepatic circulation is interrupted
 → liver cannot compensate and signs of bile salt deficiency appear (*steatorrhea, deficiency of fat soluble vitamins , cholesterol stones*).
 B12 deficiency كمان هيصير
 Megaloblastic anemia وبصير

ال interruption زي مثلاً diseases in the terminal ileum
 Crohn's disease (فشل absorption لل bile salts), قصبت ال
 terminal ileum, فميش هيصير absorption لل bile salts وال
 liver رح يحاول يعوض لكن مش هيكفي كثير، فبصير ال
 Steatorrhea



Regulation of bile secretion

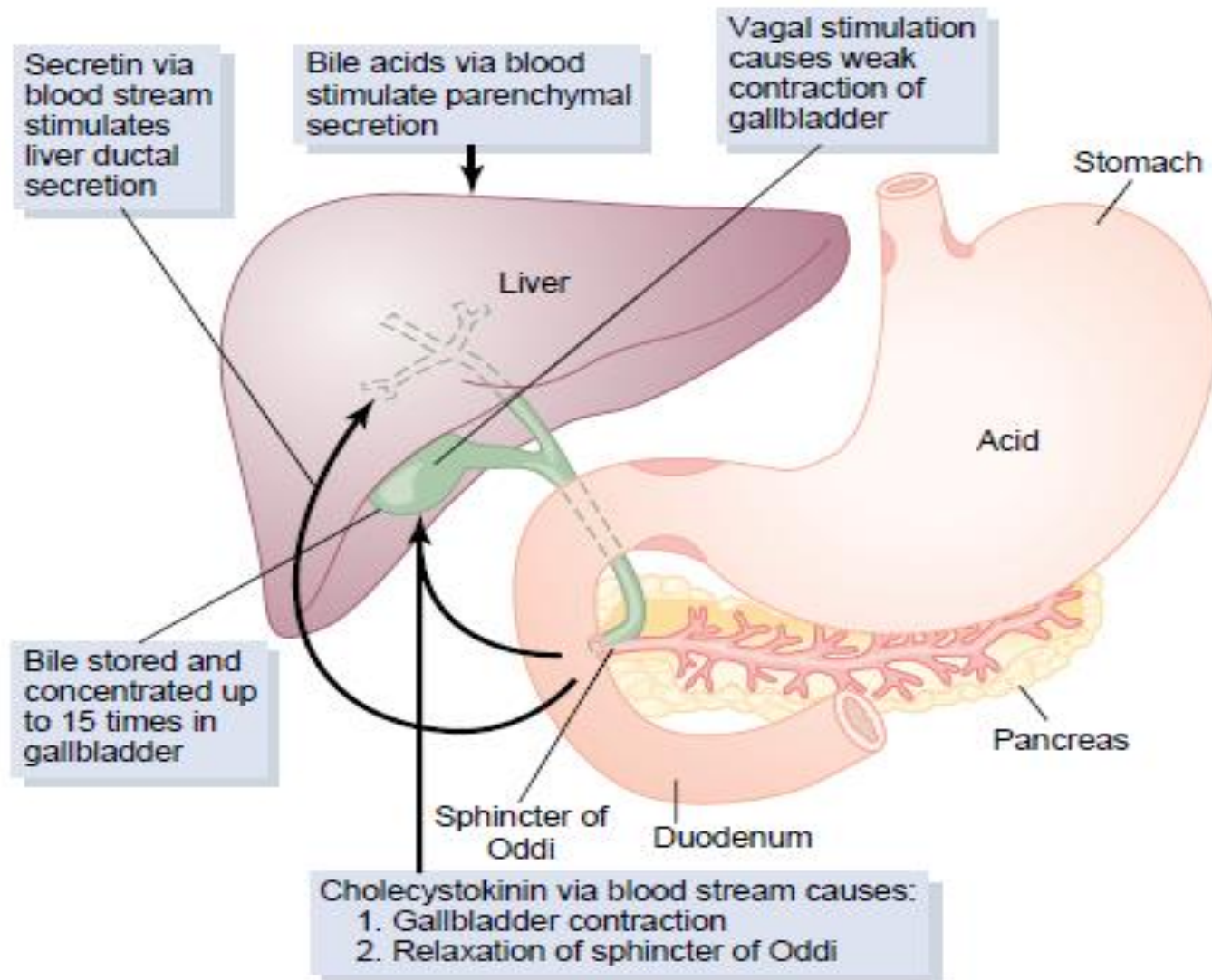
Bile secretion by the liver is increased by:-

- ^{الأهم} **Chemical mechanism**; Bile salts returned to the liver by the enterohepatic circulation stimulate further bile secretion.
- **Hormonal mechanism**; **Secretin** stimulate the aqueous alkaline portion of bile and increase bile flow. أما ال CCK يعمل contraction لل gallbladder ويعمل relaxation لل sphincter of oddi
- **Neural mechanism**; occurs in the cephalic phase of digestion . Mediated via the **Vagus nerve** & cause increased water & bicarbonate content of bile.

Choleretics are substances that increase bile formation by the liver and bile flow .e.g. bile salts & **secretin**.

Cholagogue are substances that increase move bile from the gall bladder and increase bile flow .e.g. **CCK**

هاد الي يفسر ليش لما أكل دهون بصير في مخص بالمرارة ال CCK بمشي من ال small intestine مع ال blood لل liver و انقبضت ال gallbladder وكان في حصوة صار عندك مخص و هاد بنسميه fatty dyspesia ولو ل التسكير هيصير acute cholecystitis



Liver: Bile Synthesis

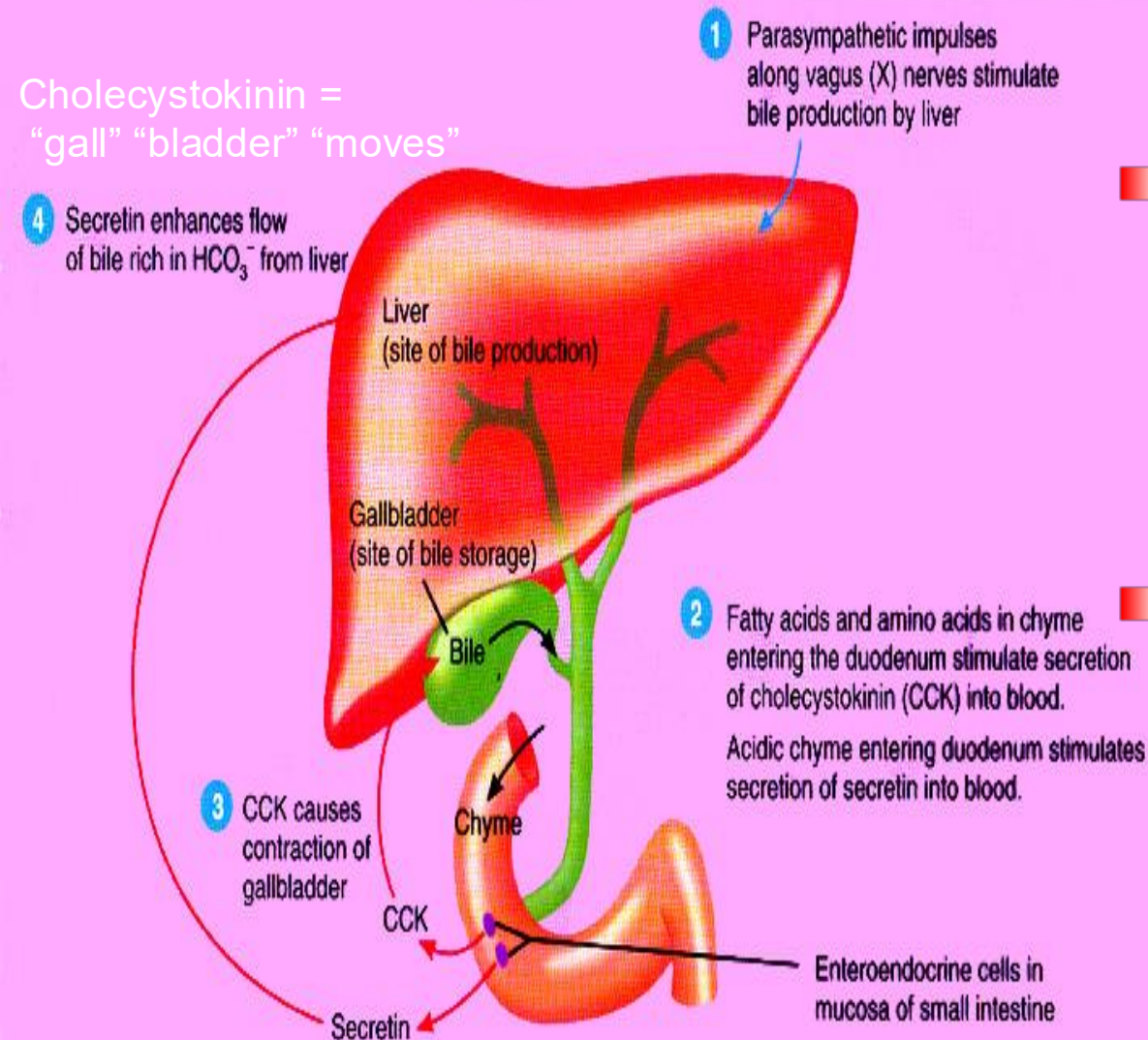
Regulation of bile production/secretion

- Nervous control from parasympathetic via Vagus nerve

- Auto regulation by sensing the presence of fatty acids and amino acids in the acidic chyme

- Hormonal control by the secretion of the Enteroendocrine, CCK and secretin, from the duodenum

Cholecystikinin =
“gall” “bladder” “moves”



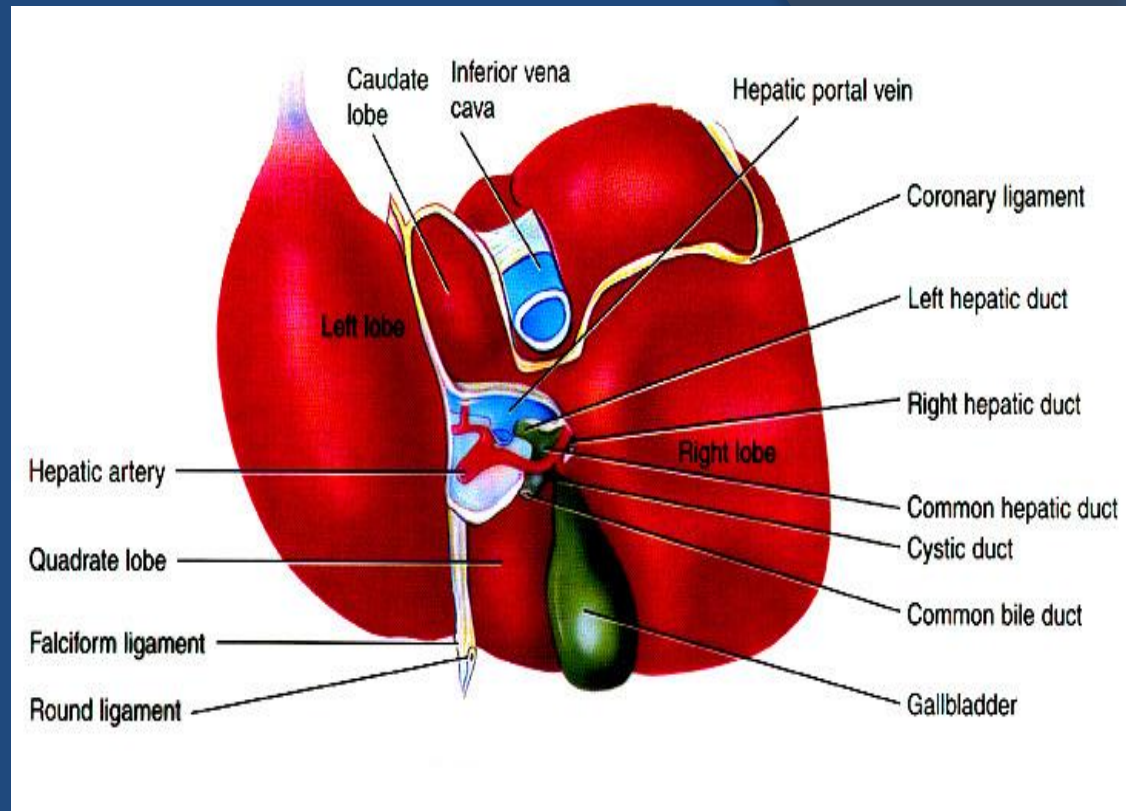
Gall Bladder

- Pear-shaped sac, 7-10 cm long

- **Physiology**

- Stores and concentrates bile between meals
- CCK stimulates bile release for fatty meals
- when the small intestine is empty, the hepatopancreatic sphincter closes, forcing bile into the gallbladder for storage

Pathology:
gallstones



Functions Gall Bladder

1-Storage of bile: between meals, the sphincter of oddi is tonically contracted, so bile flow retrograde upwards through the cystic duct to be stored in the gall bladder.

2-Concentration of bile : by active reabsorption of Na⁺, followed by passive reabsorption of water and most electrolytes, except calcium (bile salts increase 5-10 times, water content decreases to 89%).

3-Acidification of bile: due to bicarbonate reabsorption during concentration, pH= 7-7.4 (prevents **Ca²⁺** ppt and formation of gall stones).

ما يترسب في الـ acidic media
يترسب في الـ alkaline media

4-Secretion of mucus: (white bile) from mucous glands in the mucosa: it Protects the gall bladder wall against highly concentrated bile salts, gives the bile a semi fluid consistency, and acts as a lubricant in the small intestine.

- لما بتعمل عملية مرارة والمرارة منفوشة ورحت شفطتها وطلع منها white bile وما طلع الـ الأخضر، فمعناها انه الـ cystic duct is obstructed ما بقدر يدخلها الـ bile ويضله ماشي للأعضاء

5-Evacuation: by contraction of wall and relaxation of sphincter.

Bilirubin ال

Bile Pigments الزبدة انه موضوع مهم يعني

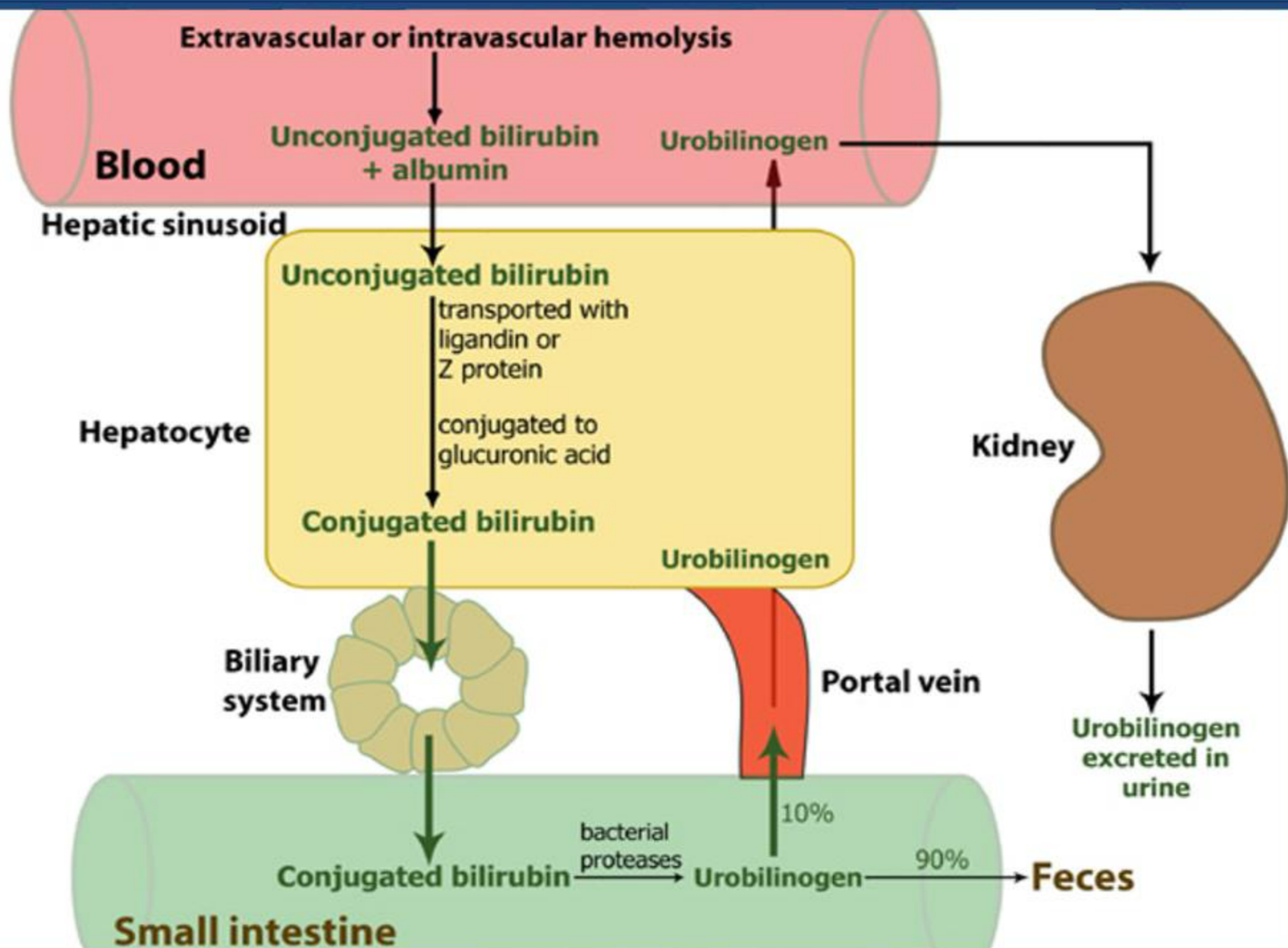
يعني Protein

- Hb of RBCs is phagocytosed by RES → Heme + Globin.
- Heme ring is opened → Iron is stored in the liver. Transferrin اسمه reticuloendothelial system. spleen في ال معناها هنا بصير اسمه Ferritin
- The remaining part of heme is converted to the Green pigment biliverdin → reduced into bilirubin → blood, combine with albumin (haemobilirubin, unconjugated, indirect or free bilirubin) → liver where albumin is detached, while bilirubin is conjugated with glucuronic acid (Conjugated or direct bilirubin). Carrier of bilirubin هنا اسمه indirect bilirubin لأنه غير albumin فلازم الشيء يحمله، فيحمله ال destruction of RBCs وينسجمه هيك عشانته ناتج عن ال يشكل 20% من ال total bilirubin بصيرله active uptake اي مرض بخلي ال spleen تكسر ال RBCs اكثر من اللازم وقبل ال 120 يوم تبعها، أي حاجة هتعمل hemolysis ← ال free bilirubin هيزيد هو المسؤول عن لون ال bile
- Conjugated bilirubin is actively transported into the bile canaliculi → golden yellow color of liver bile → Small intestine is converted to urobilinogen → most urobilinogen is converted to stercocoblinogen → Stool (stercobilin, brown color of stool). في ال colon بصيرله oxidation اول ما يطلق ويصير اسمه stercocoblin
- 5% enter the general circulation (urobilinogen) → kidneys → urine (urobilin). لما يصيرله oxidation وهاد المسؤول عن لون البول

- ال liver بعمل ثلاث حاجات، بعمل uptake لل indirect bilirubin وبعدين بعمله conjugation وبعدين بعمله secretion (بوديه ع ال bile ducts)، فلو ال liver تبعك تعبان أو خربان أو عندك hepatitis أو cirrhoses مش هيقدر يعمل هاد الكلام

- شو الفرق بين ال direct bilirubin وال indirect؟
ال indirect هو water insoluble عشان هيك بنحمل على ال albumin، أما ال direct is water soluble، شو بفيديك؟؟؟

بفيديك انه طالما ال indirect is water insoluble لازم يكون مع carrier وال carrier هو ال albumin وال albumin كبير، فمش هتلاقيه في ال urin، أما ال direct بنزل في ال urin، عشان هيك أي واحد عنده صفرة بسبب hepatitis أو ال ducts مسكرة ومش عارف يروح ع الأمعاء، هيضله في ال portal blood وبروح ع ال kidney وبنزل في ال urin وبخلي البول dark tea colour



Jaundice

خصوصاً ال eye وال mouth

- **Definition:** Yellow discoloration of skin and mucus membranes due to presence of excess level of bilirubin (free or conjugated).

زيادة ال bile salts في الدم هي التي بتعمل الحكة، أي عيان بحك هيكون عنده يا obstructive يا hepatocellular

اللي عنده total bilirubin عالي وال direct normal يكون عنده

Hemolytic jaundice

عنده صفار وعيونه صفرة بس البول يكون لونه عادي

Hepatocellular J

Obstructive J

	<u>Hemolytic jaundice</u>	Hepatocellular J	<u>Obstructive J</u>
Causes	Excessive hemolysis of RBCS Hemolytic anemia, drugs, Autoimmune disease	Liver disease Infection viral hepatitis Chemicals Like overdose of paracetamol chloroform Drugs كانوا يتسخدموه في التخدير زمان	Cholestasis Intrahepatic cirrhosis Extra-hepatic GBS Carcinoma stricture
Mechanism	↑ Production of free bill	Liver cannot uptake Conjugate and excrete bil	Liver conjugate but cannot excrete bil to intestine
Blood Bil	Haem bili ↑↑	Both ↑	Chole bili ↑↑
Bile salts	Absent	Present	Present
Urine Bili Color	Absent لانه كله unconjugated وهاد بنزلش بال urin لانه too big، هاد بروج ع ال liver	Present Chole bili Dark brown	Present Chole Bili Very dark frothy brown يعني في زي bubbles
Stool	Very dark stool لانه ال liver عمل معاه شغله	Pale stool	Very pale stool