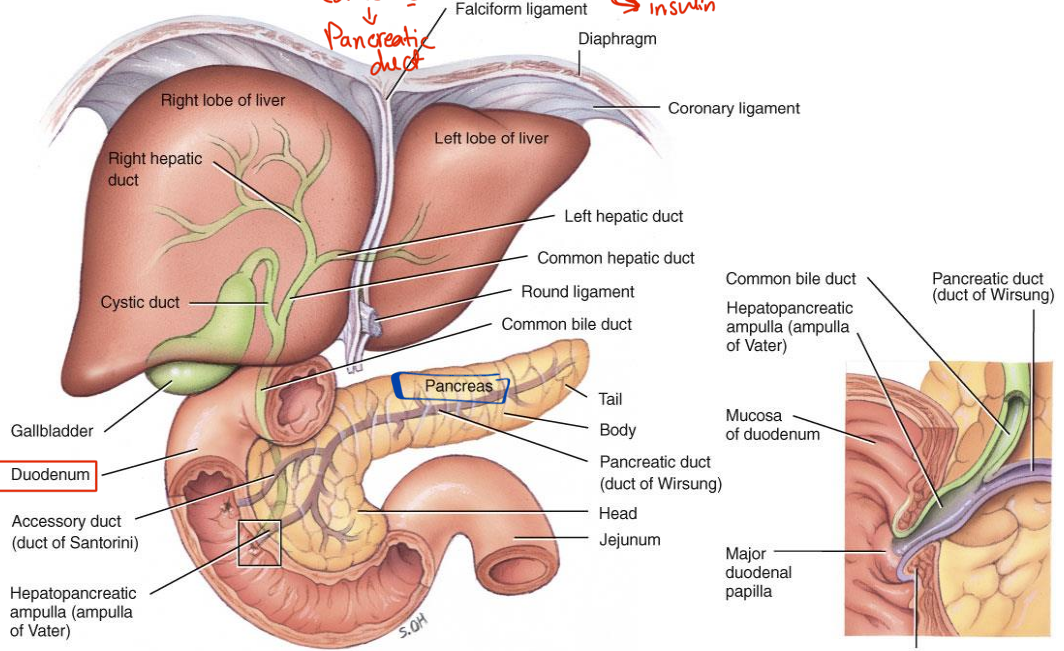


THE PANCREAS

- Head, neck, body and tail
- Head into duodenum
- Tail to spleen
- Pancreatic duct joins bile duct and connect to duodenum

عن طريق إفرازه
الغذاء وبتنزيه
فإنه إفراز
عنه يتم هضم
الدهن

exocrine & endocrine (با الدم)
↓
Pancreatic duct
↓
insulin



(a) Anterior view

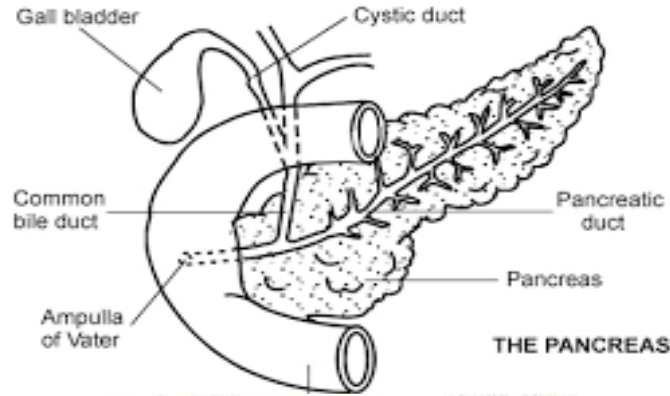
24.17a

Hormones

الذي يفرزها البنكرياس أو الكبد أو المرارة
CCK secretin GIP
التي تفرزها البنكرياس أو الكبد أو المرارة
التي تفرزها البنكرياس أو الكبد أو المرارة

التي تفرزها البنكرياس أو الكبد أو المرارة
التي تفرزها البنكرياس أو الكبد أو المرارة

The pancreas



- **Exocrine functions** → Digestive enzymes secreted by the **pancreatic Acini**

Stores inactive enzymes ^①(proteases, ^②lipases, amylases)

مخزن في الكبد في الدم

↓
Protein

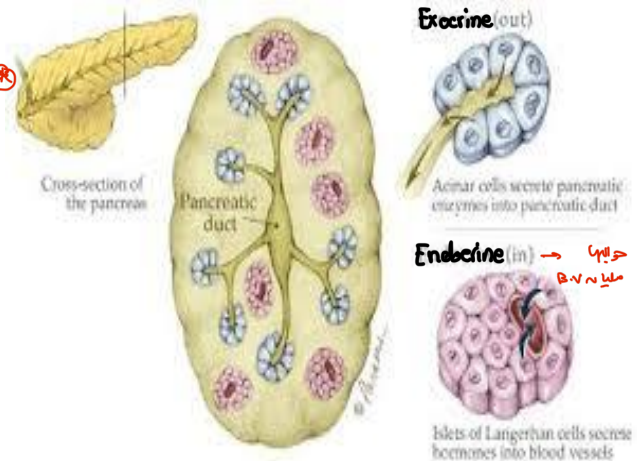
↓
fat

هذه البروتينات تفرز inactive في sphincter وتنتقل داخل duodenum

- **Endocrine functions** → hormone secretion.

- **Glucagon**: stimulates the stored glycogen in the liver to convert to glucose. Produced if the body does not have enough glucose.

- **Insulin**: made in the beta cells of the Islets of Langerhans of the pancreas. Insulin is a hormone that regulates blood glucose.



Physiologic Anatomy of the Pancreas

- Two major types of tissues

- 1) The **acini**, which secrete digestive juices into duodenum
- 2) The **islets of Langerhans**, which secrete insulin and glucagon into blood. (Two antagonistic hormones)

- 1 to 2 million islets of Langerhans, organized around small capillaries into which its cells secrete their hormones.
- The islets contain three major types of cells alpha, beta, delta cell

مریض (DM) عکس تصویر
تلفظ destruction کی صورت 70-80% مرگ

- The **beta cells** 60 % of all the cells of the islets, lie mainly in the middle of each islet and secrete insulin and amylin,
- The **alpha cells**, 25 % of the total, secrete glucagon
- The **delta cells**, about 10 %, secrete somatostatin. inhibitor
- One other type of cell, the PP cell, is present in small numbers in the islets and secretes pancreatic polypeptide.

Physiologic Anatomy of the Pancreas

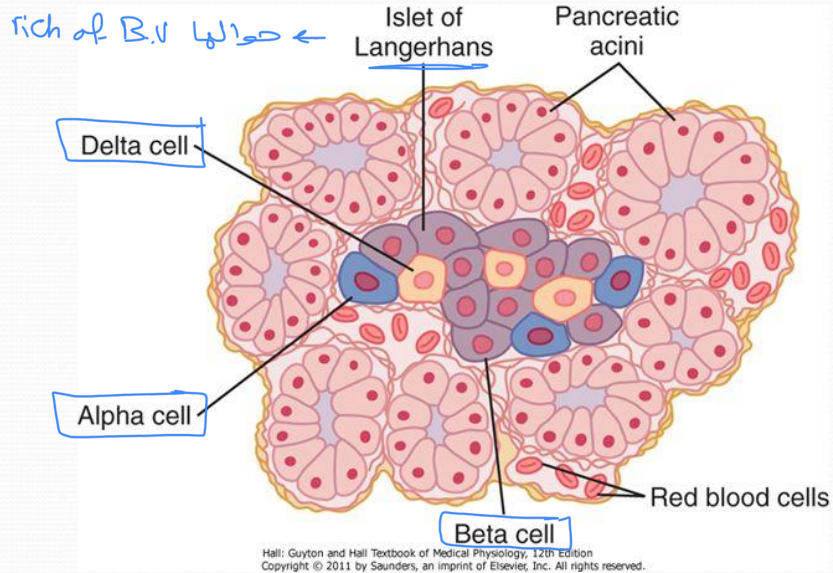


Fig. 78.1 Physiologic anatomy of an islet of Langerhans in the pancreas

Insulin: → increase uptake cell into insulin.
سبب خروصه

- secreted when the **blood glucose level is high**, which usually occurs just after eating.

- Insulin stimulates how much glucose is taken by cells

⊗ كل صومونه عنده الى Basal level

انه بيكونه الى افراز ب قليل

و لكنه بعد ما يجيو

stimulates بيطلع كثير

- In liver and muscle cells glucose is **stored as glycogen**

ATP الاشارة كفاية و دخل خليه لعضلات و خزنه

- In muscle cells the breakdown of glucose supplies energy for protein metabolism

⊗ صانك خلايا يحكمه تحييب و تدخل لكر داخلها

دوره الحاجة الى الانولين .

مثل ال Brain .

والك ال Brain في وجود الانولين يتكونه استجابيه

لـ glucose وانه بيخله جوا خلاياه اكثر

ولكن هناك خلايا ما بتقدر تحييب لكر الا يكونه

في الانولين .

→ **Diabetes** is a common hormonal disease where liver cells and all body cells are unable to take up and or metabolize glucose.

Glucagon: (Fasting state) → ↓ glucose in Blood.

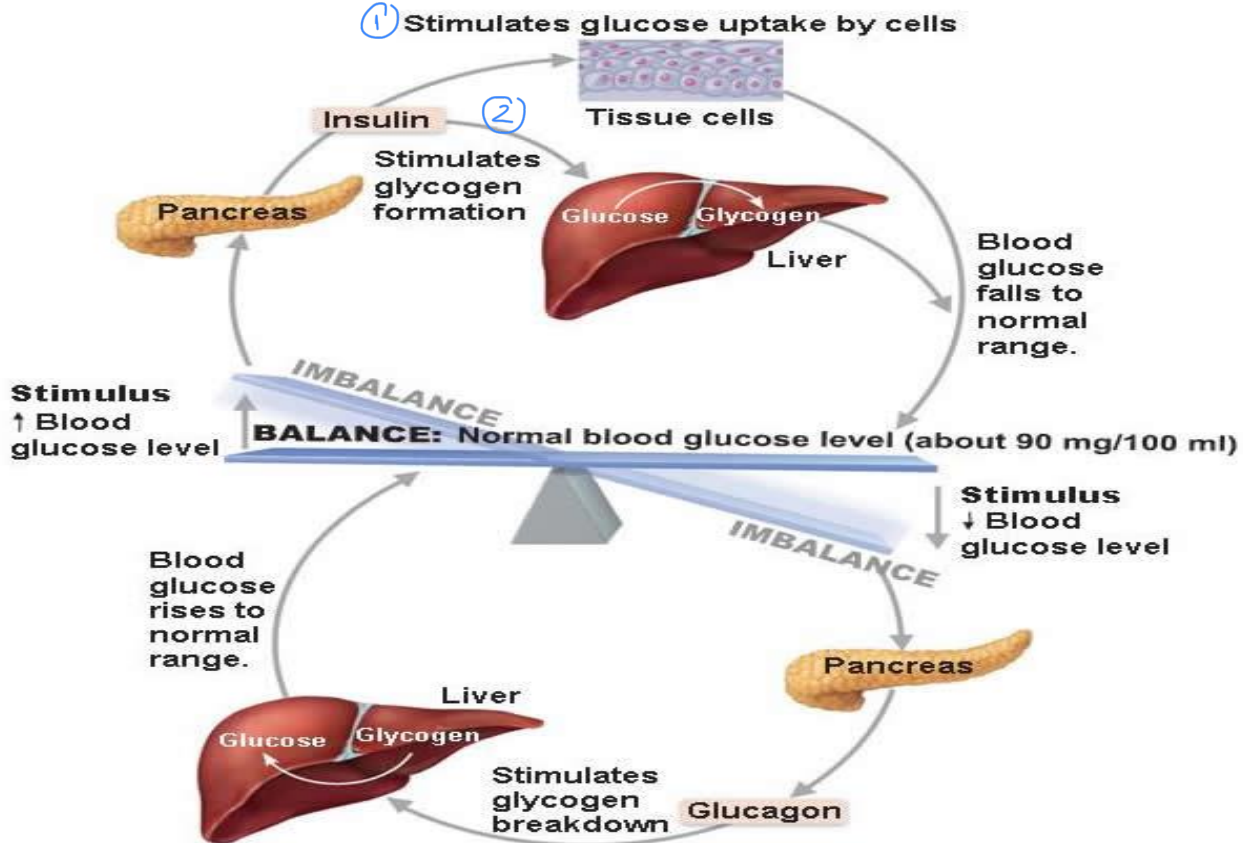
- Is secreted from the Pancreas, and this happens usually between meals when the blood glucose level is low.

- Glucagon stimulates the liver to break down glycogen to glucose to use fat and protein in preference to glucose as an energy source

- Hypoglycaemia (abnormal low glucose level in blood) بـسـرـبـ اـرـدـهـ

السكر بتكون زياده .

له بتخوف (بـيـنـقـوـتـ في Coma)

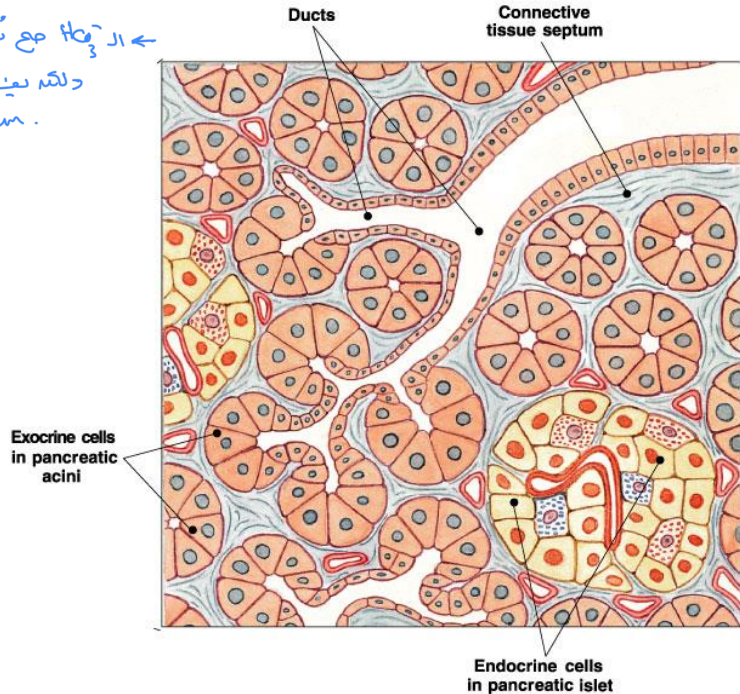


HISTOLOGY OF PANCREAS

- Acini are exocrine cells that secrete digestive enzymes into ducts
- Duct cells secrete HCO_3^- to buffer the acid chyme from stomach and raise its pH from 2-3 to 7-8

← الـ HCO_3^- مع يُفرز من الـ acini
 وذلك بغير شكل أكثر من
 duct system.

→ optimal pH
 لهذا المنزلية



عشاه الذلل الى نزل والمبيئة المعوية
 في الامعاء كانت كالتلك

هذه الخلايا ما تبخلى الانزيمات الي
 ثم افرازها تستغل فتحول الـ pH
 من 2-3 بتخليها (7-8)

SECRETION OF PANCREATIC JUICE

- Enzymes are secreted by Acinar cells
- Bicarbonate solution is secreted by Ductal cells
- About 1 liter of pancreatic juice is secreted by the pancreas per day
- Bicarbonate solution neutralize the acidity
- Enzymes digest proteins, starch and fat
- Pancreatic release is mediated both by the nervous system and by the hormone CCK

Pancreatic secretion

→ Fat & Carbohydrate & Protein digestion
 بعدی نفعی ال digestion ال Small intestine ال
 absorption ال

- The pancreatic enzymes for **digesting proteins** are:

- Trypsinogen** - makes up most of the enzymes → trypsin inhibitory elixir ال pancreas ال inactive
- Chymotrypsinogen** → inactive. → peptide bond ال amine acid ال peptide ال
- Pro-Carboxypolypeptidase** → inactive. → peptide ال chymotrypsinogen ال (amine acid) ال كى ال aromatic ring (حلقه) ال

- Trypsin and chymotrypsin break proteins into peptides (smaller proteins)

- Carboxypolypeptidase breaks peptides into amino acids → carboxyl-terminal ال amino acid ال

- These enzymes are secreted in an **inactive** form and become active in the intestinal tract

- Many of the protein-digesting enzymes, such as aminopeptidase, are secreted by the intestinal epithelium, but trypsin, chymotrypsin, and carboxypeptidase are secreted in inactive form by the pancreas. ← مزارم تكون الانزيمات inactive في الكبد لا في البنكرياس

Pancreatitis

بسبب هذه الانزيمات، يقولون لو كانت تسيطر في البنكرياس حتمًا

- Another intestinal enzyme, enteropeptidase, converts inactive trypsinogen into active trypsin. → دهن يسهل الانزيم الثاني

- Active trypsin then activates the other two.

موجود في جدار الـ Small intestine

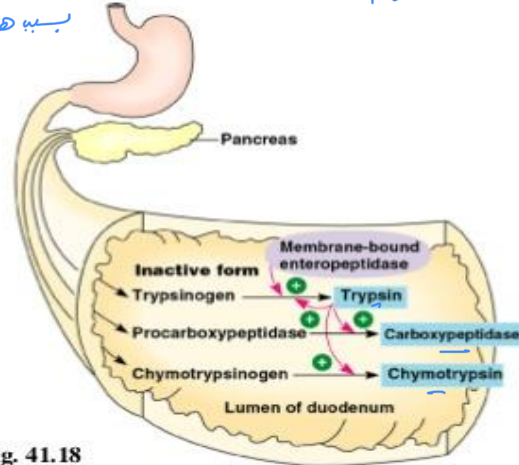
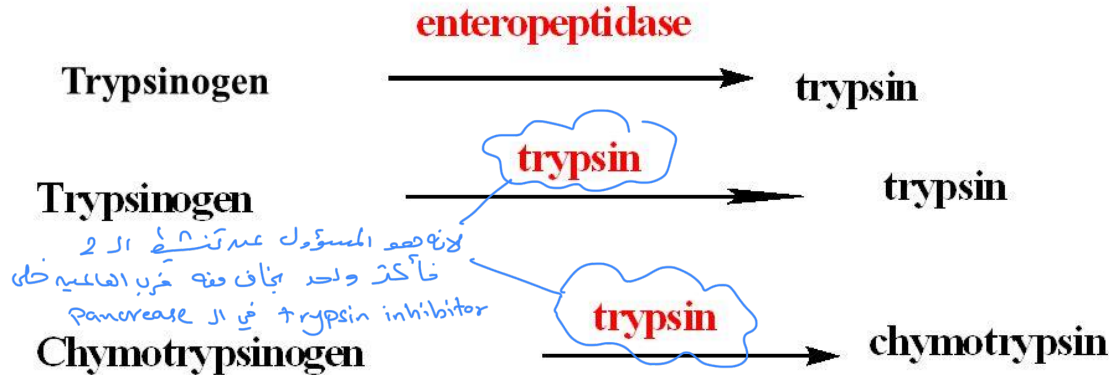


Fig. 41.18

- Trypsin is the common activator of all the pancreatic zymogens i.e activates chymotrypsinogen into chymotrypsin and pro-carboxypeptidase into carboxypeptidase and proteases into elastase.



الله أكبر

الله أكبر

الله أكبر

لا إله إلا الله

الله أكبر

الله أكبر

الله أكبر

والله الحمد.

Acute Pancreatitis

عنا فيه مشكلة الانزيمات ابي تم اكلها

- It is important these enzymes only become active in the intestinal tract otherwise if they were secreted in an active form they would digest the pancreas itself.
- They cannot be activated in the pancreas due to the **presence of a trypsin inhibitor**.
- The enzymes **become active when they meet trypsin** that is already in the intestinal tract so if the inhibitor prevents active trypsin until the intestine → then it also prevents the other proteolytic enzymes becoming active.

لو انا sphincter of oddi مسكر لاي سبب (عندما بيبي) (tumor) وال cck بيحفز ال pancreas غشاه يفرز lipase enzyme وال sphincter مسكر شيفل الانزيمات تفرز وتختزن في pancreas وحنا فيه trypsin inhibitor وحتيكون trypsin داخل pancreas
↓
activation of enzymes
↓
حتملك دمج pancreas ل

- This means the **pancreas can start to digest itself**. This is called acute pancreatitis

Pancreatic secretion

The following enzyme **breaks down carbohydrates**

- **Pancreatic amylase**

- This breaks down carbohydrates to disaccharides and trisaccharides

Fats are **broken down** by:

- **Pancreatic lipase**

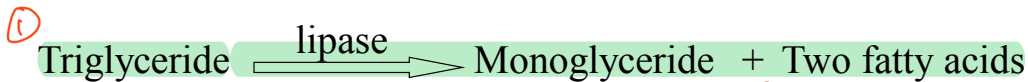
- This breaks down fat to fatty acids and monoglycerides

- **Cholesterol esterase**

- This breaks down cholesterol compounds

- **Phospholipase**

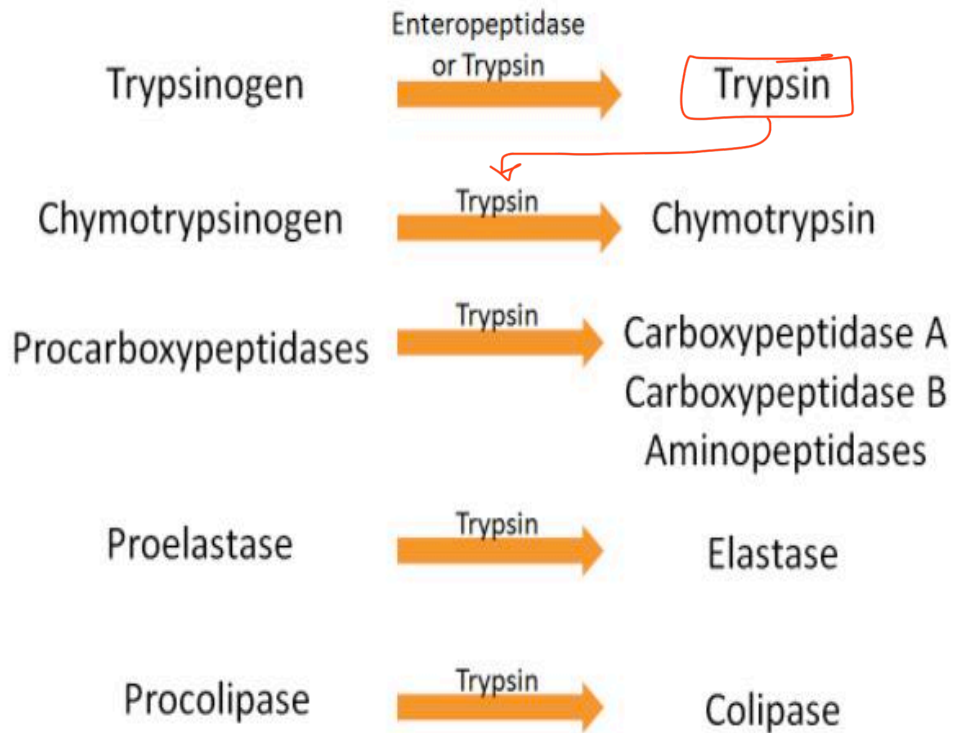
- This splits fatty acids from phospholipids



② or fat يتركز في شكل phospholipids ، في أنزيمات مختصة

- Lipase digestion requires the presence of a pancreatic protein co-factor (**colipase**).
لأن Lipase يحتاج ليتمدد بـ Co-factor وهو Lipase

- Secreted from pancreas as pro-colipase



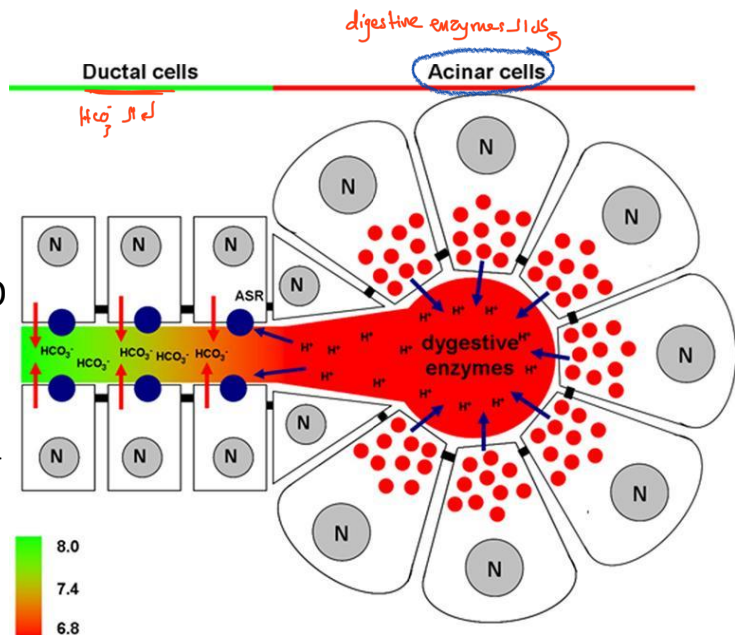
DIGESTION BY PANCREATIC ENZYMES

- Starch digestion
 - Remaining starch is digested in intestine by pancreatic amylase
 - Digestion same as in the mouth

STARCH > AMYLASE > DISACCHARIDES

Bicarbonate and the pancreas

- Secreted from the epithelial cells of the ducts that lead to the acini
- Increased secretion of pancreatic enzymes = increased secretion of bicarbonate
- Bicarbonate is made in the cells (very similar to in the red blood cell)
 - CO_2 diffuses into the epithelial cell under the action of carbonic anhydrase = $\text{CO}_2 + \text{H}_2\text{O} = \text{carbonic acid (H}_2\text{CO}_3) = \text{HCO}_3^- + \text{H}^+$
 - Bicarbonate excreted into the lumen of the duct
 - Leaves high amounts of H^+ in the cell so Na^+ move into keep pH neutral
 - The movement of Na and HCO_3 causes an **osmotic gradient** which causes osmosis of water into the pancreatic duct



1. Water (H_2O) and carbon dioxide (CO_2) combine under the influence of carbonic anhydrase (CA) to form carbonic acid (H_2CO_3).
2. Carbonic acid dissociates to form hydrogen ions (H^+) and bicarbonate ions (HCO_3^-).
3. The H^+ are exchanged for sodium ions (Na^+) by an antiporter. Sodium ions are removed by the Na^+-K^+ pump.
4. The HCO_3^- are transported into the intercalated ducts in exchange for Cl^- , which return to the lumen by a channel. Sodium ions and H_2O follow the HCO_3^- into the ducts.
5. The ions and H_2O move through the intercalated duct toward the interlobular duct.

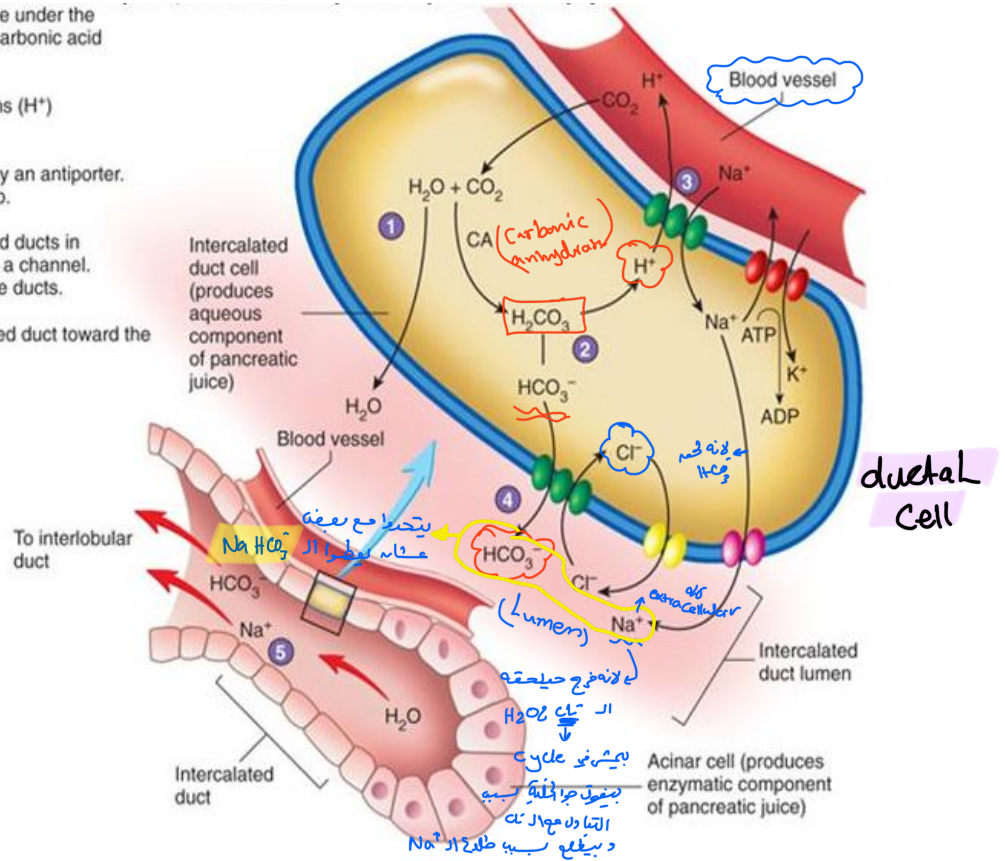
⊛ السطحات التي يتطلع :

1] H_2O

2] $NaHCO_3$

3] Na^+

الذي يحفز هذا السطح هو **secretin**



Regulation of pancreatic secretion

Three things stimulate pancreatic secretion

- **Acetylcholine** - from the enteric nervous system and parasympathetic nerves from the autonomic nervous system
- **Cholecystokinin** - secreted from the **duodenum** and **jejunum** mucosa when food enters the small intestine (lipid, stretch)
- **Secretin** - secreted from the duodenum and jejunum mucosa when highly acidic food enters the small intestine

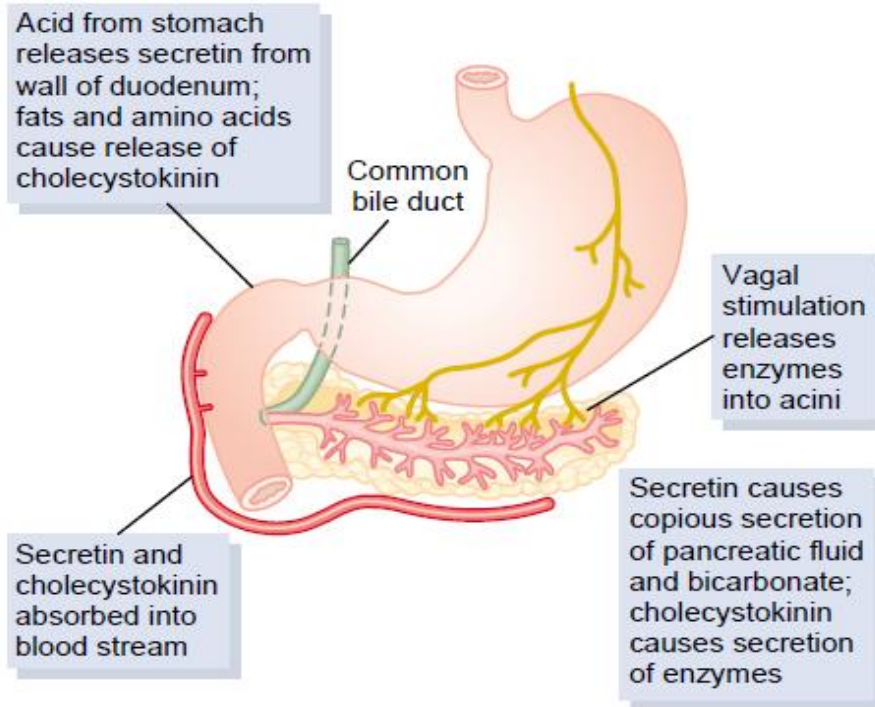
- Acetylcholine and cholecystokinin stimulate the **acinar cells** → produce digestive enzymes
- Secretin creates large amounts of bicarbonate and water secretion → this helps move the digestive enzymes from the acinar cells into the ducts.

When these enzymes are secreted together → the effect is much greater than a large quantity of just one enzyme (they help one another to cause even more secretion)

Secreted in a cephalic, gastric and intestinal phases like gastric secretion

Pancreatic secretion is greatest during the intestinal phase due to large amounts of secretin

Regulation of pancreatic secretion



THE BILIARY SYSTEM

- Bile is a non-enzyme solution secreted from **hepatocytes** (liver cells).

- The key components of bile are:

- Bile salts for fat digestion

- Bile pigments (bilirubin)

- Cholesterol

- Phospholipid - H_2O - electrolyte.

- Bile acids are steroids that combine with A.A to form bile salts.
- Bile salts have polar side chains to allow them to interact with both lipids and water, creating **water soluble droplets**.

⊗ الى بيض الـ fat ينفذ به carbohydrate & protein

• hydrophobic

↓

حلاتي الـ fat تتجمع مع بعضها ما يتوزع في الماء

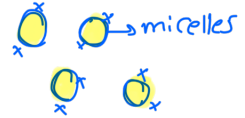
الـ digestion enzyme يتبادل تعمل

digestion به في مناطقها



عشان الـ enzyme تتحرك في وسطها

emulification
احولة من Large droplet الى Small droplet اخلوها بتقدر
تجبه في الماء . (تصير soluble).

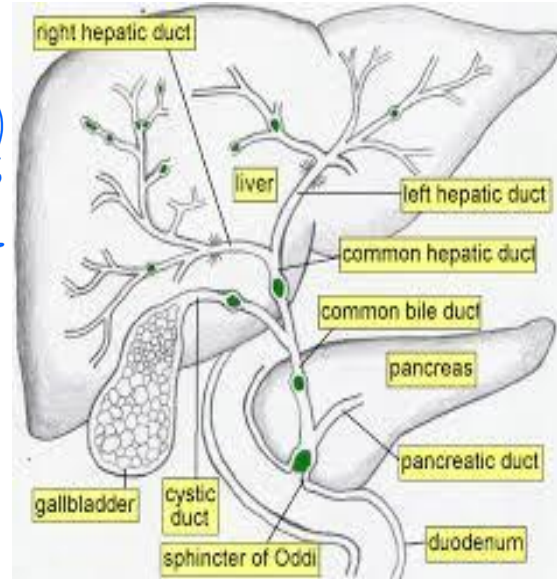


absorption بقدر يصير الي

صارت الـ surface area عتسا
اكثر عتسا تفسد بروتينا.

Functions of the Bile

- The liver secretes bile → ادره ما يتلفع هو بيلزك
- Bile functions:
 - Helps with fat digestion and absorption
Common hepatic duct في ويدونقوت في ال common hepatic duct
It does this by the bile acids (no enzymes which breakdown fat are contained within bile)
The bile acids emulsify fats (break large droplets into smaller droplets) and the formation of small micelles
This increases surface area for lipases from the pancreas to act on
The bile acids also help with absorption of digested fats through the intestinal mucosa
Bile also helps excrete waste from the body
Bilirubin and excess cholesterol and fatty acids
Neutralizes acid from stomach



(Bilirubin) is metabolic substance from RBCs.
 له يتقادم 120 يوم و بعدها يتكسر في الكبد و

Bile secretion

Bile is secreted in 2 stages by the liver

1. Initially it is **secreted by liver hepatocytes**

This secretion contains large amounts of bile salts and cholesterol

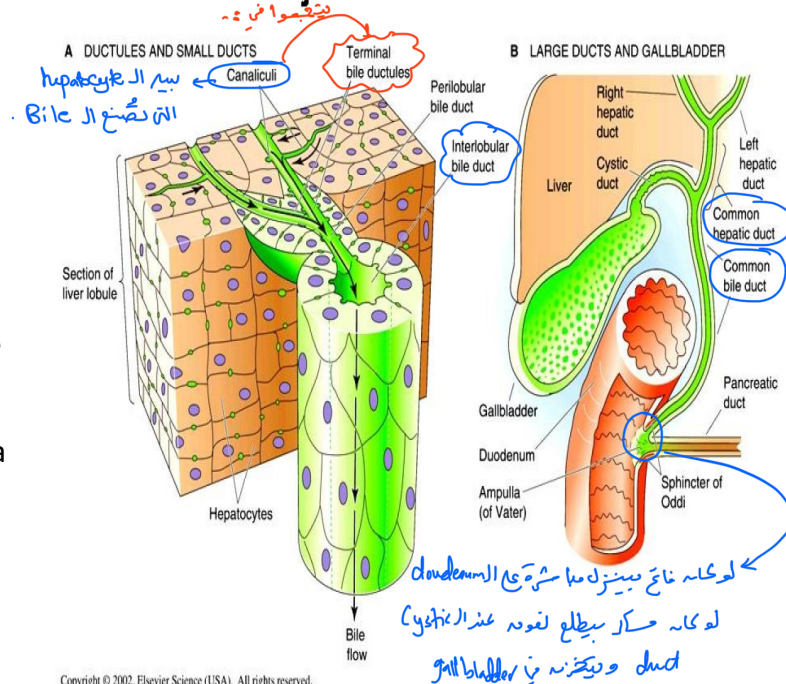
It is secreted into **bile canaliculi** (between hepatocyte)

2. In the second stage the bile in the canaliculi empties into the *terminal bile ducts* → the common *hepatic duct* → **common bile duct**

From here the bile is secreted directly into the duodenum or it can be sent to the gallbladder via the cystic duct for storage until it is needed (when the sphincter is closed)

As bile moves through the bile ducts the liver secretes a watery substances full of bicarbonate into the bile. This substances is secreted from the epithelial cells that line the ducts and ductules of the liver → this process is stimulated by secretin

Bile is secreted by the liver, stored in the gall bladder and ejected into the small intestine



The gallbladder

3. Bile is stored in the gallbladder until needed in the duodenum

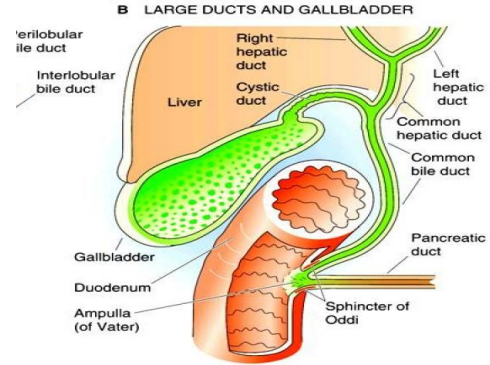
- As the bile is in the gallbladder it becomes

more concentrated

- This is because there is absorption of water and electrolytes through the gallbladder mucosa
- This is due to **active transport**

- Active transport** is the movement of ions (Na^+) from a low concentration to a high concentration across a membrane

- Sodium is moved from the bile into the gallbladder mucosa via active transport. As it moves Cl^- and water molecules follow (passive)



انتقال Na^+ من بلي إلى غشاء الخلية
من منخفض إلى مرتفع
نقل Na^+ من بلي إلى الخلية
نقل Na^+ من بلي إلى الخلية
نقل H_2O

نقل Cl^- و H_2O من بلي إلى الخلية
Passive diffusion

خلايا كبد البلي تزداد عند نسبة الكوليسترول في بلي
لذلك صار في اختلاف في بلي تيار
more concentrated بلي
لذلك صار في اختلاف في بلي تيار

- Reabsorption changes the composition of the bile
- The bile secreted from the gallbladder in the end has high concentrations of **bilirubin**, **cholesterol** and **lecithin**
- Lecithin is a fatty substance made of fatty acids and phospholipids

مكونات ال Bile

نسبهم زادت
لأنه سمي
ملي

← عاليه جداً
stones

Table 5.1: Composition of bile

	<u>Liver bile</u>	<u>Gallbladder bile</u>
Water	97.5 g/dl	92 g/dl
Bile salts	1.1 g/dl	6 g/dl
Bilirubin	0.04 g/dl	0.3 g/dl
Cholesterol	0.1 g/dl	0.3 to 0.9 g/dl
Fatty acids	0.12 g/dl	0.3 to 1.2 g/dl
Lecithin (phospholipid)	0.04 g/dl	0.3 g/dl
Na ⁺	145.04 mEq/L	130 mEq/L
K ⁺	5 mEq/h	12 mEq/L
Ca ⁺⁺	5 mEq/L	23 mEq/L
Cl ⁻	100 mEq/L	25 mEq/L
HCO ₃ ⁻	28 mEq/L	10 mEq/L

- **Bile Composition;**

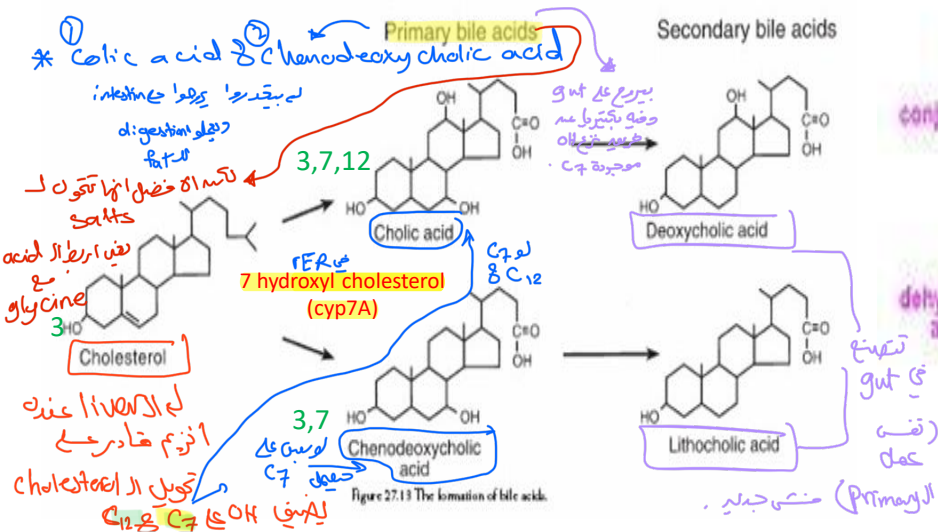
- Water (85%), الجريمية فيه
- bile salts (10%), (= acids), (Cholic, chenodeoxycholic, deoxycholic, and lithocholic acid)
- mucus
- pigments (3%), bile pigments e.g. bilirubin glucuronide
- fats (1%), such as Phospholipids (lecithin), cholesterol.
- 0.7% inorganic salts.

← من خلال الكال B. يتخلص من حرارة
وعواد زيادة في جسم
+ يحل من خلاه digestion fat

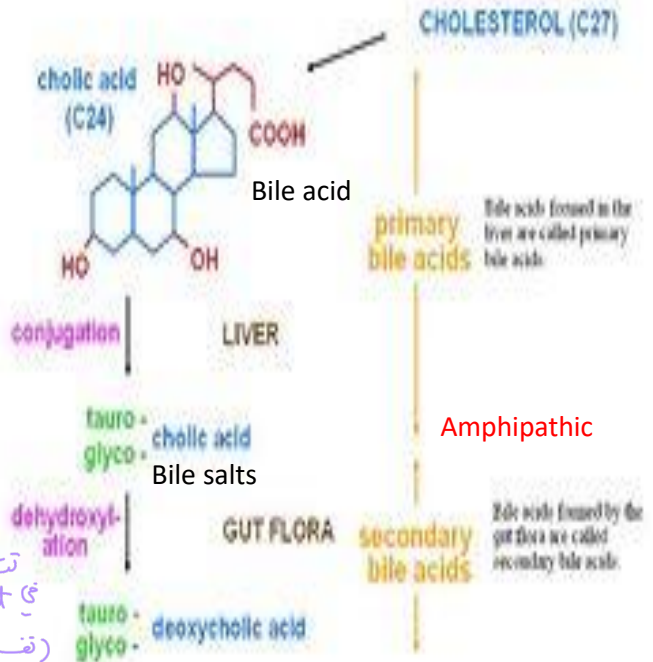
ما قام
التخلص منه جسم
صفرة في الجسم

Bile salts → کلہ ال چولسترل

- Bile salts are conjugated bile acids with either a molecule of glycine or taurine
- Bile salts are fully ionized (negatively charged) at physiological pH



SYNTHESIS OF BILE ACIDS

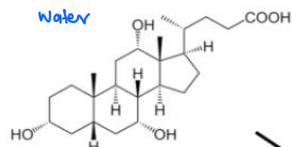


الPrimary) غنى جديد .

Bile Salts formation

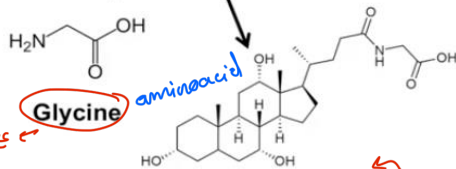
لو زادت نسبة ال acid ده Chenoodeoxycholic acid بيقول negative feedback
 7. hydroxyl cholesterol
 Primary bile acid تصنع في hepatocyte
 second تصنع في gut

hydrophobic & hydrophilic
 ↓
 interact with fat
 amphipathic group
 ↓
 interact with water



Cholic Acid

$pK_a \approx 6$



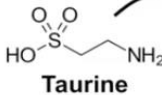
Glycine

Glycocholic Acid

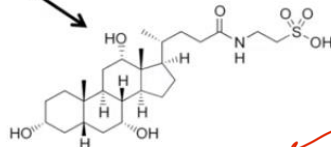
$pK_a \approx 4$

more acidic

Chenoodeoxycholic Acid



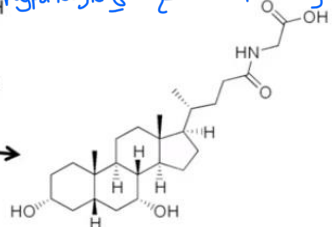
Taurine



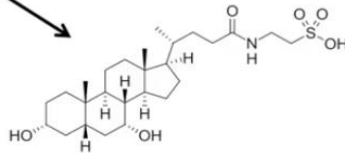
Taurocholic Acid

$pK_a \approx 2$

Glycine



Glycochenoodeoxycholic Acid



Taurochenoodeoxycholic Acid

Duodenum
 $pH \sim 6$

Conjugated Bile Acids

Potassium and Sodium Salts of Conjugated Bile Acids are known as Bile Salts

carboxylic group

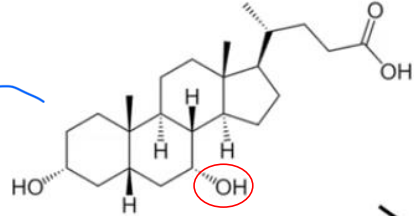
حسنتوا بكونهم
 رشتند له امولاجنٹ
 Ionized, more polar

لو ارتبطت
 عنزيم
 ال Na^+
 أو K^+
 ليقوه عنها

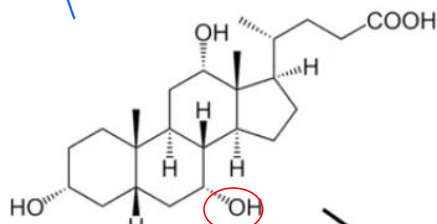
بعض ال acid
 حبيبت مع
 amino acid

مستعمله لعمل emulsification

Salt Bacteria



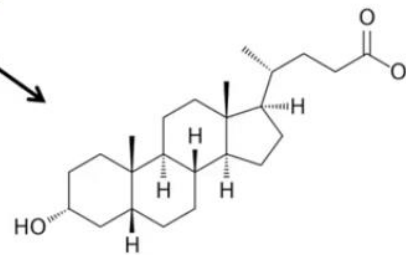
Chenodeoxycholic Acid



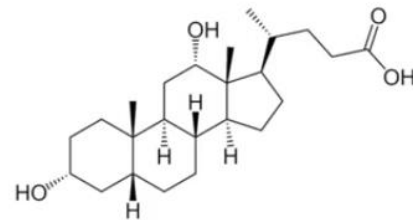
Cholic Acid

بازیدار OH الموجدع C7

Bacterial 7 α Hydroxylase

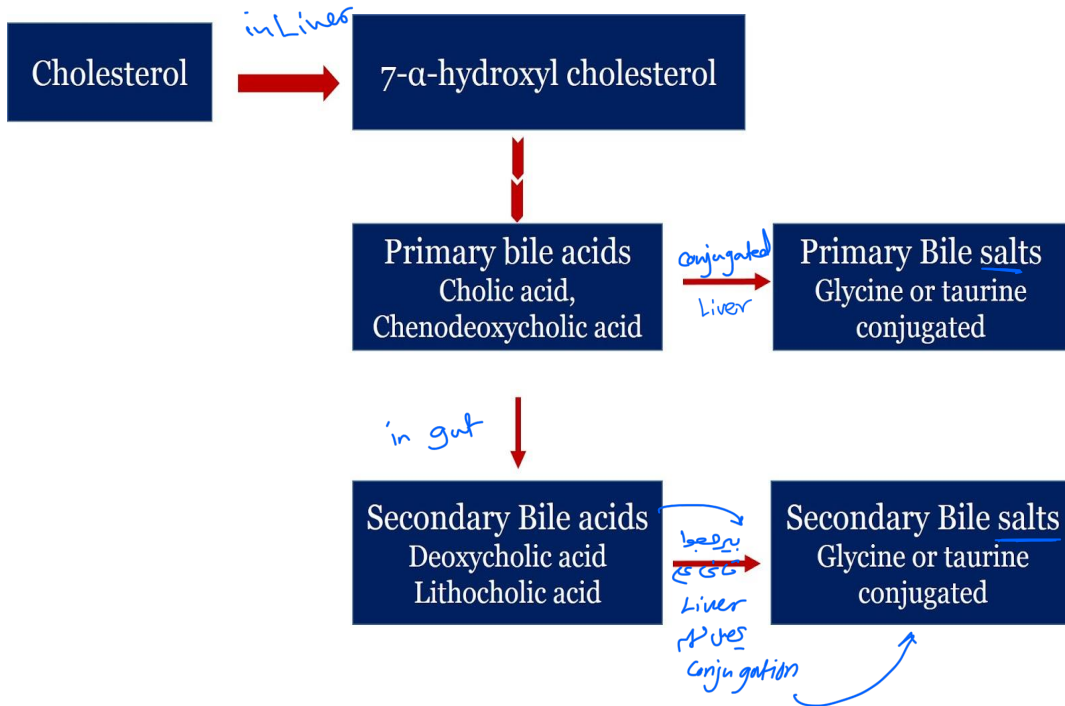


Lithocholic Acid



Deoxycholic Acid

Secondary Bile A



1 Secreted bile salts consist of 95% old, recycled bile salts and 5% newly synthesized bile salts.

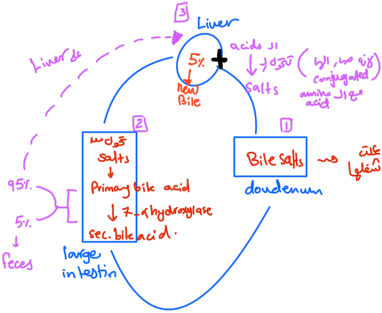
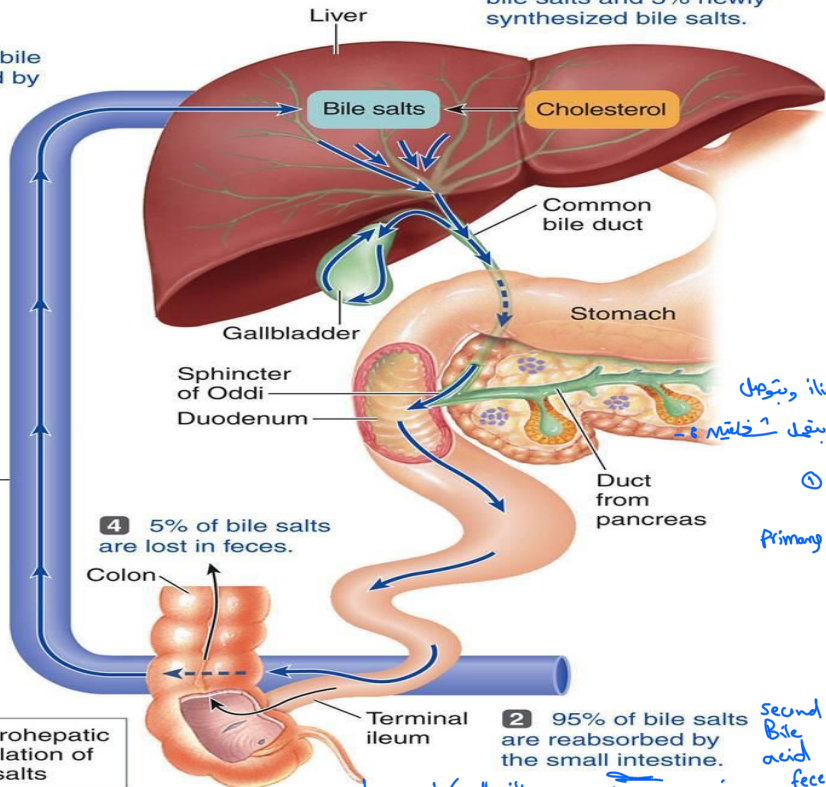
3 Reabsorbed bile salts are recycled by enterohepatic circulation.

4 5% of bile salts are lost in feces.

2 95% of bile salts are reabsorbed by the small intestine.

KEY

← = Enterohepatic circulation of bile salts



ال Bile salts مختلطة في ال small intestine وبتحول
لل large intestine ← ال large intestine بتعمل ١

١ Deconjugation: تحرير ال glycine
(amino acid) دسالة / دسالة لل Primary bile acid

٢ في بكتيريا أميبكسمة ال
إلى موجودة على ال

د تحول ال Primary Bile acid
Second Bile acid
5% من ال لا يزداد مع feces
95% من ال يمتص في ال small intestine
acids

transported ال ileum & jejunum

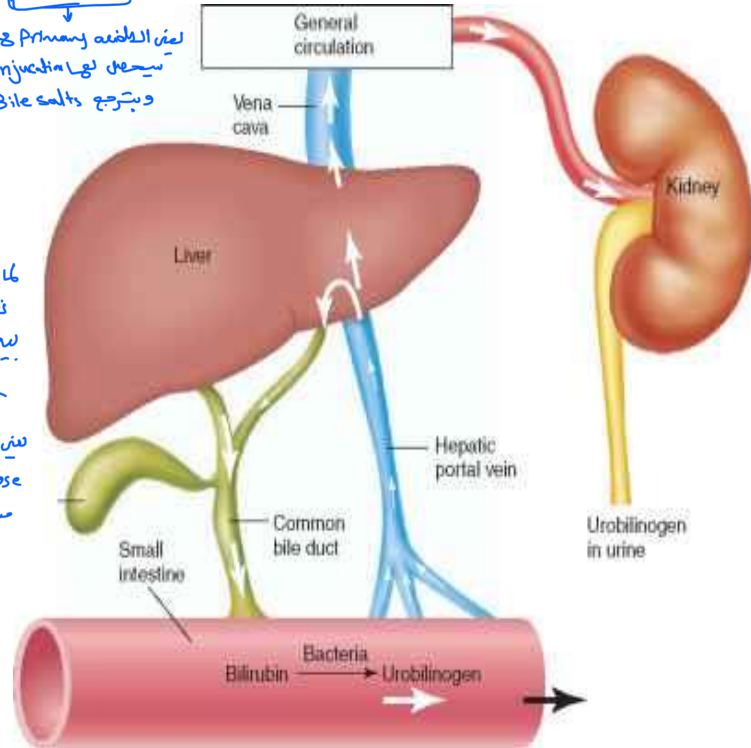
ينتقل في الدم ← ينقل مع الـ hepatic Portal vein
 5% دبالتي الـ Liver ما بد يصنع حبيبات. 95% القديم وحبيبات حبيباته.

Enterohepatic circulation

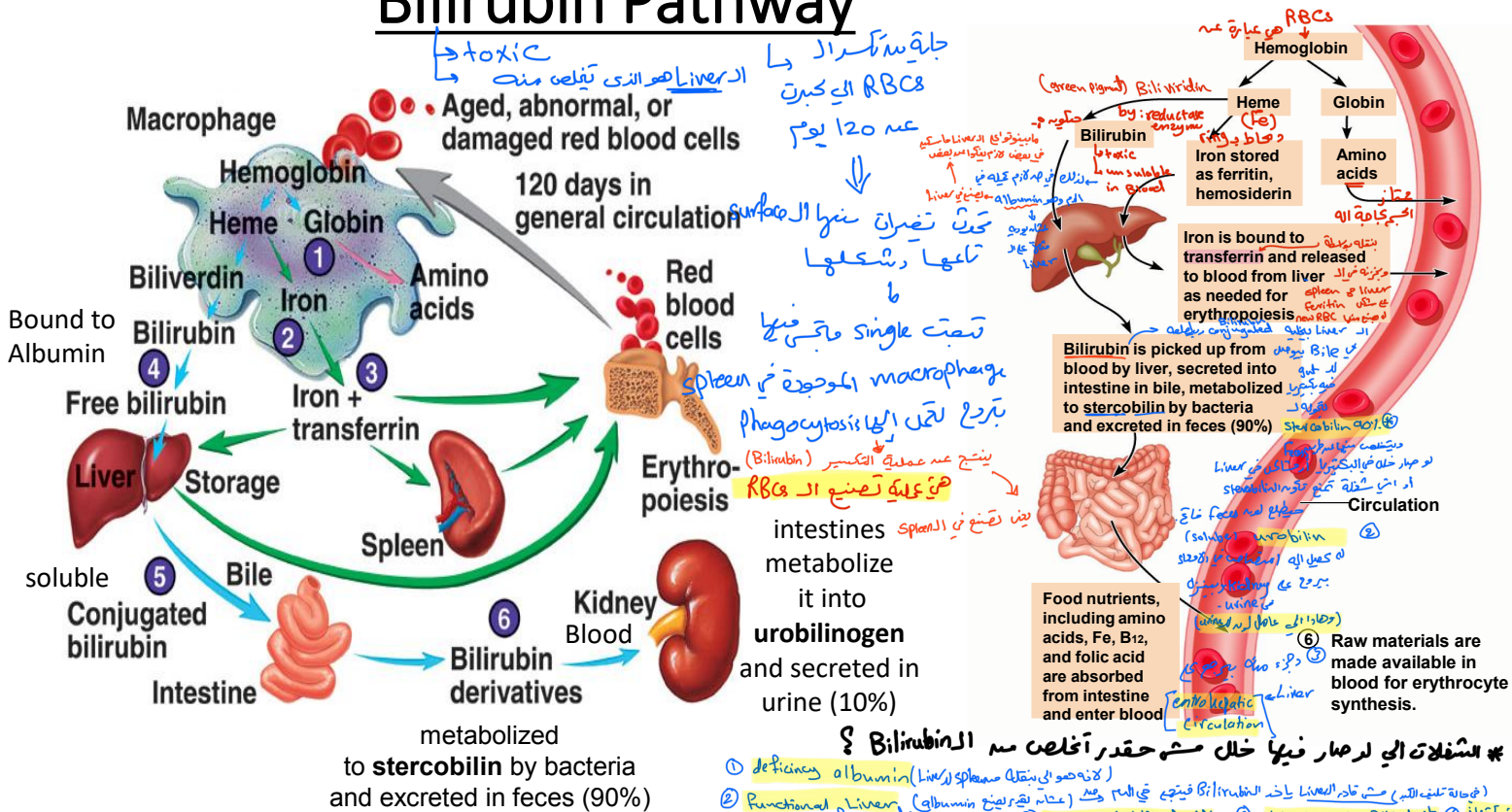


- **Enterohepatic circulation** refers to the **circulation** of biliary acids, bilirubin, drugs, or other substances from the liver to the bile, followed by entry into the small intestine, absorption by the enterocyte and transport back to the liver

ما نفع حبيبات في الدم
 نعرفت كم مصوبة
 بيشل لانه صا حبيبات
 مع الـ bile
 ↓
 في الدم اعطى
 dose
 من العلاج.

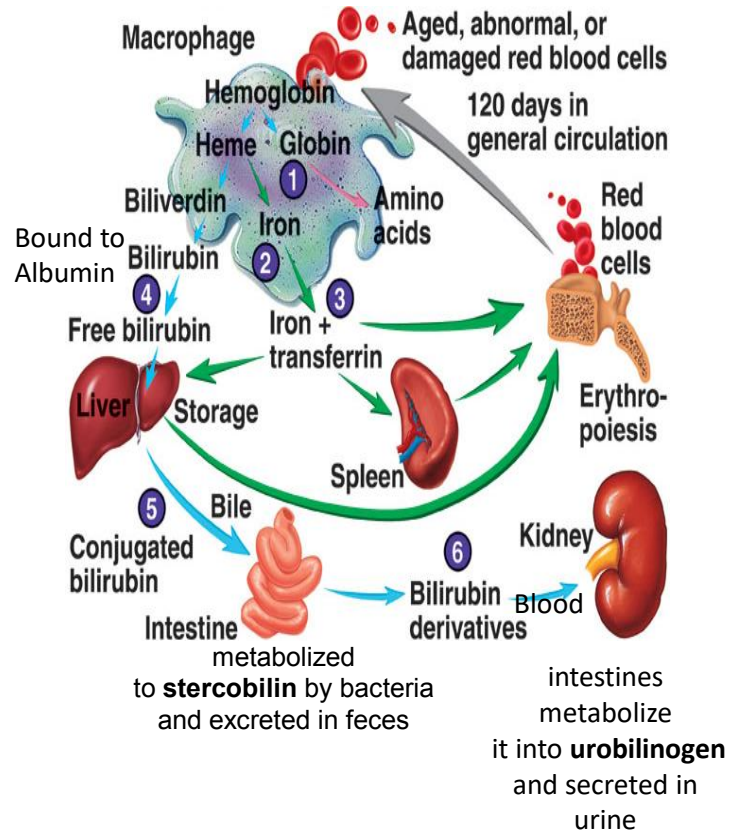


Bilirubin Pathway



Enterohepatic cycle

- Bilirubin is created through the breakdown of red blood cells
- Breakdown occurs in the spleen which is full of macrophages
- Haemoglobin is split to haem and globin
- Heme is broken down then to iron and amino acids
- The iron portion is transported in the blood as transferrin
- Amino acids are broken down into **biliverdin** which is broken down further to bilirubin
- The bilirubin is secreted from the spleen into the blood (it is carried by albumin as a transporter protein molecule)
- The bilirubin is absorbed by hepatocytes in the liver

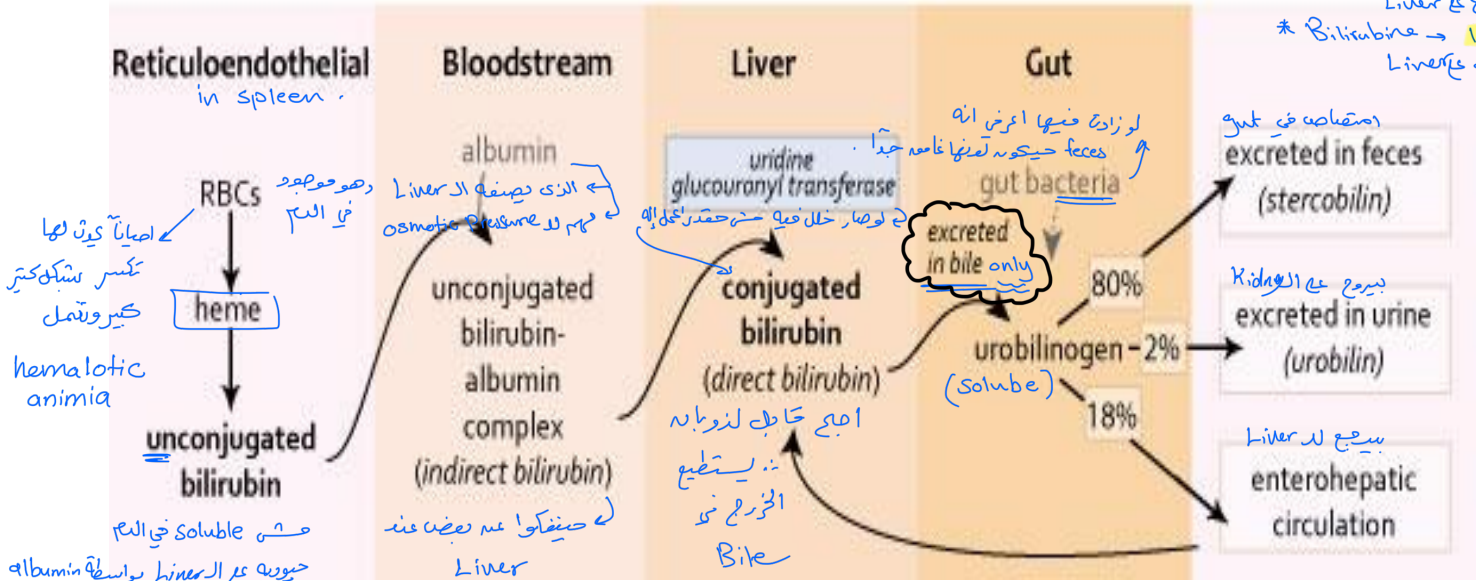


- Biliverdin (green pigment) is converted to yellow bilirubin by **biliverdin reductase** (with $\text{NADPH} + \text{H}^+$). These reactions occur in the reticuloendothelial system (spleen and lymph nodes). Bilirubin moves into the bloodstream in combination with albumin and then moves into the liver with the release of albumin

Bilirubin

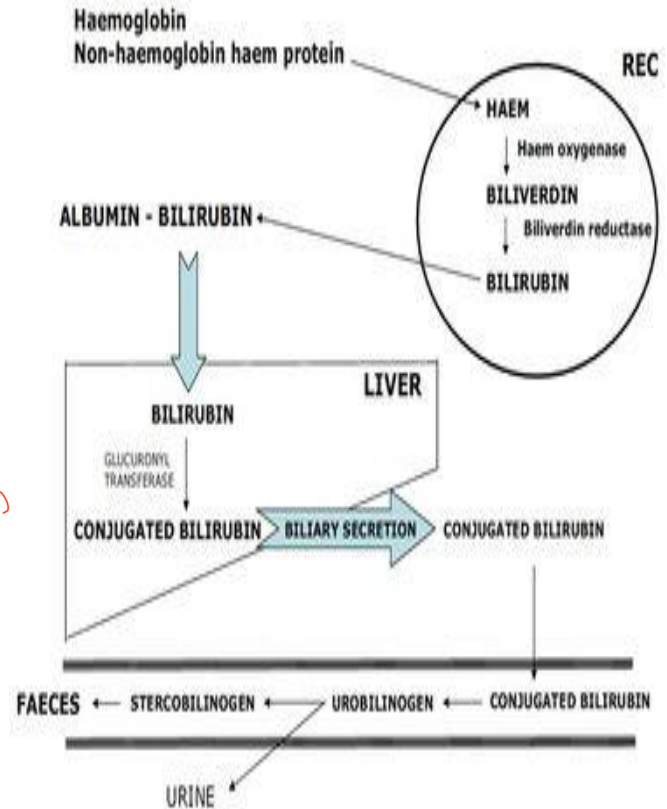
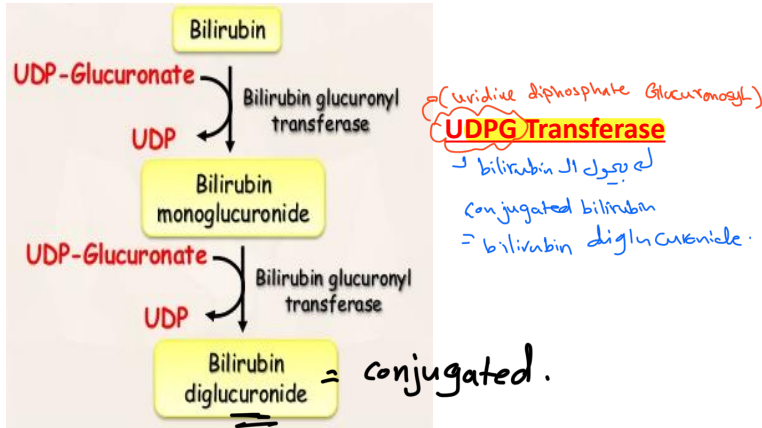
لا إله إلا أنت سبحانك انى كنت
الظالمين

- * Bile salts → 95%
يرجع إلى Liver
- * Bilirubin → 18%
يرجع إلى Liver



The Enterohepatic cycle

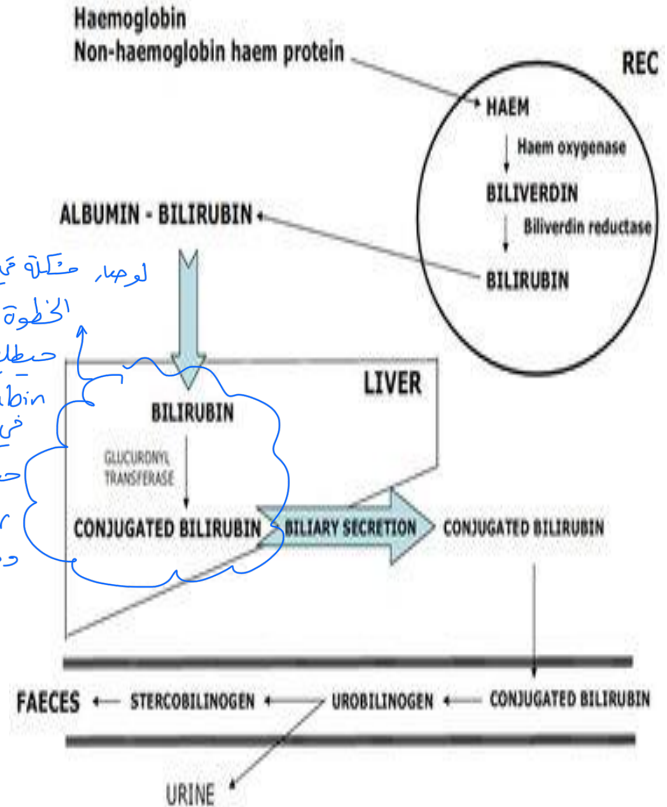
- Inside the hepatocyte (liver) the bilirubin and albumin molecule separate
- The bilirubin binds with **glucuronic acid** to form conjugated bilirubin (bilirubin glucuronide (BG))
- This conjugated bilirubin is excreted from the hepatocytes into the bile → intestines



اللهم صل وسلم وبارك على قودنا محمد

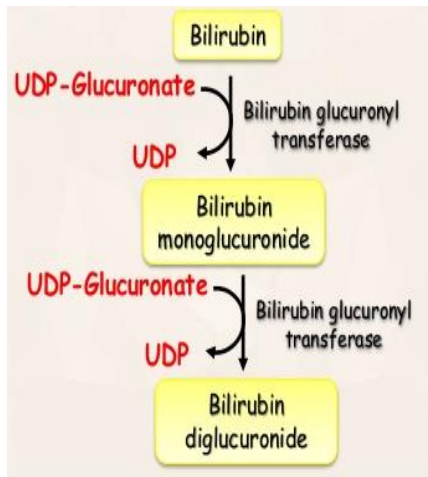
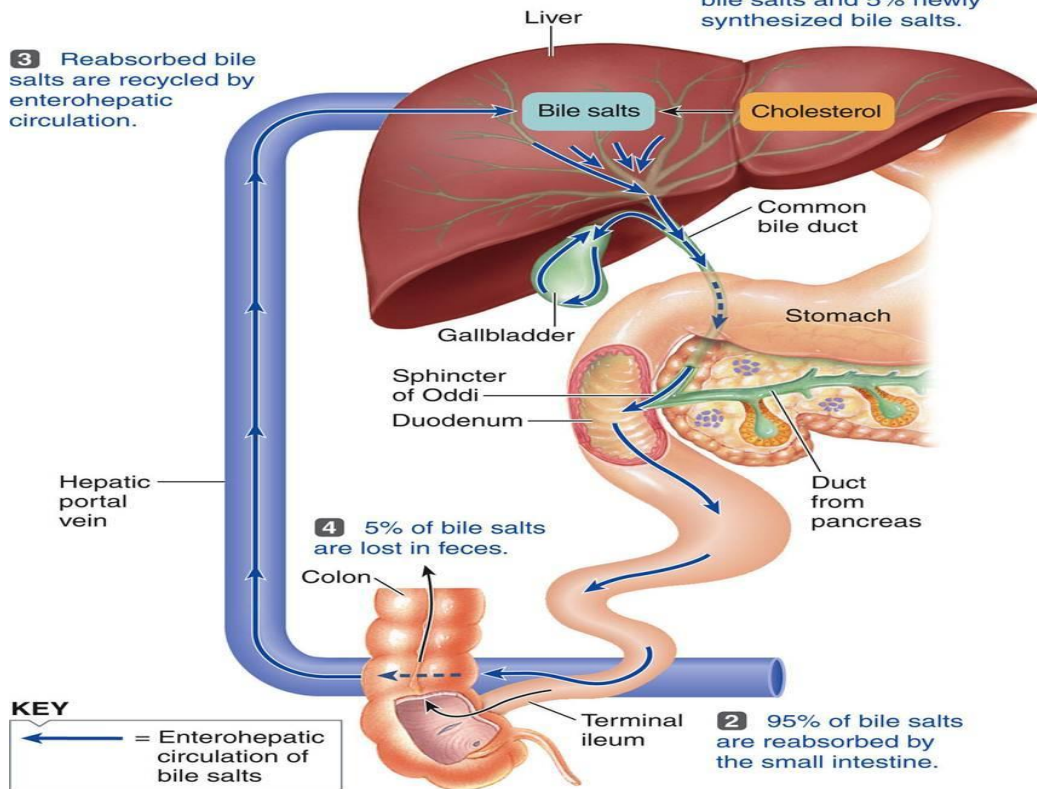
- Once in the intestine some of the conjugated bilirubin is converted into **urobilinogen** which is very soluble
- Urobilinogen is reabsorbed through the intestine to the blood. Some goes to the liver and is reexcreted into the blood and the remainder is excreted via the kidneys
- The urobilinogen that remains in the intestine is converted to **stercobilinogen** and excreted in the faeces

لوعاء مقلقة في هذه الخطوة من صطلع
Bilirubin في ال bile
صيرت في Liver
و صيرت في blood



3 Reabsorbed bile salts are recycled by enterohepatic circulation.

1 Secreted bile salts consist of 95% old, recycled bile salts and 5% newly synthesized bile salts.



المشاكل التي يمكن تصير:-

حقنه ٣ فوصان

Disease	BLOOD TEST	URINE TEST	STOOL TEST
Hemolysis (Bilirubin) BIL. ↑ RBCs له خلايا RBCs بنتاير قبل ما يصل او 120 يوم (conjugated bilirubin) BG ↑↑ HCT. ↓ + RBC ↓ + HB. (hematocrit) RBCs لانه تفسر عالي		BIL. ↑ Urobilinogen ↑ لانه تفسر RBCs كافيه ال Bilirubin ↑↑	<u>Stercobilin</u> ↑
Bile Duct Obstruction لانه ال Bile مش قادر يطالع في Intestine Conjugated Bilirubin ال حيرج في Blood BG. ↑		Urobilinogen ↓ BIL. ---- لانه مش قادر ماوصل منطقة ال Intestine	Acholic stool فائع حاله لونه
Hepatic Inflammation لانه مش قادر يفرز ال Liver BIL. ↑ BG. ↓ ↓ ↓ UPG-D transferase لانه في التهاب في Liver، مش قادر يطالع ال conjugated		Urobilinogen ↓ ↓ BIL. ↑ ↑ لانه مش قادر conjugated Bilirubin	Acholic stool
UDPG-Transferase BIL. ↑ BG. ↓ ↓		Urobilinogen ↓ BIL. ↑ ↑	Acholic stool
Bacterial Overgrowth لانه ال Intestine ال غشاه تافه Stone ال غشاه كثير غلظه	Normal	Urobilinogen ↑ ↑ ↑ BIL. ---- لانه بتضع كثير فكاه ال Stone غلظه	Very dark stool Stercobilin ↑ ↑

* ↑ Bilirubin in Blood → ↑ Bilirubin in extracellular fluid → jaundice.

Stimulation of the gallbladder

انا محتاجة ال Bile

له مش عناء الهضم ال Fat بي
انما ضي كثير مواد لازم اتخلص منها

PhosphoLipid و Cholesterol و Bilirubin

ليه لو اتهم ال انها ما بيقبل مشكله ، ب بيصير ما تاكل كميته
كبيرة من Lipid لانه ما في Gall bladder خزينة

ال Bile

- Stimulated when digested food enters the duodenum → particularly if it is a fatty food
- This causes a rhythmical contraction of the gallbladder wall
- There is relaxation of the sphincter of Oddi (where the common bile duct enters the duodenum)
- ① **Cholecystikinin** is a big stimulus for gallbladder contractions also
 - Remember this is released when fatty foods enter the duodenum
- When the duodenum is very full of fatty substances the gall bladder can empty completely within 1 hour
- The gallbladder can be made to contract through ② **parasympathetic stimulation** from the enteric nervous system and the autonomic nervous system

receptor لها

② G.B عمل contraction لا

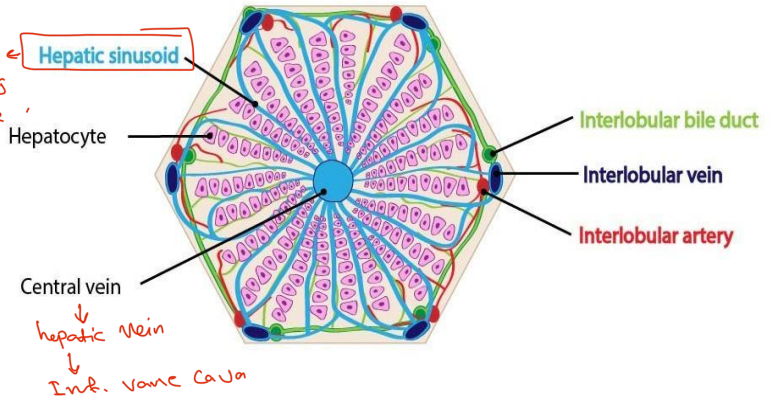
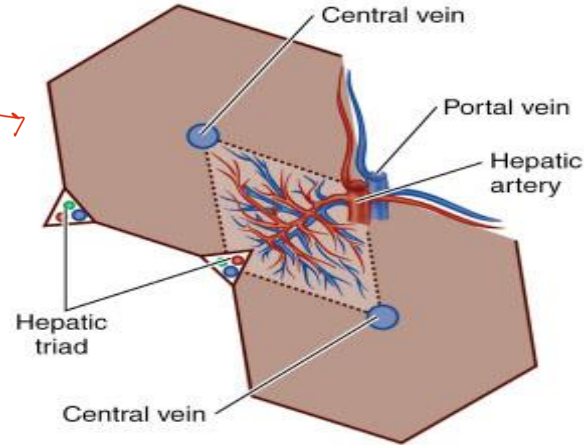
Gallstones

- As the bile becomes concentrated in the gallbladder this causes an increased concentration of bile salts, **lecithin** and **cholesterol** → لو تترسب د تجميع حصى Stone
- Cholesterol is normally insoluble in water but **bile salts** and **lecithin** help to keep it in solution → amphipathic
- Under abnormal conditions the cholesterol may precipitate out of solution and cause cholesterol gallstones → cholesterol ان تترسب و جمع حصى و تسمى cholesterol gallstones
 Insoluble حصى و جمع حصى و تسمى cholesterol gallstones
 Gallstones Cholesterol راتة الكلى و جمع حصى و تسمى cholesterol gallstones
 Gallstones Cholesterol راتة الكلى و جمع حصى و تسمى cholesterol gallstones
- The amount of cholesterol in the bile is determined by the amount of fat a person eats ← Gallstones Cholesterol راتة الكلى و جمع حصى و تسمى cholesterol gallstones
- If a person eats a lot of fat → the amount of cholesterol will be higher → more likely to precipitate out of solution to cause cholesterol gallstones
- If these gallstones move out of the gallbladder to the bile ducts → contraction of the muscle layer of the bile duct to try and push the stone along → felt as pain



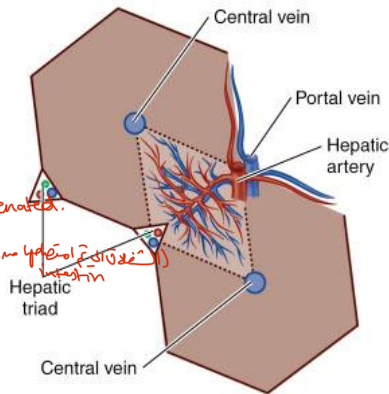
The liver

- The largest organ in the body
- **Made up of lobules**
- Lobules are formed around a **central vein**
- The central veins enters into the hepatic vein and then the vena cava
- Each lobule has **cellular plates** ← *مصفوفة الكبد*
which radiate out from the central vein - contain the hepatocytes
- **Bile canaliculi** lie between each cellular plate
- Bile canaliculi empty into the bile ducts
- Between cellular plates lie **hepatic sinusoids**

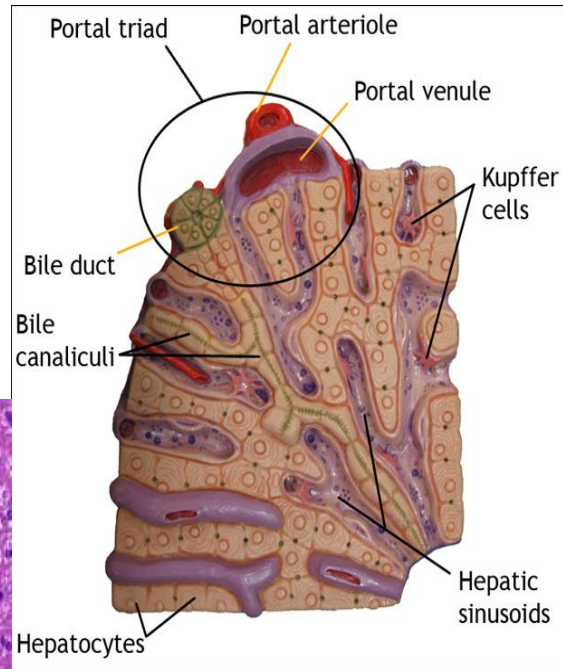
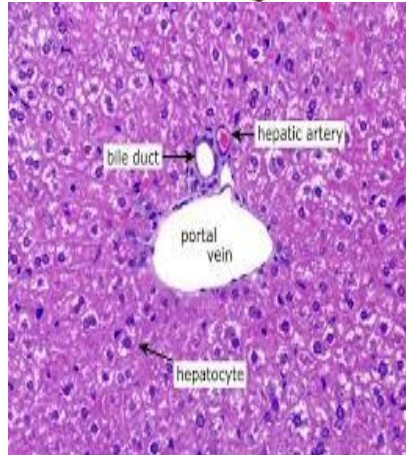


- The portal triad is the entrance to the liver lobules.
- A **portal triad** is the combination of:

- The hepatic artery 25% oxygenated.
- The portal vein (75%) nutrients (غذاء) (غذاء الدم)
- The common bile duct → بضع
قناة
Bile
- Lymphatics
- A branch of the vagus nerve



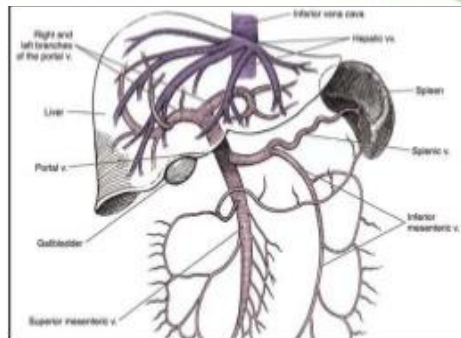
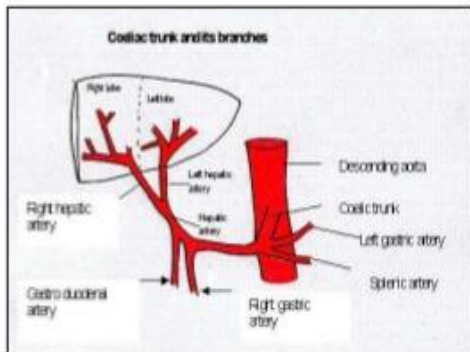
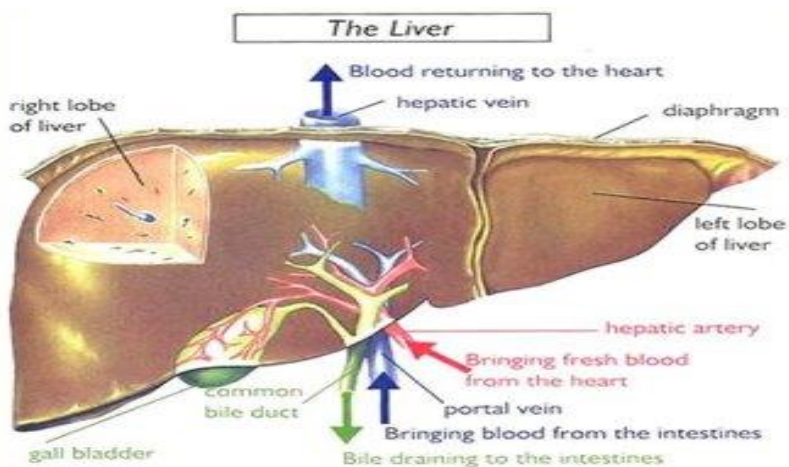
- Each portal triad is surrounded by lobules with hepatocytes
- The portal veins bring blood to the liver
- The central veins drain blood via the hepatic vein from the liver
- The pressure in the portal vein is 9mmHg and 0mmHg in the hepatic vein



Blood supply

Arterial supply is by portal vein & hepatic artery.

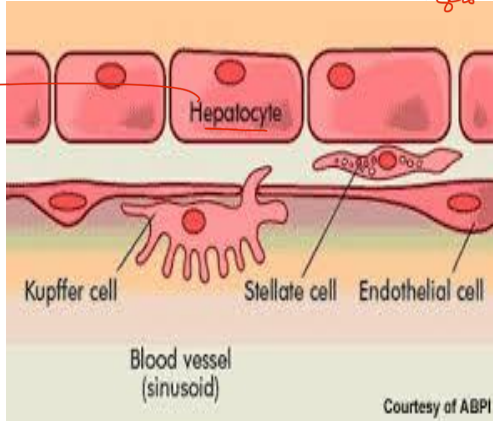
Venous drainage is by hepatic veins which drain into inferior vena cava.



= Blood Vessels

- The sinusoids and hepatocytes lie close together so the cells are continuously exposed to portal venous blood
- The sinusoids have 2 different types of cells:
 - Endothelial cells (large Pors)
 - Kupffer cells (macrophages)

تتخلص من الخلايا السامة
toxic cells



يحدث فيها تصنيع سكرات
كبدية
فأما فتحاتها فهي
exchanger

- The Kupffer cells carry out phagocytosis of bacteria that is present in the hepatic sinus blood
- The endothelial cells have large pores
- Pores mean large molecules can escape
- Lymphatics drain these spaces

Liver Function

مضغ البروتينات →

- Removing metabolic waste products, hormones, drugs, and toxins

Fat

Bilirubin مثل ال

Ammonia → urea (water soluble)

في ال urine

less toxic → more toxic
soluble → insoluble " "

- Producing bile to aid in digestion

- Processing nutrients absorbed from the digestive tract

- Storing glycogen, certain vitamins, and minerals (Iron and vitamin D, A) + Blood vessels

vit. lipid soluble

في خزنة جز في الدم ختمكم

- Maintaining normal blood sugar

glycogen
glucose
في الدم من الجلوكوز في شكله glycogen
في الدم من الجلوكوز في شكله glycogen

extra Blood of Liver

في حالة نزل ضغط أو قلة الدم في الكبد

- Synthesizing plasma proteins, albumin, and clotting factors, Fibrinogen, globulin.

Blood vessel في ال osmotic pressure
منه يخلق له ضغطا قابلا

coagulation

- Producing immune factors and removing bacteria

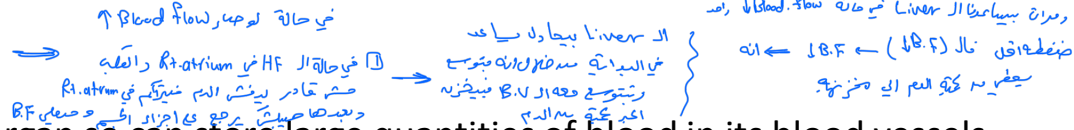
- Removing senescent red blood cells from the circulation

- Excreting bilirubin → conjugated

في ال urine
في ال urine

Functions of the liver

- Storage: الـ Liver مليان بـ B.V فيز ركب
سرور Blood الموجود في مب



The liver is an expandable organ so can store large quantities of blood in its blood vessels
 Normally it holds 10% of a persons total blood volume

In right sided heart failure there → the blood cannot move from the right ventricle to the lungs → it starts to build up in the venous system → this causes pressure on the liver and makes it expand → the liver holds an extra 0.5L to 1L of blood when this happens
 The extra blood is stored in the hepatic vein and sinusoids and causes the liver to increase in size

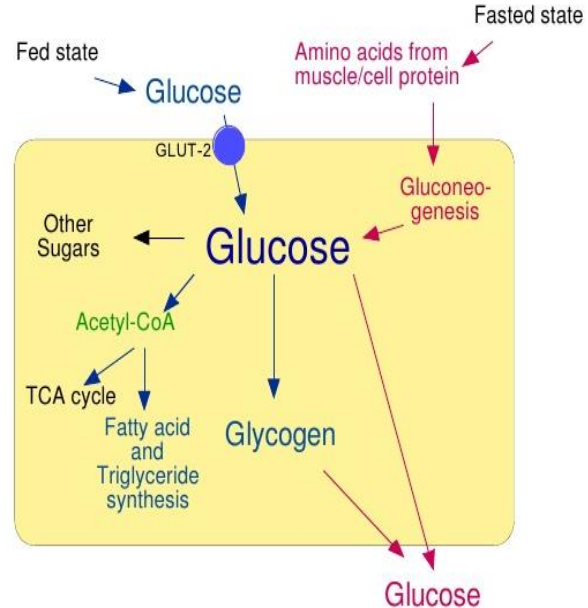
When a person's blood volume is low the liver can release stored blood to prevent preload decreasing which → a decrease in blood pressure

Metabolism in the liver - Carbohydrates

The liver helps the metabolism of carbohydrates by carrying out the following functions:

- Stores large amounts of glycogen
- Converts galactose and fructose to glucose
- Gluconeogenesis (makes glucose)

Liver and Glucose Metabolism



The liver **helps to maintain a normal blood glucose level**

Glycogen storage allows the liver to remove excess glucose from the blood → store it → and return it to the blood when blood glucose levels fall below normal. (This occurs after a meal when blood sugar levels rise and the pancreas secretes insulin)

- The blood glucose enters the liver via the portal vein and is taken into the hepatocytes
- The insulin acts on the glucose molecules to make them bind together to form a polysaccharide (GLYCOGEN)

This requires the enzyme **glycogen synthase**

- When blood glucose levels are low **GLUCAGON** is released which causes the liver to break down glycogen to glucose

(glycogenolysis) break down of amino acid

Metabolism in the liver - Carbohydrates

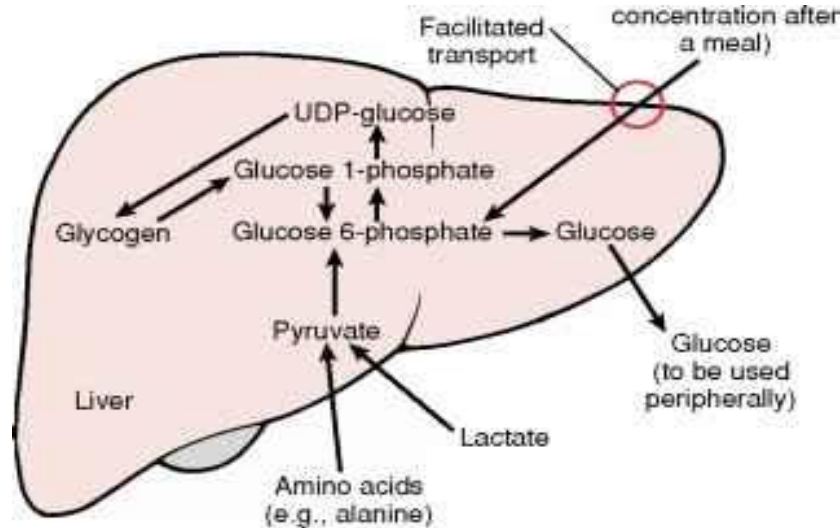
GLUCONEOGENESIS

- This is when glucose is made from non-carbohydrate substances
- It is made from lactate, glycerol (from fat breakdown) and amino acids
- This process occurs when blood glucose falls below normal levels

GALACTOSE AND FRUCTOSE TO GLUCOSE

Occurs by hydrolysis

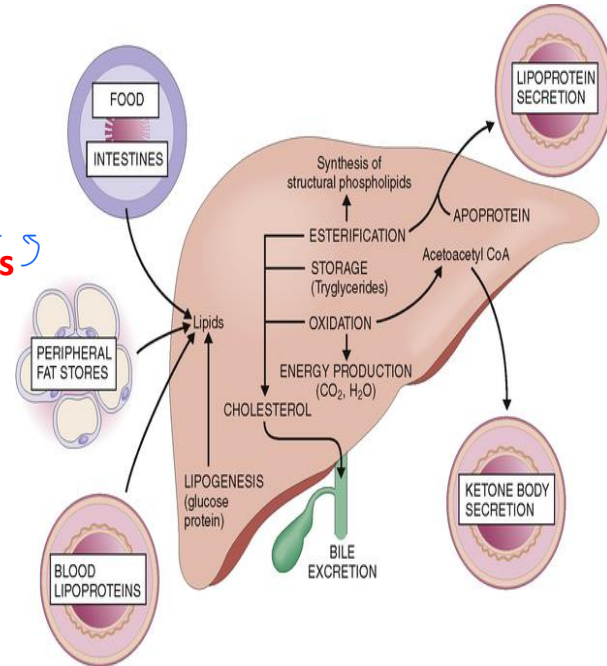
This means the fructose and galactose large “sugar” molecules are broken down to smaller sugar molecules (glucose) by water which break the bonds!



Fat metabolism

The liver affects fat metabolism by:

- **Causing breakdown of fatty acids to create energy**
 - This occurs in the mitochondria
 - Caused by **beta oxidation**
 - This causes the fatty acid to break into glycerol and fatty acids *estrogen & Progesterone*
Bile salts & bile acids
- **Synthesis of cholesterol, phospholipids and **lipoproteins**** *HDL, LDL*
 - Cholesterol synthesized in the liver is converted to bile salts
 - The rest of the cholesterol is transported via lipoproteins and carried to the blood tissues
 - Phospholipids also are created in the liver and transferred by lipoproteins
 - Cholesterol and phospholipids are used to form cell membranes
- **Synthesis of fats from proteins and carbohydrates**



Protein metabolism

The liver helps with **protein metabolism** by:

- **Deamination of amino acids** deamination في حالة زيادة عدد ال amino acid → ammonia نم تصنع ال ammonia
liver ↓ urea → excreted in urine
- This means when the body has **too much protein amino acids** are broken down further to create **ammonia**
- Ammonia is toxic to the body and so it is *eliminated as waste as urea*
- **Formation of urea** for the removal of ammonia from body fluids
- If the liver did not form urea from ammonia → the level of ammonia could get too high and cause a coma
- **Formation of plasma proteins** (transport molecules such as albumin)
اشهر ال albumin
 - When plasma protein levels fall → this causes the liver to increase the mitosis of hepatic cells and the liver increases in size to increase the amount of plasma proteins
 - If there is liver failure the amount of plasma proteins (especially albumin) falls which causes oedema

Other functions of the liver

- Storage of vitamins -Vitamin A, D and **B12**
- **Storage of ferritin**
 - Second largest storage of iron after haemoglobin
 - Stored as ferritin
 - Ferritin is made and stored in the hepatocytes
 - When iron levels in the blood become low the hepatocytes release the iron from **ferritin**
- **Formation of coagulation factors**
 - Fibrogen, prethrombin, Factor VII and **vitamin K**
 - Vitamin K is used to make prothrombin, factor VII, IX and X
 - When vitamin K is low there are less **coagulation** factors and this prevents blood coagulation
- **Removal of drugs and other substances**
 - Can detoxify drugs and secrete the waste products into the bile e.g. penicillin
 - Main route for excreting calcium is by excretion by the liver into the bile and lost in faeces

مخزن حديد في الكبد

يتم تصنيعه بكميات كبيرة في الكبد
أو في الكبد.

Jaundice

This is the yellow tint of body tissues

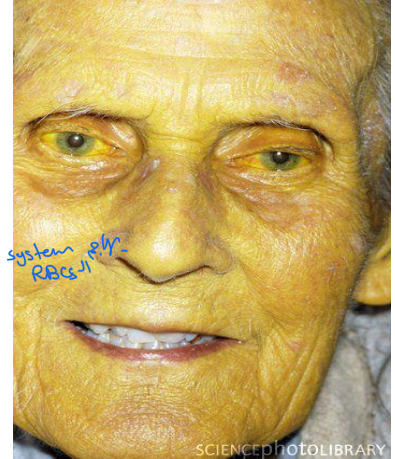
Due to excess quantities of bilirubin in extracellular tissues - can be unconjugated or conjugated

Normal levels of bilirubin are **0.5mg/dl plasma**

Skin starts to turn yellow at bilirubin levels of **1.5-2mg/dl plasma**

Causes

- 1. Increased **destruction of red blood cells** (haemolytic anemia) → increased breakdown products → increased bilirubin quantities
 - Called haemolytic jaundice
 - Liver is normal here
- 2. **Obstruction of the bile ducts** or **damage to the liver** which stops normal amounts of bilirubin being excreted into the intestine
 - Called obstructive jaundice
 - Can be due to gallstones or tumours



فَسَحٌ فِي الْخَلَاِ

Cirrhosis and other liver diseases

CIRRHOSIS:

- When the liver cells are destroyed and replaced by **fibrous tissue**
- The fibrous tissue contracts around the blood vessels and restricts their flow
- Occurs in **alcoholism**

الناسه الي بيشربو كحول

