

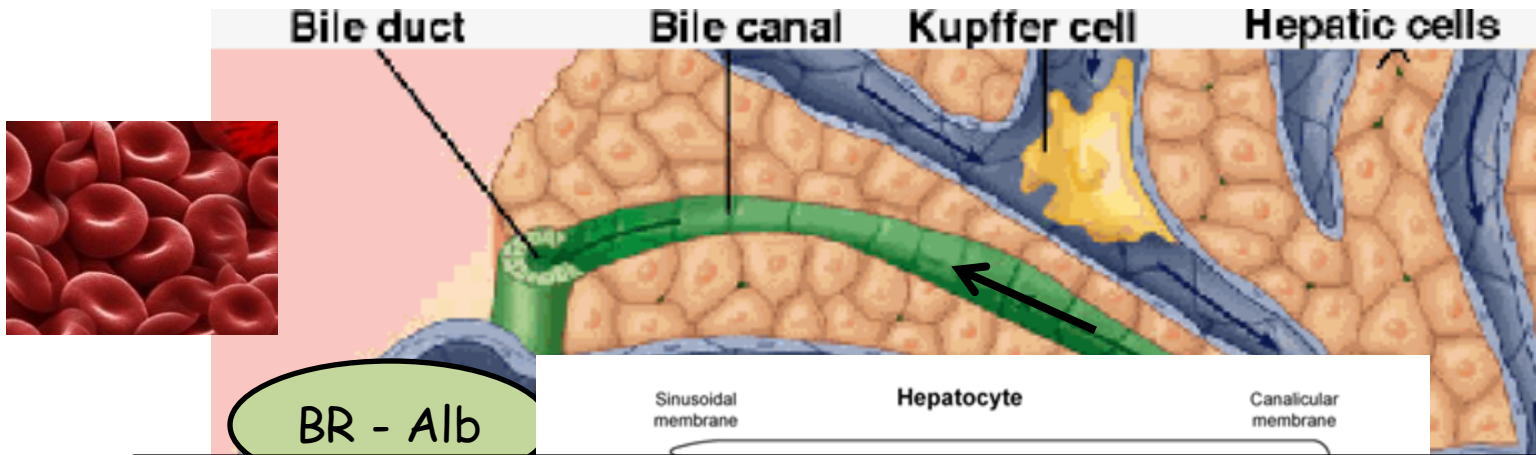
# Bilirubin Physiology - WYNTKFTB

- Bilirubin metabolism
  - Unconjugated
  - Conjugation
  - Excretion
- Enterohepatic circulation
- Implication of bilirubin metabolism
  - Urine
  - Stool
- Understand the metabolic pathway as related to the disease state of **JAUNDICE**



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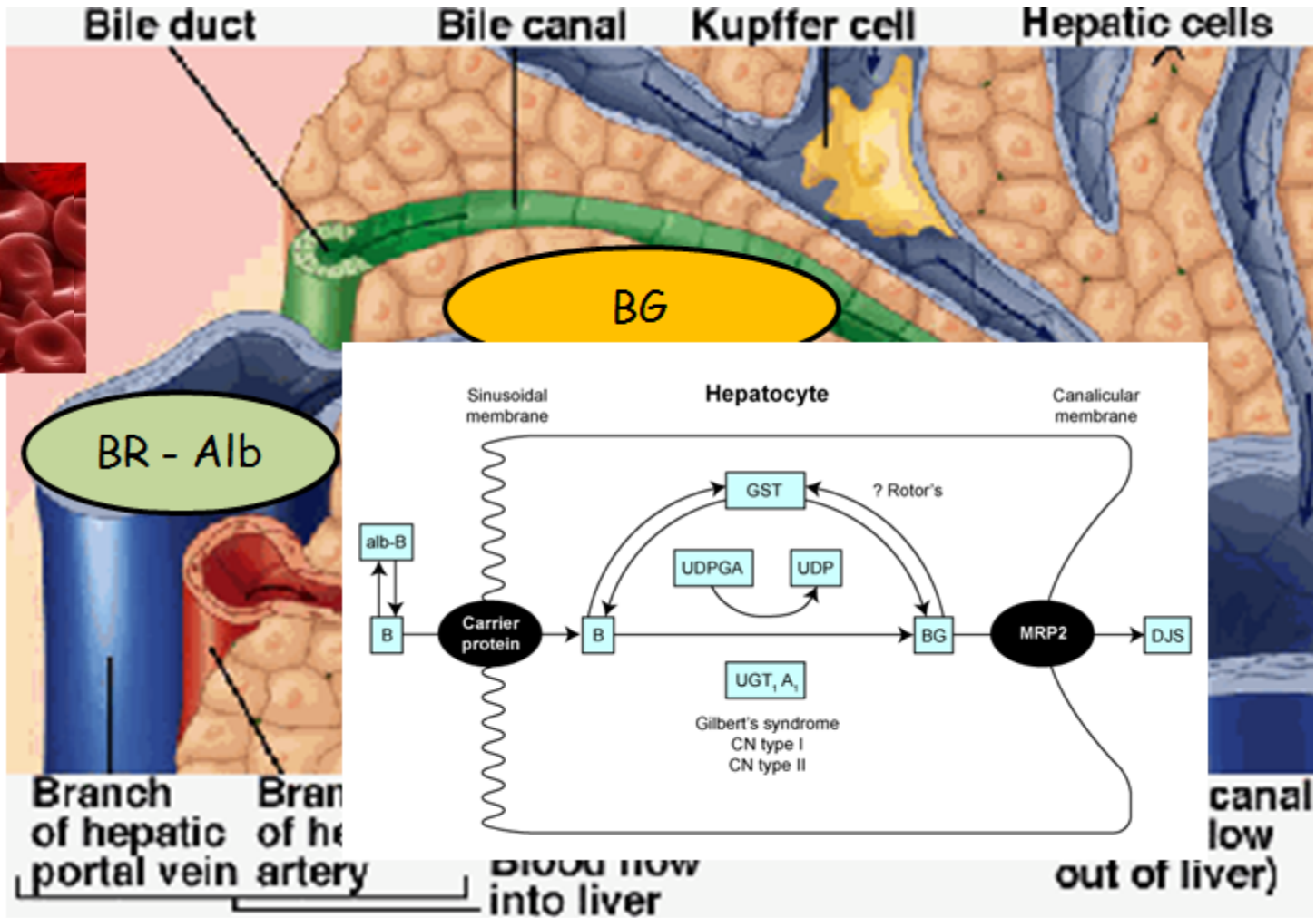
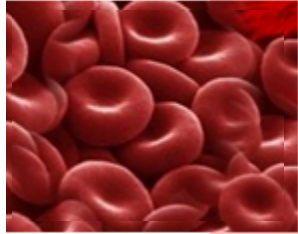


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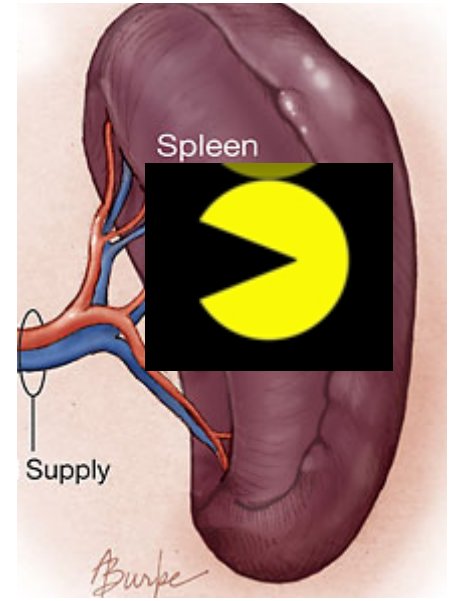
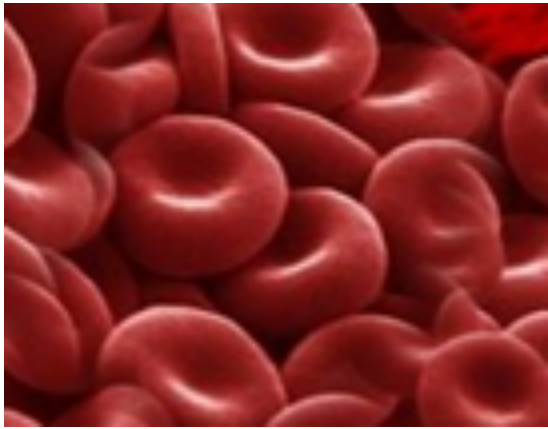
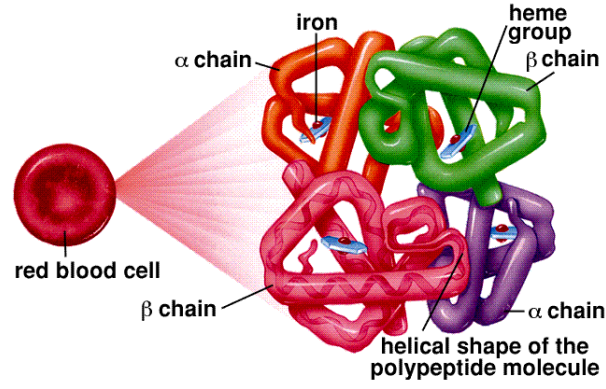


the Bilirubin  
an overview  
by howard sach

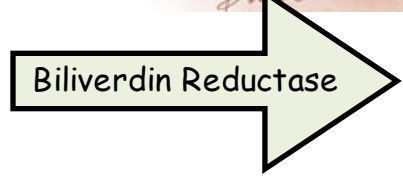
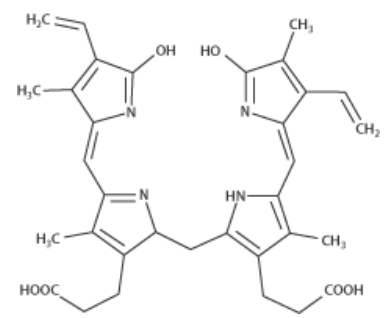
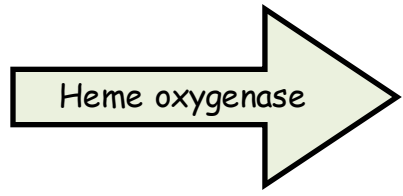
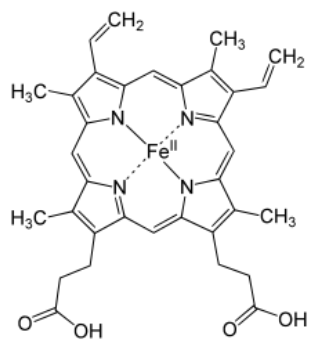
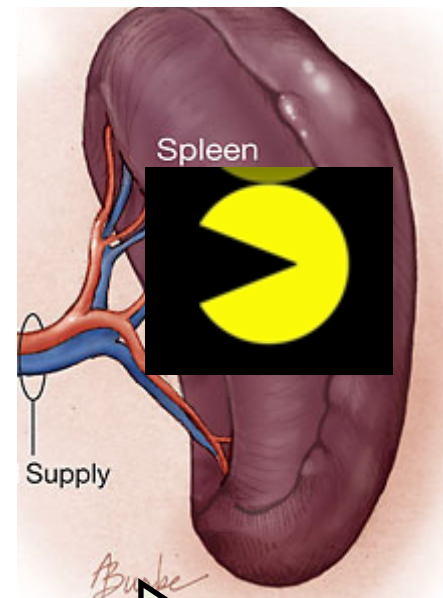
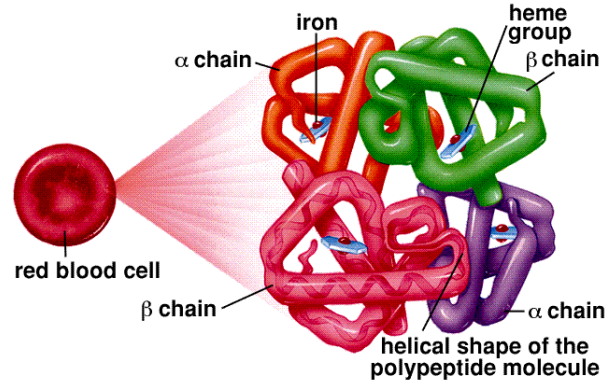
# Slo-Motion Instant Replay...



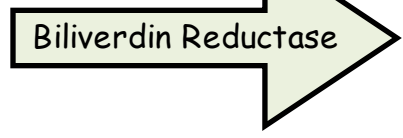
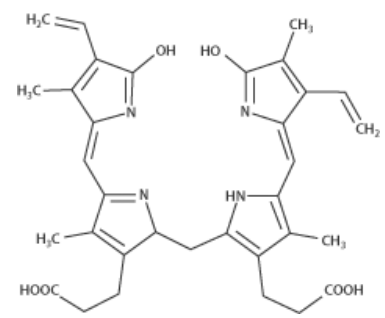
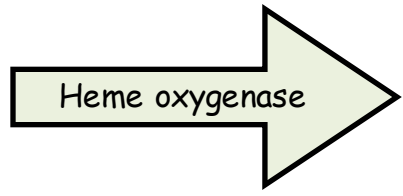
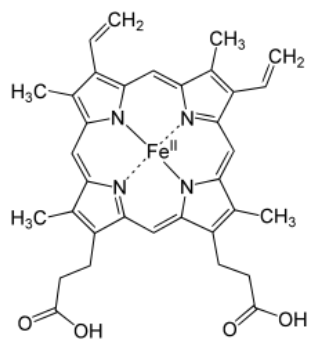
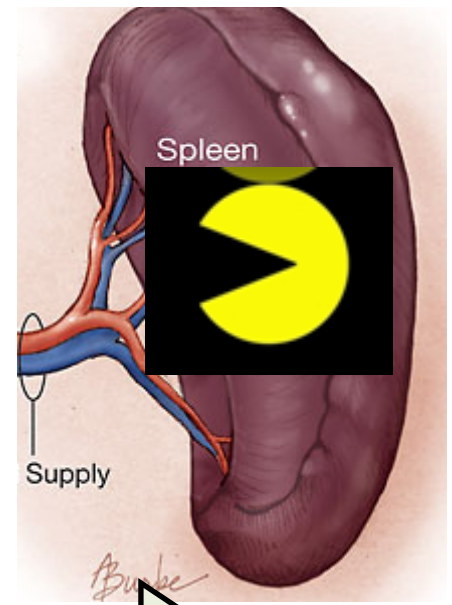
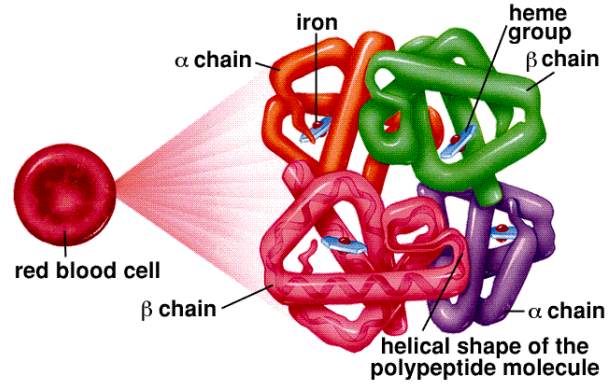
### Hemoglobin Molecule



### Hemoglobin Molecule

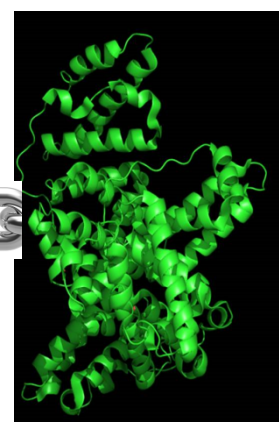
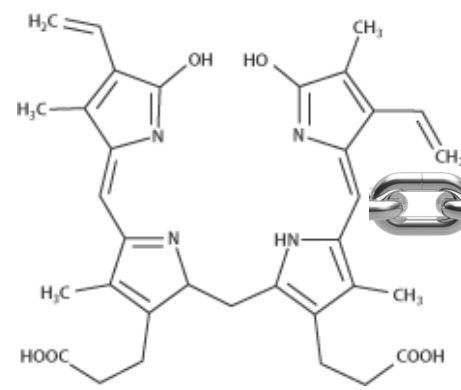


### Hemoglobin Molecule



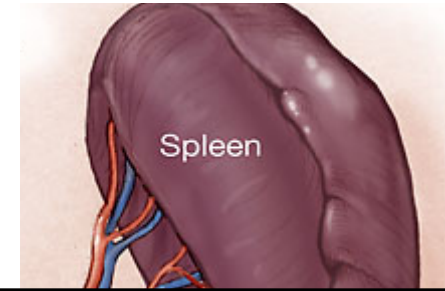
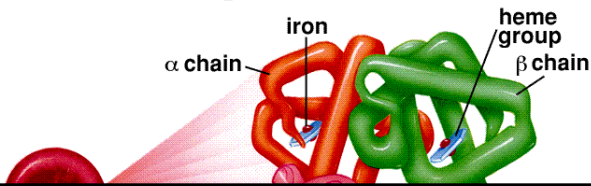
**Bilirubin  
(unconjugated)**

...not water soluble...



**Albumin**

## Hemoglobin Molecule



## Unconjugated Bilirubin ('Indirect')

### Key points:

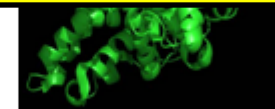
- 'Attached to albumin': too big to pass through glomerular filtration barrier.
  - Intravascular: Hemoglobin → urine
- Unconjugated: not water soluble.

How can we get too much unconjugated bilirubin in the serum?

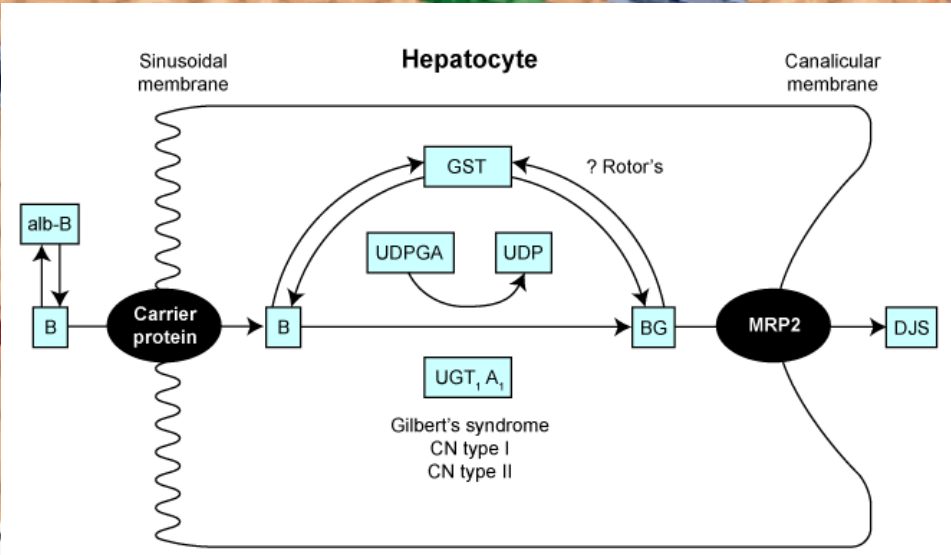
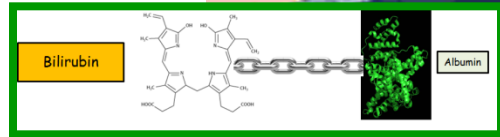
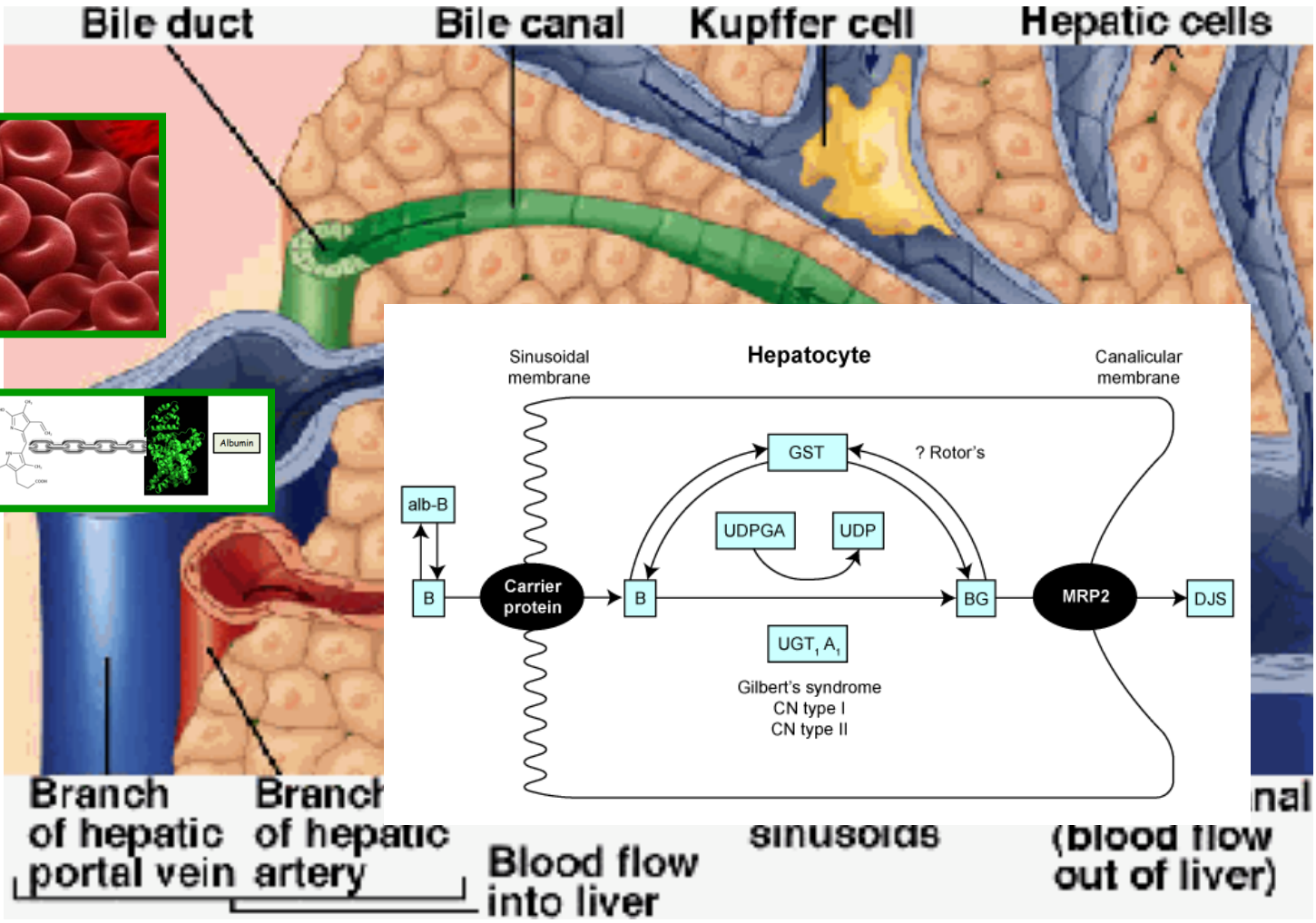
### 1. Hemolysis

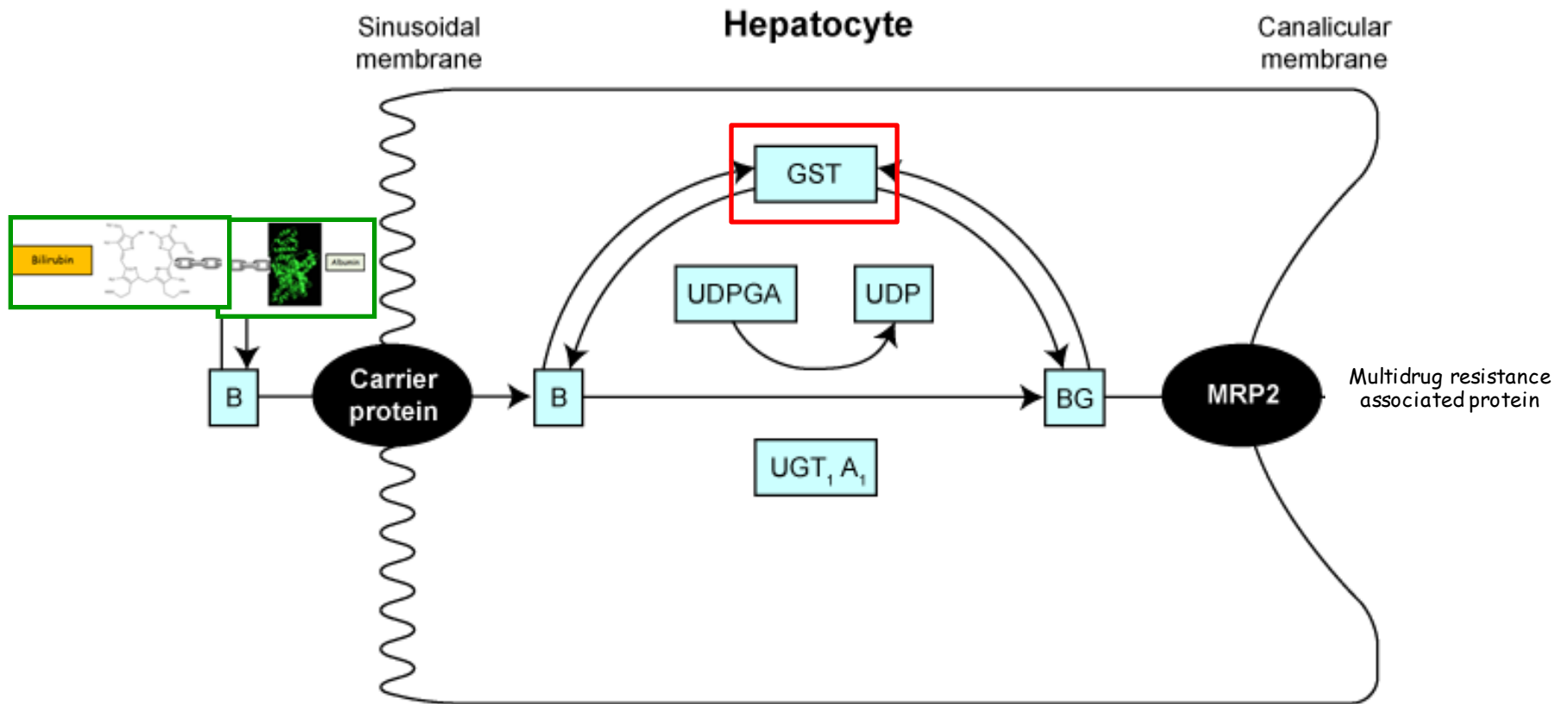
- Elevated indirect bilirubin is used as a diagnostic marker (with ↑ LDH, ↓ haptoglobin)

### 2. Conjugation defect: inherited (**Gilbert's**, Crigler-Najjar)

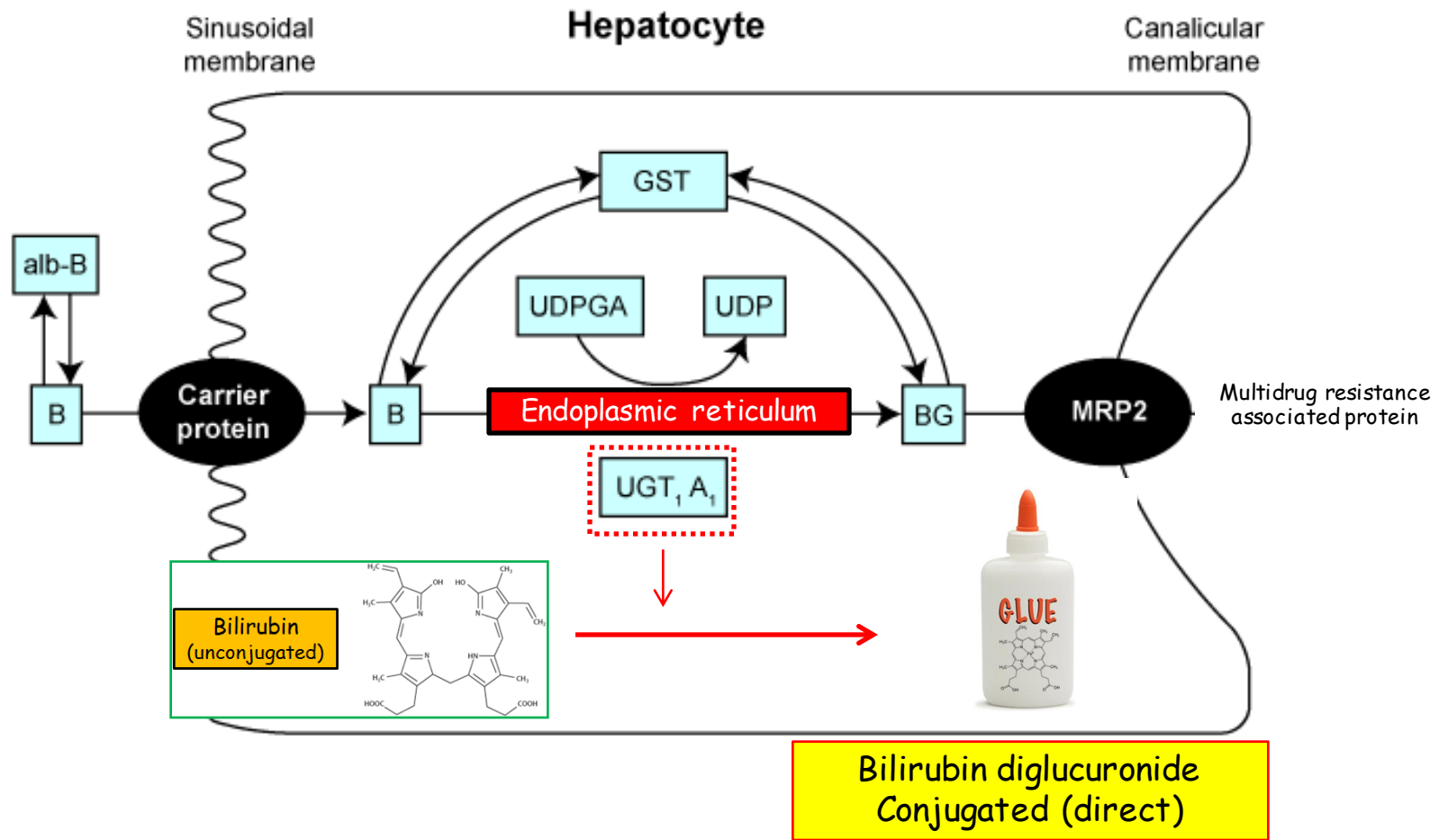








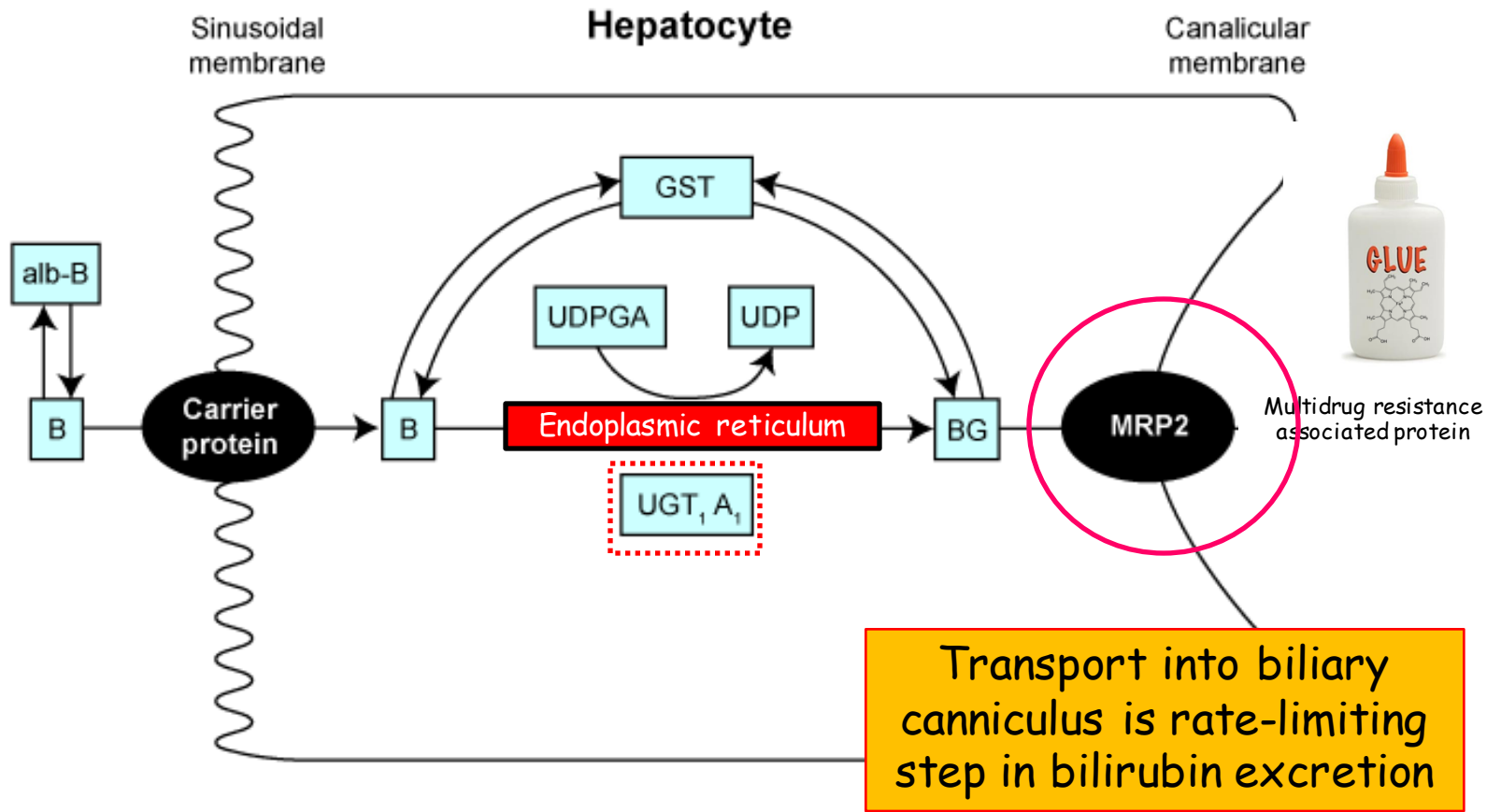
Bilirubin binds to cytosolic binding protein, **glutathione s-transferase (GST)** for transport to ER



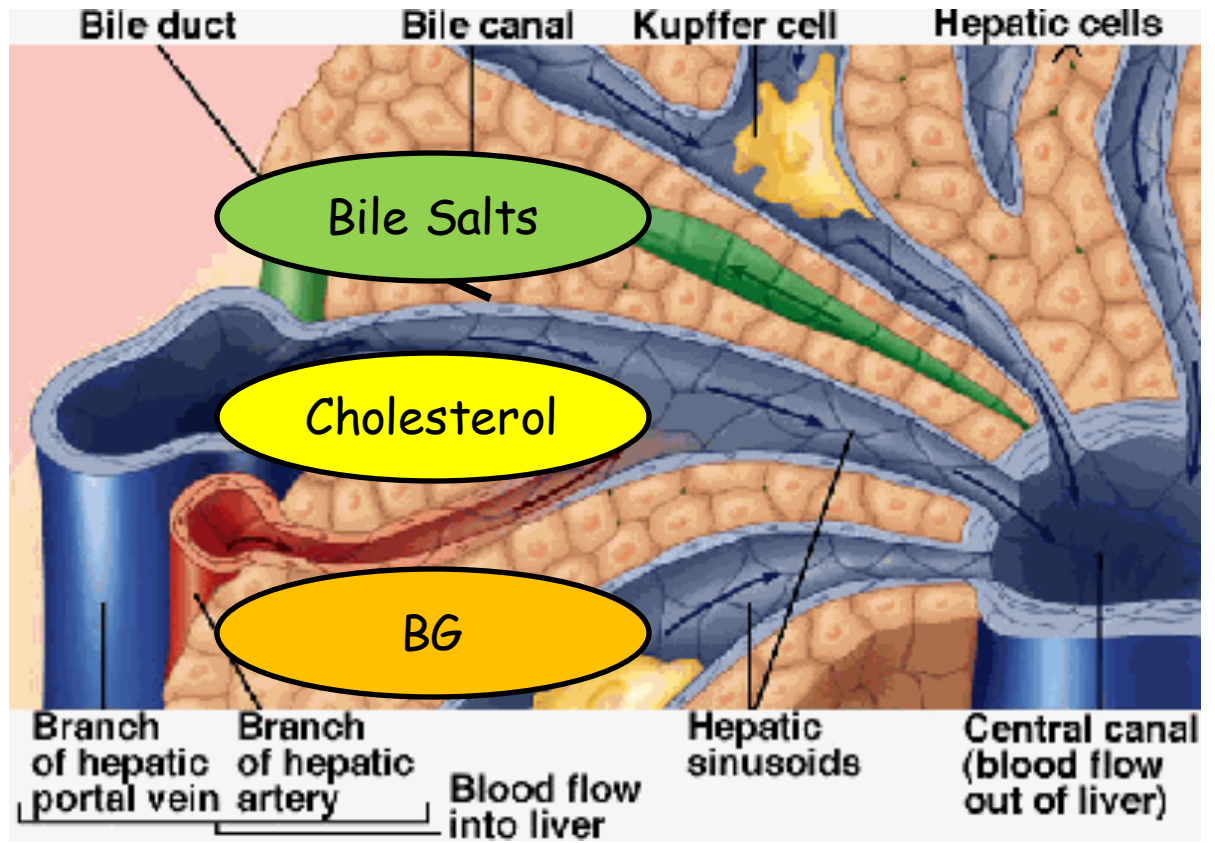
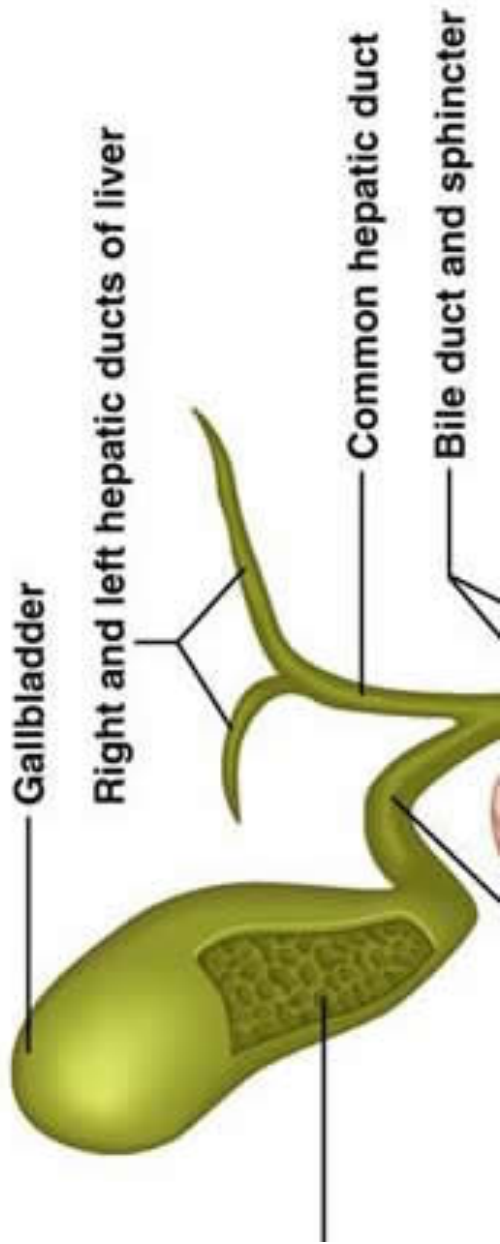
Bilirubin binds to cytosolic binding protein, glutathione s-transferase (GST) for transport to ER

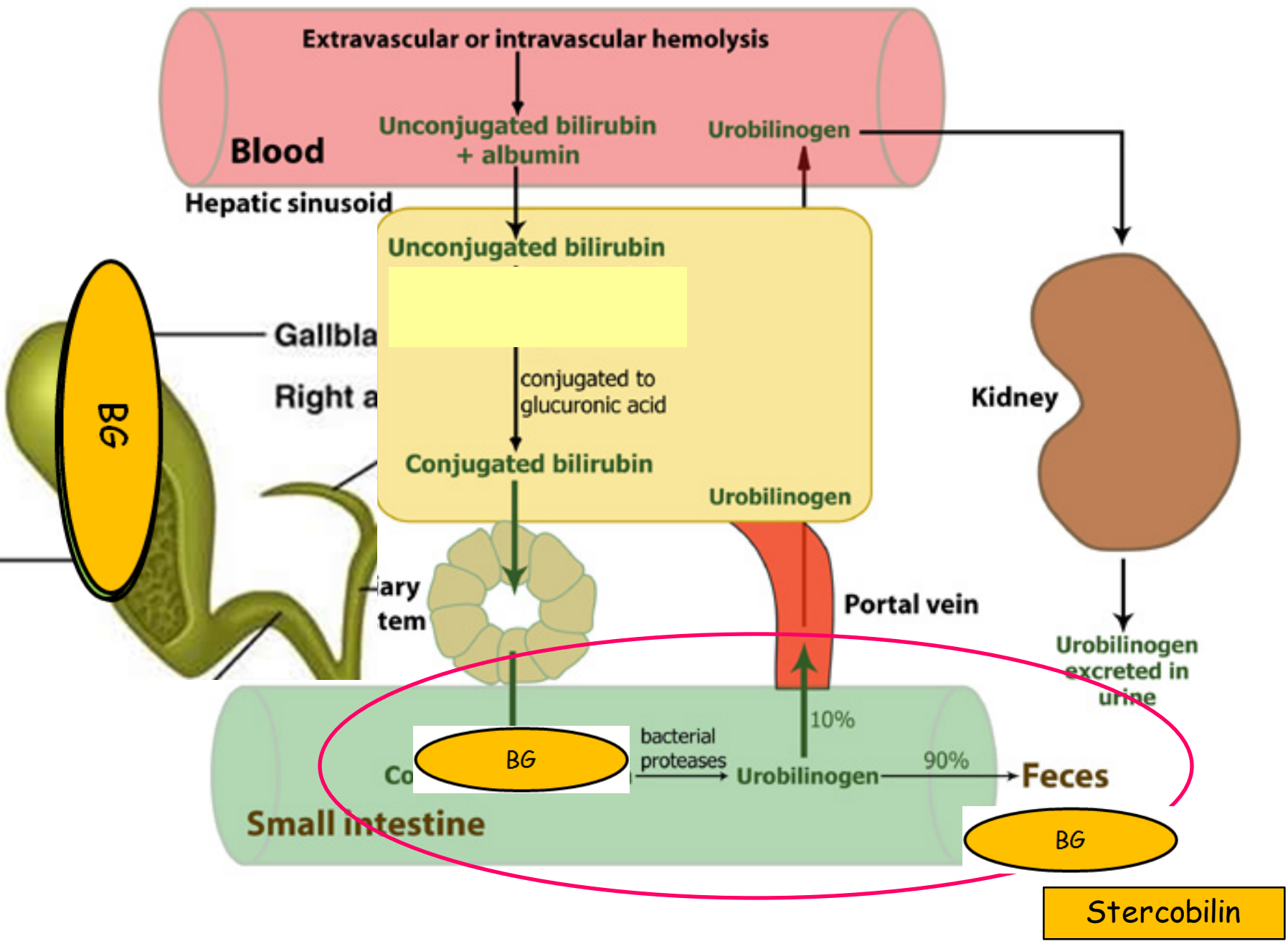
Conjugation of bilirubin is catalyzed by bilirubin-uridinediphosphate (UDP)- glucuronosyltransferase (UGT1A1). Product is **bilirubin diglucuronide**.

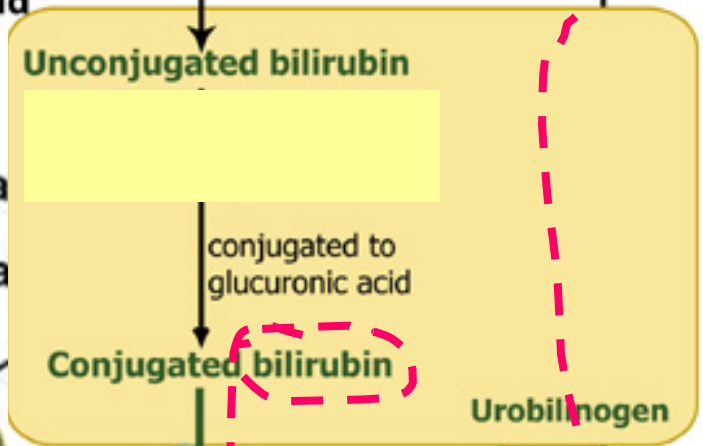
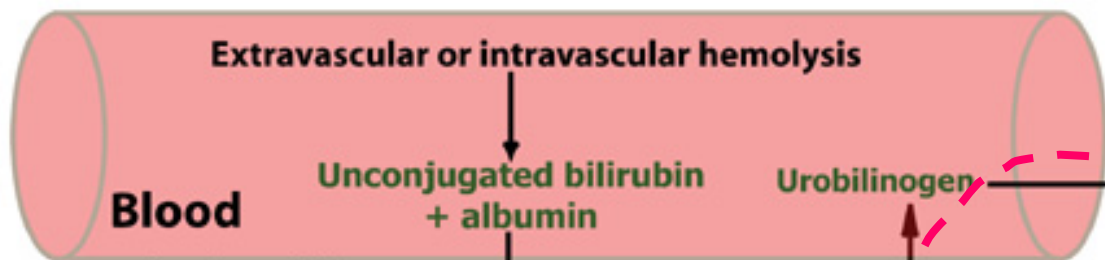
UDPGA is the donor sugar



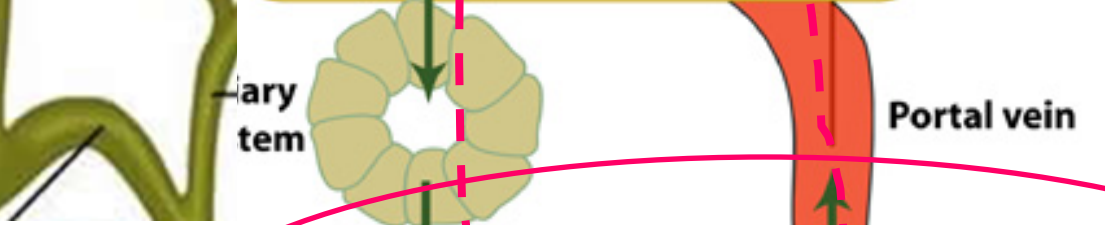
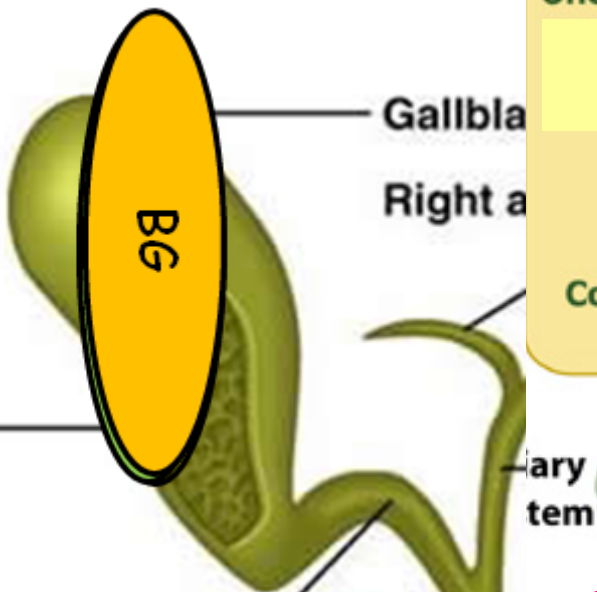
We'll return later to review all the steps that can malfunction.



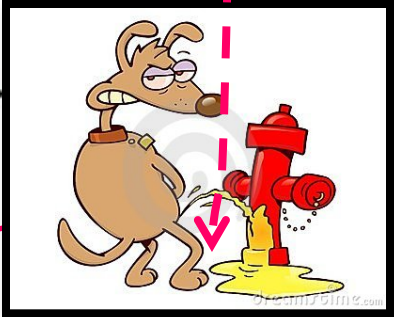





This is normal and healthy



Urobilinogen: 10%




Test	Result
COLOR URINE	Yellow
APPEARANCE URINE	Clear
SPEC GRAVITY, URINE	1.022
pH URINE	6.5
PROTEIN URINE	Negative
GLUCOSE URINE	Negative
KETONES URINE	Negative
BILIRUBIN URINE	Negative
OCCULT BLOOD URINE	Negative
NITRITE URINE	Negative
 UROBILINOGEN URINE	<b>Positive</b>
LEUKO ESTERASE UR	Negative
MICROSCOPIC ?	Not Indicated

Based on the enterohepatic circulation of bilirubin:

What disease does this patient suffer from?

What can you deduce about the enterohepatic circulation of bilirubin from this test?




Test	Result
COLOR URINE	Yellow
APPEARANCE URINE	Clear
SPEC GRAVITY, URINE	1.022
pH URINE	6.5
PROTEIN URINE	Negative
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BILIRUBIN URINE	Negative
OCCULT BLOOD URINE	Negative
NITRITE URINE	Negative
 UROBILINOGEN URINE	<b>Positive</b>
LEUKO ESTERASE UR	Negative
MICROSCOPIC ?	Not Indicated

Based on the enterohepatic circulation of bilirubin:

What disease does this patient suffer from: **no disease**


What can you deduce about the enterohepatic circulation of bilirubin from this test: **Intact**

Test	Result
COLOR URINE	Yellow
APPEARANCE URINE	Clear
SPEC GRAVITY, URINE	1.022
pH URINE	6.5
PROTEIN URINE	Negative
GLUCOSE URINE	Negative
KETONES URINE	Negative
BILIRUBIN URINE	Negative
OCCULT BLOOD URINE	Negative
NITRITE URINE	Negative
 UROBILINOGEN URINE	<b>Positive</b>
LEUKO ESTERASE UR	Negative
MICROSCOPIC ?	Not Indicated

### Urine Bilirubin:


Measures the presence of conjugated bilirubin (water soluble).

**Conjugated bilirubin** gets in urine through **reflux** into the sinusoids

Test	Result
COLOR URINE	Yellow
APPEARANCE URINE	Clear
SPEC GRAVITY, URINE	1.022
pH URINE	6.5
PROTEIN URINE	Negative
GLUCOSE URINE	Negative
KETONES URINE	Negative
BILIRUBIN URINE	<b>Positive</b>
OCCULT BLOOD URINE	Negative
NITRITE URINE	Negative
 UROBILINOGEN URINE	<b>Positive</b>
LEUKO ESTERASE UR	Negative
MICROSCOPIC ?	Not Indicated

Patient presents with jaundice. Which disorder is least likely based solely on this urinalysis?

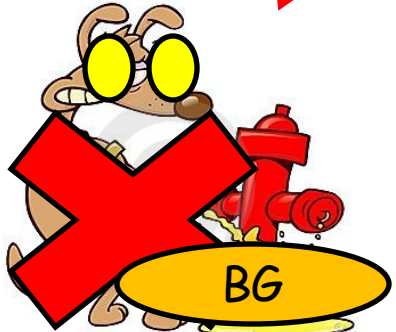
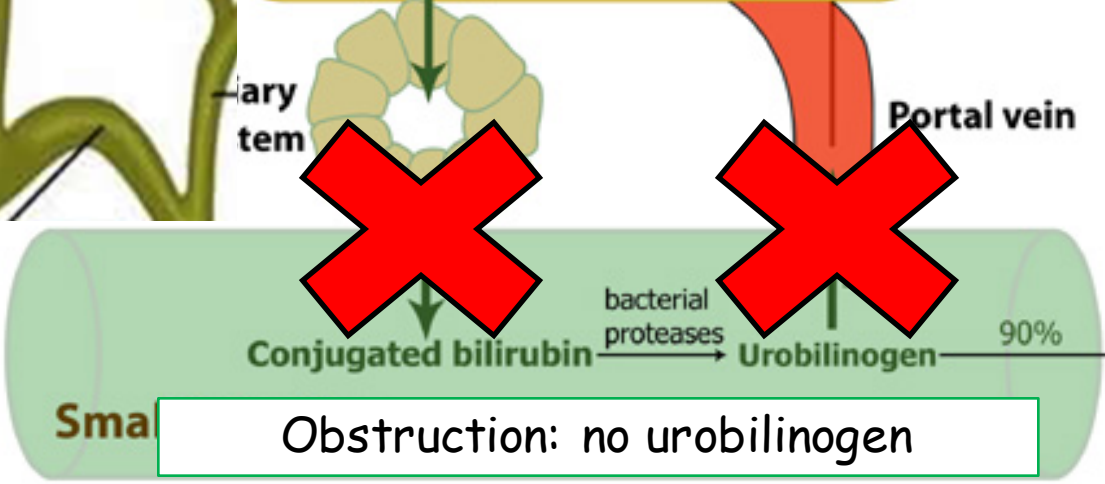
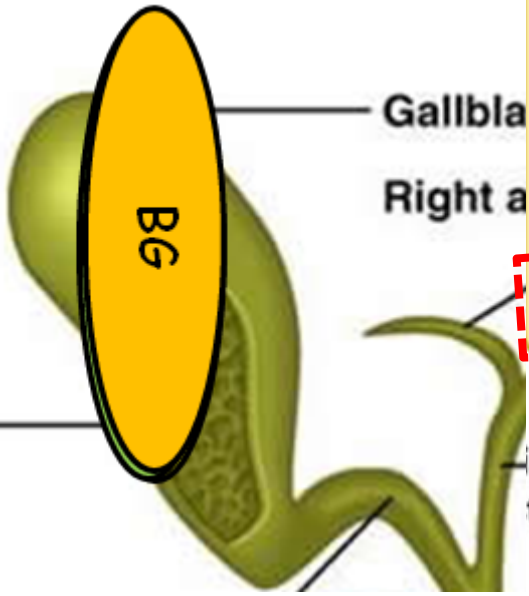
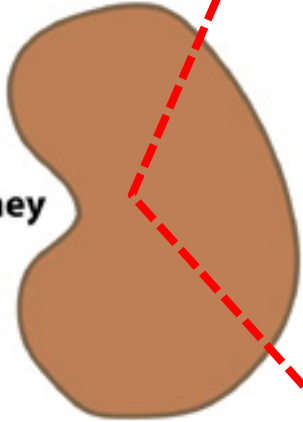
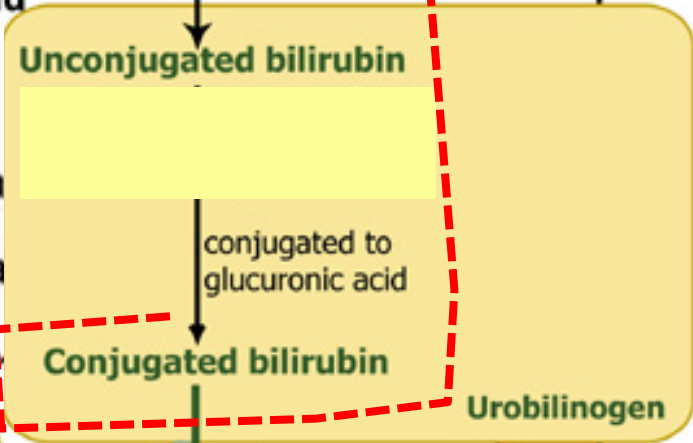
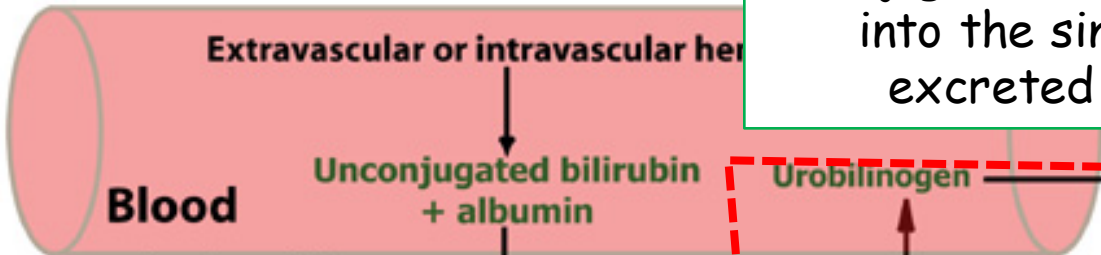
1. Cirrhosis
2. Acute infection, HBV
3. Adenocarcinoma in pancreatic head
4. Wilson's disease
5. Dubin-Johnson syndrome

Test	Result
COLOR URINE	Yellow
APPEARANCE URINE	Clear
SPEC GRAVITY, URINE	1.022
pH URINE	6.5
PROTEIN URINE	Negative
GLUCOSE URINE	Negative
KETONES URINE	Negative
BILIRUBIN URINE	<b>Positive</b>
OCCULT BLOOD URINE	Negative
NITRITE URINE	Negative
 UROBILINOGEN URINE	<b>Positive</b>
LEUKO ESTERASE UR	Negative
MICROSCOPIC ?	Not Indicated

Patient presents with jaundice. Which disorder is least likely based solely on this urinalysis?

1. Cirrhosis
2. Acute infection, HBV
3. Adenocarcinoma in pancreatic head: obstruction; no urobilinogen
4. Wilson's disease
5. Dubin-Johnson syndrome: slow excretion but intact enterohepatic circ

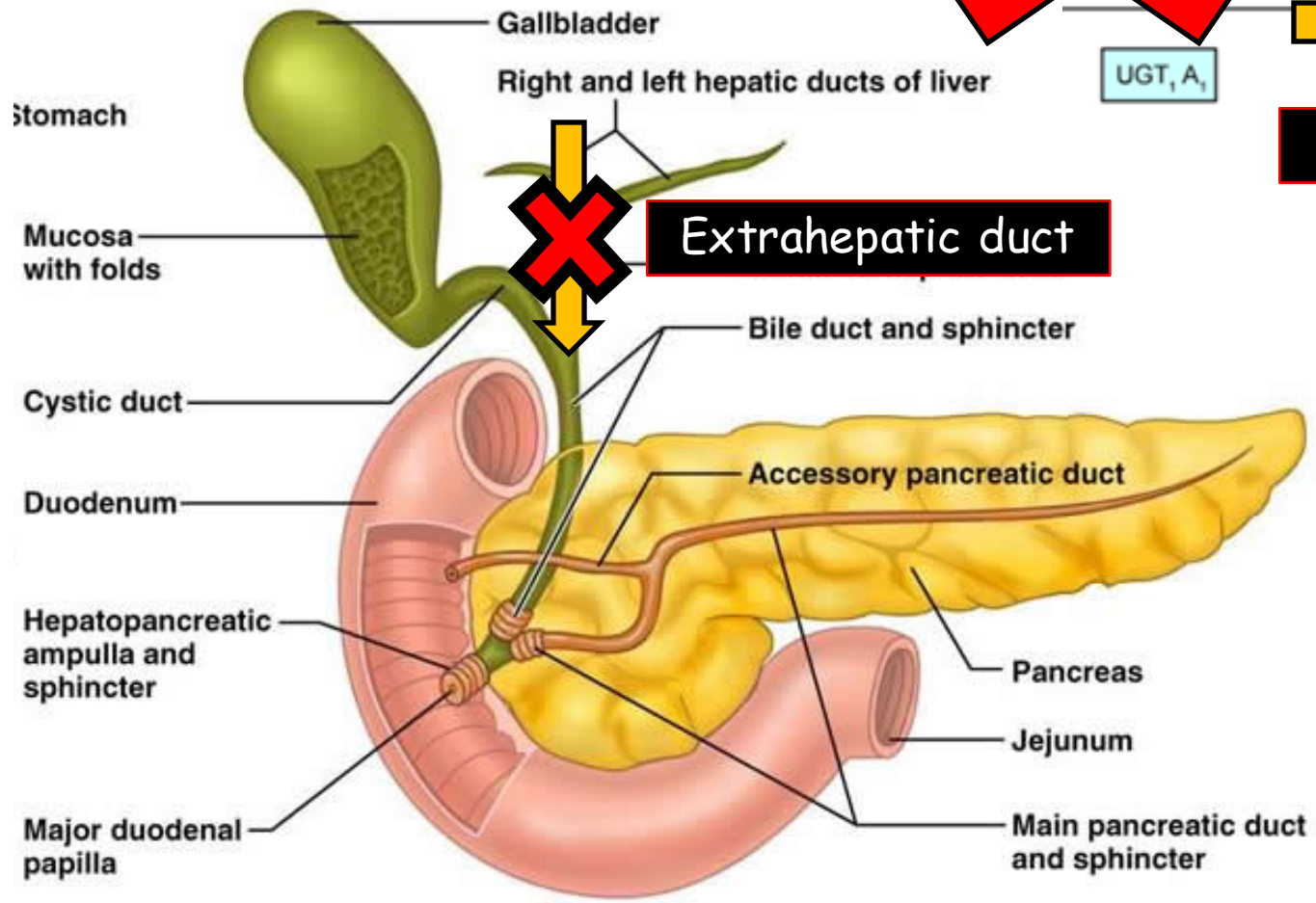
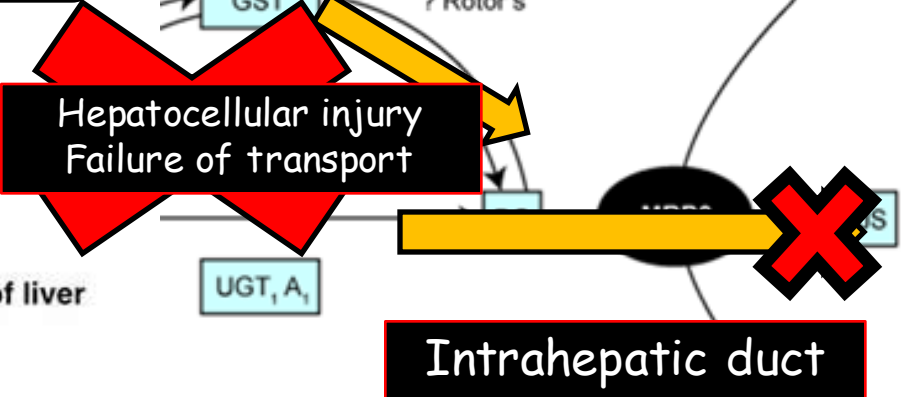
Conjugated bilirubin refluxes into the sinusoids and is excreted in the urine



# Conjugated Hyperbilirubinemia

Hepatocyte

Canalicular membrane



Stomach

Gallbladder

Right and left hepatic ducts of liver

Mucosa with folds



Extrahepatic duct

Cystic duct

Bile duct and sphincter

Duodenum

Accessory pancreatic duct

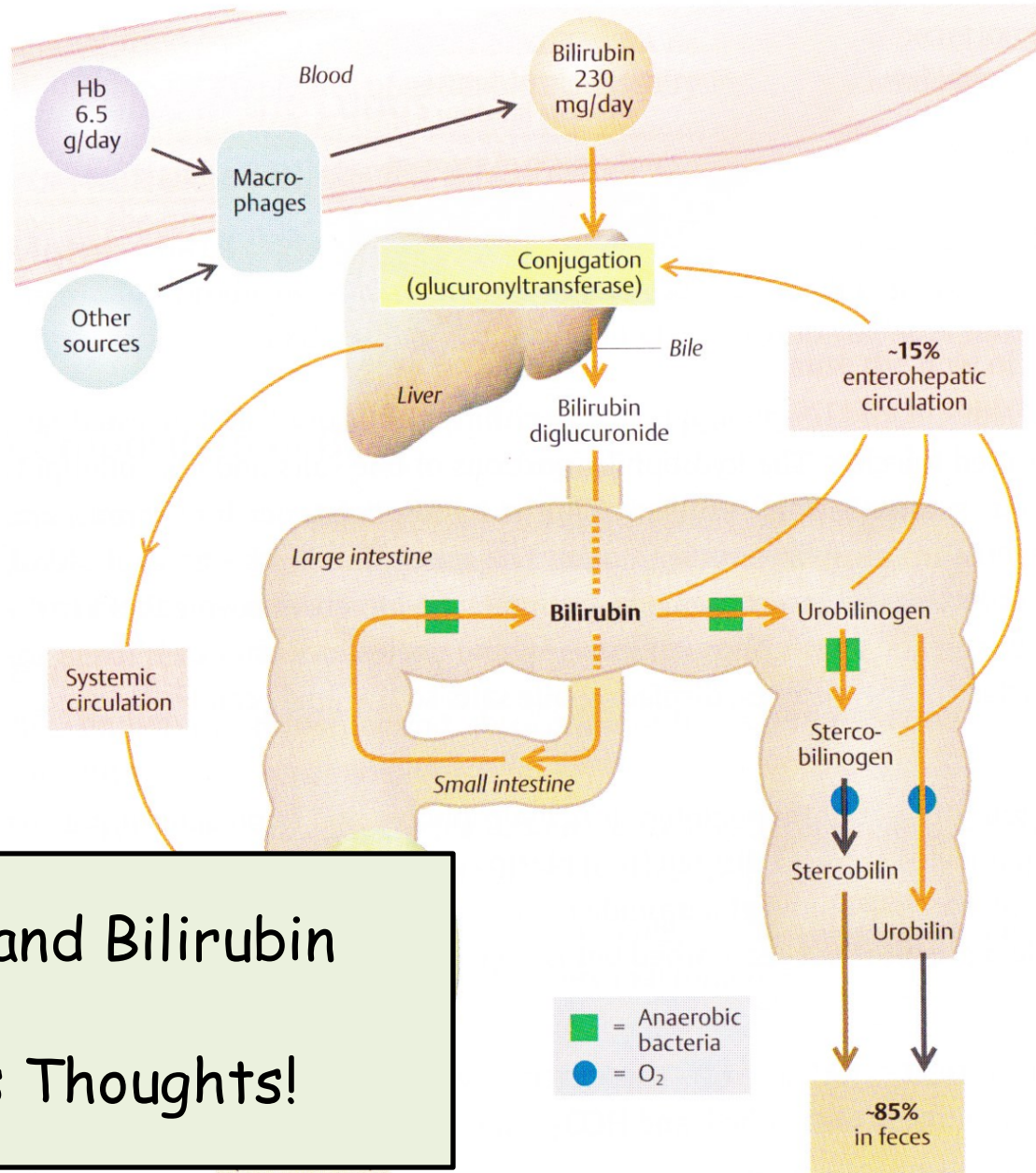
Hepatopancreatic ampulla and sphincter

Pancreas

Major duodenal papilla

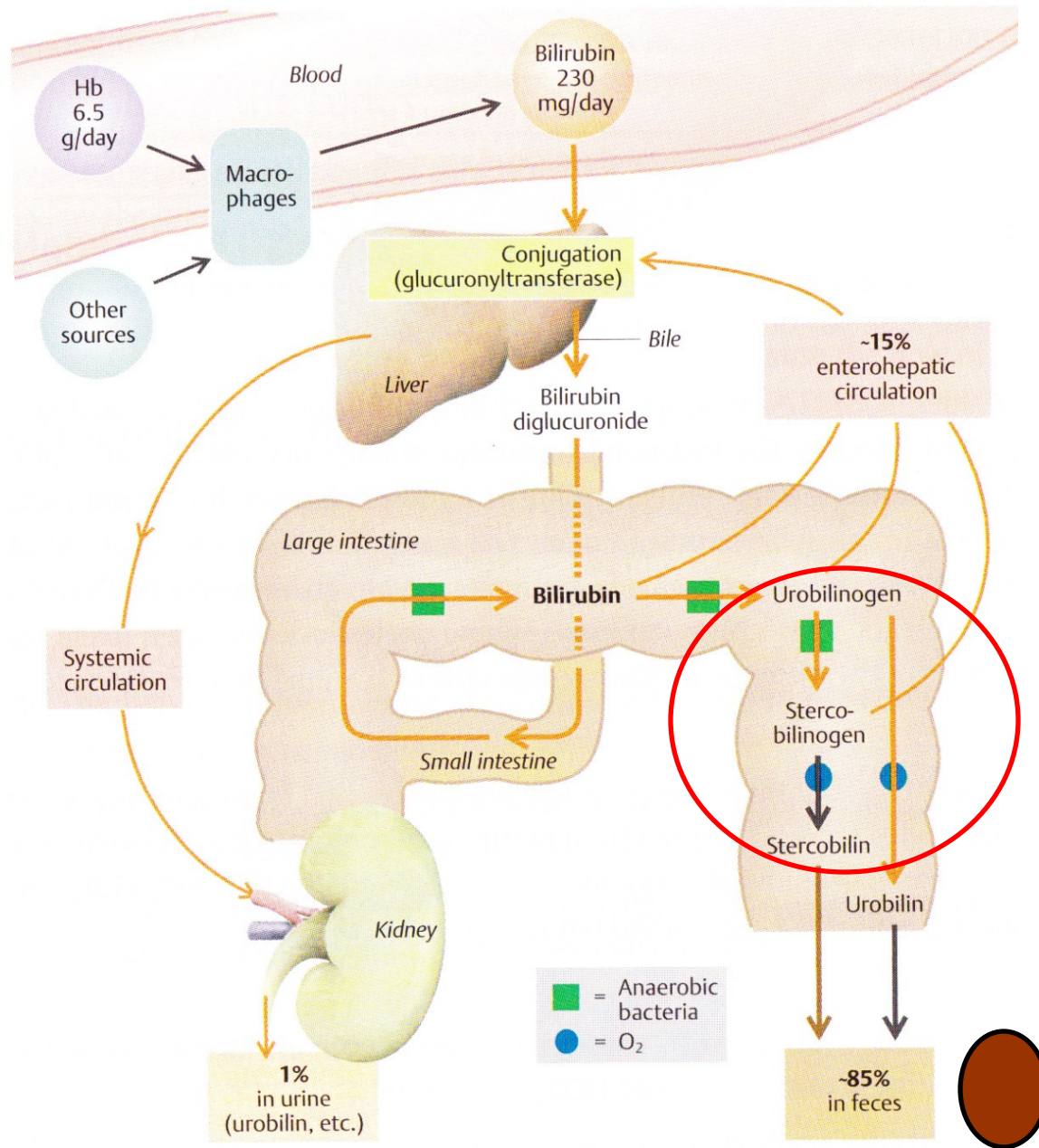
Jejunum

Main pancreatic duct and sphincter

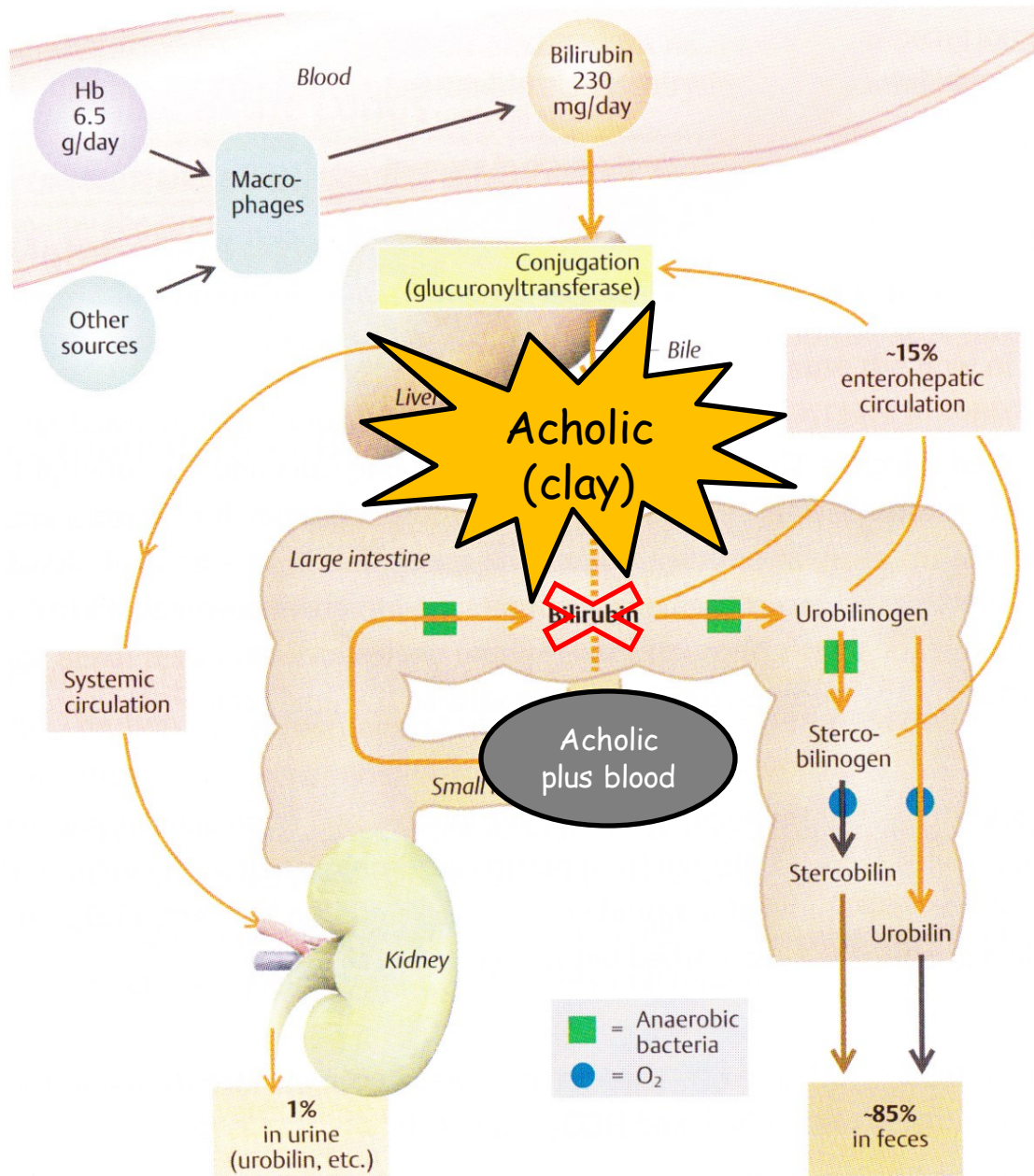


Feces and Bilirubin

Bonus Thoughts!









# Bilirubin Physiology - WYNTKFTB

- Bilirubin metabolism
  - Unconjugated: hemoglobin breakdown product
  - Conjugation: UDP-glucuronosyltransferase
  - Excretion: bile canniculi
- Enterohepatic circulation:
  - Bacterial protease convert to urobilinogen, majority in stool; minority reabsorbed and excreted in urine
- Implication of bilirubin metabolism
  - Urine: **urobilinogen implies no obstruction**
  - Stool: pale/acholic **obstruction**; silver implies blood.
- Understand the metabolic pathway as related to the disease state of **JAUNDICE**
  - **Major players include hemolysis, conjugation defects, hepatocyte dysfunction, duct disease/obstruction.**