July 30, 2018

Bilirubin Analysis and Liver Function

1. Functions of the liver
    a. Produce proteins-
        i. Regulation of clotting-
        ii. Albumin-
    b. Glucose and glycogen conversion-
    c. Lipids
    d. Digestion
        i. Bile-
    e. Detoxification-
2. Liver Blood Supply
    a. Hepatic portal circulation
    b. Hepatic artery
3. Liver production-
    a. Nutrients

i. Proteins

ii. Lipids and lipoproteins

iii. Carbohydrates

b. Bile

c. Breakdown products

4. Hemoglobin Catabolism

a. The ideal method of RBC recycling takes place extravascularly by the RE system (aka: _____ _____ _____)

i. Heme broken down into iron and protein portions

1. Iron recycled

2. Amino acids recycled

3. Biliverdin

4. Bilirubin

a. Conjugation

5. Urobilinogen

6. Urobilin/Stercobilin

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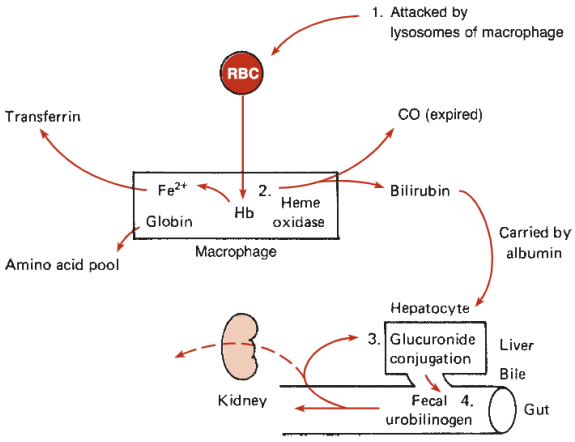
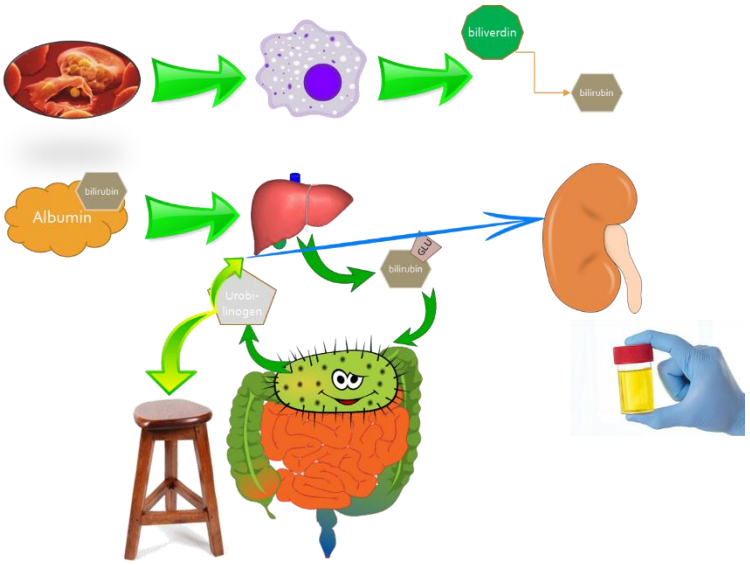


FIGURE 19-4 Extravascular degradation of hemoglobin.



b. Bilirubin

i. Unconjugated bilirubin: Non-water soluble

ii. Conjugated bilirubin: Created in the liver by conjugation with glucuronic acid by the enzyme _____

1. Known as direct bilirubin

2. Secreted in the bile via:

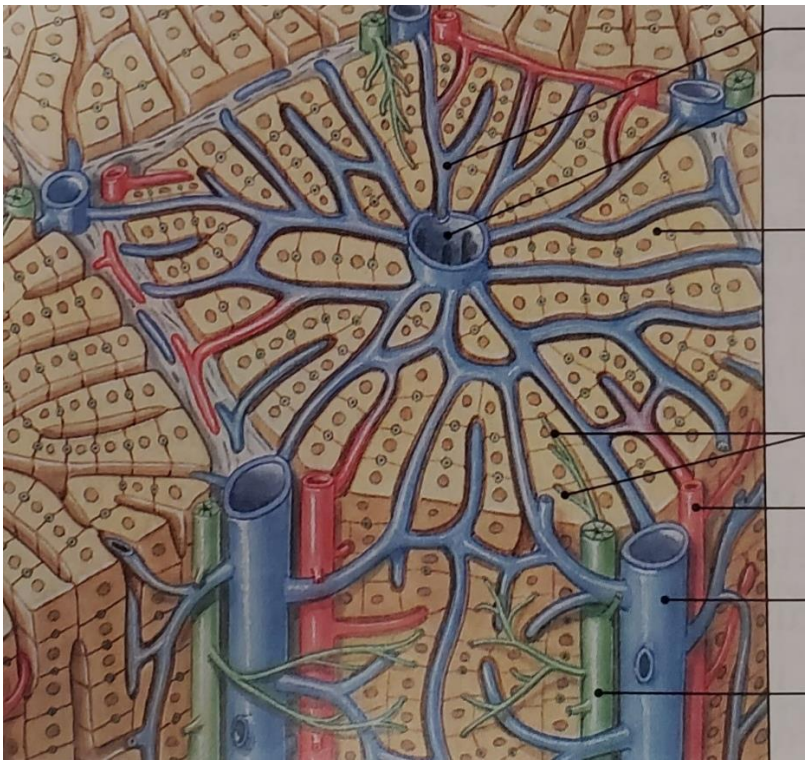
3. From there into the small intestine where bacteria metabolize into:

iii. Urobilinogen: first colorless product, produced by intestinal bacteria

1. Some reabsorbed by portal circulation

2. Moset continues and bacteria further metabolize to:

5. Liver Lobule



6. Bilirubin Testing
    a. Specimen considerations: UV light degrades, hemolysis and lipemia interfere
    b. Evelyn Malloy- Bilirubin + diazotized sulfanilic acid = _____
        i. Absorbs @ 560 nm
    c. Jendrassik-Grof method: diazonium ion and bilirubin produce azobilirubin, Abs @ 600 nm
        i. Stop reaction and shift pH at end
    d. Water soluble portion testable without “accelerant.” This means _____ bilirubin

1. Caffeine benzoate, methanol

ii. How to report indirect bilirubin?

_____-_____=_____

iii. Delta bilirubin (δ)

1. Dry slide assays:

e. Urobilinogen testing (not in lecture, an aside)

i. P-dimethylaminobenzaldehyde (Ehrlich's Reagent)

ii. Mostly performed on urine

We cannot detect a lack of urobilinogen in the urine, only normal or elevated

7. Jaundice

a. Discoloration caused by high levels of bilirubin (>2 mg/dL)

b. First visible in:

c. Classification of jaundice based on underlying cause

i. Pre-hepatic: cause is increased rate of hemolysis

ii. Hepatic: decreased ability of the liver to deal with heme breakdown products

iii. Post-hepatic: disruption in liver's excretion of bilirubin through bile duct

d. More than discoloration: kernicterus

Usually occurs with bilirubin levels greater than 20 mg/dL, preterm infants are at greater risk

i.

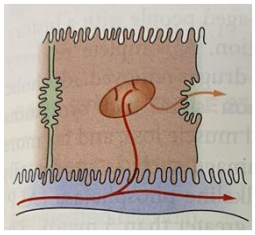
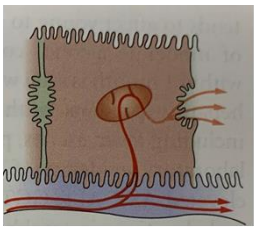
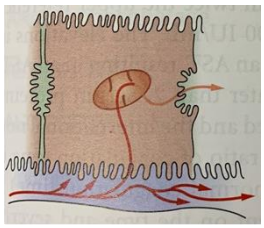
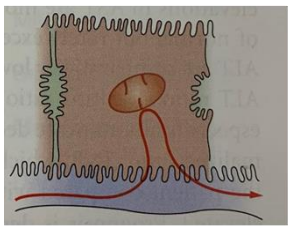
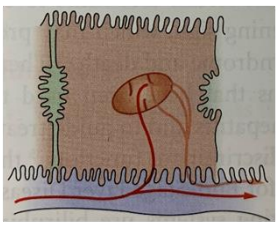
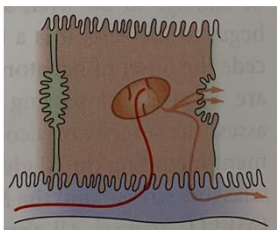
8. Prehepatic Jaundice
    a. Increased RBC turnover caused by _____
    b. Level of bilirubin usually _____
    c. Type of bilirubin present:

9. Hepatic Jaundice
    a. Bilirubin metabolism or transport is impaired
    b. Gilbert's
    c. Crigler-Najjar
    d. Dubin-Johnson
        i. Rotor
    e. Viral hepatitis
    f. Liver cancer
    g. Reye's syndrome
    h. Autoimmune
    i. Wilson's
    j. Cirrhosis
10. Posthepatic Jaundice

a. Obstructive Jaundice

b. Causes include:

c. Type of bilirubin present:

11. More about kernicterus

a. Where does the bilirubin come from?

b. What kind of bilirubin is it?

c. Why can't the body eliminate it?

d. How can it be treated?

12. Case Study 1:

a. A 65 year old female presents to the Emergency Department with:
    i. Abdominal Pain
    ii. Chills
    iii. Fever
    iv. Yellow Eyes
    v. Patient reports loss of appetite
    vi. Patient reports stools have been whitish recently
b. Lab Results:
    i. AST 38 U/L (7-40 U/L)

ii. ALT 28 U/L (0-30 U/L)
iii. Alk Phos: 452 U/L (20-120 U/L)
What does this mean?

iv. Bilirubin
Total: 6.0 mg/dL (0.1-1.5 mg/dL)
Direct: 5.4 mg/dL (0.1-0.4 mg/dL)
Indirect: ____ mg/dL (0.1-1.1 mg/dL)
What does this mean?

v. Urinalysis:
Color: Dark yellow
Bilirubin: ++
Urobilinogen: Normal/negative

13. Case Study 2:
    a. 49 Y.O. patient on Ribavirin and interferon alpha for control chronic hepatitis C that has been well controlled up to this point.
        i. Abdominal pain
        ii. Fever
        iii. Yellow eyes
        iv. Lab Results
            1. Total Bilirubin: 5.5 mg/dL
            2. Indirect Bilirubin ↑
            3. Albumin: Normal
            4. AST/ALT: Slight elevation, consistent with previous results
        v. Ribavarin Black Box Warning: "The primary clinical toxicity of ribavirin is hemolytic anemia. The anemia associated with ribavirin therapy may result in worsening of cardiac disease and lead to fatal and nonfatal myocardial infarctions."

14. Case Study 3:
    a. A 54 year old man presents with vomiting, epigastric pain, and nausea. He admits to a history of heavy drinking. Labs are as follows:
        i. Lab Results:
            1. **Alk Phos: 175 U/L (20-120 U/L)**
            2. **AST: 158 U/L (7-40 U/L)**
            3. **ALT: 92 U/L (0-30 U/L)**
            4. **GGT: 284 U/L (0- 50 U/L)**
            5. LD: 136 U/L (100-220 U/L)
            6. **T Bili: 16.7 mg/dL (0.1-1.5 mg/dL)**
            7. **C Bili: 8.9 mg/dL (0.1-0.4 mg/dL)**
            8. **Albumin: 1.7 g/dL (3.5-5.0 g/dL)**
            9. T Protein: 6.0 g/dL (6.0-8.0 g/dL)
            10. **PT: 19 sec (9-13 sec)**** What does this have to do with liver function?

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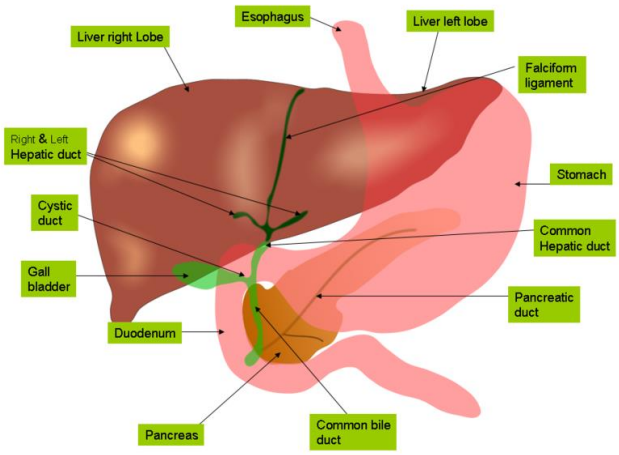
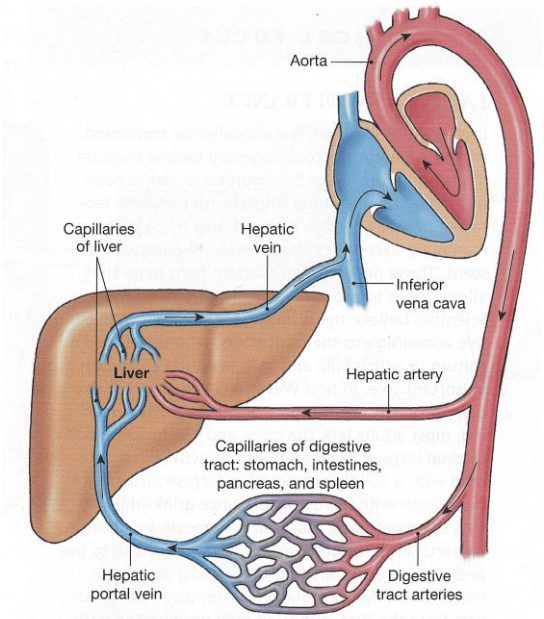
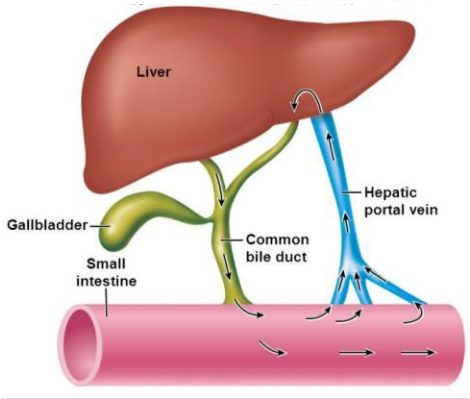




● **FIGURE 21-30** ***The hepatic portal system.*** Most nutrients absorbed by the intestine pass through the liver, which serves as a filter that can remove potentially harmful xenobiotics before they get into the systemic circulation.



	Pre-hepatic Jaundice	Hepatic Jaundice	Post-hepatic Jaundice
Total bilirubin	Normal / Increased	Increased	Increased
Conjugated bilirubin	Normal	Normal / Increased* / ?Decreased?	Increased
Unconjugated bilirubin	Increased	Increased	Normal
Urobilinogen	Increased	Normal	?Decreased? / Negative
Urine Colour	Normal	Dark	Dark
Stool colour	Normal	Normal	Pale
Alkaline phosphate levels	Normal	Slight elevation	Increased
AST & ALT levels	normal	Increased	Normal