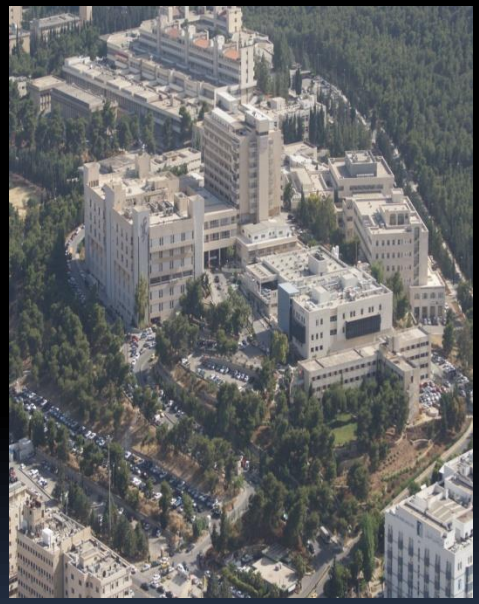
LIVER DISEASES IN CHILDREN



Fareed Khdair , MD

Associate Professor

Chief, Section of Pediatric Gastroenterology, Hepatology, and Nutrition

University of Jordan – School of Medicine

GI Modules

- Indiana University, USA
- https://radtf.iuhealth.org/radtf/

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edactic.medlib.iupui.edu/Default.ASP

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1. Testing & Demo

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Mark Feist MD

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Riley Hospital for Children
Indiana University Health

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McAfee

6:46 PM

Indiana University School of Medicine
Department of Educational Technology

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Welcome to Dr. Mark Feist's Educational Website

This website contains case-based modules which are part of a curriculum used teach residents about pediatric gastroenterology, hepatology, and nutrition. The content of this website and the curriculum is based on the needs of primary care providers faced with children who present with gastrointestinal complaints.

The multiple choice and true/false questions in the modules are the means of teaching you much of the information. Do not get discouraged if you don't know the answers; you are not expected to know all the answers as this is the first time many of you have been exposed to this information. The incorrect answers on the multiple choice questions usually have an explanation of why they are incorrect and give you a little more information about that topic; therefore, clicking on all of answers will maximize your educational experience.

Click on the link below to access the modules.

GI CASES

Are you finished? Don't forget to log off!

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8 items were found.

Shown as...	Topic	Tests	Created	Updated
CaseStudy	Nutrition View		11/22/2005	02/23/2006
CaseStudy	Abdominal Pain View		09/27/2005	02/22/2006
CaseStudy	GI Bleeding View		07/25/2005	02/17/2006
CaseStudy	Diarrhea View		06/28/2005	06/14/2006
CaseStudy	Liver Disease II View		12/22/2004	02/24/2006
CaseStudy	Liver Disease I View		08/16/2004	01/24/2006
CaseStudy	Gastroesophageal Reflux View		07/14/2004	06/05/2006
CaseStudy	Constipation View		05/05/2004	08/23/2006

Do Another Search || Home

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Nutrition

Learning Objectives:

At the end of this module you should be able to:

- Describe the composition of various infant formulas and list indications for their usage
- Choose an infant formula for different clinical situations based on the protein, carbohydrate, and fat content of the formula
- Describe normal infant nutritional requirements
- List the most common causes of failure to thrive
- Describe the different types of failure to thrive based on trends in weight, height, and head circumference
- Assess nutritional status and diagnose malnutrition
- Describe the effects of pancreatic insufficiency on nutritional status
- Describe the risks that can be associated with nutritional rehabilitation
- Identify risk factors for and the presentation of deficiencies or toxicities of various vitamins and minerals

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History: A 2-month-old male infant presents to your office because of irritability. The mother reports that the patient has become more irritable over the past few weeks and has begun to spit up after most feeds. The irritability occurs around the clock, and the patient is not sleeping well. The emesis is non-bilious, non-bloody and described as undigested formula. It usually occurs within a few minutes of completing the feeding. Mom estimates the amount of emesis as half of the volume consumed. She also states that he has a red, scaly rash on his arms, legs, and face which has gotten worse over the past few weeks.

Click on the links below for more history.

Past Medical History

Family History

Social History

Diet History

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The most likely cause of this patient's symptoms is

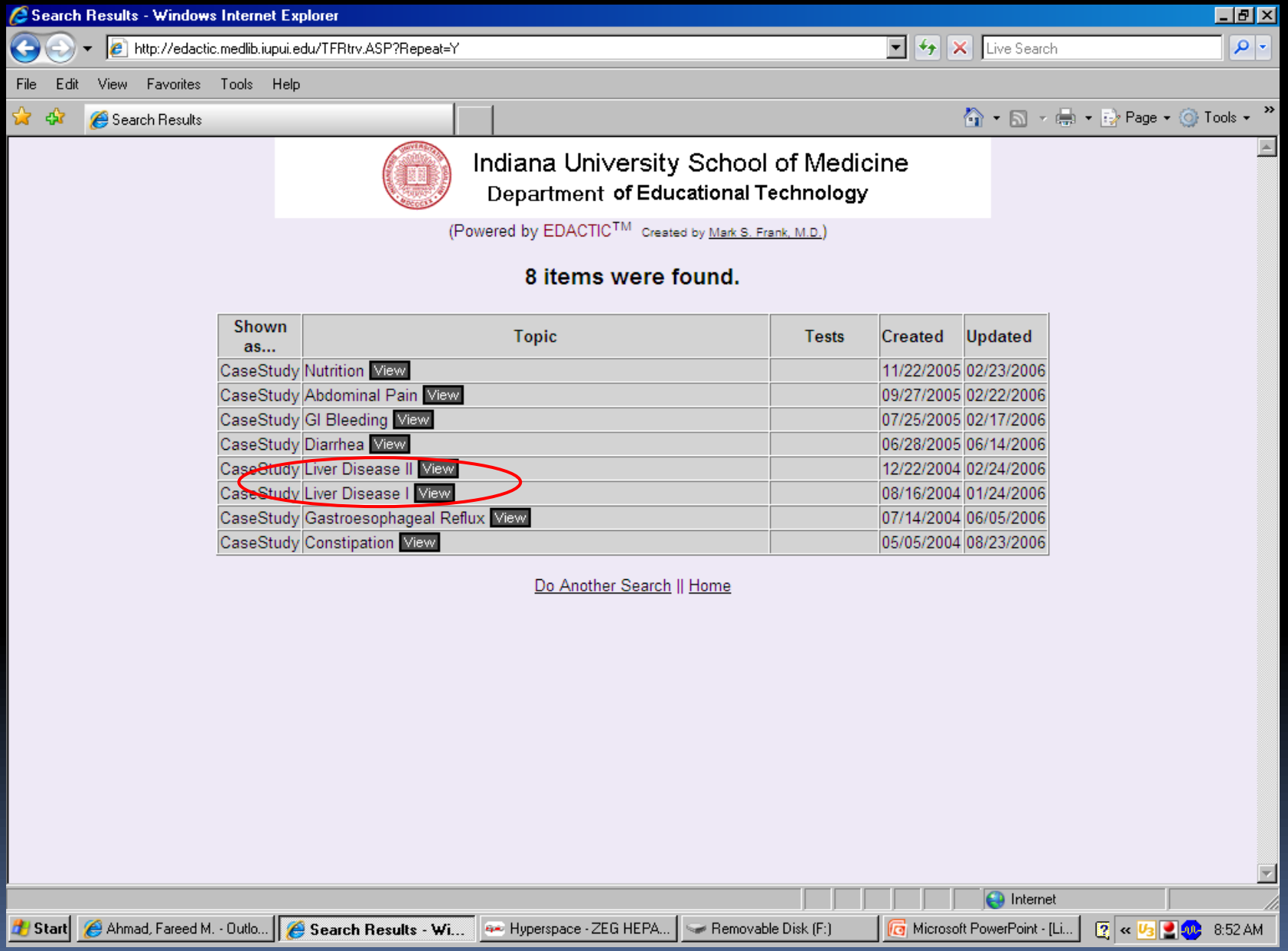
A physiologic infantile gastroesophageal reflux
B congenital alactasia (lactose intolerance)
C cow's milk protein allergy
D malrotation with midgut volvulus

The treatment of choice for this patient would be a trial of

A Nutramigen
B Isomil
C Neocate
D Enfamil Gentlease
E goat's milk

Response to therapy in this condition is usually seen

A immediately
B within 12 hours
C after 48-72 hours
D after 2 weeks


Search Results - Windows Internet Explorer
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Search Results
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CaseStudy | GI Bleeding View | | 07/25/2005 | 02/17/2006
CaseStudy | Diarrhea View | | 06/28/2005 | 06/14/2006
CaseStudy | Liver Disease II View | | 12/22/2004 | 02/24/2006
CaseStudy | Liver Disease I View | | 08/16/2004 | 01/24/2006
CaseStudy | Gastroesophageal Reflux View | | 07/14/2004 | 06/05/2006
CaseStudy | Constipation View | | 05/05/2004 | 08/23/2006
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Liver Disease

Learning Objectives:

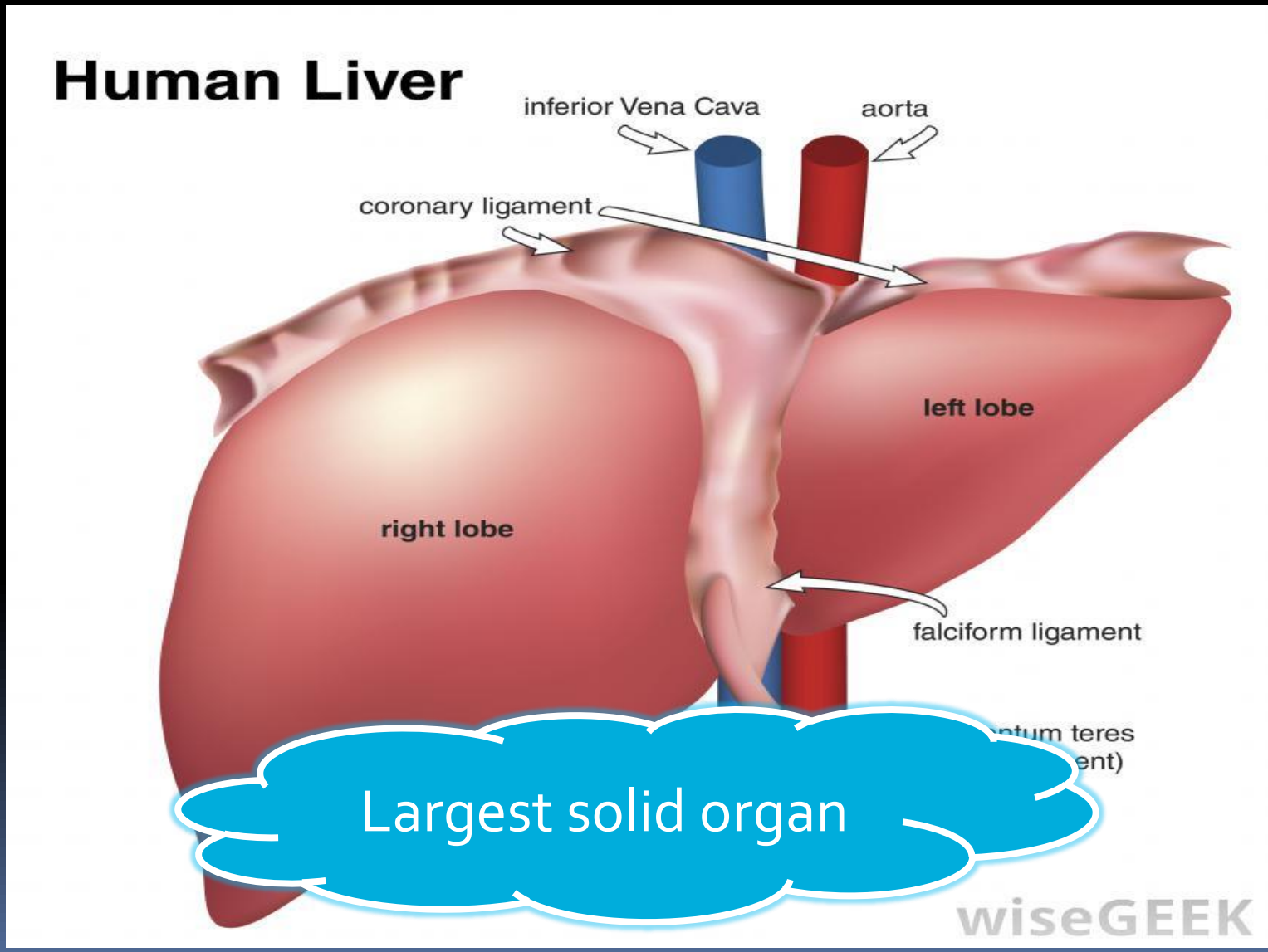
At the end of this module you should be able to:

- Differentiate pathologic from benign causes of hyperbilirubinemia
- Identify warning signs in an infant with persistent jaundice
- Initiate a diagnostic evaluation of an infant with persistent jaundice
- State the three most common causes of neonatal cholestasis
- Identify treatable conditions which may cause neonatal cholestasis
- Initiate a diagnostic evaluation of a patient who presents with acute hepatitis
- Explain the value of laboratory tests and imaging studies that are used to evaluate patients with liver disease
- Describe the presentation of a patient with acute hepatic failure and provide supportive care to the patient.

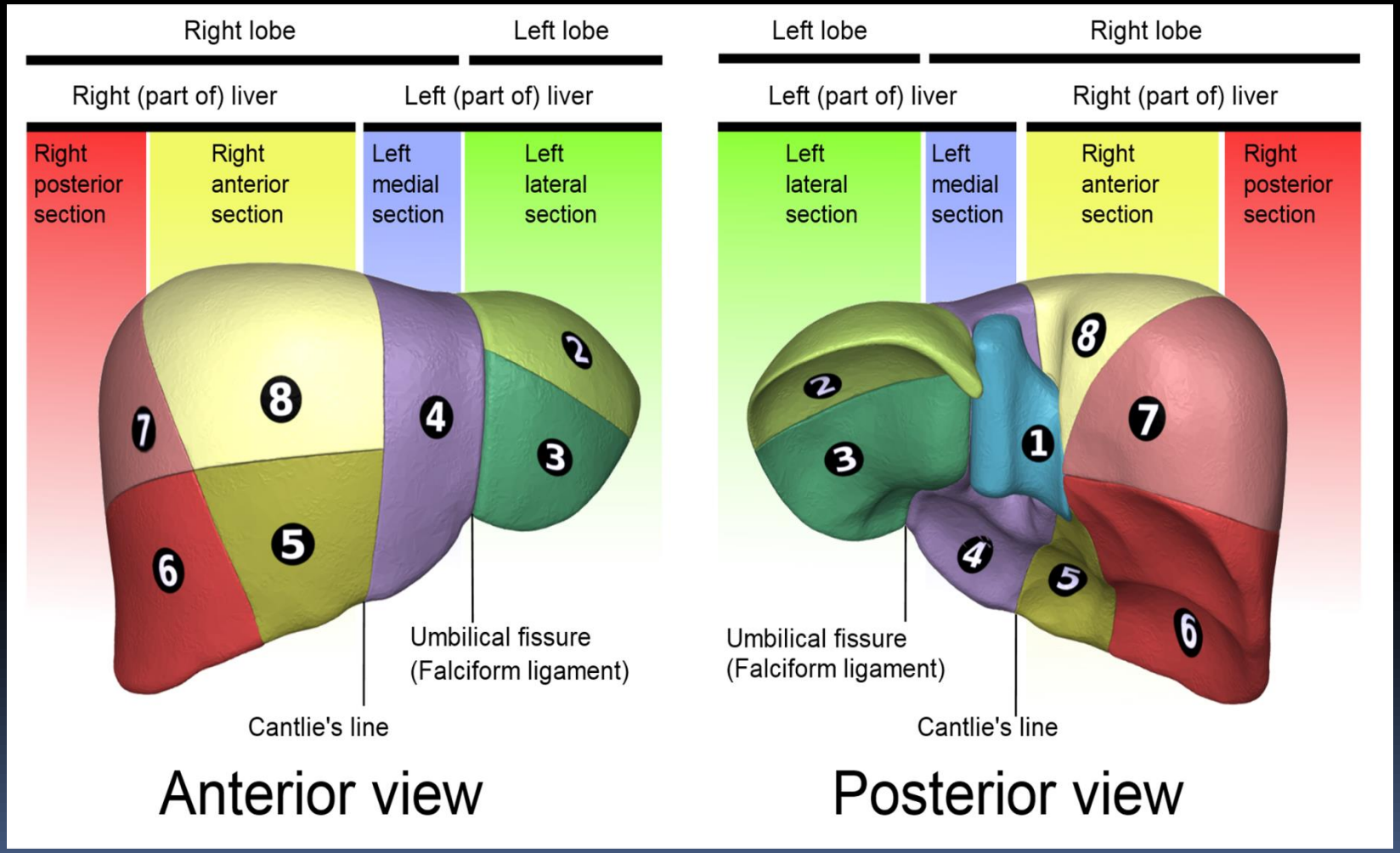
Agenda

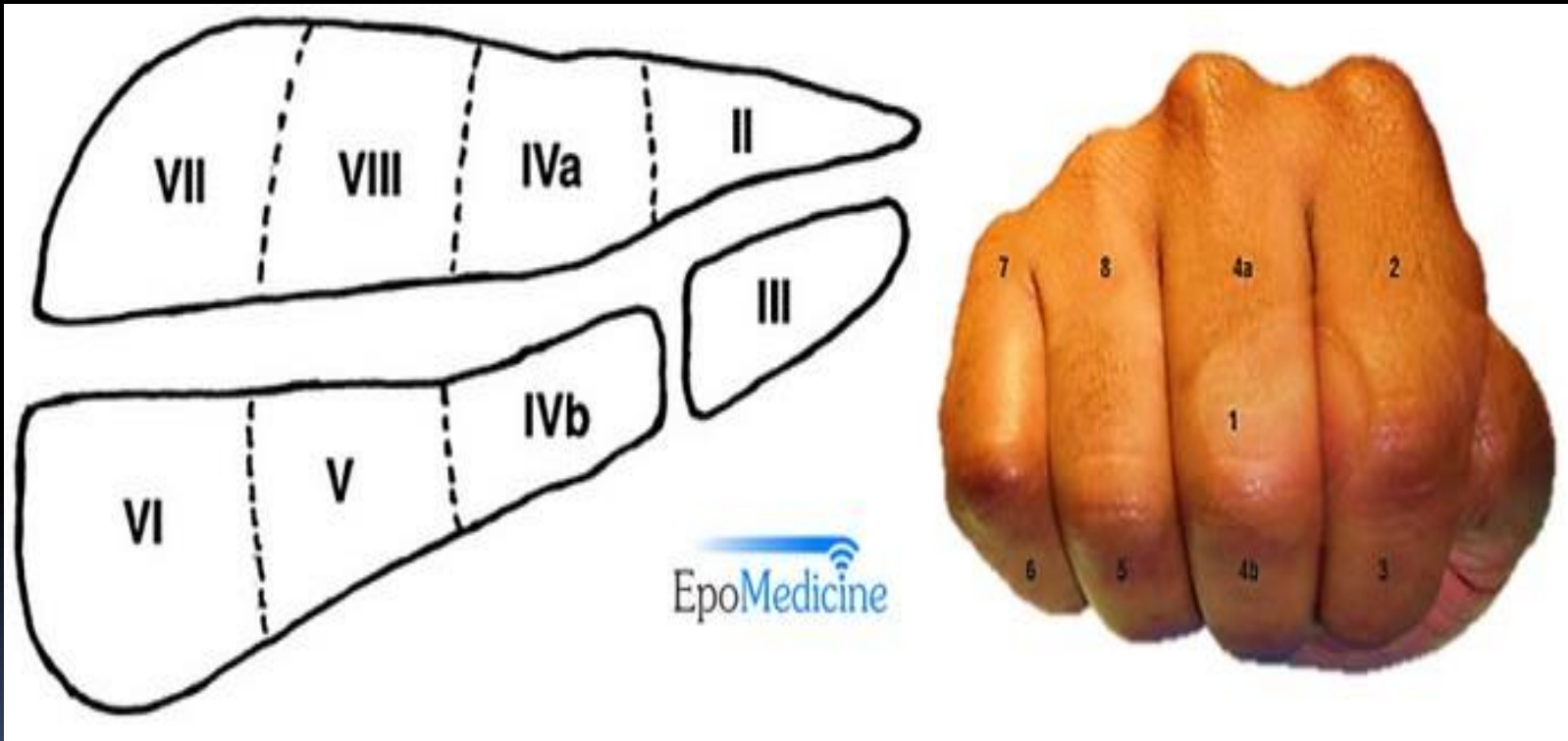
- Liver anatomy and physiology
- Spectrum of liver diseases
- Neonatal jaundice
- Red flags in the jaundiced infant
- Evaluation of the jaundiced infant
- Acute hepatitis
- Acute liver failure
- Chronic hepatitis
- How to interpret Hep B serologies
- Cases

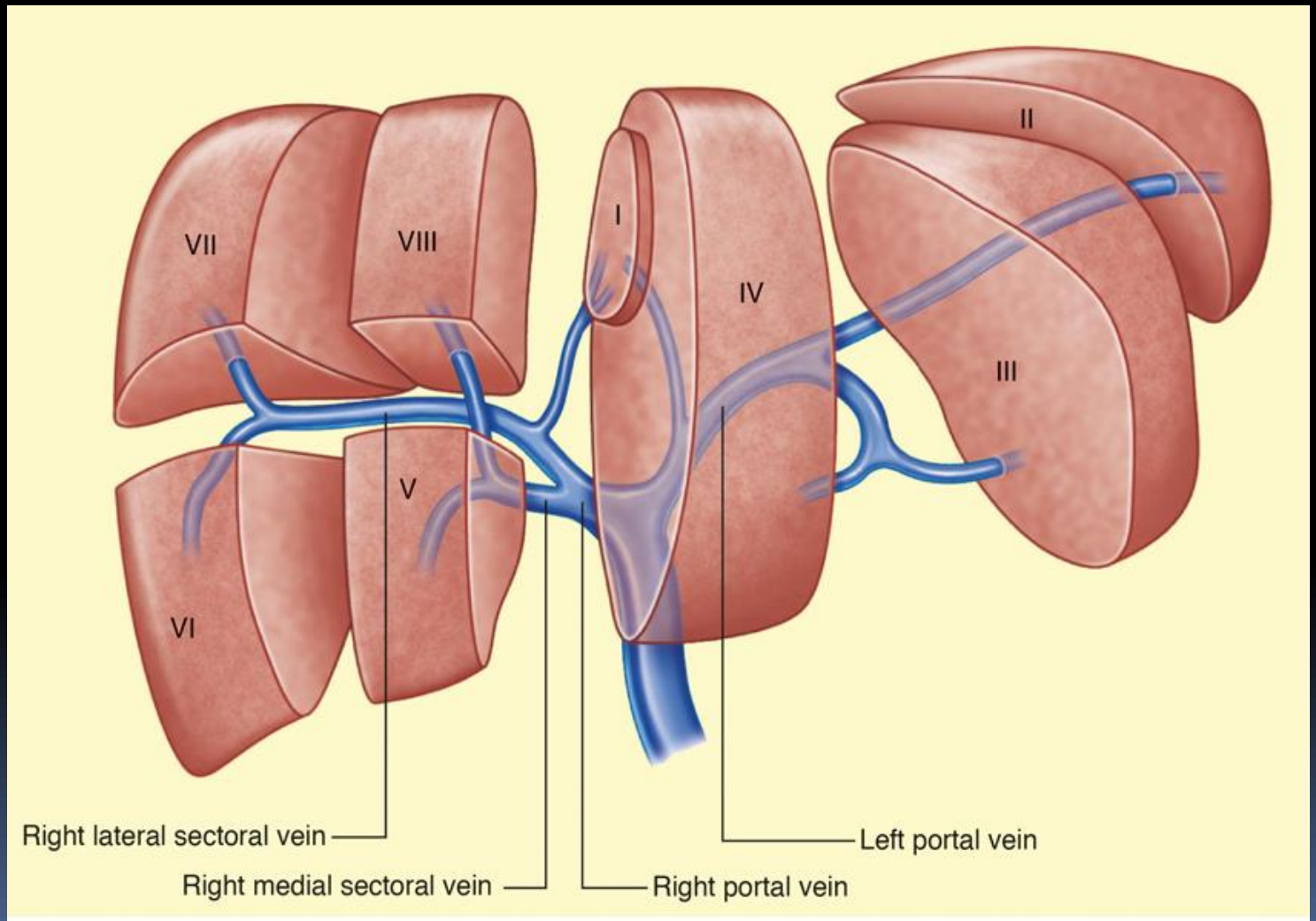
Anatomy


Human Liver
inferior Vena Cava
aorta
coronary ligament
left lobe
right lobe
falciform ligament
Largest solid organ
wiseGEEK

Liver segments

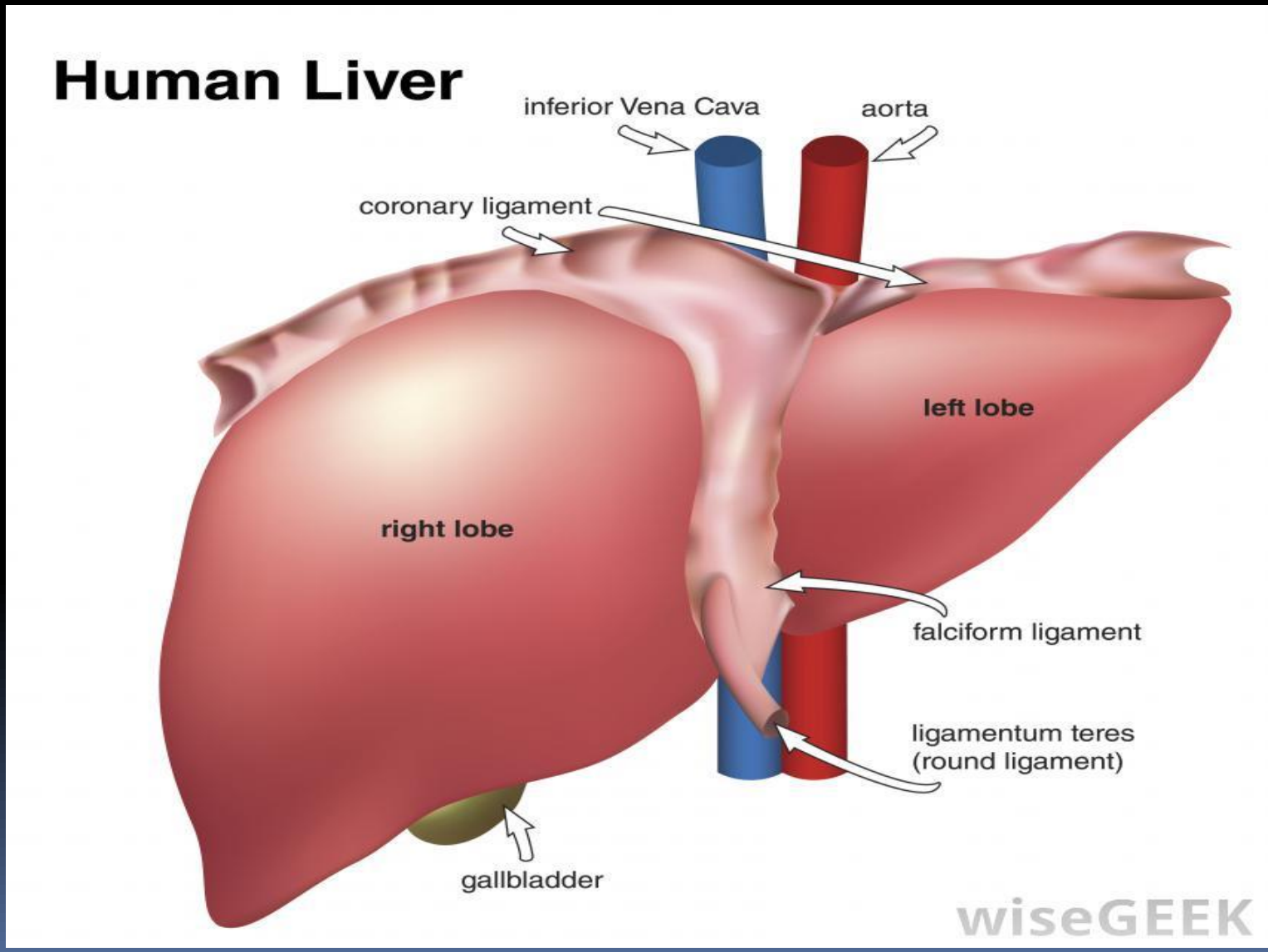



VII
VIII
IVa
II
III
IVb
V
VI
EpoMedicine
7
8
4a
2
1
6
5
4b
3

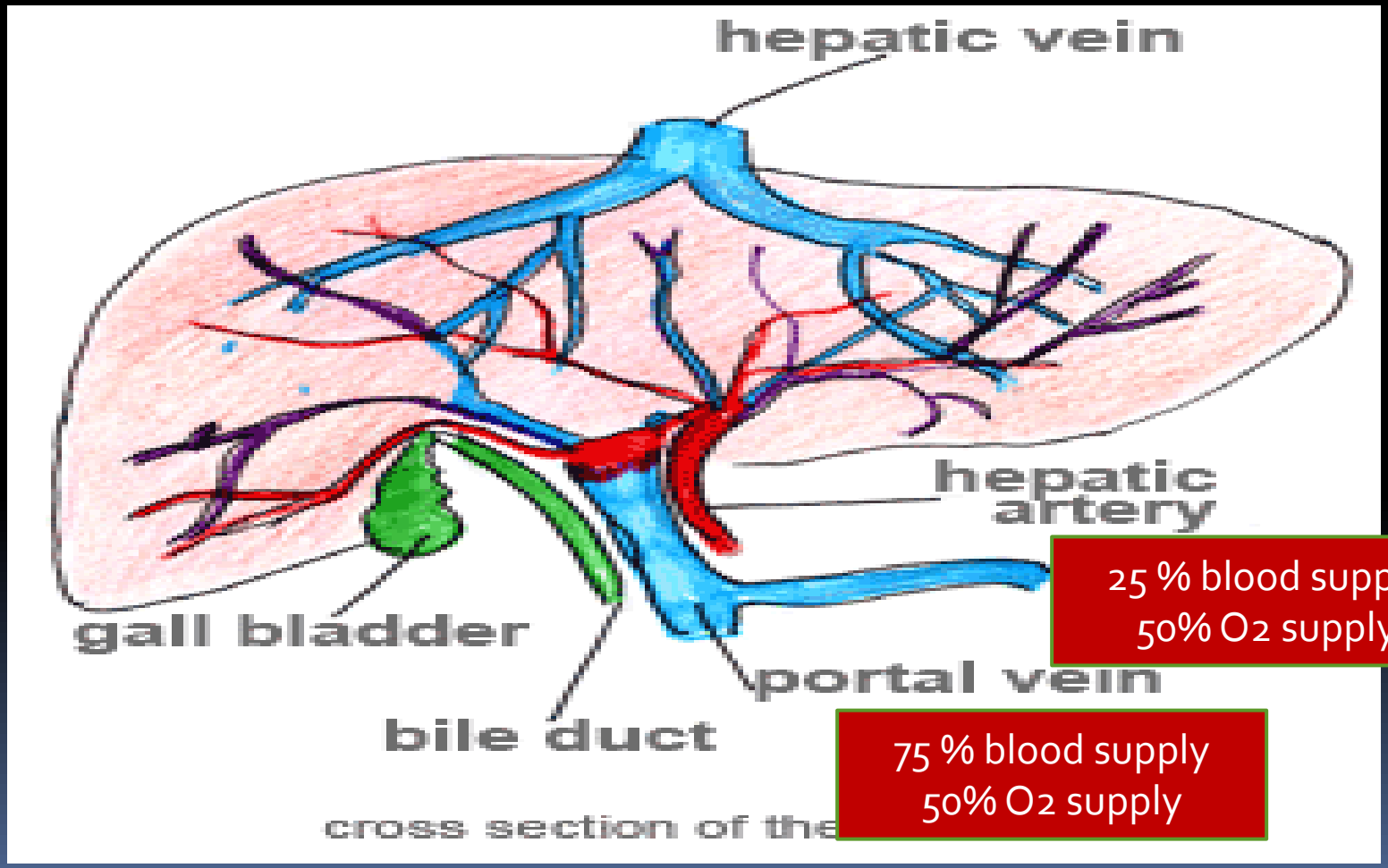


Source: Schrope B: *Surgical and Interventional Ultrasound:*
www.accesssurgery.com

Anatomy

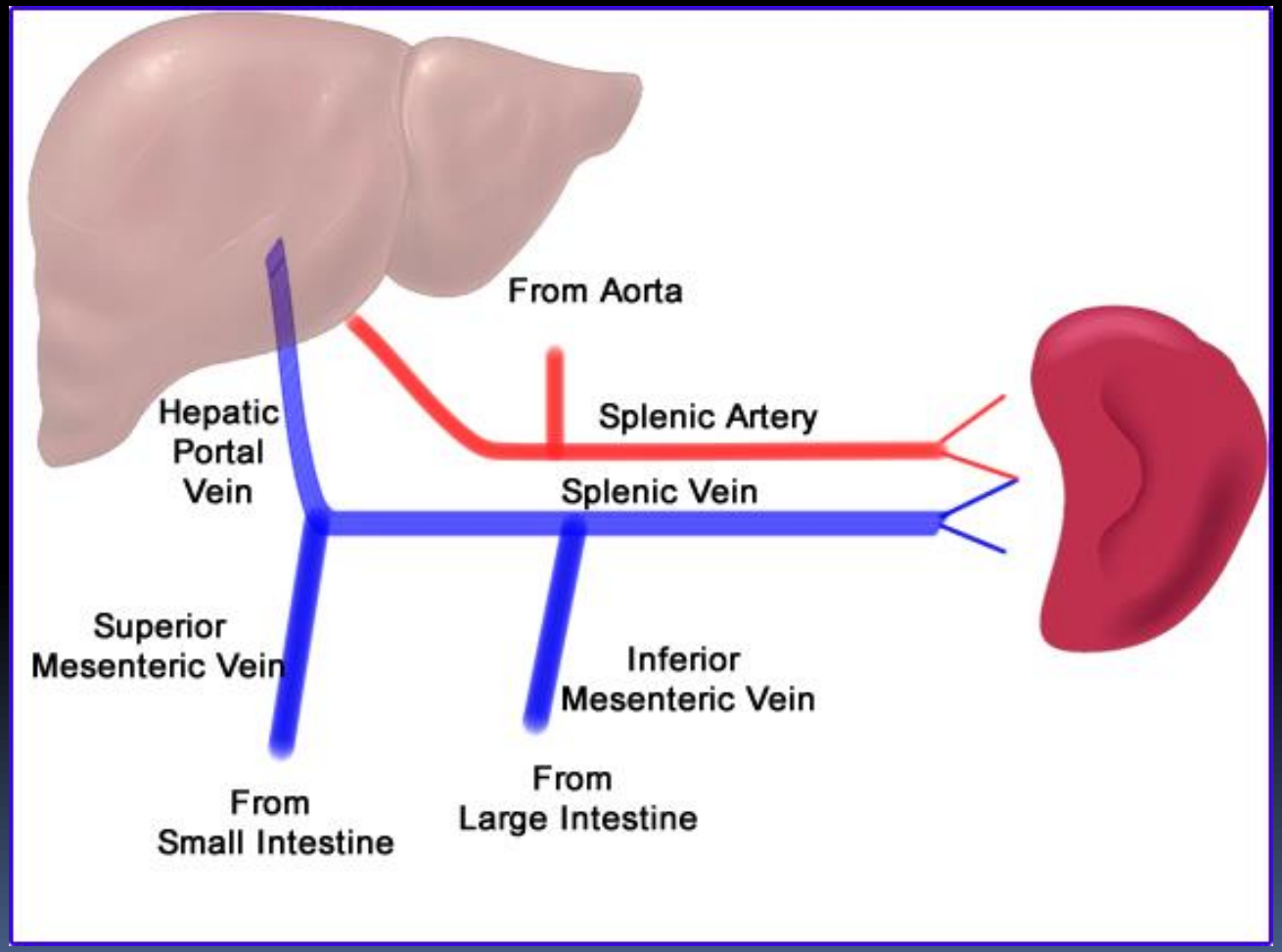

Human Liver
inferior Vena Cava
aorta
coronary ligament
left lobe
right lobe
falciform ligament
ligamentum teres
(round ligament)
gallbladder
wiseGEEK

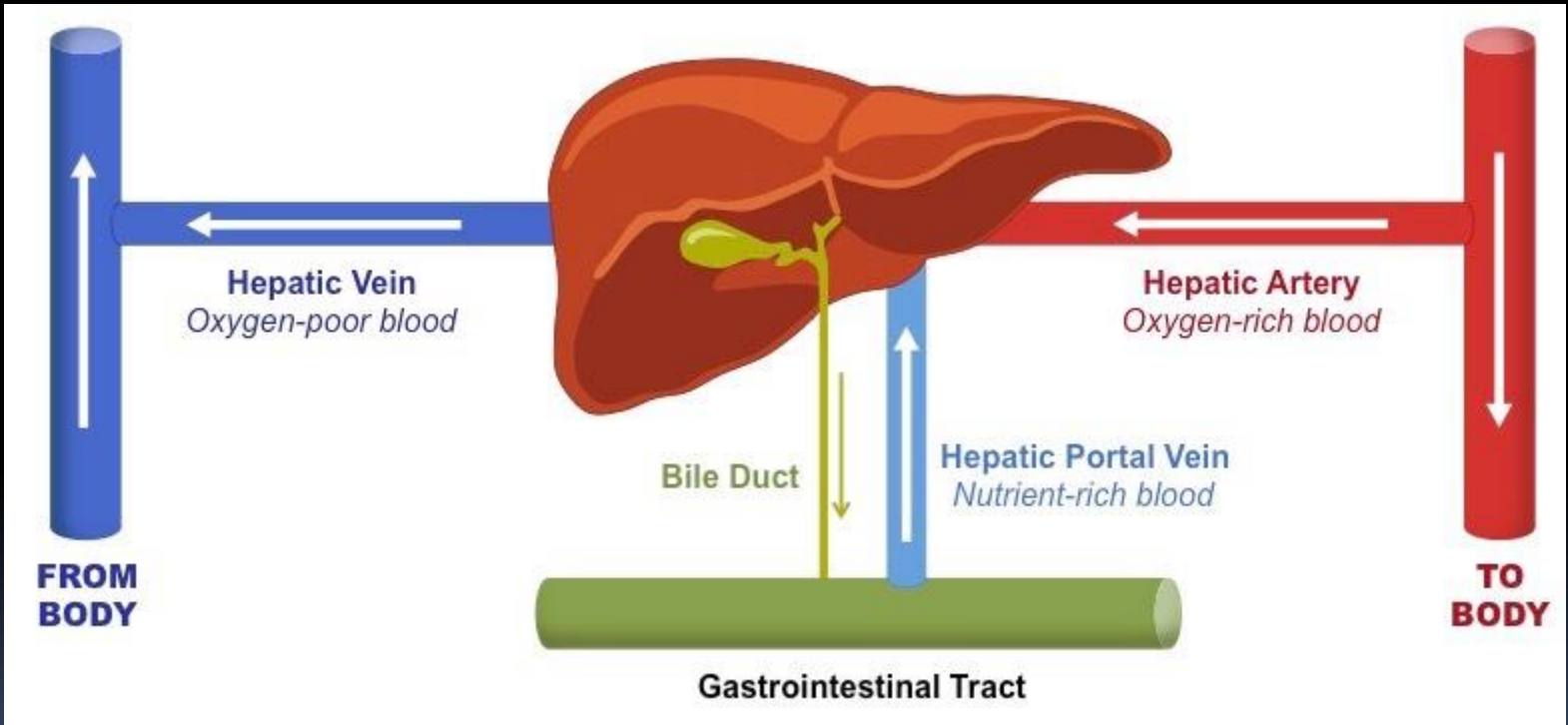
Anatomy



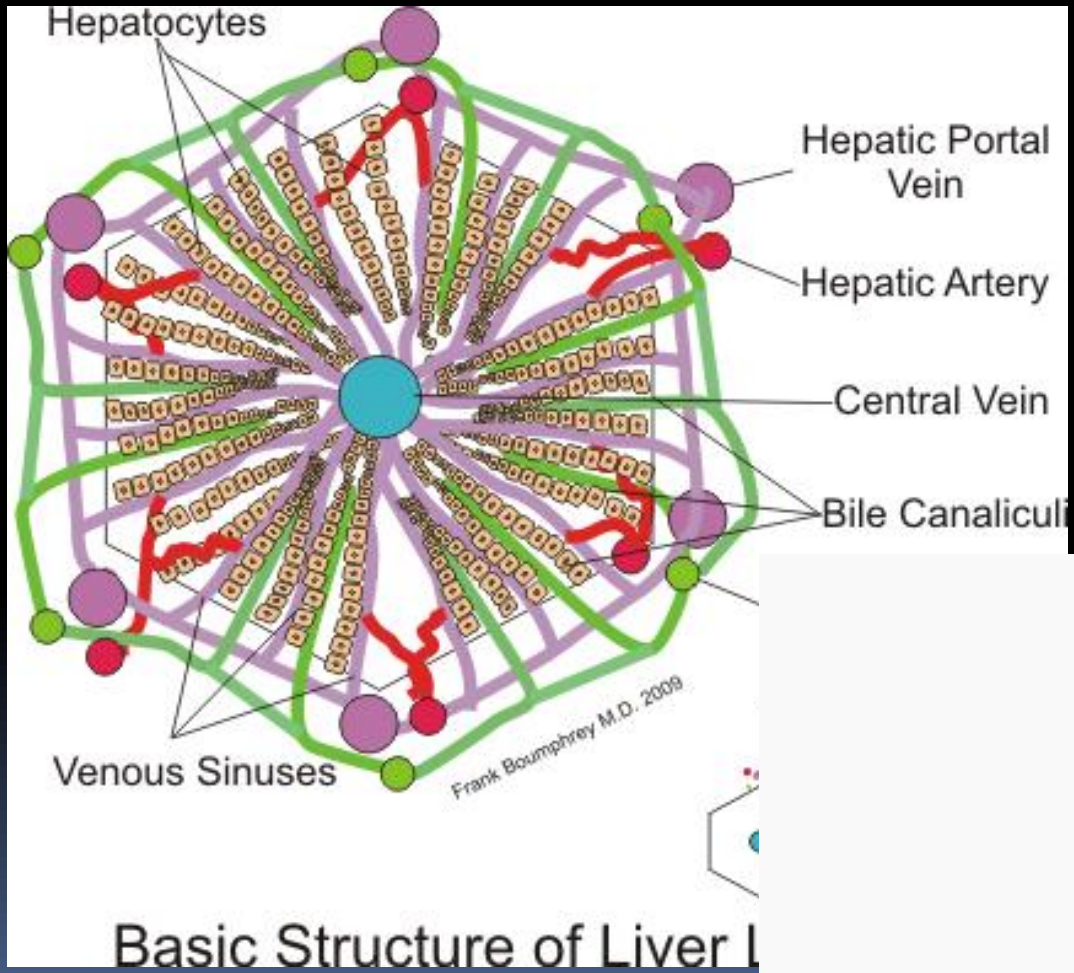
25 % blood supply
50% O2 supply

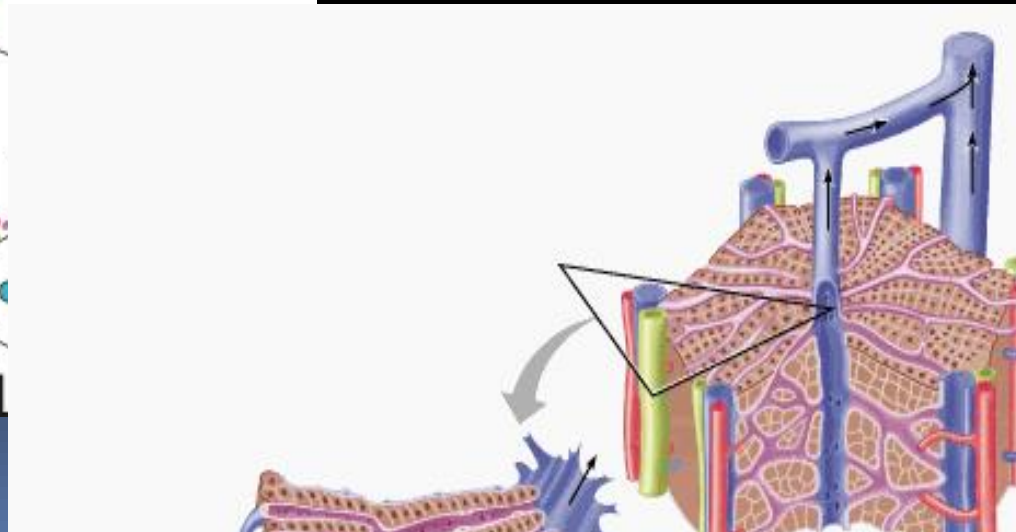
75 % blood supply
50% O2 supply


From Aorta
Hepatic
Portal
Vein
Splenic Artery
Splenic Vein
Superior
Mesenteric Vein
Inferior
Mesenteric Vein
From
Small Intestine
From
Large Intestine

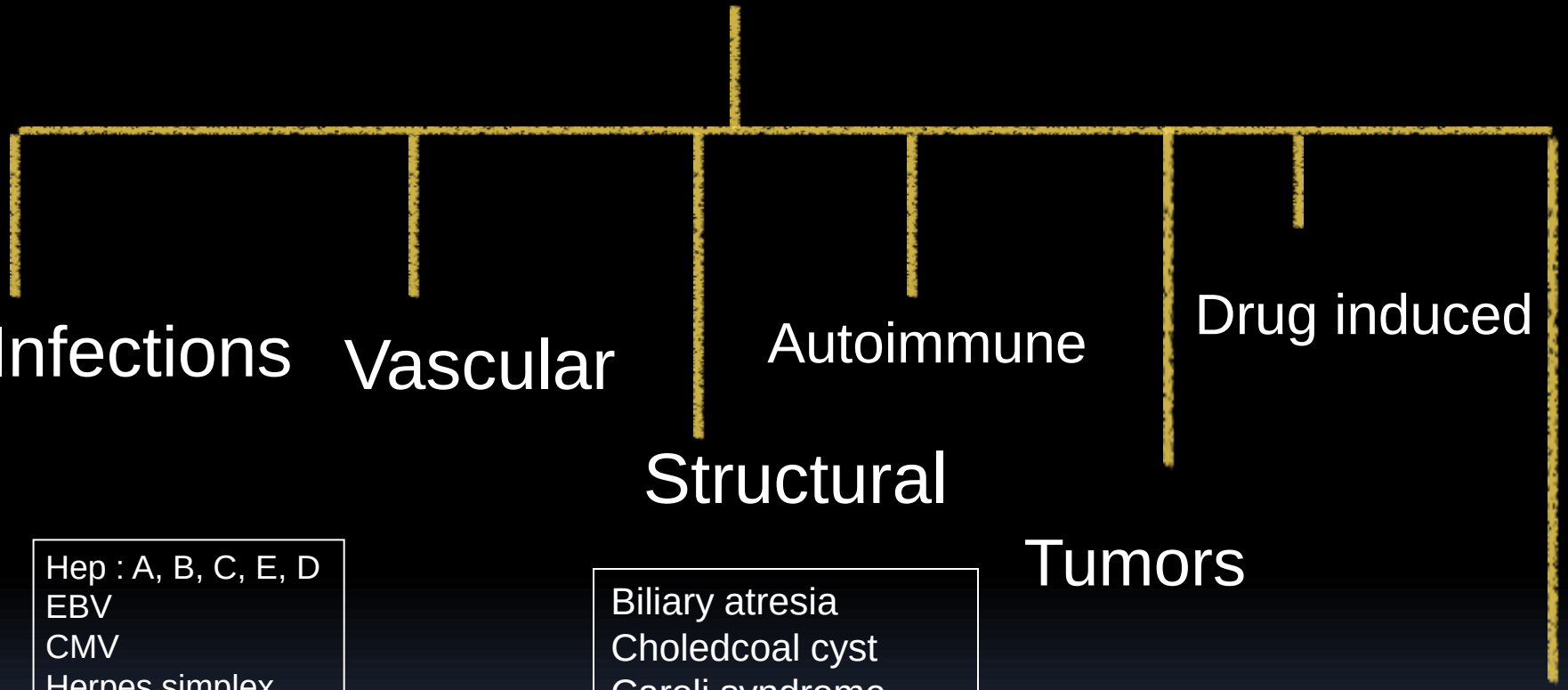

Hepatic Vein
Oxygen-poor blood
Hepatic Artery
Oxygen-rich blood
Bile Duct
Hepatic Portal Vein
Nutrient-rich blood
FROM BODY
TO BODY
Gastrointestinal Tract

Structure of liver lobule





Liver diseases



Infections

Vascular

Structural

Autoimmune

Drug induced

Tumors

Inherited Metabolic

Hep : A, B, C, E, D
EBV
CMV
Herpes simplex
HHV6
Parvovirus
Yellow fever
Dengue fever
Hantavirus

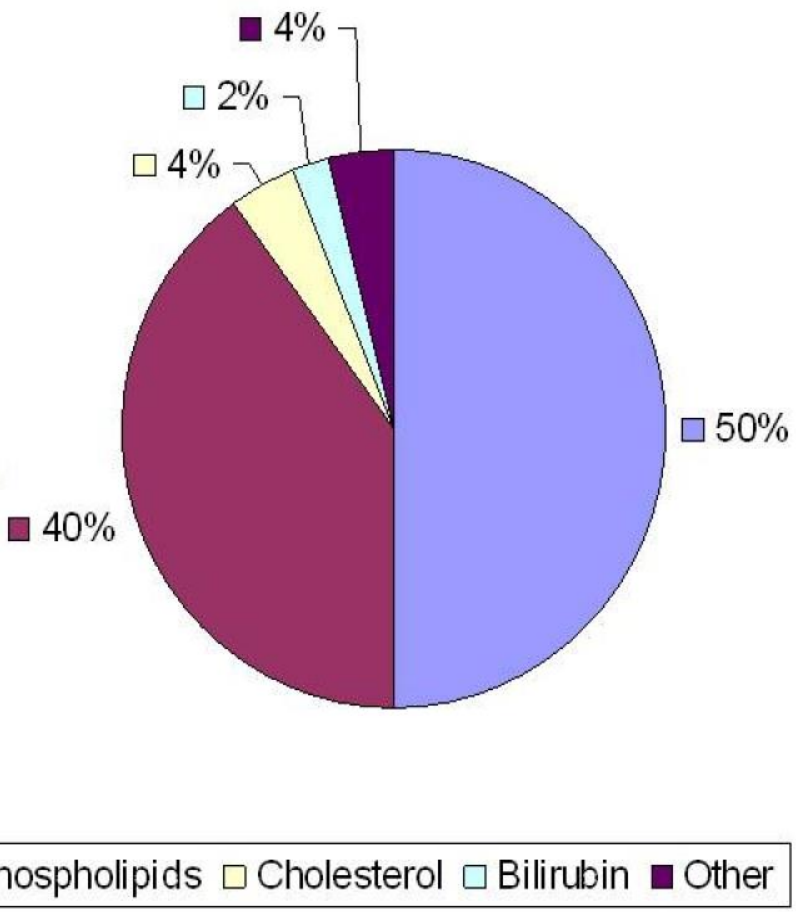
Biliary atresia
Choledcoal cyst
Caroli syndrome
Alagille syndrome
choledecholithiasis

Cholestatic disease

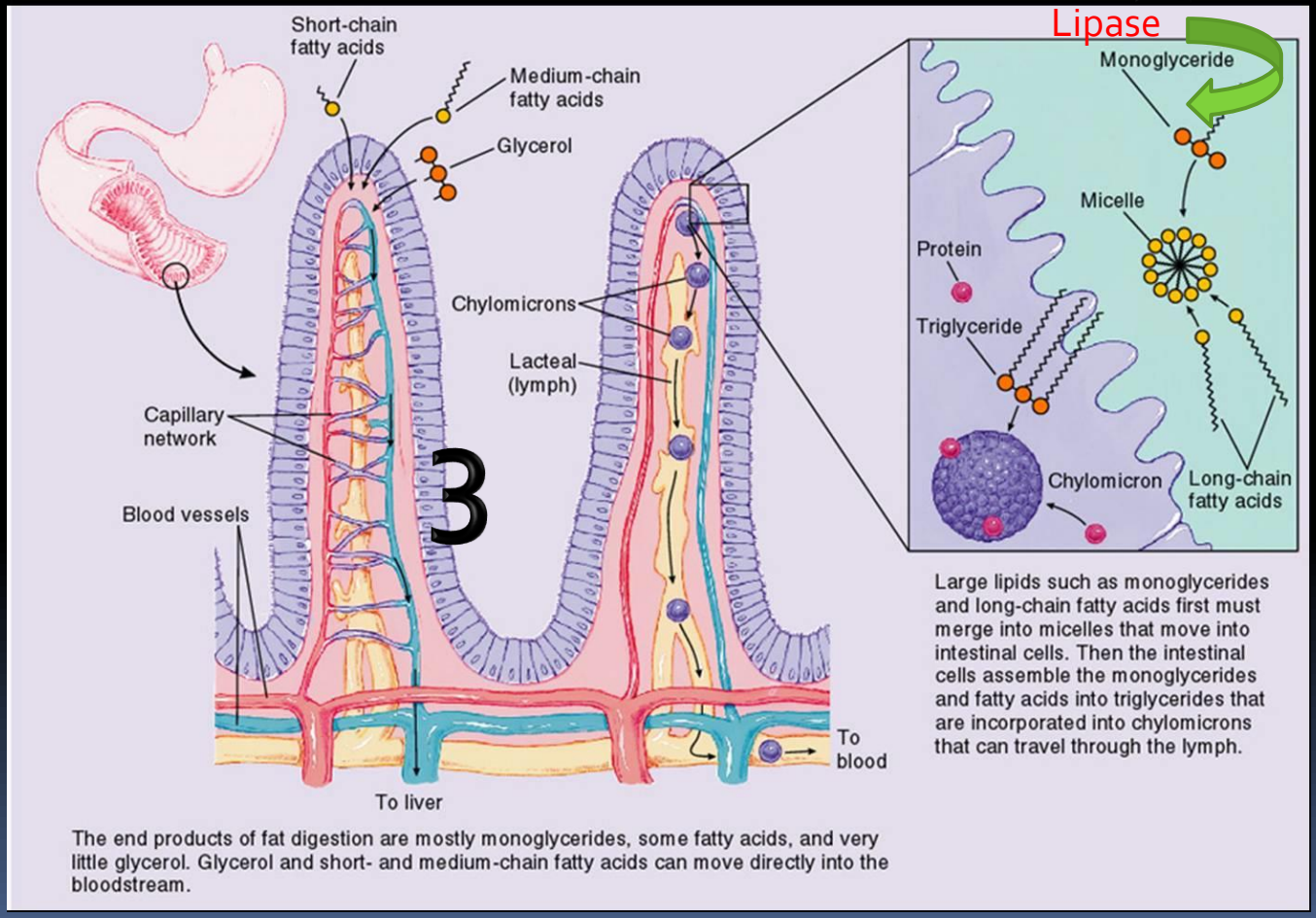
- Heterogenous group of diseases
- Different etiologies
- Affect bile

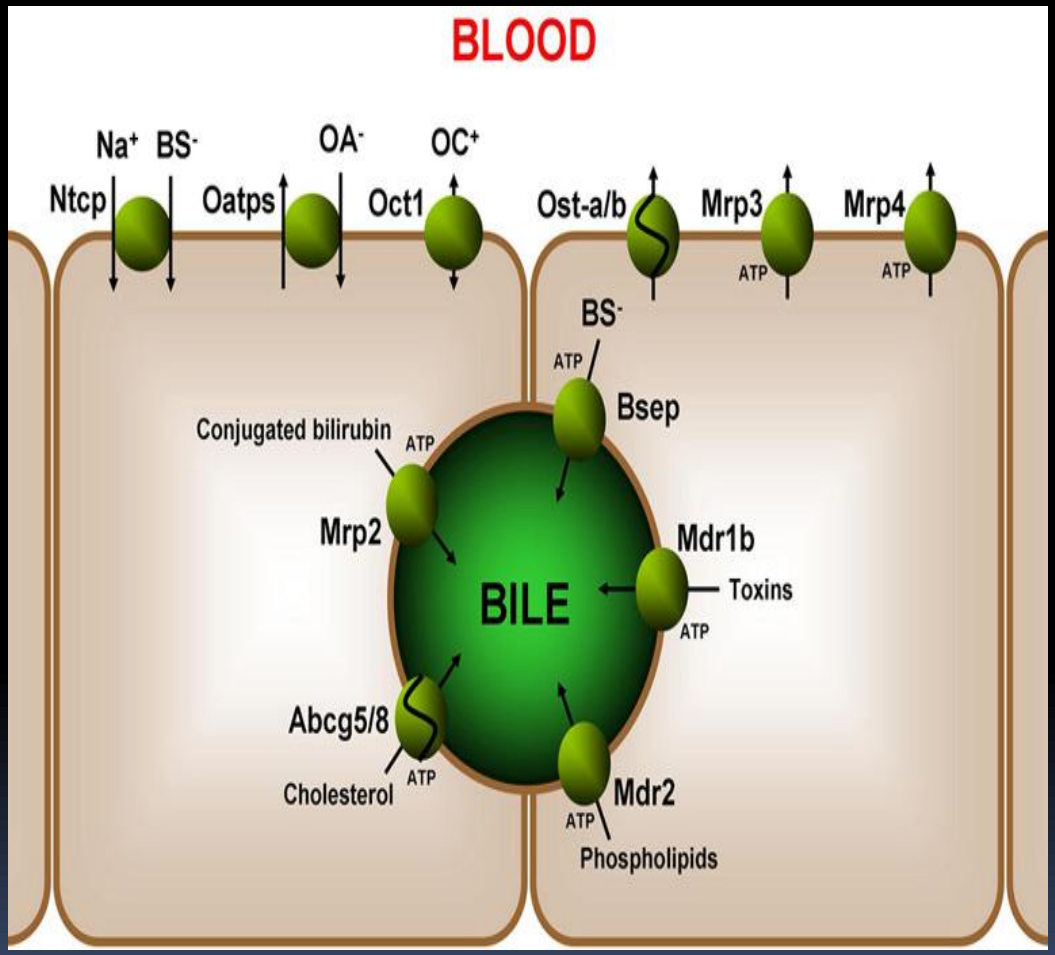
What is bile?

- **A yellowish, blue and green fluid secreted by hepatocytes**
- Composed of water, ions, bile acids, organic molecules (e.g. cholesterol, phospholipids, bilirubin)
- **Aids the process of digestion of lipids (which are insoluble in water) by emulsification**



Absorption of MCT vs LCT



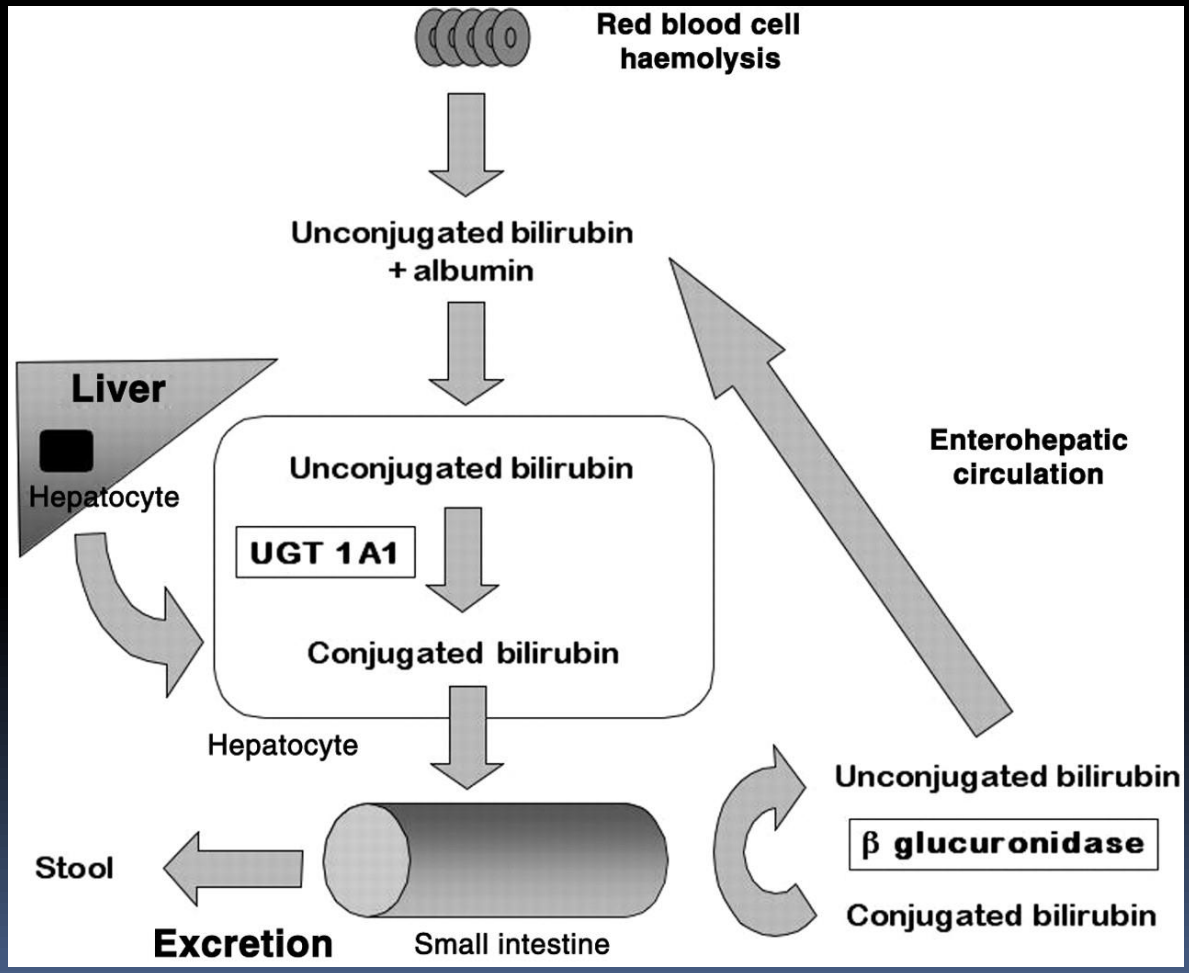

BLOOD
Na+ BS-
Ntcp
Oatps
OA-
OC+
Oct1
Ost-a/b
Mrp3
ATP
Mrp4
ATP
BS-
ATP
Bsep
Conjugated bilirubin
ATP
Mrp2
Mdr1b
BILE
Toxins
ATP
Abcg5/8
Cholesterol
ATP
Mdr2
ATP
Phospholipids

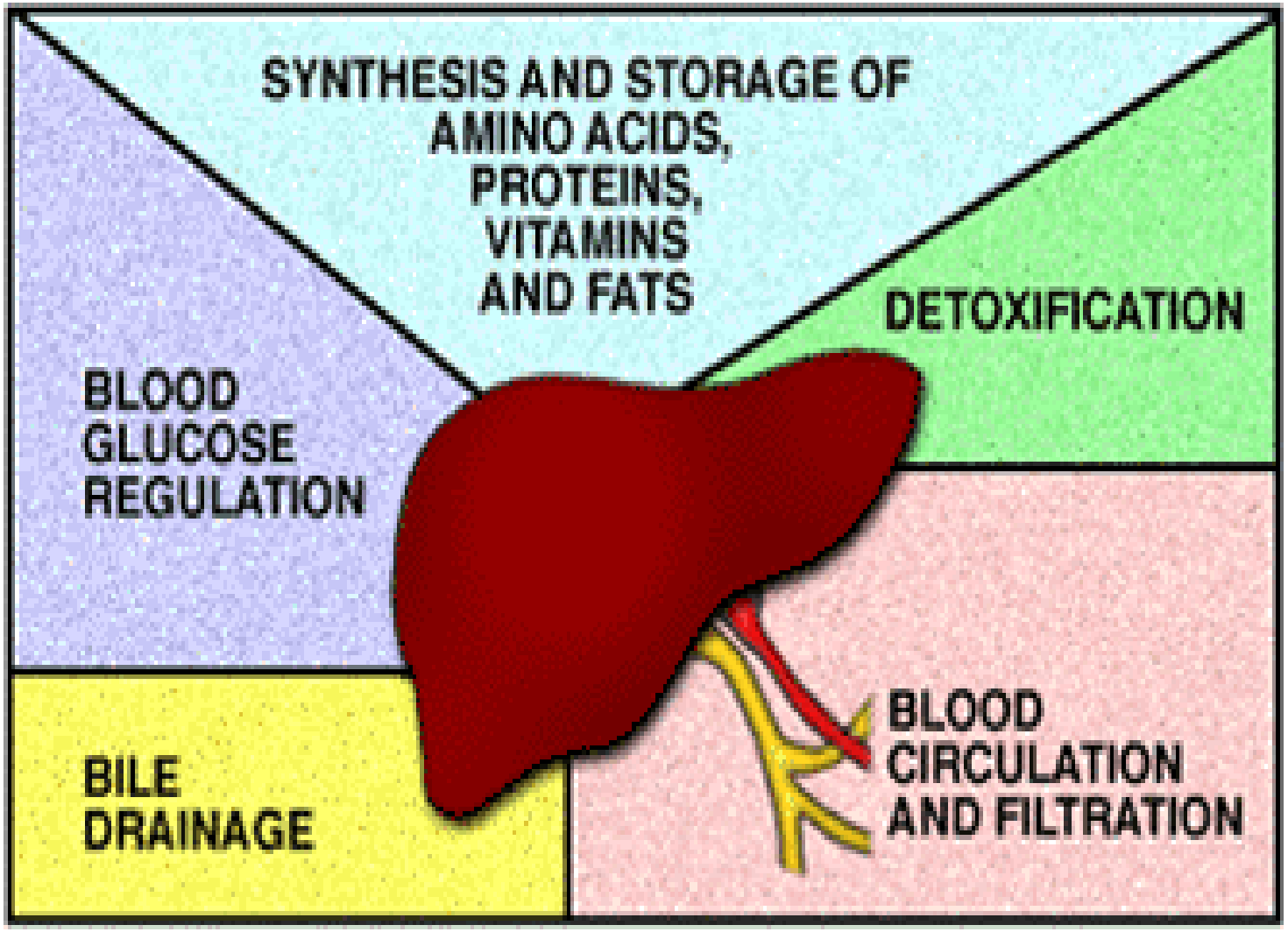
Progressive Familial Intrahepatic Cholestasis
PFIC

Laboratory parameter	*PFIC1*	*PFIC2*	*PFIC3*
GGT	Normal/low	Normal/low	Elevated
Aminotransferases	Mildly elevated	Elevated (×5)	Significantly elevated
Alkaline phosphatase	Elevated	Elevated	Elevated
Serum cholesterol	Normal	Normal	Normal
Serum bile acids	Elevated	Elevated	Elevated
Alpha-fetoprotein	Mildly elevated	Elevation more than PFIC1	Normal
Biliary bile salts	Mildly decreased	Dramatically decreased	Normal
Biliary phospholipids	Normal	Normal	Low

PFIC: Progressive familial intrahepatic cholestasis; GGT: Gamma-glutamyl transferase

Overview


Red blood cell haemolysis
Unconjugated bilirubin + albumin
Liver
Hepatocyte
Unconjugated bilirubin
UGT 1A1
Conjugated bilirubin
Hepatocyte
Enterohepatic circulation
Unconjugated bilirubin
β glucuronidase
Conjugated bilirubin
Stool
Excretion
Small intestine



LIVER FUNCTIONS

Auto regeneration

Cholestasis

- Decreased /impaired bile flow
- Either due to mechanical obstruction
- Or due to down regulation / absent transport proteins
- Direct hyperbilirubinemia
- Total bilirubin = Conjugated + Unconjugated + Delta
- Delta : conjugated bili bound to albumin

Bilirubin Measurements

The most accurate way to measure bilirubin fractions is by measuring the total bilirubin(TB), the unconjugated bilirubin(UB), and the conjugated bilirubin(CB). Often the unconjugated + conjugated bilirubin does not equal the total bilirubin measured. This difference is referred to as delta bilirubin or the delta fraction. Delta bilirubin is actually conjugated bilirubin that is covalently bound to albumin and is therefore not measured as conjugated bilirubin. Now let's look at the results of the child in the vignette as an example:

- TB = 9.0
- UB = 3.2
- CB = 4.8

The delta bilirubin, or delta fraction, in this example equals 1. This is calculated by the equation Delta = TB - (UB + CB) ; Delta = 9.0 - (3.2 + 4.8)

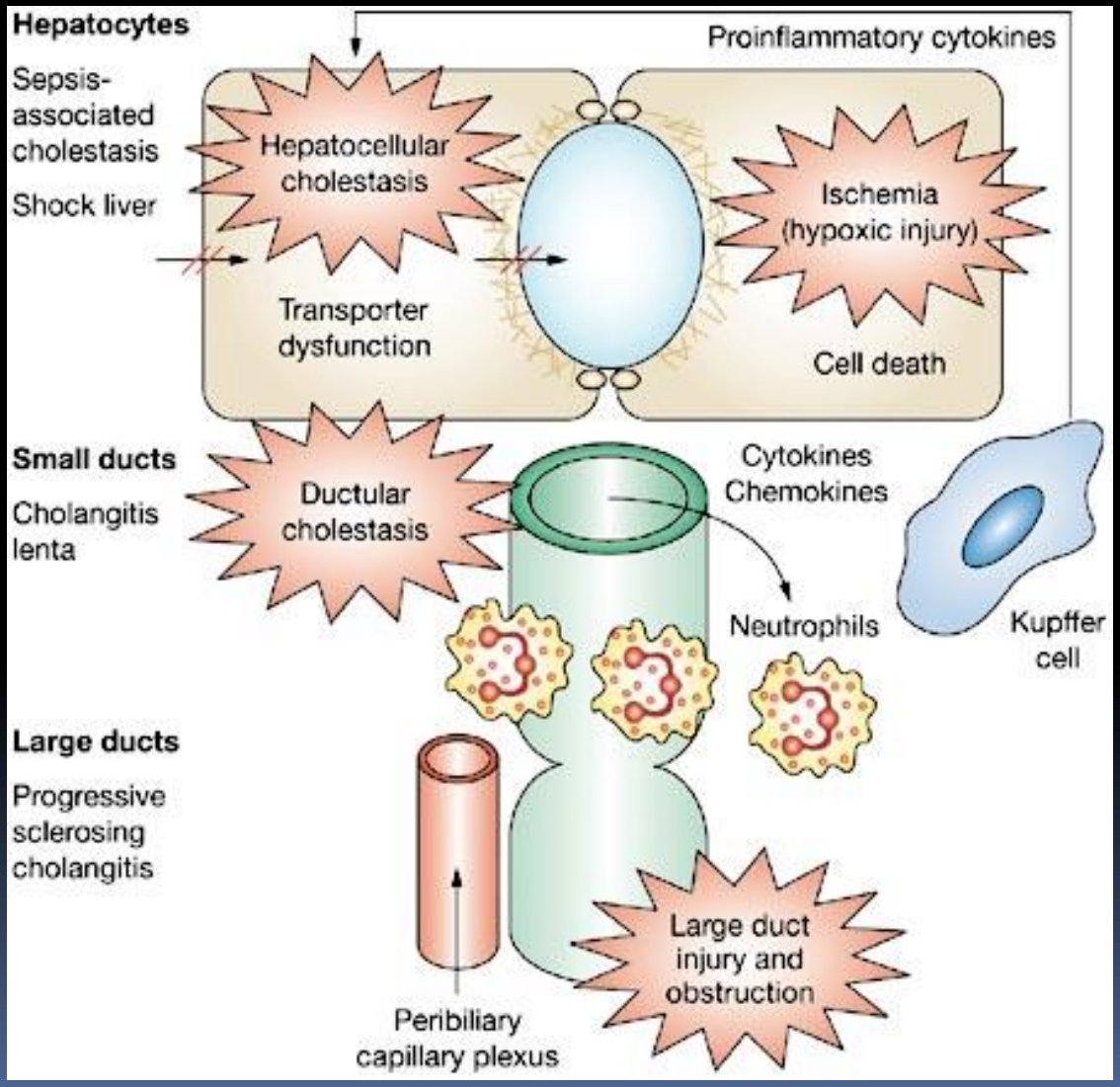
The other method of measuring bilirubin fractions is reporting the total bilirubin(TB) and the direct bilirubin(DB). This method is less accurate in measuring conjugated bilirubin in that the direct portion may contain conjugated as well as delta bilirubin.

Cholestasis by laboratory criteria has traditionally been defined as a direct (or conjugated) bilirubin that is greater than 20% of the total measured bilirubin. The child in the vignette does indeed have cholestatic jaundice as her conjugated bilirubin accounts for just over 50% of the total bilirubin. Once the diagnosis of cholestatic jaundice has been made, consultation with a pediatric gastroenterologist is indicated.

Close

cholestasis

- This results in retention of bile components in the liver , which are harmful to the hepatocytes and will lead to liver damage if left " undrained " in the hepatocytes


Hepatocytes
Proinflammatory cytokines
Sepsis-associated cholestasis
Shock liver
Hepatocellular cholestasis
Ischemia (hypoxic injury)
Transporter dysfunction
Cell death
Small ducts
Cholangitis lenta
Ductular cholestasis
Cytokines
Chemokines
Neutrophils
Kupffer cell
Large ducts
Progressive sclerosing cholangitis
Large duct injury and obstruction
Peribiliary capillary plexus

Neonatal jaundice

- Physiologic Vs pathological jaundice

Neonatal Jaundice

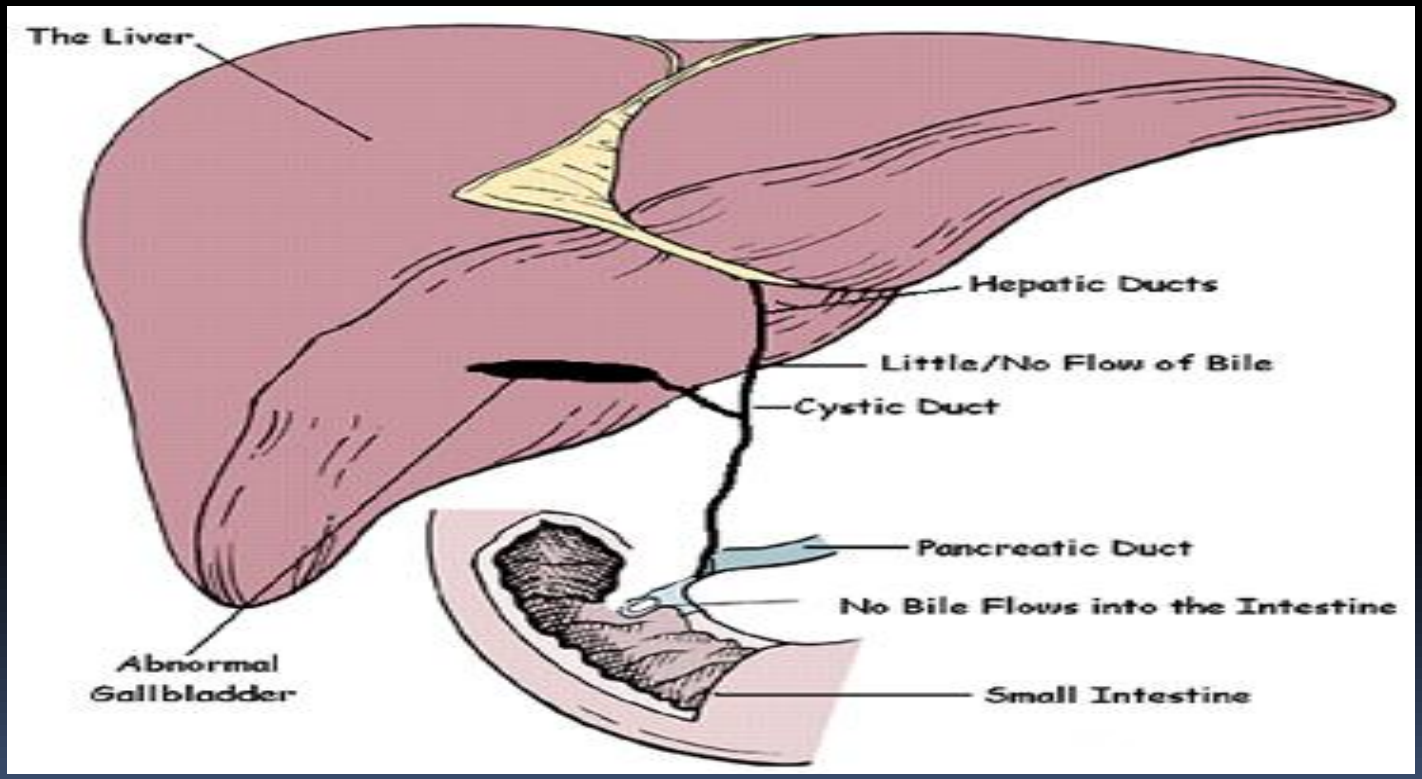
- At what age should you rule out cholestasis as the cause of neonatal jaundice?
  - 2 weeks in formula fed infants
  - 3 weeks in breastfed infants
- How can you screen for neonatal cholestasis?
  - Fractionate the bilirubin

Red Flags in the Jaundiced Infant

- by History :
  - Irritability or vomiting
  - Dark urine
  - Acholic stools
  - Poor intrauterine growth
- By Physical exam:
  - Abnormal facies
  - Microcephaly
  - Cataracts
  - Heart murmur or other signs of cardiac disease
  - Hepatomegaly
  - Splenomegaly

What does each of these suggest?

Biliary atresia

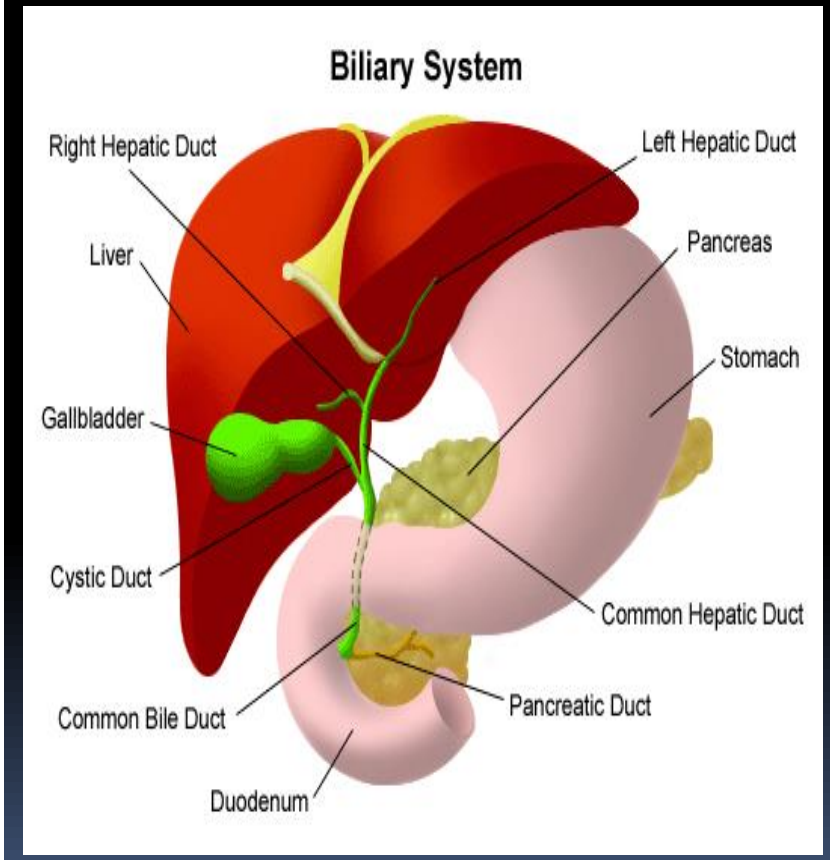


Biliary Atresia

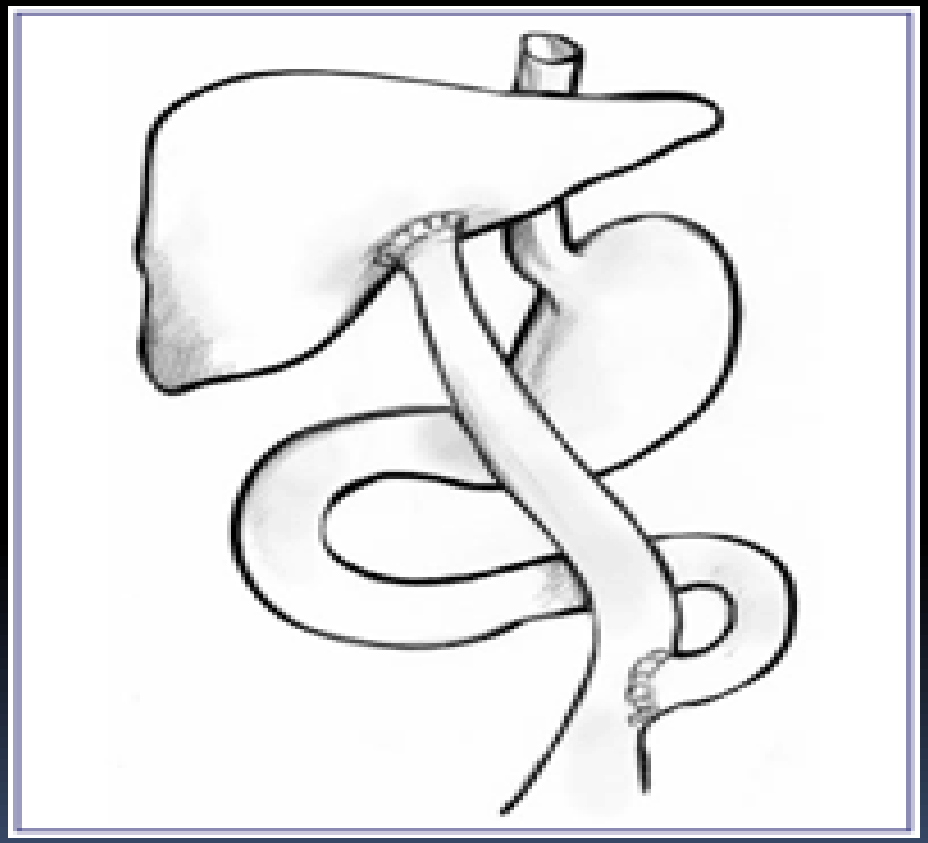
- Why is it important to rule out biliary atresia in a timely manner?
  - Earlier intervention associated with better outcome
- Are most patients well-appearing or ill-appearing at the time of presentation?
  - Well-appearing
- What surgical procedure can be done for patients with biliary atresia?
  - Kasai portoenterostomy

Kasai Portoenterostomy

Normal



Kasai



Other Causes of Neonatal Cholestasis

- Besides biliary atresia what are the two most common causes of neonatal cholestasis?
  - Idiopathic neonatal hepatitis
  - α1-antitrypsin deficiency – v.rare in our countries
- Name some other causes
  - Hypothyroidism
  - Galactosemia
  - Fructosemia
  - Tyrosinemia
  - TPN
  - Sepsis or UTI
  - Choledochal cyst
  - Alagille syndrome
  - Cystic fibrosis
  - Bile acid synthesis defects

Evaluation of the Jaundiced Infant

- The most important thing for the primary care physician to do is
- FRACTIONATE THE BILIRUBIN!!!
- If neonatal cholestasis is present consultation with a pediatric gastroenterologist is warranted
- You should review the newborn screen and at least consider blood and urine cultures

Diagnostic Testing

- What are the indications, pros, and cons of
  - Ultrasound
  - DISIDA or HIDA scan

  Di- ISopropyl – Imino- Di- Acetic scan

  Tc99
  - Liver biopsy
  - Intraoperative cholangiogram

Mx of cholestatic infant

1. Treat the cause

2. Decrease cholestasis/ improve bile flow
   Ursodeoxycholic acid URSA

3. Improve nutrition MCT formula
4. Vitamin supplement ADEK

ADEK

5 ml po q day
+
Vit K 2 mg

Mx of cholestatic infant

4- watch for cirrhosis complications

PHTN

Splenomeglly :

Ascites

Esophagela varices

Hepatorenal syndrome

Hepatopulmonary syndrome

malignancy

Acute Hepatitis

- Causes
  - Hepatitis A most common
  - Hepatitis B and C
  - EBV, CMV, other viruses
  - Non-infectious causes
- Evaluation
  - Hepatitis panel +/- EBV and CMV serologies
  - Liver *function* tests
  - If Hep B or C (+) or no cause found, refer patient

Acute Hepatic Failure

- May result from a variety of causes
- Management of these patients
  - Provide IV glucose
  - Try to lower ammonia
  - Try to correct coagulopathy
  - Transfer to transplant center

Chronic Hepatitis

- Causes
  - NASH
  - Hepatitis B or C
  - Autoimmune, Wilson's, α1-antitrypsin deficiency
  - Medication related
- Evaluation
  - Hepatitis panel
  - Liver *function* tests
  - Referral to pediatric gastroenterologist

Hepatitis B Serologies

- HBsAg =
  - infected
- Anti-HBs =
  - protected
- Anti-HBc IgM =
  - primary infection recent
- Anti-HBc IgG =
  - primary infection remote
- HBeAg =
  - viral replication or increased infectivity

Interpretation of Hep B Serologies

- Interpret these serologies
  - Anti-HBs (+) and anti-HBc (+)
    - Resolved infection
  - HBsAg (+) and anti-HBc IgG (+)
    - Chronic infection
  - Anti-HBs (+) and anti-HBc (-)
    - Immunized
  - HBsAg (+) and anti-HBc IgM (+)
    - Acute infection

You see a 18-day-old male infant for his 2-week visit. He is breastfeeding well, and his weight gain has been appropriate. Mom reports that he still looks a little jaundiced but she says that his color seems to be improving. His physical exam is unremarkable except for mild jaundice and scleral icterus.

Are there any "red flags" to suggest cholestasis?

What is the most likely cause for his jaundice?

Are there any tests that should be ordered?

How will you manage this patient?

You see a 4-week-old male infant in clinic. He is breastfeeding well, and his weight gain has been appropriate. Mom reports that his stools are almost white in color and his urine very dark brown. On physical exam, he has mild jaundice and scleral icterus and his liver is palpable 3 cm below the costal margin.

Are there any "red flags" to suggest cholestasis?

What is the most likely cause for his jaundice?

Are there any tests that should be ordered?

How will you manage this patient?

You see a 14-year-old female in clinic for fever, nausea and vomiting for the past 3 days. She reports that this morning she noticed a yellow color to her eyes and skin. Her physical exam is remarkable for jaundice, scleral icterus, and mild right upper quadrant tenderness. Labs: ALT 4000, AST 3100, alk phos 280, total bili 7.8, conj bili 5.6.

- What is your assessment of this patient?
- What is the most likely etiology?
- What other labs would you order?
  - Hep A IgM (+)
  - Coags normal, NL serum glucose
- How would you treat this patient?
- What if the Hep A IgM was (-)?

You see a 9-year-old female with jaundice. She was seen in a local ER and was told that she had hepatitis. Family history is positive for hypothyroidism in the maternal grandmother and the mother. PE: normal except jaundice. Labs from local ER: ALT 2300, AST 2200, alk phos 300, total bili 12.2, conj bili 8.8, hepatitis screen (-).

- What is your assessment of this patient?
- Are there any clues to suggest an etiology?
- What other labs would you order?
  - EBV and CMV serologies (-)
  - IgG elevated, ANA (+), anti-SMA (+)
- What is your diagnosis of this patient?
- How would you manage this patient?

Autoimmune Hepatitis

- More common in females
- Personal or family history often positive for autoimmune diseases
- Lab:
  - ANA, anti-SMA: Type I
  - Anti-LKM1: Type II
  - Elevated IgG: either
- Treatment: steroids +/- azathioprine

You see a 15-year-old male patient in clinic with fever. On physical exam you notice that he has mild scleral icterus. He states that he often notices this whenever he is sick and states that the same thing happens to his father and uncle. PE: no abdominal tenderness, no HSM. Lab: ALT, AST, alk phos normal; total bili 4.8, conj bili 0.2

- What is your assessment of this patient?
- What is the most likely etiology?
- Are there any other labs that you would order?
  - Consider labs to rule out hemolysis
- How would you treat this patient?

Gilbert's Disease

- Jaundice seen in times of illness or decreased po intake
- Autosomal recessive
- Bilirubin is UNconjugated
- Other liver labs are normal
- No signs of chronic liver disease
- No treatment is necessary

You see a 17-year-old male who presents with jaundice. Mom reports that he has become very withdrawn over the past year and has recently been diagnosed with depression. PE: liver edge palpable 6 cm below costal margin and 8 cm below midline, faint brown rings noted at edge of iris.

- What is your assessment of this patient?
- Are there any clues to suggest an etiology?
- What other labs would you order?
  - Ceruloplasmin decreased
  - 24-hour urine copper extremely elevated
- What is your diagnosis of this patient?
- How would you manage this patient?

Wilson's Disease

- Liver disease, CNS disease, psychiatric disease, signs of hemolysis
- Usually affects older children or adolescents
- Kayser-Fleischer rings highly suggestive
- Lab:
  - Decrease serum ceruloplasmin
  - Elevated 24-hour urine copper
- Treatment: penicillamine or trientine +/- zinc

Riley Hospital Indianapolis

You see a 13-year-old male in clinic for a yearly check-up. He is asymptomatic today. PE: severely obese, acanthosis nigricans present, liver palpable 3 cm below costal margin. Labs: ALT 180, AST 110, alk phos 200, bili 0.8

- What is your assessment of this patient?
- Are there any clues to suggest an etiology?
- What other labs would you order?
  - Fasting blood glucose and insulin level elevated
  - Hepatitis panel (-)
- What is your diagnosis of this patient?
- How would you manage this patient?

NASH

Non Alcholic Steato Hepatitis

- Most common liver disease in the U.S.
- Obesity and insulin resistance
- Fatty infiltration of liver with inflammation
- Must rule out other causes
- Treatment: weight loss is first line treatment

THE END

Questions