LIPIDS

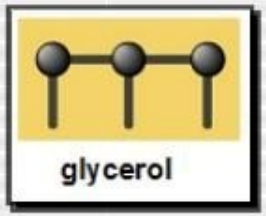
Part II: Digestion, Absorption, Transportation & Metabolism

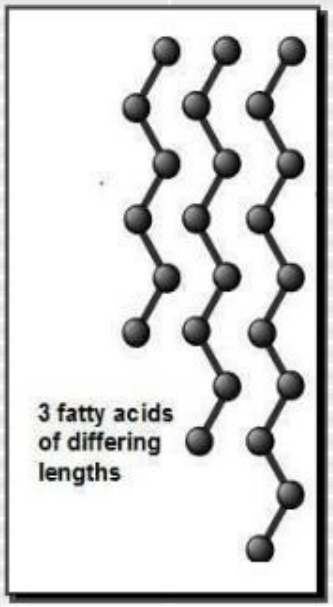
Digestion of Triglycerides

Goal:

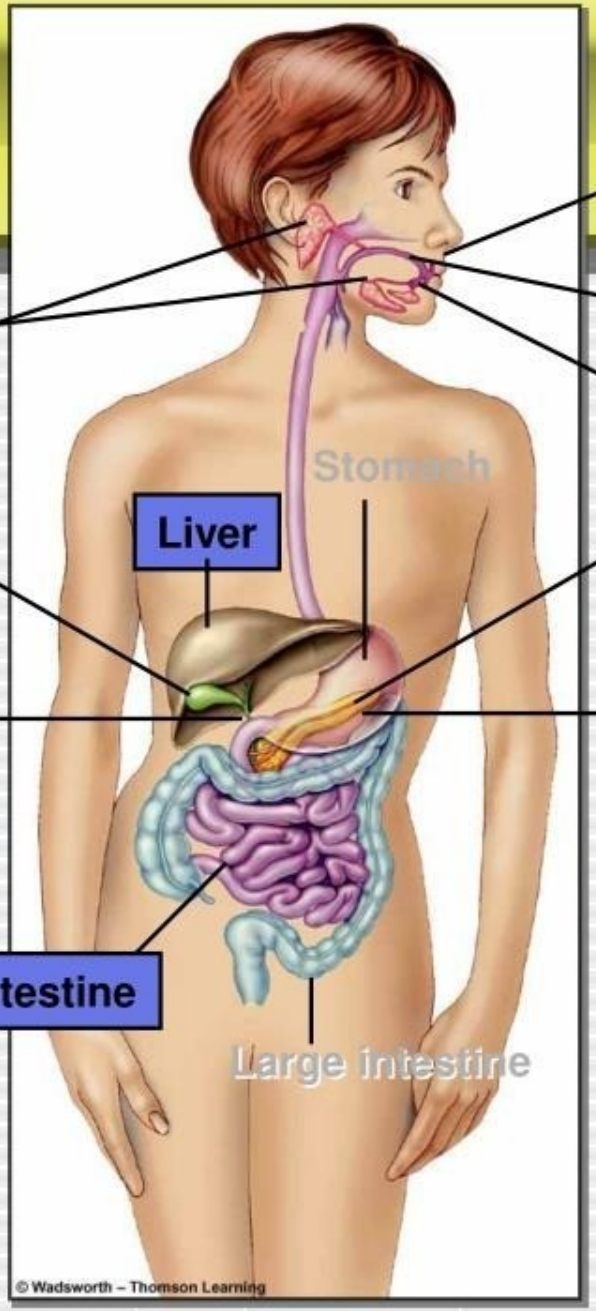
Triglyceride >>>

- monoglycerides
- glycerol
- fatty acids





Digestion


Mouth
Tongue
Salivary glands
Sublingual salivary gland
Stomach
Gallbladder
Liver
Pancreatic duct
Common bile duct
Pancreas
bile
lipases
Small intestine
Large intestine
© Wadsworth – Thomson Learning

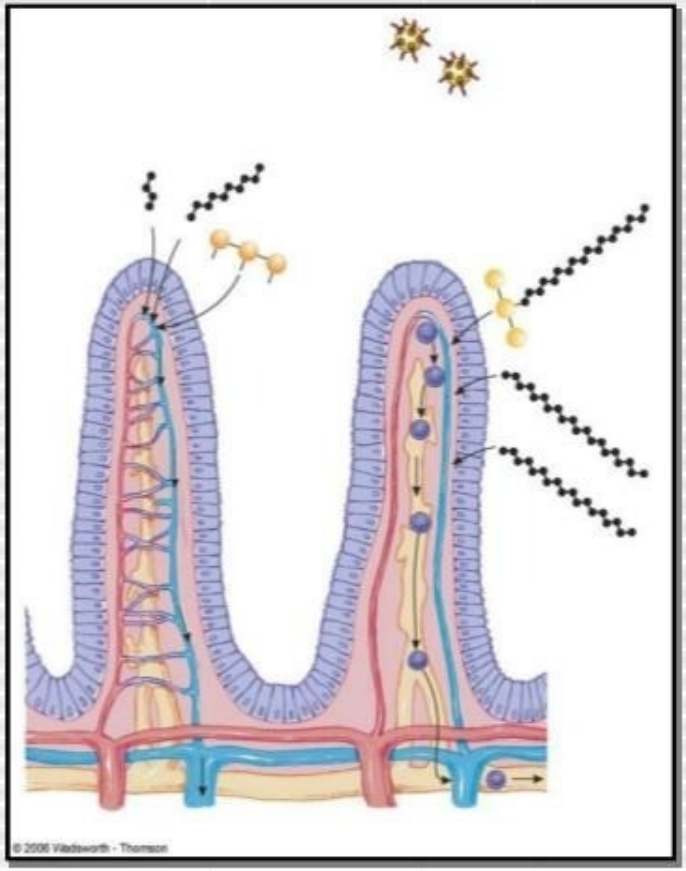
Absorption

two different routes

- small bits ➡bloodstream
  glycerol, short fatty acids

- larger bits➡ lymph

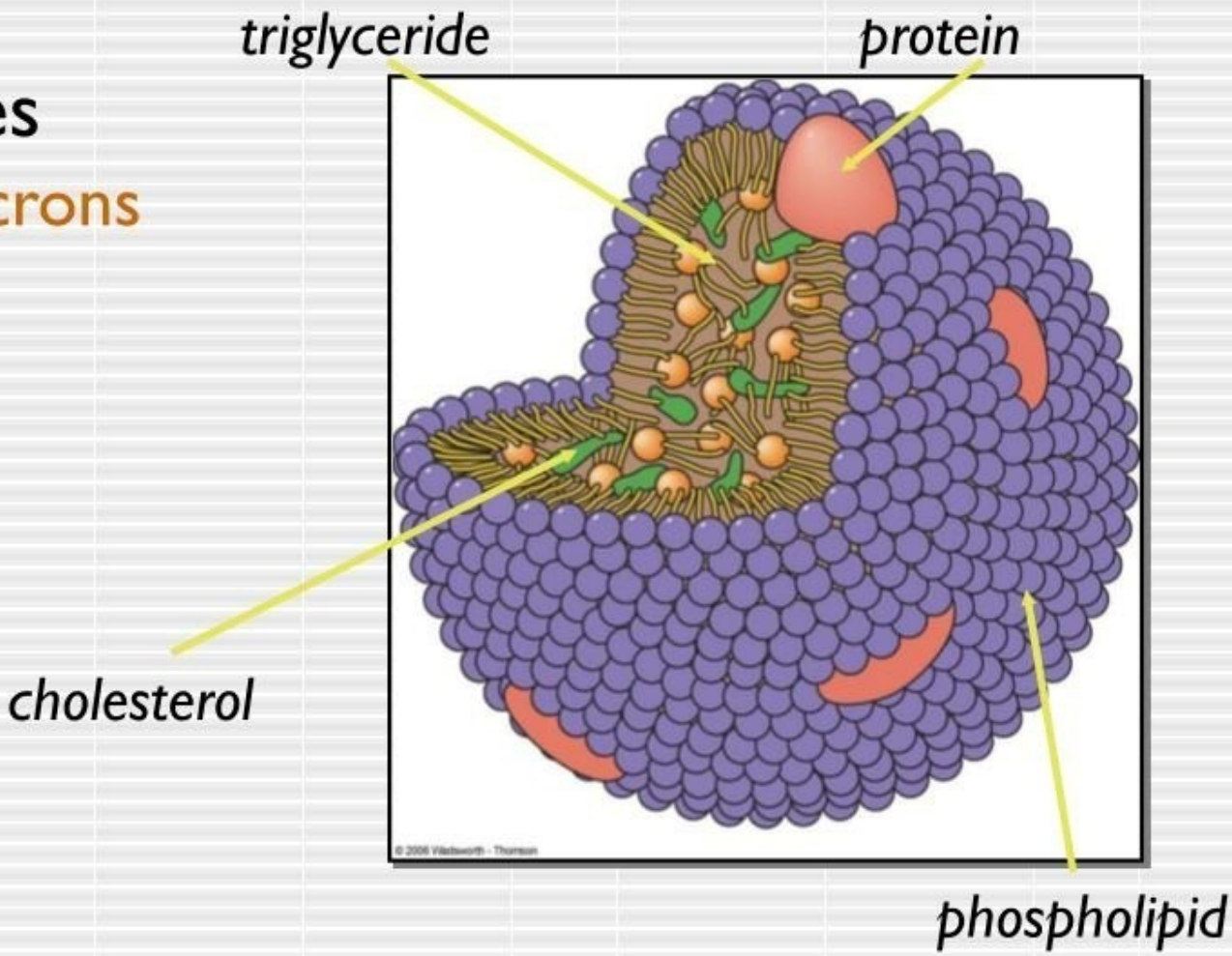
  monoglycerides, long fatty acids



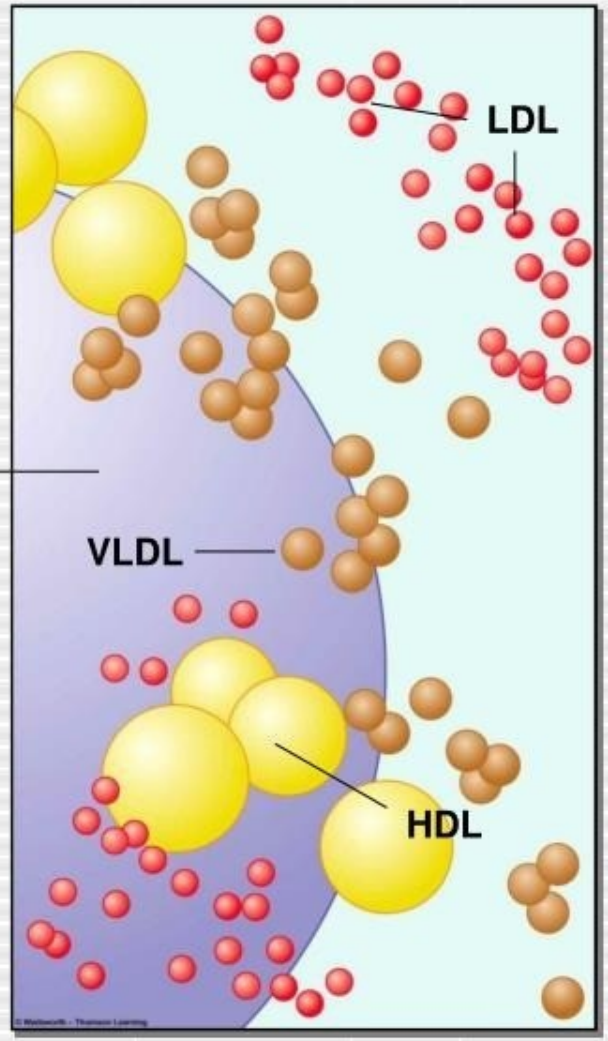
Lipoproteins = *Fat Transporters*

Four Types

- Chylomicrons
- VLDL
- LDL
- HDL



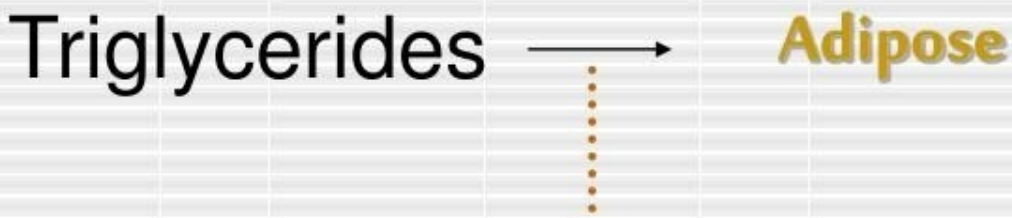
Types of Lipoproteins

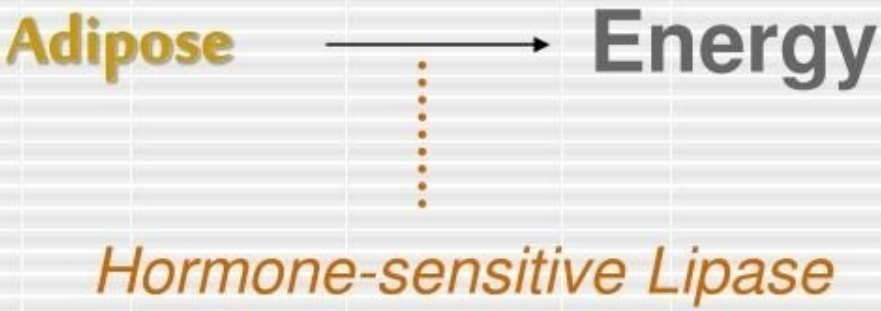


Lipoproteins Compared

Lipoprotein	Primary Ingredient	Function	Blood Test
Chylomicrons	Triglyceride	Transports fats (from intestines) to cells	"triglycerides"
VLDL	Triglyceride	Transports fats (from liver) to cells	"triglycerides"
LDL [recycled VLDLs]	Cholesterol	Transports cholesterol to tissues	"bad cholesterol"
HDL	Protein	Transports cholesterol to liver	"good cholesterol"

Fat Metabolism





LIPIDS

Part III: Lipids and Health

Function of Fats

- Energy [adipose tissue]
- Insulation
- Protects bones and organs
- Essential Fatty Acids
  - Linoleic (omega-6)
  - Linolenic (omega-3)

Eicosanoids

Heart Disease: Blood Lipid Profile

- Total Cholesterol
- LDL & HDL
- Triglycerides

Heart Disease & Fatty Acids

AVOID

High LDLs

- Saturated
- Trans

Low HDLs

- Trans
- Omega-6s

EMPHASIZE

Low LDLs

- Monounsaturated
- Omega-3s

High HDLs

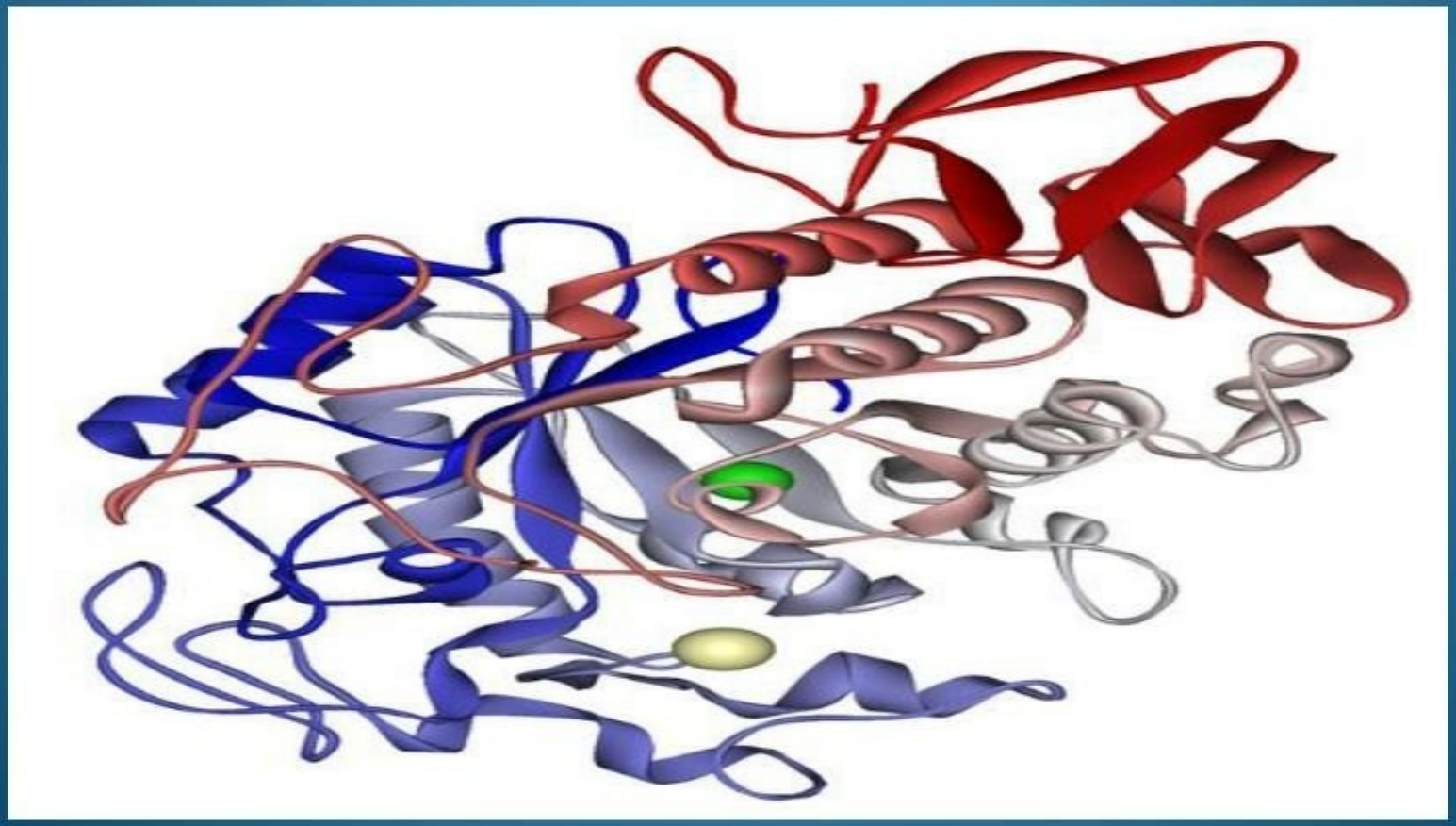
- Omega-3s

Cancer & Fat

- Total Fat
- Excess Calories
- Animal Fats
- Types of Fatty Acids
- Lack of Vegetables & Fruits and other plant foods

PHYTOCHEMICALS

Serum Amylase



AMYLASE enzyme is synthesized primarily in the pancreas and salivary glands.

- amylase (alpha-amylase or AML) helps digest starch and glycogen in the mouth, stomach, and intestine.
- In cases of suspected acute pancreatic disease, measurement of serum or urine AML the most important laboratory test.

Purpose

- To diagnose acute pancreatitis.
- To distinguish between acute pancreatitis and other causes of abdominal pain that require immediate surgery.
- To evaluate possible pancreatic injury caused by abdominal trauma or surgery

Precautions

- If the patient has severe abdominal pain, draw the sample before diagnostic or therapeutic intervention. For accurate results, it's important to obtain an early sample.
- Handle the sample gently to prevent hemolysis.

Reference values

- Normal serum amylase levels range from 25 to 160 U/L. (More than 20 methods of measuring serum AML exist, with different ranges of normal values.

Types

1. **Salivary amylase** (S-amylase) - pH 6.7
2. **Pancreatic amylase** (P-amylase) - pH 7.1

Diagnostic Use

Increased enzyme levels in humans are associated with:

- Salivary trauma, mumps and inflammation of the salivary glands.

- Acute pancreatitis and pancreatic duct obstruction due to cancer of the pancreas.

When to Get Tested?

When you have symptoms of a pancreatic disorder, such as severe abdominal pain, fever, loss of appetite

Sample Required?

Serum – heparinised plasma - urine

A blood sample drawn from a vein in the arm.

Blood was collected and allowed to stand at room temperature for 1°hour to coagulate.

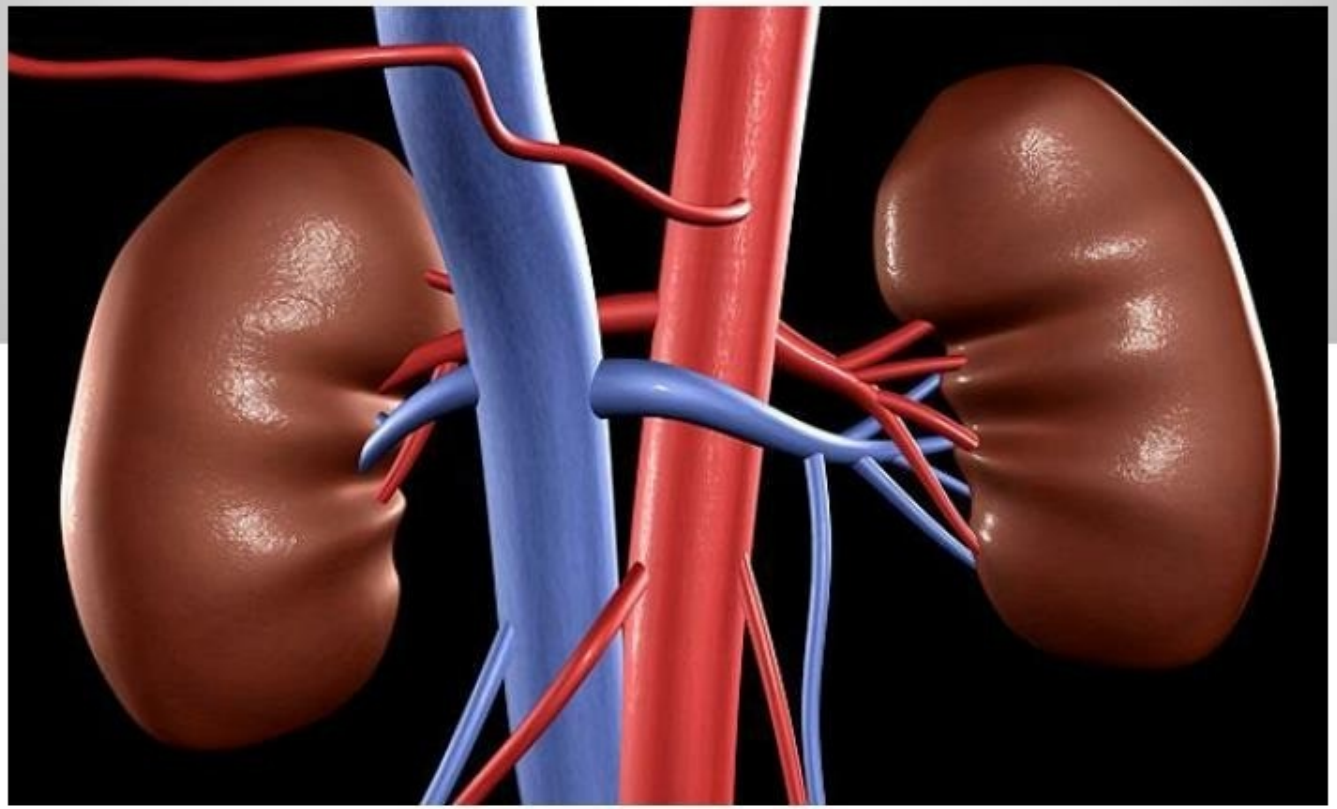
Serum was obtained by centrifugation for 30 minutes at 4°C.

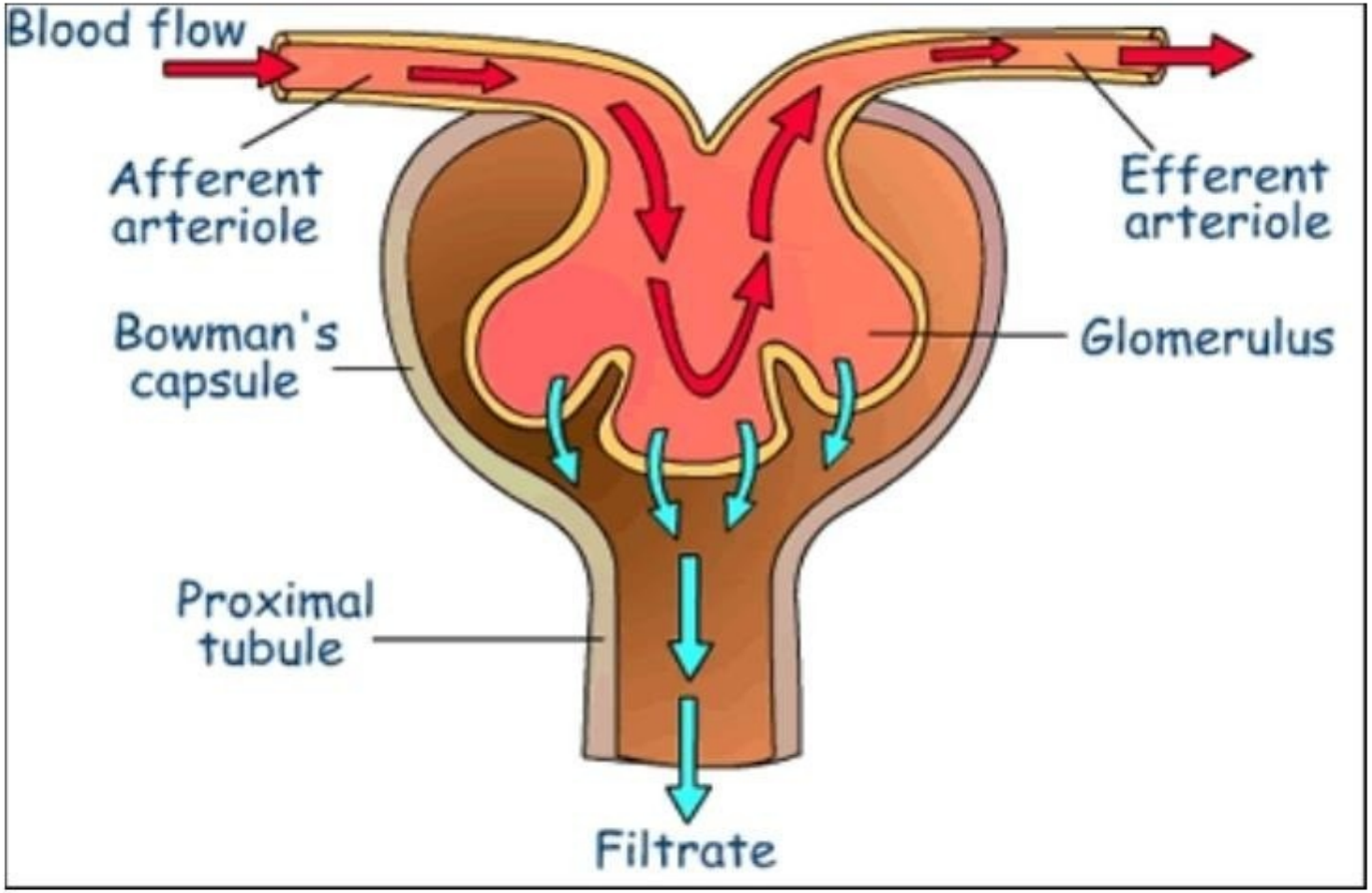
No loss of activity within 5 days at 4-25 °C.

What does the test result mean?

In acute pancreatitis, amylase in the blood increases (often to 4-6 times higher than the highest reference value, sometimes called upper limit of normal).

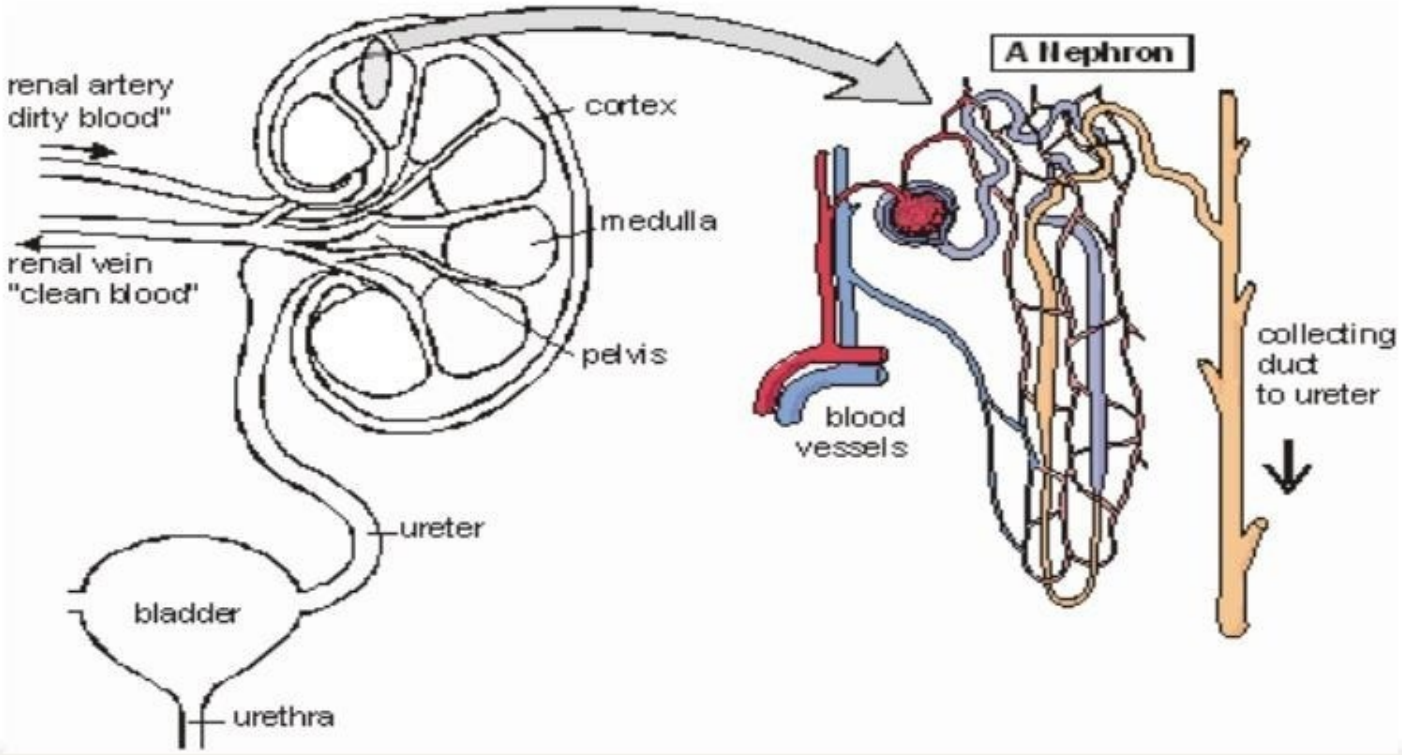
Kidney Function Test




Blood flow
Afferent arteriole
Efferent arteriole
Bowman's capsule
Glomerulus
Proximal tubule
Filtrate

Definition

Kidney function tests are common lab tests used to evaluate how well the kidneys are working. Such tests include: BUN (Blood urea nitrogen) Creatinine - blood.



Purpose

The kidneys, the body's natural filtration system, perform many vital functions, including

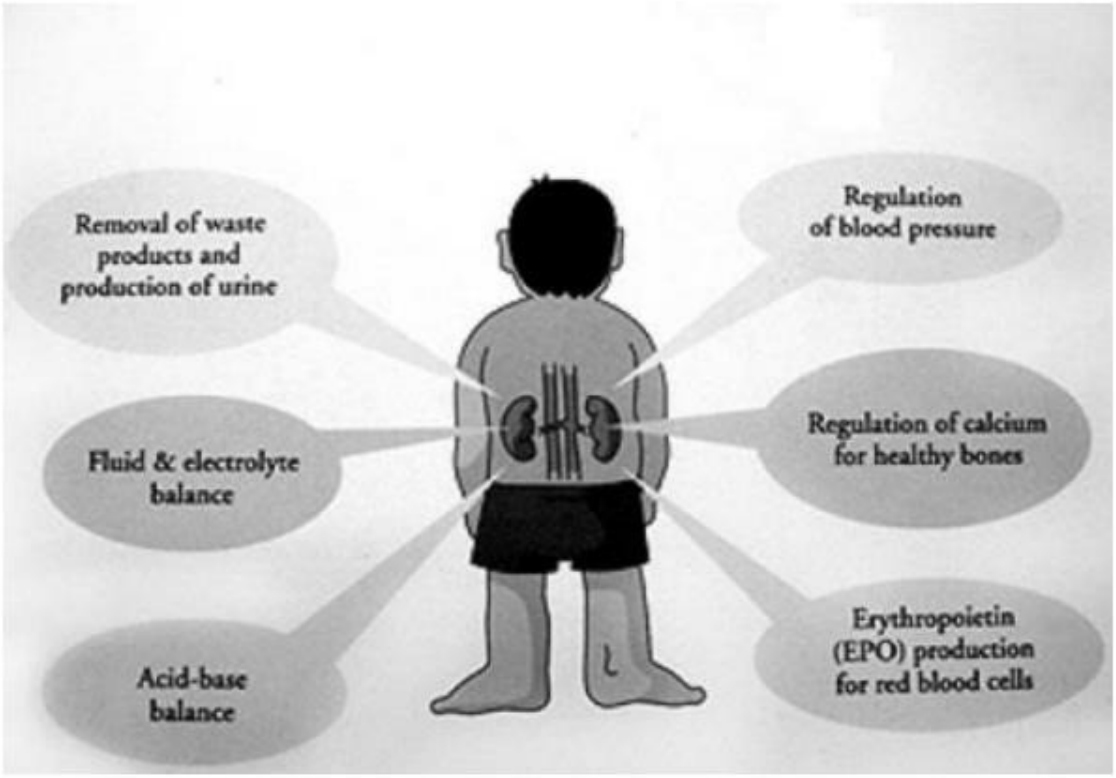
- removing metabolic waste products from the bloodstream.
- regulating the body's water balance.
- maintaining the pH (acidity/alkalinity) of the body's fluids.
- waste chemicals are filtered out and eliminated from the body (along with excess water) in the form of urine.

Kidney Function Test help to determine if the kidneys are performing their tasks adequately.

What happens when the kidney stop working?

- Waste products accumulate - Uremia.
- Fluid accumulates.
- Urine production slows or stops.
- You will feel lethargic, sleepy, sick or breathless. you will look pale .your ankles will become "puffy" this is oedema.

What do the kidneys do?



Blood Tests

➢Blood Urea Nitrogen Test (BUN)

- A blood urea nitrogen (BUN) test measures the amount of nitrogen in your blood that comes from the waste product urea.

- Urea is made when protein is broken down in your body.

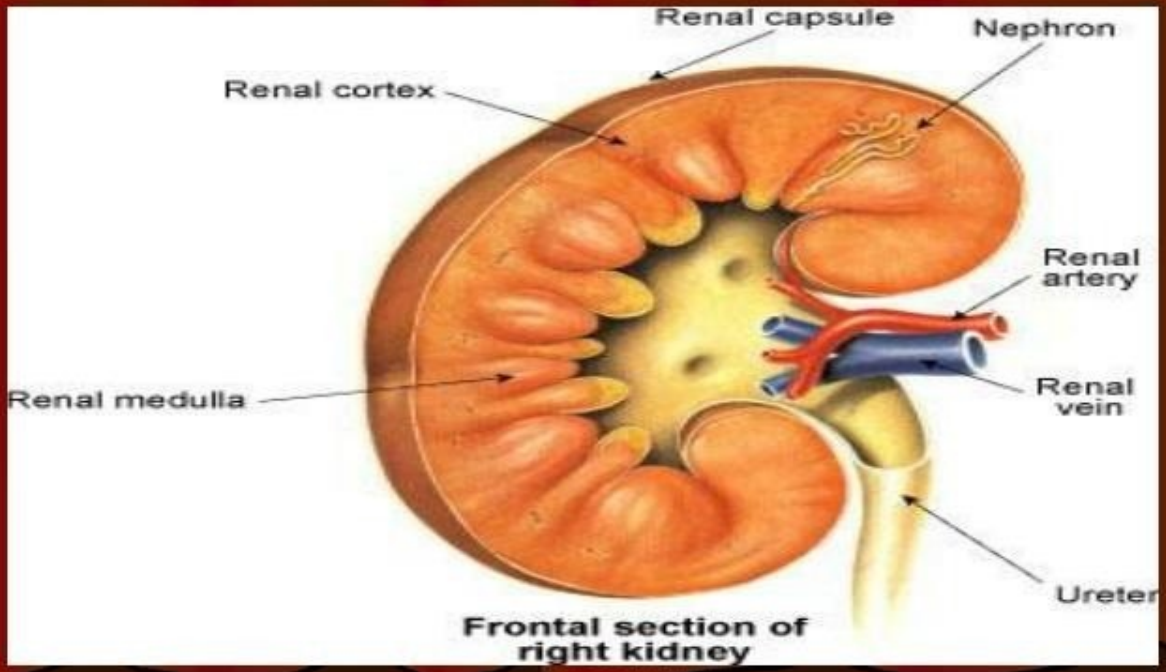
- Urea is made in the liver and passed out of your body in the urine.

- A BUN test is done to see how well your kidneys are working

Routine Kidney Function Test

- Blood urea nitrogen
- Serum Creatinine
- Serum total protein, albumin, globulin, A/G Ratio
- Blood gases, Blood PH and Bicarbonate
- Plasma and Urine Osmolarity
- Creatinine Clearance Test
- Routine Urine Examination

Creatine and Creatinine



Creatine

- Creatine is formed from glycine, arginine and methionine.

- The biosynthesis of creatine requires the following steps:

a- Transamidation: occurs in the kidney .

b-Transmethylation: occurs in the liver.

c- Phosphorylation: occurs in the Muscles.

SERUM CREATININE

- Measurement of the serum creatinine (Cr) concentration is the most commonly used method for determining the level of renal function.
- Serum Cr can be used to estimate GFR because Cr varies inversely with the level of renal function.
- Normal Cr concentrations range from **0.6 to 1.2** mg/dL (0.05-0.12 mmol/L).

- Serum creatinine level is not sensitive to mild to moderate reductions in renal function.
- When Serum Cr level changes from **0.6 to 1.2** mg/dL , this reflects a decline in GFR of approximately **50%**.
- Cr concentration of 1.2 would not draw clinical attention to a reduction of GFR.

- In humans, approximately half of creatine originates from food (mainly from fresh meat).

- Creatine can be found in urine in sever muscular dystrophy
- Creatine supplementation has been investigated as a possible therapeutic approach for the treatment of muscular, neuromuscular diseases.

Creatine phosphate

- **Creatine phosphate** found in muscle, is a high-energy compound that can reversibly donate a phosphate group to ADP to form ATP that can be used to maintain the intracellular level of ATP during the first few minutes of intense muscular contraction.

- **Note:** The amount of creatine phosphate in the body is proportional to the muscle mass.

Creatinine

- Creatinine is produced during muscle contractions from creatine phosphate.

- In the blood, creatinine is removed by filtration through the glomeruli of the kidney and is secreted into urine.

- In kidney disease, creatinine levels in the blood are elevated, whereas the creatinine clearance rate is decreased and hence the urine levels are diminished.

Creatinine Level

Creatinine test is most widely used to assess kidney function as its level is not affected with diet.

Normal Range:

Serum

Male 0.7-1.4 mg/dl

Female 0.7-1.2 mg/dl

Urine 1000-1500 mg/24h

Creatinine Clearance:

Male 98-156 ml/min

Female 95-160 ml/min

Creatinine Clearance (Routinely used)

- Creatine is a nitrogen-containing compound formed in the liver.
- Stored in muscle as creatine phosphate
- 1-2% of muscle creatine converted to creatinine (Cr) each day
- Amount of creatinine produced is related to muscle mass
- Cr is freely filtered at the glomerulus
- Cr clearance = 125 mL/ min

How to calculate Creatinine clearance

In case of a 24-h sample:

$$\mathbf{V\ (mL/min)} = \frac{\text{Total volume of urine in 24 hours}}{24 \times 60\ (\text{i.e. } 1440)}$$

$$\mathbf{Creatinine\ Clearance\ (mL/min)} = \frac{U\ (\text{mg/dL}) \times V\ (\text{mL/min})}{S\ (\text{mg/dL})}$$

Sample:

Serum, heparinised plasma and urine.

When is it ordered?

signs and symptoms of kidney dysfunction include:

- Lack of concentration.
- Poor appetite.
- Urine that is foamy, bloody, or coffee-colored.
- A decrease in the amount of urine.
- Problems urinating, such as a burning feeling
- Mid-back pain (flank).
- High blood pressure

glomerular filtration rate (GFR)

- Glomerular Filtration Rate is the volume of fluid passing through the glomerulus in a given period of time.
- Measurement is based on the concept of **clearance**: measuring urinary excretion of a substance that is completely **filtered (cleared)** from the blood by the glomeruli.

Measurement of Renal Clearance

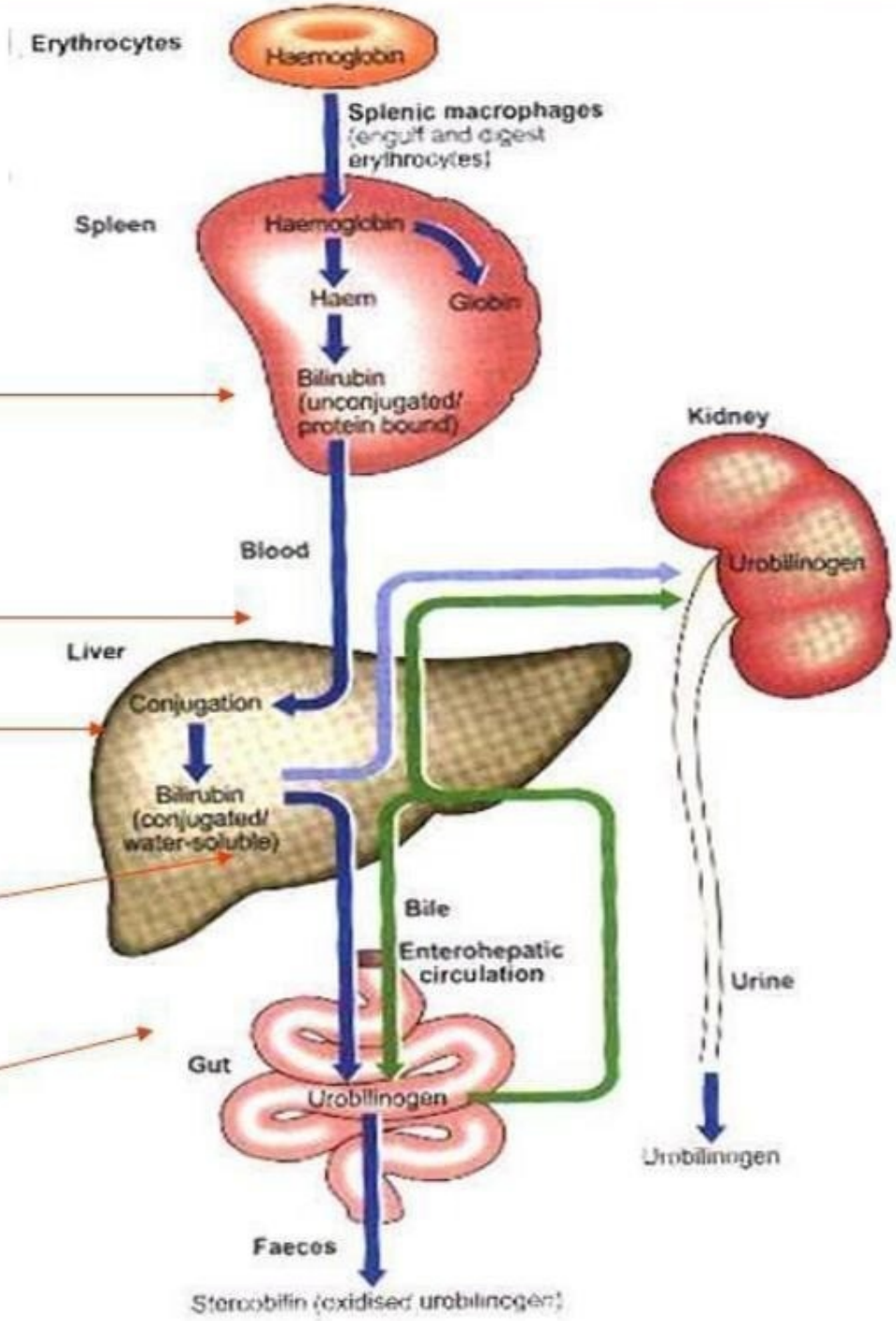
- Imagine a substance C that is freely filtered at the glomerulus and is neither reabsorbed or secreted.
- ∴ all C which is filtered will come out in urine
- Thus all the filtered plasma will be cleared of "C"
- Clearance is defined as the volume of plasma cleared of a substance in 1 min
- Thus, the clearance of "C" is 125 mL/min

Jaundice

- Yellow discoloration of sclera, skin, mucous membranes due to deposition of bile pigment
- Clinically detected with serum bilirubin 2-2.5mg/dL or ↑ (2 times normal)

Bilirubin Metabolism (Re: JAUNDICE

- PRODUCTION
- IV TRANSPORT
- UPTAKE
- CONJUGATION
- EXCRETION



What causes ↑ bilirubin?

Prehepatic	Unconjugated
Hepatic	mixed
Post-hepatic	conjugated

Causes

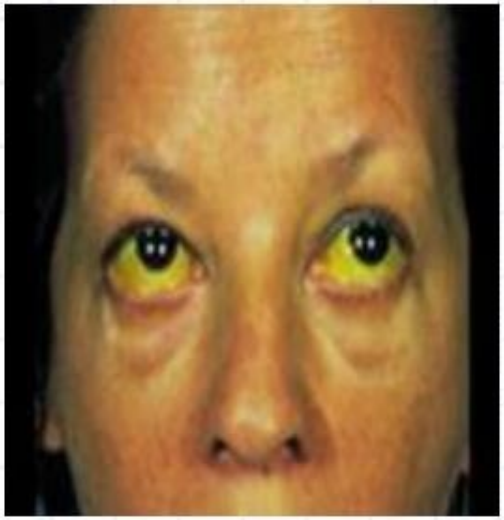
- Hepatocellular disease
- Viral infections (hepatitis A, B, and C)
- Chronic alcohol use
- Autoimmune disorders
- Drugs
- Pregnancy

Causes

- Parenteral nutrition
- Sarcoidosis
- Dubin-Johnson syndrome
- Rotor's syndrome
- Primary biliary cirrhosis
- Primary sclerosing cholangitis

Symptoms

- Yellow discoloration of the skin, sclerae and mucous membranes
- Itching (pruritus) due to deposits of bile salts on the skin
- Stool becomes light in color
- Urine becomes deep orange and foamy



Clinical Features

- Careful history and examination
- Family history (Gilbert, Rotor, Crigler-Najjar, Dubin-Johnson, Sickle Cell)
- Healthy young person with fever, malaise, myalgias = viral hepatitis (try to locate source)
- Gradually develops symptoms = hepatic/bile duct obstruction (consider liver disease/cirrhosis)
- Develops acutely with abdominal pain = acute cholangitis sec to choledocholithiasis

History that should be taken from patients presenting with Jaundice

- Duration of jaundice
- Previous attacks of jaundice
- Pain
- Chills, fever, systemic symptoms
- Itching
- Exposure to drugs (prescribed and illegal)
- Biliary surgery
- Anorexia, weight loss
- Colour of urine and stool
- Contact with other jaundiced patients
- History of injections or blood transfusions
- Occupation

Examination of patients with Jaundice

- Depth of jaundice
- Scratch marks
- Signs of chronic liver disease
- Palmar erythema
- Clubbing
- White nails
- Dupuytren's contracture
- Gynaecomastia
- Liver
- Size
- Shape
- Surface
- Enlargement of gall bladder
- Splenomegaly
- Abdominal mass
- Colour of urine and stools

Laboratory Tests

- Pigment studies
  - Serum bilirubin, direct
  - Serum bilirubin, total
  - Urine R/E for bilirubin and urobilinogen
- Alkaline Phosphatase
- Liver aminotransferrase levels
    - AST
    - ALT
  - Elevated levels usually indicate cellular damage to the liver
  - > 70% of liver cells may be damaged before LFT's become elevated

Liver Biopsy

- Used to obtain a specimen of liver tissue
- Done under local anesthesia

Autoantibody and immunoglobulin characteristics in liver disease

Liver disease	Auto antibodies	Immunoglobulin
Primary billiary cirrhosis	High titre of antimitochondrial antibody in 95% of patients	Raised IgM
Autoimmune chronic active hepatitis	Smooth muscle antibody in 70%, antinuclear factor in 60%, Low antimitochondrial antibody titre in 20%	Raised IgG in all patients
Primary sclerosing cholangitis	Antinuclear cytoplasmic antibody in 30%	

Summary

- An isolated raised serum bilirubin concentration is usually due to Gilbert's syndrome, which is confirmed by normal liver enzyme activities and full blood count
- Jaundice with dark urine, pale stools, and raised alkaline phosphatase and gamma-glutamyl transferase activity suggests an obstructive cause, which is confirmed by presence of dilated bile ducts on ultrasonography
- Jaundice in patients with low serum albumin concentration suggests chronic liver disease
- Patients with high concentrations of bilirubin (>100 micro mol/l) or signs of sepsis require emergency specialist referral
- Imaging of the bile ducts for obstructive jaundice is increasingly performed by magnetic resonance cholangiopancreatography, with endoscopy becoming reserved for the therapeutic interventions

Pre-Hepatic Disorders

Gilberts

- Failure to conjugate
- 2-5%
- Autosomal recessive
- Asymptomatic
- Bilirubin
  Unconjugated
- Normal ALT/ALP
- Worse if infection, miss a meal

Haemolysis

- Excess bilirubin production
- Unconjugated Bil ++
- Normal ALP/ALT
- Low Hb/retics++
- Splenomegaly
- Pigmented gallstones

Hepatic Disorders & Hepatic Failure

Acute & Chronic Liver Disease

- **Acute**
  - Drugs
  - Viral
  - Alcohol
  - Autoimmune
- **Chronic**
  - Biliary
    - Primary biliary cirrhosis
    - Primary sclerosing cholangitis
  - Liver cell damage (cirrhotic)
    - Alcohol
    - Autoimmune
    - Viral*
    - Haemochromatosis*
    - Wilsons*
    - A1AT*

Post-Hepatic Disorders

- **Intrinsic to the ductal system**
  - Gallstones
  - Surgical strictures
  - Infection (cytomegalovirus, Cryptosporidium infection in patients with acquired immunodeficiency syndrome)
  - Intrahepatic malignancy
    - Cholangiocarcinoma
- **Extrinsic to the ductal system**
  - Extrahepatic malignancy (pancreas, lymphoma)
  - Pancreatitis