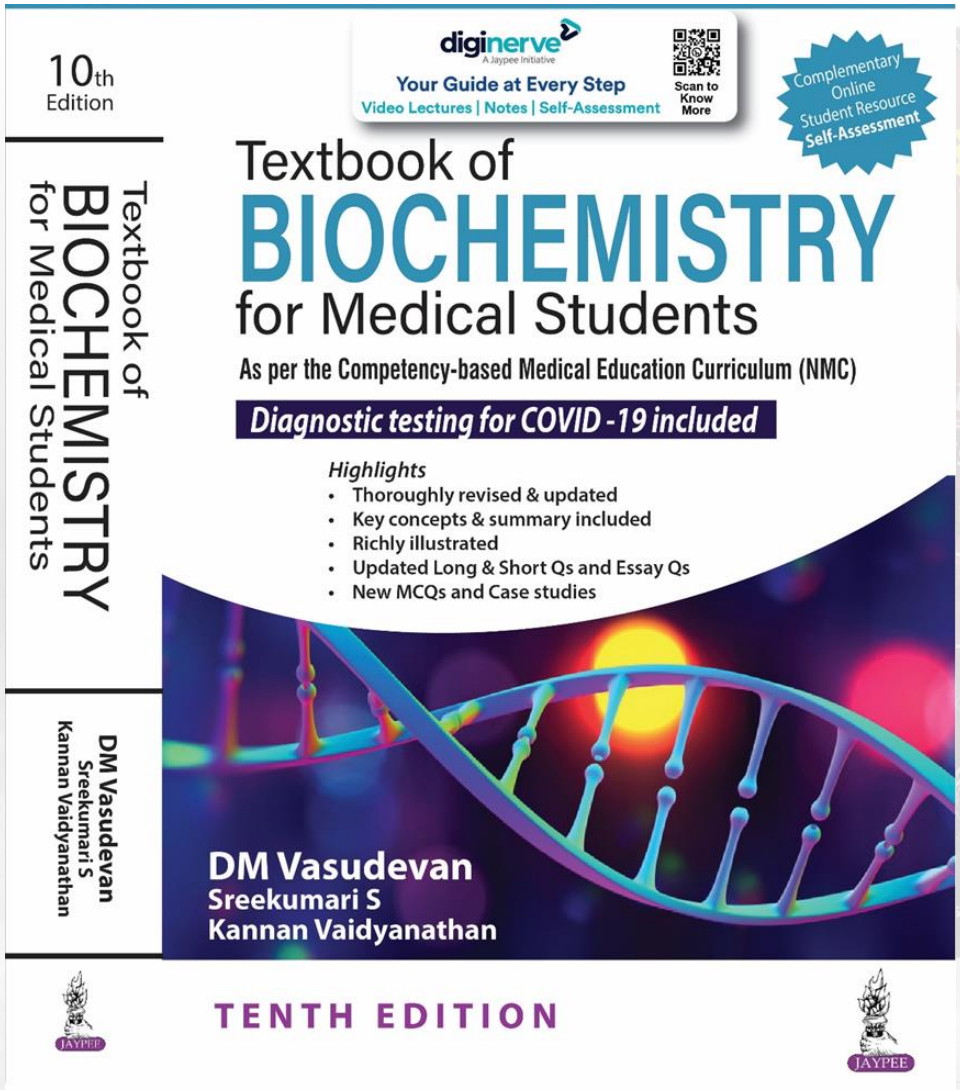
Chapter 21:

Liver Function Tests



Textbook of
BIOCHEMISTRY
for Medical Students

By DM Vasudevan, *et al.*

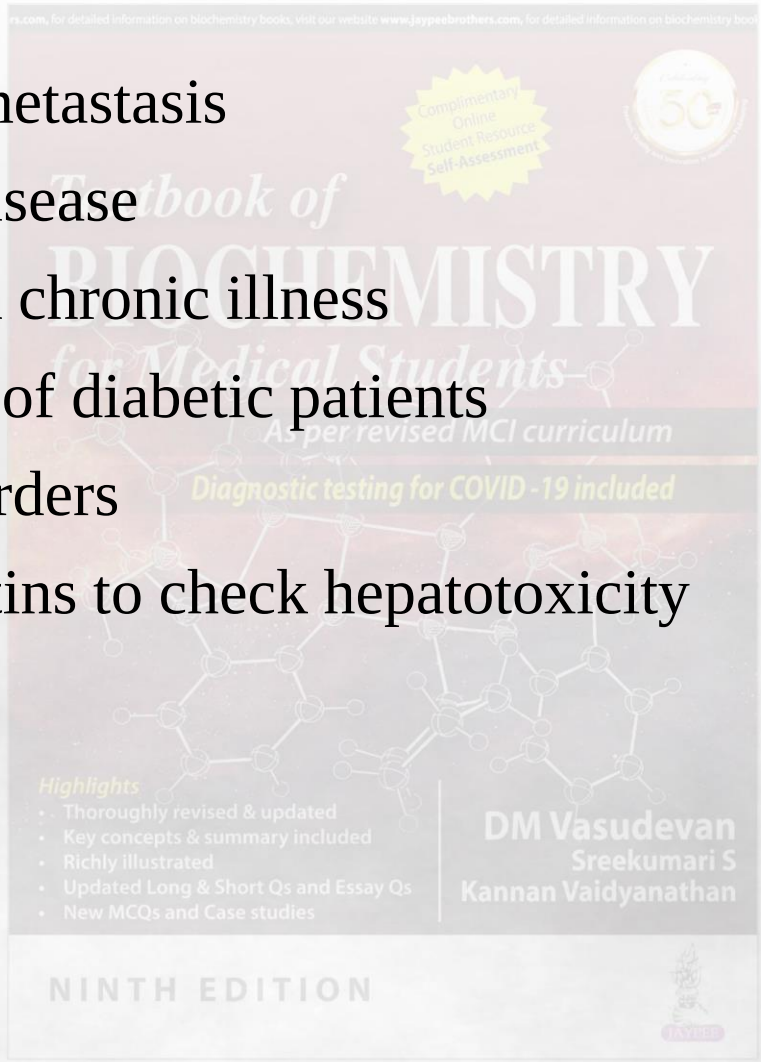
TENTH EDITION

Major Functions of Liver

1. *Synthetic function*
    a. Synthesis of plasma proteins (albumin, coagulation factors, many globulins)
    b. Synthesis of cholesterol
    c. Synthesis of triacylglycerol
    d. Lipoprotein synthesis
2. *Metabolic function*
    a. Carbohydrates: Glycolysis; glycogen synthesis; glycogen metabolism
    b. Ketogenesis; fatty acid synthesis and breakdown
    c. Protein catabolism
    d. Citric acid cycle, production of ATP
3. *Detoxification and excretion*
    a. Ammonia to urea
    b. Bilirubin (bile pigment)
    c. Drug metabolites
4. *Homeostasis:* Blood glucose regulation
5. *Storage function:* Vitamin A, D, K, B12
6. Production of bile salts; help in digestion

Indications for Liver Function Tests

1. Jaundice
2. Suspected liver metastasis
3. Alcoholic liver disease
4. Any undiagnosed chronic illness
5. Annual check up of diabetic patients
6. Coagulation disorders
7. Therapy with statins to check hepatotoxicity



Classification of Liver Function Tests

Group I (Tests of hepatic excretory function)

i. Serum: Bilirubin; total, conjugated, and unconjugated
ii. Urine: Bile pigments, bile salts and urobilinogen

Group II: Liver enzyme panel

i. Alanine aminotransferase (ALT) (Marker of liver injury)
ii. Aspartate aminotransferase (AST) (Marker of liver injury)
iii. Alkaline phosphatase (ALP) (Marker of cholestasis)
iv. Gamma glutamyl transferase (GGT) (Marker of cholestasis)

Group III: Plasma proteins (Tests for synthetic function of liver)
(Marker, chronic liver diseases)

i. Total proteins
ii. Serum albumin, globulins, A/G ratio
iii. Prothrombin time
iv. Blood ammonia

Classification of Liver Function Tests CONTINUED

Group IV: Special tests (Tests for metabolic liver disease)

i. Ceruloplasmin
ii. Ferritin and iron
iii. Alpha-1 antitrypsin (AAT)
iv. Beta-2 microglobulin (b2M)
v. Alpha fetoprotein (AFP)

Group V: Direct and indirect markers of hepatic fibrosis

i. Serum hyaluronic acid (SHA)
ii. Procollagen type I carboxy terminal peptide (PICP)
iii. Procollagen type III amino terminal peptide (PIIINP)
iv. Matrix metalloproteinases (MMPs)
v. Tissue inhibitors of MMPs (TIMPs)
vi. Transforming growth factor beta-1 (TGF Beta-1)

B. **Classification based on Clinical aspects**

Group I: Markers of liver dysfunction

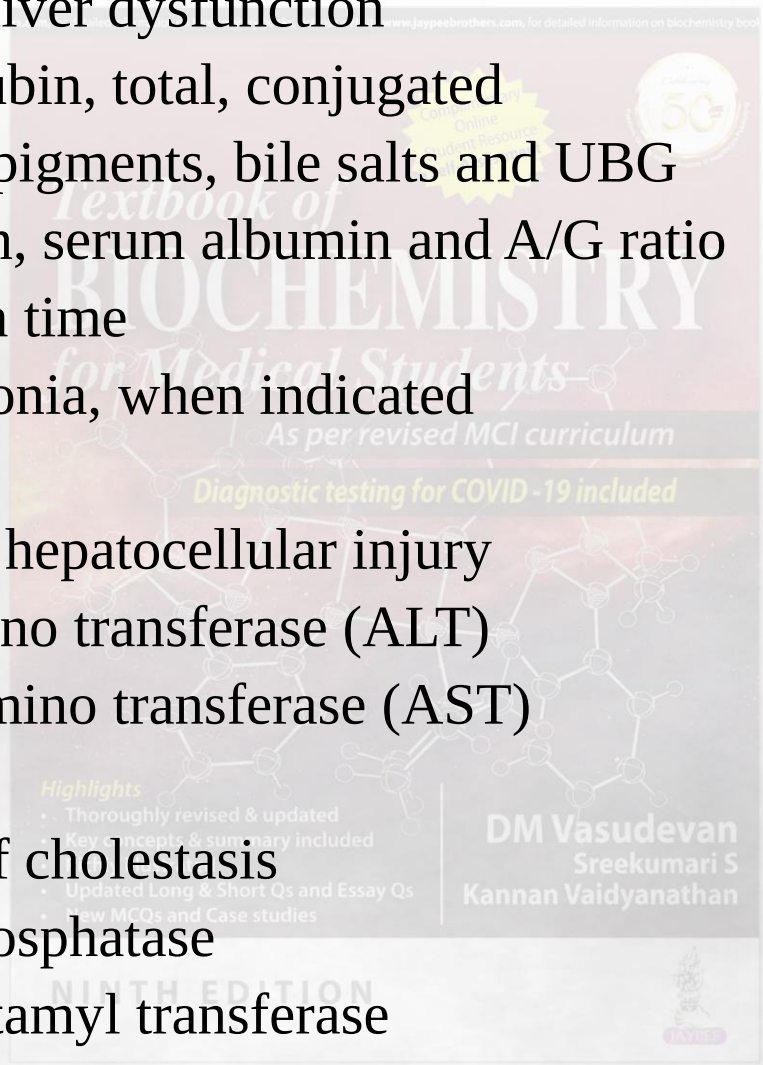
i. Serum bilirubin, total, conjugated
ii. Urine: Bile pigments, bile salts and UBG
iii. Total protein, serum albumin and A/G ratio
iv. Prothrombin time
v. Blood ammonia, when indicated

Group II: Markers of hepatocellular injury

i. Alanine amino transferase (ALT)
ii. Aspartate amino transferase (AST)

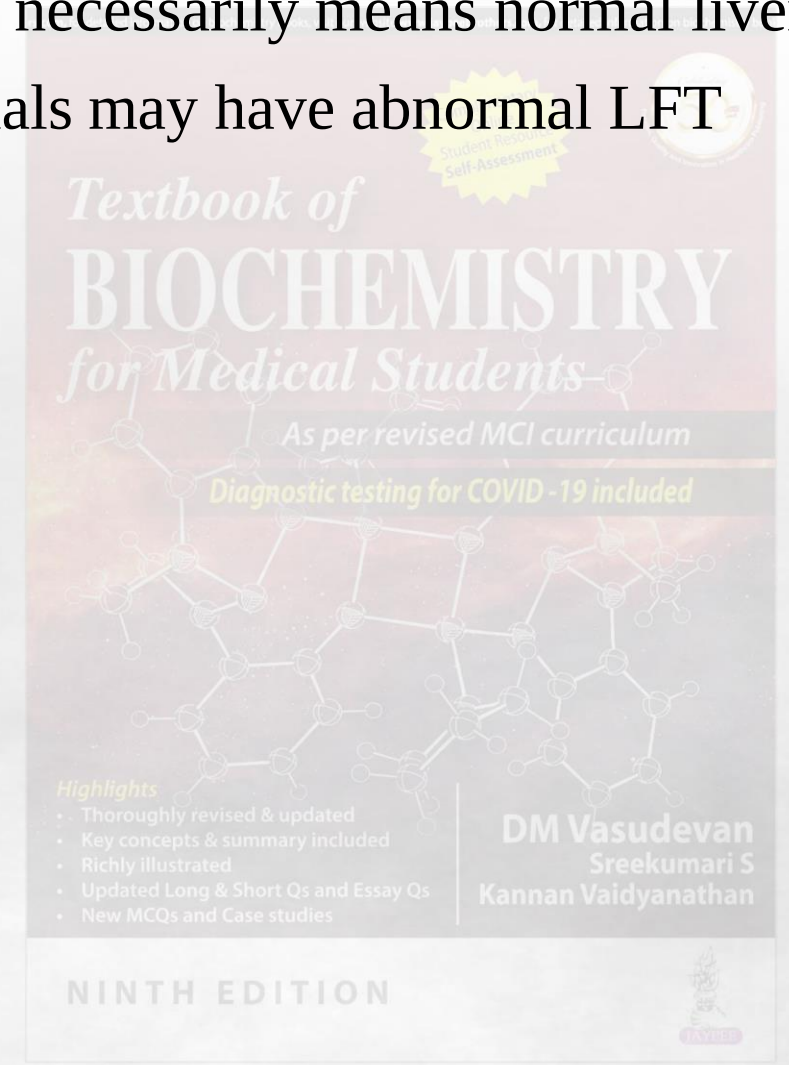
Group III: Markers of cholestasis

i. Alkaline phosphatase
ii. Gamma glutamyl transferase



Problems in Interpretation

- Normal LFT not necessarily means normal liver
- Normal individuals may have abnormal LFT



Laboratory Findings in Serum in Jaundice Cases

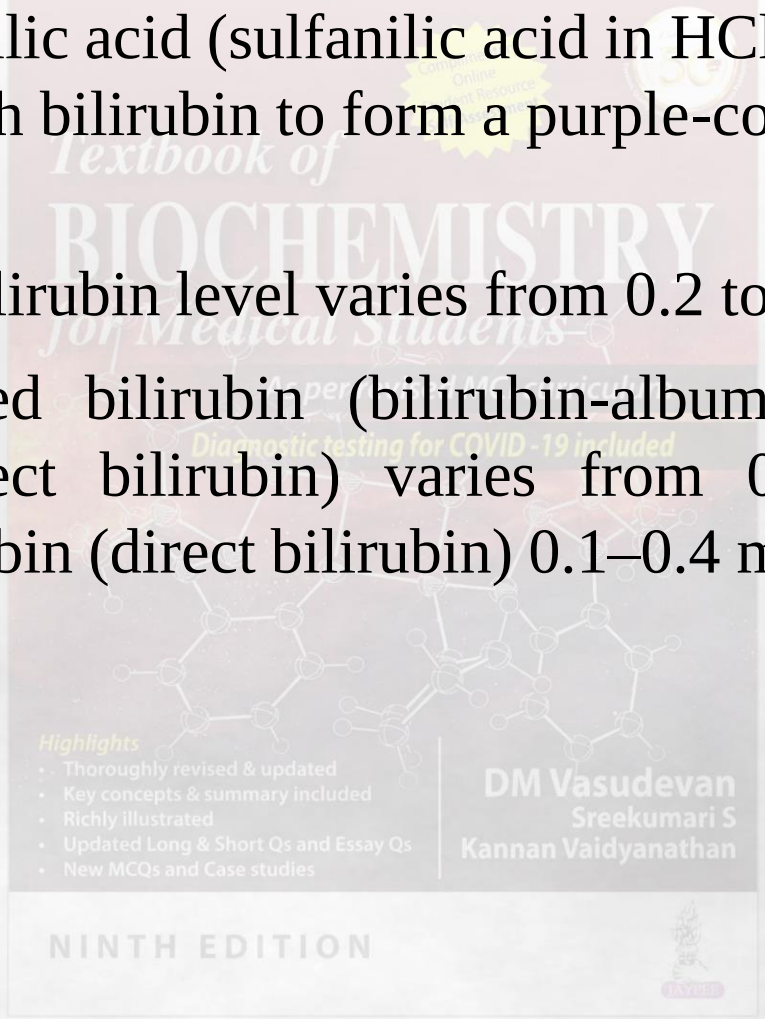
	Hemolytic jaundice	*Obstructive jaundice*	*Hepatocellular jaundice*
Total bilirubin	Elevated	Elevated	Elevated
Conjugated bilirubin	Normal	Elevated	Elevated
Unconjugated	Elevated	Normal	Elevated
Van den Bergh reaction	Indirect +ve	Direct +ve	Biphasic

Laboratory Findings in Urine in Jaundice Cases

	Hemolytic jaundice	*Obstructive jaundice*	*Hepatocellular jaundice*
Bile pigments	Absent	+++	++
Bile salts	Absent	++	+
Urobilinogen	Elevated	Absent	Normal or decreased
Positive test	Ehrlich's +ve	Fouchet's +ve	Hey's +ve

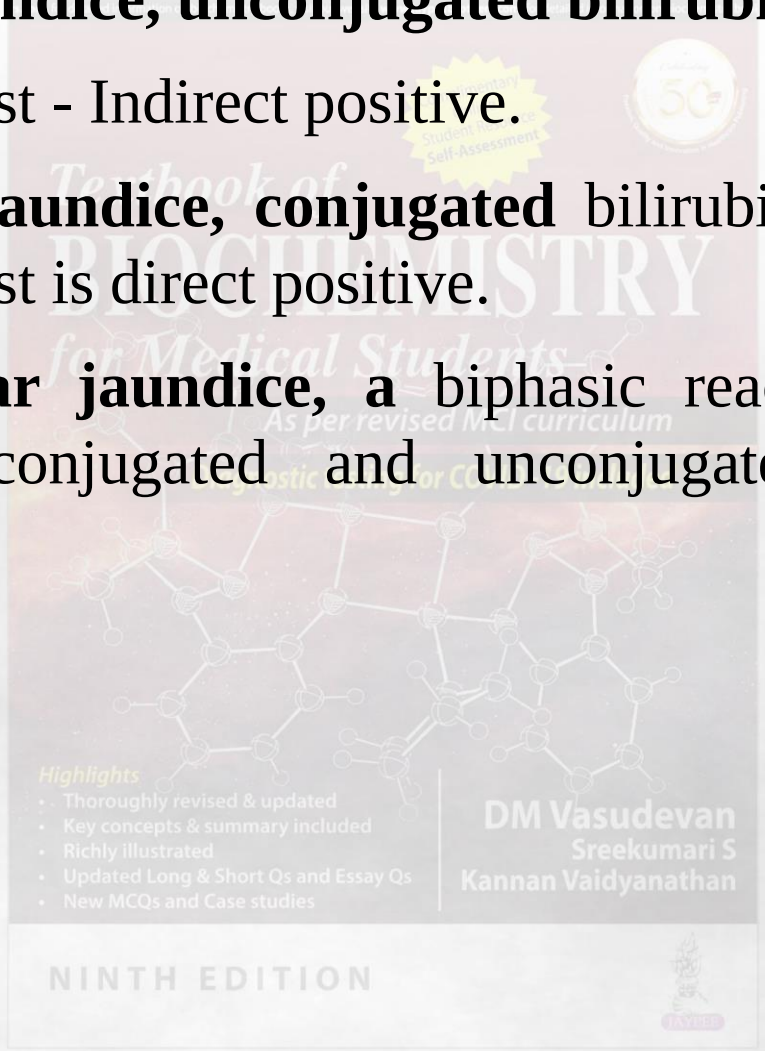
Measurement of Bilirubin

- Bilirubin is estimated by van den Bergh reaction, where diazotised sulfanilic acid (sulfanilic acid in HCl and sodium nitrite) reacts with bilirubin to form a purple-colored complex, azobilirubin.
- Normal serum bilirubin level varies from 0.2 to 0.8 mg/dl.
- The unconjugated bilirubin (bilirubin-albumin complex) (free bilirubin) (indirect bilirubin) varies from 0.2–0.7 mg/dl and conjugated bilirubin (direct bilirubin) 0.1–0.4 mg/dl.



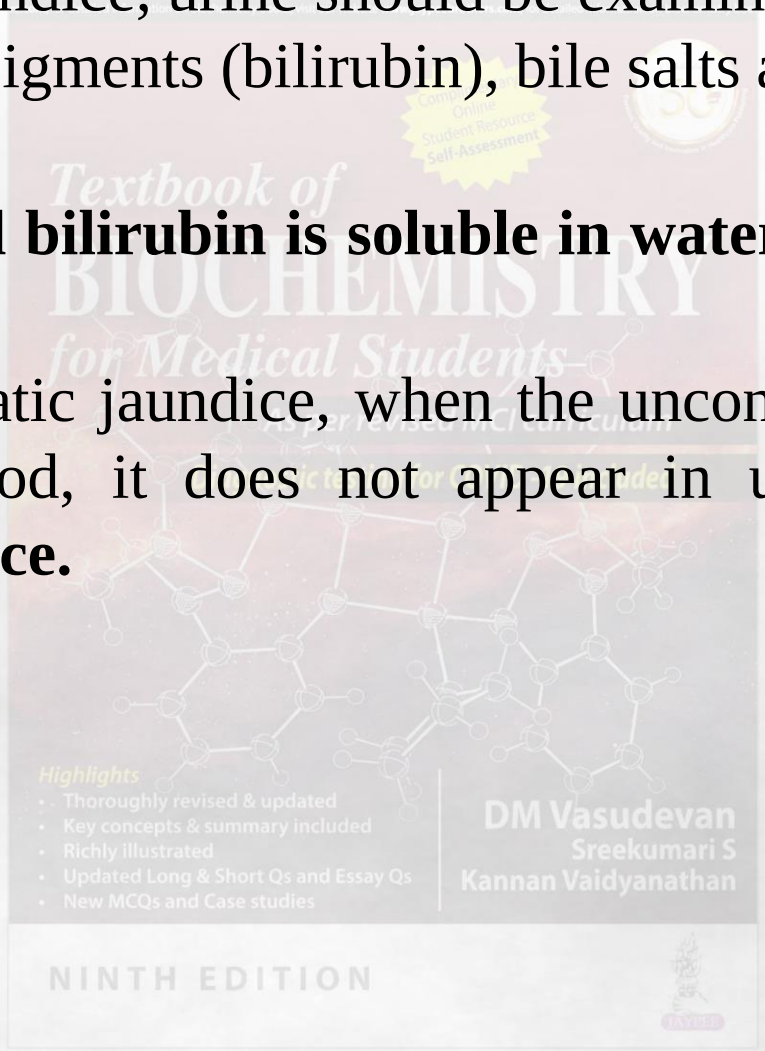
- When bilirubin is conjugated, the purple color is produced immediately on mixing with the reagent, the response is said to be van den Bergh direct positive.
- When the bilirubin is unconjugated, the color is obtained only when alcohol is added, and this response is known as indirect positive.
- If both conjugated and unconjugated bilirubins are present in increased amounts, a purple color is produced immediately and the color is intensified on adding alcohol.
- Then the reaction is called **biphasic**.

- In **hemolytic jaundice, unconjugated bilirubin** is increased.
- van den Bergh test - Indirect positive.
- In **obstructive jaundice, conjugated** bilirubin is elevated, and van den Bergh test is direct positive.
- In **hepatocellular jaundice, a** biphasic reaction is observed, because both conjugated and unconjugated bilirubins are increased.

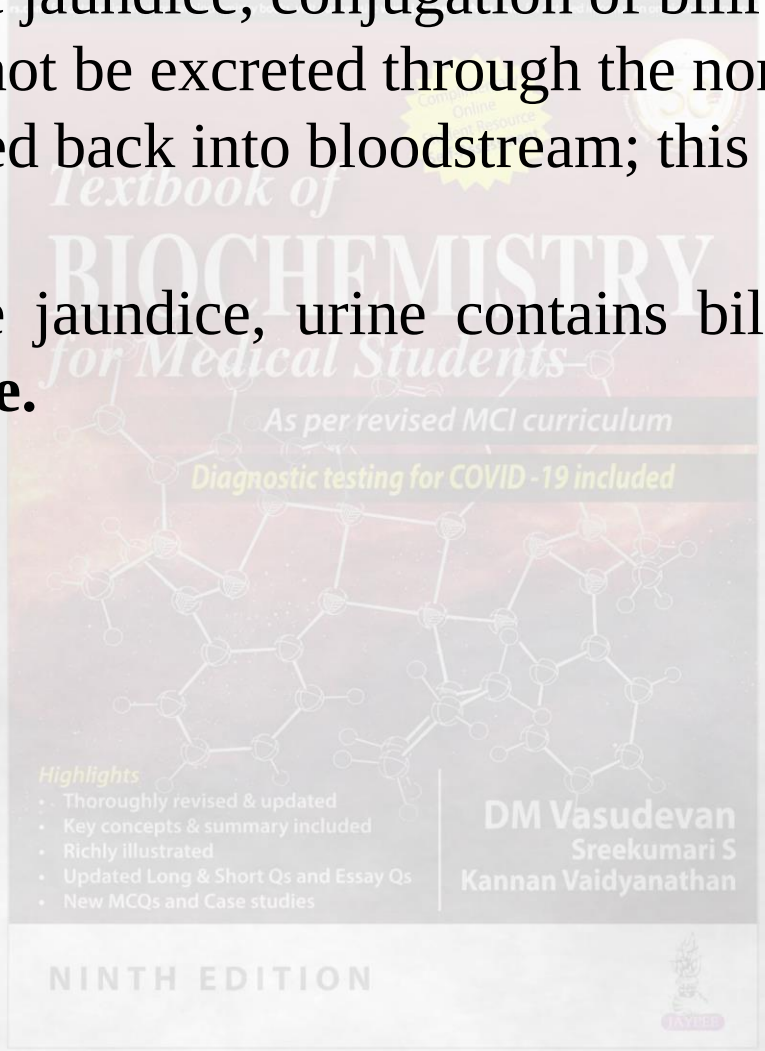


Urinary Bilirubin

- In all cases of jaundice, urine should be examined for the presence of bile pigments (bilirubin), bile salts and urobilinogen.
- **Only conjugated bilirubin is soluble in water and** is excreted in urine.
- Hence in prehepatic jaundice, when the unconjugated bilirubin is increased in blood, it does not appear in urine; hence called **acholuric jaundice.**



- But in obstructive jaundice, conjugation of bilirubin is taking place, which cannot be excreted through the normal passage, and so it is regurgitated back into bloodstream; this is then excreted through urine.
- So in obstructive jaundice, urine contains bilirubin; it is called **choluric jaundice.**

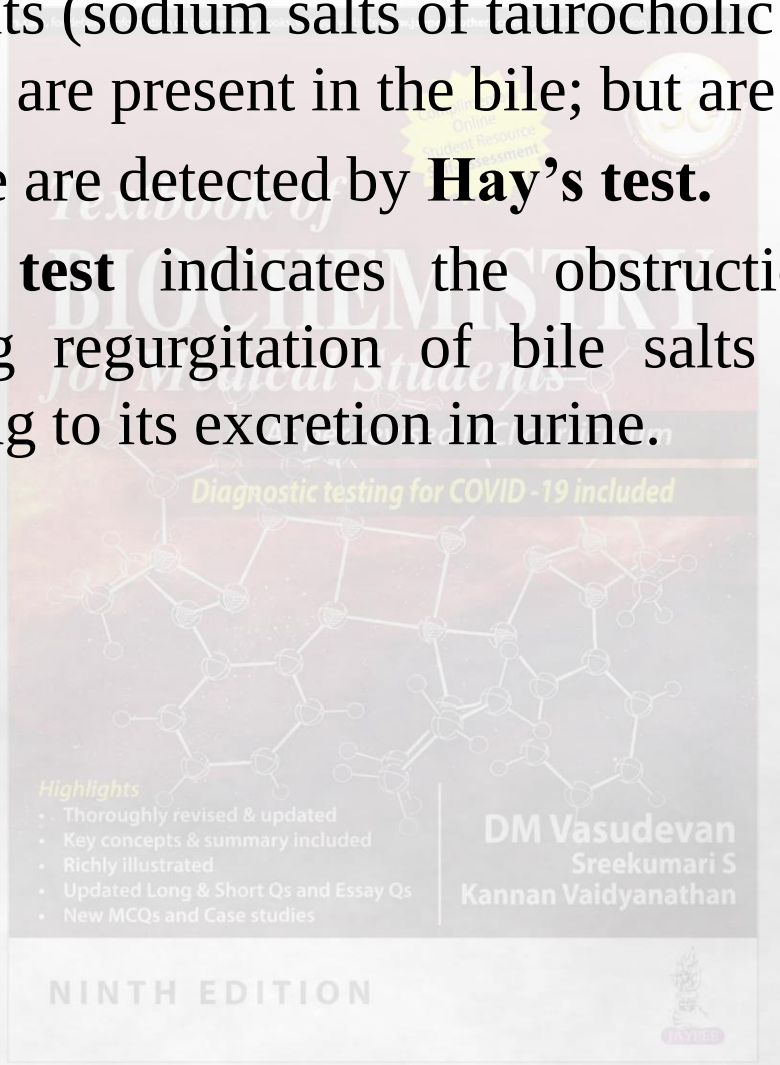


Urinary Urobilinogen

- In cases of obstruction, bile is not reaching the intestine and so urobilinogen may be decreased or absent in urine.
- **In hepatocellular jaundice, urobilinogen is initially** elevated, then decreases or disappears when the obstructive stage sets in and reappears when obstruction is cleared.
- Urobilinogen is absent in urine, when there is obstruction to bile flow.
- The **first indication of the recovery is the reappearance of urobilinogen** in urine.
- **In hemolytic anemias, urobilinogen is increased.**
- **Bilirubin is detected by Fouchet's test and** urobilinogen by Ehrlich's test.

Urine Bile Salts

- Normally bile salts (sodium salts of taurocholic acid and glycocholic acid) are present in the bile; but are not seen in urine.
- Bile salts in urine are detected by **Hay's test.**
- **Positive Hay's test** indicates the obstruction in the biliary passages causing regurgitation of bile salts into the systemic circulation leading to its excretion in urine.



Tests useful to Distinguish Different Types of Jaundice

Speci-men	*Test*	*Prehepatic or hemolytic or retention jaundice*	*Hepatocellular jaundice*	*Posthepatic or obstructive or regurgitation jaundice*
Blood	Unconjugated bilirubin (van den Bergh indirect test)	++	+	Normal
Blood	Conjugated bilirubin (van den Bergh direct test)	Normal	Excretion is rate-limiting. It is the first impaired activity. In early phase, it is increased	++
Blood	Alkaline phosphatase (40–125 U/L)	Normal	2–3 times increased	10–12 times increased

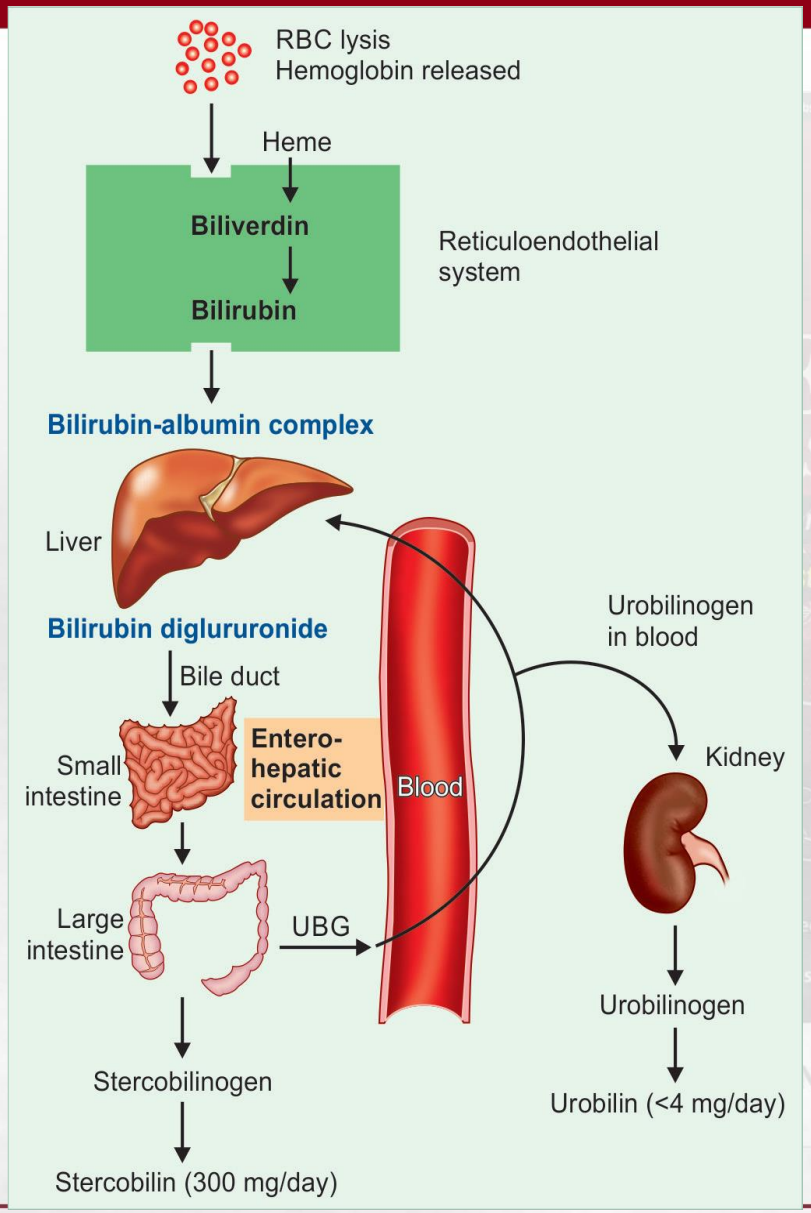
Continued

Tests useful to Distinguish Different Types of Jaundice

Speci-men	*Test*	*Prehepatic / hemolytic or retention jaundice*	*Hepatocellular jaundice*	*Posthepatic/ obstructive / regurgitation jaundice*
Urine	Bile salt (Hay's test)	Absent	Absent	Present
Urine	Conjugated bilirubin (Fouchet's)	Absent	Present	Present
Urine	Urobilinogens (Ehrlich test)	+++	Increased in early phases; later decreased as production is low.	Absent
Feces	Urobilins	++	Normal or decreased	Clay-colored

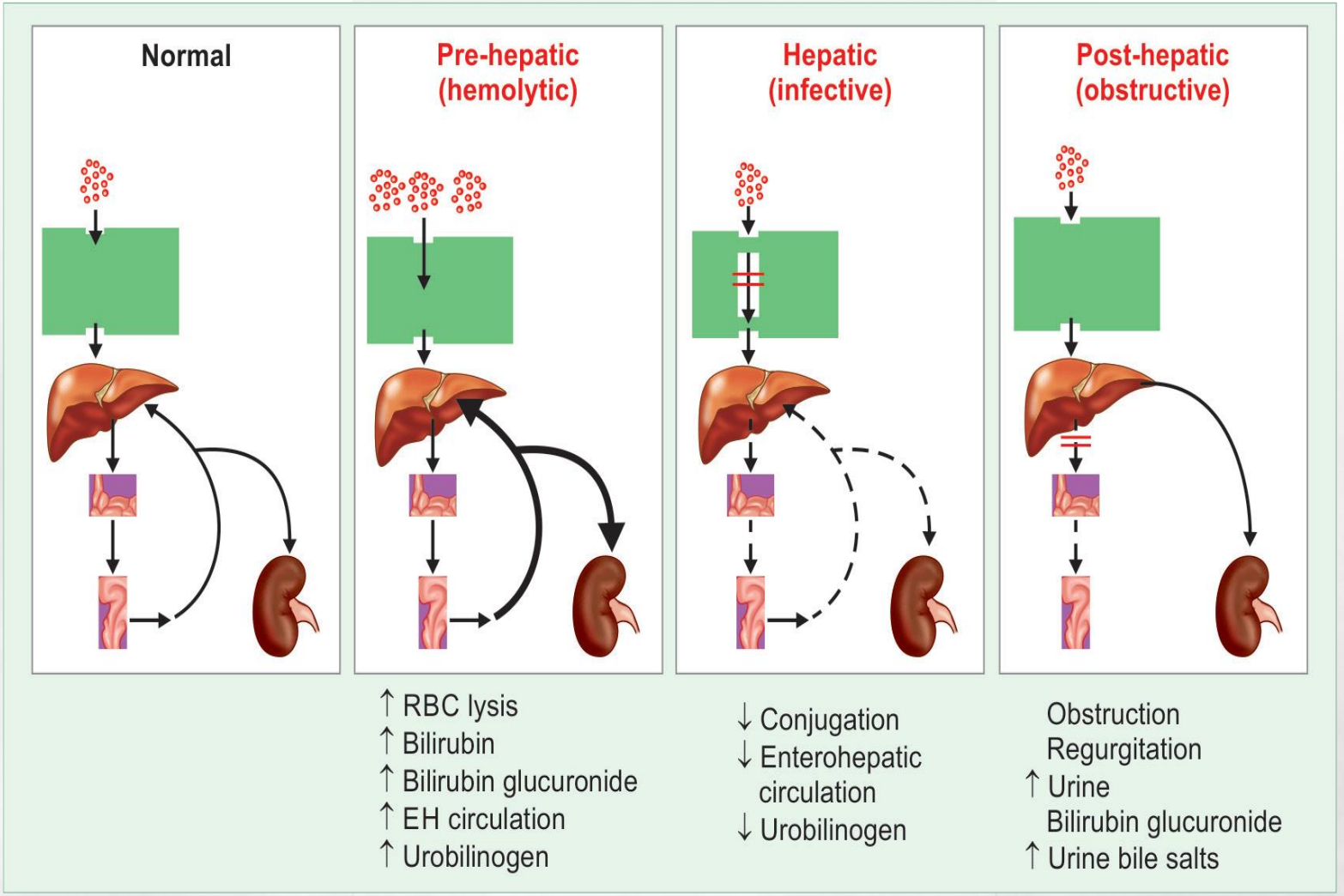
Classification of Jaundice

Type of bilirubin	*Class of jaundice*	*Causes*
Unconjugated	Prehepatic or hemolytic	Abnormal red cells; antibodies; drugs and toxins; thalassemia; hemoglobinopathies Gilbert's syndrome; Crigler-Najjar syndrome
Unconjugated and conjugated	Hepatic or hepatocellular	Viral hepatitis; toxic hepatitis; intrahepatic cholestasis
Conjugated or obstructive	Posthepatic	Extrahepatic cholestasis; gallstones; tumors of bile duct; carcinoma of pancreas; lymph node enlargement in porta hepatis



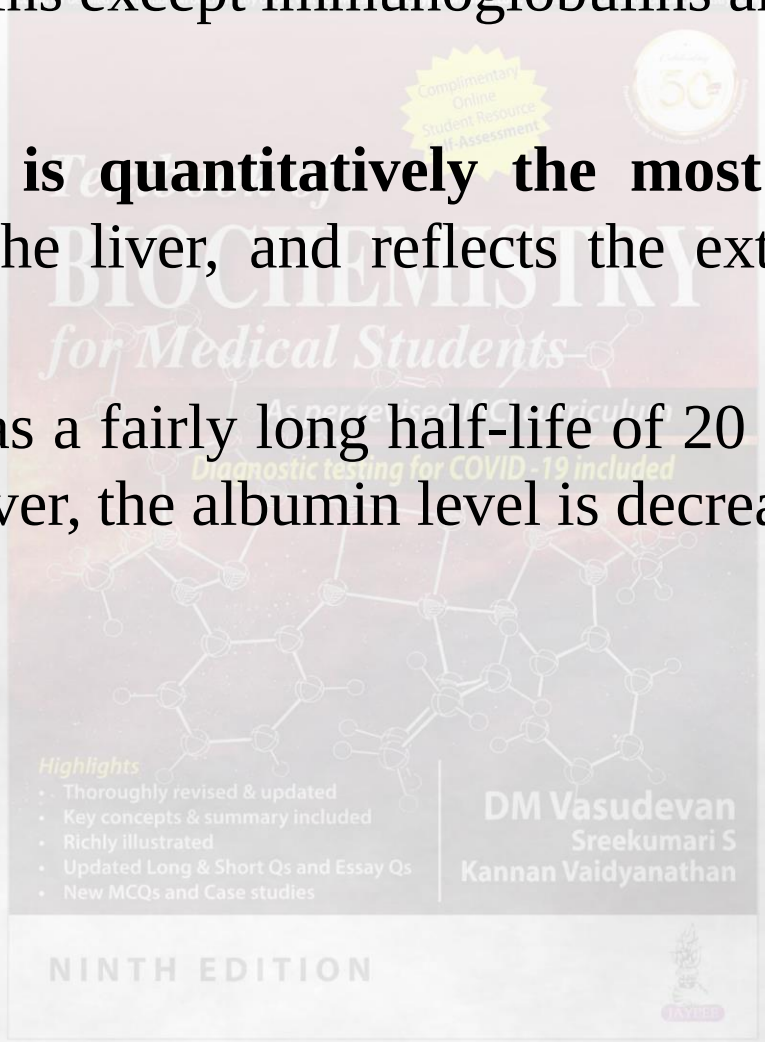
Bilirubin Metabolism

Comparison of Different Types of Jaundices



Serum Albumin Level

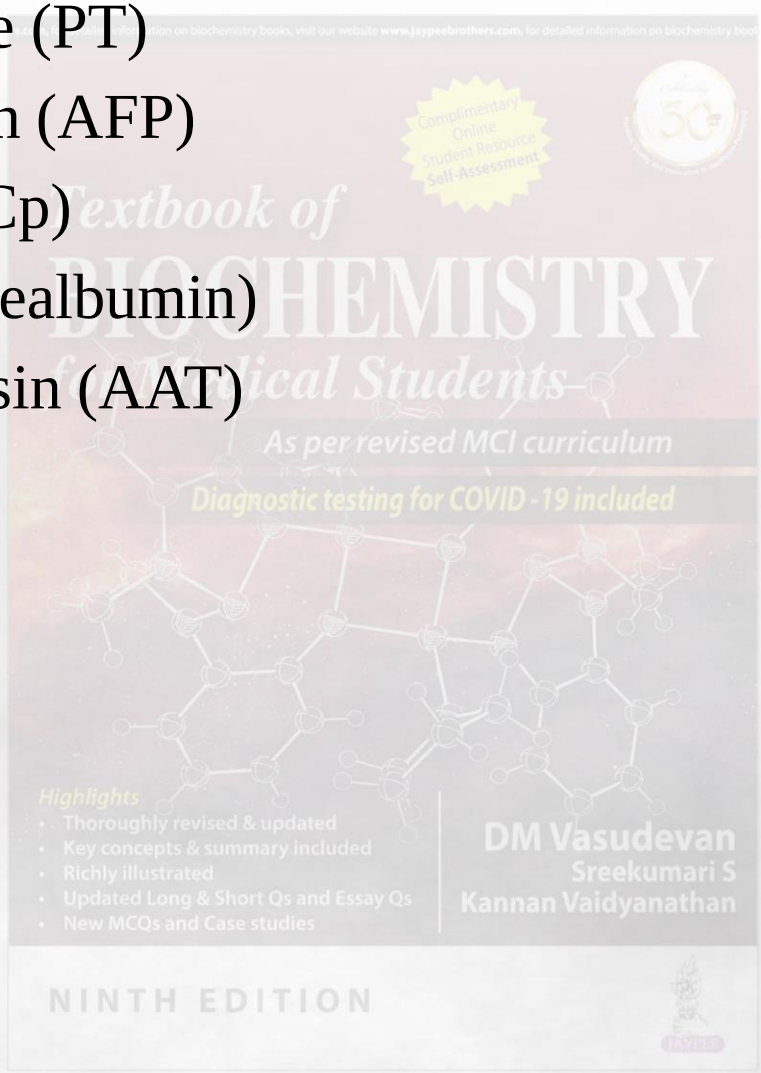
- All plasma proteins except immunoglobulins are synthesized by the liver.
- Serum **albumin is quantitatively the most** important protein synthesized by the liver, and reflects the extent of functioning liver cell mass.
- Since albumin has a fairly long half-life of 20 days, in all chronic diseases of the liver, the albumin level is decreased.



- A reversal in A/G ratio is often the rule in cirrhosis, due to hypoalbuminemia and associated hypergammaglobulinemia.
- Normal albumin level in blood is 3.5 to 5 g/dl; and globulin level is 2.5 to 3.5 g/dl.
- The turn-over rates of haptoglobin and transferrin are lesser than albumin; hence they are useful to identify the recent changes in liver functions.
- **SERUM IMMUNOGLOBULINS**
- Immunoglobulins are produced by B lymphocytes,
- Alpha and beta globulins synthesized mainly by hepatocytes.
- Gamma globulins increased in chronic liver diseases (chronic active hepatitis, cirrhosis)

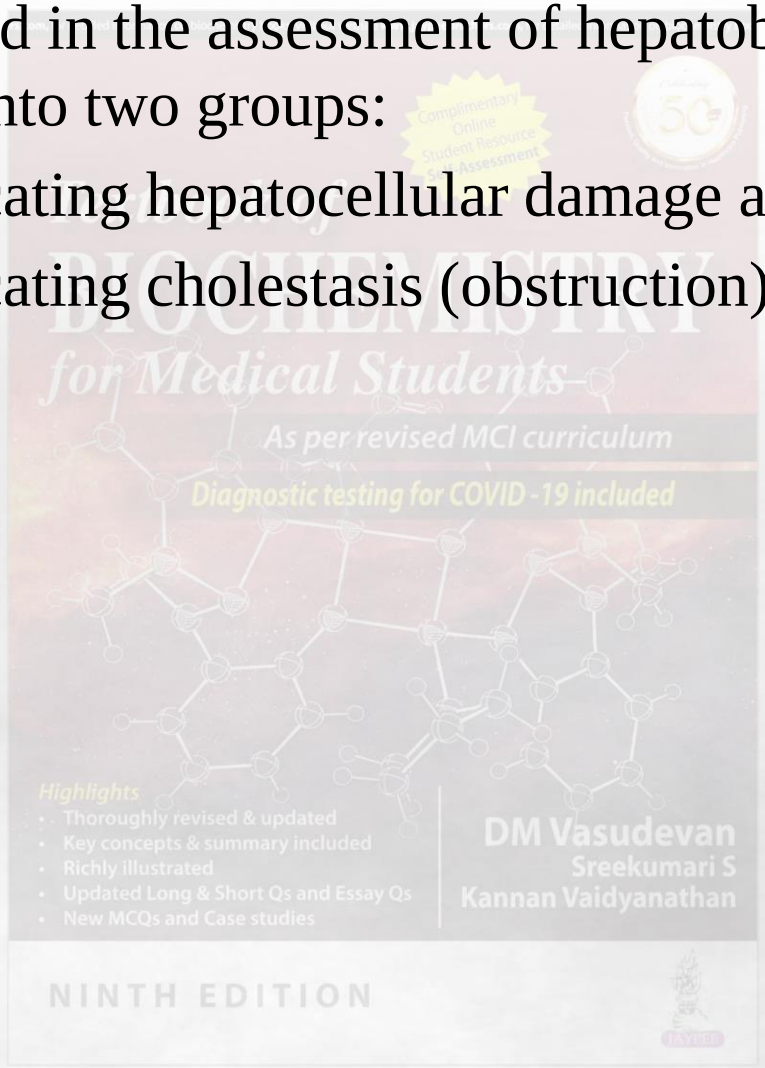
Other Tests Based on Synthetic Function

- Prothrombin time (PT)
- Alpha-fetoprotein (AFP)
- Ceruloplasmin (Cp)
- Transthyretin (Prealbumin)
- Alpha-1 antitrypsin (AAT)
- Haptoglobin



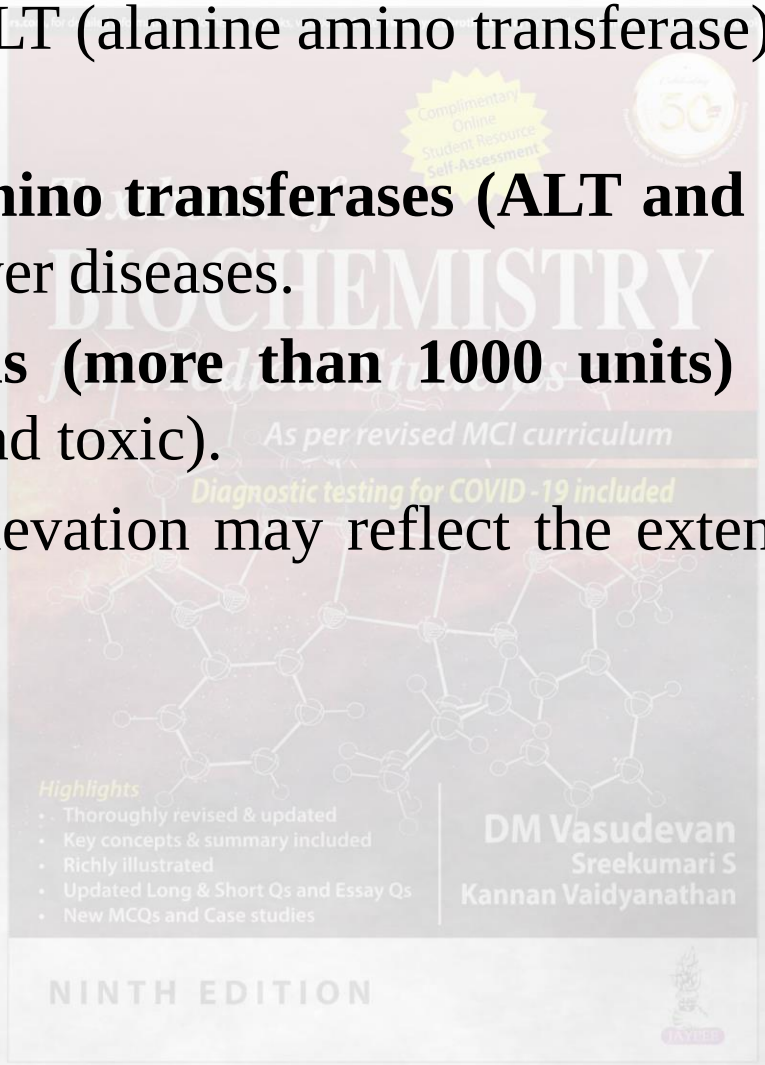
Tests based on Serum Enzymes (Liver Enzyme Panel)

- The enzymes used in the assessment of hepatobiliary disease may be divided into two groups:
  (a) Those indicating hepatocellular damage and
  (b) Those indicating cholestasis (obstruction).



Enzymes Indicating Hepatocellular Damage

- Normal serum ALT (alanine amino transferase) is 10-35 IU/L.
- **The levels of amino transferases (ALT and** AST) in serum are elevated in all liver diseases.
- **Very high levels (more than 1000 units) are** seen in acute hepatitis (viral and toxic).
- The degree of elevation may reflect the extent of hepatocellular necrosis.



- Lowering of the level of transaminases indicates recovery, but a sudden fall from a very high level may indicate poor prognosis.
- Elevation of ALT is more in cases of hepatic disease compared to AST.
- AST > ALT in **alcoholic liver disease.**
- In alcoholic liver disease, the actual values show only mild elevation; but a ratio of AST/ALT more than 2 is quite suggestive.
- **Moderate elevation of amino transferases** often between 100-300 U/L is seen in **alcoholic** hepatitis, autoimmune hepatitis, Wilson's disease and nonalcoholic chronic hepatitis.
- **Minor elevation less than 100U/L is seen in** chronic viral hepatitis (hepatitis C), fatty liver and in nonalcoholic steatohepatitis (**NASH).**

Clinical Significance of AST/ALT Ratio

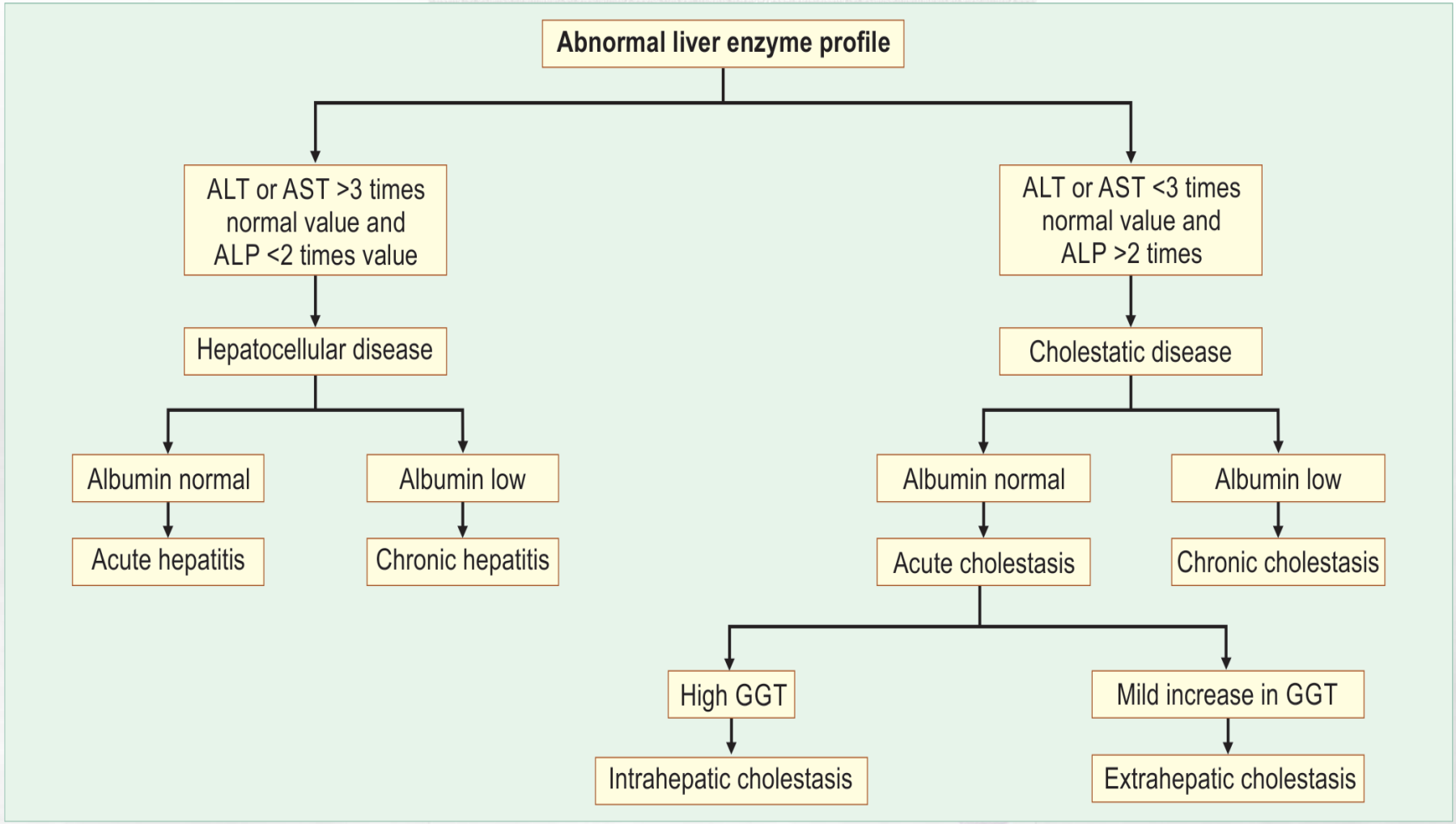
Normal AST: ALT ratio is 0.8. A ratio >2 is seen in:

- Alcoholic hepatitis
- Hepatitis with cirrhosis
- Nonalcoholic steatohepatitis (NASH)
- Liver metastases
- Myocardial infarction
- Erythromycin treatment

ALT higher than AST is seen in:

- Acute hepatocellular injury
- Toxic exposure
- Extrahepatic obstruction (cholestasis)

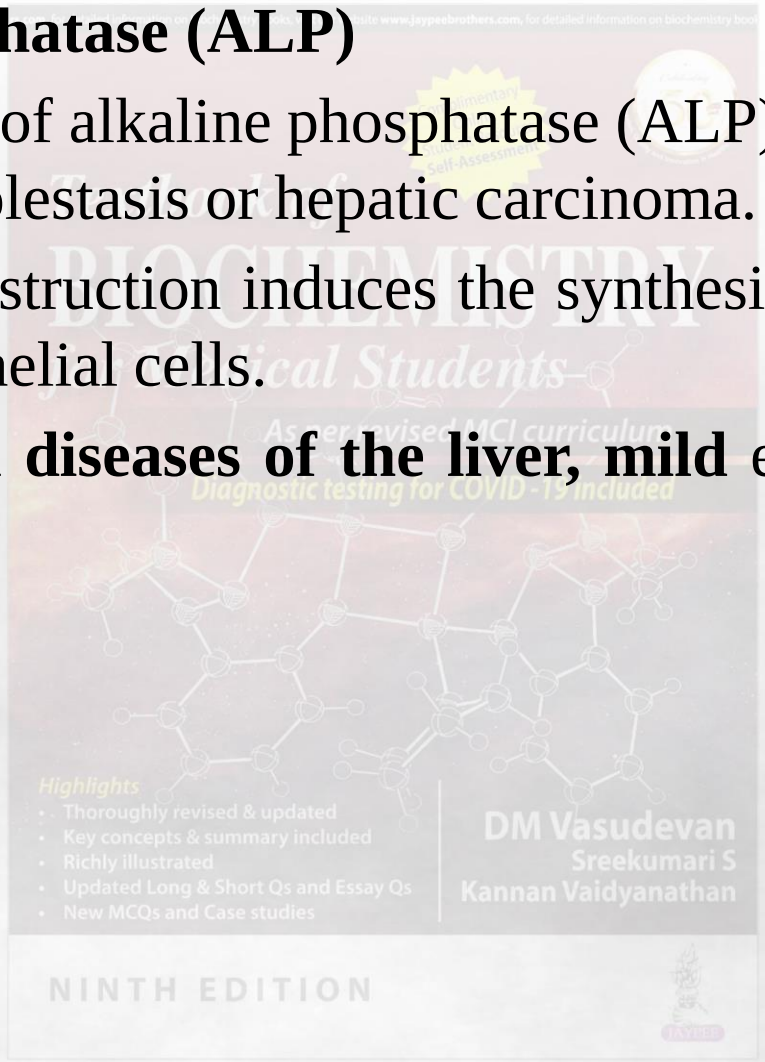
Algorithm for Diagnosis of Liver Diseases



Markers of Obstructive Liver Disease

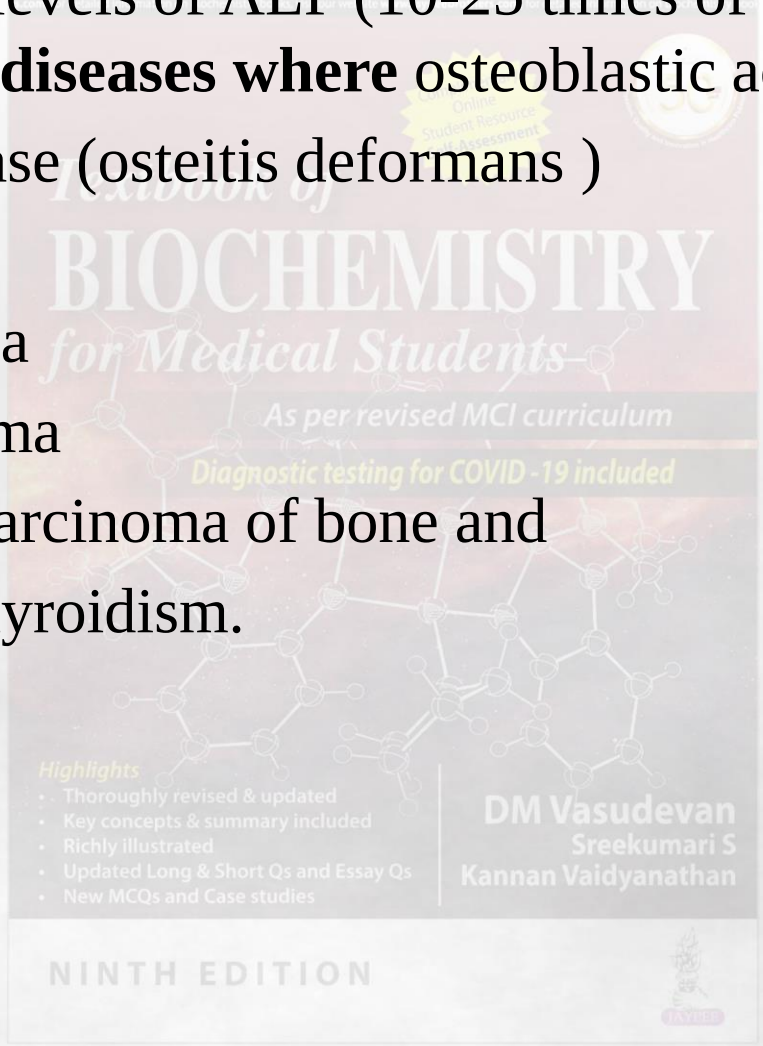
1. **Alkaline Phosphatase (ALP)**

- Very high levels of alkaline phosphatase (ALP) are noticed in patients with cholestasis or hepatic carcinoma.
- The bile duct obstruction induces the synthesis of the enzyme by biliary tract epithelial cells.
- In **parenchymal diseases of the liver, mild** elevation of ALP is noticed.

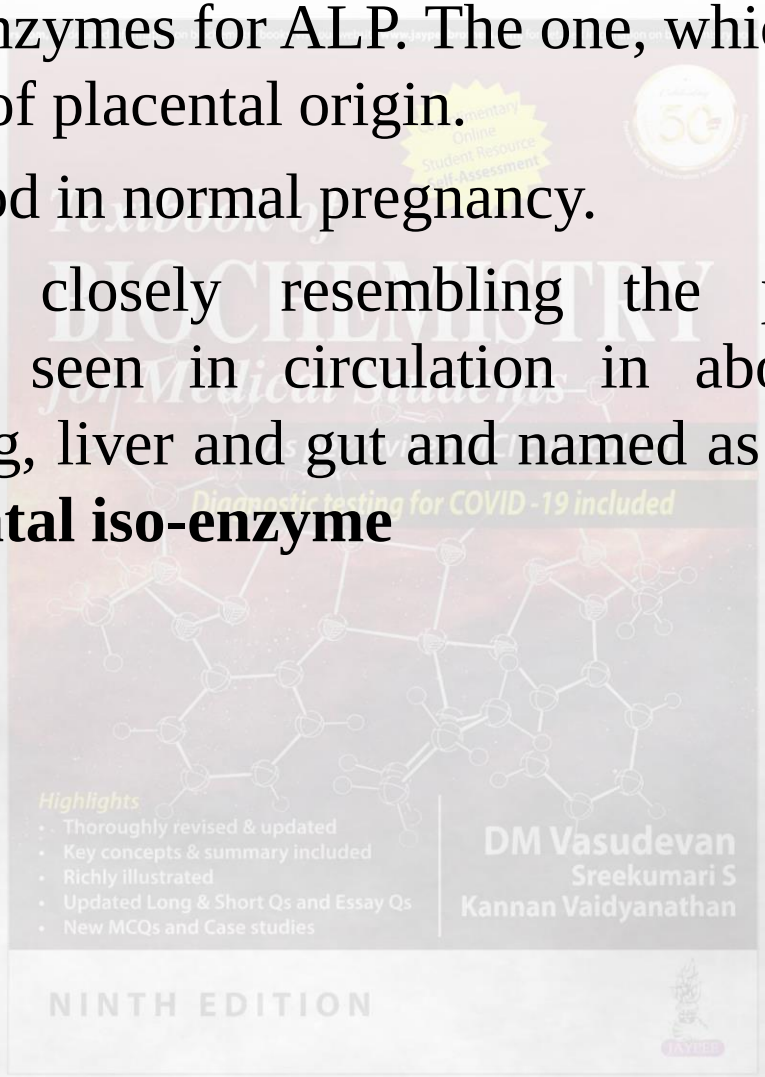


- In hepatitis, inflammatory edema produces an obstructive phase, during which ALP level is elevated.
- Very high levels of ALP (10-12 times of upper limit) may be noticed in extrahepatic **obstruction** (obstructive jaundice) caused by gallstones or by pressure on bile duct by carcinoma of head of pancreas.
- Intrahepatic cholestasis may be due to virus (infective hepatitis) or by drugs (chlorpromazine).
- ALP is produced by epithelial cells of biliary canaliculi and obstruction of bile with consequent irritation of epithelial cells leads to secretion of ALP into serum.

- Drastically high levels of ALP (10-25 times of upper limit) are seen in **bone diseases where** osteoblastic activity is enhanced.
  - Paget's disease (osteitis deformans)
  - Rickets
  - Osteomalacia
  - Osteoblastoma
  - Metastatic carcinoma of bone and
  - Hyperparathyroidism.

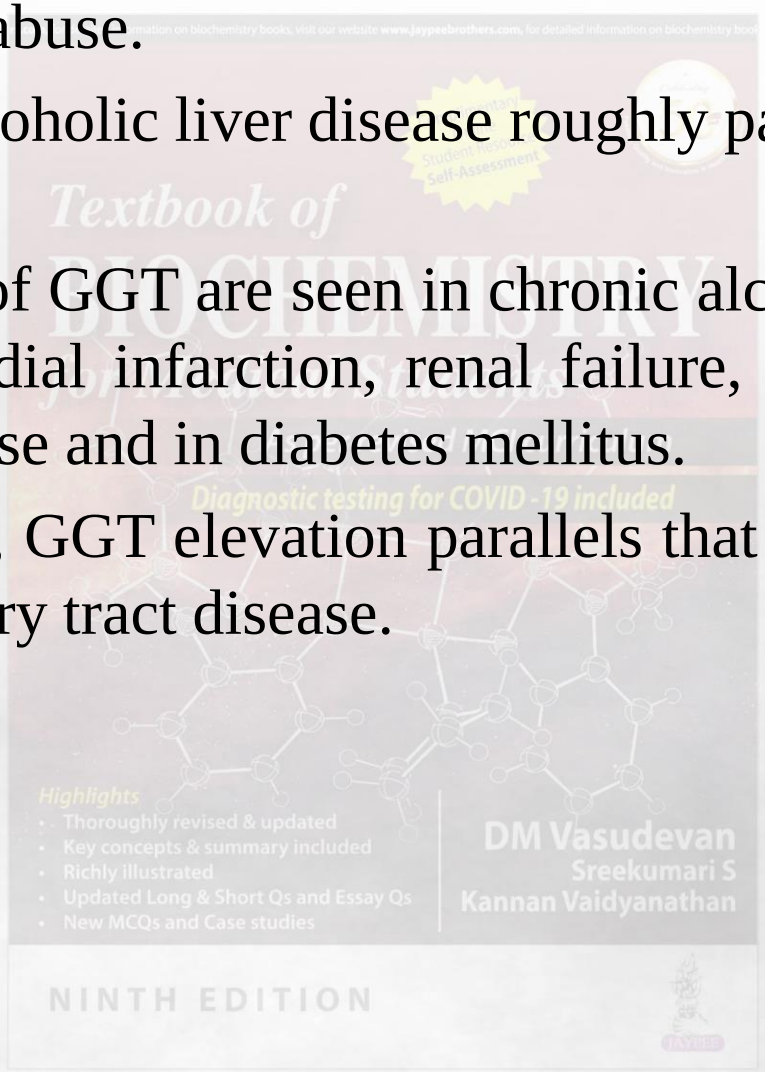


- There are 6 iso-enzymes for ALP. The one, which is inhibited by phenylalanine is of placental origin.
- It is found in blood in normal pregnancy.
- An iso-enzyme closely resembling the placental form is characteristically seen in circulation in about 15% cases of carcinoma of lung, liver and gut and named as **Regan iso-enzyme or carcinoplacental iso-enzyme**



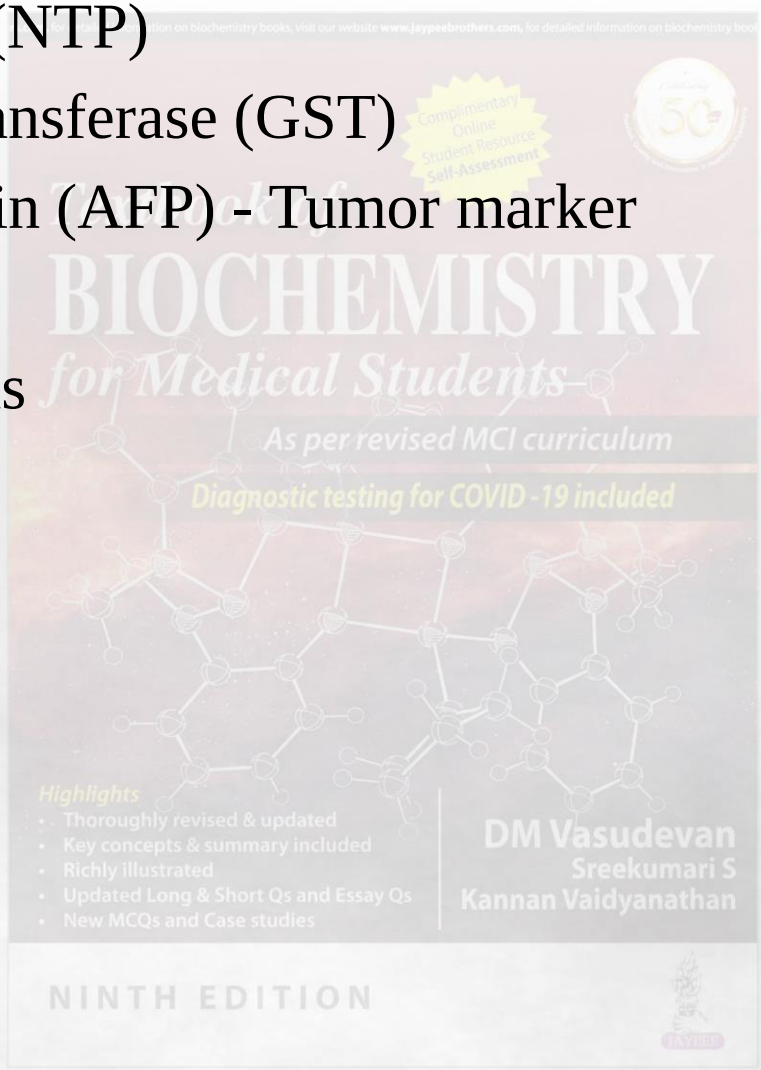
Gamma Glutamyl Transferase (GGT)

- Detects alcohol abuse.
- GGT level in alcoholic liver disease roughly parallels the alcohol intake.
- Elevated levels of GGT are seen in chronic alcoholism, pancreatic disease, myocardial infarction, renal failure, chronic obstructive pulmonary disease and in diabetes mellitus.
- In liver diseases, GGT elevation parallels that of ALP and is very sensitive of biliary tract disease.



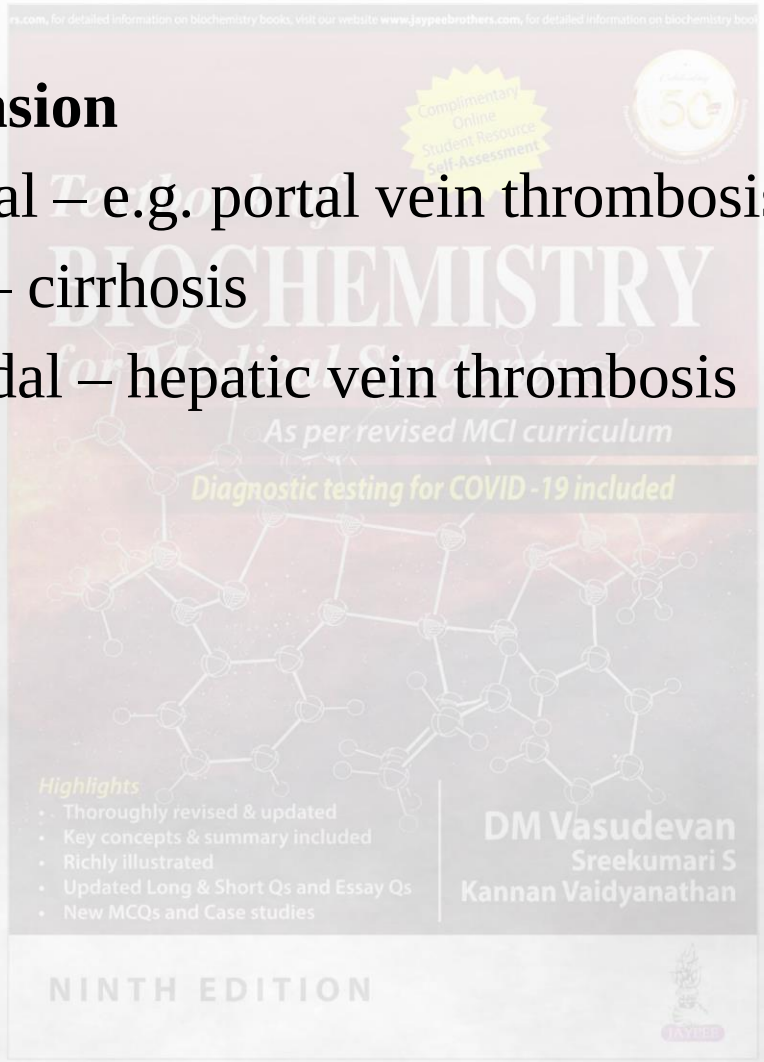
Other Tests

- 5’ Nucleotidase (NTP)
- Glutathione S transferase (GST)
- Alpha feto protein (AFP) - Tumor marker
- Ammonia
- Immunoglobulins
- Auto antibodies



Clinical Manifestations of Liver Dysfunction

- **Jaundice**
- **Portal Hypertension**
  a. Presinusoidal – e.g. portal vein thrombosis
  b. Sinusoidal – cirrhosis
  c. Postsinusoidal – hepatic vein thrombosis
- **Ascites**



Clinical features of liver failure

Liver

- Loss of metabolic function
- Decreased gluconeogenesis leading to hypoglycemia
- Decreased lactate clearance leading to lactic acidosis
- Decreased ammonia clearance leading to hyperammonemia
- Decreased synthetic capacity leading to coagulopathy
- Portal hypertension

Lungs: Adult respiratory distress syndrome

Adrenal gland: Inadequate glucocorticoid production contributing to hypotension

Brain

- Hepatic encephalopathy
- Cerebral edema
- Intracranial hypertension

Causes of Cholestatic Liver Disease

Extrahepatic cholestasis

- Cholelithiasis (stone in gallbladder)
- Carcinoma head of pancreas
- Portal lymphadenopathy
- Chronic pancreatitis
- Biliary stricture
- Parasites (liver flukes) (rare in India)

Causes of Cholestatic Liver Disease Continued

Intrahepatic cholestasis

- Alcoholic cirrhosis
- Primary biliary cirrhosis
- Nonalcoholic steatohepatitis (NASH)
- Viral hepatitis (cholestatic phase)
- Protoporphyria
- Dubin-Johnson syndrome

Drugs

- Androgens, chlorpromazine
- Chlorpropamide, nitrofurantoin
- Erythromycin, phenytoin
- Cyclosporin, captopril

Causes of Hepatocellular Damage

1. Viruses: HAV, HBV, HCV, herpes, adenovirus
2. Alcohol
3. Toxins: Carbon tetrachloride, chloroform, mushroom, aflatoxin, arsenic
4. Immunological: Autoimmune hepatitis, NASH
5. General diseases: Wilson's disease, hemochromatosis, AAT deficiency, porphyrias, sarcoidosis, amyloidosis
6. Neoplasm: Hepatocellular carcinoma, metastatic liver disease, lymphoma
7. Bacterial infections: TB, leptospirosis, brucella, abscesses
8. Parasites: Helminths, amoebiasis, plasmodia, leishmania
9. Drugs: Salicylate, tetracyclines, methotrexate, isoniazid, rifampicin, halothane, methyldopa, valproate

Immunological Tests for Liver Diseases

IgG level is increased in chronic hepatitis, alcoholic and autoimmune hepatitis. It shows a slow and sustained increase in viral hepatitis. **Ig M** shows a marked increase in primary biliary cirrhosis and a moderate increase in viral hepatitis and cirrhosis. **Ig A** is increased in alcoholic cirrhosis and primary biliary cirrhosis.

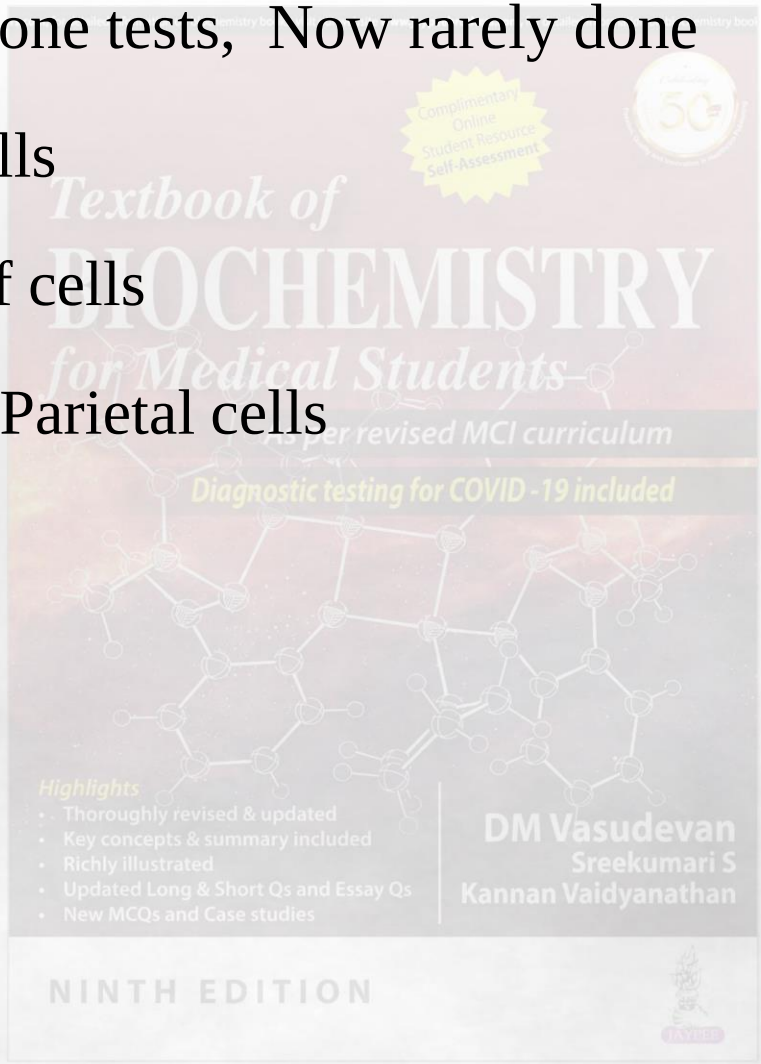
Autoantibodies: Autoimmune chronic hepatitis is due to defective suppressor T cells leading to the production of autoantibodies against hepatocyte surface antigens. Commonly encountered autoantibodies in hepatic autoimmune disorders are: a) antinuclear antibodies b) antibody against double-stranded DNA, c) anti-smooth muscle (actin) antibody, d) asialoglycoprotein receptor autoantibody and e) anti-mitochondrial antibody.

Liver Regeneration

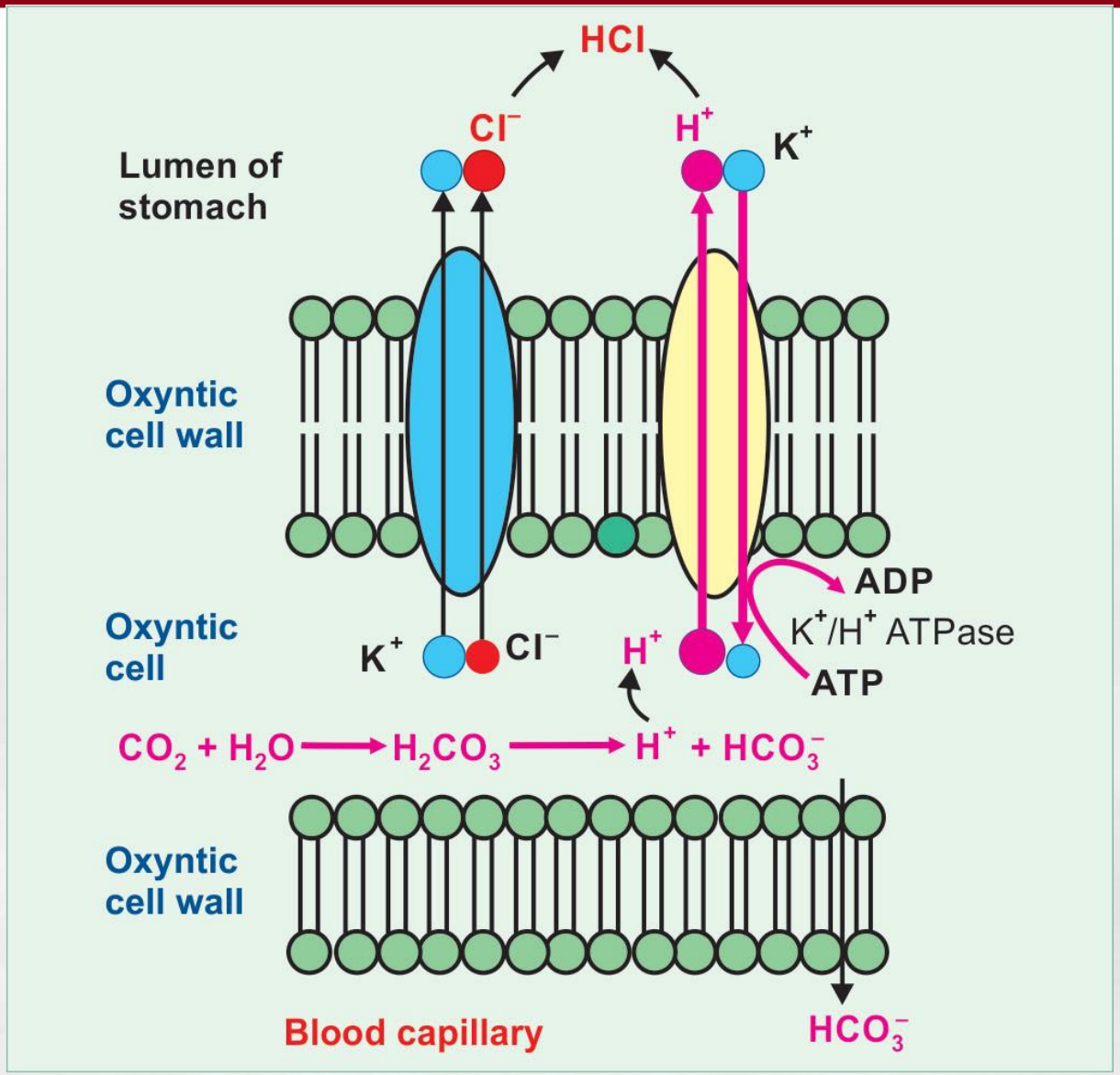
- About 90% of liver can be removed and still the remaining liver cells divide replacing the lost cells within weeks.
- Lipocytes in liver store vitamin A and other retinoids.
- Hepatocytes, when damaged, release a protein which causes lipocytes to be transformed into myofibroblast-like cells.
- Once activated, these are the sites for the synthesis of connective tissue and extracellular matrix proteins.
- After severe liver injury, liver cells regenerate.
- But this is chaotic and may result in hepatic fibrosis.
- Repetitive injury leads to fibrosis, otherwise complete regeneration occurs.

Gastric Function Tests

- Once routinely done tests, Now rarely done
- HCl - Parietal cells
- Pepsingen - chief cells
- Intrinsic factor - Parietal cells

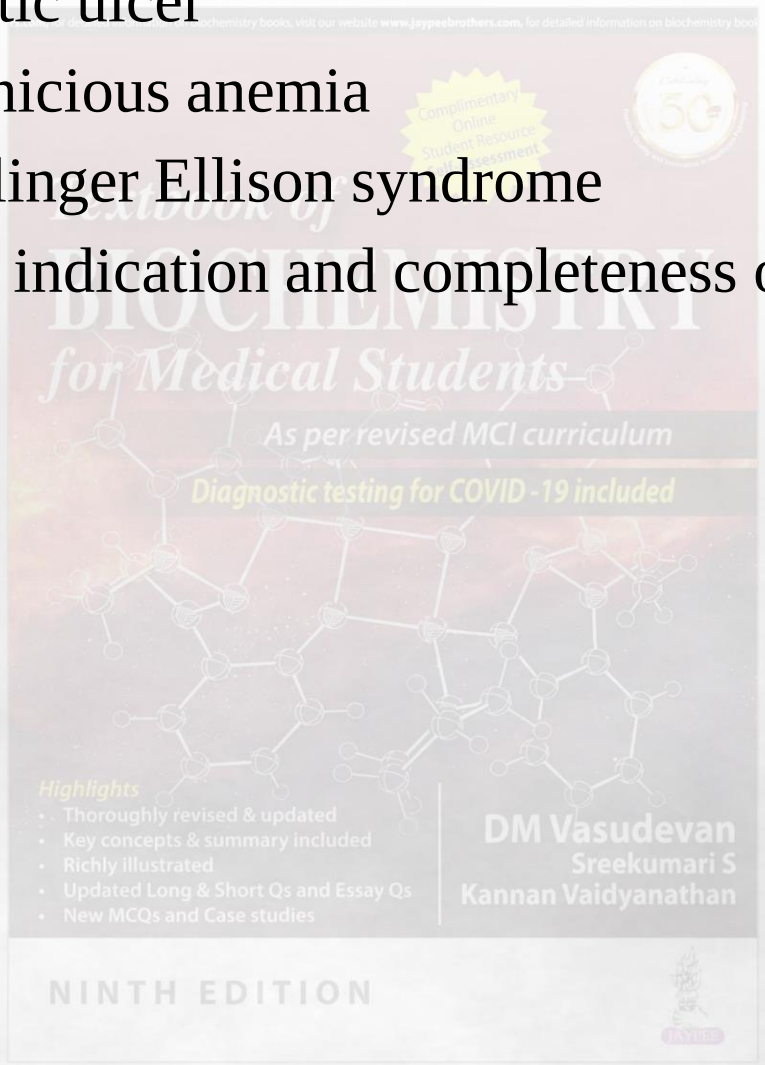


Mechanism of HCl secretion by Gastric Cells



GFT: Indications

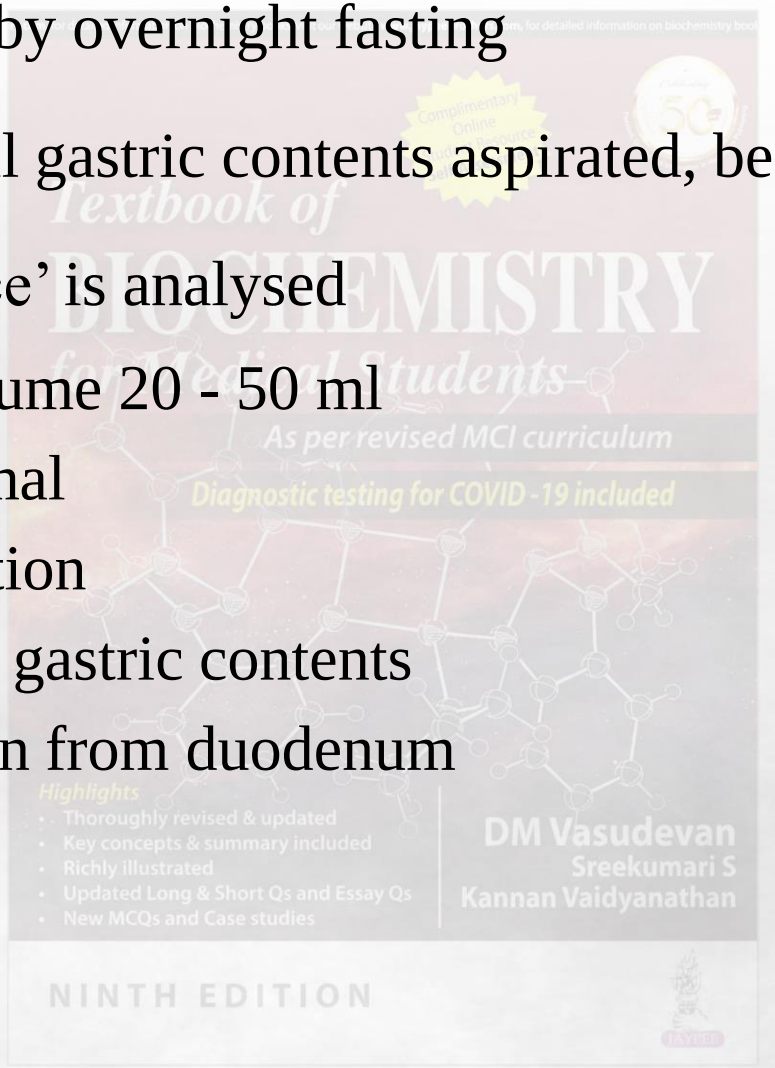
- Diagnosis of Peptic ulcer
- Exclusion of Pernicious anemia
- Diagnosis of Zollinger Ellison syndrome
- Determination of indication and completeness of vagotomy



Examination of Resting Juice

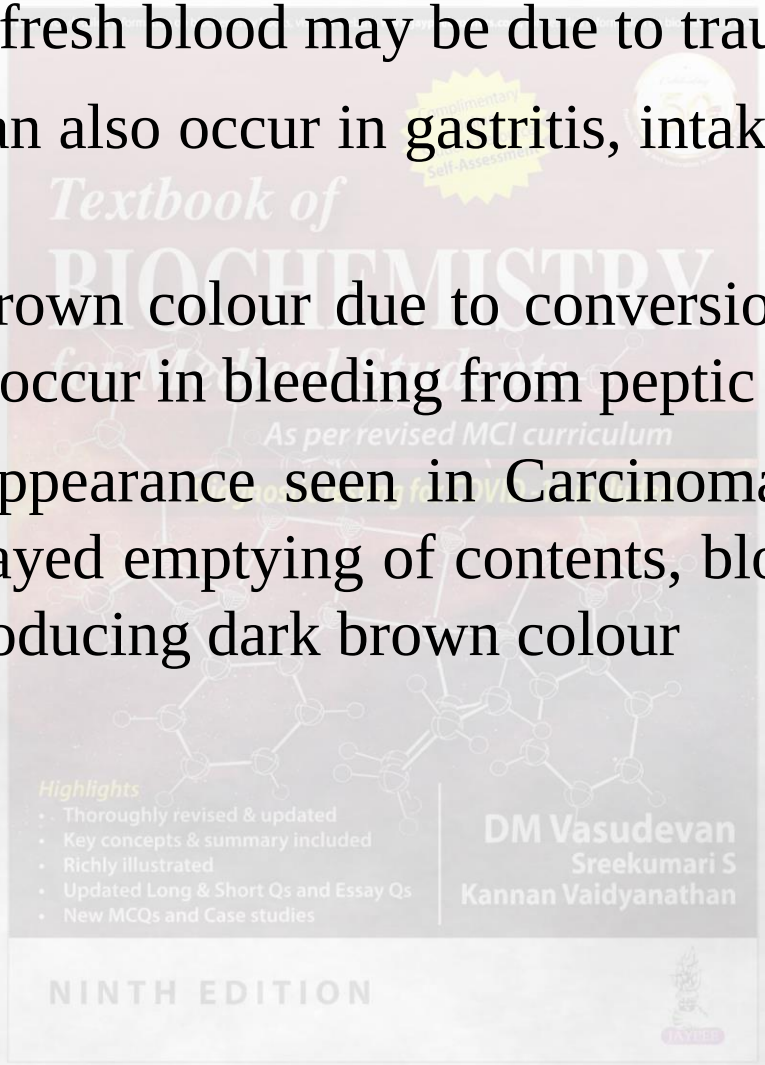
- Patient prepared by overnight fasting
- In the morning all gastric contents aspirated, before food
- The 'Resting juice' is analysed

- Resting juice volume 20 - 50 ml
- > 100 ml: abnormal
  - Hyper secretion
  - Retention of gastric contents
  - Regurgitation from duodenum



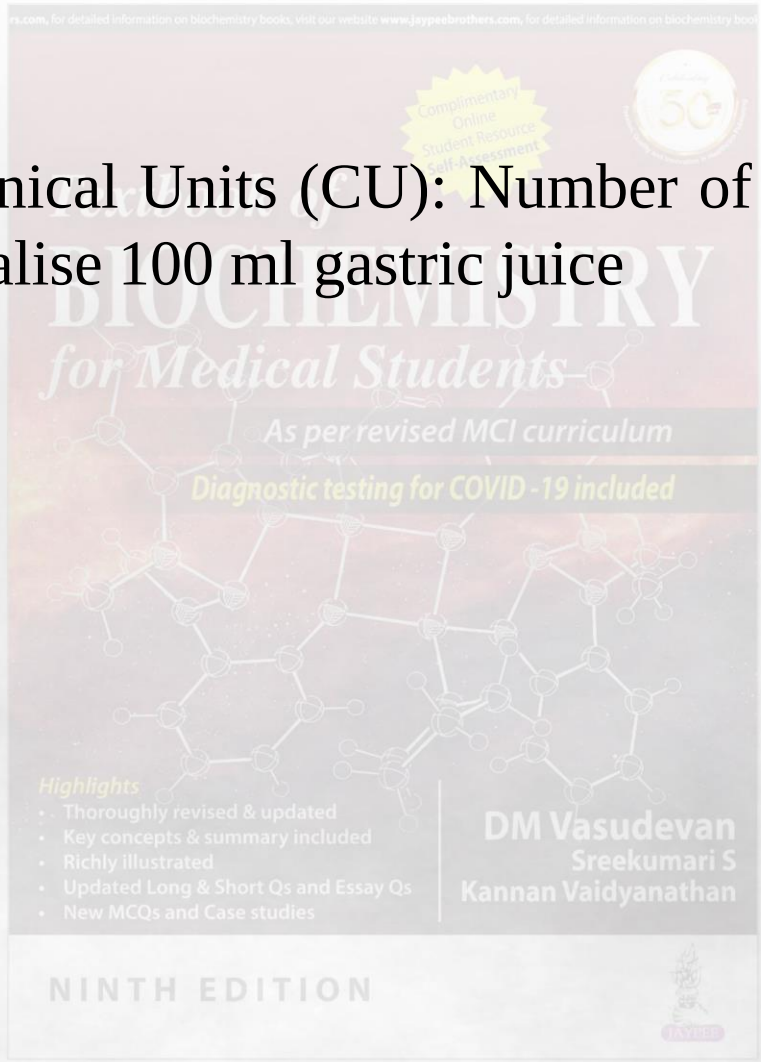
Resting Juice

- Small amount of fresh blood may be due to trauma by the tube
- Fresh bleeding can also occur in gastritis, intake of medicines like aspirin
- Brown/reddish brown colour due to conversion of blood to acid hematin by HCl: occur in bleeding from peptic ulcer
- Coffee ground appearance seen in Carcinoma Stomach: due to bleeding and delayed emptying of contents, blood get mixed with food residues, producing dark brown colour



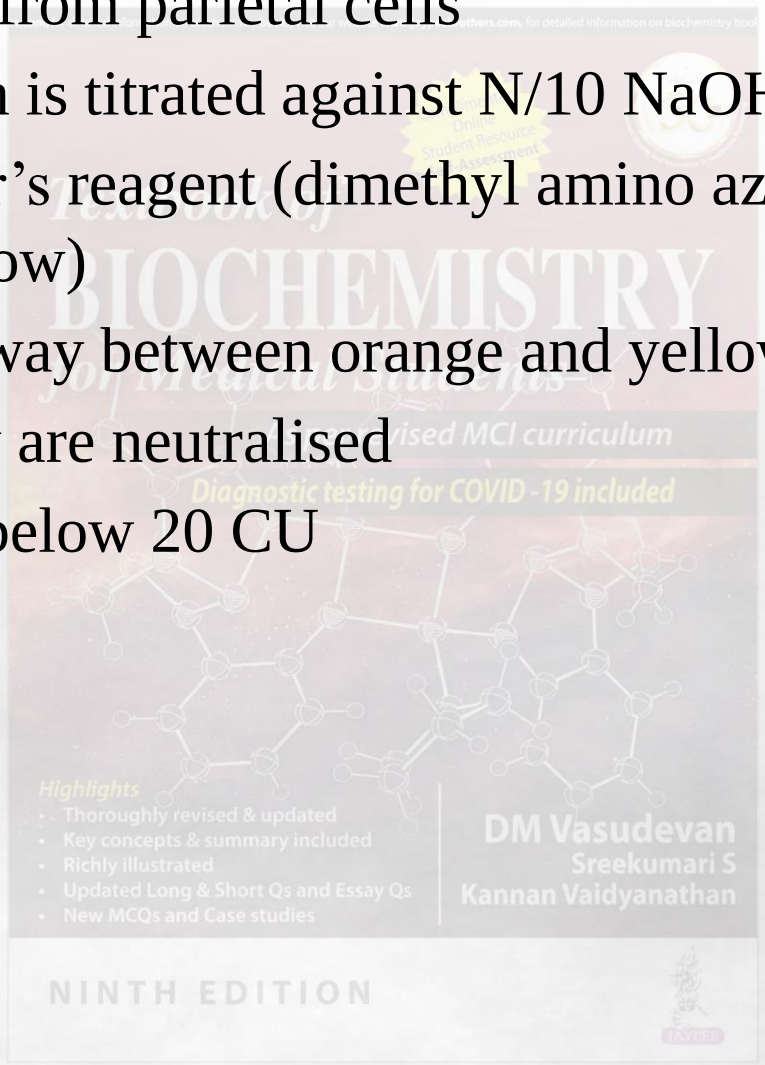
Resting Juice: Acidity

- Free acidity
- Total acidity
- Expressed as Clinical Units (CU): Number of ml of N/10 NaOH required to neutralise 100 ml gastric juice



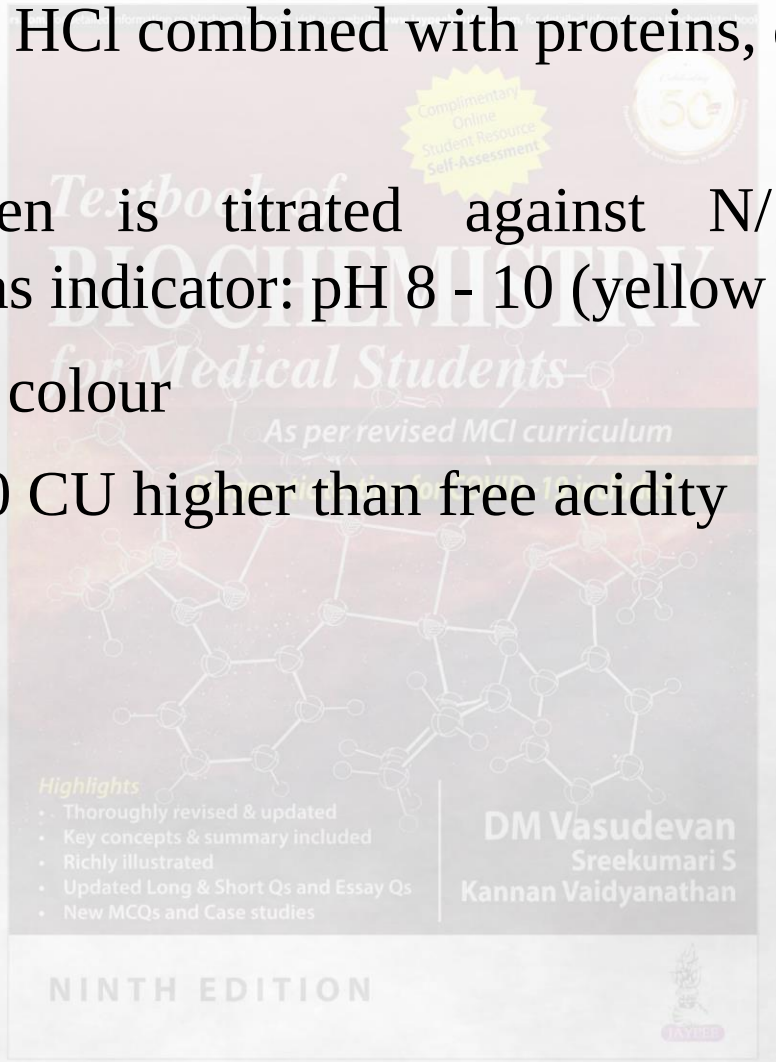
Free Acidity

- Denotes the HCl from parietal cells
- Filtered specimen is titrated against N/10 NaOH
- Indicator: Topffer's reagent (dimethyl amino azo benzene) 2.9 - 4 (red - yellow)
- End point is midway between orange and yellow (pH: 3.5)
- Strong acids only are neutralised
- Normal value is below 20 CU



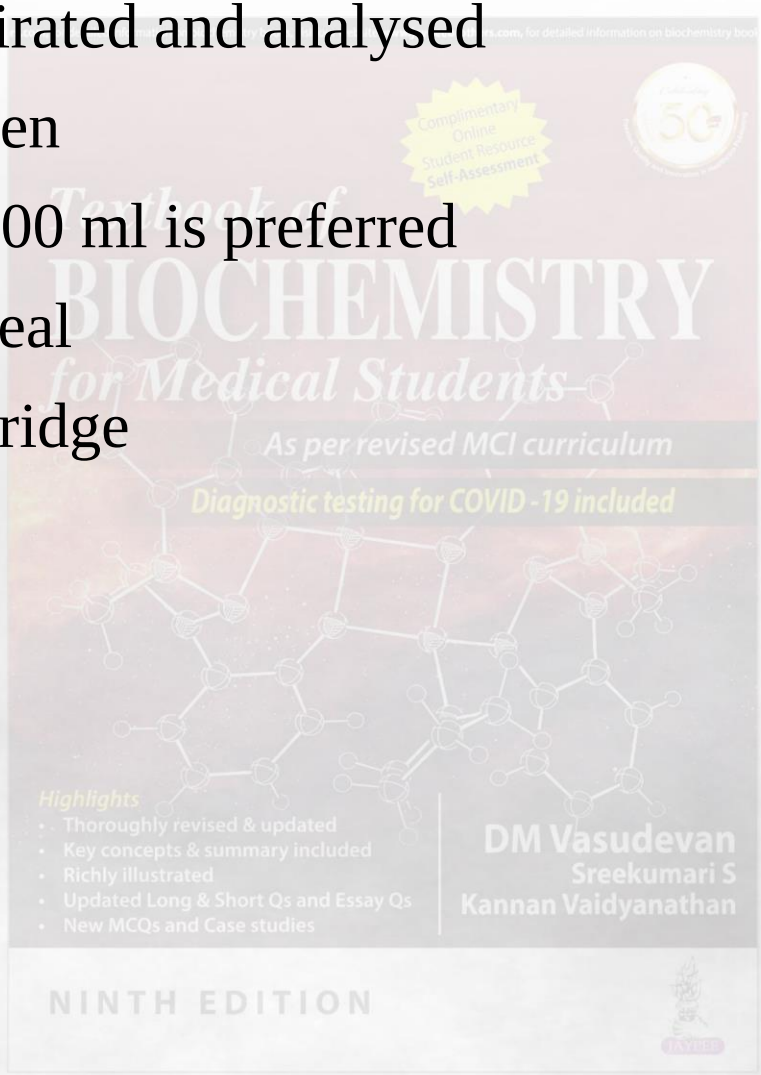
Total Acidity

- Include free HCl, HCl combined with proteins, organic acids like lactic acid
- Filtered specimen is titrated against N/10 NaOH using phenolphthalein as indicator: pH 8 - 10 (yellow - red)
- End point is pink colour
- Total acidity is 10 CU higher than free acidity



Fractional Test Meal

- Resting juice aspirated and analysed
- A test meal is given
  - Rice water, 300 ml is preferred
  - Ewald test meal
  - Oat meal porridge
  - Riegel meal

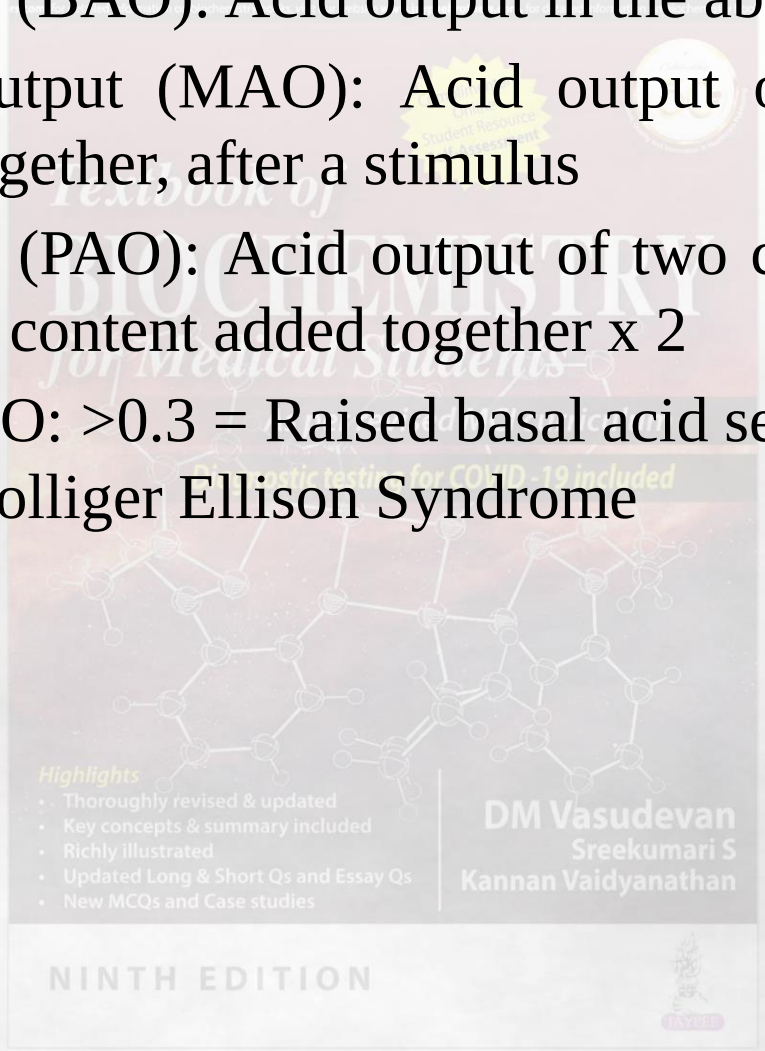


Fractional Test Meal

- 10 ml gastric juice aspirated at 15 minutes interval
- After 3 hours remaining contents, if any, is aspirated
- Contents filtered and analysed for bile, blood, mucus, starch and acidity
- Free acid appear after 15-45 minutes
- Raise to maximum by 15-30 minutes and then decrease
- Free acid is normally 15 - 45 CU
- Total acidity is 10 CU higher
- Normally no blood, nor significant amount of bile

Acid Secretion

- Basal acid output (BAO): Acid output in the absence of all stimuli
- Maximal acid output (MAO): Acid output of four continuous samples added together, after a stimulus
- Peak acid output (PAO): Acid output of two continuous samples with highest acid content added together x 2
    - BAO/PAO: >0.3 = Raised basal acid secretion
      >0.6 = Zolliger Ellison Syndrome



Normal Hydrochloric Acid Secretion

	Acid output in mmol/hour			
	Men		Women	
	Lower Limit	Upper Limit	Lower limit	Upper limit
Basal acid output	—	10	—	5.5
Maximal acid output	7	45	5	30
Peak acid output	12	60	8	40

Causes for Hyperacidity and Hypoacidity

Hyperacidity is seen in:

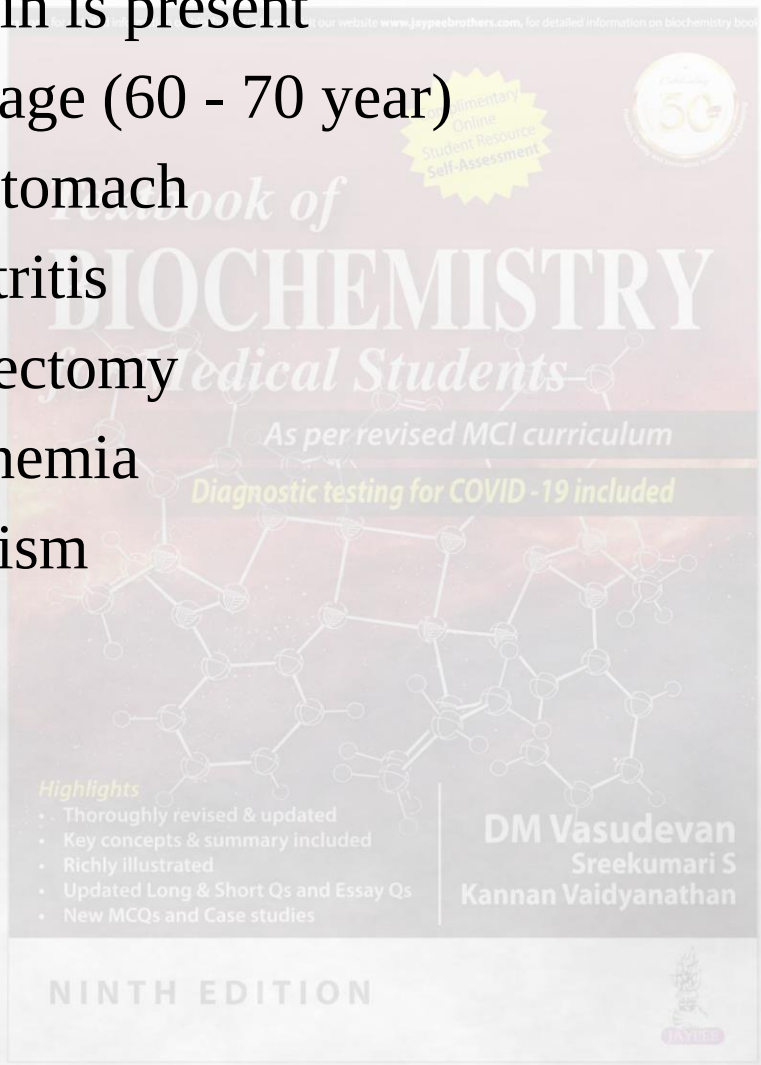
i. Duodenal ulcer
ii. Gastric cell hyperplasia
iii. Carcinoid tumors
iv. Zollinger-Ellison syndrome
v. Multiple endocrine neoplasia (MEN)
vi. Excessive histamine production as in systemic mastocytosis and basophilic leukemia

Hypoacidity is seen in:

i. Gastritis
ii. Gastric carcinoma
iii. Partial gastrectomy
iv. Pernicious anemia
v. Chronic iron deficiency anemia

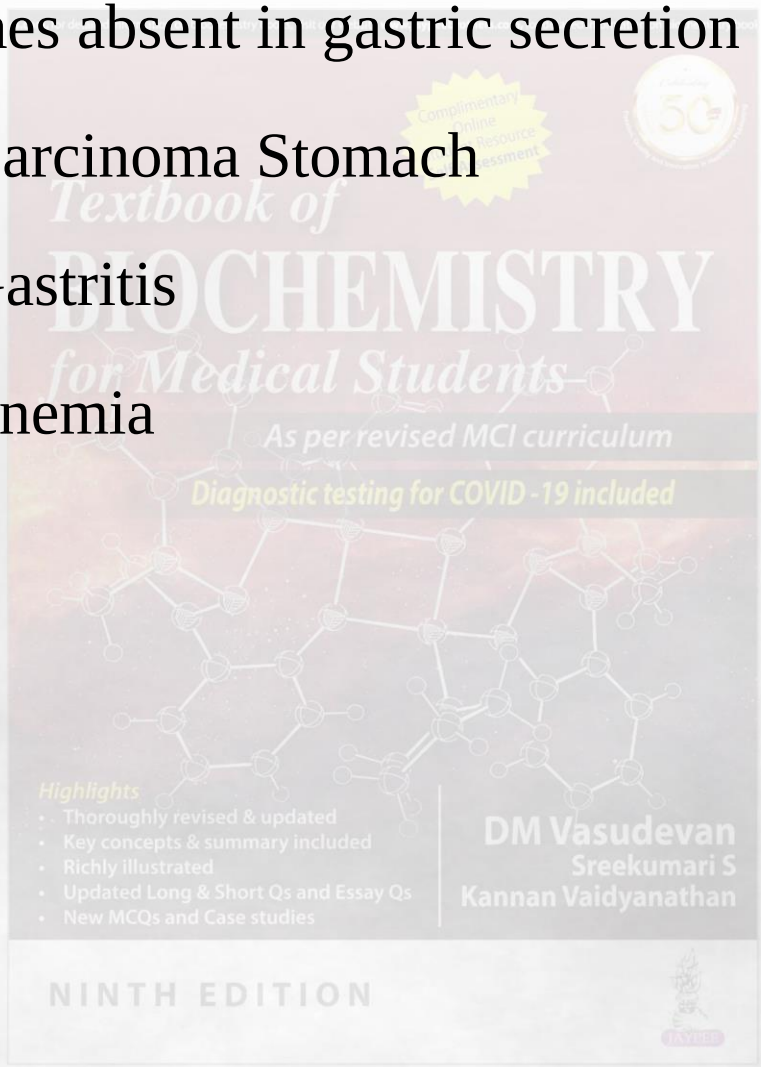
Achlorhydria

- No HCl; but pepsin is present
  - Usual in old age (60 - 70 year)
  - Carcinoma Stomach
  - Chronic Gastritis
  - Partial Gastrectomy
  - Pernicious anemia
  - Hypothyroidism
  - Myxoedema



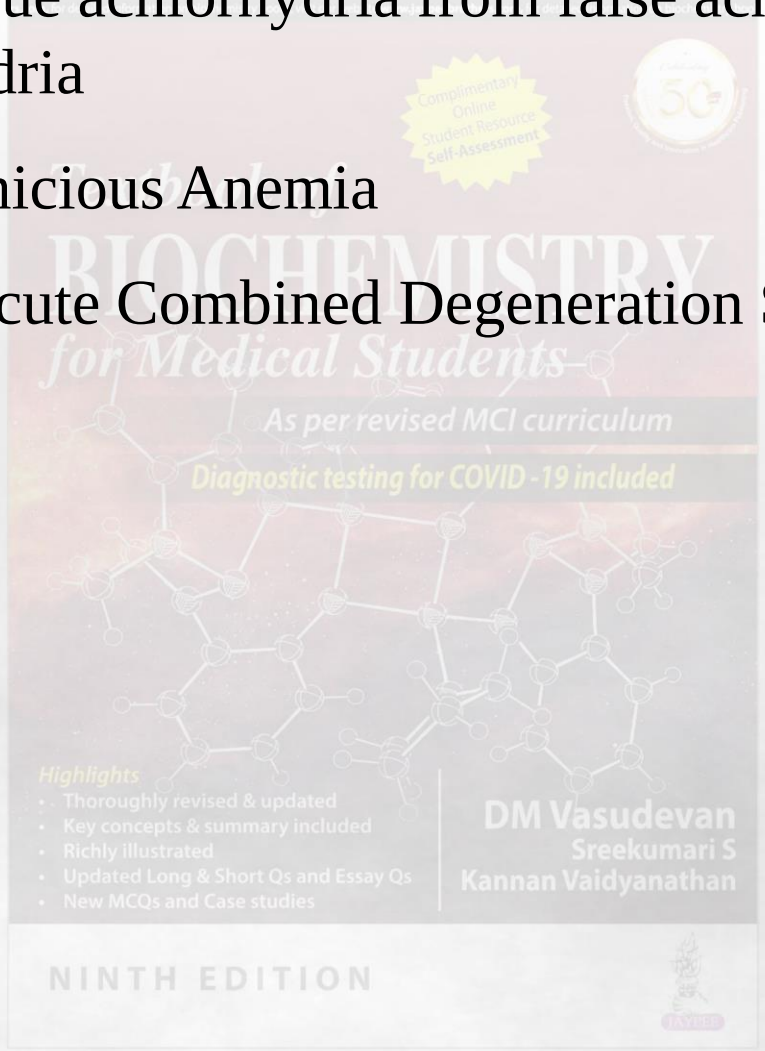
Achylia Gastrica

- Acids and Enzymes absent in gastric secretion
  - Advanced Carcinoma Stomach
  - Advanced Gastritis
  - Pernicious anemia



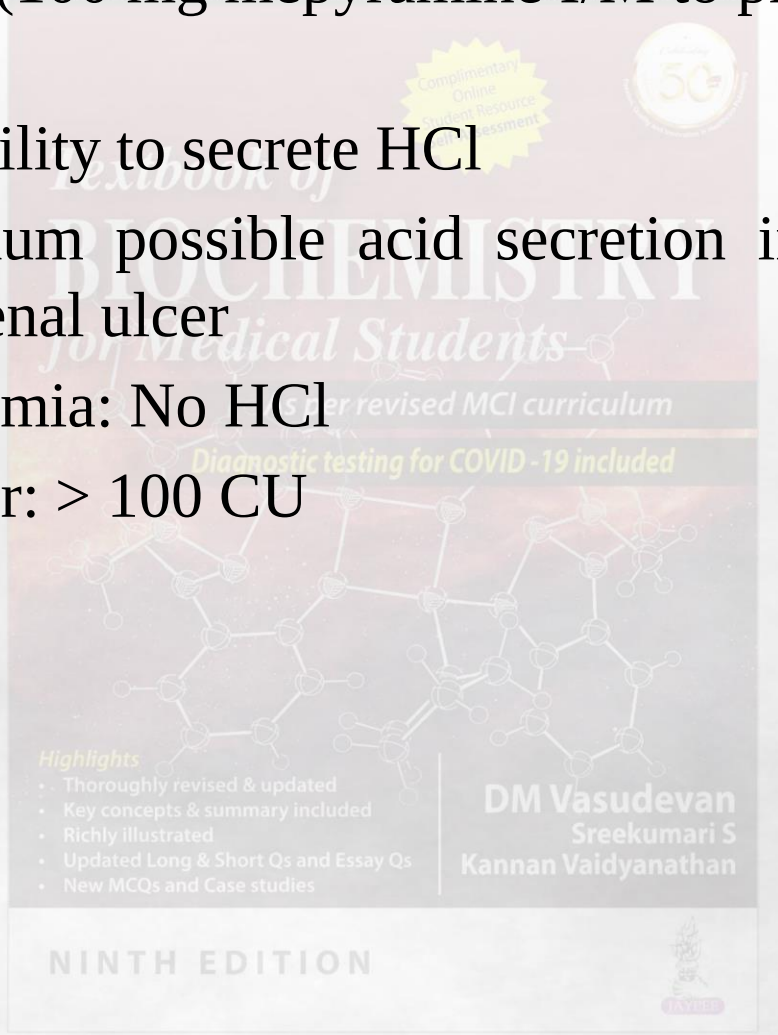
Histamine Stimulation Tests: Indications

- To differentiate true achlorhydria from false achlorhydria and hypochlorhydria
- Diagnosis of Pernicious Anemia
- Dignosis of Subacute Combined Degeneration Spinal Cord



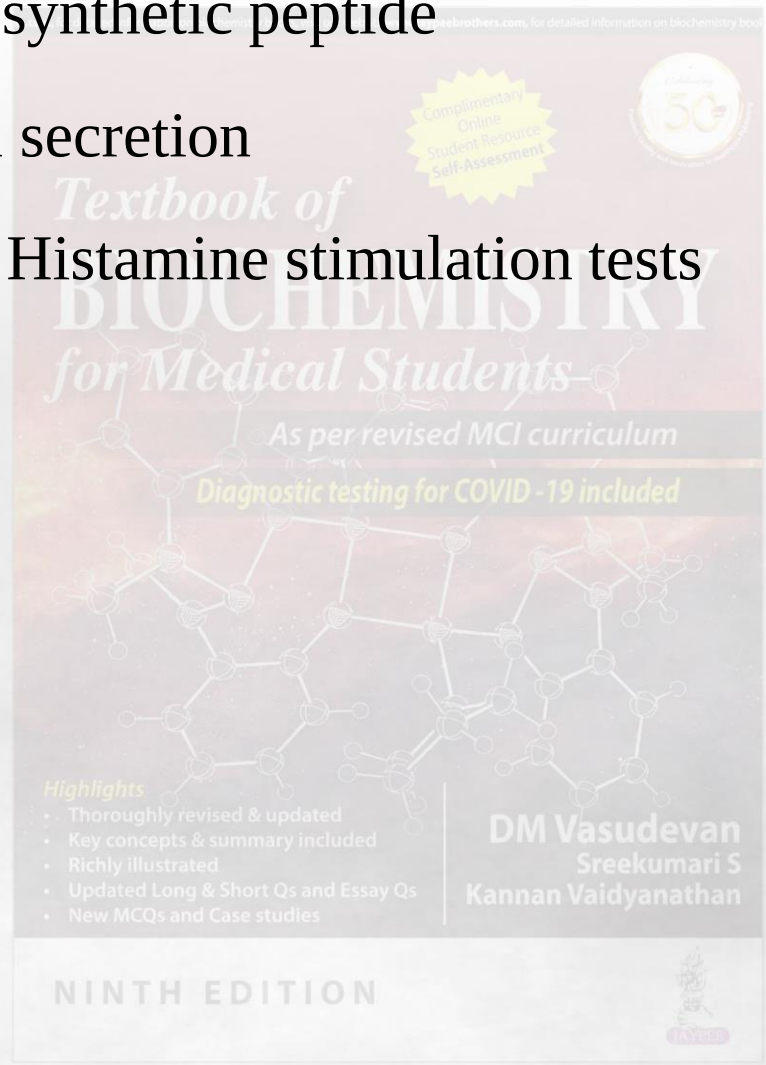
Augmented Histamine Test

- 0.04 mg/Kg S/C (100 mg mepyramine I/M to prevent severe reactions)
- To show the inability to secrete HCl
- To show maximum possible acid secretion in the diagnosis & surgery of Duodenal ulcer
- In pernicious anemia: No HCl
- In Duodenal ulcer: > 100 CU



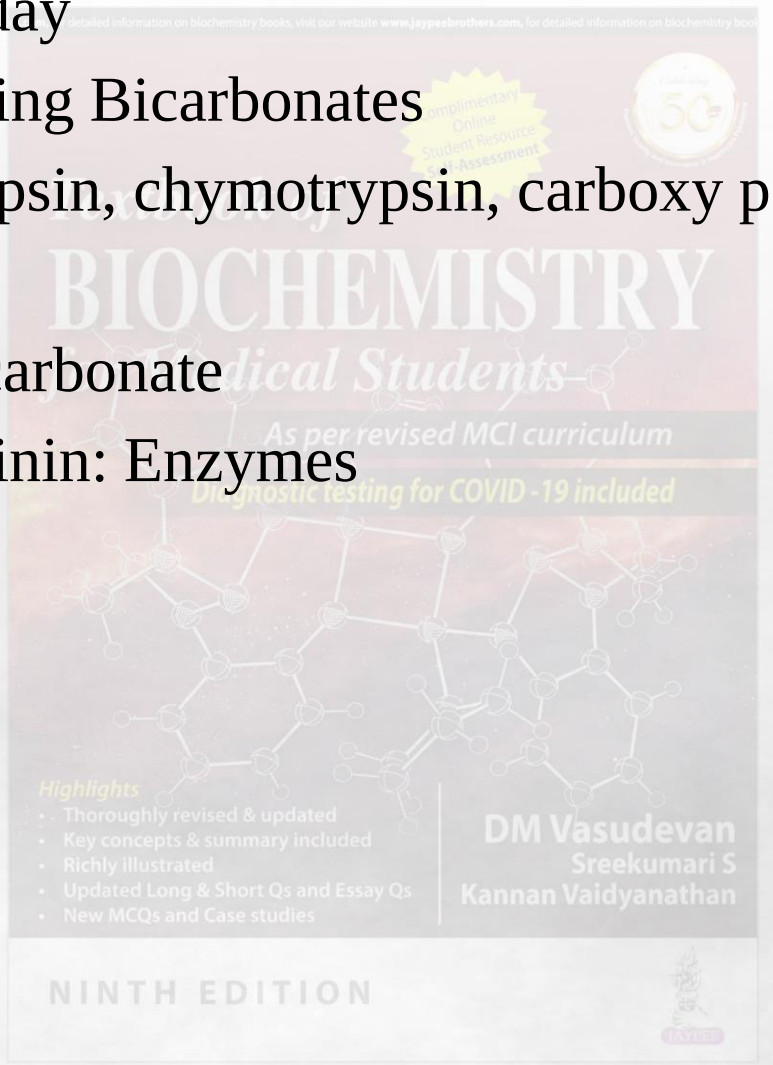
Pentagastrin Stimulation Test

- Pentagastrin is a synthetic peptide
- It stimulates HCl secretion
- Test is similar to Histamine stimulation tests



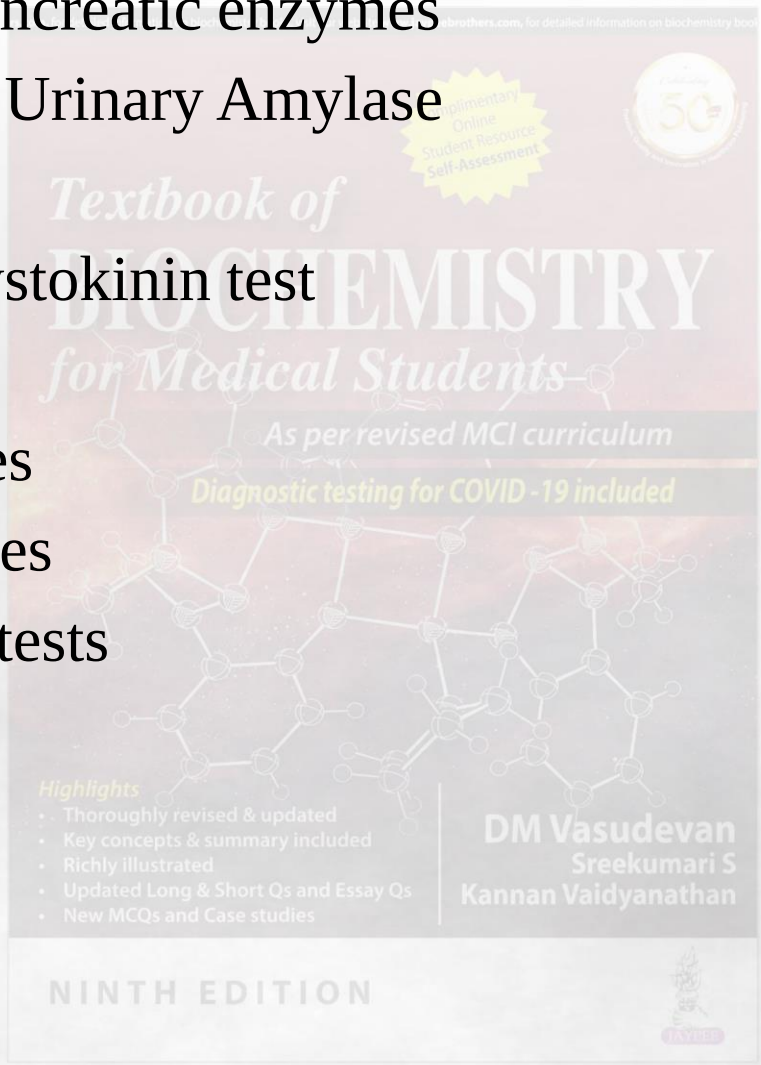
Pancreatic Secretion

- 1000 - 2500 ml/day
- Alkaline containing Bicarbonates
- Zymogens of trypsin, chymotrypsin, carboxy peptidase, elastase
- regulated by:
  - Secretin: Bicarbonate
  - Cholecystokinin: Enzymes



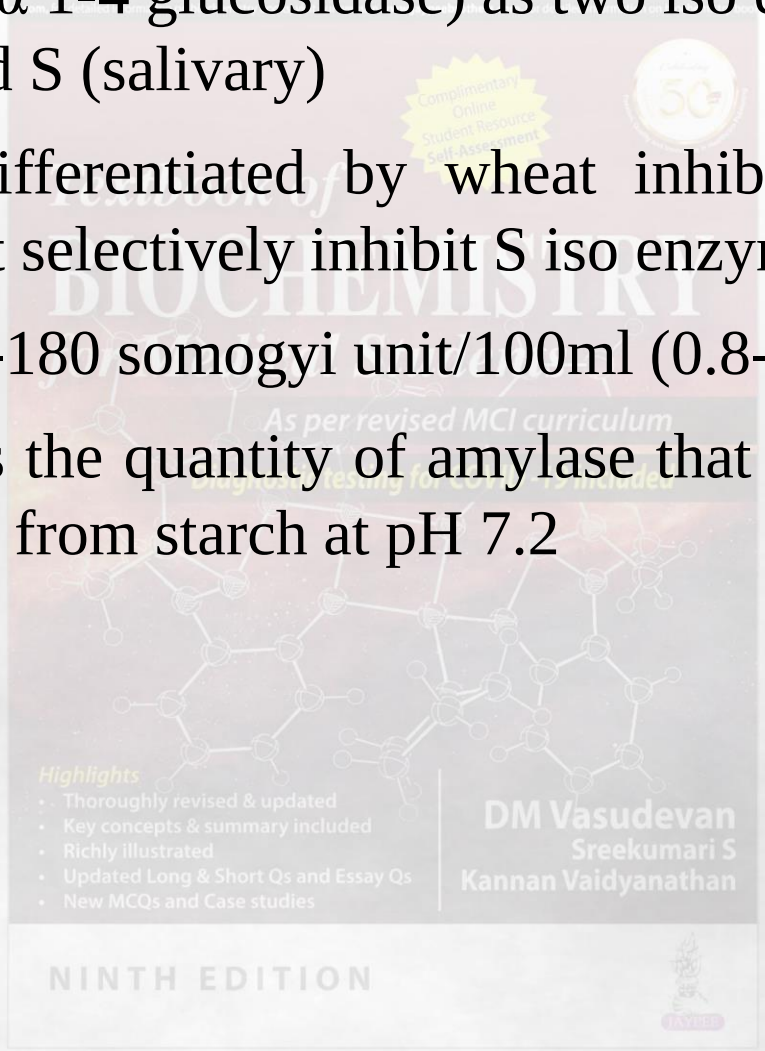
Pancreatic Function Tests

- By measuring pancreatic enzymes
- Serum Amylase, Urinary Amylase
- Serum Trypsin
- Secretin Cholecystokinin test
- Lundh test
- Sweat electrolytes
- Fat balance studies
- Starch tolerance tests



Serum Amylase

- Serum Amylase (α 1-4 glucosidase) as two iso enzymes:
  P (pancreatic) and S (salivary)
- These can be differentiated by wheat inhibition test (Protein inhibitor in wheat selectively inhibit S iso enzyme)
- Normal level: 80-180 somogyi unit/100ml (0.8-3.2 IU/L)
- 1 somogyi unit is the quantity of amylase that will produce 1 mg of reducing sugar from starch at pH 7.2

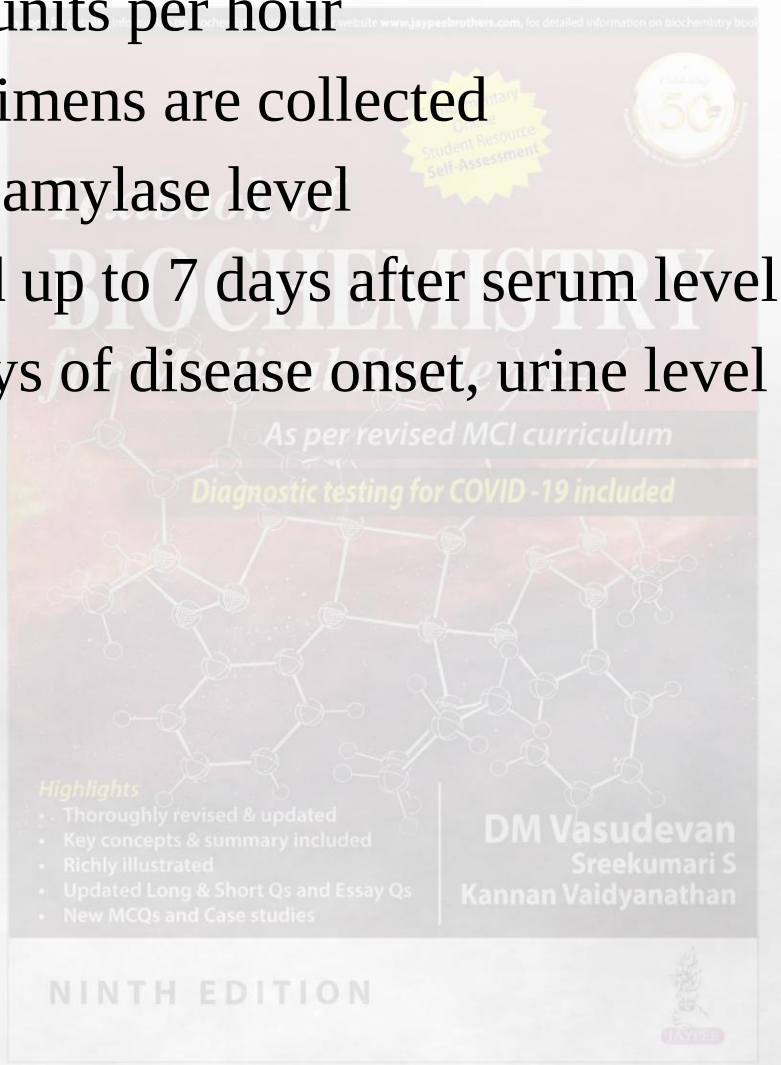


Serum Amylase

- In inflammation of pancreas and salivary glands, and in their duct obstruction, enzymes are regurgitated to blood, excreted in urine
- In a/c pancreatits, S.amylase increase within 6-24 hours, returns to normal by 3-5 days
- Also increase in:
  - Mumps
  - Pseudocyst of Pancreas
  - Pancreatic duct obstruction due to stricture, spasm, stones or Carcinoma
  - Diabetic acidosis
  - Peptic ulcer perforation
  - Renal insufficiency

Urinary Amylase

- 40 - 250 somgyi units per hour
- Timed urine specimens are collected
- Parallel to serum amylase level
- Remains elevated up to 7 days after serum level returns to normal
- So after a few days of disease onset, urine level is more dignostic



Clearance Ratio

$$CR = \frac{\text{Ur Am}}{\text{Sr Am}} \times \frac{\text{Sr Cr}}{\text{Ur Cr}} \times 100$$

Ur Am: Urinary Amylase

Sr Am: Serum Amylase

Sr Cr: Serum Creatinine

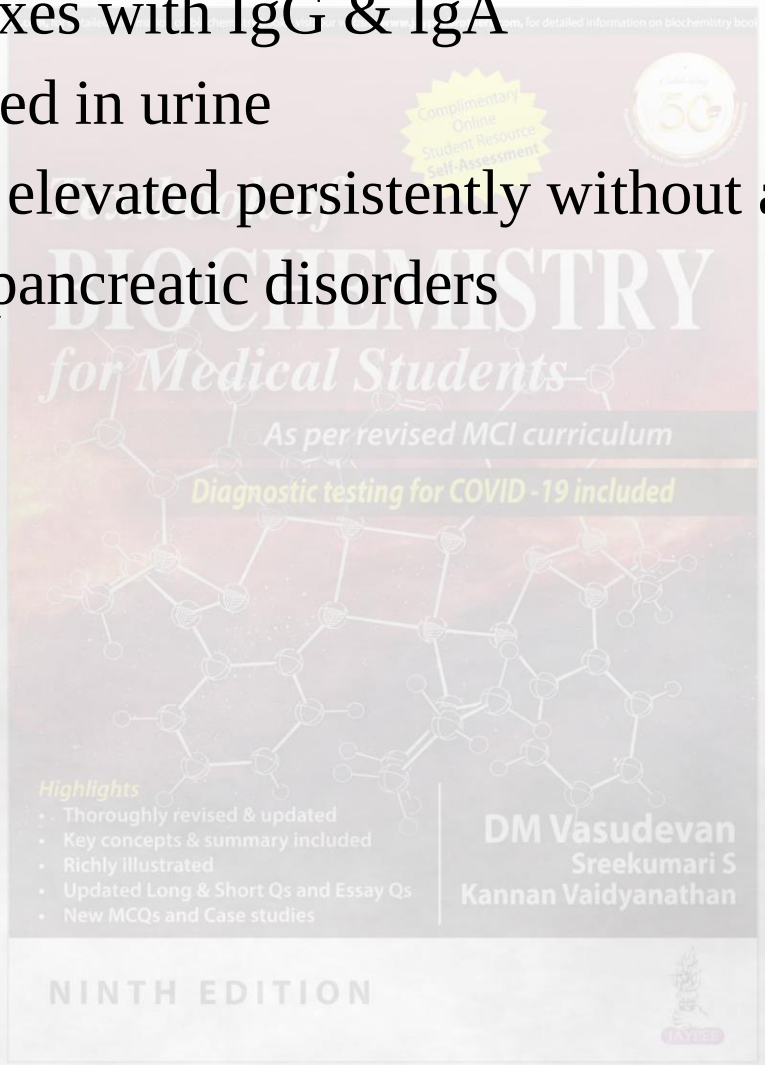
Ur Cr: Urinary Creatinine

Normal : 1 - 4.4%

A/c Pancreatits : 7 - 15%

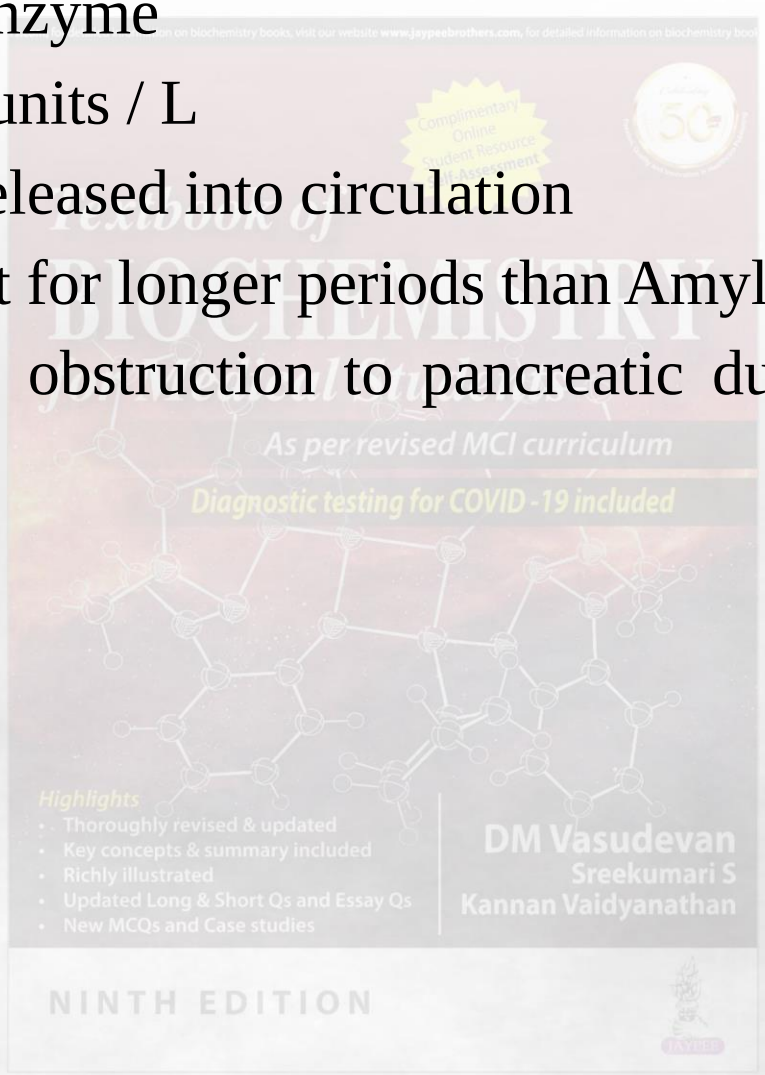
Macro Amylasemia

- Amylase complexes with IgG & IgA
- Cannot be excreted in urine
- Amylase level is elevated persistently without any symptoms
- Early marker of pancreatic disorders



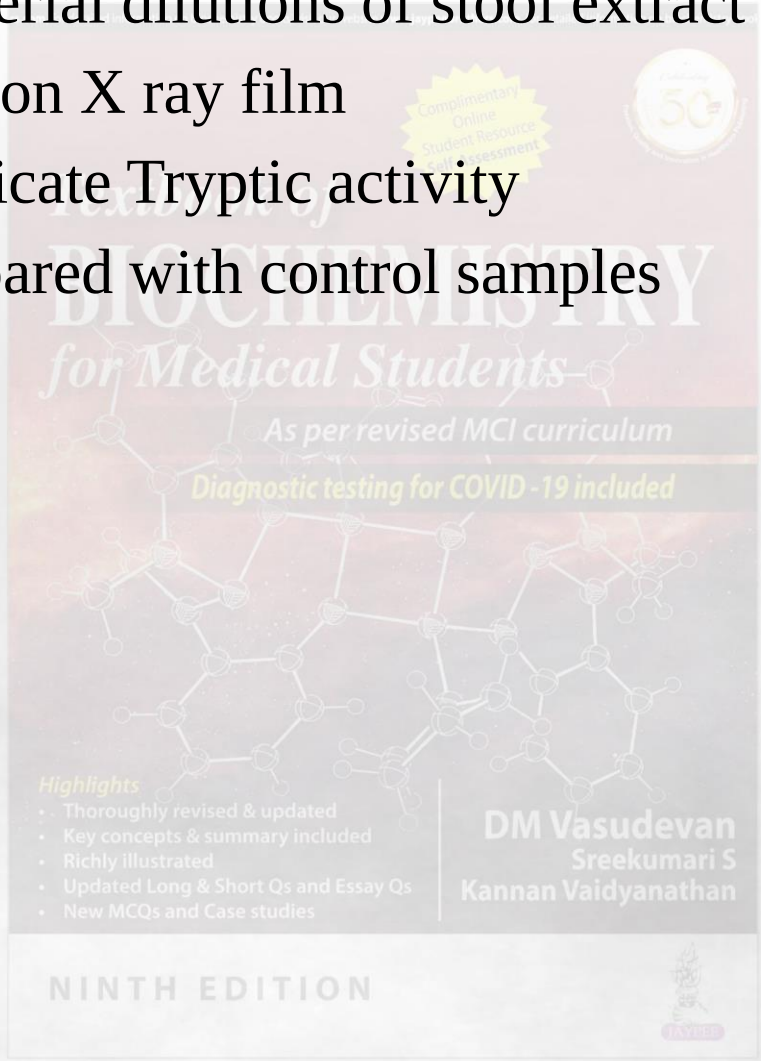
Serum Lipase

- Major lipolytic enzyme
- Normal: 0 - 150 units / L
- In Pancreatitis, released into circulation
- High level persist for longer periods than Amylase
- Also elevated in obstruction to pancreatic ducts by stone or neoplasm



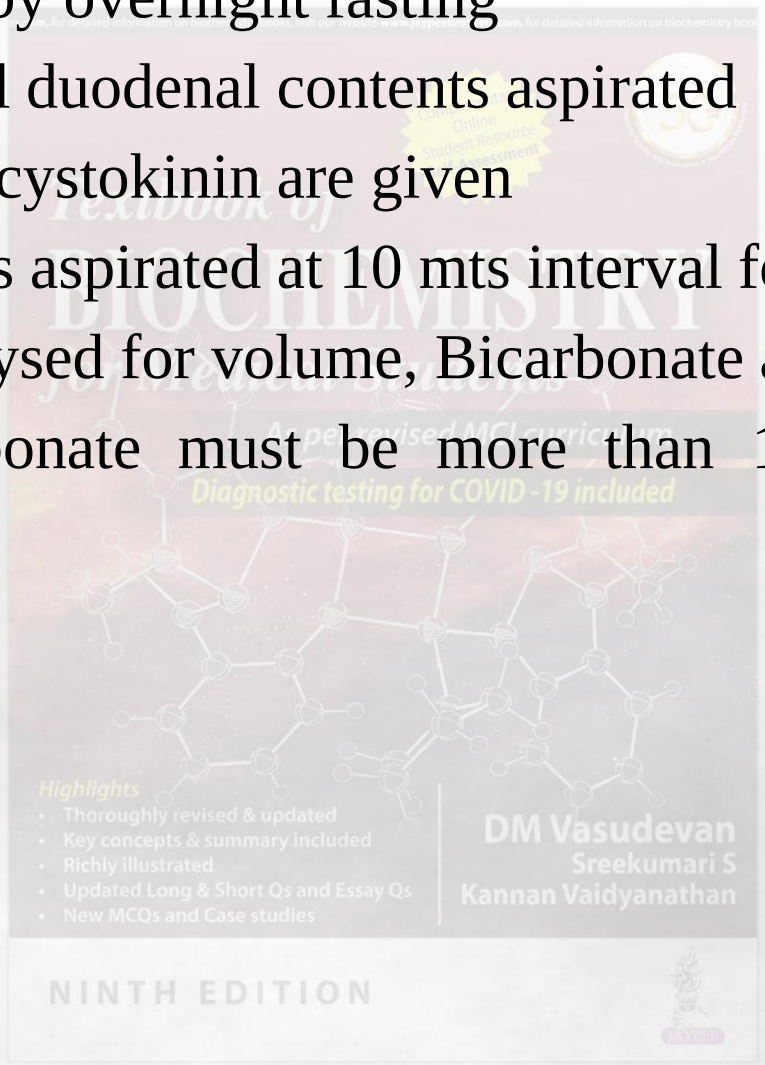
Trypsin

- Tested by using serial dilutions of stool extract
- Drops are placed on X ray film
- Translucency indicate Tryptic activity
- This can be compared with control samples



Secretin Cholecystokinin Test

- Patient prepared by overnight fasting
- In the morning all duodenal contents aspirated
- Secretin & Cholecystokinin are given
- duodenal contents aspirated at 10 mts interval for 80 mts
- each sample analysed for volume, Bicarbonate and Amylase
- Normally Bicarbonate must be more than 15 mmol/L at 30 minutes



Pancreatic Function Tests

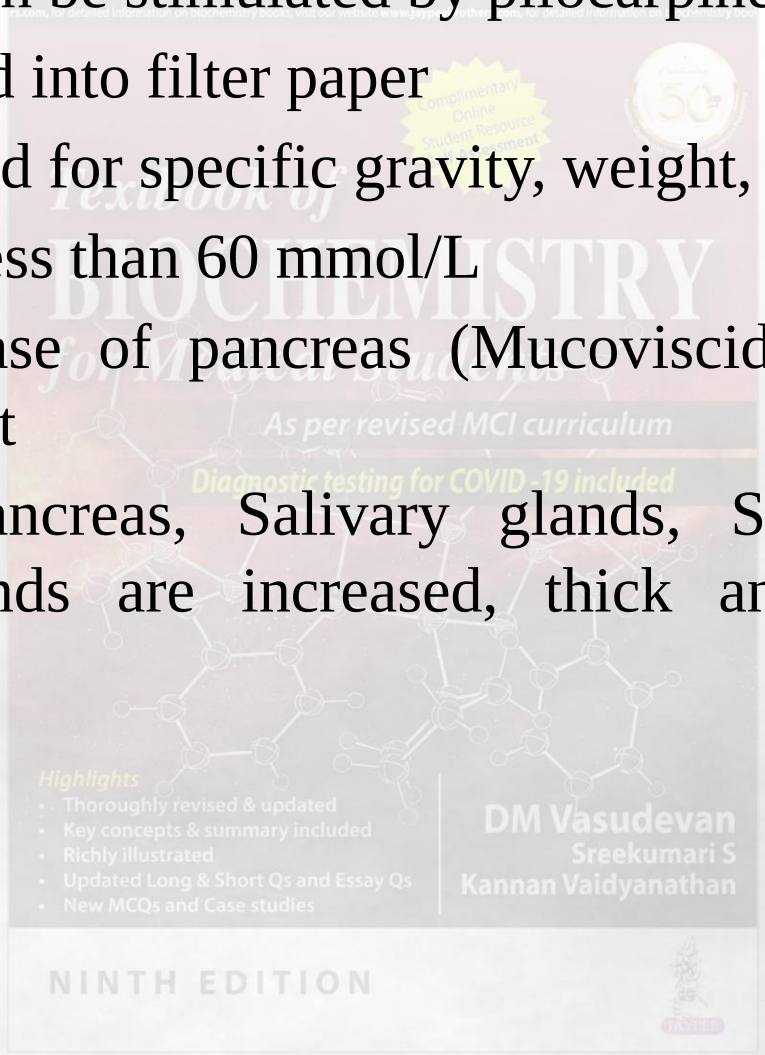
	Volume	Bicarbonate	Amylase
Normal	150-200 ml/hr	70 mmol/L/hr	200 u/hr
A/c Pacreatitis	⬇	⬇	⬇
Ca Pancreas	N / ⬇	⬇	⬇
Duct obstruction	⬇	N	N

Lundh Test

- Test meal contain milk powder, vegetable oil and glucose
- (6% fat, 5% protein, 15% CHO)
- Duodenal contents aspirated and 500 ml test meal given
- Again duodenal contents aspirated at 30 mts interval, for 2 hrs
- Substances like Benzoyl Arginine ethyl ester is incubated with aspirate
- Benzoic acid liberated by trypsin is estimated
- Tryptic activity can be calculated
  - Normal in Carcinoma Pancreas
  - Decreased in C/c pancreatits

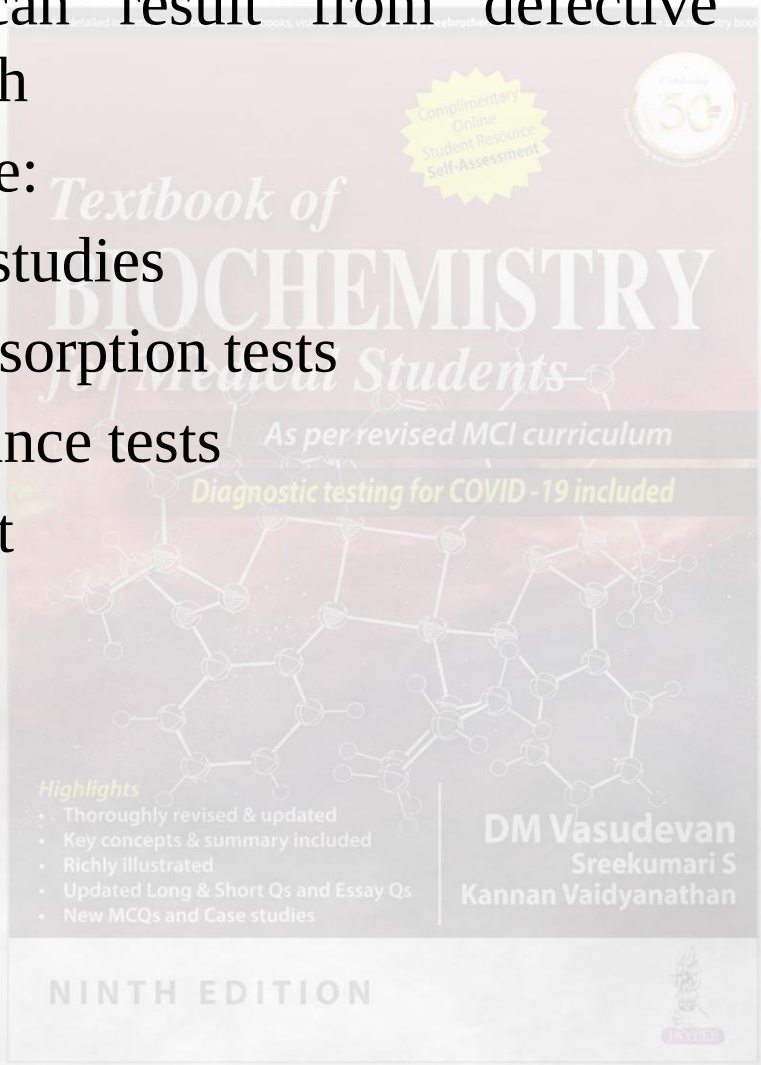
Sweat Electrolytes

- Sweat secrtion can be stimulated by pilocarpine
- Sweat is absorbed into filter paper
- Sweat is examined for specific gravity, weight, volume, Na^+, Cl^-
- Normally Cl^- is less than 60 mmol/L
- Fibrocystic disease of pancreas (Mucoviscidosis): Na^+ & Cl^- increased in sweat
- Secretion of Pancreas, Salivary glands, Sweat glands and Peritracheal glands are increased, thick and viscid in this condition



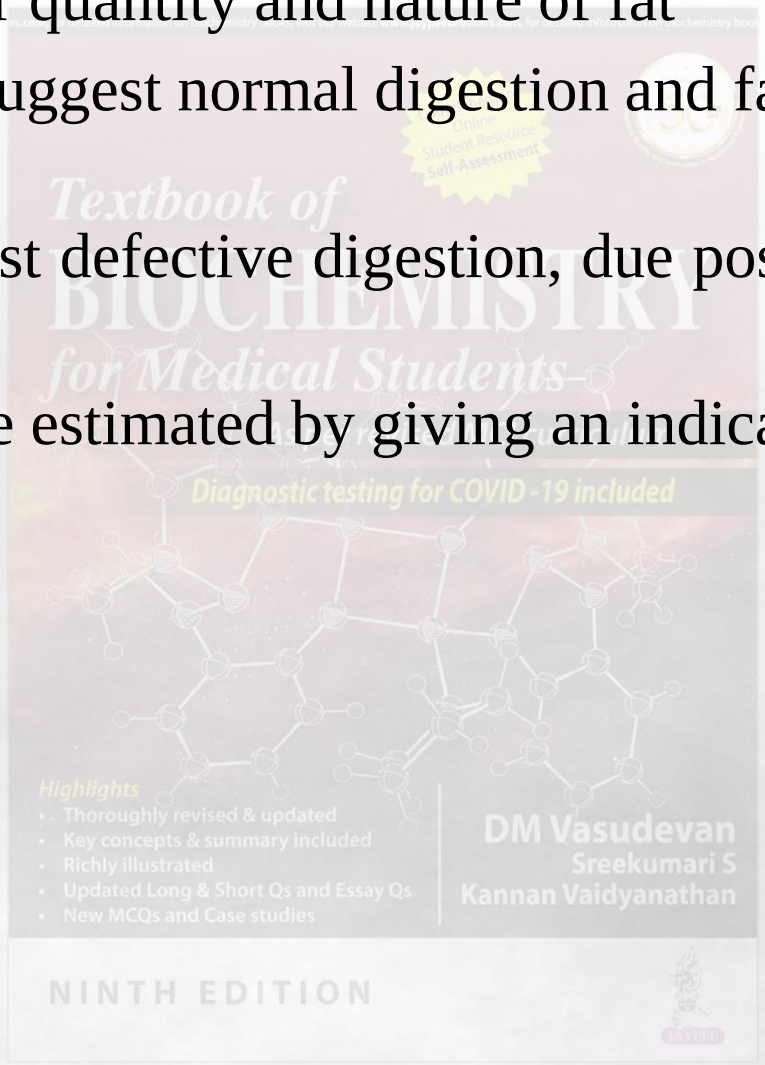
Studies on Malabsorption

- Malabsorption can result from defective digestion, absorption or both
- Common tests are:
  - Fat balance studies
  - D Xylose absorption tests
  - Starch tolerance tests
  - Schilling test



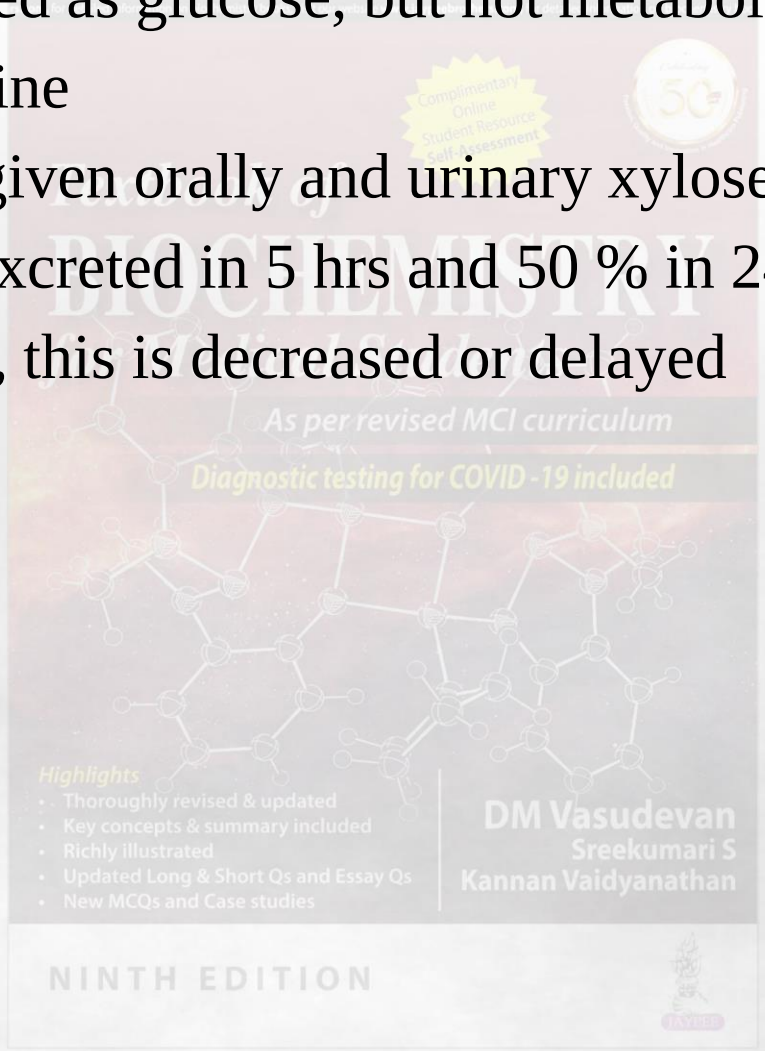
Fat Balance Studies

- Feces is tested for quantity and nature of fat
- Split fatty acids suggest normal digestion and faulty absorption
- Neutral fat suggest defective digestion, due possibly to pancreatic dysfunction
- 24 hour fat can be estimated by giving an indicator like carmine



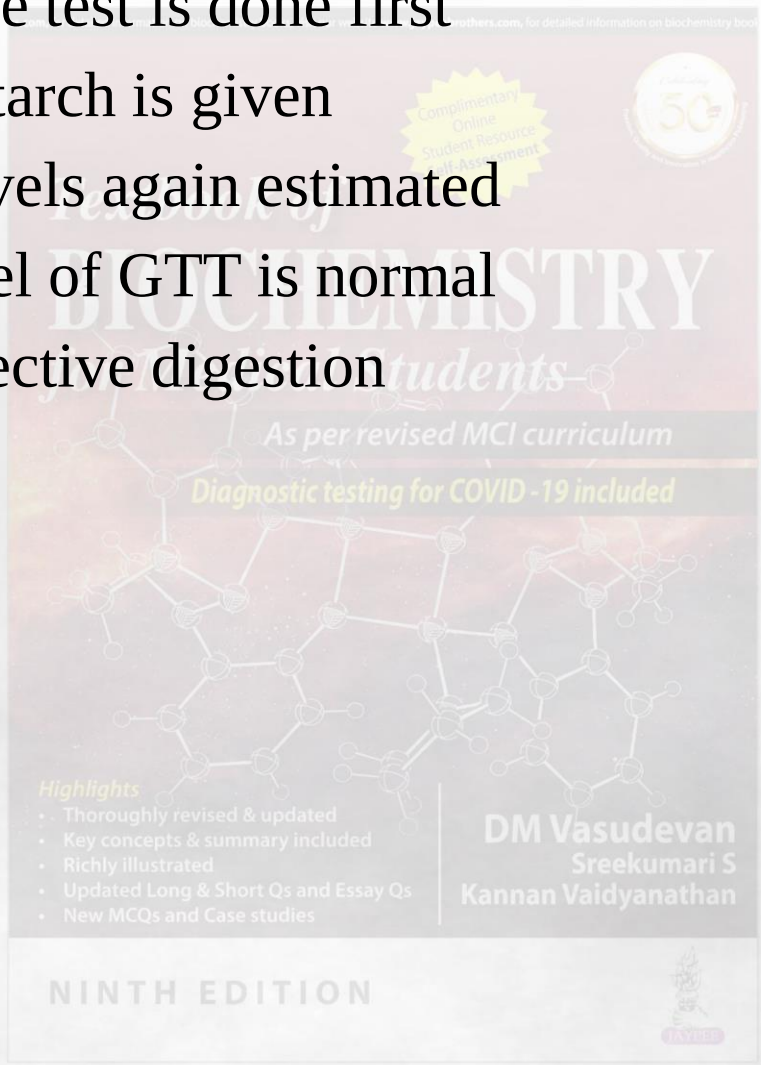
D Xylose Absorption Test

- D xylose: absorbed as glucose, but not metabolised rapidly
- So excreted in urine
- 25 gm xylose is given orally and urinary xylose is estimated
- Normally 25 % excreted in 5 hrs and 50 % in 24 hrs
- In malabsorption, this is decreased or delayed



Starch Tolerance Test

- Glucose Tolerance test is done first
- 100 gm soluble starch is given
- Blood glucose levels again estimated
- 80 % of peak level of GTT is normal
- Decreased in defective digestion



Schilling Test

- 1 µgm Co^{60} labeled Vit B_{12} is given orally
- Excess of normal B_{12} is given parenterally; to saturate free binding sites to ensure excretion of labeled B_{12}
- In defective absorption radioactivity is minimal in urine