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Textbook of Medical Biochemistry

MN Chatterjea
Rana Shinde

9th Edition

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CHAPTER 37

LIVER FUNCTION TESTS

Major Concepts

A. To know various functions of liver.
B. To classify the liver function tests and their interpretations.
C. To learn how to use various tests collectively to evaluate the liver dysfunction.

Specific Objectives

A. 1. Review anatomy and physiology of liver. (Not included in the text, but students are advised to do so before studying this chapter.)
   2. Learn in detail, various functions of liver such as metabolic functions, secretory functions, excretory functions, hematologic functions, protective functions, storage functions.
B. 1. Learn the classification of various liver function tests based on different functions of the liver.
   2.
   - Learn the details of van den Bergh test; and total direct bilirubin estimation and it's interpretation.
   - Classify jaundice and learn the liver function tests associated with it and their usefulness.
   - Study glucose, galactose, fructose and epinephrine tolerance tests and the implication of these tests in assessing liver dysfunction.
   - Learn the tests of protein, albumin estimation, fibrinogen estimation, and flocculation and turbidity tests.
   - Study the tests based on lipid metabolism such as cholesterol-cholesteryl ester ratio and the interpretation.
   - Learn hippuric acid test and its importance and detoxication functions of the liver.
   - Learn details of excretory function tests such as BSP retention test, Rose-Bengal dye test, bilirubin-tolerance test and their interpretations.
   - Study the details of tests based on hematological functions of liver such as, prothrombin time, prothrombin index and its interpretation.
   - Learn the details of tests based on amino acid catabolism such as estimation of ammonia, ammonia tolerance test, glutamine estimation in CSF and their importance in assessment of liver function.
   - Activities of several enzymes are elevated in liver dysfunction, such as ALP, GPT, OCT, GGT, etc. How these can be useful in differential diagnosis.
C. Normally more than one test is indicated to assess the liver function. Learn how different tests can be employed and used collectively for assessment of liver function.

INTRODUCTION

Numerous laboratory investigations have been proposed in the assessment of liver diseases. From among these host of tests, the following battery of blood tests: Total bilirubin and VD Bergh test, total and differential proteins and A: G ratio and certain enzyme assays as aminotransferases, alkaline phosphatase and γ-GGT have become widely known as ***Standard Liver Function Tests (LFTs).***

Urine tests for bilirubin and its metabolites and the prothrombin time (PT) and index (PI) are also often included under these headings; but tests such as Turbidity/flocculation test, Icteric index, etc. are now becoming outdated. ***Second generation*** LFTs attempt to improve on this battery of tests and to gain a genuine measurement of liver function, i.e. quantitative assessment of functional hepatic mass. These include the capacity of the liver to eliminate exogenous compounds such as aminopyrine or caffeine or endogenous compounds such as bile acids which have gained much importance recently. However, such investigations are not yet routinely or widely used due to lack of facilities and are useful for research purpose only. Hence in our discussion we will confine to "Standard LFTs" which are routinely done and possible in any standard laboratory. It is stressed that with the advent of more sophisticated techniques for the diagnosis of liver diseases, ***particularly ultrasound and CT scanning together with percutaneous and endoscopic cholangiography and liver biopsy, routine use of standard LFTs is being questioned now.***

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FUNCTIONS OF THE LIVER

Liver is a versatile organ which is involved in metabolism and independently involved in many other biochemical functions. Regenerating power of liver cells is tremendous.

Although details of the various functions performed by liver have been discussed under their respective places, a summary of these functions is given below in brief, so that students can easily group the tests of liver associating with its functions.

1. Metabolic Functions

Liver is the key organ and the principal site where the metabolism of carbohydrates, lipids, and proteins take place.

- Liver is the organ where NH_3 is converted to urea.
- It is the principal organ where cholesterol is synthesised, and catabolised to form bile acids and bile salts.
- Esterfication of cholesterol takes place solely in liver.
- In this organ absorbed monosaccharides other than glucose are converted to glucose, viz., galactose is converted to glucose, fructose converted to glucose.
- Liver besides other organs can bring about catabolism and anabolism of nucleic acids.
- Liver is also involved in metabolism of vitamins and minerals to certain extent.

2. Secretory Function

Liver is responsible for the formation and secretion of bile in the intestine. Bile pigments-bilirubin formed from haem catabolism is conjugated in liver cells and secreted in the bile.

3. Excretory Function

Certain exogenous dyes like BSP (bromsulphthalein) and Rose Bengal dye are exclusively excreted through liver cells.

4. Synthesis of Certain Blood Coagulation Factors

Liver cells are responsible for conversion of preprothrombin (inactive) to active prothrombin in the presence of vit. K. It also produces other clotting factors like factor V, VII and X. Fibrinogen involved in blood coagulation is also synthesised in liver.

5. Synthesis of Other Proteins

Albumin is solely synthesised in liver and also to some extent α-and β-globulins.

6. Detoxication Function and Protective Function

Kupffer cells of liver remove foreign bodies from blood by phagocytosis. Liver cells can detoxicate drugs, hormones and convert them into less toxic substances for excretion.

7. Storage Function

Liver stores glucose in the form of glycogen. It also stores vit. B_{12}, vit A, etc.

8. Miscellaneous Functions

Liver is involved in blood formation in embryo and in some abnormal states, it also forms blood in adult.

CLASSIFICATI ON OF LFTs

Tests used in the study of patients with liver and biliary tract diseases can be classified according to the specific functions of the liver involved.

I. *Tests based on abnormalities of bile pigment metabolism:*

(N.B: Students must revise their knowledge on haem catabolism)

- Serum bilirubin and VD Bergh reaction
- Urine bilirubin
- Urine and faecal urobilinogen

II. *Tests based on liver's part in carbohydrate metabolism:*

- Galactose tolerance test
- Fructose tolerance test

III. *Tests based on changes in plasma proteins:*

- Estimation of total plasma proteins, albumin and globulin and determination of A:G ratio.
- Determination of plasma fibrinogen
- Various flocculation tests
- Amino acids in urine

IV. *Tests based on abnormalities of lipids:*

- Determination of serum cholesterol and ester cholesterol and their ratio.
- Determination of faecal fats

V. *Tests based on detoxicating function of liver:*

- Hippuric acid synthesis test.

VI. *Excretion of injected substances by the liver (excretory function):*

- Bromsulphthalein test (BSP retention test)
- I^{131}-Rose Bengal test

VII. *Formation of prothrombin by liver:*

- Determination of prothrombin time and index

VIII. *Tests based on amino acid catabolism:*

- Determination of blood NH_3
- Determination of glutamine in CS fluid ***(Indirect liver function test)***

IX. *Tests based on drug metabolism:*

- MEGX test
- Antipyrine breath test

X. *Determination of serum enzyme activities.*

TESTS BASED ON ABNORMALITIES OF BILE PIGMENT METABOLISM

1. VD Bergh Reaction and Serum Bilirubin

Principle: Methods for detecting and estimating bilirubin in serum are based on the formation of a purple compound **azo-bilirubin** where bilirubin in serum is allowed to react with a freshly prepared, solution of VD Bergh's diazo-reagent.

VD Bergh Reaction

Consists of two parts: Direct reaction and indirect reaction. The latter serves as the basis for a quantitative estimation of serum bilirubin (given ahead).

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Ehrlich's diazo-reagent: This is **freshly prepared** before use. ***It consists of two solutions:***

Solution A: Contains sulphanilic acid in conc. HCl.

Solution B: Sodium nitrite in water. Fresh solution is prepared by taking 10 ml of solution A + 0.8 ml of solution B.

Procedure: Take 0.3 ml of serum into each of two small tubes. Add 0.3 ml of DW to one which serves as **Control** and 0.3 ml of freshly prepared diazo-reagent into second **('test').** Mix both tubes and observe any colour change.

Basis of the reaction: Coupling of diazotised sulphanilic acid and bilirubin if present produces a ***"reddish-purple" azo-compound.***

Responses: **Three** different responses may be observed:

(i) ***Immediate direct reaction:*** Immediate development of colour proceeding rapidly to a maximum.

(ii) ***Delayed direct reaction:*** Colour only begins to appear after 5 to 30 minutes and develops slowly to a maximum.

(iii) ***Indirect reaction:*** No direct reaction is obtained. Colour develops after addition of methanol.

2. Determination of Serum Bilirubin

Indirect reaction is essentially a method for the quantitative estimation of serum bilirubin.

Principle: Serum is diluted with DW and methanol added in an amount insufficient to precipitate the proteins, yet sufficient to permit all the bilirubin to react with the diazo-reagent.

N.B: Absolute methanol gives a clear solution than 95 per cent ethanol.

Colour developed is compared with a standard solution of bilirubin similarly treated.

Note: Bilirubin is a costly chemical hence an artificial standard may be used.

Artificial Standard: It is a methyl red solution in glacial acetic acid of pH 4.6 to 4.7, which closely resembles the colour of azo-bilirubin.

Note: ***Before interpretation, students should know about 'Jaundice' and its causes.***

JAUNDICE

In jaundice, there is yellow colouration of conjunctivae, mucous membrane and skin due to increased bilirubin level. **Jaundice is visible when serum bilirubin exceeds 2.4 mg/dl.**

Classification of Jaundice:

I. Rolleston and McNee (1929), as modified by Maclagan, (1964): They classified jaundice in **three groups:**

(a) Haemolytic or pre-hepatic jaundice: In this, there is increased breakdown of Hb, so that liver cells are unable to conjugate all the increased bilirubin formed.

Causes: Principally there are **two categories:**

(i) ***Intrinsic:*** Abnormalities within the red blood cells by various haemoglobinopathies, hereditary spherocytosis, G-6-PD deficiency in red cells and favism.

(ii) ***Extrinsic:*** Factors external to red blood cells e.g. incompatible blood transfusion, haemolytic disease of the newborn (HDN), autoimmune haemolytic anaemias, in malaria, etc.

(b) Hepatocellular or hepatic jaundice: In this, there is disease of the parenchymal cells of liver. This may be divided into **3 groups,** although there may be overlappings.

(i) ***Conditions in which there is defective conjugation:*** There may be a reduction in the number of functioning liver cells, e.g. in chronic hepatitis, in this all liver functions are impaired or there may be a specific defect in the conjugation process, e.g. in Gilbert's disease, Crigler-Najjar syndrome, etc. In these the liver function is otherwise normal.

(ii) ***Conditions such as viral hepatitis and toxic jaundice:*** In this, there is extensive damage to liver cells, associated with considerable degree of intrahepatic obstruction resulting in appreciable absorption of conjugated bilirubin.

(iii) ***"Cholestatic" Jaundice:*** This occurs due to drugs, (drug-induced) such as chlorpromazine and some steroids in which there is mainly intrahepatic obstruction, liver function being essentially normal.

(c) Obstructive or posthepatic jaundice: In this, there is obstruction to the flow of bile in the extrahepatic ducts, e.g. due to gallstones, carcinoma of head of pancreas, enlarged lymph glands pressing on bile duct, etc.

II. Rich's Classification of Jaundice

According to this classification jaundice is divided into mainly **two groups:**

(i) ***Retention Jaundice:*** In this, there is impaired removal of bilirubin from the blood, or excessive amount of bilirubin is produced and not cleared fully by liver cells. This group includes haemolytic jaundice and those conditions which are characterised by impaired conjugation of bilirubin.

(ii) ***Regurgitation Jaundice:*** In this, there is excess of conjugated bilirubin and it includes obstructive jaundice and those liver conditions in which there is considerable degree of intrahepatic obstruction (cholestasis).

Interpretations

(a) ***VD Bergh reaction:*** Correlation of different types of VD Bergh reaction is based on the fact how bilirubin reacts differently with the Diazo-reagent according to whether or not, it has been conjugated.

- Bilirubin formed from Hb and not passed through liver cells is called ***unconjugated bilirubin*** and it ***gives an indirect reaction.***
- On the other hand, bilirubin which has passed through liver cells and undergoes conjugation is called ***conjugated bilirubin*** and ***gives direct reaction.***

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TESTS BASED ON LIVER'S PART IN CARBOHYDRATE METABOLISM

The tests are based on tolerance to various sugars since liver is involved in removal of these sugars by glycogenesis or in conversion of other monosaccharides to glucose.

1. Glucose Tolerance Test

- Not of much value in liver diseases
- Although glucose tolerance is sometimes diminished, it is often difficult to separate the part played by the liver from other factors influencing glucose metabolism.

2. Galactose Tolerance Test

Basis: The normal liver is able to convert galactose into glucose; but this function is impaired in intrahepatic diseases and the amount of blood galactose and galactose in urine is excessive.

Advantages of this test

- It is used primarily ***to detect liver cell injury.***
- It can be performed in presence of jaundice.
- As it measures an intrinsic hepatic function, it ***may be used to distinguish obstructive and non-obstructive jaundice.***

Note: In prolonged obstruction, if untreated, secondary involvement of liver leads to abnormality in the galactose tolerance.

Methods: This can be of **two types:**

(a) ***Oral galactose tolerance test (Maclagan)*** and

(b) ***IV galactose tolerance test.***

(a) ***Oral galactose tolerance test (Maclagan):*** The test is performed in the morning after a night's fast. A fasting blood sample is collected which serves as "control". 40 gm of galactose dissolved in a cup-full of water is given orally. Further blood samples are collected at 1/2 hourly intervals for two hours (similar to GTT).

Interpretations

- ***Normally or in obstructive jaundice:*** 3 gm or less of galactose are excreted in the urine within 3 to 5 hours and the blood galactose returns to normal within one hour.
- ***In intrahepatic (Parenchymatous) jaundice:*** The excretion amounts to 4 to 5 gm or more during the first five hours.

Galactose index (Maclagan)

It is obtained by adding the four blood galactose levels.

Interpretations

- Upper normal limit of normal was taken as 160.
- In healthy medical students, range varied from 0 to 110 and in hospital patients not suffering from liver disease the value ranged from 0 to 160.
- ***In liver diseases*** very high values are obtained.
- In infective and toxic hepatitis values up to about 500 are seen, decreasing slowly as the clinical condition improves.
- ***In cirrhosis of the liver*** increased values may be obtained up to 500, depending on the severity of the disease.

(b) ***IV galactose tolerance test (King):*** The test is performed in the morning after a night's fast. A fasting blood sample is collected which serves as "control". An IV injection of galactose, equivalent to 0.5 gm/kg body weight is given as a sterile 50 per cent solution. Blood samples are collected after five minutes, ½ hour, 1 hour, 1½ hours, 2 hours and 2½ hours after IV injection and blood galactose level is estimated.

Interpretations

- ***A normal response*** should have a curve beginning on the average at about 200 mg galactose/100 dl, falling steeply during the one hour and reaching a figure between 0 to 10 mg% by end of 2 hours.
- In most cases of ***obstructive jaundice*** similar results are obtained, unless there is parenchymal damage.
- ***In parenchymatous diseases*** with liver cell damage, ***the fall in blood galactose takes place more slowly.*** Normally no galactose is detected in 2½ hours sample, but ***in parenchymatous disease, value is greater than 20 mg/dl.***

3. Fructose Tolerance Test

Method

50 gm of fructose given to the fasting patient as for GTT. Fasting blood sugar is estimated and blood sugar is estimated in samples is taken at ½ hourly intervals for 2½ hours after taking the oral fructose. The usual methods for estimation of blood sugar measures both the glucose and fructose present.

Interpretations

- ***Normal response*** shows little or no rise in the blood sugar level. The highest blood sugar value reached during the test should not exceed the fasting level by more than 30 mg%.
- Similar result is obtained in most cases of ***obstructive jaundice*** cases (provided no parenchymal damage).
- ***In infectious hepatitis*** and parenchymatous liver cells damage: Rise in blood sugar is greater than above, but the increases obtained are never very great.

4. Epinephrine Tolerance Test (Storage Function)

Principle: The response to epinephrine as evidenced by elevation of blood sugar is a manifestation of glycogenolysis and is directly influenced by glycogen stores of liver.

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Method

The patient is kept on a high carbohydrate diet for three days before the test. After an overnight fast, the fasting blood sugar is determined. 0.01 ml of a 1 in 1000 solution of epinephrine per kg body weight in injected. The blood sugar is then determined in samples collected at 15 minutes intervals up to one hour.

Interpretations

- ***Normally*** in the course of an hour, the rise in blood sugar over the fasting level exceeds by 40 mg% or more.
- ***In parenchymal hepatic diseases*** the rise is less.
- It is of much use for diagnosis of ***glycogen storage diseases***, specially in ***von Gierke's disease***, in which blood glucose rise is not seen due to lack of glucose-6-phosphatase.

TESTS BASED ON CHANGES IN PLASMA PROTEINS

1. Determination of Total Plasma Proteins and Albumin and Globulin and A:G Ratio:

This yields most useful information in chronic liver diseases. Liver is the site of albumin synthesis and also possibly of some of α-and β-globulins.

Interpretations

- ***In infectious hepatitis*** quantitative estimations of albumin and globulin may give normal results in the early stages. ***Qualitative changes may be present, in early stage rise in β-globulins and in later stages γ-globulins show rise.***
- ***In obstructive jaundice*** normal values are the rule, as long as the obstructive jaundice is not associated with accompanying liver cell damage.
- ***In advanced parenchymal liver diseases and in cirrhosis liver*** the albumin is grossly decreased and the globulins are often increased, so ***that A:G ratio is reversed, such a pattern is characteristically seen in cirrhosis of the liver***. The albumin may fall below 2.5 gm% and may be a contributory factor in causing oedema in such cases. Fractionation of globulins, reveals that the increase is usually in the γ-globulin fraction, but in some cases there is a smaller increase in β-globulins.

Note:

- ***The severity of hypoalbuminaemia in chronic liver diseases is of diagnostic importance and may serve as a criterion of the degree of damage.***
- A low serum albumin which fails to increase during treatment is usually a poor prognostic sign.

2. Estimation of Plasma Fibrinogen

Fibrinogen is formed in the liver and likely to be affected if considerable liver damage is present.

- ***Normal value*** is 200-400 mg%.
- Values below 100 mg% have been reported in ***severe parenchymal liver damage***. Such a situation is found in severe acute insufficiency such as may occur in:
  - ***Acute hepatic necrosis***
  - ***Poisoning from carbon tetrachloride***
  - ***In advanced stages of liver of the cirrhosis.***

3. Flocculation Tests

The tests have become outdated and not routinely carried out.

Principle: Flocculation tests depend on an alteration in the type of proteins present in the plasma. The alteration may be either quantitative or qualitative and most frequently involves one or more of the globulin fractions.

(a) Thymol turbidity and flocculation test: The degree of turbidity produced when serum is mixed with a buffered solution of thymol is measured. Turbidity produced is compared with a set of protein standards, or turbidity is read in a colorimeter against a $BaSO_4$ standard.

Maclagan unit: Maclagan expressed the results in units, so that a turbidity equivalent to that of 10 mg/100 ml protein standard is one unit.

Basis of the reaction: The thymol turbidity test requires lipids (phospholipids). ***The turbidity/and flocculation in this test is a complex of "lipothymoprotein".*** The thymol seems to decrease the dispersion and solubility of the lipids, and the proteins involved is mainly β-globulin, though some γ-globulin is also precipitated.

Interpretations

- ***Normal range*** is 0 to 4 units.
- It measures only an acute process in the liver, but the degree of turbidity is not proportional to the severity of the disease.
- ***In infectious hepatitis,*** it is highest soon after the onset of the jaundice, but frequently remains raised for several weeks.
- Sera with high β-and γ-globulin fractions, due to other causes may give a positive test.
- ***A negative thymol test in the presence of jaundice is very useful for distinguishing between hepatic and extrahepatic jaundice.***

Thymol flocculation: After the turbidity has been measured, the tubes are kept in the dark for overnight and read the degree of flocculation if any. Flocculation is graded as –ve no flocculation, +ve flocculation as +, ++, +++ and ++++.

(b) Zinc sulphate turbidity test: When a serum having an ***abnormally high content of γ-globulin*** is diluted with a solution containing buffered $ZnSO_4$ solution,

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a turbidity develops. The amount of turbidity is proportional to concentration of γ-globulin. Turbidity is measured as discussed in thymol turbidity test.

Interpretations

- ***Normal range:*** Varies from 2 to 8 units.
- All cases of cirrhosis of liver gives +ve results.
- ***In infectious hepatitis:*** γ-globulin is increased in later stage. ***$ZnSO_4$ turbidity becomes +ve later as compared to thymol turbidity which becomes +ve early.***
- It may be +ve in other cases where there is increase in γ-globulin.

Other turbidity/and flocculation test viz, cephalin-cholesterol flocculation test, Takata-Ara test, etc. have become obsolete.

4. **Amino acids in urine (Aminoaciduria):** The daily excretion of amino acid nitrogen in normal health varies from 80-300 mg. Aminoaciduria found in severe liver diseases is of **overflow type,** with accompanying increase in plasma amino acids level.

CLINICAL IMPORTANCE

In severe liver diseases like acute yellow atrophy and sometimes in advanced cirrhosis of liver crystals of certain amino acids may be found in urinary deposits microscopically.

- ***Tyrosine crystals:*** Tyrosine crystallises in sheaves or tufts of fine needles.
- ***Leucine crystals:*** Leucine has spherical shaped crystals, yellowish in colour, with radial and circular striations.

Solubility: Both are insoluble in acetone and ether but soluble in acids/and alkalies. Tyrosine is only slightly soluble in acetic acid and insoluble in ethanol, whereas leucine is soluble in the former and slightly soluble in the latter.

TESTS BASED ON ABNORMALITIES OF LIPIDS

- **Cholesterol-Cholesteryl Ester Ratio**

The liver plays an active and important role in the metabolism of cholesterol including its synthesis, esterification, oxidation and excretion.

Interpretations

- Normal total blood cholesterol ranges from 150-250 mg/dl and approx. 60 to 70 per cent of this is in esterified form.
- ***In obstructive jaundice,*** an increase in total blood cholesterol is common, but the ester fraction is also raised, so that % esterified does not change.
- ***In parenchymatous liver diseases,*** there is either no rise or even decrease in total cholesterol and the ***ester fraction is always definitely reduced.*** The degree of reduction roughly parallels the degree of liver damage.
- ***In severe acute hepatic necrosis,*** the total serum cholesterol is usually low and may fall below 100 mg/dl, whilst there is marked reduction in the % present as esters.

TESTS BASED ON THE DETOXICATING FUNCTION OF THE LIVER

HIPPURIC ACID TEST OF QUICK

Principle

1. Best known test for the detoxicating function of liver.
2. Liver removes benzoic acid, administered as sodium benzoate, either orally or IV, and combines with amino acid glycine to form hippuric acid. The amount of hippuric acid excreted in urine in a fixed time is determined. (Refer chapter on detoxication).
3. The test thus depends on ***two factors***
   (i) The ability of liver cells to produce and provide sufficient glycine and
   (ii) The capacity of liver cells to conjugate it with the benzoic acid.
4. ***For reliable result, renal function must be normal.*** If there is any reason to suspect renal impairment, a urea clearance test should be done simultaneously.

Methods: Both oral and IV forms of the hippuric acid test are in use.

1. ***Oral hippuric acid test:*** Dissolve 6.0 gm of sodium benzoate in approx 200 ml of water. The test may be started 3 hours after a light breakfast of toast and tea. Food should not be given until late in the test. The patient empties the bladder, the urine being discarded. The patient is allowed to drink the sodium benzoate solution and **time is noted.** The bladder is again emptied 4 hr later. Any urine passed during this 4 hours is kept and added to that passed at the end of 4 hours. The amount of hippuric acid excreted in this 4 hours period is estimated.

Interpretations

- ***Normally,*** at least 3.0 gm of hippuric acid, expressed as Benzoic acid or 3.5 gm of sodium benzoate should be excreted in health.
- Smaller amounts are found when there is either acute or chronic liver damage. Amounts lower than 1.0 gm may be excreted by patients with infectious hepatitis.

2. ***IV Hippuric Acid Test***

Indications: Normally oral test is preferred. An IV test is indicated:

- When there is impairment of absorption due to absorption defects.
- If there is accompanying nausea/vomiting.

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Procedure

1.77 gm of sodium benozate dissolved in 20 ml of DW as a sterile solution given IV. Shortly before the injection, the patient empties the bladder, which is discarded. The bladder is emptied after ***one hour*** and ***two hours after the injection.***

Interpretations

- ***In normal health,*** hippuric acid equivalent to at least 0.85 gm of sodium benzoate, or to 0.7 gm of benzoic acid should be excreted in the one hour, or equivalent to 1.15 gm of benzoic acid in the first two hours.
- Excretion of smaller amounts more than above indicate the presence of liver damage.

TESTS BASED ON EXCRETORY FUNCTION OF LIVER

1. BSP Retention Test (Bromsulphthalein Test)

Principle

1. The ability of the liver to excrete certain dyes, e.g. BSP is utilised in this test.
2. In normal healthy individual, a constant proportion (10 to 15% of the dye) is removed per minute. In hepatic damage and insufficiency, BSP removal is impaired by cellular failure, as damaged liver cells fail to conjugate the dye or due to decrease blood flow.
3. ***Removal of BSP by the liver involves conjugation of the dye as a mercaptide with the cysteine component of glutathione.*** The reaction of conjugation of BSP with glutathione is ***rate-limiting***, and thus it exerts a controlling influence on the rate of removal of the dye.

Procedure

With the patient fasting, inject IV slowly, an amount of 5 per cent BSP solution, which contains 5 mg of BSP/Kg, body weight. Withdraw 5 to 10 ml of blood, 25 and 45 minutes after the injection and allow the specimens to clot. Separate the sera and estimate the amount of the dye in each sample.

Interpretations

- ***In normal*** healthy individual not more than 5 per cent of the dye should remain in the blood at the end of 45 minutes. The bulk of the dye is removed in 25 minutes and less than 15 per cent is left at the end of 25 minutes.
- ***In Parenchymatous liver diseases*** removal proceeds more slowly. In advanced cirrhosis removal is very slow and ***40 to 50 per cent of the dye is retained in 45 minutes sample.***

Contraindication: Since the dye is removed in bile after conjugation, this test can only be used in cases in which there is no obstruction to the flow of bile. Hence ***the test is of no value if obstruction of biliary tree exists (obstructive jaundice).***

CLINICAL SIGNIFICANCE

- BSP-excretion test is ***a useful index of liver damage,*** particularly when the damage is diffuse and extensive.
- **The test is most useful:**
  - **In liver cell damage without jaundice**
  - **In cirrhosis of the liver**
  - **In chronic hepatitis**.

2. Rose-Bengal Dye Test

Rose-Bengal is another dye which can be used to assess excretory function. 10 ml of a 1 per cent solution of the dye is injected IV slowly.

Interpretation: Normally 50 per cent or more of the dye disappears within 8 minutes.

I^{131}-labelled Rose-Bengal: I^{131}-Rose-Bengal has been used where isotope laboratory is present. I^{131}-labelled Rose-Bengal is administered IV. Then count is taken over the neck and abdomen. Initially, count is more in neck and practically nil over abdomen. ***As the dye is excreted through liver, neck count goes down and count over abdomen increases.***

Interpretation

- ***In parenchymal liver diseases*** high count in the neck persists and there is hardly a rise in count over abdomen, as the dye is retained.

3. **Bilirubin tolerance test:** 1 mg/kg body weight of bilirubin is injected IV. If more than 5 per cent of the injected bilirubin is retained after 4 hours, the excretory and conjugating function of the liver is considered abnormal. The bilirubin excretion test has been recommended by some authorities as a better test of excretory function of the liver as compared to dye tests as bilirubin is a normal physiologic substance and the dyes are foreign to the body. But the test is not used routinely and extensively due to its high cost.

Note: The three substances listed above, with the exception of BSP, are excreted almost entirely by the liver. No significant amounts are taken up by RE cells.

FORMATION OF PROTHROMBIN BY LIVER

Determination prothrombin time: Prothrombin is formed in the liver from ***inactive "preprothrombin"*** in presence of vitamin K. ***Prothrombin activity is measured as prothrombin time (PT).*** The term prothrombin time was given to time required for clotting to take place in citrated plasma to which optimum amounts of "thromboplastin" and Ca^{++} have been added. The "one-stage" technique introduced by Quick, the prothrombin time is related inversely to the concentration not only to prothrombin, but also of factors V, VII and X and it can be more sensitive

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to a lack of VII and X than to prothrombin alone. In spite of above restriction, as it is simple and quick in performance, it is still much used.

Interpretations

- ***Normal value:*** Normal levels of prothrombin in control give prothrombin time of approx 14 seconds. (Range: 10-16 Sec). Results are always expressed as patient's prothrombin time in seconds to normal control value.
- ***In parenchymatous liver diseases:*** Depending on the degree of liver cells damage plasma prothrombin time may be increased from 22 to as much as 150 secs.
- ***In obstructive jaundice:*** Due to absence of bile salts, there may be defective absorption of vitamin K, hence PT is increased, as prothrombin formation suffers.

Note

- From above, it is observed that PT is increased both in obstructive jaundice and in diseases of liver cells damage. Hence ***PT cannot be used to differentiate between them.***
- ***However, if adequate vitamin K is administered parenterally, the PT returns rapidly to normal in uncomplicated obstructive jaundice, whereas in liver damage the response is less marked.***

Other Clinical Uses

- PT is used mostly in controlling anticoagulant therapy.
- Determination of PT is also used to decide whether there is danger of bleeding at operation in biliary tract diseases.

Prothrombin index

Prothrombin activity is also sometimes expressed as ***"prothrombin index" in %,*** which is the ratio of prothrombin time of the normal control to the patient's prothrombin time multiplied by 100. Thus,

$$\text{Prothrombin index} = \frac{\text{PT of normal control}}{\text{PT of patient}} \times 100$$

Normally index is 70 to 100 per cent. The "critical level" below which bleeding may occur is not fixed one, but there is always a possibility of this occurring if prothrombin index is below 60 per cent.

TESTS BASED ON AMINO ACID CATABOLISM

1. Determination of blood NH_3: Nitrogen part of amino acid is converted to NH_3 in the liver mainly by transamination and deamination (transdeamination) and it is converted to urea in liver only (Refer Chapter on Protein Metabolism).

Other sources of NH_3

Following are the other sources of ammonia:

- NH_3 is formed from nitrogenous material by bacterial action in the gut.
- In kidneys, by hydrolysis of glutamine by ***glutaminase.***
- From pyrimidines catabolism: A small amount of NH_3 is formed from catabolism of Pyrimidines.

Interpretations

- ***Normal range:*** Blood ammonia varies from 40 to 75 µg ammonia nitrogen per 100 ml of blood.
- ***In parenchymal liver diseases:*** The ability to remove NH_3 coming to liver from intestine and other sources may be impaired. Increases in NH_3 can be found in more advanced cases of cirrhosis of the liver, particularly when there are associated neurological complications. In such cases blood levels may be over 200 µg/100 ml. Very high values may be obtained in hepatic coma.

2. Ammonia tolerance test: An ammonia tolerance test has been devised to test the ability of the liver to deal with NH_3 coming to it from the intestine.

Procedure

The patient should come for the test after overnight 12 hours fast, only small amounts of fluids can be taken during that time. Take fasting specimen of blood for NH_3 determination. After that, give by mouth 10 gm of ammonium citrate dissolved in water and flavoured with fruit juice/lemon. Take blood samples after 30, 60, 120 and 180 minutes and determine blood NH_3.

Note: In patients with increased initial levels, give smaller doses, e.g. only 5 grams.

Interpretations

- ***In normal healthy persons:*** Little increase is found; blood NH_3 levels remaining within normal range.
- ***In advanced cirrhosis of the liver:*** Marked rise to twice the initial level or more, exceeding 200 to 300 µg% are seen.
- Considerable increases are also seen when there is a collateral circulation and in patients who have a portocaval anastomosis.

3. Determination of glutamine in CS Fluid (An Indirect Liver Function Test)

Glutamine, the amide of glutamic acid, is formed by *glutamine synthetase* by glutamic acid and NH_3.

Glutamine in CS fluid can be estimated by the method of **Whittaker** (1955). The glutamine is hydrolysed to glutamic acid and NH_3 by the action of dilute acid at 100 degree centigrade. A correction is made for a small amount of NH_3 produced from urea. No other substances

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present in CS fluid were found to form NH_3 under above conditions.

Interpretations

- *The normal range* found to be 6.0 to 14.0 mg%.
- *In infectious hepatit is* found is range from 16 to 28 mg%, but is usually less than 30 mg%.
- *In cirrhosis of the liver* the increase is more; depending on the severity. It varies from 22 to 36 mg% or more.
- *In hepatic coma* increase is very high, ranging from 30 to 60 mg% or more.
- *In other types of coma, normal values are obtained.*

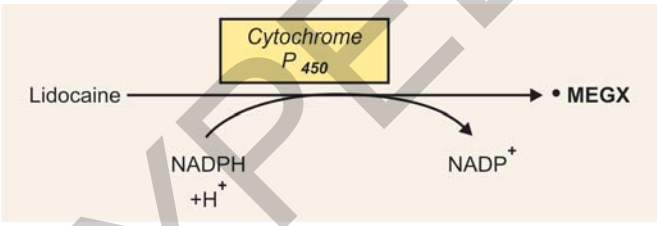
Note: ***Some authorities put 40 mg% as a critical level. Prognosis of the case is fatal if CS fluid glutamine level is more than 40 mg%, in case of cirrhosis of the liver and hepatic coma.***

TESTS BASED ON DRUG METABOLISM

The capacity of the liver to metabolise certain drugs can successfully be used as a measure of hepatic function. Tests based on drug clearance or metabolite formation kinetics reflect the actual functional state of the liver and are therefore called ***dynamic liver function tests***. Tests based on the rate of metabolite formation are of particular interest.

1. MEGX Test

Principle: ***Lidocaine*** is rapidly converted to its primary metabolite ***monoethyl glycine xylidine*** (MEGX) by the hepatic microsomal cytochrome P_{450} system. A loss of hepatic cytochrome P_{450} activity or major changes in hepatic blood flow (due to portosystemic shunting) result in decreased MEGX formation. ***Lidocaine metabolite formation has been used as an index of hepatic function.***



Procedure

An IV bolus injection of a small lidocaine test dose, 1 mg/kg, is given. Blood sample is taken before the injection. Another blood sample is taken 15 or 30 minutes after the injection. MEGX is determined in the serum by use of an automated fluorescence polarisation immuno-assay within about 20 minutes in both the samples.

Interpretations

- The highest MEGX test results are observed in liver donors with unimpaired organ function and in normal healthy subjects.
- Liver recipients with uncomplicated postoperative course show somewhat lower test results.
- In patients with ***cirrhosis of the liver,*** the increase of MEGX concentration in serum is much less marked and decrease value is dependant on disease severity.

Note

- The test is rapid and easy to function
- Potential sources of extrahepatic MEGX formation seem to have no noticeable influence on the test.

2. Antipyrine breath test:

Antipyrine like lidocaine is also metabolised by cytochrome P_{450} system. When given orally it is absorbed from intestine completely, not bound to plasma proteins and metabolised by liver only.

Procedure: C^{14}-labelled aminopyrine (dimethyl amino antipyrine) is given orally in dosage of 1 to 2 microcurie. Breath samples are collected for 2 and 24 hours and analysed.

Interpretations

- Normal subjects excrete 5 to 8 per cent of the administered dose in 2 hours.
- Patients with hepatitis and cirrhosis excretes only 2 to 3 per cent.

VALUE OF SERUM ENZYMES IN LIVER DISEASES

Quite a large number of enzyme estimations are available which are used to ascertain liver function.

They can be divided into **2 groups**

I. Most commonly and routinely done in the laboratory.
II. Not routinely done in the laboratory.

Most commonly and routinely employed in laboratories are two:

A. Serum transaminases (amino transferases), and
B. Serum alkaline phosphatase.

A. Serum Transaminases (Amino transferases)

Interpretations

- Normal ranges for these enzymes are as follows:
  - **SGOT** (aspartate transaminase): 4 to 17 IU/L (7 to 35 units/ml)
  - **SGPT** (alanine transaminase): 3 to 15 IU/ L (6 to 32 units/ml)
- Both these enzymes are found in most tissues, but the relative amounts vary. ***Heart muscles are richer in SGOT, whereas liver contains both but more of SGPT.***
- Increases in both transaminases are found in liver diseases, with SGPT much higher than SGOT.
- Their determination is of limited value in differential diagnosis of jaundice because of considerable overlapping.
- ***But their determination is of extreme use in assessing the severity and prognosis of parenchymal liver***

SECTION FIVE

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diseases specially acute infectious hepatitis and serum hepatitis. In these two conditions, highest values in thousand units are seen.

- ***Screening test:*** Also useful as a screening test in outbreak of infectious hepatitis (viral hepatitis), it is the most sensitive diagnostic index. The increase can be seen in prodromal stage, when jaundice has not appeared clinically. ***Such cases can be isolated and segregated from others***, so that spread of the disease can be checked.
- Very high values are also obtained in toxic hepatitis, due to carbon tetrachloride poisoning. Increases are comparatively less in drug hepatitis (cholestatic) like chloropromazine.
- In obstructive jaundice (extrahepatic) also increases occur, but usually do not exceed 200 to 300 IU/L.

B. Serum Alkaline Phosphatase

Alkaline phosphatase enzyme is found in a number of organs, mostly in bones and liver, then in small intestine, kidney and placenta. ***Placental isoenzyme of alkaline phosphatase is heat-stable.***

Interpretations

- ***Normal range*** for serum ALP as per King-Armstrong method is 3 to 13 KA Units/100 ml (23 to 92 IU/L).
- ***It is used for many years in differential diagnosis of jaundice.*** It is increased in both infectious hepatitis (viral hepatitis) and posthepatic jaundice (extrahepatic obstruction) but ***the rise is usually much greater in cases of obstructive jaundice.*** **Dividing Line which has been suggested is 35 KA units/100 ml.** ***A value higher than 35 KA units/100 ml is strongly suggestive of diagnosis of obstructive jaundice***, in which very high figures even up to 200 units or more may be found. There is certain amount of overlapping mostly in the range of 30 to 45 KA Units/100 ml.
- Very high values are occasionally found in certain liver diseases, e.g. xanthomatous biliary cirrhosis in which there is no extrahepatic obstruction.
- Higher values are also obtained in ***space-occupying lesions of liver,*** e.g.
  - ***Abscess***
  - ***Primary carcinoma (hepatoma)***
  - ***Metastatic carcinoma***
  - ***Infiltrative lesions like lymphoma***
  - ***Granuloma and amyloidosis.***

A diagnostic triad suggests:
- ***High serum ALP***
- ***Impaired BSP-retension*** and
- ***Normal/or almost normal serum bilirubin.***

- Serum ALP is found to be normal in haemolytic jaundice.

Mechanism of increase in ALP in liver diseases

Increase in the activity of ALP in liver diseases is not due to hepatic cell disruption, nor to a failure of clearance, but rather **to increased synthesis of hepatic ALP.** The stimulus for this increased synthesis in patients with liver diseases has been attributed to bile duct obstruction either extrahepatically by stones, tumours, strictures or intrahepatically by infiltrative disorders or ***space-occupying lesions.***

Note

- The relation of the amino transferase to ALP level may provide better evidence than either test alone, as to whether or not the jaundice is cholestatic.
- **High ALP with low amino transferase activity is usual in cholestasis and the converse occurs in non-cholestatic jaundice.**
  It is, however, stressed that there are several intrahepatic causes of cholestasis such as primary biliary cirrhosis, acute alcoholic hepatitis and sclerosing cholangitis in which laparotomy is inappropriate. ***Hence, even after a confident diagnosis of cholestatic jaundice based on the LFTs, further investigation to define the site of obstruction is imperative.***

II. Other Enzymes (not done routinely)

Other enzymes which have been found to be useful but not routinely done in the laboratory are discussed below briefly:

1. Serum 5′-Nucleotidase

This enzyme hydrolyses nucleotides with a phosphate group on carbon atom 5′ of the ribose, e.g. adenosine 5′-P. On hydrolysis it produces adenosine and inorganic PO_4. These nucleotides are also hydrolysed by non-specific phosphatases such as alkaline phosphatase present in the serum. However, 5′-nucleotidase is inactivated by nickel, hence if hydrolysis is carried out with and without added nickel, the difference gives the 5′-nucleotidase activity.

Interpretations

- ***Normal range*** is 2 to 17 IU/L
- ***Liver diseases***
  - ***Serum 5′ nucleotidase is raised along with serum ALP in diseases of liver and biliary tract in a roughly parallel manner.*** It is thus highest in post-hepatic obstructive jaundice frequently over 100 units. **It has added advantage over serum ALP in that enzyme is not affected in bone diseases.**
  - Smaller increases are found in hepatic jaundice, e.g. in infectious hepatitis, in some cases of which normal results are obtained.
- ***Bone diseases***
  5′ nucleotidase is normal in patients with increased serum ALP in bone diseases such as Paget's disease.

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7. Serum SHBD (Hydroxy Butyrate Dehydrogenase): An enzyme acting on α-OH butyric acid has been identified in the serum and studied as a diagnostic aid in liver diseases.

Interpretations

- *Normal* serum HBD between 56 to 125 IU/L
- *In liver diseases* elevated levels of this enzyme is observed in acute viral hepatitis. Also elevated level is seen in myocardial infarction.

Ratio of LDH/SHBD

To differentiate the liver diseases and acute myocardial infarction:

$$\text{Ratio of } \frac{\text{LDH}}{\text{SHBD}} \text{ has been found more useful}$$

- Normal ratio of $\frac{\text{LDH}}{\text{SHBD}} = 1.18$ to 1.60
- ***Less than 1.18 is observed in most cases of myocardial infarction. Greater than 1.60 is observed in liver diseases.***
- In infectious hepatitis, the ratio is frequently > 2.0. In chronic hepatitis and obstructive jaundice the ratio ranged from 1.6 to 2.0.

8. Serum Aldolase and Phosphohexose Isomerase: These are both markedly increased in serum of patients with acute hepatitis. No increase is found in cirrhosis, latent hepatitis or biliary obstruction.

9. Serum Amylase

Liver is a major, if not the only source of amylase found in the serum under normal physiologic conditions. Studies have shown low serum amylase levels in liver diseases like acute infectious hepatitis.

10. Serum Sorbitol Dehydrogenase (SDH)

The enzyme catalyses the following reaction:

$$\text{Sorbitol} + \text{NAD}^+ \xrightleftharpoons{\text{SDH}} \text{Fructose} + \text{NADH}$$

Interpretations

- *Normal value:* Normal values for serum found to be less than 0.2 m-IU.
- Striking elevation seen in ***acute viral hepatitis*** and carbon tetrachloride poisoning up to 17 m-IU. In viral hepatitis, values of SDH return to normal before transaminases.
- *In chronic hepatitis and in obstructive jaundice:* Serum levels of SDH are normal or only slightly elevated.
- Myocardial and other extrahepatic diseases do not lead to elevated levels.

Advantages

- Like OCT, it is a *hepatospecific enzyme.*
- The serial estimation is of immense value in diagnosis and follow up for prognosis of infectious hepatitis.
- Also of immense value in differential diagnosis of jaundice.
- Enzyme has been recently demonstrated in small amount in kidney and prostate but no increase in activity in the diseases of these organs noted.

11. Serum γ-Glutamyl Transferase (γ-GT)

- *Normal range:* 10 to 47 IU/L
- **Recently, the importance of this enzyme in alcohol abuse has been stressed.**

The activity of this microsomal enzyme has been found to increase in most of hepatobiliary diseases but, largely because of the enzyme's wide tissue distribution, the specificity of a high value is very low. Unlike the amino transferases, the elevated levels do not necessarily indicate liver cell disruption but may be due to enzyme induction by drugs such as, phenobarbitone, phenytoin, warfarin and alcohol.

- These severe limitations have meant that this test has now *only two, practical uses*

(a) ***An elevated γ-GT implies that an elevated ALP is of hepatic origin,*** and

(b) Secondly, it may be useful in screening for alcohol abuse. ***Sudden increase in γ-GT in chronic alcoholics suggests recent bout of drinking of alcohols.***

Table 37.1 shows the enzyme assays as per priorities useful in detecting alterations in liver diseases.

Table 37.2 shows the differentiating features of three types of jaundice.

Table 37.1: Enzyme assays as per priorities useful in detecting alterations in liver diseases

Alterations detected	*Principal enzyme assays*
• Hepatocellular damage/or increased permeability of liver cells.	1. Transaminases (amino transferases) (AST and ALT) 2. Ornithine carbamoyl transferase (OCT) 3. Sorbitol dehydrogenase (SDH)
• Extrahepatic or intrahepatic obstruction	1. Alkaline phosphatase (ALP) 2. 5'-Nucleotidase 3. γ-GT 4. LAP
• Protein synthesis	1. Pseudocholinesterase
• Alcohol abuse	1. γ-GT

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Table 37.2: Differentiation of three types of jaundice

	Haemolytic or prehepatic jaundice	*Hepatic or parenchymatous jaundice*	*Obstructive or posthepatic jaundice*
I. Causes:	Due to excessive haemolysis (a) Intrinsic defects in RB cells (b) Extrinsic causes external to RB Cells	Disease of parenchymal cells of liver viz. Viral hepatitis, toxic jaundice Cirrhosis of the liver	Due to obstruction of biliary passage (a) Extrahepatic gallstones, tumors, enlarged lymph nodes, etc (b) Intrahepatic cholestasis.
II. Clinical findings:			
(a) Degree of jaundice	Usually low +	Marked jaundice ++ to +++	Marked Jaundice ++ to +++
(b) Faeces	Dark coloured	Variable, usually pale	Clay coloured
III. Biochemical findings: Based on bile pigment metabolism:			
1. VD Bergh reaction	Indirect, may be delayed positive	Biphasic	Direct
2. Type of bile pigment in circulation	Unconjugated bilirubin	Mixture of conjugated and unconjugated bilirubin	Conjugated bilirubin
3. Serum bilirubin	Usually low 3 mg to 5 mg%	High, up to 20 mg%	Very high, may be up to 50 mg%
4. Bile Pigments in urine:			
• Bilirubin	Not detected	Present	Present ++
• Urobilinogen	Increased ++	May be increased + or normal	Decreased or Absent
5. Faecal Stercobilinogen	Increased ++	Decreased	Decreased or Absent
IV. Steatorrhoea:	Not present	Present	Present
V. Other biochemical features:			
1. Prothrombin time (PT)	Normal	Increased	Increased, After parental vit K becomes normal
2. Turbidity and flocculation tests			
• Thymol turbidity	Negative	++ to +++	Negative
3. Enzyme assays:			
• Amino transferase activity ALT (S-GPT)	Usually normal	Marked increase +++ to ++++ (goes in thousand units). Usually 500 to 1500 IU/L or may be more	Increased to ++. Usually 100 to 300 IU/L Do not exceed 300 IU/L
• Alkaline Phosphatase (ALP)	Normal	Increased slightly (+) ***usually less than 30 KA Units %***	Marked increase 30 to 100 KA units %, ***more than 35 KA units % suggests obstructive jaundice.***
• 5'-Nucleotidase	Normal	Increased (+) Slight	Marked increase ++ to +++

I. Question (Essay type and short notes)

1. Enumerate various functions of the liver. Describe any one test based on its detoxication function in details.
2. What are the various liver function tests? Describe any one test based on conjugation mechanism.
3. Enumerate various functions of liver. Describe the liver function tests based on excretion of bilirubin.
4. Classify liver function tests. Describe the tests based on bile pigment metabolism.
5. Classify the liver function tests. Describe the liver function test based on either
   a. Excretory function or
   b. Detoxicating function
6. Describe briefly the liver function tests.
7. What are the conjugation tests performed for the assessment of liver function? Give details of the oral and the IV procedure.
8. Enumerate the diverse metabolic tests performed for the assessment of liver function.
9. Name liver function tests and give an account of certain enzyme estimations used as liver function tests.
10. Enumerate the tests performed to assess liver function and discuss the excretory tests.

Short Notes

a. Liver function test based on dextoxication.
b. Hippuric acid test
c. Vanden Bergh test
d. Direct and indirect Van den Bergh test
e. Prothrombin time and vit K.
f. Hippuric and synthesis test
g. Galactose tolerance test
h. BSP retention test
i. Liver function tests based on protein metabolism
j. Biochemical tests for obstructive liver disease
k. Liver function tests, related to carbohydrate metabolism
l. Bilirubin metabolism and the measurement of serum bilirubin
m. Use of enzyme estimations as liver functions tests.

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II. MCQs (Give one correct answer)

1. In a case of jaundice, there is no trace of bile pigments in urine, the most probable diagnosis is:
   a. Infections hepatitis b. Obstructive jaundice
   c. Serum hepatitis d. Haemolytic jaundice
   e. None of the above
2. The following enzyme activities are often increased along with the diseases as mentioned in each:
   a. Hepatic bilirubin, UDP—Glucuronyl transferase and Gilbert's syndrome
   b. Gammaglutamyl oxidase and viral hepatitis
   c. Alkaline phosphatase and cholestatic and obstructive jaundice
   d. Gammaglutamyl transferase and obstructive jaundice
   e. Serum amylase and obstructive jaundice
3. Jaundice is clinically detected in sclerae when serum bilirubin concentration reaches above:
   a. 0.5 to 1 mg/100 ml b. 1 to 2 mg/100 ml
   c. 2 to 3 mg/100 ml d. 3 to 4 mg/100 ml
   e. >5 mg/100 ml
4. When jaundice results from hepatitis, the unconjugated fraction of total serum bilirubin is usually:
   a. At least 50% b. Less than 50%
   c. 50 to 85% d. 85 to 90%
   e. 90–100%
5. Patients with hepatocellular jaundice as compared to those with purely obstructive jaundice, tend to have:
   a. Higher serum alkaline phosphatase, LDH and ALT activity
   b. Higher serum alkaline phosphatase activity, lower LDH and ALT activity
   c. Lower serum alkaline phosphatase activity, LDH and ALT activity,
   d. Lower serum alkaline phosphatase activity, higher LDH and ALT activity
   e. None of the above
6. If results of the serum bilirubin, alkaline phosphatase, LDH and ALT determination suggest obstructive jaundice, the ideal confirmatory test would be:
   a. Serum ICD b. Protein electrophoresis
   c. Serum 5-Nucleotidase d. Serum OCT
   e. None of the above
7. The slow moving fraction of LDH isoenzyme LD5 (M4) is typically elevated in patients with:
   a. Myocardial infarction
   b. Cerebrovascular accident (stroke)
   c. Pancreatitis
   d. Hepatitis
   e. In all of the above
8. Drugs can cause jaundice by all of the following mechanisms except:
   a. By causing haemolysis
   b. By selective toxic effects on kupffer cells of liver
   c. By causing intrahepatic cholestasis
   d. By competition with bilirubin for albumin binding site
   e. By direct toxic effect on hepatic cells
9. Prothrombin time in obstructive jaundice:
   a. Normal
   b. Decreases
   c. Becomes normal after vit K injection
   d. Increases after vit K injection,
   e. None of the above.
10. Prothrombin time in parenchymal disease of the liver:
    a. Normal
    b. Decreases
    c. Increases
    d. Becomes normal after parenteral vit K injection
    e. None of the above.
11. Overflow aminoaciduria is one of the abnormalities observed in patients with:
    a. Acute hepatic necrosis b. Obstructive jaundice
    c. Cholecystitis d. Nephrotic syndrome
    e. Hepatoma
12. In which of the following conditions the plasma activities of both ALP and GGT are likely to be increased:
    a. Carcinoma of prostrate
    b. In trimester of normal pregnancy
    c. Osteomalacia
    d. Alcoholic cirrhosis
    e. Infectious hepatitis.
13. Increased unconjugated bilirubin is found in all of the following except:
    a. hemolytic anemia
    b. Crigglar Najjar syndrome
    c. Gilbert's syndrome
    d. Dubin-Johnson syndrome
    e. Physiological jaundice in infants.
14. In the liver, a substantial proportion of the activity of the following enzyme is membrance bound:
    a. Aspartate Aminotransferase
    b. Alanine Aminotransferase
    c. Lactate dehydrogenase
    d. Alkaline phosphatase
    e. Ornithine Transcarbamoylase

Fill in the blanks

1. The purple colored complex formed in Vanden Bergh test in called_____.
2. Certain drugs such as chlorpromazine cause_____ jaundic while gall stones may cause_____ jaundice.
3. Presence of bilirubin in urine without the presence of_____ is strongly suggestive of obstructive jaundice.
4. In advanced parenchymal liver diseases and cirrhosis of liver albumin is_____ and globulins are_____.
5. A complete absence of faecal_____is strongly suggestive of malignant obstruction obstruction.
6. In parenchymal liver, diseases in fall in blood galactose in galactose tolerance test takes place_____.
7. Epinephrime tolerance test is of much use in glycogen storage disease specially_____.
8. In advanced parenchymal liver diseases and in cirrhosis liver the albumin is grossly_____.

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9. Amino acid involved in hippuric acid test is _____.
10. The enzyme which is used for differential diagnosis of jaundice is_____.

Answers to MCQs

1. d. 2. c. 3. c 4. b 5. d 6. c
7. d 8. b 9. c 10. c 11. a 12. d
13. d 14. d.

Answers to the fill in blanks

1. Azobilirubin
2. Cholestatic/obstructive
3. Urobilinogen
4. Decreased/increased
5. Urobilinogen
6. Slowly
7. Von-Gierke's disease
8. Decreased
9. Glycine
10. Alkaline phosphatase

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