INDOCYANINE GREEN EXCRETION AS A TEST FOR HEPATIC BLOOD FLOW

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Master Degree in Clinical Pathology

by

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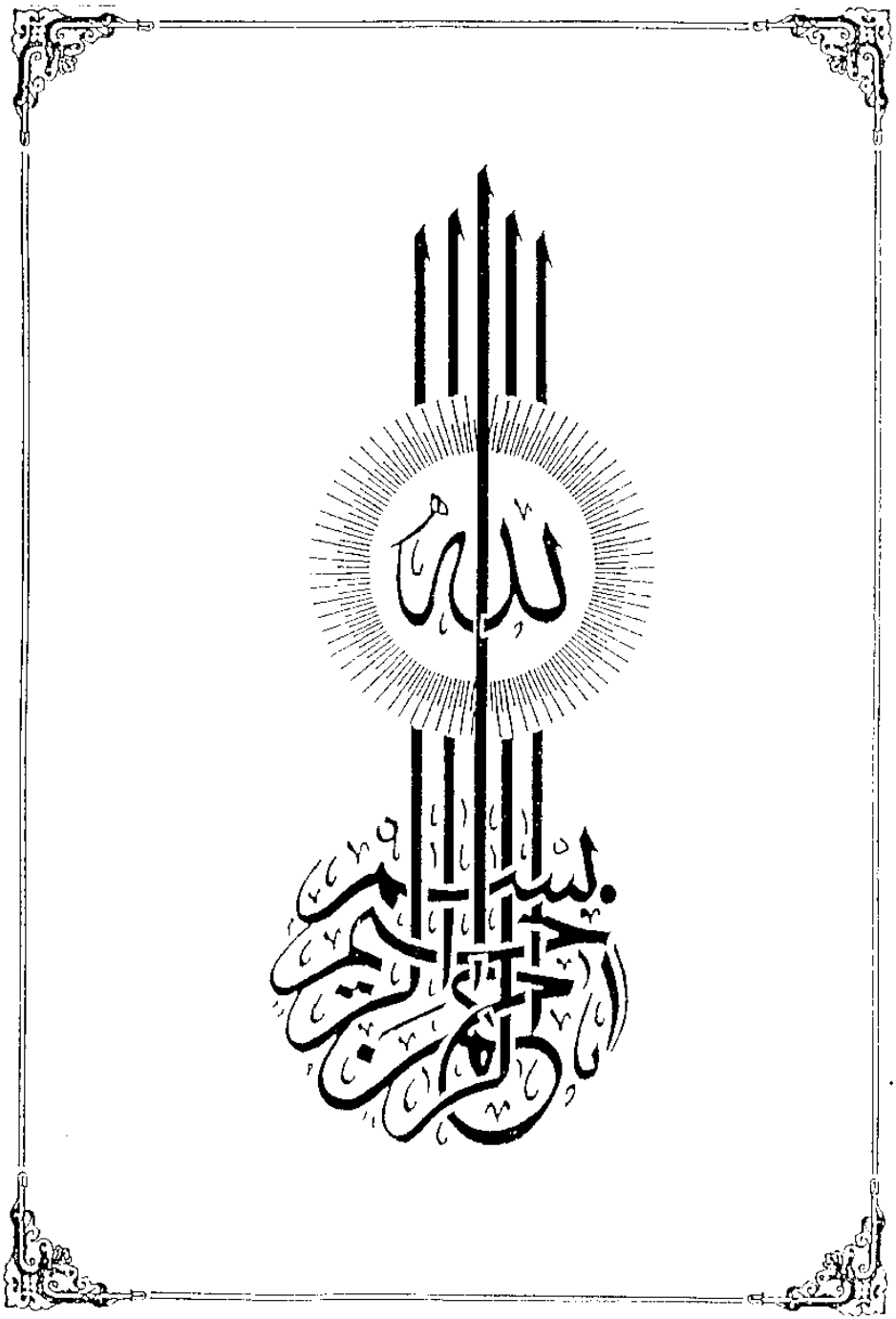
بسم الله الرحمن الرحيم

" رب اشرح لى صدرى ويسّر لى أمرى وأحلل عقدة من لسانى
يفقهوا قولى "

صدق الله العظيم

IN THE NAME OF GOD, THE MERCIFUL,
THE COMPASSIONATE

MY LORD, RELIEVE MY MIND
& EASE MY TASK FOR ME
& LOOSEN A KNOT FROM MY TONGUE
THAT THEY MAY UNDERSTAND MY SAY



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Faten El Borolossy

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INTRODUCTION

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AIM OF STUDY

Liver cirrhosis is considered one of the major health problems in Egypt. This is clearly due to the high incidence of Bilharziasis and viral hepatitis. Clinical signs and symptoms of liver cirrhosis are only manifested at later stages due to the large functional reserve capacity of the liver. That is why laboratory diagnosis of liver cirrhosis is extremely important.

Many liver function tests are used for diagnosis of liver cirrhosis. Unfortunately, many of them, as serum bilirubin, are within normal in early stages. Elevation of liver enzymes is also mild. One of the best investigations for early diagnosis of liver cirrhosis is the ability of the liver to excrete certain dyes; this is because dye excretion is largely dependant on the efficiency of hepatic blood flow which is markedly affected in the very early stages of cirrhosis.

Bromosulfophthalein (BSP) is largely used in this respect and it is considered one of the best sensitive indicators of early liver cirrhosis before the appearance of jaundice. However, the BSP test suffers some drawbacks.

Indocyanine green (ICG) is recently used for measurement of hepatic blood flow by the indicator-dilution method. It is recommended as the most sensitive test of liver function.

The aim of this study is to review the value of ICG as a test for hepatic blood flow and hepatic excretory power in comparison with BSP and to clarify the recent applications of ICG excretion test.

Anatomy and Patho-physiology of the Liver

Anatomy & Pathophysiology of the Liver:

In order to evaluate all the tests described for the liver, it is necessary to describe the structure and function of the liver and the hepatic parenchymal cells. It should be pointed out that the liver, portal vein, bile ducts, pancreas and duodenum form a functional unit within the upper abdomen. Diseases affecting any one of these organs thus often affect neighbouring systems. Hepatic functions should therefore not only be tested in primary hepatic disorders, but also if secondary involvement of the liver is suspected. (Fig. 1).

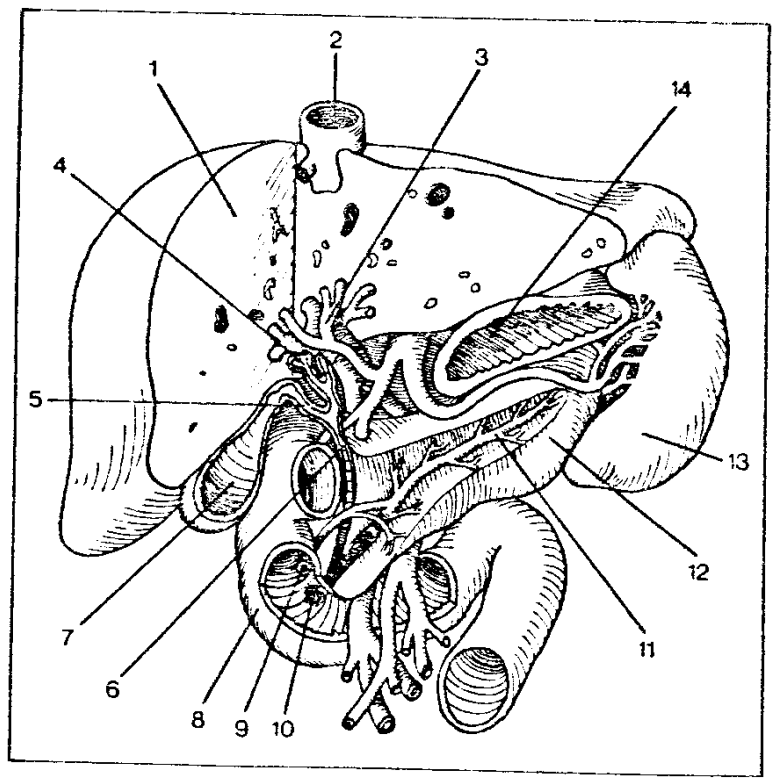

Fig. 1 Diagram showing the functional unit consisting of the liver,portal vein, biliary tract, pancreas and duodenum

Key to the "hepato-entero-pancreatic system"

1 Liver
2 Vena cava
3 Vena portae (R. dext.)
4 Hepatic duct (ductus hepaticus R. dext.)
5 Cystic duct (ductus cysticus)
6 Common bile duct (ductus choledochus)
7 Gall bladder
8 Duodenum
9 Papilla duodeni minor
10 Papilla duodeni major
11 Pancreatic duct (ductus pancreaticus)
12 Pancreas
13 Spleen
14 Stomach

Structure of the Liver & Biliary Tract:

The liver is a large organ (1200 - 1600 g) shaped like a wedge with its base to the right. It has two major lobes, the larger right one being about six times the size of the left in the normal adult. The right lobe lies behind the rib cage with its upper border at about the level of the fifth rib. The smaller left lobe is tongue-shaped and its apex reaches to the dome of the left cupola of the diaphragm (Last, 1982).

The circulatory system of the liver is characterised by a dual blood supply. Approximately 80 percent of this blood supply enters from the portal vein and 20 percent from the hepatic artery. This rich flow of blood, amounting to about 1500 ml per minute, brings oxygen and nutrient material to the liver.

There is also an extensive system of lymph vessels that carries the interstitial fluid or liver lymph into the general circulation.

A network of bile ducts transports substances secreted or excreted by the liver cells for a storage in

the gall bladder and subsequently into the digestive tract.

The liver is the largest gland of the human body and it is a central metabolic organ. It is composed of a multitude of functional units called lobules. A branch of the hepatic vein forms the central core of the lobule, which is surrounded by the hepatic parenchymal cells arranged in plates or sheets of one cell thickness. These plates or sheets form the walls of spaces or lacunae, which are divided into two systems of irregular tunnels containing the portal tracts and the central hepatic vein. In most instances, the two systems of tunnels run in planes perpendicular to each other. The portal tracts contain branches of the portal vein, the hepatic artery, bile ducts, and lymph vessels. The portal vein and hepatic artery supply the blood that flows through special capillaries called sinusoids, which empty into the central hepatic vein at right angles. The walls of the simusoids are lined with reticuloendothelial cells, called Kupffer cells, which are phagocytic cells. Between the cell plates and the sinusoids are spaces, the space of Disse, which contain interstitial fluid that functions in the transfer of nutrients and waste products between the liver cells and

the blood. Most of the hepatic parenchymal cells are polygonal and their surface area is increased by the presence of microvilli on their outer surface (Tietz, 1976) (Fig. 2).

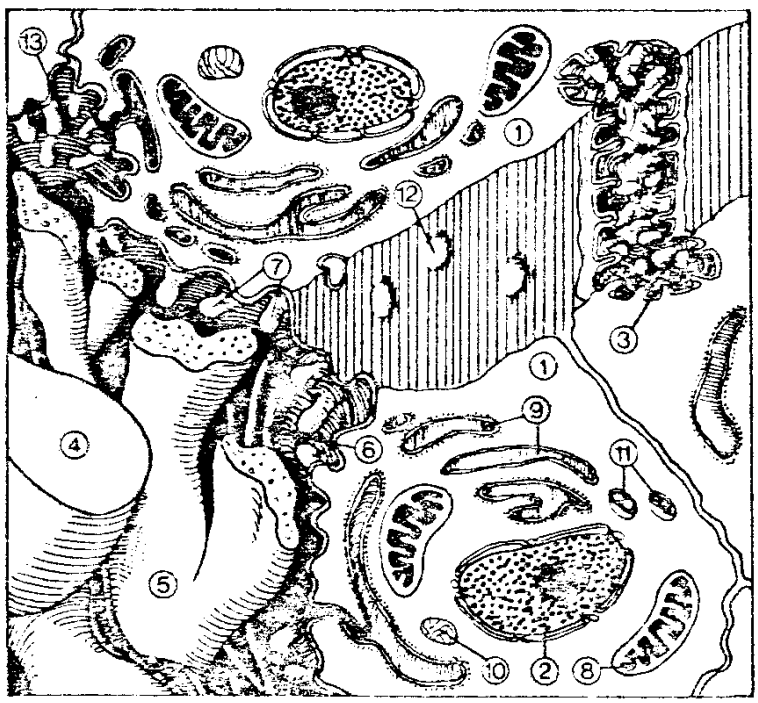

Fig. 2 Schematic representation of neighbouring hepatic cells

1 Hepatic parenchymal cells seen in section
2 Nucleus with nuclear pores
3 Bile canaliculus with microvilli
4 Erythrocyte seen in section
5 Stellate Kupffer cell
6 Reticulin fibres in the space of Disse
7 Microvilli of the outer cell membrane
8 Mitochondrion
9 Smooth and granular endoplasmic reticulum
10 Lipid droplet
11 Lysosomes
12 Intercellular sites of adhesion
13 Triangular intercellular space with microvilli

Small bile canaliculi or bile capillaries are formed by grooves in contact surfaces of liver cells that fit together to form a cylindrical tube. The canaliculi form polygonal networks that surround each liver cell and carry the bile to small ductules which in turn form bile ducts. The bile ducts then empty into the hepatic duct (Ductus hepaticus), there is one hepatic duct for each of the right and left liver lobes. The hepatic ducts join outside the liver forming the common hepatic duct (ductus hepaticus communis) which unites with the cystic duct (ductus cysticus) to form the common bile duct (ductus choledochus). The common bile duct is the last element of the biliary tree, it normally enters the duodenum together with the pancreatic duct (Last, 1982).

The gross appearance of a cut section of the liver would be a pattern of red dots representing the central veins of the lobules, separated by greyish dots that represent the portal tracts, all against the brown background of liver tissue. The central veins are from 0.3 to 1.0 mm apart. The liver cells are approximately polyhedral in shape, with a diameter of about 30 um. Each gram of liver tissue contains about 200 million cells, of which 170 million are parenchymal and 30 million are sinusoidal epithelial cells (Rains and Ritchie, 1984).

Pathophysiological Basis of Diagnostic Procedures used in Clinical Chemistry:

Many metabolic processes take place within the hepatic cells, in fact most of the chemical reactions carried out in the human body occur in these cells. Many different groups of substances are metabolised, but only a few of the basic reactions can be described.

* Carbohydrates: Excess glucose is stored in the form of glycogen. Free glucose can be released from this store when required. Galactose and fructose are fed into the carbohydrate metabolic pathway.

* Lipids: Neutral lipids are stored in the liver. Depending on the metabolic state, fatty acids are either degraded or used in the synthesis of phosphatides. Bile acids, bile salts and cholesterol are produced mainly in the liver.

* Proteins: The liver is the central organ for the synthesis of blood proteins. Some of the amino acids released during digestion are degraded, the nitrogen liberated during deamination is used to produce urea. The rest of the amino acids are utilised in the synthesis of albumin, the clotting factors and