LIVER DISEASE IN THE PERINATAL PERIOD

ESSAY

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By

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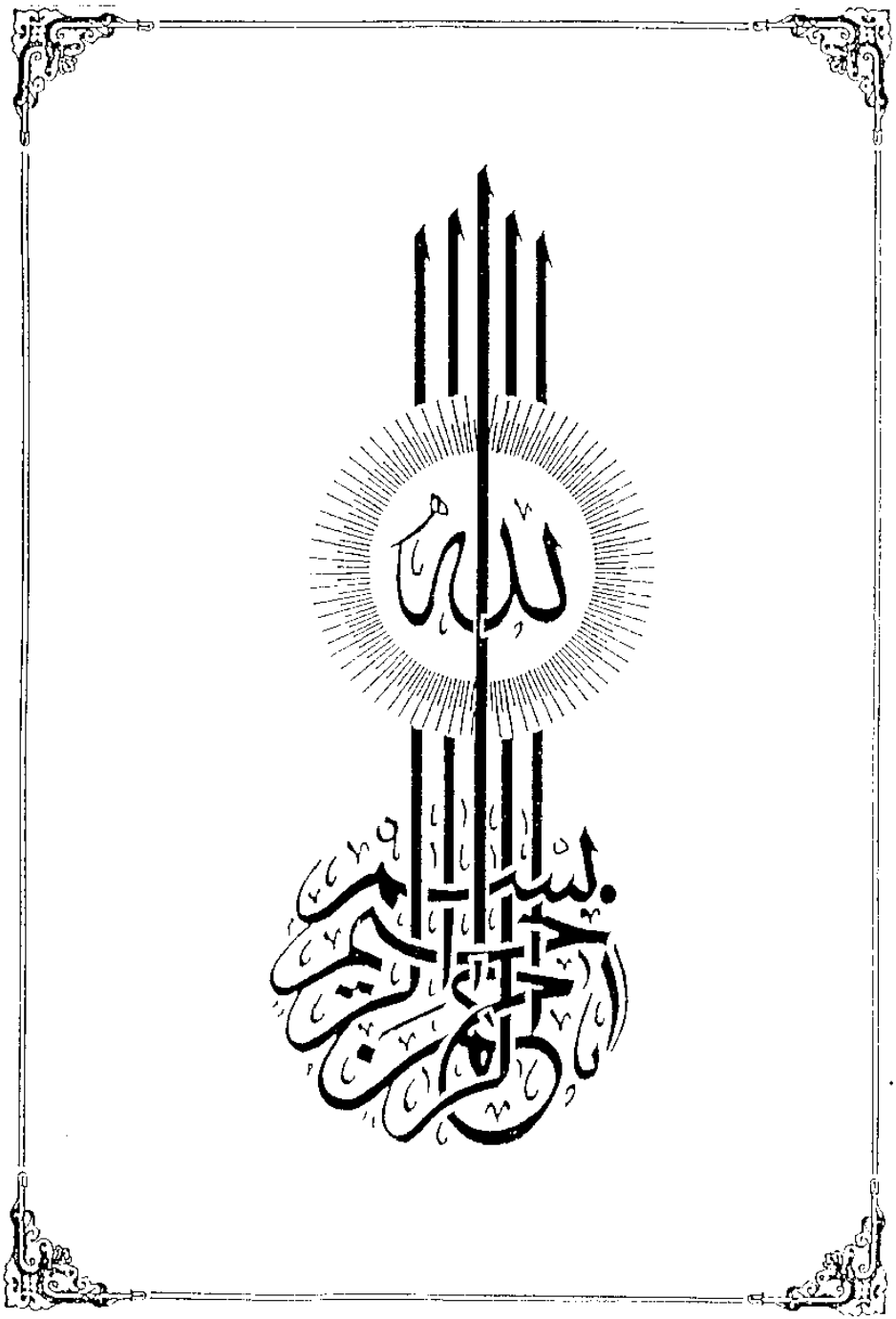
بسم الله الرحمن الرحيم

"وقل رب زدني علما"

صدق الله العظيم



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AIM OF WORK

Hepatic dysfunction may reflect an insult occurring in utero and manifest during infancy. Possible causes of liver disease may vary from a structural or functional development abnormality to specific inborn errors in metabolism.

The aim of this essay is to give a comprehensive review of the most recent data dealing with liver diseases in perinatal period.

AN INTRODUCTION

AND

REVIEW OF LITERATURE

PART (I)

AN INTRODUCTION TO THE LIVER

1- Developmental Hepatology:

- Morphologic development of the human hepatobiliary system.
- Neonatal liver morphology.
- Development of hepatic function.

2- Reticuloendothelial system and host defense.

3- Manifestation and mechanisms of liver dysfunction.

- Hepatomegaly.
- Hepatosplenomegaly.
- Jaundice.

DEVELOPMENTAL HEPATOLOGY

Since many hepatic lesions in infancy result from morphologic or biochemical maldevelopment of the liver, this section will be devoted to a review of normal hepatobiliary development in the human embryo and fetus.

Morphologic development of the human hepatobiliary system:

The liver develops very early in organogenesis. The first sign being a thickening of the ventral part of endodermal epithelial tube (Fig. 1) near the future duodenum in the 2.5 mm (18th day), embryo. By the 22nd day this grows into a well formed hepatic diverticulum which forms a caudal cystic part, the future gall bladder and a cephalic hepatic bud, the future liver. In the 28th day embryo irregular and poorly formed hepatic cell plates in the form of ridges grow out of hepatic bud and weave into the vascular mesenchyme of septum transversum, between the two vitelline veins. This vascular tissue later differentiates into sinusoids and other hepatic vasculature. Hepatoblasts and hepatocytes develop not only from the endoblastic epithelium of the hepatic, but also from the coelomic epithelium of mesenchymal origin (Du Bois, 1963).

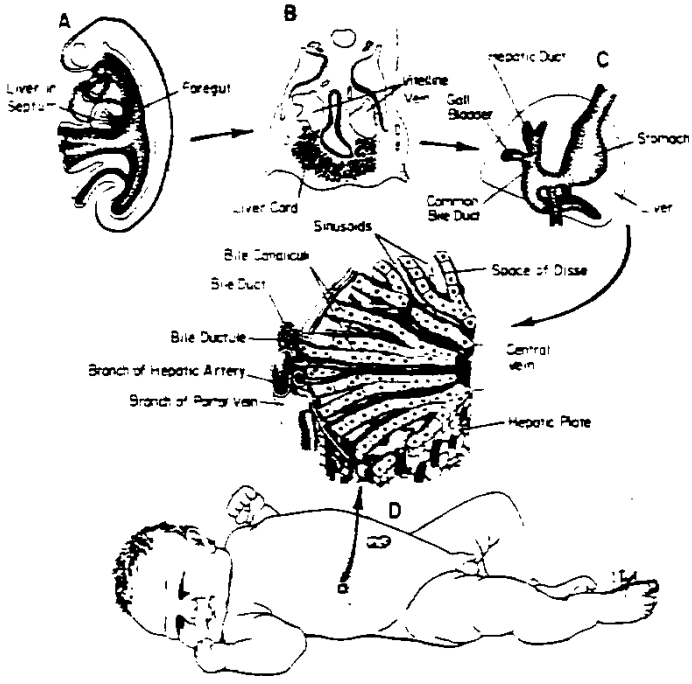

Fig. (1): Developmental changes of the liver and biliary tract (Andres et al., 1977).

Thus, the liver parenchyma has a dual origin, the anterior part is predominantly endodermal, while the posterior part is predominantly mesodermal. The junctional area is equally shared by the two (Andres et al., 1977).

The comparative developmental changes of the early and late gestational liver are illustrated in Fig. (1).

Early development of the extrahepatic biliary tract and gall-bladder in man:

The caudal part of the hollow hepatic diverticulum elongates and becomes obliterated due to the active migration of epithelial cells into its original lumen (Arey, 1974).

The elongation becomes the common bile duct, hepatic ducts, and possibly the larger proximal intrahepatic bile ducts. The cystic duct appears as the gall bladder becomes further separated from the duodenum by the elongation of the common bile duct.

As early as four to five weeks of gestation, the future biliary tree is intact but remains as a solid epithelial cord. Sequential recanalization in man then occurs as follows: Common bile duct, five weeks; hepatic duct, six weeks; cystic duct, seven weeks; and gall bladder, 7.5 weeks.

Biliary tract development is completed by ten weeks of gestation. It is presumed that arrest in development for any reason (intrauterine infection) may contribute to various abnormalities i.e. biliary atresia (Elias, 1963).

The development of the liver is associated with marked changes in the primordial vitelline veins, which give rise to the portal and hepatic veins, and the umbilical veins send branches into the liver. During the sixth to eighth weeks period of embryogenesis, however, the entire umbilical venous system disappears except for the distal left umbilical vein, which remains throughout fetal life and supplies the liver with oxygenated blood. In addition, some of the hepatic sinusoids coalesce, giving rise to a large diagonal channel, the ductus venosus. It continues in direct line from a branch of the umbilical vein to the hepatic vein; thus shunting the oxygenated blood directly to the heart. Final vascular development is completed by the eighth week of fetal life (Andres et al., 1977).

Any insult or compromise in vascularization may affect intrauterine hepatobiliary development and extrauterine circulation leading to altered hepatic function such as impaired

hepatic uptake of bilirubin. Radical changes take place in the hepatic circulation at birth (Witzleben, 1975). Umbilical vessels are obliterated and the flow of well-oxygenated venous blood delivered to the liver during fetal life abruptly shifts to less well-oxygenated portal venous blood. This adaptive response may partly contribute to the evidences of liver dysfunction in the first one to two weeks of extrauterine life such as mild elevation in serum transaminase and bilirubin values. Furthermore, the ductus venosus which normally constricts soon after birth, may remain open in the presence of neonatal distress. Consequently, blood is diverted away from the liver sinusoids and liver function is further compromised (Andres et al., 1977).

Neonatal liver morphology:

The liver of neonates and infants is relatively large, constituting approximately 5% of body weight (Wilson et al., 1963). The liver at birth is made up of four incompletely separated lobes. Each consists of the "classical" structural units known as hepatic lobules. The lobule is a small roughly hexagonal piece of tissue containing anastomosing plates of parenchymal cells, along with a system of blood sinusoids enveloped by perisinusoidal space. It comprises a histologic unit with a

central vein (smallest subdivision of the hepatic vein) and sinusoids extending outwards toward the periphery in which portal triads (branches of hepatic artery, portal vein and interlobular bile duct) encircling the periphery of each lobule are encountered.

Bile produced by hepatic cells is secreted into the bile canaliculi located between parenchymal cells flow in toward bile ductules near the lobule periphery and then to the larger interlobular bile ducts in the portal tract (portal triad with associated connective tissue, lymphatic vessels, and nerves) (Andres et al., 1977).

Bile flow continues to the duodenum via larger proximal interlobular bile ducts and hepatic ducts which unite in the porta hepatis to form the common hepatic duct, and then to the common bile duct. Blood from branches of the hepatic artery and portal vein flows in the opposite direction to bile, and mixes as it passes through the sinusoids to the central vein (Arey, 1974).

Development of hepatic function:

The functional development of the liver is essential to survival in the intrauterine and extrauterine environment.