ALPHA-FETO PROTEIN IN ACUTE VIRAL HEPATITIS

THESIS

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BY

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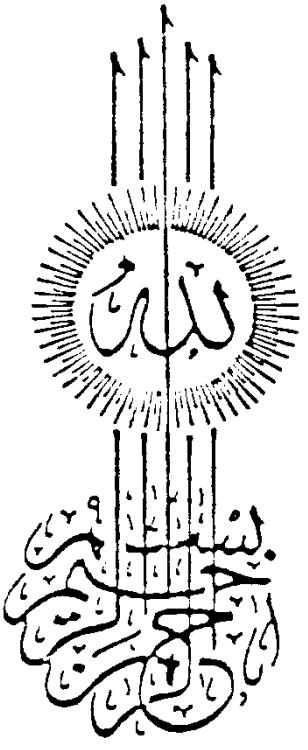
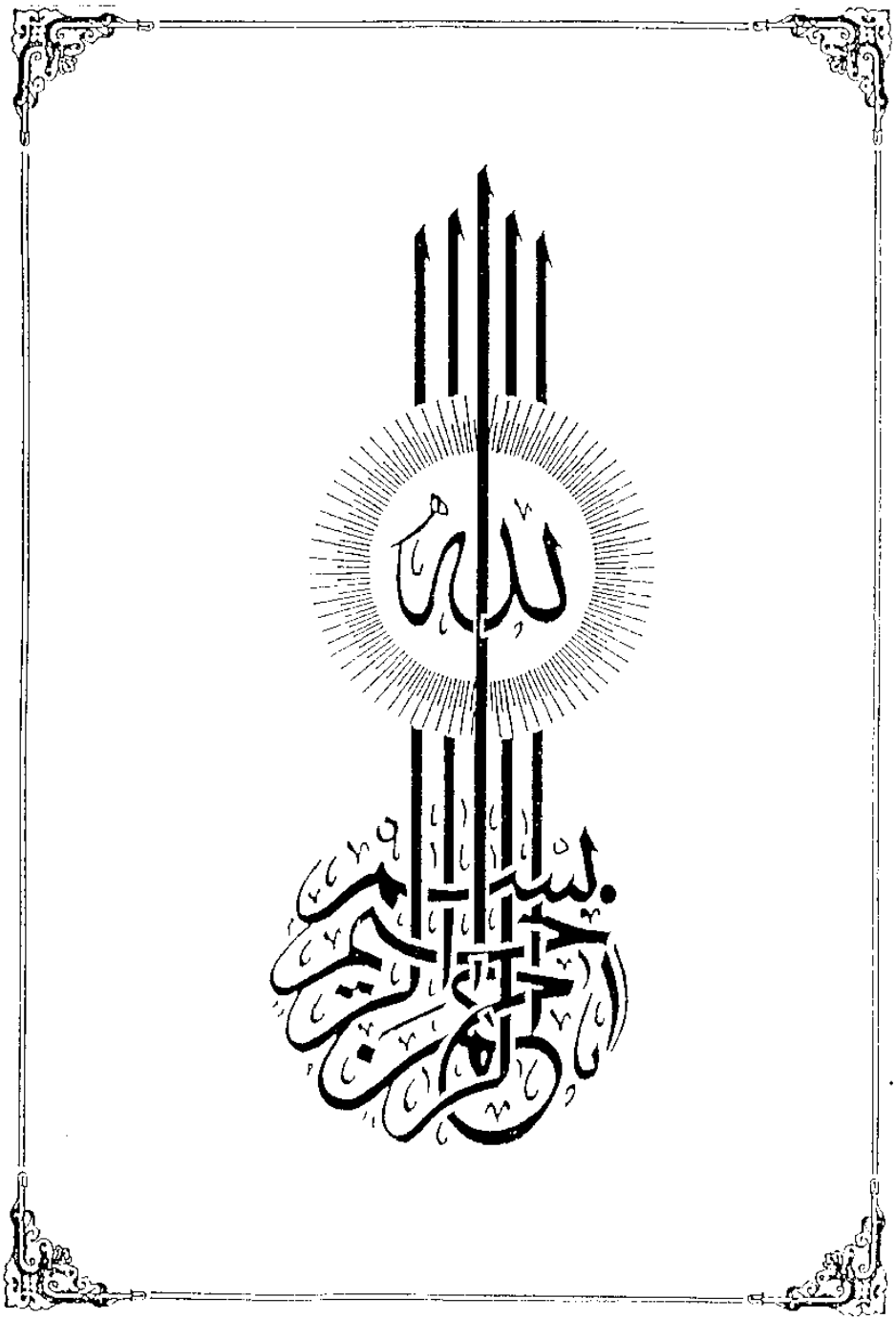


"وَعَلَّمَكَ مَا لَمْ تَكُنْ تَعْلَمُ وَكَانَ فَضْلُ اللَّهِ عَلَيْكَ عَظِيمًا"

صدق الله العظيم

سورة النساء: آية رقم ١١٣



TO MY

MOTHER....

ACKNOWLEDGEMENT

"I would Like to Offer my Limitless Thanks to my God for aiding me in this thesis.

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CONTENTS

Introduction

INTRODUCTION

Alpha-fetoprotein [AFP] is an alpha-I-globulin belongs to group of plasma proteins. Sometimes called fetospecific proteins, which are present in high concentration in fetal sera but absent or not detectable in healthy adults (Karel Kithier, 1981).

It was first identified in 1956 during electrophoresis experiment on plasma protein of fetus of a few weeks old by Halbrecht and Klibanski, Bergstrand and Czar as a protein which migrated between albumin and alpha-I-globulins.

It was found that [AFP] reaches a peak level of 3-4 mg/ml around the 12th week of gestation, which is synthesized by the fetal liver, yolk sac, and also by cells in gastro-intestinal tract, (M.O. El Haileg, et al., 1977).

After the 14th week of gestation the level of AFP declines exponentially and by 34 weeks synthesis is virtually shut off. By two years of age sera AFP levels have reached 1-2 ng/ml or 1:20,000 that present at birth, and this low level persists into adult life, (James P.Nolan, 1979).

Ableve in 1971 observed that AFP, reapears in sera of mice with transplacental hepatocellular carcinoma. This observation since then has been extended to primary hepatomas of a number of other animal species, including man.

The significance of an elevated serum AFP concentration in diagnosis of hepatocellular carcinoma was now soon well decumented [Wepsic et al., 1979] Tatorinov [1964] considered AFP as an immunological marker which could be used in clinical diagnosis of hepatocellularcarcinoma and in epidemiological surveys.

It was found later that human embryonal cell carcinoma such as testicular and ovarian tumours elaborate large quantities of AFP, [Shuster et al., 1974].

Increased level of (>40 ng/ml) of AFP have been demonstrated in a variety of non neoplastic hepatic disorders. The serum concentration is more frequently increased in those disorders in which there are prominent hepatocellular necrosis and inflammation, and highest values were observed in patients with viral hepatitis, [Bloomer et al., 1975].

The aim of our present study is to determine the serum level of AFP in cases of acute viral hepatitis in order to exclude any clinical correlation.

Review of Literature

PROPERTIES OF ALPHA-FETO PROTEIN

PROPERTIES OF ALPHA-FETOPROTEIN

Physicochemical properties :

Alpha-fetoprotein is a glycoprotein with a molecular weight 64,000-70,000. It contains 3-4 percent carbohydrate and consists of a single polypeptid chain, [Ruoslahti et al., 1971 & 1974].

Hexose, hexosamine and sialic acid present in a ratio of 2.2: 1.2: 0.9 by weight, [Purves et al., 1970].

It carries physico-chemical properties very similar to albumin but human AFP is slightly larger than albumin. Failure of immunological cross reactions as well as difference in their N and C terminal amino acid sequences indicates presence of extensive structural differences between native forms of human albumin and AFP. The alpha-fetoprotein molecule contains high content of cystein but with no disulphide bonding. It also shows cathodal electrophoric modility, [Shuster, et al., 1974].

Physiological function of alpha-fetoprotein:

There are several striking structural and functional similarities between AFP and albumin which have led to the

suggestion that AFP serves as a fetal albumin. The high concentration of AFP and albumin in plasma helps to control the osmotic pressure of intravascular fluid, also in binding and transport of metabolities and metabolic effectors. Alpha-fetoprotein has been implicated in suppression of immune response of maternal estrogen. Antibodies raised against purified native human AFP do not react with albumin, although antisera raised against the unfolded polypeptide chain of either protein cross react strongly, [Karel Kithier 1981 & Micheal B, et al., 1982].

Reports from several laboratories have indicated that AFP may function as an immunosuppressive agent, capable of blocking several in vitro parameters of T-cell function such as mitogen stimulating or mixed leucocyte culture, and AFP synthesis also be related to immunodepression in patients with liver disease, [Gunner H. et al., 1975].

The animal studies of Murgita and Tomasi 1975, provided clear evidence that AFP caused immunosuppressive effect in vitro. They also reported that AFP may induce a local immuno-suppressive effect which occured at a very low concentration. Thus significant immunosuppressive effect at local site of AFP

production might occur in absence of elevated serum concentration. However no evidence of an immunosuppressive effect of AFP in vivo has so far been provided.

Production of alpha-fetoprotein :

Alpha-fetoprotein is produced in organ originally derived from yolk sac. The main AFP production organ is the fetal liver which stems from a bud from the primitive forgut in turn a yolk sac dervitative, [Gitlin, 1971]. The other cell type, although at first sight a seemingly unrelated one is the germinal cell. They originate in the dorsocaudal portion of the yolk sac where they migrate later on the gonadal ridges which later becomes differentiated into gonads. Alpha-fetoprotein is also synthesized by the cells of gastrointestinal tracts, [Gitlin, 1967].

At a cellular level, most hepatocytes are initially involved in AFP synthesis by sixth week of gestation of foetal life, but as the serum level of AFP commences to fall, the numbers of hepatocytes involved in its synthetic process declines and tend to be those situated around the central vein. The kupffer cells, bile ducts, epithelial and haemopoietic cells do not appear to synthesis AFP at any time. It