SERUM ALPHA FETO-PROTEIN IN ELDERLY PREGNANT WOMEN

THESIS SUBMITTED

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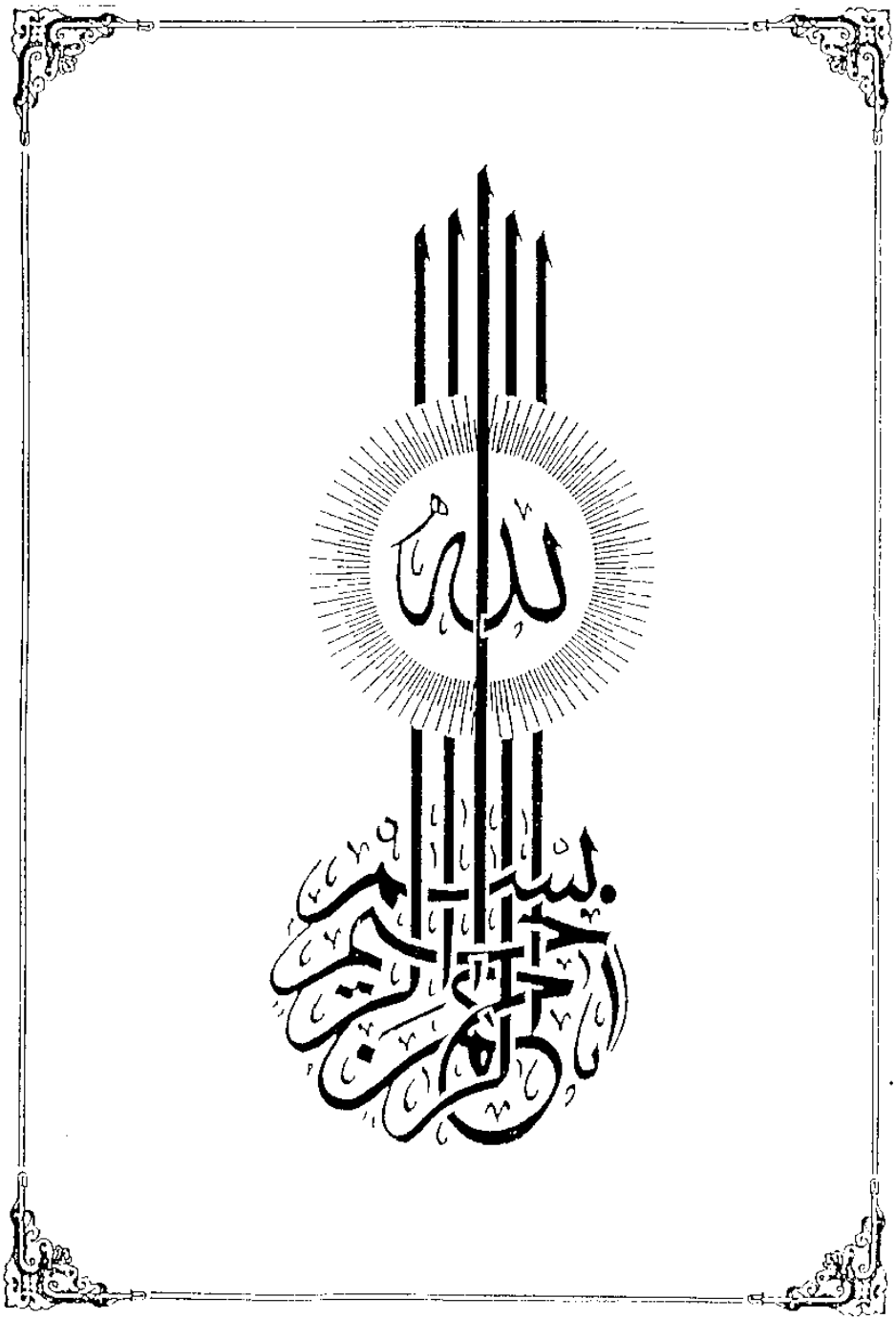

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DEDICATION

TO THE SOUL OF MY DEAR FATHER , TO MY MOTHER ,

BROTHERS MOHAMED AND HASSEN AND MY SISTER MONA

FOR THEIR EVERLASTING SELFLESS

LOVE AND ENCOURAGEMENT

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Review of Literature

THE REVIEW OF THE LITERATURE

1. THE REVIEW OF ALPHA FETO-PROTEIN :

1.1 Historical perspective of AFP in genesis of neural tube defects (NTD) and for aneuploid conceptions .

Alpha-Fetoprotein (AFP) was the first recognized oncofetal antigen and the first tumor marker with wide spread use in clinical medicine.

AFP was discovered in 1956 (Bergstrand and Czar , (1956) as a new protein with a mobility seen only in the serum of early fetuses.

Abelev et al (1963) demonstrated that this glyco-protein was present in large quantities in sera of new born mice and sera from adult mice with transplanted hepatomes.

Its clinical importance was established as a marker of primary hepatomes(Tatarinov,1964)and teratocarcinomas of the testis and ovaries (Abelev et al , 1967).

Van Furth and Adinolfi (1969) established that AFP is the major serum protein of the human fetus.

Clinical interest in AFP was centered on its usefulness as a tumor marker until its importance in obstetrics emerged from the work of the Finnish group on its relationship to spontaneous abortion and IUFD (Seppala and Ruoslahti,1972) and that of the Scottish group on its relationship to open neural tube defects [Brock and Sutcliffe,(1972);Brock and Scrimgeour,(1972)].

Brock and Sutcliffe (1972) reported that AFP was elevated in amniotic fluid samples with open neural defects (NTD) both spina bifida and anencephaly ,they suggested that elevated levels of AFP might also be found in maternal serum samples from NTD-affected pregnancies .

These observations were of importance especially in the United Kingdom where NTD-affected pregnancies are as frequent as 8/ 1000 births .

Further reports from this area rapidly confirmed the diagnostic reliability of Amniotic fluid AFP (AFAFP) levels for antenatal diagnosis of NTD. By the following year clinical testing of AFAFP levels was in use in the UK,USA and Scandanavia [(Allan et al,1973);(Harris et al ,1974);(Milunsky and Alpert,1974)].

This procedure was reserved for patients who were known to be at high risk for NTD because one or more of their children were affected ,an approach which could prevent only 5% of affected pregnancies at best (Wald et al,1978).

Reports on the applications of maternal serum AFP level to screen all pregnancies for NTD followed in the first foot steps of AFAFP measurements [(Leek et al,1973) ;(Brock et al,1973) ;(Seller et al 1974) ;(Harris et al, 1974) ;(Wald et al,1974)].

Some conflicting reports on the accuracy of maternal serum AFP levels together with the realization that there were many possible sources of false positive elevations led to the organizations of the United Kingdom collabortive study in 1975 .

The study groups initial report on serum AFP screening in 19148 pregnancies appeared in 1977 (report on UK collaborative study ,1977).

More expanded analysis of U.K experience have appeared [(Bennett et al,1978) ; (Ferguson Smith et al , 1978) ;(Wald et al , 1979) ;(Woolfson et al , 1979)].

1.2 Chemical structure :

Alpha fetoprotein belongs to a category of oncofetal antigens,proteins which show strong expression in fetal and embryonic tissues and disappear in the corresponding adult tissues but reappear in the presence of certain types of tumors (Brock,1980).

It is very similar to albumin in amino-acid composition and size with a molecular weight of 69,000 D , the homology between their amino-acid consequences suggested that these two proteins once had a common ancestor and ancestoral gene[(Ruoslahti and Seppala,1971) ;(Bennett , 1981)].

It is formed of a single polypeptide chain but differs from albumin in that it is a glycoprotein with 3-4% carbohydrate content and it migrate with alpha one globulins in electrophoresis (CowChock and Jackson,1980).

AFP is the oldest known protein in vertebrate evolution and has been identified in all studied species of fishes, birds and mammals (Adinolfi and Lessof ,1975).

The mammalian AFPs are immunologically cross reactive in their native states suggesting that little mutation in this protein has occured (Cowchock and Jackson, 1980).

1.3 :AFP Heterogeneity :

Human AFP is heterogenous protein and when subjected to isoelectric focusing resolves into at least two (and possible more) different fractions (Alpert et al,1972).

These two major fractions have differential affinity for the lectin concavalin A (con A). Crossed immunoelectrophoresis of AFP with the first dimensional run being made in the presence of high concentrations of the lectin will clearly separate the two isoprotein (kerckaert et al, 1979).

Alternatively AFP may be fractionated by affinity chromatography on columns of (Con A) linked to an insoluble matrix (Ruostlahti et al ,1978).

A major proportion of AFP from all human tissues binds to (Con A binding) while a smaller proportion passes through the column without being retarded (Con A non-binding).

Ruoslahti et al (1978) suggested that Con A binding AFP is synthesized in the liver while the non-binding fraction is derived from the yolk sac. The heterogeneity of AFP has been exploited in the early antenatal diagnosis of neural tubal defects.

Smith et al (1979b),pointed out that the increased levels of amniotic fluid AFP (AFAFP) found in anencephaly and spina bifida was probably by transudation of fetal serum components.

Since this AFP is synthesized by the fetal liver , it should be mainly of the Con A binding fraction.It has been found that analysis of AFP fractions in the amniotic fluid in NTD has shown a higher concentration of the Con A binding fraction and a low concentration of the Con A non-binding fraction [(Smith et al, 1979); (Ruoslahti et al,1979); (Hindersson et al ,1979); (Brock , 1979b)] .

But these are limitations in the practical use of this heterogeneity in diagnosing NTD . These include contamination by fetal blood which will falsely raise the Con A binding fraction in the amniotic fluid, and the total AFAFP level as well.