SOMATOMEDIN-C AND C-PEPTIDE IN UMBILICAL CORD OF UNCONTROLLED DIABETIC MOTHERS.

THESIS

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By

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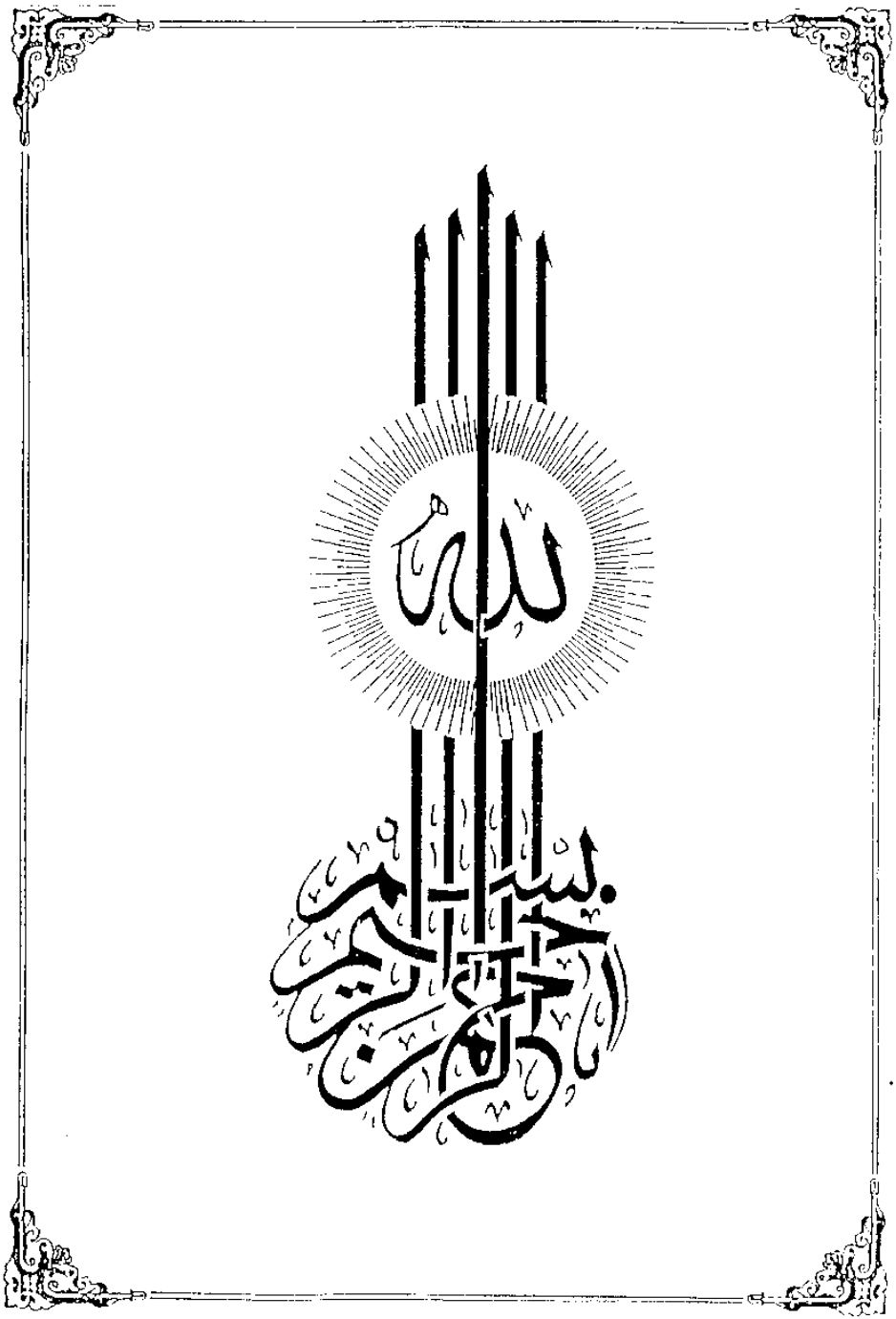

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CONTENT

INTRODUCTION AND AIM OF THE WORK

INTRODUCTION:

Although it is likely that fetal or placental hormones play a pivotal role in the stimulation and modulation of fetal growth there is little evidence that the traditionally known or classical hormone secreted by the fetal endocrine gland have any significant effect in the fetus, the only exeption is insulin.

In several studies on the human positive correlation have been observed between birth weight and umbilical cord venous insulin concentration (Roe T.F. et al, 1973 ; Hill D.E.,1978; Rosenberg A.M.et al,1980).

Several investigators have considered the possibility that insulin might augment fetal growth throught the stimulation of somatomedin production (Hill D.J.and Milner R.D.,1980; Spencer G.S.et al,1983).

Since infants of diabetic mothers are good example for hyperinsulinemic babies, also macrosomia is a common association in such infant particular attention will be focused in this work on the possible role of insulin and somatomedins in fetal growth in such infants.

AIM OF THE WORK :

The aim of the work is to study some hormonal profile in three groups of subjects normal,pre-diabetic and uncontrolled diabetic in the form of cord c-peptide, somatomedin-c, glucose taking the glycosylated hemoglobin of the mother as a marker of uncontrolled diabetic state.

REVIEW

CHAPTER I

SOMATOMEDINS.(Sm).

Introduction:

Growth hormone administration in vivo increases sulphate incorporation into cartilage chondroitin sulphate, the hormone also increases incorporation of amino acid into cartilage protein and thymidine incorporation into DNA, these effects are not seen when growth hormone is added to cartilage in vitro (Daughaday W.H. 1971).

However, the in vitro addition of serum from growth hormone treated animals has resulted in increased incorporation of sulfate, amino acids and thymidine. These results have indicated that the effects of growth hormone on cartilage are not direct but are brought about by the induction by growth hormone of a factor that cirulates in blood and mediates the effect of the hormone on cartilage, this substance initially called sulfation factor is now referred to as somatomedins.(Daughaday W.H.1971).

Origin of Sm :

Although sm does not appear to be stored in any tissue it is believed that the liver is a major source

since **sm** is produced by hepatocyte cultures (Spencer E.M.1979), moreover **sm** content is found to be higher in hepatic than in portal vein blood and serum concentration of **sm** are reduced by hepatectomy or hepatocellular diseases.(Takano K.et al, 1979).

The liver is probably not the only organ involved in **sm** production, however since other tissues have been found to produce **sm** in cell of organ culture. D'Ecrole and associates have shown that **sm** is produced by explants of a variety of fetal mouse tissues.(D'Ecrole A.J.1980).

Isolation of sm :

Factor that appear to be regulated by growth hormone and have cartilage stimulating activity include **sm-A, sm-C,** insulin like growth factor 1 and 2 (IGF I & IGF II) and multiplication stimulating activity, although **sm-B** exhibit some dependence on growth hormone, it does not stimulate cartilage and therefore is not included.(Richler M.M.et al 1977).

The **sm** are a family of polypeptides with growth promoting and insulin like activity, these polypeptides were initially isolated from several sources including human serum using a variety of bioassays (van Wyk J.J.et al 1974).

It has been established that the amino acid sequence of **sm-c** is identical to that of IGF-I (Klapper D.C.et al 1983). Multiplication stimulating activity (M.S.A.) has recently been sequenced and found to be similar in amino acid composition to IGF-II.(Marquart H.et al 1981).

Fetal biosynthesis of sm :

All fetal tissue appear to produce **sm**, both fetal tissue extracts and media harvested from fetal cells contain **sm**, although cellular synthesis has been indicated in these studies, the most elegant demonstration of fetal biosynthesis has come from the isolation from fetal cells of **mRNA** coding for **sm** (Sara V.R.and Hall K.1984).

Recently IGF-II gene expression has been demonstrated in a variety of fetal tissues, including kidney, liver, adrenals and striated muscle (Scott J.1985), a human fetal liver c-DNA library was used for the isolation of IGF-II gene (Dull T.J.et al,1984). In the rat IGF-II mRNA species are expressed in a variety of neonatal tissues. (Soares M.B.et al 1985).

The mechanism which regulate fetal **sm** biosynthesis remain to be elucidated, unlike the adult, the fetal production appear to be independent of growth hormone

(Sara, V.R.and Hall,K.1984), rather the growth hormone homologue placental lactogen may be of importance. In rat fibroblasts derived from fetal donors Avine placental lactogen and not growth hormone stimulates IGF-II synthesis (Adams S.O.et al 1983).

In contrast when fibroblasts were derived from adult donors, the production of IGF-1 was stimulated by both placental lactogen and growth hormone, other hormones such as insulin and growth factors such as epidermal growth factor and platelet derived growth factor have been implicated as possible regulators of fetal **sm** biosynthesis.(Sara,V.R.and Hall,K.1984).

Biological action of sm in the fetus :

The importance of **sm** for fetal growth was first suggested by in vitro studies demonstrating their biological action on fetal cells and tissues. In a wide variety of species and cellular types, the **sm** have been shown to stimulate DNA synthesis and cell proliferation, protein synthesis and glucose uptake and metabolism.(Sara, V.R.and Hall, K.1984).

It was found that there was a significant increase of **sm** in cord blood in full term neonates than in light

fordate newborns and premature which might be the cause of or at least related to the rapid increase in weight during the weeks immediately before birth this suggests that **sm** has a role in fetal growth.(Khattab A.K.et al,1984).Hyper-insulinism has been postulated as a possible stimulus to **sm** (Sandra L.et al 1981),which could be of clinical significance for the macrosomia seen in infants of diabetic mother where intrauterine fetal hyperinsulinism is implicated (Sosenko I.R.1979).

Effect of sm in body tissues :

In cartilage, they stimulate sulfate uptake, amino acid transport and synthesis of RNA, DNA, protein and chondroitin sulfate.(Daughaday W.H.et al 1975). In fat they promote glucose oxidation and decrease lipolysis. (Underwood L.E.et al 1972).

Apparantly IGF-I and IGF-II exert their acute metabolic effect through the insulin receptor, indirect evidence in favor of this concept stems from experiment in which the insulin receptor of adipocytes has been destroyed by short trypisinisation this procedure does not abolish only the antilipolytic effect of insulin and its stimulatory effect on glucose metabolism but it also abolish the corresponding effect of IGF I and II (Zapf J.et al 1981).