THE ROLE OF CERVICAL MUCUS PROLACTIN IN INFERTILITY

Thesis

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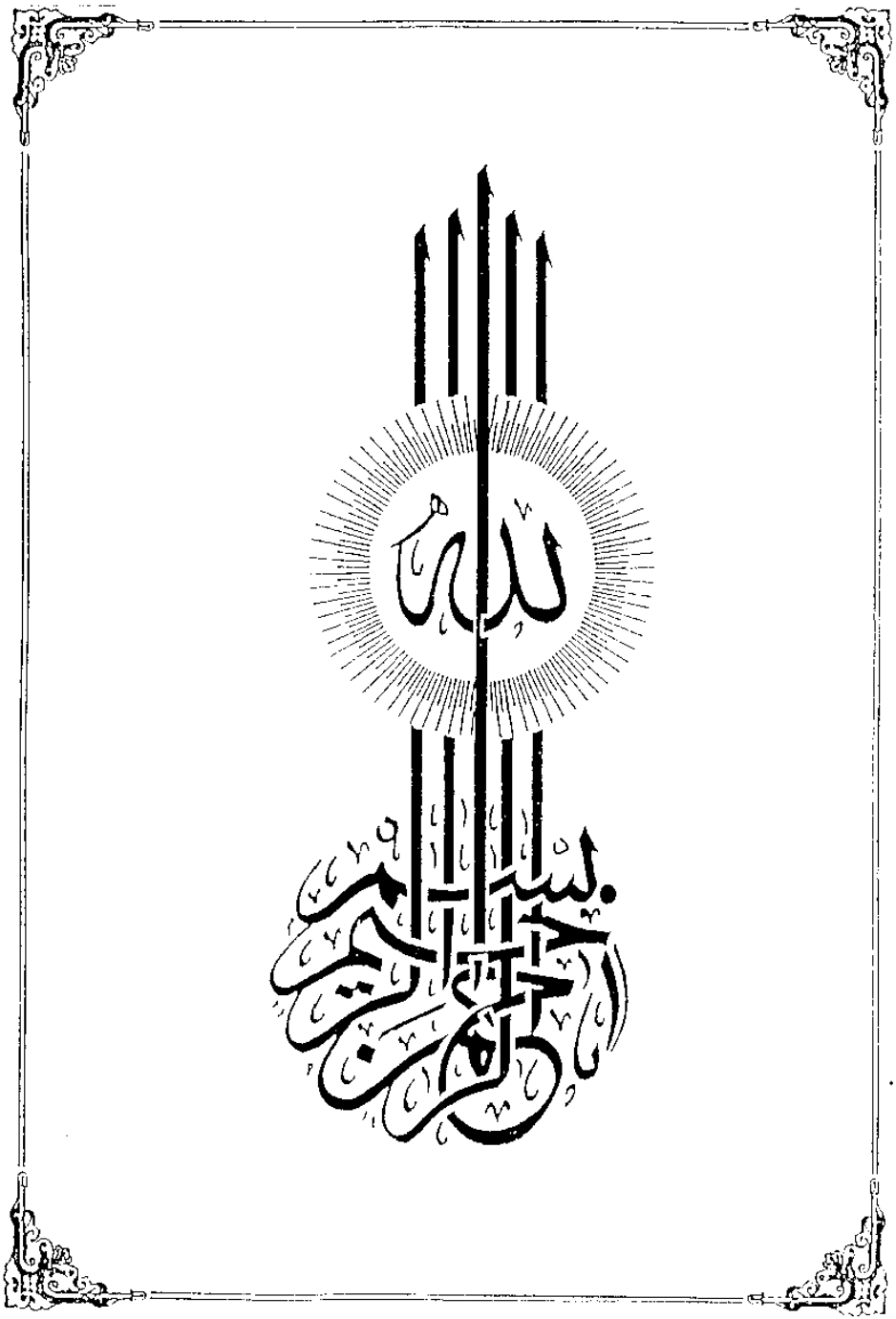

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ABBREVIATIONS

P.I.F.	=	Prolactin inhibitory factore
E_2	=	estrogen
P	=	Progesteron
h.PRL	=	Human prolactin
PRL	=	Prolactin
H.S.G.	=	Hystrosalpingogram
B.B.T.	=	Basal Body temperature
L.P.D.	=	Luteal phase defect.

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INTRODUCTION AND AIM OF WORK

INTRODUCTION AND AIM OF THE WORK

Prolactin was first isolated and indentified as a separate pitutary hormone in humans in 1971. (Hwang, 1972). Prolactin is known to be present in different body fluids including milk (Frantz, 1973), Semen, amniotic fluid (Friesen et al., 1973) as well as the pituitary gland and blood. Sheath et al. (1976), reported that cervical mucus contains prolactin. These body fluids and secretions were found to contain higher levels of prolactin than does serum.

Specific prolactin receptors are now known to be present not only in the mammary gland, but have also been found in the adrenal gland, ovary, liver, Kidney and prostate (Friesen et al., 1973 and Rajaniemi et al., 1974).

It has been postulated that tissues binding prolactin may be potential sites of action of prolactin. Prolactin hormone has been implicated in infertility, it was found that elevation of serum prolactin may produce anovulation (through its hypoestrogenic effect) that does not respond to clomiphene therapy. Treatment with bromoergocryptine may allow either spontaeneous ovulation or subsequent responsiveness to clomiphene (Hirvonen et al., 1976).

Hyperprolactinemia may also produce corpus luteum dysfunction (Mc Natty, 1977) and thus cause or contribute to the infertility.

Therefore, it was of interest to examine the cervical mucus for the presence of prolactin. Also, in this work we try to reveal the possible relation (If present) between cervical and serum prolactin in infertile women and to compare these results with normal control group.

PROLACTIN

Molecular structure of PRL :

Prolactin is a protein with no known carbohydrate content and a molecular weight approximating 20.000 (Saxena, 1977).

It is a polypeptide Hormone of 199 amino acids and is synthesized and secreted in the pituitary gland by lactotrophic cells containing eosinophilic granules. In several species, including human, specific prolactin producing cells (lactotrophs) have been identified by histologic techniques induding immunohistochemistry (Ash and Silverman, 1982).

PRL has been localized immunohistochemically within pituitary acidophils of all species studied including primates. (Phifer et al., 1972).

Prolactin is unique in that in many species phylogenetically related to human it is implicated in multiple physiologic processes, including control of water and electrolytes homeostasis, regulation of growth and development, . metabolic effects control of reproductive functions, and synergystic actions with antagonists of steroid hormone effects (Bern, 1968).

Mechanism of action of prolactin :

Once prolactin released into the circulating system, PRL binds to specific receptors inducing production of cyclic AMP-dependent protein kinase, an early event in a series of biologic

activities that result in the production of multiple specific proteins. Specific prolactin receptors have been found in crude membrane fractions of many tissues, including the mammary gland, adrenal gland, testis, ovary, liver and kidney. The half life of circulating PRL is 15 minutes. Its metabolic clearance rate is approximatelly 46 $\pm$ 1 ml/m/m^2 and its production rate is about 211 $\pm$ 75 u gm/day/m^2 (Cooper et al., 1979).

Most studies indicate that PRL acts on receptors which are located on the outer membrane of the target cells (Fraser, 1979). PRL is able to induce its own receptors and may also assist in the induction of receptors of other hormones, for example LH receptors in corpus luteum and oestrogen receptors in various tissues.

Posner et al. (1975) found that the receptor proteins have an extremely short half life and need to be continually replaced. They emphasized the importance of relating plasma levels to receptor concentration and receptor occupation. Interaction of PRL with the same cell membrane receptors and translation of the altered state of the membrane into intracellular signal to the nucleus modifies intranuclear transcription. This is coordinated to provide the ribosomal, transfer and messenger R N As required for the synthesis of milk proteins and other inducible proteins and secretion of milk products (Turkington, 1972).

Function of prolactin :

Specific functions of prolactin in the female are recognized in its action on the mammary gland in post partum location in the regulation of reproductive cycle, in the maintenance of pregnancy and in fetal growth by an effect on the metabolism of the mother (L'Hermite et al., 1972). In males, PRL may affect adrenal functions in terms of water regulation and electrolyte balance, and also the functions of the prostate, seminal vesicles and testis (Friesen et al., 1972b).

The large quantities of PRL in amniotic fluid throughout pregnancy may be involved in osmoregulation of the fetus, preparing it for the transition from an equatic environment. The most important actions of PRL in human femal reproduction may be summarized as follows (Archer, 1980).

(1) Menarchial years :

- Mammotrophic action.
- Possibly luteolytic action.

(2) Pregnancy :

- Amniotic fluid:
  * osmoregulatory function.
  * Maturation of lung surfactant.
- Possible role in pre eclampsia.
- Developement of breast for lactation.

(3) Puerperium :

- Initiation of lactation.

Synthesis, storage and secretion of PRL :

Production of prolaction occurs in lactotropic cells, which coexist with GH producing cells in the lateral wing of the anterior pitutary gland. Histologic examination by light microscopy demonstrates that lactotropic cells contain acidophilic granules that can be differentiated from those somatotrophic cells by the uptake of carmosin or erythrocin stains. However, classification of cell types by light microscopy is of little use in accounting for individual hormones secreted by anterior pitutary. Electron microscopy and immunohistochemical staining techniques indicate that prolactin-secreting cells possess distinct morphologic features: Lamellar pattern of the rough endoplasmic reticulum, large secretory granules (400-900 mm in diameter) and polymorphism of their secretory granules (Hopkins, 1973).

In the lactotrophic cells, prolactin is synthesized within cisterns of the rough endoplasmic reticulum and packed by Golgi apparatus into small membrane bound granules, which are used to form larger mature secretory granules. these granules lie in the cytoplasm until their contents are secreted by exocytosis resulting from fusion of granule membrane with the surface membrane itself (Chang, 1978).