Ain Shams University
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STEROIDOGENESIS

AN ESSAY

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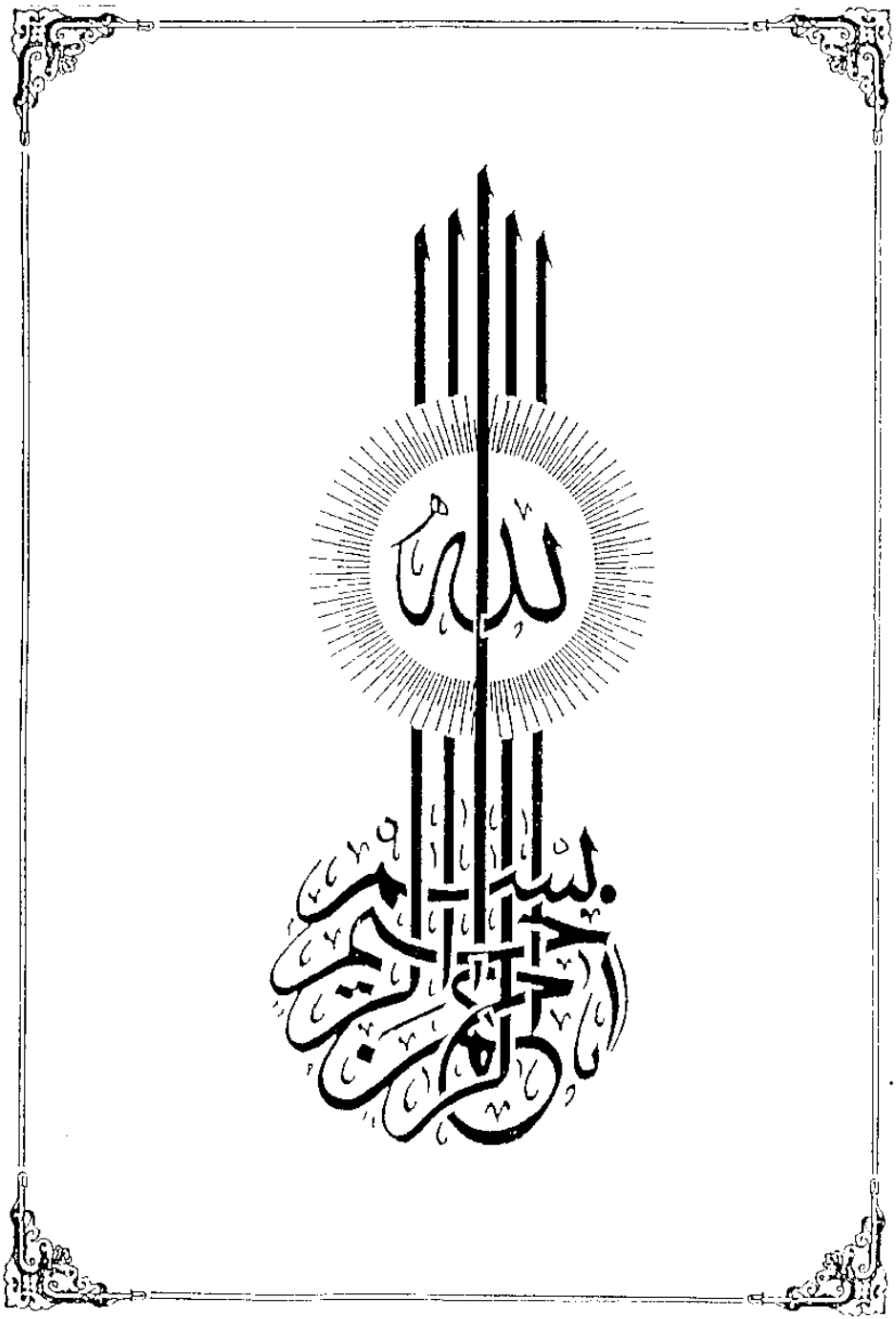
بسم الله الرحمن الرحيم

« وقل رب أدخلنى مدخل صدق وأخرجنى مخرج صدق واجعل لى
من لدنك سلطانا نصيرا »

صدق الله العظيم

«سورة الإسراء ، الآية ٨٠»



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To The Memory

of

My Parents.

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AIM OF THE WORK

Study of various aspects of steroidogenesis in the human body (ovary, testis, adrenal gland subcutanous fat and fetoplacental unit).

CHAPTER I

INTRODUCTION

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INTRODUCTION

The over all steroid biosynthesis pathway is based primarily on the pioneering work of *K.J. Ryan* and his coworkers. These pathways follow the fundamental pattern displayed by all steroid producing endocrine organs. As a result, it should be no surprise that the normal human ovary produces all three classes of sex steroids, estrogen, progestins and androgens.

The importance of ovarian androgens is appreciated not only as obligate precursors to estrogen but also as clinically important secretory products.

The ovary is distinguished from the adrenal gland in that it is deficient in 21 hydroxylase and 11 ß hydroxylase enzymes.

Glucocorticoids and mineralocorticoids, therefore are not produced in normal ovarian tissue.

Steroidogenesis in the feto-placental unit does not follow the conventional mechanism of hormone production within a single organ, rather the final products result from critical interactions and interdependence of separate organ systems which individually do not posses the necessary enzymatic capabilities. It is helpful to view the process as consisting of a fetal compartment, a placental compartment and a maternal compartment.

Separately the fetal and placental compartments lack certain steroidogenic activities. Together however, they are complementary and form a complete unit, which utilizes the maternal compartment as a source of basic building materials and as a resource for clearance of steroid.

CHAPTER II

HORMONES

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HORMONES

The term, hormone, (from the Greek Hormaein, to excite) was first applied by Byliss and Starling in the early 1900's to describe secretin, which is released into the blood by the duodenal mucosa and stimulates flow of pancreatic juice (*Goodman*, 1974).

Hormones are physiological regulators which are effective in minute quantities, synthesized by living cells in glands which secrete directly into the blood stream, transported by the circulating blood to specific target organs located at a site distant from the gland of synthesis where they exert specific actions (*Martin*, 1976).

The Chemical Nature of Hormones

Hormones synthesized from amino acids

Modified amino acids

These are sometimes called amine hormones. The group includes epinephrine and norepinephrine derived from the amino acid tyrosine, serotonin, and melatonin derived from tryptophan. Thyroxine obtained through iodination and condensation of two tyrosine molecules is usually included in this classification.

Small peptides

Thyrotropin release factor is a tripeptide, several other hypothalamic hormones seem to be small peptides or polyamines. The best known

neurohypophysial hormones (vasopressin oxytocin, vasotocin, etc.) are octapeptides which are chemically related to one another.

Larger peptides

This group includes active forms of the gastrins with 17 amino-acid moieties, glucagons with 29, and calcitonins with 32. Adrenocorticotrophic hormone seems to contain 39 aminoacid components.

Proteins

Authors differ on where they draw the line between large peptides and small proteins. Insulin molecules contain 20 or 21 amino acid α chains joined by sulfhydryl bridges to 29-31 amino acid ß chains. Parathyroid hormones have 80-85 amino acids. Growth hormone contains 191 amino acids.

Glycoproteins

Some adenohypophysial hormones contain carbohydrate components. These include, thyroid stimulating hormone, follicle stimulating hormone and luteinizing hormone. Chorionic gonadotropins are also glycoproteins.

Non-protein hormones

Steroids

Lipid-soluble hormones secreted by the ovary, testis, adrenal cortex, and placenta are derived from cholesterol, which contains 27 carbon atoms. Glucocorticoids and mineralocorticoids from the adrenal contain 21 carbons as does progesterone; androgens 19 and estrogens, 18 carbon atoms. Vitamin D and its metabolites are chemically related to these.

Other non-proteins

Prostaglandins are cyclic fatty acids (*Martin,* 1976)

Storage and Secretion of Hormones

There is no single way in which all the endocrine glands store and secrete their hormones. However, several general patterns occur for most of the hormones. For instance all the protein hormones are formed by the granular endoplasmic reticulum of the glandular cells in the same manner that other secretory proteins are formed. However, the initial protein formed by the endoplasmic reticulum almost never is the final hormone itself. Instead, it is larger than the active hormone and is called a preprohormone. Then, this large protein is further cleaved, usually while still in the endoplasmic reticulum, to form a smaller protein called the prohormone. This in turn is transported in the E.R. transport vesicles to the Golgi apparatus where still another section of the protein is cleaved; in this way the final active protein hormone is formed. The Golgi apparatus usually also compacts the hormone molecules into small membrane-encapsulated vesicles called secretory vesicles or secretory granules. These then remain stored in the cytoplasmic compartment of the endocrine cell until a specific signal, such as a nerve signal, another hormonal signal, or a local chemical or physical signal, comes along to cause secretion.

The 2 groups of hormones derived from tyrosin, the thyroid and adrenal medullary hormones are both formed by the actions of enzymes in the cytoplasmic compartments of the granular cells. In the case of theadrenal medullary hormones norepinephrine and epinephrine, these are then absorbed into performed vesicles and stored until they are to be secreted.

The thyroid metabolic hormones, thyroxine and triiodothyronine on the other hand, are formed as component parts of a large protein molecule called thyroglobulin, and this is then stored in large follicles within the thyroid gland. When the thyroid hormones are to be secreted specific enzymes systems within the thyroid glandular cells cleave the thyroglobulin molecule, thereby allowing the thyroid hormones to be released in the blood.

For the steroid hormones secreted by the adrenal cortex, the ovaries, or the testes the amount stored in the glandular cells are usually quite small, but large amounts of precursor molecules, especially cholesterol and various intermediates between cholesterol and the final hormones, are present in the cells. Upon appropriate stimulation, enzymes in these cells can within minutes cause the chemical conversions to the final hormones followed almost immediately by secretion (*Guyton*, 1986).

Control of Hormone Secretion Rate

Without exception, the rate of secretion of every hormone that has ever been studied is itself controlled very exactly by some internal control system. In most instances, this control is exerted through a negative feedback mechanism as follows:

1. The endocrine gland has a natural tendency to oversecrete its hormone.
2. Because of this tendency, the hormone exerts more and more of its control effect on the target organ.
3. The target organ in turn performs its function.
4. But when too much function occurs, usually some factor about the function then feeds back to the endocrine gland and causes a negative