SERUM CORTISOL LEVELS IN NORMAL PRIMIGRAVIDA AND WOMEN WITH PRE ECLAMPSIA

THESIS
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CONTENTS

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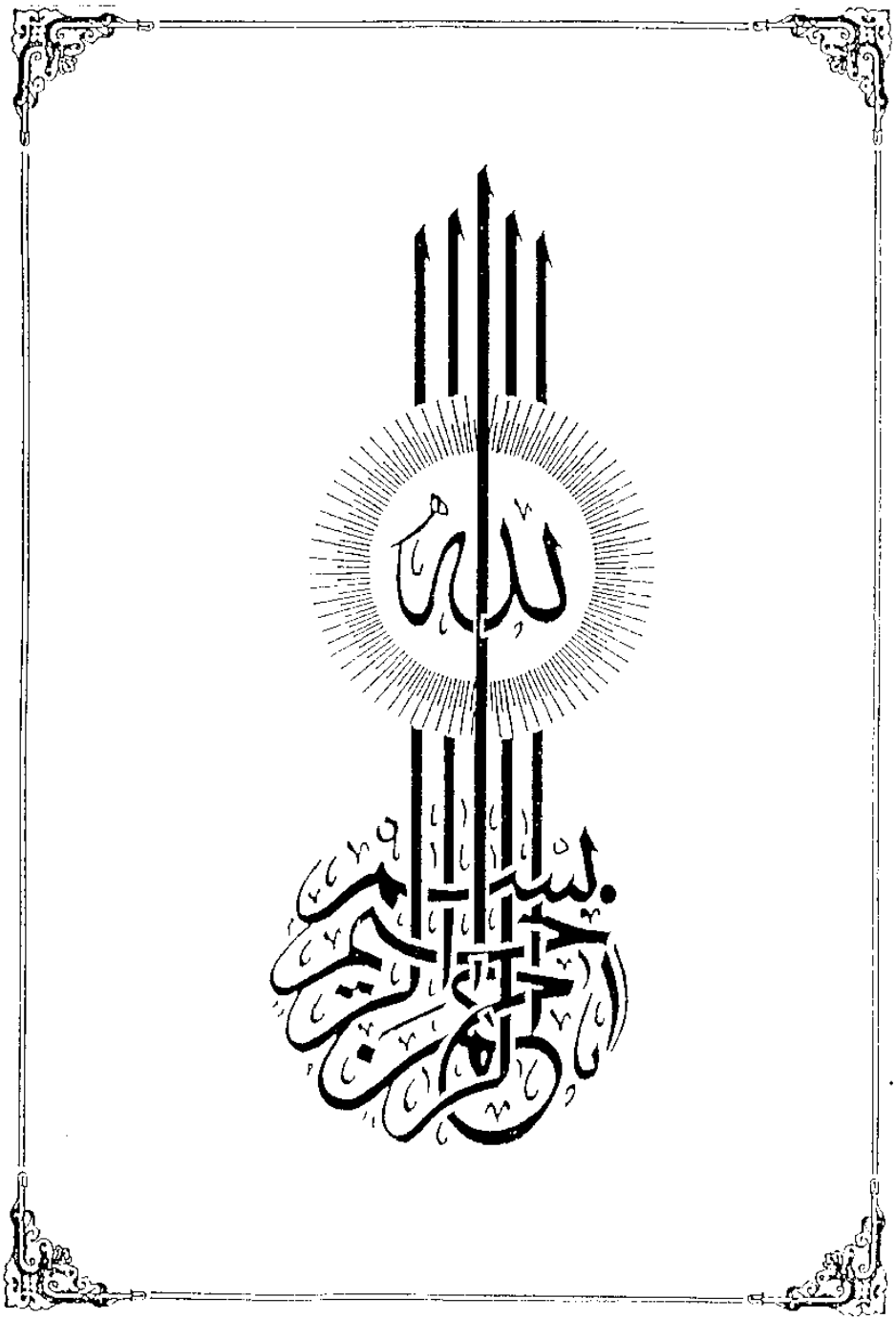

INTRODUCTION

Cortisol is among the most important biologically active steroids secreted by human adrenal cortex. Cortisol is the major glucocorticoid secreted by the human adrenal and normally the most abundant unconjugated steroid in the peripheral blood (Peterson, 1983).

The maternal plasma cortisol increase progressively throughout gestation (Carr et al., 1981).

Mukherjee and Swyer (1972) suggest that pregnancy is associated with increased adrenal responsiveness to adrenocorticotropic hormone (ACTH) stimulation, with the maintenance of normal hypothalamic feed back relationship. The failure of this mechanism may be implicated in the development of pre-eclampsia.

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AIM OF THE WORK

The aim of this work is to study the levels of serum cortisol in normal primigravida and women with pre-eclampsia and to see if the difference is significant with the severity of the clinical symptoms.

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Anatomy of the Suprarenal Gland:

The adrenal glands are paired organs that lie near the superior poles of the kidney embeded in adipose tissue. They are about 4-6 cm long, 1-2 cm wide, and 4-6 mm thick, and together weight about 8 g (Junqueira et al., 1986).

The right suprarenal gland is somewhat triangular in outline and its anterior surface touches the inferior vena cava posteriorly and medially and the liver laterally. The left adrenal is less triangular and more crescentic in outline, lies along the anterior medial border of the left kidney, and its lower half is in contact anterioly with posterior surface of the pancreas and splenic vessels. The gland are enclosed in a tough connective tissue capsule and embeded in adipose tissue. This connective tissue capsule penetrates into the deeper parts of the gland. It is contiguous with the septa which divides the organ into its characteristic zonal layers.

In addition, the glands are surrounded by renal fasia to which they are quite firmly attached (Soffer et al., 1961).

Blood Supply:

The adrenals are supplied by numerous small arteries arising from the phrenic arteries, the aorta, and the renal arteries and occasionally by branches from the ovarian and intercostal arteries. These vesseles penetrate the gland along connective tissue trabeculae and break up into a network of sinusoidal capillaries that extend radially into large venous lacunae in the medulla. Venules collect into a large central vein that runs as an axis through the gland and empties on the left into the renal vein and on the right into the inferior vena cava (Liddle, 1981).

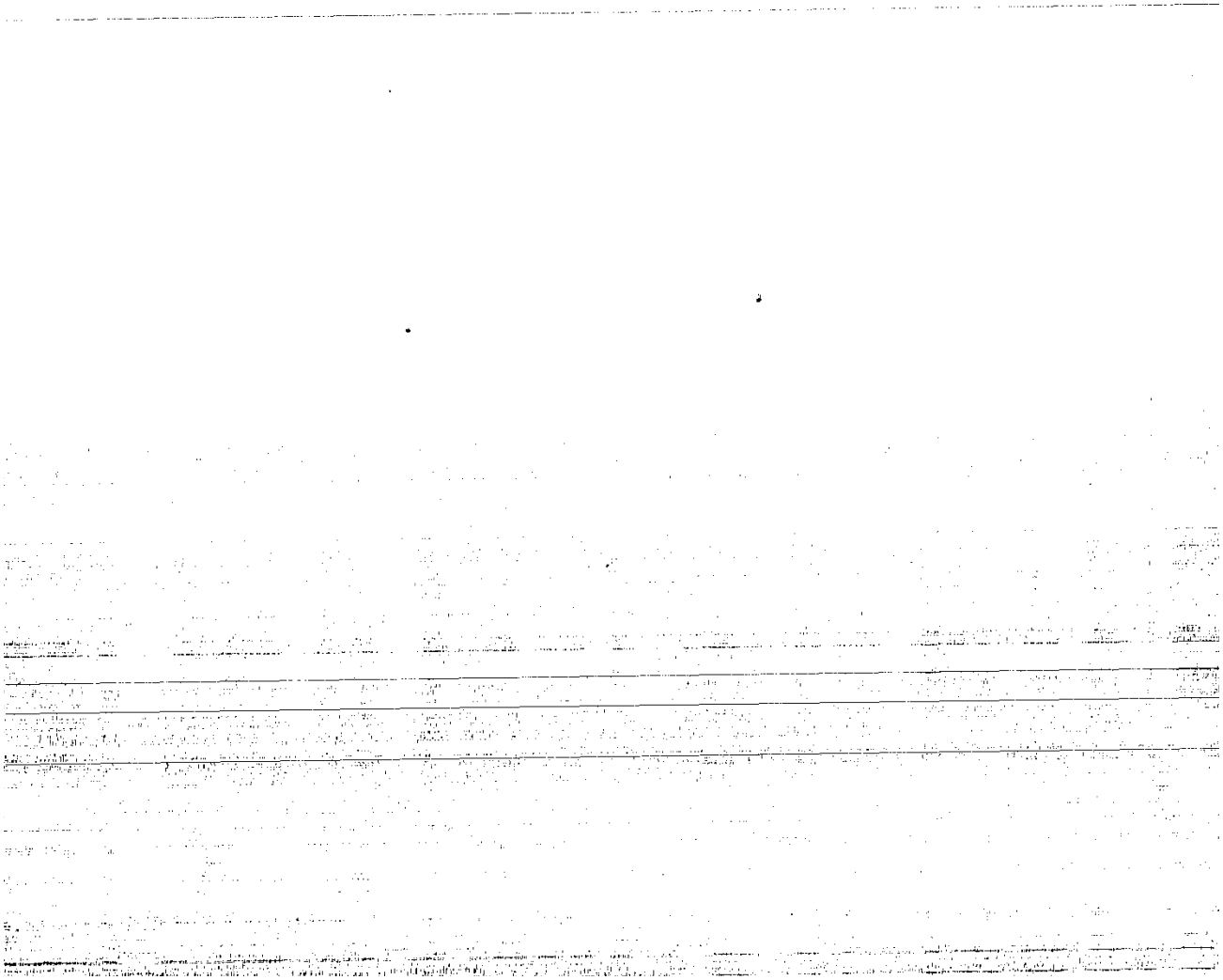
Histology:

The adrenal cortex can be subdivided into 3 concentric layers which, in humans, are usually not sharply defined, the zona glomerulosa, the zona fasciculata, and the zona reticularis.

The zona glomerulosa secretes mineralocorticoids, primarily aldosterone, which are involved with maintenance of electrolyte and water balance. The zona fasciculata and probably the zona reticularis secrete the glucocorticoids cortisone and cortisol which are concerned with the regulation of carbohydrate, protein, and fat metabolism. Androgens and perhaps estrogens are produced in small amount in these 2 zones. The glomerulosa, fasciculata, and reticularis zones occupy respectively, 15%, 65%, and 7% of the total volume of the adrenals. The layer immediately beneath the connective tissue capsule is the zona glomerulosa, in which the columnar or pyramidal cells are arranged in closely packed, rounded, or arched clusters surrounded by capillaries. The next layer of cells is known as the zona fasciculata because the cells are arranged in straight cords, one or two cells thick, that run at right angles to the surface of the organ and have capillaries between them.

The innermost layer of the cortex, between the zona fasciculata and the medulla, contains cells disposed in irregular cords forming an anastomosing network and is called the zona reticularis.

Cells of the adrenal cortex do not store their secretory products in granules; rather, they synthesize and secrete steroid hormones only upon demand (Junqueira et al., 1986).



PHYSIOLOGY OF THE ADRENOCORTICAL GLAND

Chemistry of the Adrenal Steroids:

The adrenal cortex produces a number of potent hormones all of which are steroid derivates. All steroid hormones have a cyclopentanoperhydrophenanthrene ring system as their chemical nucleus. Most naturally occurring steroids contain alcohol side chains and therefore usually referred to as sterols (Grodsky,1979).

The adrenocortical steroids are of 2 structural types: those that have a 2- carbon side chain attached at position 17 of the D ring and contain 21 carbon atoms ("C_{21} steroids"), and those that have a keto or hydroxyl group at position 17 and contain 19 carbon atoms ("C_{19} steroids"). The C_{21} steroids that have a hydroxyl group at the 17 position in addition to the side chain are often called 17-hydroxycorticoids or 17- hydroxycorticosteroids. The C_{19} steroids have androgenic activity.

All secreted C_{21} steroids have both mineralocorticoids and glucocorticoid activity.

The C_{21} steroids secreted by the adrenal have a Δ^4 -3- keto configuration in the A ring.

In most naturally occurring adrenal steroids, 17-hydroxy group are in the α configuration, while 3-, 11-, 21- hydroxy group are in the β configuration (Ganong, 1985).

Biosynthesis of Adrenocortical Hormones:

Kinetic studies of the conversion of plasma cholesterol to cortisol in humans demonstrate that under both basal conditions and ACTH stimulation the primary source of secreted cortisol is the circulating cholesterol (Borkowski et al., 1967).

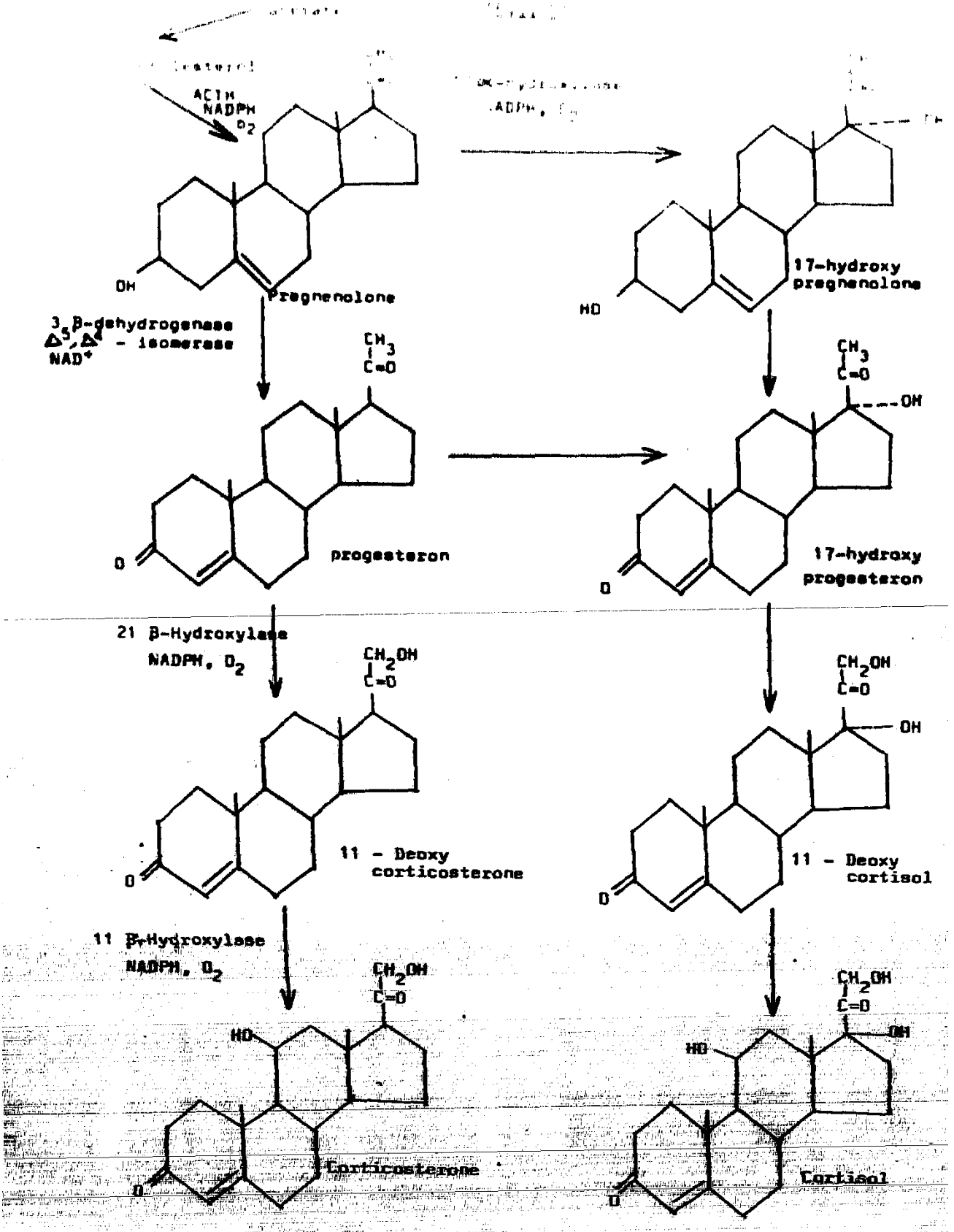
The source of cholesterol for steroid synthesis are cholesterol up take from low density lipoprotein, de novo synthesis of cholesterol within the adrenocortical cells, and hydrolysis of stored cholesterol esters (Peterson, 1983).

Conversion of cholesterol pregnenolone by the desmolase enzyme complex in the adrenal mitochondria is the rate-limiting step in adrenal steroid biosynthesis. Pregnenolone is modified both hydroxylation reactions and by 3 β-hydroxyoxidation and double-bond isomerization to form cortisol. Dehydrogenation of the 3 β-hydroxyl group is accomplished by 3 β-hydroxysteroid dehydrogenase, with NAD^+ as hydrogen acceptor .

The double bond is then rearranged by $\Delta^{4,5}$ - 3-ketosteroidisomerase. Hydroxylation at 11 β, 17 α and 21 positions are catalyzed by monoxygenases (Smith et al., 1983).

All biosynthetic reactions are carried out by both the maternal and fetal adrenals. Although the placenta can carry out some of these reactions, it does not passess 17, 20 desmolase, C_{21}, 17α-, 11 β-, or 18 methyl mixed function oxidases (Diczfalusy et al.,1974).

Steps of biosynthesis of adrenocortical hormones are shown in figure (1).



Outline of hormone biosynthesis in the zona fasciculata and zona reticularis of the adrenal cortex (after Ganong, 1985).

CORTISOL CIRCADIAN RHYTHM

The episodic secretion of cortisol in normal subjects has been well established (Hellman et al., 1970; Weitzman et al., 1971).

The diurnal variation of adrenal cortical activity has been well correlated with a preceeding change in the level of corticotrophin in the blood (Ney et al., 1963).

In man and higher mamals the secretion of ACTH appear to be episodic in nature, the number and duration of episodes increasing to be a peak between 3 and 8 A.M. with a nadir at 18 to 24 hr. This change in frequency of episodes causes the familiar circadian rhythm in ACTH and cortisol.

ACTH secretion is dependent on the prior secretion of CRF, and it can be assumed that the episodes are initiated by pulsatile release of CRF (Jones,1979).

The biological clock responsible for the diurnal ACTH rhythm is apparently located in the suprachiasmatic nuclie of the hypothalamus (Ganong, 1985).

The periodicity of the circadian rhythm is not dependant on the negative feed back of cortisol (Gallagher et al., 1973).