HYPOGONADISM IN FEMALE

Essay

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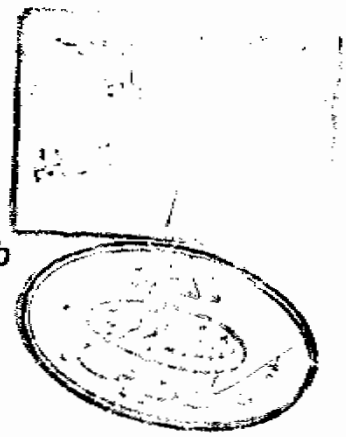

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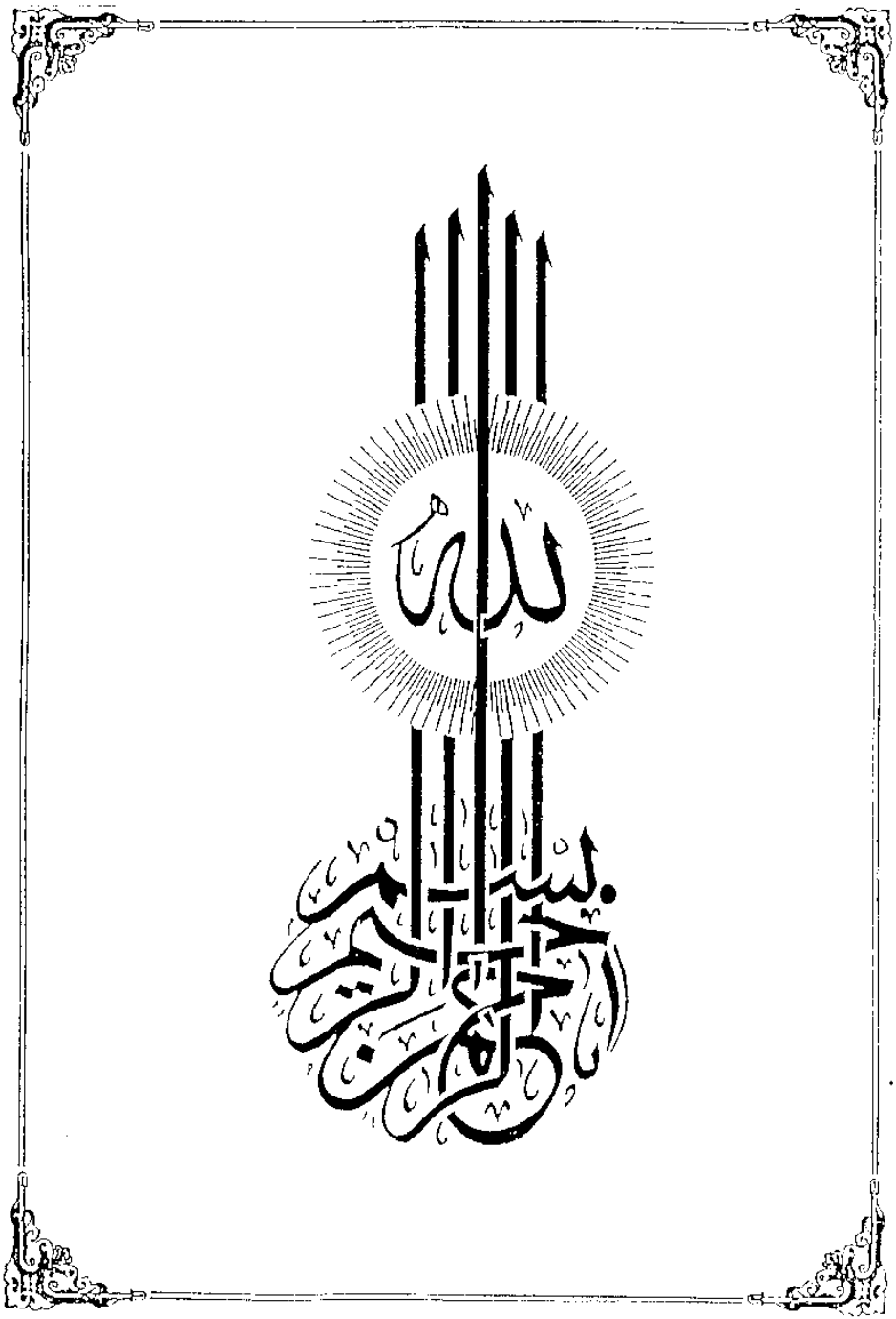

LIST OF ABBRAVIATIONS

ACTH	Adreno-cortico-tropic hormone
ACTH	Adreno-corticotropic hormone
CDGP	Constitutional delay of growth and puberty
CNS	Central nervous system
DHA	Dehydroepiandrosterone
DHAS	Dehydroepiandrosterone sulfate
DHT	Dihydrotestosterone
E_1	Esterone
E_2	Estradiot
FSH	Follicle stimulating hormone
GH	Growth hormone
GHRH	Growth hormone releasing hormone
GnRH	Gonadotropin releasing hormone
HCG	Human chorionic gonadotropins
hGH	Human growth hormone
HH	Hypogonadotropin hypogonadism
HLAs	Human leucocyte antigens
hMG	Human menopausal gonadotropin
LH	Leuteinizing hormone
LHRH	Luteininzing hormone releasing hormone
LTC_4	Leukotrienes
n	Number
P.O	per oral
PHV	Peak height velocity
r-hGH	Recombinant human growth hormone
SC	Subcutaneous

SD	Standard deviation
SDS	Standard deviation score
T3	Triiodothyronine
T4	Thyroxine = tetraiodothyronine
TDF	Testis - determining factor
TRF	Thyrotropin releasing factor
TSH	Thyroid stimulating hormone
Xp -	Deletion of the short arm of X chromosome
Xq -	Deletion of the long arm of X chromosome

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Introduction And Aim of The Work

Introduction and aim of the work

Puberty is the stage of transition from the sexually immature to the potentially fertile stage during which secondary sexual characteristics appear (Rosenfield,1990).It is the physiological stage that leads to reproductive capability, manifested by ovulation in the female. Major physical changes occur during this process, leading to acceleration of somatic growth; the adolescent growth spurt (Moris,1979 and Styne,1986).

Hypogonadism is defined as delay or absence in either the onset or completion of puberty and it may be associated with poor somatic growth (Forfar and Arneil,1983). The age at which hypogonadism is said to be present is defined as more than two standard deviation above the mean for normal puberty (Behrman and Kliegman,1990).

The understanding of the wide range of normal variation is necessary in arriving at a decision to persue pathologic causes of hypogonadism (Rallison,1986).

Hypogonadism may be attributed to hypothalamic, pituitary or gonadal disorders or due to other endocrine or systemic disorders. Constitutional delay of growth and puberty is the commonest differential diagnosis of hypogonadotropic hypogonadism (Sizonenko,1978 and Rallison,1986).

The aim of this study is to throw light on the normal determination and differentiation of female sex, review the physical and endocrinal changes which occur during female puberty. Current mechanisms by which puberty may be initiated will be explained. Also to discuss the etiology of hypogonadism in female and the

clinical manifestation of different types of hypogonadism. Finally to put a methodological procedure for diagnosis and differential diagnosis of hypogonadism in female, besides, the designation of therapeutic management of female hypogonadism.

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FEMALE SEXUAL DIFFERENTIATION

Normal Determination & Differentiation Of Sex

Determination of sex and sexual differentiation are sequential processes that involve successively the establishment of chromosomal (genetic) sex in the zygote at the moment of conception , the determination of gonadal (primary) sex, and the regulation by gonadal sex of differentiation of the genital apparatus that defines the phenotypic sex (Austin and Edwards ,1985).

So sexual development and differentiation is a complex process involving events at several genetic and embryological levels. At the first level, fertilization ,and during the immediate post fertilization cell cleavages, the sex chromosomes constitution is established in the zygote. This may be normal,46 XX or 46 XY or may consist of some abnormalities in all cells (such as all being 45,X or 47,XXY) or abnormality in mosaic pattern (such as 46,XX/45,X or 45,X/47,XXY). At the second level, the differentiation of the paired genital ridges into gonads , between the fifth and sixth post fertilization week , changes occur independently on each side of the embryo. These changes depend on a series of events initiated by the Y chromosome (Langman,1969).

Sex determination is concerned with control of development of the primary or gonadal sex(ovaries or testes),and sex differentiation with the events subsequent to gonadal organogenesis. These processes are regulated by at least 30 specific genes located on sex chromosomes or autosomes that act through a variety of mechanisms , including organizing factors , sex steroid and peptide secretions and specific tissue receptors. Both male and female embryos possess indifferent ,

common primordia that have an inherent tendency to feminize unless there is an active interference by musculinizing factors , i.e. an ovary differentiates unless the indifferent embryonic gonad is diverted by testis-organizing factor(H-Y antigen)regulated by the Y chromosome (Davis,1981).

Moreover , female differentiation of the somatic structures (the internal and external genital tracts) occurs independently of gonadal hormones and will emerge in the absence of fetal testes whether ovaries are present or not. Thus, the sexual dimorphism in phenotype that results from sex differentiation in placental mammals is mediated by the fetal testis and its dual hormonal secretions , and not by the ovary(Byskov,1981).

The presence of a Y chromosome is associated with the induction of testis. However , the presence of a Y chromosome does not invariably result in testicular differentiation , and the absence,using classic cytogenetics,of a demonstrable Y chromosome does not guarantee ovarian development. Until recently,it was thought that the factor responsible for the induction of the testis was the Y chromosomes-encoded minor histocompatibility antigen called H-Y antigen. However,new evidence suggests that this plasma membrane protein is coded for by a region of the Y chromosome that does not appear to be directly associated with the presence or absence of a testis (Wiberg,1987).

If the H-Y antigen has a role in testicular development it may be in tissue organization since the protein's structure is suggestive of a cell adhesion type of molecule;so called CAM protein (Page etal.,1987).

Recently, molecular genetic techniques that can probe for the presence of specific DNA sequences too small to be detected by cytogenetics, appear to have localized a Y chromosome "testis-determining factor" or TDF. This region of DNA is a small fraction of the Y chromosome located in the distal part of the short arm adjacent to the terminal pseudoautosomal region. When this small region of the Y is absent, the individual fails to develop testes, when present, regardless of how little else of the Y is present, the testes develop (Lippe,1990).

Similarly, using molecular genetic techniques, including cloning a segment of this TDF region , there was an observation suggesting that this gene encodes a protein with multiple fingers that bind to nucleic acids in a sequence - specific manner , thereby regulating the transcription of other genes downstream in the process from TDF (Page,etal,1987).

This model for the role of TDF that invokes the action and products of several genes, including genes located on the X-chromosome as well as on autosomes , is important since a single TDF gene alone cannot explain all examples of genetic disorders of sexual differentiation (Lippe,1990).

Biological Functions of X Chromosomes

The biological functions of the X chromosomes are complex. Genes on the X-chromosome have a critical influence on sex determination in both the female and male and on the differentiation of the somatic sex structures in the male . In addition , over 100 gene loci unrelated to sex development are X-linked (Mckusick,1983).