A REVIEW ON

POLYCYSTIC OVARIAN DISEASE

THESIS

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BY

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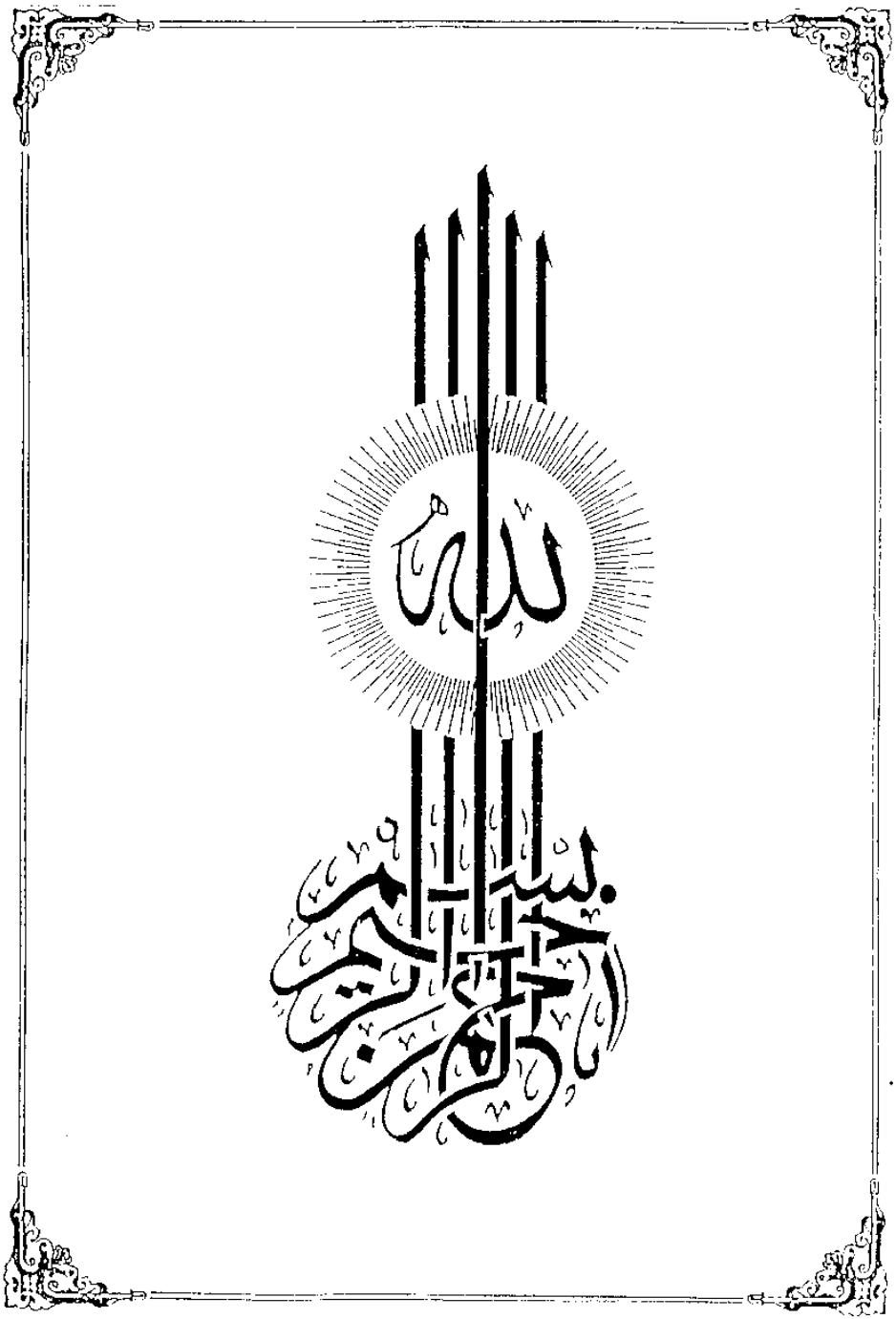

C O N T E N T S

INTRODUCTION

HISTORICAL BACKGROUND

Gross sclerocystic changes in the human ovary were clearly described by Chereau in 1845, and partial resection of such ovaries was being practiced before 1897 in Europe by Gusserow, Martin, Wiedow, Zweifel, and others.

In the American literature, Findley described wedge resection for "cystic degeneration of the ovary" as early as 1904.

Although occasional reports about this condition continued to appear over the years, more interest was aroused in 1935 when this anatomical abnormality was related by Stein and Leventhal to a clinical syndrome consisting of "menstrual irregularity featuring amenorrhea, a history of sterility, masculine type hirsutism, and less consistently, retarted breast development and obesity.

Little of significance occured to alter the situation untill the last two decade, when a continuing evaluation of polycystic ovarian disease and a revolution of the knowledge of hypothalamic pituitary-ovarian relationship began to shed new light on the problem.

INCIDENCE

Searching for patients with polycystic ovarian disease on the basis of infertility, amenorrhea, and hirsutism preselects the symptomatology associated with the anatomical changes. It is of particular importance to study the incidence of polycystic ovarian disease as observed under other circumstances.

In one series of 12.160 unselected gynacologic laparotomies (Varap, Niemineva K., 1951), for example, an incidence of 1.4% of polycystic ovaries was reported.

In large groups of infertile women prevalences of 0.6% to 4.3% have been noted (McGoofan L.S., 1954, Breteche J., 1952).

In a series of 740 consecutive autopsies (including an unspecified number of young girls and old women), bilateral polycystic ovaries were found in 3.5% (Sommers S.C., Wadman P.J., 1956).

Evidently the gross anatomical lesion is fairly common.

Increasing use of the laparoscope will undoubtedly change our perception of this disorder still further.

Clearly, the "syndrome" of Stein and Leventhal identified only a small and empirically selected fraction of the much larger number of patient who actually have polycystic ovarian disease.

It follows that adherence to this set of clinical criteria will deprive many women of the benifit of appropriate medical and surgical therapy.

Since the gross anatomical lesion of sclerocystic ovarian disease is relatively common. It is necessary to re-examine the frequency of revelant signs and symptoms in patient who have been surgicaly explored.

In 1962 a comprehensive review of published cases of surgically proven polycystic ovarian disease (Goldzieher J.W., Green J.A., 1962) found the frequencies for the major clinical features as summarized in table (1).

Amenorrhea was present in only about 50% of cases, infertility 74%, hirsutism in 69%, and obesity in 41%.

In some recent series (Yen S.S.C., Chaney C., Gudd H.L., 1976) the incidence of obesity prior to menarche has been as high as 90%. In contrast the usual clinical impression, cyclic menses occured in 12%

and evidence of ovulation in early one-fourth of the patients.

Thus, the allegedly characteristic signs and symptoms are not found with sufficient consistency to justify the designation of a syndrome.

PREDISPOSING FACTORS TO POLYCYSTIC OVARIAN DISEASE

Stein & Leventhal (1935) discussed two possible causes of the syndrome.

Firstly, they suggested that the ovarian changes might be due to abnormal hormonal stimulation from the anterior pituitary.

Secondly, they postulated that the thickened ovarian tunica might prevent immature follicles from ripening and reaching the surface of the ovary.

The latter explanation is clearly invalid as these patients can ovulate spontanously and usually respond well to ovulation induction therapy.

Recently the biochemical and endocrinologic data that bear on the causes of polycystic ovarian disease are so voluminoss. These causes can only be touched upon here.

Agreement is still lacking about whether the primary defect resides in the hypothalamus, the pituitary, the ovary or the adrenal.

However, there are certain factors, the presence of which seems to be necessary or contributory to the aetiology of the disease.

Age:

In observation which has its bearing on the possible aetiology of polycystic ovarian disease is that the syndrome is usually seen in the 2nd and 3rd decade of life.

Declerq and Van De Calseyde (1977) in a series of patients with polycystic ovarian disease noticed that their mean age in years to be 25 y.

Some investigators (Yen et al., 1976) are theorizing that the factor initiating the self perpetuating process of chronic anovulation (which is one of the main features of polycystic ovarian disease) is an abnormality in the pubertal process.

This abnormality is responsible for the pathogenesis of polycystic ovarian disease may be an exaggerated adrenarche (Yen et al., 1976).

In the latter process there is over production of adrenal androgen both in adipose tissue and the

central nervous system (pituitary system). Thus providing an inappropriate steroidal feed back, which would initiate chronic anovulation.

Obesity:

This feature in the polycystic ovarian patient aside from being part of the symptom complex of the disease. It is in itself pre-existent before its onset and may be one of the determining factor in initiating the disease process.

The observation that the peripheral conversion of androgen into oestrogen (estrone) is facilitated by the body fat (Siiteri and McDonald, 1973).

Obesity, which occuring at puberty or later in the reproductive years, is one mechanism of the onset of polycystic ovarian disease.

Siiteri and MacDonald, (1973); MacDonald et al., (1978); and Edman et al., (1978) reported that the extraglandular aromatization of androgens increases with increasing body weight.

Thus, at puberty or later, obesity could be the initiating factor in polycystic ovarian disease.

The initiation is by increasing estrone production and consequently altering pituitary gonadotropin secretion (Yen, 1980).

Bates and Whitworth (1982) found that simple weight loss reduced plasma androgen in some women with androgen excess and restored cyclic ovulation.

GENETIC ASPECTS IN POLYCYSTIC OVARIAN DISEASE

There have been sporadic reports of abnormal karyotypes in patients with polycystic ovarian disease.

But that reports have not been confirmed in systematic studies of sizable groups of individuals.

Several investigators (Cooper et al., 1968; Givens et al., 1971; and McDonough et al., 1972) have provided information regarding familial patterns in polycystic ovarian disease.

The findings in one study of 18 families (Cooper et al., 1968) were compatable with autosomal dominant transmission.

Others (Givens et al., 1971) have believed that X-linked transmission could not be ruled out.

The broad range of clinical findings (from a small cystic ovary on one side and a streak ovary on the other side, to Turner phenotypes with polycystic ovaries, and mosaicism such as 46XX/45X) are consistent with the variability of X-linked disorders in general.

Twins with polycystic ovaries and a normal sibling have been reported (McDonough et al., 1972).

All three siblings had elevated urinary pregnanetriol levels.

In two families in which there were women with polycystic ovarian disease, three of the women had low testosterone values and high luteinizing hormone/ Follicle stimulating hormone ratio (Givens et al., 1971).

The genetics implications of 3 B-Ol-dehydrogenase deficiency in some patients with polycystic ovarian disease (Axelord et al., 1965; Lobo et al., 1980; and Lorber et al., 1978) remain to be clarified.

Emotional stress

The menarche and ultimately ovulation result from activation of the hypothalamic pituitary ovarian system to its final step of its maturation.

The above is thought to result from a signal originating in the central nervous system.