بسم الله الرحمن الرحيم

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الالكتروني والميكروفيلم

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COLOUR DOPPLER CHANGES IN POLYCYSTIC OVARY AND ITS RELATION TO DIFFERENT THERAPEUTIC MODALITIES

Thesis
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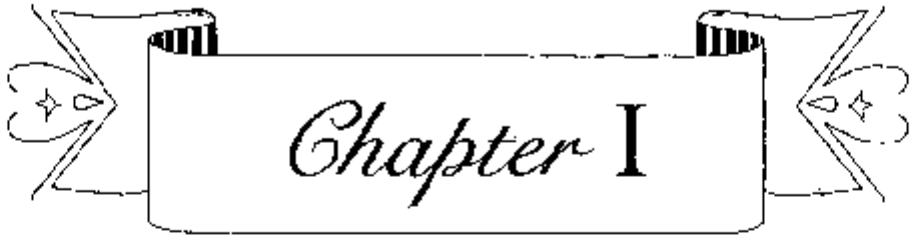

INTRODUCTION

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Polycystic ovarian syndrome (PCOS) has been a subject of interest and investigations for over 50 years. Because it is not a discrete disease, however, but rather a spectrum of symptomatology, pathology, and laboratory findings, a complete description of its etiology and pathogenesis has not been elucidated. What has evolved is the concept of polycystic ovarian syndrome as a self perpetuating cycle resulting in a state of chronic hormonal imbalance; representing a spectrum of manifestations, involving contribution from the hypothalamus, pituitary, ovaries, and adrenal and extraglandular tissues[1] and is usually associated with oligo-ovulation, hirsutism, infertility and unique ovarian morphology.[2]

Historical background:

Gross sclerocystic changes in the human ovary were first described by Chereau in 1845, and partial resection of such ovaries was being practiced before 1897 in Europe by Gusserow et al..[3] Several years later, Findley[4] 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[5] to a clinical syndrome consisting of "menstrual irregularity featuring amenorrhea, a history of sterility, masculine type of hirsutism, and less consistently retarded breast development and obesity. At this point of time no mention was made of a hormonal abnormality. However, it is now known that clinical and biochemical variability are very common in these patients, and if one were to adhere strictly to the original

description for diagnosis, a large number of cases would go undetected. Consequently, the eponym "Stein-Leventhal Syndrome" has fallen into disuse, and polycystic ovarian syndrome (PCOS) has been adopted as the generic description for a broad spectrum of abnormalities in women with a characteristic endocrine dysfunction.[6] The spectrum of symptoms and signs of PCOS was complied in by Goldzieher an Axelrod[7] from 1,079 cases reported in the scientific literatures.

Prevalence of polycystic ovaries in anovulatory, hirsute and normal subjects:

Although it is well recognized that women with PCOS frequently present with infertility,[8] there are few data in the literature which address the question of how common polycystic ovaries are in women with anovulatory infertility. Franks et al[9] assessed the prevalence of polycystic ovaries in a population of patients attending a gynecological endocrine clinic with menstrual disturbances, hirsutism or both (Table 1). The vast majority of women with oligomenorrhea were found to have polycystic ovaries on ultrasound (87%) but, more surprisingly, those with regular ovulatory cycles who presented with hirsutism also had a high prevalence of polycystic ovaries (92%). The appearance of polycystic ovaries in women with regular ovulatory cycles was an important finding since it suggests that the polycystic ovary represents a primary ovarian abnormality rather than the response of the ovary to chronic anovulation.[10]

Table 1. Prevalence of polycystic ovaries on ultrasound in women with anovulation and/or hirsutism[9]

Presenting symptoms	Prevalence of PCO (%)	LH (U/ml)		T (nmol/L)	
		Median	Range	Mean	SD
Oligomenorrhea	87	13.9	4.0-42	3.3	1.2
Hirsutism (regular cycle)	92	9.9	5.0-15	2.6	0.9
Normal controls	-	5.3	2.0-14	1.7	0.4

Polson et al[1] examined a large group of volunteers from the normal population. All these women considered themselves to be normal and had not presented to a physician for treatment of menstrual disturbances or symptoms of hyperandrogenemia. They found that 22% of 257 women who presented for ultrasound scans had polycystic ovaries. There was a strong correlation between the cycle history and the ovarian appearance, so that the majority of women in the normal population who had polycystic ovaries had slightly irregular cycles. Furthermore, although the mean and median serum LH concentrations in women with polycystic ovaries were not different from those in women with normal ovaries, there was a difference in the distribution of LH concentrations such that there was a preponderance of higher levels in those with polycystic ovaries.

Structure of the Polycystic Ovary:

1. Histological features:

There have been numerous studies documenting the morphology of the polycystic ovary,[8,12-18] but few have made a concerted attempt to quantitate the histological features which distinguish the polycystic from the normal ovary. Hughesdon,[19] reported that polycystic ovaries obtained after a full thickness wedge resection were typically increased in size, although normal sized ovaries with all the other characteristic histological features of polycystic ovaries were observed. An important feature of the polycystic ovary was that, although the average number of the primordial follicles was the same as in a normal ovary, the number of ripening and atretic follicles are doubled (Table 2). Thus all stages of folliculogenesis are increased in the polycystic ovary but the proportion of immature, mature and atretic follicles are similar to those observed in the normal ovary. There is a tendency for the tunica to be increased and to contain many collagen fibers. There is a slight increase in the cortical stroma but the subcortical stroma is greatly increased (5 times) with the appearance of many small blood vessels and nerves, particularly in the hilar region. Small nests of hilar cells (which on electron microscopy show features of steroid-secreting cells) are also commonly found in the polycystic ovary.[20]

The increased stroma which is so characteristic of the polycystic ovary appears to be derived primarily from atretic follicles. During atresia there is a striking hypertrophy of the theca cells[20] which then disperse into the interstitial tissue, often accumulating around small blood vessels.[19] It is the increased population of the atretic follicles which accounts for the previously described "theca cell hyperplasia", but it is

important to realize that this is probably a normal function of atresia itself rather than an abnormality which affects developing follicles in the polycystic ovary. Primary mesenchymal hyperplasia may also contribute to the increase in stroma but appears to play a lesser part in the genesis of the polycystic ovary than the theca-derived cells.[19]

Table 2. Ovarian cross-sectional area and follicle count in polycystic and control ovaries[19]

	size (cm^2)	Primordial Follicles	Follicle count/section		
			Immature	Mature	Atretic
Polycystic ovaries	9.7	81	3.7	1.4	12.4
normal	5	80	1.8	0.7	5.2

It remains unclear whether the increased androgen production from the polycystic ovary is simply a feature of the increased number of (luteinizing hormone-responsive) theca-interstitial cells or whether the cells themselves are qualitatively different, in their steroidogenic capacity, from those in the normal ovary.

2. *Ultrasound diagnostic criteria of polycystic ovaries*:

The increased number of follicles, and in particular the medium-sized to large antral follicles (2-10 mm in diameter) can be readily visualized using high resolution ultrasound scanning. Ultrasound will also demonstrate the increased stroma which typifies the polycystic ovaries.[9,12,22,23] The basis of the diagnosis (using the transabdominal route of scanning) is the finding of ten or more follicles, in one plane, together with increased stroma. Identification of increased stroma is relatively straightforward when the overall ovarian volume is increased (i.e. greater than 9 cm^2)

but is more difficult to assess if the ovary is of normal volume The appearance then has to be differentiated from that of the so-called multifollicular ovary.[21] This is observed during normal puberty and in women with mild or partially-recovered weight loss-related hypothalamic amenorrhea and is associated with a slowing of luteinizing hormone pulses.[24] In such cases the ovary is normal in size or slightly increased in volume and there is an increased number of follicles. However, the stroma is not increased and can be distinguished quite clearly from the normal-sized polycystic ovary. It is clear that transvaginal ultrasonography allows the definition of a larger number of small follicles than transabdominal scanning does even in the normal ovaries.[24]

3. Correlation of ultrasound with histology

It is important, when possible, to support the findings of ultrasound by those of histology. In a recent study Saxton et al[25] showed an excellent correlation between the morphological appearance as observed on ultrasound and that seen on histology. These observations lend confidence to the assertion that ultrasound can be reliably used for the diagnosis of polycystic ovaries.

4. Color Doppler

In the last decade Doppler ultrasound has gained importance in obstetrics and gynecology. Doppler ultrasound gives information about blood flow.

Potentials of Doppler ultrasound application in gynecology ar still not very well explored. However, despite tremendous efforts and research interest from all around the world, promising results from Doppler research in Gynecology are still far from

practical and routine clinical application. There are many objective and subjective reasons for that situation such as: low results reliability and reproducibility, high technique complexity, inadequate education and knowledge of pelvic haemodynamics, lack of standardization in Doppler measurements, cost-benefits issues (Doppler machines are usually very expensive), question whether Doppler should be used as a screening tool or as a secondary or even tertiary test, interpretation of results, time consuming procedure, etc...

For intelligent and successful application of the technique to medical diagnosis,an understanding of Doppler physics, its possibilities and limitations are necessary. Flow can be detected even in vessels that are too small to image e.g. ovarian vessels. Doppler ultrasound can determine the presence or absence of flow, flow direction, and flow character.