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A REVIEW- ON POLY CYSTIC OVARY SYNDROME

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ABSTRACT
Polycystic ovarian syndrome (PCOS) affects 4% to 12% of women of reproductive age. The lack of well defined diagnostic criteria makes identification of this common disease confusing to many clinicians. Also, with the varied manifestations of the disorder a patient may present to any one of several providers: an internist, family practitioner, nurse practitioner, pediatrician, gynecologist, dermatologist, or endocrinologist. Furthermore, the most distressing aspect of PCOS for any given patient may change over time, from hirsutism as a teenager to infertility as a young adult–potentially requiring several different providers along the way. It is important, therefore, that those caring for these patients understand not only the management issues pertinent to their specialty, but also appreciate the other potential health risks in these women. Recent insights into the pathophysiology of PCOS have shown insulin resistance to play a substantial role and as such have brought the long-term issues of type 2 diabetes mellitus and its resultant increased risk of coronary artery disease to the forefront. No longer can irregular menses and/or hirsutism be thought of as benign nuisances.

KEY WORDS
PCOs, hirsutism, insulin resistance.

INTRODUCTION:

Polycystic ovary syndrome (PCOS) is a condition that causes irregular menstrual periods because monthly ovulation is not occurring and levels of androgens (male hormones) in women are elevated [1]. The condition occurs in about 5 to 10 percent of women. The elevated androgen levels can sometimes cause excessive facial hair growth, acne, and/or male-pattern scalp hair thinning. Most, but not all, women with PCOS are overweight or obese, and they are at higher than average risk of developing diabetes and obstructive sleep apnea.

Although PCOS is not completely reversible, there are a number of treatments that can reduce or minimize bothersome symptoms [2]. Most women with PCOS are able to lead a normal life without significant complications.

Cause:

The cause of polycystic ovary syndrome (PCOS) is not completely understood. It is believed that abnormal levels of the pituitary hormone luteinizing hormone (LH) and high levels of male hormones (androgens) interfere with normal function of the ovaries.

Normal menstrual cycle — the brain (including the pituitary gland), ovaries, and uterus normally follow a sequence of events once per month; this sequence helps to prepare the body for pregnancy [3].

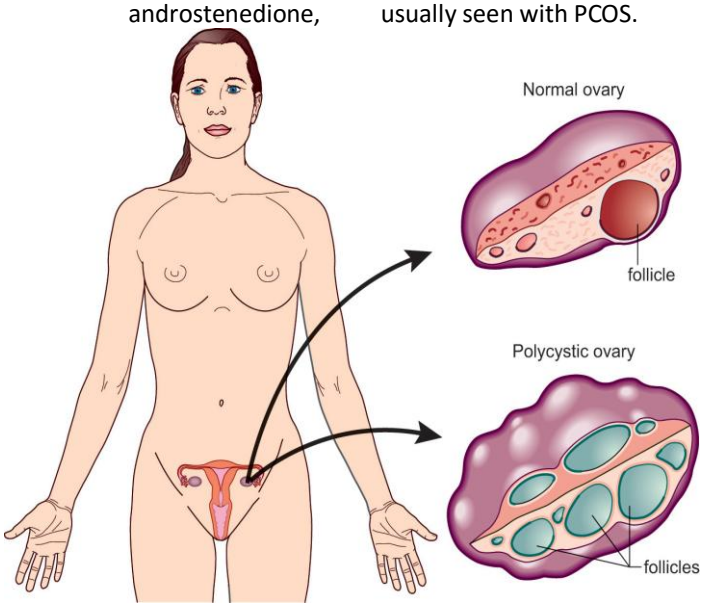
Two hormones, follicle-stimulating hormone (FSH) and LH, are made by the pituitary gland. Two other hormones, progesterone and estrogen, are made by the ovaries.

During the first half of the cycle, small increases in FSH stimulate the ovary to develop a follicle that contains an egg (oocyte)[4]. The follicle produces rising levels of estrogen, which cause the lining of the uterus to thicken and the pituitary to release a very large amount of LH. This midcycle "surge" of LH causes the egg to be released from the ovary (called ovulation)[5]. If the egg is fertilized by a sperm it develops into an embryo which travels through the fallopian tube to the uterus. After ovulation, the ovary produces both estrogen and progesterone, which prepare the uterus for possible embryo implantation and pregnancy.

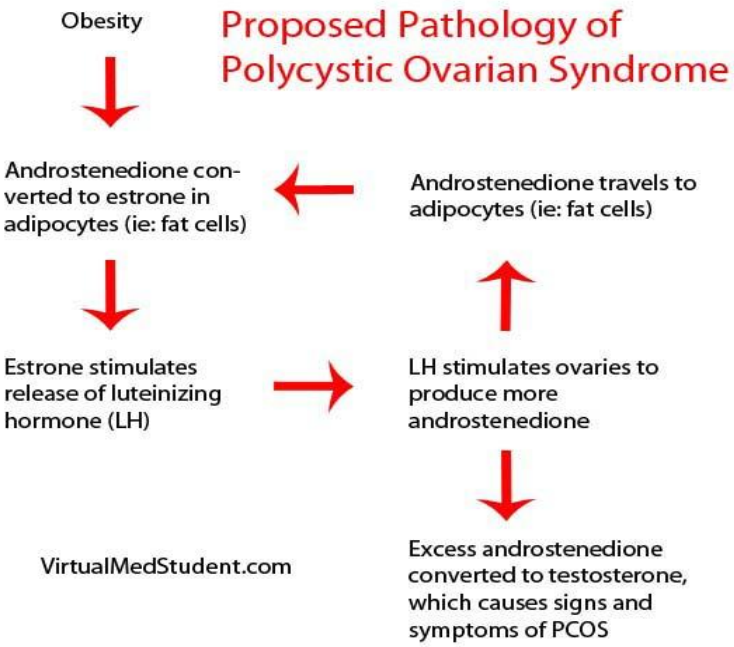
Menstrual cycle in PCOS — In women with PCOS, multiple small follicles (small cysts 4 to 9 mm in diameter) accumulate in the ovary, hence the term polycystic ovaries. None of these small follicles are capable of growing to a size that would trigger

ovulation [6]. As a result, the levels of estrogen, progesterone, LH, and FSH become imbalanced.

Androgens are normally produced by the ovaries and the adrenal glands. Examples of androgens include testosterone, androstenedione, dehydroepiandrosterone (DHEA), and DHEA sulfate (DHEA-S). Androgens may become increased in women with PCOS because of the high levels of LH, but also because of high levels of insulin that are usually seen with PCOS.



Pathophysiology of PCOS:



PCOS symptoms

Menstrual irregularity — If ovulation does not occur, the lining of the uterus (called the endometrium) does not uniformly shed and regrow as in a normal menstrual cycle. Instead, the endometrium becomes thicker and may shed irregularly, which can result in heavy and/orprolonged bleeding[7]. Irregular or absent menstrual periods can increase a woman's risk of endometrial overgrowth (called endometrial hyperplasia) or even endometrial cancer [8].

Weight gain and obesity — PCOS is associated with gradual weight gain and obesity in about one-half of women. For some women with PCOS, obesity develops at the time of puberty [9].

Hair growth and acne — Male-pattern hair growth (hirsutism) may be seen on the upper lip, chin, neck, sideburn area, chest, upper or lower abdomen, upper arm, and inner thigh. Acne is a skin condition that causes oily skin and blockages in hair follicles [10].

Insulin abnormalities — PCOS is associated with elevated levels of insulin in the blood. Insulin resistance and hyper insulinemia can occur in both normal-weight and overweight women with PCOS[11]. Among women with PCOS, up to 35 percent of those who are obese develop impaired glucose tolerance ("prediabetes") by age 40 years, while up to 10 percent of obese women develop type 2 diabetes. The risk of these conditions is much higher in women with PCOS compared with women without PCOS [12]. A family history of diabetes, overweight and obesity, as well as race and ethnicity (particularly African American and Hispanic) can increase the likelihood of developing diabetes among women with PCOS [13].

Infertility — many women with PCOS do not ovulate regularly, and it may take these women longer to become pregnant. An infertility evaluation is often recommended after 6 to 12 months of trying to become pregnant [14].

Heart disease — Women who are obese and who also have insulin resistance or diabetes might have an increased risk of coronary artery disease, the narrowing of the arteries that supply blood to the heart [15]. It is not known for sure if women with PCOS are at increased risk for this condition. Both weight loss and treatment of insulin abnormalities can decrease this risk [16].

Sleep apnea — Sleep apnea is a condition that causes brief spells where breathing stops (apnea) during sleep. Patients with this problem often experience fatigue and daytime sleepiness [17]. In addition, there is evidence that people with untreated sleep apnea have an increased risk of insulin resistance, obesity, diabetes, cardiovascular problems, such as high blood pressure, heart attack, abnormal heart rhythms, or stroke. This risk may be changes in heart rate and blood pressure that occur during sleep [18].

PCOS diagnosis

Baseline screening laboratory studies for women suspected of having PCOS include the following:

Thyroid function tests (eg, TSH, free thyroxine)

- Serum prolactin level
- Total and free testosterone levels
- Free androgen index
- Serum hCG level
- Cosyntropin stimulation test
- Serum 17-hydroxyprogesterone (17-OHPG) level
- Urinary free cortisol (UFC) and creatinine levels
- Low-dose dexamethasone suppression test
- Serum insulinlike growth factor (IGF)–1 level[19]
- Other tests used in the evaluation of PCOS include the following:
- Androstenedione level
- FSH and LH levels
- GnRH stimulation testing
- Glucose level
- Insulin level
- Lipid panel

The following imaging studies may be used in the evaluation of PCOS:

- Ovarian ultrasonography, preferably using transvaginal approach[20]
- Pelvic CT scan or MRI to visualize the adrenals and ovaries[21]

PCOS Treatment:

Oral contraceptives — Women with PCOS occasionally ovulate, and oral contraceptives are useful in providing protection from pregnancy[22]. Although an OC allows for bleeding once per month, this does not mean that the PCOS is "cured;" irregular cycles generally return when the OC is stopped [23].

Progestin — Another method to treat menstrual irregularity is to take a hormone [24]called progestin (sample brand name: Provera) for 10 to 14 days every one to three months[25]. This will induce a period in almost all women with PCOS, but it does not help with the cosmetic concerns (hirsutism and acne) and does not prevent pregnancy. It does reduce the risk of uterine cancer [26].

Hair treatments — in women with PCOS, hormonal treatment of excess hair growth is typically approached in a two step process [27]. The first step is to prescribe an estrogen-progestin contraceptive (ie, a birth control pill)[28]. If after six months of hormone treatment sufficient improvement in excess hair growth has not been achieved [29], a second medication called spironolactone, an antiandrogen, is added [30]. If hormone treatment with an estrogen-progestin results in a satisfactory reduction in excess hair growth, this therapy is continued [31].

Weight loss — Weight loss is one of the most effective approaches for managing insulin abnormalities, irregular menstrual periods, and other symptoms of PCOS [32]. For example, many overweight women with PCOS who lose 5 to 10 percent of their body weight notice that their periods become more regular [33]. Weight loss can often be achieved with a program of diet and exercise [34].

Metformin — Metformin (sample brand name: Glucophage) is medication that improves the effectiveness of insulin produced by the body [35]. It was developed as a treatment for type 2 diabetes but may be recommended for women with PCOS in selected situations [36].

If a woman does not have regular menstrual cycles [37], the first-line treatment is a hormonal method of birth control, such as birth control pills[38]. If the woman cannot take birth control pills, one alternative is to take metformin;[39] a progestin is usually recommended, in addition to metformin, for six months or until menstrual cycles are regular[40].

Metformin may help with weight loss [41]. Although metformin is not a weight-loss drug, some studies have shown that women with PCOS who are on a low-calorie diet lose more weight when metformin is added [42]. If metformin is used, it is essential that diet and exercise are also part of the recommended regimen because the weight that is lost in the early phase of metformin treatment may be regained over time [43].

Treatment of infertility — If tests determine that lack of ovulation is the cause of infertility, several treatment options are available. These treatments work best in women who are not obese[44].

The primary treatment for women who are unable to become pregnant and who have PCOS is weight loss [45]. Even a modest amount of weight loss may allow the woman to begin ovulating normally. In addition, weight loss can improve the effectiveness of other infertility treatments [46].

Clomiphene is a US Food and Drug Administration (FDA)-approved oral medication that stimulates the ovaries to release one or more eggs [47]. It triggers ovulation in about 80 percent of women with PCOS, and about 50 percent of these women will become pregnant [48].

If a woman does not ovulate or is unable to conceive with clomiphene, gonadotropin therapy (follicle-stimulating hormone [FSH] injections) may be recommended [49]. Ovulation occurs in almost all women with PCOS who use gonadotropin therapy; approximately 60 percent of these women become pregnant [50].

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