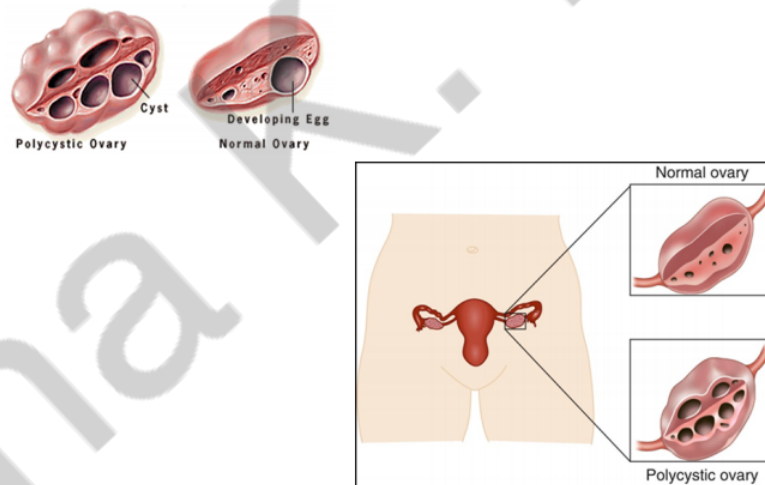# *Polycystic Ovary Syndrome*

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INTRODUCTION

Polycystic Ovary Syndrome (PCOS), also known as the Stein-Leventhal Syndrome, is the most common hormonal disorder in women of reproductive age. The main features of PCOS include irregular periods, excess androgen levels, and polycystic ovaries[1]. Androgen hormones are responsible for binding to androgen receptors, thus regulating the development and maintenance of male characteristics. It is for this reason that one of the defining features of a woman with PCOS, along with other symptoms, is the development of excess facial or body hair. Polycystic ovaries describe enlarged ovaries that contain many fluid-filled follicles that surround the eggs. These polycystic ovaries can be up to 8mm in size, and are unable to release an egg, meaning that ovulation does not occur. Figure 1 shows a polycystic ovary in comparison to a normal ovary.

Figure 1: Normal compared to a polycystic ovary, retrieved from Nutrition Therapy and Pathophysiology[2].

As is evidenced, the polycystic ovary is larger than normal, with multiple bubble-like follicles developing on the surface as partially mature eggs that swell up, but fail to open. In a woman with PCOS, these follicles can reach up to 25 or more in number. On the other hand, the normal ovary has a single developing egg, which is eventually released. Types of PCOS can be classified into four major groups: insulin-resistant, pill-induced, inflammatory, and hidden

polycystic ovary syndrome[3]. Each type has its own prevalence and causes, and thus its own approach to treatment. There are both genetic and environmental factors that influence the development of PCOS, regardless of the type. Although there is no cure for PCOS, the symptoms can be managed using a treatment plan, and today it is possible to live a relatively normal life with this syndrome.

DIAGNOSIS

The modern diagnostic criteria can be traced back to the 1800s, with the discovery of polycystic ovaries. However, at this time there was no known connection to a larger cause. Later in the 1990s, the National Institutes of Health (NIH) and National Institute of Child Health and Human Development (NICHD) recognized menstrual irregularity and hyperandrogenism as part of the syndrome's potential symptomatic traits. The first diagnostic criteria for PCOS was published by American gynecologists Irving F. Stein, Sr. and Michael L. Leventhal. They suggested that for a patient to be diagnosed as having Stein-Leventhal syndrome, they must have enlarged ovaries, obesity, anovulation, and excessive hair growth, also known as hirsutism[2]. Since this discovery, the criteria of diagnosis has been up for debate, with some arguing the collection of symptoms as being a gynecological problem, and other insights suggesting it is more of a multisystem disorder. This is due to the fact that there is a wide spectrum of symptoms possible, hence the use of the word "syndrome" in the name, and not all are experienced by women with PCOS. For example, only 15% of people with PCOS have cysts in their ovaries[4]. Due to the fact that not all the symptoms are experienced by women who have PCOS, an alternative diagnosis was decided upon, that is used today. While used interchangeably with PCOS, the Stein-Leventhal syndrome is primarily used for the subset of women with all the original symptoms intended for its criteria.

The Rotterdam criteria was first sponsored by the NIH/NICHD in a consensus workshop. At the time, it was suggested that a person has PCOS if they have all of the following: oligoovulation, which is abnormalities in the menstrual cycle, signs of androgen excess, and the exclusion of other disorders that can result in the first two symptoms[5]. Over time, this criteria was further researched so that the definition is wider. According to the 2003 Rotterdam criteria, diagnosis requires the presence of at least two of the following: hyperandrogenism, ovulatory dysfunction, and polycystic ovaries[6]. The 2009 Androgen Excess and PCOS society criteria, on the other hand, specifies that the patient must have clinical or biochemical evidence of hyperandrogenism, and either oligomenorrhea, which is defined as menstrual cycle length of greater than 35 days, and/or polycystic ovaries. The primary difference here is that in order for a patient to have PCOS, they have to have evidence of high levels of androgenism. Figure 2 indicates a table taken from a medical journal that compares and summarizes the 1990 NIH criteria, the 2003 Rotterdam criteria, and the 2009 Androgen Excess and PCOS society criteria.

Table 1. Criteria for Diagnosis of PCOS

Clinical finding	National Institutes of Health criteria, 1990 (must have both of the findings marked below)	Rotterdam criteria, 2003 (must have any two of the findings marked below)	Androgen Excess and PCOS Society, 2009 (must have A plus either B or C)
Hyperandrogenism*	X	X	A
Oligomenorrhea	X	X	B
Polycystic ovaries		X	C

PCOS = polycystic ovary syndrome.

*—Clinical or biochemical evidence of excess androgen.

Information from reference 19.

Figure 2: A comparison of the different diagnostic criterias, retrieved from AAFP[6].

In addition to the previous criteria specifics, the diagnostic workup should consider the patient's history and physical examination. These include the menstrual history, weight fluctuations, subcutaneous findings, and their impact on the PCOS symptoms. It is worth noting

that the International Diabetes Federation (IDF) has different waist circumference measurements when determining central obesity, depending on the ethnicity of the individual. This is shown in Figure 3, which outlines the different waist circumference cut-offs in the different ethnic groups.

Category	Measurement
Caucasian, African American, Hispanic, and Native American males	>40 inches (>102 c m)
Caucasian, African American, Hispanic, and Native American females	>35 inches (>88 c m)
Asian males	≥35.4 inches (≥90 c m)
Asian females	≥31.5 inches (≥80 c m)

Figure 3: Waist circumference measurement cut offs for each ethnic category, retrieved from Nutrition Therapy and Pathophysiology[2].

ETIOLOGY AND PREVALENCE

With different criterias to diagnose PCOS, it can be difficult to pinpoint the exact statistical prevalence of those with PCOS. According to the World Health Organization (WHO), 116 million women worldwide as of 2010 were affected by PCOS[7]. A study using the Rotterdam criteria concluded that around 18% of women had PCOS, and approximately 70% of them were previously undiagnosed. Evidently, there needs to be a deeper understanding of the syndrome in order to reduce the number of undiagnosed cases. The different types of PCOS exhibit varying prevalence, with some being more easy to diagnose than others. Insulin-resistant PCOS is the most common type, with 70% of PCOS women being insulin-resistant[2]. This, along with pill-induced PCOS, is the more easily-diagnosable type. Inflammatory and Hidden PCOS can be significantly more difficult to diagnose, with the former more commonly misdiagnosed, and the latter showing too few outward symptoms.

While genetics plays a large role in the prevalence of the syndrome, risk factors such as obesite, lack of physical exercise, and other environmental factors play an important role. In fact, a study showed that there is a much lower prevalence of 5% in lean individuals compared to 28% in those that are overweight and obese[2]. The genetic component of PCOS is what requires the

most understanding, as it can help with targeting the diagnosis of those who exhibit little to no symptoms. Although PCOS is more commonly associated with women since the existence of ovaries is needed to exhibit the abnormalities that characterize the syndrome for what it is, 80% of paternal transmission occurs when the father is affected with the gene, compared to only 45% in material transmission[2]. This supports the argument that despite the fact that either parent can transmit the gene, the father carrying the gene can more likely impact the children. For this reason, it is suggested that any female sibling of a person with PCOS should be tested, even if there are no outward symptoms. In these cases, more than half of all these female siblings end up having some degree of PCOS. Men will not experience the same symptoms, but may have hypothyroid, metabolic syndrome, heart problems, poor lipid profile, the inability to grow a full beard, or premature balding[2].

PATHOPHYSIOLOGY

To better understand the causes behind the physiological symptoms of people in PCOS, it is important to address the pathophysiology involved. Figure 4 outlines the pathophysiology of PCOS in a flowchart. As can be seen, the combination of genetics, obesity, living a sedentary lifestyle, and high androgen levels, directly results in insulin-resistance and increased GnRH pulsatile release. These cause an increase in LH:FSH ratio, due to an increase in LH by the anterior pituitary gland,[8] and hyperinsulinemia respectfully. Hand-in-hand, these two contribute directly to the hyperandrogenism found in PCOS patients, which then leads to anovulation and/or polycystic ovaries. Anovulation, or the absence of egg release, can result in anovulatory bleeds, decreased progesterone levels, and subfertility. The decreased levels of progesterone allows for the uncontrolled increase of estrogen, which increases the risk of endometrial cancer.
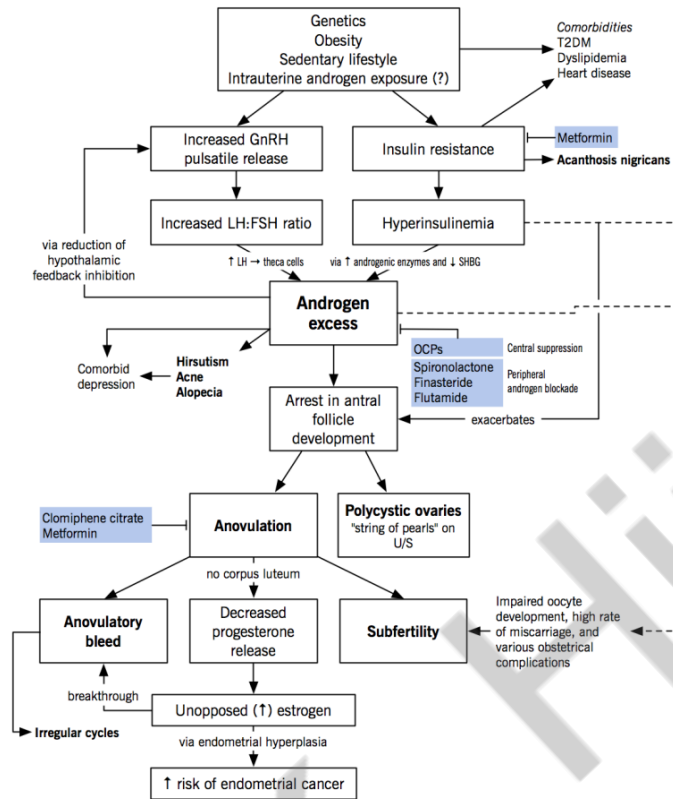
Genetics
Obesity
Sedentary lifestyle
Intrauterine androgen exposure (?)

Comorbidities
T2DM
Dyslipidemia
Heart disease

Increased GnRH pulsatile release

Insulin resistance — Metformin
Acanthosis nigricans

Increased LH:FSH ratio

Hyperinsulinemia

via reduction of hypothalamic feedback inhibition

↑ LH → theca cells

via ↑ androgenic enzymes and ↓ SHBG

Androgen excess

Comorbid depression

Hirsutism
Acne
Alopecia

OCPs
Spironolactone
Finasteride
Flutamide

Central suppression

Peripheral androgen blockade

Arrest in antral follicle development

exacerbates

Clomiphene citrate
Metformin

Anovulation

Polycystic ovaries
"string of pearls" on U/S

no corpus luteum

Anovulatory bleed

Decreased progesterone release

Subfertility

Impaired oocyte development, high rate of miscarriage, and various obstetrical complications

breakthrough

Unopposed (↑) estrogen

Irregular cycles

via endometrial hyperplasia

↑ risk of endometrial cancer

Figure 4: An outline of the pathophysiology of PCOS, retrieved from McMaster Pathophysiology Review[9].

Insulin-resistance in women with PCOS is not limited to overweight and obese women, however, having high abdominal fast can accelerate the insulin-resistence seen in this group. The fat cells in the body mobilize free fatty acids, which block the insulin action. This increases the levels of triglycerides, apolipoprotein B, and adenosine triphosphate in the blood, and as a result, VLDL production increases. High levels of VLDL can cause plaque to be deposited on the artery walls, accelerating inflammation. Additionally, inflammatory adipokines suppress insulin signaling, and inflammatory signals TNF-α, IL-6, LPS, and saturated free fatty acids activate inhibitory molecules, which suppress insulin signaling as well, and thus contributing to insulin resistance.

TREATMENT

In addition to the steps needed to be taken for a diagnosis to be made, a standard assessment using various tests is conducted to narrow down the target of treatment. A

gynecologic ultrasonography helps with locating the follicles, and a laparoscopic examination can help reveal the thickened outer surface of the ovary, although a laparoscopy is not routine for confirming a diagnosis of PCOS. Elevate blood levels of androgens, including androstenedione and testosterone, can be shown through biochemical tests. Although not necessary, blood tests of the LH:FSH ratio, if tested on the same day of the menstrual cycle, can help with the diagnosis. Finally, it is always worth testing glucose tolerance in women with risk factors, so to better prepare the treatment plan.

The two types of medications that can help PCOS include oral contraceptives and metformin. Oral contraceptives increase the sex hormone binding globulin production, allowing an increase in binding of free testosterone. This is done to reduce hirsutism symptoms, as well as to regulate normal period cycles. Metformin, commonly used in type 2 diabetes mellitus to reduce insulin resistance, can be used for similar purposes. Moreover, Metformin also supports ovarian function, and with helping to return to normal ovulation[10]. Metformin can cause various side effects, with diarrhea being a common experience in those who take it. This is due to the increase in intestinal chloride secretion, a direct result of the AMP-cAMP & AMPK mediation counterbalance that occurs when taking the medication[11].

There are also surgical procedures that can be used to help treat, or even cure, PCOS[12]. These, however, should only be considered after the patient has attempted medication, lifestyle changes, and medical nutrition therapy, extensively. Ovarian surgery is an option for those who have unmanageable symptoms, and do not wish to have any pregnancies in the future. In this surgery, electrocautery is used to abolish the parts of the ovaries. It is not guaranteed that this procedure will provide permanent results, or fix the problem of irregular menstrual cycle and ovulation. Furthermore, there are risks in doing such surgeries, including injury to the bowel,

bladder, and blood vessels. As a result of this procedure, it is possible for a woman to enter menopause early.

MEDICAL NUTRITION THERAPY

Before considering medication or surgical procedures, the patient is advised to make adjustments to their lifestyle through diet and exercise. Losing weight is one of the main objectives, especially since any success body fat can worsen clinical features, such as hyperinsulinemia and hyperandrogenism. Weight loss can help counteract these conditions and improve menstrual function by decreasing androgen levels and insulin resistance. Most times, lifestyle changes are targeted even if the patient is also taking medication, as a way to increase their chances of overcoming the symptoms. For example, the use of Metformin can aid with weight loss, as it lowers appetite with its insulin-controlling mechanisms. All-in-all, the American Association of Clinical Endocrinologists recommend a goal of 5-15% weight loss[13]. This may be difficult for some women, so the use of consistency in careful diet planning to help reduce symptom severity and risk factors is vital in ensuring that they feel some sort of progress, thus reducing the risk of developing issues in self-esteem, depression, anxiety, and eating disorders.

Various goals for PCOS are outlined in the Nutrition Care Manual[14]. For starters, they are recommended to eat a variety of fruits and vegetables every day, as well as nutrient-rich whole grains that are a good source of dietary fiber. Examples of these include bulgur, amaranth, whole-grain barley, buckwheat, oats, brown rice, quinoa, whole rye, and popcorn. Furthermore, the protein-rich foods they should target include lean meats and poultry, adding eggs to meals and snacks to add fullness and help manage blood sugar levels. In addition, foods high in omega-3 fatty acids are highly recommended, such as fatty fish, seeds, oils, and nuts. Finally, it is advised to stick to low-fat dairy foods, and limit foods and drinks that are high in added

sugars. In regards to lifestyle change specifications, it is suggested to eat 4 to 6 times a day, and to engage in some form of physical activity each day.

PROGNOSIS

According to the Nutrition Care Manual, women with PCOS are at a high risk for developing cardiovascular disease, type 2 diabetes mellitus, and metabolic syndrome. Therefore, when developing their nutrition goals, one should take this into consideration, and also target preventing any of these conditions[14]. Lesser-known risks of those with PCOS include the development of hypertension, sleep apnea, autoimmune thyroiditis, acanthosis nigricans, non-alcoholic fatty liver disease, and depression and/or anxiety. All of these are related to weight gain, however it is not clear if body dissatisfaction predominantly contributes to the emotional disturbances found in PCOS[2] .

CONCLUSION

Although there are no known prevention precautions to take with PCOS, being educated on the risk factors, genetic impact, and environmental triggers, can make a difference between someone who progresses it to a point of developing further complications, and someone that catches it early enough to make the necessary nutritional interventions. Regardless of the medical and technological advancements made in the healthcare industry, one thing that remains certain is the current and future need to take multidisciplinary action when dealing with syndromes such as PCOS. Furthermore, more attention needs to be paid to the men who are carriers but do not have outward symptoms, as they play a large role in passing the genes on that put their children at risk. All of these improvements that can help reduce the impact of PCOS, and thus the emotional and financial strain of those diagnosed with or close to someone diagnosed with PCOS, come down to targeting the education system of future generations, and of those already in the healthcare system.

REFERENCES

1. Polycystic ovary syndrome. nhs.uk. Published October 20, 2017. Accessed November 27, 2020. https://www.nhs.uk/conditions/polycystic-ovary-syndrome-pcos/

2. Nelms M, Sucher K. Nutrition Therapy & Pathophysiology. 4th ed. Cengage Learning; 2020.

3. Types of PCOS | Symptoms of PCOS | Treatment of PCOS. indiraivf. Published May 30, 2019. Accessed November 27, 2020. https://www.indiraivf.com/types-of-pcos/

4. Dunaif A, Fauser BCJM. Renaming PCOS—A Two-State Solution. J Clin Endocrinol Metab. 2013;98(11):4325-4328. doi:10.1210/jc.2013-2040

5. Scott R. Polycystic Ovarian Syndrome. Medscape. Published 2019. Accessed November 27, 2020. https://emedicine.medscape.com/article/256806-overview#showall

6. Williams T, Mortada R, Porter S. Diagnosis and Treatment of Polycystic Ovary Syndrome. AFP. 2016;94(2):106-113.

7. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. Accessed November 27, 2020. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6350784/

8. Luteinizing Hormone LH | Hormone Health Network. Accessed November 27, 2020. https://www.hormone.org/your-health-and-hormones/glands-and-hormones-a-to-z/hormones/luteinizing-hormone

9. Polycystic ovarian syndrome (PCOS) | McMaster Pathophysiology Review. Accessed November 27, 2020. http://www.pathophys.org/pcos/

10. Metformin in polycystic ovary syndrome: systematic review and meta-analysis. Accessed November 27, 2020. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC259161/

11. Ovarian surgery to cure PCOS. Conquer. Published January 29, 2020. Accessed November 27, 2020. https://conquerpcos.org/ovarian-surgery-to-cure-pcos/

12. Metformin (Glucophage) and Weight Loss. Accessed November 27, 2020. https://www.diabetes.co.uk/diabetes-medication/metformin-weight-loss.html

13. Garvey WT, Mechanick JI, Brett EM, et al. American Association of Clinical Endocrinologists and American College of Endocrinology Comprehensive Clinical Practice Guidelines for Medical Care of Patients with Obesity. Endocr Pract. 2016;22 Suppl 3:1-203. doi:10.4158/EP161365.GL

14. NutritionForPolycysticOvarianSyndrome(PCOS)FINAL.pdf. Accessed November 27, 2020. https://scandpg01-prd.s3.amazonaws.com/resources/DOCS/FactSheets/NutritionForPolycysticOvarianSyndrome(PCOS)FINAL.pdf