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Polycystic ovary syndrome: Diagnosis and management

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Abstract: *Polycystic ovary syndrome (PCOS) is a common endocrine disorder. Patients may present with a combination of hyperandrogenism symptoms, menstrual irregularities, metabolic syndrome, infertility, acne, and obesity. PCOS diagnosis is based on three diagnostic guidelines. Treatment options include oral contraceptive pills, antiandrogens, and metformin. NPs can improve diagnosed patients' quality of life through education about this disorder.*

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Polycystic ovary syndrome (PCOS) is a common endocrine, metabolic, and menstrual disorder in women.¹ Stein and Leventhal first discussed PCOS in 1935 when patients presented with a host of endocrine issues, such as amenorrhea, polycystic ovaries, and hirsutism.² It is now acknowledged as a disorder that can affect women for the duration of their lives and can present with variable signs and symptoms.³

Gynecologists and endocrinologists have managed this disorder in the past, but increased disorder

prevalence has led to primary care management as well. PCOS prevalence is now between 6% and 10% based on the US National Institutes of Health (NIH) criteria and as high as 15% when based on the broader Rotterdam criteria.⁴ A prevalence of 15% to 20% is possible under other guideline criteria.⁵ The prevalence necessitates that primary care NPs broaden their knowledge base about PCOS to help patients manage symptoms and address complications that may arise from PCOS, such as difficulty becoming pregnant.

Keywords: *acne, fertility, hirsutism, hyperandrogenism, insulin resistance, lifestyle management, metabolic syndrome, obesity, PCOS, polycystic ovary syndrome, primary care*

■ Clinical presentation

NPs should suspect PCOS if a reproductive-age woman presents with any of the following hyperandrogenism symptoms: acne, hirsutism, and/or male pattern baldness.⁵ PCOS should be even higher on the differential list if the patient also presents with irregular menstrual cycles and/or infertility. Patients also may present with obesity and insulin resistance symptoms. The symptoms of obesity and insulin resistance also are found in metabolic syndrome, and research suggests that women with PCOS have an increased incidence of metabolic syndrome.³ Women with a PCOS diagnosis can present with one or more of the above signs and symptoms.

Acne lesions are graded on a mild, moderate, or severe scale. This is often a subjective scale, unless face planes are divided and lesions are individually counted. Acne in patients with PCOS often is composed of severe cystic lesions. Acne with this diagnosis is related to hyperandrogen production and the sebaceous glands and follicles in the skin.⁶ Acne resistant to treatment indicates an even a stronger correlation to PCOS.⁶ It is important for NPs to examine menstrual cycle patterns in patients with acne as they may indicate potential PCOS diagnosis.^{3,7}

Hirsutism is seen in patients with PCOS with hyperandrogen production. Hirsutism develops gradually in these patients and intensifies with weight gain.⁶ Hirsutism is seen in about 70% of patients with PCOS.⁴ Hirsutism in PCOS is often seen on the upper lip, chin, face, chest, back, abdomen, arms, and thighs.³ Hirsutism severity can fluctuate with patients and the severity can be graded using the Ferriman-Gallwey Scale.⁸ This scale is subjective in nature and often is not necessary for diagnosis.

Male pattern baldness related to hyperandrogen production is seen in 10% of patients with PCOS.⁹ Women with hyperandrogenemia experience various hair-loss patterns; typically hair loss occurs at the vertex, crown, or in a diffuse pattern, whereas women with more severe hyperandrogenemia may see bitemporal or frontal hairline hair loss.⁶ This can be a very psychologically distressing presentation to a patient and may be the only presenting symptom of concern.

Alongside hyperandrogen symptoms, obesity and insulin resistance symptoms can also present problems for patients with undiagnosed PCOS. Studies

on obesity in PCOS have shown variable numbers, but the prevalence of obesity in PCOS may be as high as 76%.^{10,11} Increased body mass index (BMI) is connected to insulin resistance and hyperandrogen symptoms.⁴ Insulin resistance affects up to 65% to 70% of patients with PCOS.^{12,13} Insulin resistance may lead to metabolic-type symptoms that have a negative impact on a patient's overall health.¹⁴

Irregular menstrual cycles are a common chief complaint for patients in primary care. Women with PCOS may present with menstrual cycles that suggest infrequent menstrual bleeding (previously referred to as oligomenorrhea), amenorrhea, or unpredictable bleeding.^{3,15,16} Only 30% of patients with PCOS will have normal menstrual cycles.¹⁷ Women who are amenorrheic have the most severe hyperandrogen symptoms with their PCOS.⁴ It is imperative to discuss patients' menstrual cycles at each primary care visit, as this information can be essential in diagnosing PCOS.

Infertility with PCOS is frequently not evaluated until women attempt to conceive. Infertility is related

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to the anovulation that can occur in patients with PCOS. Menstrual cycles longer than 35 days are suggestive of anovulation.⁴ Cycle lengths of more than 32 days warrant further evaluation.⁶ Clinicians calculate cycle length by counting from the day the menstrual cycle starts to the day before the next cycle starts. Forty percent of patients with PCOS experience infertility.³

Adolescents. Adolescent females may present with similar symptoms for PCOS as adults. Biologic changes with puberty can trigger irregular cycles and acne, and anovulatory cycles are a normal finding as menstrual cycles are regulating.^{4,18} It is crucial that labs are drawn and for the patient to meet the criteria for PCOS before an accurate diagnosis can be made.⁴ During adolescent years, it may take time to establish a consistency of presenting symptoms and track the history of menstrual cycles. If there is a concern for PCOS, clinicians need to educate adolescent patients to track menstrual cycles to establish cycle length.

Perimenopause and menopause. Patients who are experiencing perimenopause and menopause

can often be even more challenging to diagnose with PCOS, as it is a disorder that is mainly symptomatic during reproductive years. They may report a long history of irregular cycles and hyperandrogen symptoms, but these symptoms do not continue as menstruation ceases.¹⁹ Reviewing menstrual cycle and hyperandrogenism histories during childbearing years may lead a healthcare provider to be suspicious of a past PCOS diagnosis.¹⁵ If not diagnosed before menstruation ceases, perimenopausal and menopausal women may only present with secondary symptoms associated with PCOS, such as obesity and metabolic symptoms.¹⁹

■ Diagnosis

Differentials. When evaluating for PCOS, it is important to rule out other endocrinopathies. Differential diagnoses for patients who have PCOS can include endocrine tumors, pseudo-PCOS related to obesity, insulin resistance, sex development disorders, virilizing congenital adrenal hyperplasia, ovarian steroidogenic blocks, thyroid disease, hyperprolactinemia, and androgenic drugs.^{5,15,20} After those are excluded, diagnostic criteria and labs can be considered, leading toward a PCOS diagnosis.

PCOS guidelines. As with all patients, begin with a thorough history and physical exam before beginning diagnostic studies. There are three diagnostic guidelines for PCOS: the NIH Criteria (1990), Rotterdam Criteria (2003), and the Androgen Excess and PCOS Society criteria (2009).²¹⁻²³ The NIH criteria requires the following: hyperandrogenism and oligomenorrhea in the absence of other androgen disorders.²¹ The Rotterdam Criteria must have two of the following: hyperandrogenism, oligomenorrhea, and/or polycystic ovaries.²² Lastly, the Androgen Excess and PCOS Society criteria require that patients with PCOS have hyperandrogenism and either oligomenorrhea or polycystic ovaries.²³ Each of these criteria require that patients have hyperandrogenism symptoms to establish a diagnosis of PCOS. Patients may show clinical or biochemical evidence to meet that hyperandrogenism standard.²⁴ The most commonly used guideline is the Rotterdam Criteria; the Endocrine Society recommends using this guideline.¹⁵

Labs and diagnostics. If a patient meets PCOS criteria under one of the guidelines, NPs should draw labs to confirm diagnosis. The initial lab panel should include a pregnancy test and thyroid panel, and also check prolactin, 17-hydroxyprogesterone, and testosterone levels.²⁴ Free testosterone is a more sensitive

measurement of androgen excess than a total testosterone level.⁶

New evidence has emerged linking elevated anti-müllerian hormone with PCOS.²⁵ This specialty lab cannot often be drawn in primary care clinics but is available in endocrinology and gynecology clinics. No international standard exists, so this lab is not included in current guidelines but this could shift in the future as more evidence emerges.⁵

Historically, luteinizing hormone (LH) and follicular stimulating hormone (FSH) levels were tested and the ratio was observed. If there was a 1:3 ratio between the two hormones, PCOS was suspected. This is not thought to be the case any longer, as the ratio can be misleading related to when it was drawn during the patient's menstrual cycle.⁵ If lab work establishes androgen excess, patients can continue to be worked up for PCOS.

Pelvic transvaginal ultrasound can help patients meet PCOS diagnostic criteria, but it is not necessary for diagnosis. If ovaries are observed to have 12 or more follicles by ultrasound, then they can be classified as polycystic ovaries.²⁴ Transvaginal ultrasound technology has improved to more frequently identify smaller follicles, improving diagnosis for PCOS. It is still important for NPs to look at overall ovarian size. A patient with PCOS not only will have more than 12 follicles but the ovary itself also must have a volume larger than 10 mL.⁶ If polycystic ovaries are diagnosed by ultrasound, patients can meet that standard for diagnostic criteria.

Adolescents. Adolescent females have cystic ovaries under normal conditions, so an ultrasound will not lead to a definitive diagnosis. Therefore, pelvic ultrasound is not critical for diagnosis in adolescents younger than age 17.⁶ If an adolescent patient has hyperandrogen symptoms with infrequent menstrual periods (oligomenorrhea), the NP can diagnose PCOS.¹⁵ After PCOS is diagnosed, it is not necessary to do fertility evaluation until the patient is ready to conceive.⁵ This is related to both fertility evaluation cost and limited clinician resources.

Perimenopause and menopause. If not diagnosed before the onset of menopausal symptoms, the presentation of PCOS in this patient population can be complex; patients who have reached perimenopause or menopause (roughly beginning in the mid-40s) do not fit into the other diagnostic criteria for PCOS.¹⁵ Testosterone levels and androgen levels go down in women who are in menopause, making the cardinal labs for PCOS noneffective for diagnosing.¹⁹ Postmenopausal

changes that occur lead healthy women to develop ovarian cysts; therefore, an ultrasound is not a helpful PCOS diagnostic in this patient population.¹⁹ If PCOS is not diagnosed before menopause, clinicians should not make this diagnosis. These patients do not meet diagnostic criteria.^{19,21-23}

■ Management

Treatment of patients with PCOS includes lifestyle changes and pharmacotherapy. (See *Educating patients with PCOS on lifestyle improvements*.) Treating hyperandrogenism and its effects are the primary goals of therapy for patients with PCOS. Before starting patients on any medication, it is important to discuss the risks and benefits with the patient so they understand the medication's role in PCOS treatment. Oral contraceptive pills (OCPs) are used for the treatment for patients not wanting to conceive.^{24,28} Estrogen-progestin combination pills help with hormone regulation and have the best chance at improving hyperandrogenism.²⁹ OCPs suppress LH production and lead to overall reduced androgen production.⁴ OCPs not only can improve a patient's hirsutism and/or acne, but also improve menstrual regularity.

To broaden overall options for patients, levonorgestrel intrauterine devices (IUDs) can be used for patients who do not reliably take OCP to prevent unwanted pregnancy. However, for PCOS treatment, both OCPs and an IUD, or an IUD with the addition of oral metformin, are necessary to help manage PCOS symptoms.²⁹ OCP use does include risks and is not meant for every patient. Smokers who are older than 35, those with a strong family history of heart disease, patients with a personal history of thromboembolic disorder of cerebrovascular disease, patients with clotting disorders, patients with an active or personal history of breast cancer, and patients with markedly impaired liver function should not be prescribed OCPs, as the risks outweigh the benefits.³⁰

Acne and hirsutism symptoms can also be treated using other means if OCP management is not preferred. Mild hirsutism can be treated cosmetically by depilatory and epilatory means.⁸ Cosmetically, electrolysis and laser hair removal are being used more frequently as a permanent means to managing hirsutism. Antiandrogens can help hirsutism and male pattern hair loss; these include spironolactone and finasteride in the US.²⁸ Finasteride and spironolactone are used off-label for treating hirsutism. Spironolactone is an androgen receptor blocker

Educating patients with PCOS on lifestyle improvements

PCOS can cause long-term health consequences if not treated appropriately. Patients with PCOS are at an increased risk for diabetes mellitus, gestational diabetes, heart disease, hypertension, dyslipidemia, sleep apnea, stroke, depression, and anxiety.²⁶ Education should be a large portion of the visit for patients with PCOS. Most of the risks previously discussed are preventable diseases, and education can play a major role in helping patients acquire lifestyle improvements and help prevent those diseases.

Lifestyle improvements, such as weight loss, can improve PCOS symptoms in all patient populations (adolescents and beyond). Decreasing BMI is challenging for patients with insulin resistance associated with PCOS. Encouraging lower-calorie diets and increased intake of fruits and vegetables can be a helpful way to lose weight. Weight loss attrition is high; patients with PCOS who do lose weight often later regain weight and PCOS symptoms reemerge.²⁷ It is important to educate patients about behavioral strategies for weight loss that can be maintained throughout the patient's lifespan.²⁶ Reducing body weight can decrease incidence of type 2 diabetes mellitus, gestational diabetes, dyslipidemia, and other cardiovascular risk factors.¹⁵ Additionally, weight loss can aid in ovarian function improvement and can stimulate ovulation. PCOS is an early risk factor for metabolic syndrome, and the risk increases with the age of diagnosis.¹⁸ This is why early intervention with lifestyle modifications is imperative to improving the patient's health and quality of life.

and has the potential to decrease excessive hair growth in women.²⁸ Finasteride is a 5 α -reductase inhibitor and blocks endogenous steroids, which can cause excessive hair growth.²⁸ Of the two, spironolactone is prescribed more frequently in the US.⁶ Antiandrogens must be used alongside contraception therapy because of their teratogenic effects and potential to feminize male fetuses.^{4,28} Acne, if not improved with spironolactone or contraceptives, can be treated with isotretinoin in severe cases. NPs who prescribe isotretinoin must be registered with the iPLEDGE program. This program was initiated to help prevent the teratogenic effects that isotretinoin can have on a fetus, but it is still used for male and female patients.³¹ Prescribers, patients, and pharmacists must be registered for the patient to be dispensed isotretinoin.³¹

If the patient has insulin resistance and/or obesity, lifestyle changes are encouraged first. Weight management can significantly help patients with PCOS.¹⁵ If an obese patient fails weight-loss efforts, metformin is suggested to manage PCOS symptoms and improve insulin resistance. Metformin does not have a specific approved

indication for PCOS, however it can help decrease hyperandrogenism and restore ovarian function.⁶ Metformin can also help reduce onset of diabetes by improving fasting blood glucose levels, reducing triglyceride and low-density lipoprotein cholesterol levels, and facilitating weight loss.¹⁴ Contraindications for metformin include patients with severe kidney impairment (with an estimated glomerular filtration rate below 30 mL/min/1.73 m²), and in patients with acute or chronic metabolic acidosis (including diabetic ketoacidosis).³² Metformin should be stopped for different intervals of time if patients are exposed to I.V. iodinated contrast for imaging, for patients having surgical or other procedures that may increase the risk of volume depletion, hypotension, and kidney impairment from restricted food and fluid intake before the procedure, or those suffering from tissue hypoxia.³²

Adolescents. Metformin or OCPs are used as first-line treatment for many adolescents with PCOS. Metformin has been shown to decrease metabolic syndrome effects, help with weight loss, and restore menstruation.⁶ It also can help with hyperandrogen symptoms.⁶ Many parents are hesitant to allow their adolescent child to take OCPs as they fear this leads to increased sexual activity, so metformin can provide an alternative for treatment. OCPs have the same effects on adolescents as they do on adult patients; therefore, they are an option for PCOS treatment for patients in this age population. It is important to evaluate and complete labs prior to starting OCPs in adolescents when PCOS is suspected. Often, healthcare providers start OCPs without considering PCOS first, especially in those who are sexually active and at risk for an unwanted pregnancy; however, prescribing OCPs can mask PCOS symptoms long term, so prescribers should consider PCOS before prescribing OCPs. PCOS symptoms can be psychologically difficult during adolescence, especially if acne and hirsutism are severe, so PCOS treatment is recommended for this age population to ensure continued stable psychological and social development.

Conception and pregnancy. When patients with PCOS desire to conceive, focusing on menstrual patterns is important to see if ovulation is occurring. Anovulation is the most common cause for irregular menstrual cycles. Clomiphene is indicated first line to treat anovulation.¹⁵ Potential risks to using clomiphene can include multiple pregnancy, ovarian hyperstimulation, thromboembolism, and/or visual disturbances.²⁴ If clomiphene is not effective, then metformin is often

added to assist in ovulatory regulation along with improving insulin resistance.¹⁵ Weight loss is recommended for patients who are trying to conceive.³ Due to these mainstays of treatment for patients with PCOS trying to conceive and newer PCOS fertility protocols, pregnancy rates for patients with PCOS have risen.²⁸ This is encouraging news because patients with PCOS have historically been given low statistical success for healthy pregnancies.

It is important to optimize health and lifestyle before patients with PCOS try to conceive. This can aid in a healthier pregnancy and fetal development.⁴ Lifestyle modifications should include decreasing BMI, decreasing caffeine intake, cessation of alcohol and smoking, and improving overall health. When pregnancy is established in patients with PCOS, there is an increased chance for spontaneous miscarriage.³ PCOS also can lead to a 40% to 50% chance of gestational diabetes.⁴ It is important to monitor pregnant patients with PCOS closely to ensure a healthy pregnancy ensues.

Perimenopause and menopause. Although PCOS cannot be diagnosed in this patient population, symptoms can still be managed in perimenopausal or menopausal women with suspected PCOS. Metformin can help this population with insulin resistance. Medications to manage hirsutism can be prescribed.

■ Implications for practice

Primary care NPs can manage patients with PCOS, a common endocrinopathy that primarily presents with symptoms in women of childbearing age, but that can affect women across the lifespan. Patients with PCOS can present with hyperandrogenism symptoms along with menstrual irregularities. Medications such as OCPs, antiandrogens, and/or metformin are common treatment options. Education regarding lifestyle improvements and BMI reduction can be significantly impactful for a patient with PCOS. Ensuring the patient is educated on long-term health consequences of PCOS is important and may help improve their long-term quality of life. 

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