POLYCYSTIC OVARIAN SYNDROME

Polycystic ovarian syndrome (PCOS) is a clinical diagnosis characterized by oligo-ovulation, hyperandrogenism, and often the presence of polycystic ovaries. A common disorder, PCOS affects about 10% of reproductive-age women.[1] Women often present with amenorrhea or oligomenorrhea, hirsutism with acne and male-pattern hair growth, weight gain, and difficulty with fertility. PCOS is associated with an increased risk of developing diabetes mellitus and cardiovascular disease.

Diagnostic criteria for PCOS vary by organization, although all include a component of ovarian disease and the exclusion of alternative diagnoses (refer to Table 1.). Differential diagnosis includes thyroid disease, hyperprolactinemia, androgen-secreting tumors, adrenal hyperplasia, and Cushing's syndrome. Depending on a woman's presenting symptoms, consider laboratory testing that includes a pregnancy test, TSH (thyroid stimulating hormone), prolactin, total and free testosterone levels, dehydroepiandrosterone (DHEA) sulfate, morning 17a-hydroxyprogesterone, and 24-hour urine cortisol level. Transvaginal ultrasound may show characteristic changes associated with PCOS, but is not required for the diagnosis if the hormonal features of PCOS are present.

TABLE 1. DIFFERING CRITERIA FOR POLYCESTIC OVARIAN SYNDROME AMONG ORGANIZATIONS [2]

| Organization | Criteria | Ovarian Dysfunction | Ovarian Morphology | Hyperandrogenism |
|---|---|--|---|---|
| National Institutes of Health (1990) [3] | Both of the following and exclusion of related disorders | Oligo- ovulation (less than 6 menses per year) | Not applicable | Clinical or biochemical (not specified) |
| Rotterdam Group (2003) [4] | Any two of three of the following and exclusion of related disorders | Oligo- anovulation (nonspecified) | Polycystic ovaries (>12 follicles 2 to 9 mm, or ovarian volume >10mL) | Clinical or biochemical (free testosterone or free testosterone index) |
| Androgen Excess Society (2006) [5] | Hyperandrogenism as critical, with addition of at least one ovarian marker and exclusion of related disorders | Oligo- anovulation and/or polycystic ovaries | Oligo- anovulation and/or polycystic ovaries | Clinical or biochemical (free testosterone) |

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PCOS results from various endocrine and metabolic abnormalities, including hypothalamic-pituitary dysfunction, abnormal ovarian hormone production, and hyperinsulinemia. These imbalances perpetuate a sequence of elevated testosterone, abnormal estrogen to progesterone ratio, insulin resistance, and dysregulation of the hypothalamic-pituitary feedback system.[2]

Treatment of PCOS is directed at:

- Decreasing insulin resistance
- Reducing hyperandrogenism
- · Managing diabetes and cardiac disease if present
- Addressing fertility concerns

Lifestyle modifications should be emphasized to improve insulin sensitivity and promote weight loss. Conventional approaches include insulin sensitizers such as metformin, oral contraceptive pills with low androgenic activity, progestins for endometrial protection, and antiandrogens for symptoms of hirsutism. For guidance regarding therapeutic approaches, refer to Family Practice Notebook's <u>Progestin Androgenic Activity</u>. The American College of Obstetricians and Gynecologists reviews the evidence behind these treatments in a 2018 practice bulletin.[5]

Research supports the use of many integrative approaches that should also be considered.

1. WEIGHT LOSS

Work with women to develop a weight loss plan, as even 5% loss of initial body weight can result in significant improvements in metabolic and hormonal balance, especially in women with a body mass index (BMI) greater than 30.[6]

2. MOVING THE BODY

Encourage regular, moderate physical activity, as evidence shows this helps with weight loss and improves ovulation and insulin resistance.[5]

3. FOOD & DRINK

Recommend a low-carbohydrate, low-glycemic-index, high-fiber diet in women with PCOS.[2] For more information, refer to the Whole Health tool "Glycemic Index." Treat inflammation with the anti-inflammatory diet. Consider omega-3 fatty acid supplementation of 1,000-2,000 mg of EPA (eicosapentaenoic acid) and DHA (docosahexaenoic acid) daily if inadequate dietary intake. For more information, refer to the "Food & Drink" overview.

4. ESTROGEN DOMINANCE

Treat estrogen dominance, which may contribute to hormonal imbalances. Approaches include a diet high in cruciferous vegetables, avoidance of xenoestrogens, and promotion of

a healthy intestinal microbiome. For more information, refer to the Whole Health tool, "Estrogen Dominance."

5. SUPPLEMENTS AND BOTANICALS

Note: Please refer to the <u>Passport to Whole Health</u>, Chapter 15 "Biologically Based Approaches: Dietary Supplements" for more information about how to determine whether or not a specific supplement is appropriate for a given individual. Supplements are not regulated with the same degree of oversight as medications, and it is important that clinicians keep this in mind. Products vary greatly in terms of accuracy of labeling, presence of adulterants, and the legitimacy of claims made by the manufacturer.

Supplements and botanicals may help improve the symptoms of PCOS, including insulin resistance and hyperandrogenism.

Vitamin D regulates insulin secretion. Lower levels may be associated with higher BMI and insulin resistance. A meta-analysis of 11 trials demonstrated that vitamin D supplementation in women with PCOS may improve insulin sensitivity. Consider supplementing to 2,000 units daily, or higher doses if indicated by serum 25-OH vitamin D levels.[7]

Inositol mediates insulin activity in the body. Supplementation with D-chiro-inositol (DCI) has been shown to improve insulin sensitivity and ovulation, decrease triglyceride and testosterone levels, and support weight loss.[2] D-pinitol, more accessible commercially, increases serum levels of DCI and decreases glucose levels, although research findings are mixed. The suggested dose of both DCI and pinitol is 600 mg twice daily. Both are generally well tolerated.[8]

Chromium is a mineral that improves insulin function and decreases blood glucose levels. A meta-analysis of seven trials found that chromium supplementation improved BMI, free testosterone, and fasting insulin in PCOS.[9] The FDA reports that chromium can be used safely in doses of 200 mcg daily for up to six months; in many studies, 1,000 micrograms daily has been used safely. There is insufficient information, however, to comment on safety in long-term use. The suggested dose is 200 to 1,000 mcg of chromium picolinate in divided doses daily. Interactions with medications can occur, especially thyroid hormone. Side effects include headache, sleep disturbances, and mood issues. Avoid chromium in people with kidney disease.[10]

N-acetylcysteine (NAC) is a precursor to glutathione, a powerful antioxidant. It is used in many conditions, and some evidence supports its use in improving insulin sensitivity and decreasing inflammation.[2] The suggested dose is 1,200 to 1,800 mg daily in divided doses. NAC is generally well tolerated, with occasional nausea reported.

Cinnamon (*Cinnamomum cassia*) has been shown to decrease blood glucose levels. A small study of 15 women with PCOS showed that one-fourth to one-half teaspoon of cinnamon powder improved insulin resistance.[11] The suggested dose is one-fourth to 1 teaspoon of powdered cinnamon or 200-300 mg of cassia extract.[12]

Licorice (*Glycyrrhiza glabra*) has antiandrogenic effects. It can be taken alone, and it also works well with spironolactone to counter its side effects of hyperkalemia and low blood pressure. The suggested dose is 500 mg standardized to 6%-15% glycrrhizin. Due to its mineralocorticoid properties, short-term and closely monitored use is recommended. Toxicities include hypokalemia, hypertension, and fluid retention.[13]

Chaste tree berry (*Vitex agnus-castus*) is often used to treat menstrual irregularities occurring in PCOS, although supporting research is limited. Thought to shift the estrogen-progesterone balance toward progesterone, chaste tree berry may help with menstrual cycle regularity and ovulation.[14] The suggested dose is typically 20-240 mg per day of crude herb. Although generally well tolerated, side effects include headache, GI disturbance, acne, and rash.[15]

6. POWER OF THE MIND

Women with PCOS have increased sympathetic nervous system activity, in addition to anxiety and depression.[2] Consider stress management, relaxation exercises, and breathing exercises to improve heart rate variability. For more information, refer to "Heart Rate Variability and Arrhythmias" Whole Health tool. Although women with PCOS may benefit from additional mind-body techniques and alterative modalities, at this time little research exists to document their efficacy specifically for PCOS.

7. OTHER COMPLEMENTARY AND INTEGRATIVE HEALTH APPROACHES

Acupuncture. A Cochrane review found insufficient high-quality evidence to support the use of acupuncture for the treatment of menstrual irregularity or pregnancy in women with PCOS.[16] Due to limitations in the included studies and its low risk profile, it would be reasonable to consider acupuncture as an adjunctive therapy. A few small studies have shown that women with PCOS receiving acupuncture had increased rates of ovulation and decreased sympathetic tone.[17]

For more information on PCOS in relation to fertility and reproductive health, refer to the "Reproductive Health" Whole Health overview.

RESOURCE LINKS

- "<u>Estrogen Dominance</u>": https://www.va.gov/WHOLEHEALTHLIBRARY/tools/estrogen-dominance.asp
- "Food and Drink": https://www.va.gov/WHOLEHEALTHLIBRARY/self-care/foodand-drink.asp
- "Glycemic Index": https://www.va.gov/WHOLEHEALTHLIBRARY/tools/glycemicindex.asp
- "<u>Heart Rate Variability and Arrhythmias</u>": https://www.va.gov/WHOLEHEALTHLIBRARY/tools/heart-rate-variability-and-arrhythmias.asp

- Passport to Whole Health: https://www.va.gov/WHOLEHEALTHLIBRARY/docs/Passport_to_WholeHealth_FY 2020 508.pdf
- <u>Progestin Androgenic Activity</u>: http://www.fpnotebook.com/gyn/pharm/PrgstnAndrgncActvty.htm
- "Reproductive Health": https://www.va.gov/WHOLEHEALTHLIBRARY/professional-care/reproductivehealth.asp

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