Polycystic ovarian syndrome (PCOS) is the most common endocrine abnormality of reproductive-aged women. This chronic condition affects 5 million to 6 million females in the United States. In addition, an estimated 50% to 75% of cases remain undiagnosed.
PCOS is classified by the presence of two of the following three criteria: (a) oligo- and/or anovulation; (b) clinical and/or biochemical signs of hyperandrogenism; and (c) polycystic ovaries, all in the absence of other known etiologies. Women with PCOS may seek care from physicians in various medical specialties, including endocrinology, internal medicine, obstetrics and gynecology, dermatology and family medicine. Therefore, physicians in these specialties must understand management of the short- and long-term complications associated with PCOS.

**Short-term complications**

Following are short-term complications related to PCOS, as well as treatment options.

- **Menstrual irregularities**
  
  The prevalence of menstrual dysfunction in women with PCOS is 14.6% to 22.8%, and irregularities range from amenorrhea to menorrhagia with a classic peripubertal onset.

  **Recommendations:** A modest weight reduction of 5% can return menses to normal. Combination oral contraceptives (COCs) or progestins are also effective at regulating the menstrual cycle in these patients. Metformin has been shown to have positive effects on ovulatory dysfunction and hyperandrogenism, ultimately restoring normal menstruation.

- **Hyperandrogenism**
  
  Cutaneous hyperandrogenism manifests as hirsutism, acne and androgenic alopecia. Its prevalence in the PCOS population in the form of acne is 15% to 25%; hirsutism, 65% to 75%; and alopecia, 5% to 50%.

  **Recommendations:** COCs are beneficial for all forms of cutaneous hyperandrogenism; however, the selection of a low-androgenic progestin component is essential. Anti-androgens, such as spironolactone, flutamide or finasteride can then be added if acceptable results are not achieved, but these medications must be used in conjunction with COCs due to known risk of congenital anomalies.

  Efornithine, a topical medication, has been shown to be effective in hirsute women, and waxing, shaving, depilatories, electrolysis and laser treatments are alternative options for hirsutism. Topical retinoids and antimicrobials or oral antibiotics can be effective in the treatment of acne. Limited data support the use of topical minoxidil in the treatment of alopecia. Hyperandrogenism has also been shown to improve with dietary modification.

- **Infertility**
  
  Infertility due to anovulation affects 75% of women with PCOS. Other agents used in ovulation induction include metformin and thiazolidinediones. Referral to a reproductive endocrinologist is appropriate if CC fails to achieve pregnancy. Treatment with exogenous gonadotropins or laparoscopic ovarian surgery such as ovarian diathermy is second-line intervention. The ovarian wedge resection has been abandoned, secondary to increased adhesion formation. The recommended third-line intervention is in vitro fertilization.

- **Obesity**
  
  Obesity in the PCOS patient tends to be central (android) or visceral in its distribution. The prevalence of obesity is 40% to 60% in this population. This epidemic exacerbates insulin resistance, ovulatory and menstrual dysfunction and pregnancy outcome. Obesity is associated with increased prevalence of metabolic syndrome, glucose intolerance, cardiovascular risk factors and sleep apnea.
**Recommendations:** Lifestyle modification is crucial. Modest amounts of weight loss have been shown to restore spontaneous ovulation and menstruation and to improve insulin sensitivity. No particular type of dietary modification has been shown to be superior. Anti-obesity medications, such as orlistat, sibutramine and rimonabant, and surgical weight loss have been found to be effective and even more sustainable in the long term for weight loss. Metformin has also appeared to have some benefit.

### Insulin resistance and hyperinsulinemia

Insulin resistance and compensatory hyperinsulinemia affect 40% to 70% of women with PCOS independent of obesity. The strongest predictors of insulin resistance in a patient with PCOS are body mass index, hyperandrogenemia, and hirsutism. Insulin resistance is also associated with obstructive sleep apnea, nonalcoholic steatohepatitis (or, nonalcoholic fatty liver disease) and metabolic abnormalities such as metabolic syndrome, dyslipidemia and type 2 diabetes mellitus (T2DM), which are all more prevalent in these patients. Hyperinsulinemia also exacerbates cutaneous hyperandrogenism.

**Recommendations:** Weight reduction and medications such as metformin and thiazolidinediones have all been shown to decrease insulin resistance.

### Dyslipidemia

Lipid abnormalities, including elevated low-density lipoprotein cholesterol levels, triglyceride levels, total cholesterol to high-density lipoprotein cholesterol ratios, and decreased high-density lipoprotein cholesterol levels are found in women with PCOS. The prevalence of abnormal lipid levels, according to National Cholesterol Education Program criteria, approaches 70% in these patients. PCOS patients have higher concentrations of smaller- and higher-density LDL particles.

**Recommendations:** Lifestyle modification with diet, exercise and weight loss is essential. HMG-CoA reductase inhibitors (statins) have been shown to effectively treat dyslipidemia and decrease levels of circulating androgens. Other treatments include nicotinic acid and fibrates.

### Obstructive sleep apnea (OSA)

Patients with PCOS have a higher risk for obstructive sleep apnea, even when compared with obese non-PCOS control subjects. Insulin resistance seems to be a better predictor of sleep-disordered breathing. Glucose tolerance is directly related to the severity of sleep apnea in these patients.

**Recommendations:** Weight loss, avoidance of alcohol, sleep position changes, avoidance of medications that inhibit the central nervous system and positive airway pressure have been shown to be effective.

### Pregnancy loss

Pregnant women with PCOS have a 30% to 50% increased risk of early spontaneous abortion.

**Recommendations:** Weight reduction and medications such as metformin have been shown to reduce first trimester spontaneous abortion (SAB) rates. The optimum time to discontinue metformin has yet to be elucidated.

### Pregnancy complications

Women with PCOS also have an increased risk of preterm delivery, hypertensive disorders, gestational diabetes and perinatal mortality. Maternal and neonatal risk are increased by iatrogenic multiple gestation from infertility treatment.

**Recommendations:** Metformin continued during pregnancy decreases rates of gestational diabetes.
Long-term complications
Following are long-term complications related to PCOS, as well as treatment options.

- Endometrial hyperplasia and carcinoma
  The chronic unopposed estrogen exposure in PCOS increases the risk of endometrial hyperplasia and endometrial carcinoma. An increased incidence of endometrial hyperplasia and atypia in the obese PCOS patient has been observed. PCOS patients have other risk factors for endometrial cancer including chronic hyperinsulinemia, increased concentrations of serum insulin-like growth factor, hyperandrogenemia and obesity.

- Metabolic syndrome:
  Metabolic syndrome is associated with an increased risk of cardiovascular disease (CVD) and T2DM. Metabolic syndrome occurs in up to 43.6% of women with PCOS. Specifically for the PCOS patient, the presence of three of the following provides the diagnosis of metabolic syndrome:
  - abdominal obesity (waist circumference, >35 inches)
  - triglycerides, >150 mg/dL
  - high-density lipoprotein cholesterol, >50 mg/dL
  - blood pressure, >130 systolic and/or >85 diastolic mm Hg
  - fasting glucose level, 110 mg/dL to 126 mg/dL, and/or two-hour glucose tolerance test result, 140 mg/dL to 199 mg/dL.

  Recommendations: Treatment starts with lifestyle modification such as diet and exercise to reduce weight. Prevention of T2DM is achieved by administration of oral hypoglycemic metformin and thiazolidinediones. Use of lipid-lowering and antihypertensive therapies is effective in reducing cardiovascular risk.

- T2DM/Impaired glucose intolerance
  Fifty percent to 75% of women with PCOS have T2DM or prediabetes. The conversion rate from impaired glucose tolerance to frank diabetes is fivefold to tenfold higher in women with PCOS.

  Recommendations: Women should be screened with a fasting glucose test followed by a two-hour glucose test after ingesting a 75-gram glucose load. Management involving lifestyle modification, including diet, exercise and weight reduction, and an oral hypoglycemic and insulin should be initiated. Lifestyle modification has been shown to be the superior treatment for improving insulin sensitivity, reducing weight, decreasing the incidence of T2DM and metabolic syndrome and improving risk factors for CVD.

- Cardiovascular disease
  Insulin-resistant states are associated with a greater susceptibility to coronary artery disease. Women with PCOS have increased CVD risk factors such as obesity, metabolic syndrome, hypertension, T2DM and dyslipidemia. These women exhibit greater endothelial dysfunction, arterial stiffness in the internal and external carotid arteries, presence of carotid and aortic plaque, increased thickness of intima media layers of the carotid artery and coronary artery and cerebrovascular artery calcification. Increased early left ventricular diastolic dysfunction, lower ejection fraction and a 7.1-times-higher risk than a non-PCOS patient for developing a myocardial infarction. Death from CVD is more common in women with PCOS. These risk factors could be the result of inflammation because C-reactive protein levels are elevated in PCOS patients.

  Recommendations: Women with PCOS should be screened for cardiovascular risk by determination of body mass index, fasting lipid and lipoprotein levels, and metabolic syndrome risk factors. Management focuses on modifying the CVD risk factors.

- Nonalcoholic steatohepatitis (NASH)
  The prevalence of nonalcoholic steatohepatitis is increased in the PCOS patient and is associated with obesity, T2DM, and hyperlipidemia. Insulin resistance may be the key mechanism leading to hepatic steatosis.
**Recommendations:** There is no proven effective therapy for nonalcoholic steatohepatitis, although modification of risk factors is recommended.33

**Psychological disorders**

The prevalence of depression in PCOS patients is reported to be as high as 40%.44 Depression has been associated with insulin resistance, impaired glucose intolerance and obesity. Patients with PCOS may have low self-esteem and poor self-image.35 They can suffer from social withdrawal, eating disorders, and anxiety and may attempt suicide.

**Recommendations:** Treatment should include behavioral and psychological interventions adjunctive to standard medical care.45

**Final notes**

PCOS is a complex medical condition that requires a multidisciplinary team approach for optimal treatment. It is important to understand that PCOS is a syndrome, not a disease, reflecting multiple potential etiologies with variable clinical expression of these and other features in adolescents and adults with this syndrome.

PCOS treatments must be directed at addressing the immediate goals of patients and preventing short- and long-term complications. By addressing these complications and making lifestyle changes that are supported by appropriate pharmacologic interventions with continuous surveillance, patients’ quality of life can be improved.

**References**


42. Polycystic Ovarian Syndrome A ssociation, Inc. Telephone: (800) 370-2943 http://www.nichd.nih.gov/womenshealth

American Association of Clinical Endocrinologists Telephone: (904) 353-7878 http://www.aace.com

American Society for Reproductive Medicine Telephone: (202) 638-5577 http://www.asrm.org

Center for Applied Reproductive Science Telephone: (423) 461-8880 http://www.ivf-et.com


Polycystic Ovarian Syndrome Association, Inc. Telephone: (800) 467-6663 http://www.hormone.org

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For more information

You can find out more about PCOS by contacting womenshealth.gov at (800) 994-9662 or the following organizations:

Women’s Health Research, National Institute of Child Health and Human Development, NIH, HHS Telephone: (800) 370-2943 http://www.nichd.nih.gov/womenshealth

American Association of Clinical Endocrinologists Telephone: (904) 353-7878 http://www.aace.com

American Society for Reproductive Medicine Telephone: (202) 638-5577 http://www.asrm.org

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