Patient education: Polycystic ovary syndrome (PCOS) (Beyond the Basics)

AUTHORS: Robert L Barbieri, MD, David A Ehrmann, MD
SECTION EDITORS: Peter J Snyder, MD, William F Crowley, Jr, MD
DEPUTY EDITOR: Kathryn A Martin, MD

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PCOS OVERVIEW

Polycystic ovary syndrome (PCOS) is a condition that causes irregular menstrual periods, symptoms of excess androgens (acne, hirsutism, and scalp hair loss), and ovaries that appear "polycystic" on pelvic ultrasound. The condition occurs in approximately 5 to 10 percent of females. Many females with PCOS are overweight or obese, and they are at higher-than-average risk of developing type 2 diabetes, sleep apnea, fatty liver, and depression. For females with PCOS who want to become pregnant, fertility medications may be needed to induce ovulation.

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

PCOS CAUSES

Reproductive system abnormalities — The cause of PCOS is not completely understood. With regards to the reproductive system, 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. To explain how these hormones cause symptoms, it is helpful to understand the normal menstrual cycle.

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. 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. Normal menstrual periods occur about every 25 to 35 days.

During the first half of the cycle, small increases in FSH stimulate the ovary to develop a follicle that contains an egg (oocyte). 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) approximately 36 to 48 hours following the LH surge (figure 1). 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 females with PCOS, menstrual cycles are typically irregular. Pelvic ultrasound shows small follicles around the periphery of the ovary, often described as a "string of pearls." None of these small follicles are capable of growing to a size that would result in ovulation. As a result, the levels of estrogen, progesterone, LH, and FSH become imbalanced.

Androgens are normally produced by the ovaries and the adrenal glands. An example of an androgen is testosterone. Androgens may become increased in females with PCOS because of the high levels of LH but also because of increased levels of insulin that are usually seen with PCOS. (See 'Insulin abnormalities' below.)

Metabolic system abnormalities — The metabolic system controls the processing of carbohydrates, fats, and proteins. Important hormones in the metabolic system include insulin, glucagon, glucagon-like peptides, and many others.

Insulin abnormalities — PCOS is associated with elevated levels of insulin in the blood. Insulin is a hormone that is produced by specialized cells within the pancreas; insulin regulates blood glucose levels. When blood glucose levels rise (after eating, for example), these cells produce insulin to help the body use glucose for energy.

- If glucose levels do not respond to normal levels of insulin, the pancreas produces more insulin. Excess production of insulin is called **hyperinsulinemia**.
- When increased levels of insulin are required to maintain normal glucose levels, a person is said to be **insulin resistant**.
- When the blood glucose levels are not completely controlled, even with increased amounts of insulin, the person is said to have **glucose intolerance** (sometimes referred to as "prediabetes").
- If blood glucose levels continue to rise despite increased insulin levels, the person may have impaired glucose tolerance, often referred to as "prediabetes," which can ultimately lead to development of **type 2 diabetes**.

These conditions are diagnosed with blood tests. (See "Patient education: Type 2 diabetes: Overview (Beyond the Basics)".)

Insulin resistance and hyperinsulinemia can occur in both normal-weight and overweight females with PCOS. Among females with PCOS who are obese, there appears to be a three-fold increase in risk for prediabetes when compared with females without PCOS who are obese; 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 females develop type 2 diabetes. 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 females with PCOS.

PCOS SYMPTOMS

The changes in hormone levels described above cause the classic symptoms of PCOS, including absent or irregular and infrequent menstrual periods, increased body hair growth or scalp hair loss, acne, and difficulty becoming pregnant. (See "Patient education: Androgenetic alopecia in men and women (Beyond the Basics)".)

Signs and symptoms of PCOS usually begin around the time of puberty, although some females do not develop symptoms until late adolescence or even into early adulthood. Because hormonal changes vary from one female to another, patients with PCOS may have mild to severe acne, facial hair growth, or scalp hair loss.

Menstrual irregularity — If ovulation does not occur, the ovaries do not produce progesterone, and the lining of the uterus (called the endometrium) becomes thicker and may shed irregularly, which can result in heavy and/or prolonged bleeding. Irregular or absent menstrual periods can increase a female's risk of endometrial overgrowth (called endometrial hyperplasia) or even endometrial cancer.

Females with PCOS usually have fewer than six to eight menstrual periods per year.

Weight gain and obesity — PCOS is associated with gradual weight gain and obesity in approximately one-half of females. For some females with PCOS, obesity develops at the time of puberty.

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. (See "Patient education: Hirsutism (excess hair growth in females) (Beyond the Basics)" and "Patient education: Acne (Beyond the Basics)".)

Infertility — Many females with PCOS do not ovulate regularly, and it may take these females longer to become pregnant. For females with PCOS who desire pregnancy but have irregular periods, the fertility evaluation should start immediately as the chance of becoming pregnant is low without treatment. (See 'Treatment of infertility' below.)

Heart disease — Females who are obese and who also have insulin resistance or diabetes might have an increased risk of coronary artery disease, which increases the risk of having a heart attack. It is not known with certainty if females with PCOS are at increased risk for this condition. Both weight loss and treatment of insulin abnormalities can decrease this risk. Other treatments (eg, cholesterol-lowering medications [statins], and treatments for high blood pressure) may also be recommended. (See "Patient education: High cholesterol and lipids (Beyond the Basics)" and "Patient education: High blood pressure treatment in adults (Beyond the Basics)".)

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. In addition, there is evidence that people with untreated sleep apnea have an increased risk of insulin resistance, obesity, diabetes, and cardiovascular problems, such as high blood pressure, heart attack, abnormal heart rhythms, or stroke.

Sleep apnea may occur in up to 50 percent of females with PCOS. The condition can be diagnosed with a sleep study, and several treatments are available. (See "Patient education: Sleep apnea in adults (Beyond the Basics)".)

Other problems — Females with PCOS are at increased risk of other problems that can impact quality of life. These include:

- Depression and anxiety – There are treatments that can help with these problems, including therapy as well as medications. (See "Patient education: Depression in adults (Beyond the Basics)".)
- Sexual dysfunction – Females with PCOS are more likely than other females to experience lower sexual satisfaction. (See "Patient education: Sexual problems in females (Beyond the Basics)".)
- Eating disorders – These include bulimia and binge eating. Females with PCOS do not appear to be at increased risk of developing anorexia.

If you think you might be experiencing any of these problems, talk with your health care provider. There are often treatments that can help.

Symptoms after menopause — Less is known about PCOS symptoms after menopause. Research suggests that females with PCOS may continue to have high androgen levels after menopause (when monthly periods normally stop), but that they decline to normal after approximately age 70. However, even females who have been through menopause and whose hormone levels are returning to normal can have symptoms like excess hair growth. (See 'Hair growth and acne' above.)

PCOS DIAGNOSIS

There is no single test for diagnosing PCOS. You may be diagnosed with PCOS based upon your symptoms, blood tests, and a physical examination. Expert groups have determined that a female must have two out of three of the following to be diagnosed with PCOS:

- Irregular menstrual periods caused by anovulation or irregular ovulation.
- Evidence of elevated androgen levels. The evidence can be based upon signs (excess hair growth, acne, or male-pattern balding) **or** blood tests (high androgen levels).
- Polycystic ovaries on pelvic ultrasound.

In addition, there must be no other cause of elevated androgen levels or irregular periods (eg, congenital adrenal hyperplasia [classic or nonclassic], androgen-secreting tumors, or hyperprolactinemia).

Blood tests are usually recommended to determine whether another condition is the cause of your signs and/or symptoms. If you have irregular periods, blood tests for pregnancy, prolactin level, thyroid-stimulating hormone (TSH), and follicle-stimulating hormone (FSH) should be done. Insulin levels are not used to diagnose PCOS, partly because insulin levels are high in people who are above normal body weight and because there is no level of insulin that is "diagnostic" for PCOS.

If PCOS is confirmed, blood glucose and cholesterol testing are usually performed. An oral glucose tolerance test is the best way to diagnose prediabetes and/or diabetes. A fasting glucose level is often normal even when prediabetes or diabetes is present. Many clinicians who treat PCOS patients also recommend testing for sleep apnea with questionnaires or overnight sleep studies in a sleep laboratory. In females with moderate to severe hirsutism (excess hair growth), blood tests for testosterone and dehydroepiandrosterone sulfate (DHEAS) may be recommended.

Females with PCOS and obesity are at particularly high risk for fatty liver (also called nonalcoholic steatohepatitis) and should be screened for signs of increases in liver fat and fibrosis.

All females who are diagnosed with PCOS should be seen on a routine basis by a health care provider for the metabolic and reproductive issues that may occur. In addition,

depression and anxiety are common in females with PCOS.

PCOS TREATMENTS

Oral contraceptives — Combination oral contraceptives (COCs; with combined estrogen and progestin) are the most commonly used treatment for regulating menstrual periods in females with PCOS. COCs are also effective for treating hirsutism and acne by suppressing ovarian androgen overproduction. A skin patch and vaginal ring are also available for contraception. Some females choose intrauterine devices (IUDs) containing a type of progesterone to minimize uterine bleeding and protect against uterine cancer. However, unlike COCs, patch, and ring, the IUD is not effective for treating acne or facial hair.

Females with PCOS occasionally ovulate, and COCs are useful in providing protection from pregnancy. Although taking a COC in a cyclical manner, with hormone-free days each month, results in bleeding once per month, this does not mean that the PCOS is "cured"; irregular cycles generally return when the COC is stopped. (See "Patient education: Absent or irregular periods (Beyond the Basics)".)

COCs decrease the body's production of androgens. Antiandrogen drugs (such as spironolactone) decrease the effect of androgens. These treatments can be used in combination to reduce and slow hair growth. COCs and antiandrogens can also reduce acne.

Side effects — Some females who take birth control pills (not just those with PCOS) stop having monthly bleeding or develop irregular spotting and bleeding. Irregular bleeding usually resolves after a few menstrual cycles.

Many females worry that they will gain weight on the pill. In general, this is not a concern with the currently available low-dose pills. Some females develop nausea, breast tenderness, and bloating after beginning the pill, but these symptoms usually resolve after two or three months.

The pill is safe and effective, although it slightly increases the risk of blood clots in the legs or lungs; this is a rare complication in young, healthy females who do not smoke, but it is more of a concern in females who are obese and in older females. (See "Patient education: Hormonal methods of birth control (Beyond the Basics)".)

Progestin — Another method to treat menstrual irregularity is to take a hormone called progestin (sample brand name: Provera) for 10 to 14 days every 1 to 3 months. This will induce a period in almost all females with PCOS, reducing the risk of overgrowth of endometrial cells thereby lowering the risk of endometrial hyperplasia, 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.

Hair treatments — Excess hair growth on the face and/or other parts of the body can be removed by shaving or use of depilatories, electrolysis, or laser therapy. Many females worry that these treatments cause hair to grow faster, although this is not true. (See "Patient education: Hirsutism (excess hair growth in females) (Beyond the Basics)".)

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

Scalp hair loss can be treated with medications in some situations. Other options include hair replacement and wigs. (See "Patient education: Androgenetic alopecia in men and women (Beyond the Basics)".)

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

There are a number of options available to treat obesity. These options are identical to those recommended for females without PCOS and include diet and exercise, weight loss medications (although their use is limited), and weight loss surgery. (See "Patient education: Losing weight (Beyond the Basics)".)

Weight loss surgery may be an option for severely obese females with PCOS. Females can lose significant amounts of weight after surgery, which can restore normal menstrual cycles, reduce high androgen levels and hirsutism, and reduce the risk of type 2 diabetes. (See "Patient education: Weight loss surgery and procedures (Beyond the Basics)".)

Metformin — Metformin (sample brand name: Glucophage) is a medication that improves the effectiveness of insulin produced by the body, reducing insulin resistance and hyperinsulinemia. It was developed as a treatment for type 2 diabetes but may be recommended for females with PCOS in selected situations.

- If a female does not have regular menstrual cycles, the first-line treatment is a hormonal method of birth control, such as birth control pills. If the female cannot take birth control pills, one alternative is to take metformin; a progestin is usually recommended, in addition to metformin, for six months or until menstrual cycles are regular. (See 'Progestin' above.)

- Metformin may help a bit with weight loss. Although metformin is not a weight-loss drug, some studies have shown that females with PCOS who are on a low-calorie diet lose slightly more weight when metformin is added. 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.

Metformin is not usually recommended for females with PCOS who have difficulty becoming pregnant, because it is not as effective as other treatments for ovulation induction, letrozole, and clomiphene. (See 'Treatment of infertility' below.)

An expert group does not recommend metformin for females with PCOS in whom excessive hair growth (hirsutism) is of primary concern. Birth control pills alone, or in combination with an antiandrogen medication, are a better option. (See "Patient education: Hirsutism (excess hair growth in females) (Beyond the Basics)".)

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 females who are not obese.

A treatment option for females who are unable to become pregnant and who have PCOS is weight loss. Even a modest amount of weight loss may allow the female to begin ovulating normally. In addition, weight loss can improve the effectiveness of other infertility treatments. (See "Patient education: Evaluation of infertility in couples (Beyond the Basics)".)

Letrozole is a medication that is now used to induce ovulation in females with PCOS. Studies have shown that live birth rates are higher in obese females with PCOS when they are treated with letrozole rather than clomiphene, the drug used in the past. Many experts now recommend letrozole as the first choice of treatment for females with PCOS who want to conceive.

If a female does not ovulate or is unable to conceive with letrozole or clomiphene, gonadotropin therapy (follicle-stimulating hormone [FSH] injections) is sometimes recommended. However, this treatment can cause multiple pregnancies, including triplets and quadruplets, particularly in patients with PCOS. In modern practice, IVF will often be suggested rather than FSH injections if clomiphene and letrozole do not result in a pregnancy. The risk of multiple gestations is lower with single-embryo transfer IVF cycles when compared with FSH injections. (See "Patient education: Infertility treatment with gonadotropins (Beyond the Basics)".)

WHERE TO GET MORE INFORMATION

Your health care provider is the best source of information for questions and concerns related to your medical problem.

This article will be updated as needed on our website (www.uptodate.com/patients). Related topics for patients, as well as selected articles written for health care professionals, are also available. Some of the most relevant are listed below.

Patient level information — UpToDate offers two types of patient education materials.

The Basics — The Basics patient education pieces answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials.

Patient education: Polycystic ovary syndrome (The Basics)
Patient education: Hirsutism (excess hair growth in women) (The Basics)
Patient education: Ovarian cysts (The Basics)
Patient education: Absent or irregular periods (The Basics)

Beyond the Basics — Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are best for patients who want in-depth information and are comfortable with some medical jargon.

Patient education: Androgenetic alopecia in men and women (Beyond the Basics)
Patient education: Hirsutism (excess hair growth in females) (Beyond the Basics)
Patient education: Acne (Beyond the Basics)
Patient education: Type 2 diabetes: Overview (Beyond the Basics)
Patient education: High cholesterol and lipids (Beyond the Basics)
Patient education: High blood pressure treatment in adults (Beyond the Basics)
Patient education: Sleep apnea in adults (Beyond the Basics)
Patient education: Absent or irregular periods (Beyond the Basics)
Patient education: Hormonal methods of birth control (Beyond the Basics)
Patient education: Losing weight (Beyond the Basics)
Patient education: Weight loss surgery and procedures (Beyond the Basics)
Patient education: Evaluation of infertility in couples (Beyond the Basics)
Patient education: Ovulation induction with clomiphene or letrozole (Beyond the Basics)
Patient education: Infertility treatment with gonadotropins (Beyond the Basics)

Professional level information — Professional level articles are designed to keep doctors and other health professionals up-to-date on the latest medical findings. These articles are thorough, long, and complex, and they contain multiple references to the research on which they are based. Professional level articles are best for people who are comfortable with a lot of medical terminology and who want to read the same materials their doctors are reading.

Definition, clinical features, and differential diagnosis of polycystic ovary syndrome in adolescents
Clinical manifestations of polycystic ovary syndrome in adults
Etiology and pathophysiology of polycystic ovary syndrome in adolescents
Diagnosis of polycystic ovary syndrome in adults
Epidemiology, phenotype, and genetics of the polycystic ovary syndrome in adults

Metformin for treatment of the polycystic ovary syndrome
Management of hirsutism in premenopausal women
Treatment of polycystic ovary syndrome in adolescents
Treatment of polycystic ovary syndrome in adults

The following organizations also provide reliable health information.

- National Library of Medicine

  (www.nlm.nih.gov/medlineplus/healthtopics.html)

- Hormone Health Network

  (https://www.hormone.org/diseases-and-conditions/polycystic-ovary-syndrome)

- US Department of Health and Human Services

  (https://www.womenshealth.gov/a-z-topics/polycystic-ovary-syndrome)

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