

Polycystic ovary syndrome (PCOS)

How is PCOS diagnosed?

Polycystic ovary syndrome (PCOS) is a common hormonal disorder that affects 5-10% of women. The diagnosis of PCOS is made by a woman having two of the following three characteristics:

1. inability to release an egg from the ovaries on a regular (monthly) basis (chronic anovulation),
2. increased male hormone levels and/or an increase in hair in the midline of the body (hyperandrogenism), and
3. polycystic-appearing ovaries on ultrasound. Because of the variable nature of PCOS, its diagnosis is based upon the combination of clinical, ultrasound, and laboratory features.

Women who have PCOS have irregular, infrequent menstrual cycles; hirsutism (increased hair growth); acne; and/or infertility. Many women with PCOS have ovaries that are enlarged with many small poorly functioning follicles that are visible on ultrasound.

Polycystic Ovary Syndrome

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Polycystic ovary syndrome is a condition associated with hormonal imbalances that cause the ovaries to overproduce androgens. It is a common cause of hirsutism. In patients with PCOS, multiple small follicles develop in the ovaries that appear as cysts, hence the term "polycystic." These small cysts are actually immature ovarian follicles that failed to mature and ovulate.

What risks do women have with PCOS?

Lack of ovulation in women with PCOS results in continuous exposure of their uterine lining (endometrium) to estrogen without progesterone. This may cause excessive thickening of the uterine lining and possible abnormal bleeding. The bombardment of estrogen without ovulation may lead to uterine cancer or pre-cancer.

Metabolic syndrome is more common in women with PCOS. This condition is characterized by abdominal obesity, cholesterol abnormalities, hypertension, and insulin resistance/diabetes mellitus. Each of these increases the risk of heart disease.

Obesity is noted in over 50% of women with PCOS. Diet and exercise that result in weight loss improves the frequency of ovulation, enhances the ability to get pregnant, improves fertility, lowers the risk of diabetes, and lowers androgen levels in many women with PCOS.

How is infertility in women with PCOS treated?

Ovulation may often be induced with clomiphene citrate (CC), an orally-administered fertility medication. If consistent ovulation is not noted with CC, the use of the oral medication letrozole may be considered as it is an effective ovulation induction agent. Gonadotropins (injectable fertility medications) may be used to induce ovulation if CC or letrozole do not result in ovulation or pregnancy. However, gonadotropins are associated with a higher risk of multiple pregnancy and/or overstimulation of the ovaries (ovarian hyperstimulation syndrome). Therefore, PCOS patients must be monitored very carefully when gonadotropins are utilized. In vitro fertilization (IVF) may also be an option for patients with PCOS.

How is PCOS treated in women not actively seeking to become pregnant?

If fertility is not an immediate concern, hormonal therapies are usually successful in temporarily correcting the problems associated with PCOS. Oral contraceptive pills (OCs) are commonly prescribed to reduce hirsutism and acne, maintain regular menstrual periods, prevent endometrial cancer, and prevent pregnancy. OCs may be combined with medications that decrease androgen action, such as spironolactone, to improve hirsutism. Eflornithine® cream has been approved to reduce facial hair and is applied directly on any affected areas on the face. Hair removal methods such as electrolysis and laser are also helpful.

Treatment with medications that increase the body's sensitivity to insulin, such as metformin, may help improve ovulation and may reduce the risk of developing diabetes or metabolic syndrome. However, metformin should not be used exclusively for fertility purposes.

Overall, treatment for PCOS should be individualized to the needs of the patient.

POLYCYSTIC OVARY SYNDROME

PCOS is a term used to describe a common hormonal disorder that causes the ovaries to produce excessive amounts of androgens. The ovaries may become enlarged with many small follicles that appear like cysts (fluid-filled sacs) (Figures 2 and 3). Symptoms of PCOS include hirsutism; acne; irregular, absent, or heavy menstrual periods; lack of ovulation; and infertility. More than 50% of PCOS patients also are overweight or obese, but that is not part of the definition, and some women are of normal weight. The most common cause of hirsutism is PCOS. Despite persistent questions surrounding the cause of PCOS, many advances have been made in treating this disorder.

Figure 2

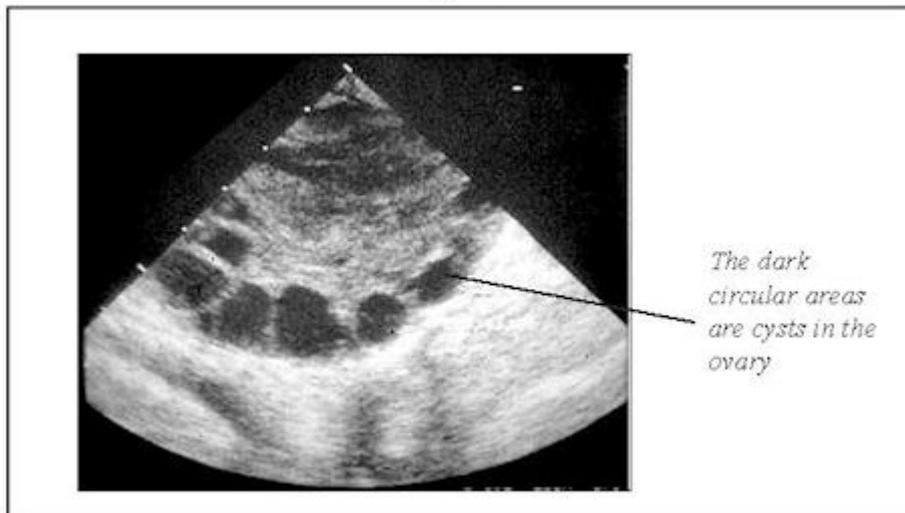


Figure 2. Ultrasound picture of a polycystic ovary.

Figure 3

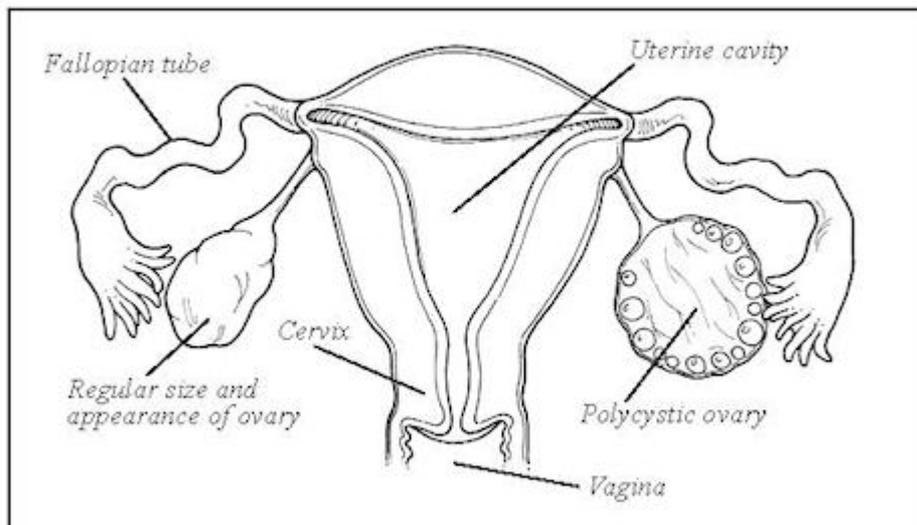


Figure 3. The polycystic ovary may become enlarged with many small cysts.

Normal Menstrual Function

In order to understand PCOS, it is important to understand how hormones control normal ovarian function. The pituitary gland, located at the base of the brain, controls egg and hormone production by releasing two hormones, follicle-stimulating hormone (FSH) and luteinizing hormone (LH). As the menstrual period begins, FSH stimulates a follicle in the ovary to begin growing. The follicle produces the hormone estrogen and contains a maturing egg. Luteinizing hormone stimulates the cells surrounding the follicle to produce significant amounts of androgens. The enlarging ovarian follicle (containing an egg) appears as a small cyst on the surface of the ovary that can be detected by ultrasound.

About 2 weeks before the onset of the next menstrual period, the follicle ruptures and releases (ovulates) the egg. The cells lining the collapsed follicle begin to produce the hormone progesterone. The follicle is now known as a corpus luteum and secretes estrogen and large quantities of progesterone throughout the second half of the menstrual cycle, which is called the luteal phase.

After ovulation, the egg is picked up by the fallopian tube. If the egg is fertilized, it remains in the fallopian tube for 3 or 4 days and then enters the uterus. The estrogen and progesterone secreted during the luteal phase have prepared the uterus to receive a fertilized egg (embryo). If the egg is not fertilized or the embryo fails to implant in the uterus, the secretion of estrogen and progesterone declines about two weeks after ovulation, and the lining of the uterus is shed. This results in menstruation, and the cycle begins again.

Abnormal Menstrual Function

The ovulatory cycle is easily affected by hormonal abnormalities. Overproduction or underproduction of certain hormones can have devastating results. Excess LH or insulin may cause the ovaries to overproduce androgens.

Insufficient FSH may impair ovarian follicle development and prevent ovulation, resulting in infertility. Eventually, the multiple small cysts formed in the ovary from follicles that failed to mature and ovulate result in the PCOS appearance on ultrasound. Not all women with PCOS have ovaries with this appearance.

Lack of ovulation in PCOS results in continuous high levels of estrogen and insufficient progesterone. Unopposed by progesterone, ongoing estrogen exposure may cause the endometrium to become excessively thickened, which can lead to heavy and/or irregular bleeding (dysfunctional or anovulatory uterine bleeding). Over many years, endometrial cancer may result due to continuous stimulation by high levels of estrogen unopposed by progesterone.

DIAGNOSING PCOS

You should describe all of your symptoms to your physician as specifically as possible. PCOS may be suspected by your medical history and physical examination. To confirm the diagnosis and exclude certain other conditions, your physician may measure your blood hormone levels and perform an endometrial biopsy to make sure no precancerous cells are present in your uterus. Because PCOS is not fully understood, it often is difficult to determine why it occurs.

Early Diagnosis

If you have had menstrual irregularity and/or progressive hirsutism since puberty, you should be evaluated for PCOS. If you are diagnosed with PCOS and you have female children, you should watch them for symptoms and inform them that they are at risk, since there is a genetic tendency to inherit the syndrome. Early treatment of PCOS may decrease the development of acne and hirsutism.

Long-term Considerations

Women with PCOS are at risk for metabolic syndrome. Metabolic syndrome is when women develop multiple risk factors for heart disease. Metabolic syndrome is common in women with PCOS, even adolescents. Women may have prediabetes, particularly those with insulin resistance, and may be at an increased risk for diabetes, heart disease, cholesterol abnormalities, and endometrial cancer (Figure 4). If you are diagnosed with PCOS, you and your physician should discuss the long-term health consequences and any additional testing that should be done.

Figure 4

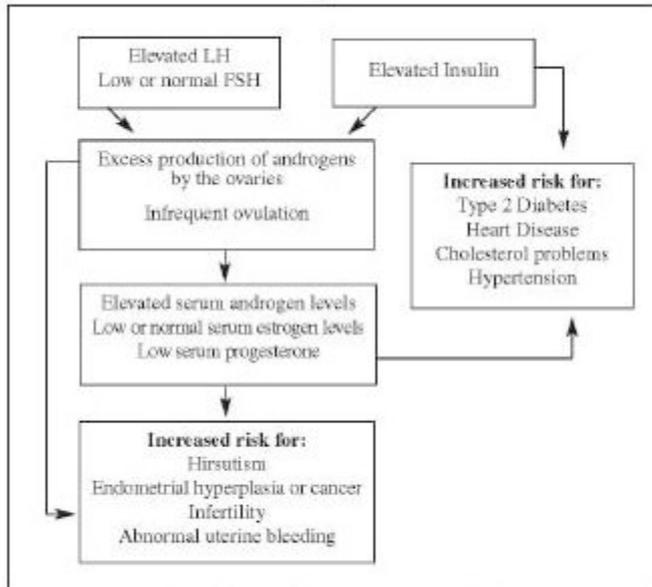


Figure 4. Potential consequences of PCOS.

PCOS TREATMENT

If you are diagnosed with PCOS, treatment will depend upon your goals. Some patients may be concerned primarily with fertility, while others are more concerned about menstrual cycle regulation, hirsutism, or acne. Regardless of your primary goal, PCOS should be treated because of the long-term health risks such as heart disease and endometrial cancer.

Weight Loss

Obesity commonly is associated with PCOS. Fatty tissues produce excess estrogen, which in turn contributes to insufficient FSH secretion by the pituitary gland. Insufficient FSH prevents ovulation and may worsen PCOS. In addition, obesity is associated with the development or worsening of insulin resistance, which may further increase androgen production by the ovaries.

Weight loss improves the hormonal condition of many PCOS patients. If you are overweight, ask your physician to recommend a weight-control plan or clinic. Area hospitals and support groups also are helpful. Although tempting, fad diets and diet pills usually are not effective and in many cases cause additional health problems.

Increasing physical activity is an important step in any weight reduction program. Start slowly with an aerobic activity such as walking or swimming. Increase speed and distance gradually. Regular activity improves state of mind as well as aiding in weight reduction. Recommendations include 3 to 4 exercise periods each week with at least 30 minutes of aerobic exercise. Extreme cases of obesity, unresponsive to medical management and behavioral modification, may be treated with bariatric surgery. Surgical risks have decreased over time and many procedures are performed in a minimally invasive way.

Hormonal Treatment

Hormonal treatment frequently is successful in temporarily correcting the problems associated with PCOS. If treatment is stopped, however, symptoms usually reappear. If you are not trying to conceive, birth control pills may be your best hormonal treatment. Birth control pills decrease ovarian hormone production and help reverse the effects of excessive androgen levels. However, birth control pills are not recommended if you smoke and are over age 35. If you also have hirsutism, your physician may prescribe spironolactone, alone or combined with birth control pills. Rarely, GnRH analogs may be used to decrease ovarian androgen production.

If you are not concerned with fertility or contraception, and hirsutism is not a problem, you can take progesterone at regular intervals to regulate your menstrual bleeding and prevent the endometrial problems associated with excessive estrogen exposure.

Ovulation Induction

If fertility is your immediate goal, ovulation may be induced with clomiphene citrate. Clomiphene is simple to use, is relatively inexpensive, and works well to induce ovulation in many patients. Clomiphene causes the pituitary gland to increase FSH secretion. Sometimes increasing the dosage or the length of treatment is necessary. Approximately 10% of pregnancies with clomiphene are twins; triplets or more are rare. Your physician also may recommend a steroid drug designed to suppress the adrenal gland to supplement clomiphene therapy. If consistent ovulation is not noted with clomiphene, the use of another oral medication, letrozole, may be considered. Whether letrozole results in the same pregnancy rates as clomiphene citrate remains to be determined. Letrozole is not approved by the FDA for induction of ovulation. Letrozole should not be given to pregnant women because it might lead to abnormalities of the reproductive system in any resulting children.

If clomiphene or letrozole do not induce ovulation, or you do not get pregnant within six ovulatory cycles, your physician may prescribe gonadotropins. There are many types of gonadotropins used alone or in combination for ovulation induction. They include human menopausal gonadotropin (hMG), purified human follicle-stimulating hormone (hFSH), recombinant follicle-stimulating hormone (rFSH), and human chorionic gonadotropin (hCG). Gonadotropins are more expensive and have a higher incidence of side effects such as hyperstimulation (excessive swelling) of the ovaries and a higher rate of multiple pregnancy such as twins or triplets.

Your needs and response to therapy will determine the appropriate medication for ovulation induction. For additional information, consult the ASRM patient information booklet titled "Medications for Inducing Ovulation" and the patient fact sheet titled Insulin-sensitizing Agents.

In very rare cases, ovulation is not achieved with either clomiphene or gonadotropins, and ovarian surgery may be tried to stimulate ovulation. Surgical procedures such as ovarian drilling may be performed through laparoscopy. Although these procedures have helped some patients to ovulate, they also may

have adverse effects on future fertility by causing adhesions (scar tissue) and are generally treatments of last resort.

Metabolic Changes

PCOS increases the risk of metabolic disorders. If you have been diagnosed with PCOS, it is important to be screened for risks associated with metabolic disorders such as cardiovascular disease, diabetes and prediabetes, elevated cholesterol levels, and high blood pressure. It is important to have these risk factors assessed and treated.

PSYCHOLOGICAL ASPECTS OF HIRSUTISM AND PCOS

Dealing with hirsutism and PCOS can be emotionally difficult. You may feel unfeminine, uncomfortable, or self-conscious about your excessive hair growth or weight, as well as worried about your ability to have children. Even though you may be embarrassed to share these feelings with other people, it is very important that you talk to your physician as soon as possible to explore the medical and cosmetic treatments available to treat these disorders. It also is important for you to realize that these are very common problems experienced by many women.

Hirsutism is a common disorder that usually can be treated successfully with hormonal medication. Following medical treatment, electrolysis or laser treatment can be used to permanently reduce or remove any remaining unwanted hair. If other female family members have experienced excessive hair growth, you should watch for early signs of hirsutism in yourself and your children, especially during adolescence. Hirsutism is frequently a result of PCOS. Both hirsutism and PCOS are easier to treat when diagnosed at a young age.

PCOS can cause hirsutism, acne, irregular or heavy menstrual periods, lack of ovulation, and infertility. It also is associated with an increased risk of diabetes, uterine cancer, high cholesterol, and heart disease. Despite questions surrounding the causes of PCOS, advances have been made in both understanding and treating the condition. If you are diagnosed with hirsutism or PCOS, your goals and concerns can be addressed in a relatively short period of time, and treatment often is successful.

What is the link between PCOS and insulin/glucose abnormalities?

As many as 70% of women with PCOS have decreased sensitivity to insulin due to increased weight. This causes those women to overproduce that hormone. Higher levels of insulin are needed to keep sugar levels under control in overweight PCOS patients. The resulting high levels of insulin may contribute to excessive production of male hormones (such as testosterone) and can lead to problems with ovulation (timely release of an egg). Women with PCOS who are not overweight should not be treated for insulin resistance.

In addition to reproductive problems, women with PCOS have a higher chance of developing medical problems such as type 2 (non-insulin dependent) diabetes, high blood pressure, and heart disease. Even young adolescents and thin women with PCOS may develop these complications. Women with PCOS also are at greater risk of complications during pregnancy, including pregnancy-induced high blood pressure, diabetes during pregnancy (gestational diabetes), preterm birth, and increased fetal and neonatal death.

How is insulin resistance diagnosed?

Insulin resistance may be suspected based on clinical features such as a darkening of the skin around the neck. Fasting laboratory tests may be performed but are not routinely recommended. If a patient is thought to have insulin resistance, a glucose tolerance test (GTT) should be administered to rule out diabetes.

What are the options to treat insulin resistance?

Weight loss, improved nutrition, and exercise are very important. Behavioral change should be the first line of therapy for an overweight woman with PCOS.

Drugs approved by the Food and Drug Administration (FDA) for the treatment of type 2 diabetes have shown promise for PCOS. These drugs, known as insulin sensitizing agents, improve the body's response to insulin.

The best-studied insulin sensitizing agent available for women with PCOS is metformin. Metformin reduces circulating insulin and androgen (male hormone) levels and restores normal ovulation in some women with PCOS. Gastrointestinal irritation, especially diarrhea and nausea, is a common side effect. These symptoms usually improve after a few weeks and can be lessened if the dose is slowly increased.

Lactic acidosis is a rare but serious adverse effect of metformin. This is a build-up of acid in the blood stream caused by inefficient metabolism. It can cause deep and rapid breathing, vomiting, abdominal pain, lethargy and heart-rhythm disturbances. Metformin is not recommended for patients with kidney, lung, liver, or heart disease. Metformin should also be temporarily stopped prior to surgery or X-ray procedures that use intravenous contrast because of the increased risk of lactic acidosis. Similarly, metformin should not be used by anyone on a lowcarbohydrate diet.

Metformin and other thiazolidinediones have been shown to reduce hyperandrogenism (an increase in male hormone levels and excessive hair growth) and restore ovulation in some PCOS patients. Pioglitazone is not commonly used for PCOS patients and if needed should be supervised by an experienced physician.

In obese PCOS women, especially those with insulin and glucose problems, bariatric (weight loss) surgery may be an effective treatment. In some, surgery can significantly reduce obesity and reduce or eliminate insulin resistance. However, proper nutrition and exercise are still necessary for continued results.

Ovarian Drilling for Infertility

If you have polycystic ovary syndrome (PCOS), you may have very irregular cycles. This usually means that you may have difficulty getting pregnant because you don't ovulate or release an egg on a regular basis. This medical condition changes the amount of important substances, called hormones, that your body produces. You end up with too much testosterone (yes, women, not just men, produce testosterone!) and insulin.

Certain medications may be helpful in making the cycles or some hormone levels more normal in these patients. Birth control pills can make you have a monthly cycle, but will prevent you from becoming pregnant. Clomiphene, a fertility drug that is taken by mouth, may help you ovulate on a more regular basis. Metformin lowers insulin levels and is generally reserved for PCOS patients who have problems with insulin levels. All of these drugs may improve the symptoms of PCOS.

The use of a surgical procedure called ovarian drilling can help promote normal menstrual cycles and lower testosterone levels. This may make it easier for you to get pregnant.

What happens if I have too much testosterone?

High levels of testosterone cause some symptoms of PCOS. You may have more body hair than most women. In addition, you may be overweight. Your periods may be irregular. Your ovaries may not release eggs every month, so you probably don't ovulate regularly and you may have a difficult time becoming pregnant.

What is ovarian drilling?

In patients with PCOS, your ovaries typically have a thick outer surface and you may produce more testosterone than women without PCOS. Ovarian drilling breaks through the thick outer surface and the drilling also reduces the amount of testosterone your ovaries make. In this laparoscopic (minimally invasive) procedure, a tiny camera attached to a thin telescope is inserted into a small incision (surgical opening) below your belly button. Special tools are inserted at other on your belly. These tools make very small holes in your ovaries, which help reduce testosterone production. You may get your period regularly and you should start to ovulate.

Will I get pregnant after ovarian drilling?

Your chances of pregnancy are good as long as your menstrual cycles become more regular and no other problems make it hard for you to conceive. In the year after ovarian drilling, about half of the patients get pregnant. You are less likely to get pregnant with twins or triplets after ovarian drilling than if you are taking fertility drugs. However, your cycles may become irregular again as time goes by.

Sometimes menstrual cycles do not become more regular after this surgery, but it may be easier to induce ovulation with fertility drugs after the surgery.

What are the risks of ovarian drilling?

This surgery could cause injury to your intestines, bladder, blood vessels, and ureter. You could also have bleeding, an infection, or a reaction to anesthesia. There is a risk of death, but it is rare.

If there is too much damage to the ovary, you may run out of eggs at a younger age and go through menopause (which is when you stop getting your period). After the surgery, adhesions or scar tissue can form between the ovaries and the fallopian tube, which carries the egg out of the ovary into the uterus. If you develop adhesions, it may be more difficult for you to get pregnant.