Beyond Infertility

Polycystic Ovary Syndrome (PCOS)



U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES NATIONAL INSTITUTES OF HEALTH *Eunice Kennedy Shriver* National Institute of Child Health and Human Development

PCOS Description

Fast Facts	
Common Names:	Polycystic Ovary Syndrome Polycystic Ovarian Syndrome PCOS Hyperandrogenism Androgen Excess Syndrome
Medical Name:	Polycystic Ovary Syndrome
Common Symptoms Include (But are not limited to):	 Infertility Menstrual irregularities Hirsutism—excess body and facial hair Acne or oily skin Acanthosis nigricans—patches of thickened and dark brown or black skin Fluid-filled sacs or cysts on the ovaries
Common Treatments:	 Lifestyle changes—such as weight loss and exercise Medications—such as oral contraceptives and insulin sensitizers Cosmetic methods for removing excess hair, such as plucking, shaving, or waxing
How many people are affected by the condition?	Because the exact definition of PCOS is still being debated, the exact number of women affected is unknown. Estimates suggest that between 5 percent and 10 percent of females of reproductive age are affected by PCOS. ¹



Polycystic ovary syndrome, or PCOS, is the most common cause of female infertility related to the absence of ovulation (called anovulatory infertility—see *Ovulation 101* for details). In fact, most women don't find out that they have PCOS until they try to get pregnant, but are not successful. However, research shows that many of the features and some of the symptoms of PCOS are present before a girl has her first menstrual period—and that the impact of PCOS goes beyond infertility.

The *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), part of the National Institutes of Health (NIH) within the U.S. Department of Health and Human Services, has supported research on the possible causes and treatments for PCOS for several decades. In 1990, the NICHD sponsored a meeting of experts to define the first set of features for

diagnosing PCOS.² The NICHD is continuing its efforts to learn more about this far-reaching condition and its many effects.

This booklet explains the broad range of PCOS symptoms, describes the conditions associated with PCOS, outlines possible treatment options, and summarizes the latest PCOSrelated research efforts of the NICHD.

Most women don't find out that they have PCOS until they try to get pregnant, but are not successful.

PCOS Description

What is PCOS and how is it diagnosed?

The term "polycystic ovary" or PCO refers to the multiple fluid-filled sacs or cysts that grow on one or both of the ovaries of many women with the condition. Many women with polycystic ovaries have symptoms of PCOS. But, the cysts don't have to be present for a woman to be diagnosed with PCOS.

A woman who has two of the following three features may be diagnosed with PCOS:³

- Chronic absence of **ovulation** (the process that releases a mature egg from the ovary) that leads to menstrual irregularities (please see *Ovulation 101* for more details about normal ovulation and menstruation)
- High levels of **androgens** (a type of hormone) that do not result from other causes or conditions

The first step in diagnosing PCOS is to rule out other conditions that cause similar symptoms.

• Cysts on one or both ovaries (as detected by ultrasound)

Women who are diagnosed with PCOS may have symptoms of PCOS, but no cysts on their ovaries. Similarly, some women have cysts on their ovaries but no symptoms of PCOS.

The exact definition of PCOS is still being debated. The first step in diagnosing PCOS is to rule out other conditions that cause similar symptoms. Some of these conditions include:



- Adrenal glands that make too much hormone (called adrenal hyperplasia)
- The body produces too much of the hormone cortisol (called Cushing's syndrome)
- Problems with the function of the thyroid gland
- A pituitary gland that makes too much of the hormone prolactin (called hyperprolactinemia)



Once a health care provider rules out these and other conditions, he or she will do the following before making a diagnosis of PCOS:

- Take a full family history, which is important because PCOS symptoms often run in families.
- Conduct a complete physical exam.
- Obtain blood samples or conduct other tests to determine a woman's hormone levels, specifically her androgen levels.

How many women are affected by PCOS?

Because the exact definition of PCOS is still being debated, the exact number of women affected is unknown. Estimates suggest that between 5 percent and 10 percent of females age 18 to 44 are affected by PCOS in some way.¹

What causes PCOS?

Researchers and health care providers do not know what causes PCOS at this time.

Because the symptoms of PCOS tend to run in families, the syndrome is probably caused, at least in part, by a change (or mutation) in one or more genes. However, because of the complex pattern of how PCOS symptoms change from one generation to the next, gene mutations are probably not the only cause of PCOS.

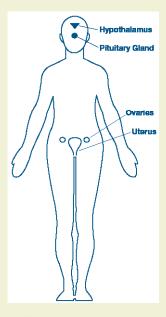
It is likely that PCOS results from a combination of factors, including genes and environmental features. Recent research conducted in animal models also suggests that, in some cases, the origins of PCOS may occur in the womb.

Ovulation 101

Ovulation is the term used to describe the process of releasing a mature egg from the ovary for fertilization or pregnancy. A woman's body goes through this process about every 24 to 32 days if she is not pregnant.

In general, ovulation involves the following body parts:

- **Hypothalamus** (pronounced high-poe-THAL-amus)—the part of the brain that functions as the main control for the body's reproductive system. The hypothalamus works like a thermostat in a furnace in that it controls the levels of different **hormones**—chemicals that control functions in the body—and other chemicals in the body. Some hormones get functions going in the body; other hormones cause functions to stop.
- **Pituitary** (pronounced pitt-OO-ih-terry) **gland**—the body's master gland. The pituitary sends out hormones to control the other glands in the body, including the ovary (see below).
- **Ovaries**—the source of eggs in a woman's body. The ovaries have **follicles**, which are small clusters of cells with a hollow space in the center, in which eggs mature. The ovaries also make hormones—such as **estrogen** and **androgens**—to maintain a woman's health.



• Uterus—where a woman carries a baby, also called the womb. The uterus has different layers; its innermost layer or lining is called the endometrium—endo means "inside" and metrium (pronounced MEE-tree-um) means "womb." The endometrium functions as a bed for an embryo when a woman is pregnant. If no pregnancy occurs, then the endometrium is shed as a menstrual flow, or period.

These parts interact with one another to coordinate a woman's monthly menstrual cycle.

- The hypothalamus keeps track of the level of natural estrogen in the woman's body.
- When the level gets low, the hypothalamus sends an order to the pituitary gland telling it that the body needs more estrogen.

- The pituitary gets the order and responds by sending out follicle-stimulating hormone (FSH), a hormone that causes the ovarian follicles to grow and mature, and luteinizing hormone (LH), a hormone that directs the ovary to make hormones such as estrogen and androgens. Mature follicles make estrogen and other substances. The pituitary continues to make FSH until the mature ovarian follicles make enough estrogen. If the follicles don't make enough estrogen, the level of FSH goes even higher.
- When the level of estrogen gets high enough, the hypothalamus and pituitary know that there is an egg ready to be released from a mature follicle. To get this egg to the uterus so that it can be fertilized, the pituitary sends out a large burst of LH.
- LH breaks open the mature follicle to release the egg, allowing it to move toward the uterus. The level of LH is only high during the time an egg is being released. This burst is the basis for home ovulation detection kits.
- The empty follicle then starts making progesterone, the hormone that prepares the uterus for pregnancy. Increased levels of progesterone cause the endometrium to change in preparation for pregnancy, should it occur. Once the endometrium is properly prepared, it can support an embryo and allow the embryo to grow.
- If the egg is fertilized, it sends out a hormone called human chorionic gonadotropin (HCG) to let the body know that it's there. HCG is similar to LH and causes the empty follicle to keep making progesterone, the hormone needed for pregnancy. Pregnancy tests measure the level of HCG. If HCG is present, then it's likely that a woman is pregnant.
- If there is no signal, that is, no HCG is present because the egg wasn't fertilized, the empty follicle stops making progesterone. Without progesterone, the endometrium starts to break down, and the woman's body sheds it as her menstrual period. Then the cycle begins again.

PCOS Symptoms

What are the symptoms of PCOS?

Many women are not aware that they have PCOS until they go to their health care providers with concerns about the following:

- Infertility
 - Many women with PCOS are infertile.⁴
 The American Society for Reproductive Medicine defines infertility as the inability of a woman younger than age 30 to get pregnant after 12 months of having unprotected intercourse; the inability of a woman older than age 30 to get pregnant after 6 months of having unprotected intercourse; or the inability to carry a pregnancy to delivery.⁵ Most women

Most women with infertility related to PCOS can be treated and do become pregnant.

with infertility related to PCOS can be treated and do become pregnant. However, some women with infertility related to PCOS will not respond to treatment and don't become pregnant.⁶

- Women with PCOS who do get pregnant are at higher risk for pregnancy complications⁷ (see Are women with PCOS at greater risk for pregnancy complications? for more information).
- Menstrual and ovulation irregularities—Problems with menstruation or ovulation are common in PCOS, and most women with the condition have menstrual irregularities,⁸ such as:
 - No menstrual periods called amenorrhea (pronounced AY-menn-or-ee-uh)
 - Periods only now and then—called oligomenorrhea (pronounced oh-ligg-OH-menn-or-ee-uh)
 - Very heavy periods
 - Bleeding but no ovulation (called anovulatory periods)

- **Excess hair growth**—More than 70 percent of women with PCOS experience hirsutism (pronounced herr-SOO-tiz-um), or excess hair growth.⁶ Excess hair usually grows on the face, chest, and abdomen in patterns that are more common in males.
- Severe acne, late-onset acne, or persistent acne that doesn't respond to other treatments The majority of women with severe acne have PCOS.⁹ PCOS is also common in women who didn't have acne until later in life (after the teenage years) and in those who have acne that does not respond to conventional treatments or that remains in spite of treatment.

After discussing these problems with their health care providers, many women find out that other troublesome features they have are actually associated with PCOS, such as very oily skin and patches of thickened, dark brown or black skin, called acanthosis nigricans (pronounced AY-kann-tho-siss NIH-gri-kanns). All of these things taken together are usually a clear indication of PCOS.

Because many women don't consider these problems to be "symptoms" of any condition, they often don't mention the concerns to their health care providers. As a result, many women with PCOS aren't diagnosed until cysts are found on their ovaries. In some studies, between 70 percent and 100 percent of women with PCOS had cysts on their ovaries.^{10,11}

What causes the symptoms of PCOS?

In general, higher than normal levels of **androgens** (male hormones) in the body cause most symptoms of PCOS.

The ovaries produce **hormones**—chemicals that control functions in the body. One of the hormones that the ovaries make is estrogen, sometimes called the "female hormone" because women need higher amounts of it than men do for normal health. The ovaries also make androgens, sometimes called "male" hormones because men need higher amounts of them than women do for normal health. Both males and females require certain levels of both of these hormones for normal health.

The hormone levels are out of balance in women with PCOS: They have higher than normal levels of androgens and may have lower than normal levels of estrogen. The high levels of androgens can:

- Cause problems with ovarian follicle growth and development, which may prevent the release of eggs.
- Make immature follicles on the ovaries bunch together, forming large lumps or cysts.
- Create the other symptoms of PCOS, including excess hair growth and acne.

Conditions Associated with PCOS

Are there other health concerns associated with PCOS?

Recent research shows that women with PCOS are at higher risk than women who don't have PCOS for a variety of health concerns, and many don't occur until later in adulthood. These other conditions are not yet considered "symptoms" of PCOS, but they do occur in a high number of women with PCOS. The presence of these other conditions can influence treatment decisions for women with PCOS. If left untreated, they can have a negative impact on a woman's health.



Most of these other conditions have their own treatments, and many treatments are used in combination to address both PCOS symptoms as well as symptoms of the other condition. This booklet discusses the treatments for the symptoms of PCOS and its associated conditions in the *What are the treatments for PCOS*? section. The following tables present descriptions of the conditions associated with PCOS.

Women with PCOS are at higher risk than women who don't have PCOS for a variety of health concerns, and many don't occur until later in adulthood.

Insulin Resistance

What is it?

To understand insulin resistance, you need to know a little bit about how the body uses food:

- Your stomach and intestines break down (or digest) the food you eat into a simple sugar called glucose. Glucose is your body's main source of energy.
- After digestion, glucose passes into your blood and is ready for your cells to use as energy. The amount of glucose in your blood is your blood glucose level or blood sugar level.
- Your cells need the hormone insulin to get the glucose out of the blood. Insulin "opens" your cells so that glucose can get in and become energy.
- Normally, the body makes the right amount of insulin so that the level of glucose in the blood stays within a healthy and balanced range.

Insulin resistance means that the cells don't use the insulin the body makes. As a result, higher than normal levels of insulin are needed to get glucose into the cells for energy.

What problems does it cause?

Insulin resistance can cause the body to store more fat and can make that fat hard to lose.

Continued problems with glucose and insulin can also lead to the **metabolic syndrome** and **diabetes** (these conditions are described on pages 11

and 12).

Insulin resistance can also upset the balance of hormones in the body. In particular, it can cause the body to make more androgens—a main feature of PCOS.

The appearance of dark patches of skin, called acanthosis nigricans, is usually a sign of insulin resistance.⁹ This condition is also common in women with PCOS.

How common is it in women with PCOS?

Current studies suggest that 50 percent to 70 percent of women with PCOS have some level of insulin resistance.¹²

Impaired Glucose Tolerance

What is it?

Your cells require a certain amount of insulin to use glucose for energy.

In most cases, the body automatically makes more insulin to keep blood sugar levels within a healthy range.

But sometimes the body stops making extra insulin, or the cells don't use the insulin available. As a result, the blood glucose level gets higher.

Impaired glucose tolerance means that blood sugar levels are higher than normal.

The level may be only slightly higher than normal, or it may be higher than normal only at certain times of the day.

What problems does it cause?

Impaired glucose tolerance affects your body's supply of energy and your overall health.

Impaired glucose tolerance also causes the body to store more fat and can make that fat hard to lose.

Continued problems with glucose and insulin can also lead to the **metabolic syndrome** and **diabetes** (these conditions are described on pages 11

and 12).

How common is it in women with PCOS?

Impaired glucose tolerance and type 2 diabetes are present in about 40 percent of women with PCOS.¹³

The American College of Obstetricians and Gynecologists (ACOG) recommends that women diagnosed with PCOS be screened for impaired glucose tolerance.¹⁴

In addition, a small number of non-obese women with PCOS have impaired glucose tolerance.¹³ Obesity can sometimes cause or worsen impaired glucose tolerance. Because the condition is present in a high number of women who aren't obese, it is likely that PCOS actually causes impaired glucose tolerance in some other way, unrelated to obesity.

Metabolic Syndrome

What is it?

The metabolic syndrome is a group of characteristics that put a person at higher risk for certain problems. These features are all related to metabolism—all the physical and chemical processes in the body that create and use energy. Some features of the metabolic syndrome include:

- Insulin resistance or impaired glucose tolerance (described on pages 9 and 10)
- Central obesity—most of the body's extra fat is stored on the trunk of the body
- High blood pressure
- High blood cholesterol

The metabolic syndrome is sometimes considered a precursor or sign of diabetes because it means that the body has trouble balancing insulin and glucose levels. Many people with the metabolic syndrome later develop diabetes.

What problems does it cause?

The metabolic syndrome is a risk factor for both **diabetes** and **cardiovascular disease** (described on pages 12 and 14).

The metabolic syndrome also makes the body more likely to produce high levels of androgens. Remember that high levels of androgens cause many of the symptoms of PCOS.

How common is it in women with PCOS?

About one-third to one-half of women with PCOS have the metabolic syndrome.¹⁵

Women with PCOS are twice as likely as women in the general population to have the metabolic syndrome.¹⁵

Conditions Associated with PCOS

Diabetes

What is it?

Your cells require a certain amount of insulin to use glucose for energy.

In diabetes, the body either stops making extra insulin, or it doesn't properly use the insulin that is available. As a result, the blood glucose level gets higher.

If the level is high often enough, or on a regular basis, the person has diabetes.

What problems does it cause?

Like impaired glucose tolerance, diabetes leads to problems with the way your cells get and use glucose, which can affect your body's energy supply and your overall health.

Consistently high levels of glucose in the blood cause damage to organs, such as your eyes and your kidneys.

Having diabetes places a person at higher risk for **cardiovascular disease** (described on page 14).

How common is it in women with PCOS?

Impaired glucose tolerance and type 2 diabetes are present in about 40 percent of women with PCOS.¹³

The incidence of diabetes is five- to ten-fold higher in women with PCOS than among women in the general population.¹⁶

Obesity

What is it?

Obesity is a condition in which the body stores more fat than is healthy for a person based on his or her height and body type.

Obesity has a variety of causes. In general, obesity occurs when a person takes in more calories than the body uses—either the person eats too much food, or the person isn't physically active enough.

For some people, obesity results because their bodies don't use calories and nutrients properly. Imbalanced hormone levels, missing enzymes, and even genetic mutations can lead to obesity.

What problems does it cause?

Storing extra fat body can get in the way of how the body works. For example:

- Obesity makes the heart work much harder to pump blood through the body, a situation that increases risk for high blood pressure and heart attack.
- Obesity can throw insulin and glucose levels out of balance, which can lead to the **metabolic syndrome** or **diabetes** (described on pages 11 and 12).
- It can upset the balance of hormones in the body, leading to such problems as insulin resistance and impaired glucose tolerance.

How common is it in women with PCOS?

Up to 70 percent of women with PCOS are obese.⁷

Cardiovascular Disease (Heart Disease and High Blood Pressure)

What is it?

Cardiovascular disease is a group of disorders that includes problems related to the heart and blood vessels. It can include:

- Coronary artery disease narrowing or blockage of the blood vessels that bring blood to the heart
- Coronary heart disease problems with the arteries as well as outcomes, such as chest pain or scar tissue, related to these problems
- Cardiomyopathy (pronounced car-dee-OH-my-AH-puh-thee) – diseases of the heart muscle, including an enlarged heart
- Heart failure—the heart doesn't pump enough blood to the body
- High blood pressure
- Arteriosclerosis or atherosclerosis conditions related to a thickening or stiffening of the walls of blood vessels
- High blood cholesterol

What problems does it cause?

Cardiovascular disease can lead to heart attack or stroke (when blood flow to the brain is interrupted or when a blood vessel in the brain ruptures).

Heart disease is the leading cause of death among women in the United States.¹⁷

Cardiovascular disease is also a major cause of disability and illness, especially among women.

How common is it in women with PCOS?

Several studies have found women with PCOS to be at increased risk for cardiovascular disease.³

In addition, research shows that simply having PCOS, by itself, is associated with higher rates of most risk factors for cardiovascular disease, including the metabolic syndrome, diabetes, high blood pressure, obesity, **obstructive sleep apnea** (described on page 15), and high blood cholesterol.¹² For these reasons, cardiovascular disease is a major concern for all women with PCOS.

ACOG recommends that women with PCOS be screened for factors related to cardiovascular disease.¹⁴ However, it is important to note that studies do not show an increase in cardiovascular events (such as heart attack) in women with PCOS.¹⁴

Obstructive Sleep Apnea

What is it?

Obstructive sleep apnea occurs when someone does not get enough air into the lungs during sleep. This situation leads to lower oxygen levels in the blood.

Many people with obstructive sleep apnea snore loudly, pause in their breathing for several seconds, and then resume normal breathing with a snort or choking sound.

What problems does it cause?

Obstructive sleep apnea is a known risk factor for cardiovascular disease.

In addition, the quality of sleep is lower in those who have obstructive sleep apnea, meaning they are less well rested and sleepier during the day.

Because it is also associated with obesity and the metabolic syndrome, obstructive sleep apnea can be a significant concern for women with PCOS.

How common is it in women with PCOS?

Women with PCOS are at significantly higher risk for obstructive sleep apnea than are women who do not have PCOS.¹⁸

Furthermore, obese women with PCOS are at even higher risk for obstructive sleep apnea than are non-obese women with PCOS.

PCOS Treatments

What are the treatments for PCOS?

Because PCOS includes a broad range of symptoms, health care providers may use a variety of treatments to address the problems of PCOS.

The number-one recommendation of health care providers for women with PCOS is **lifestyle changes**, such as eating a lower calorie diet, losing weight, and getting more physical activity. Losing weight and being more physically active can minimize many PCOS symptoms and associated conditions. For example:

- Even a 5-percent weight loss in women with PCOS can have positive effects on insulin resistance, impaired glucose tolerance, and the metabolic syndrome.¹⁴
- Women with PCOS who lose weight are more likely to have restored ovulation, improved pregnancy rates, lower levels of androgens, and lower blood pressure.
- For many women, weight loss triggers a cascade of changes that get rid of a number of PCOS symptoms, such as acne, without other medication or intervention.

Currently, no single diet or activity plan is known to be more effective than another in helping women with PCOS. Talk to your health care provider about designing a plan specific to your health status and health needs.

It is also important for women with PCOS to talk about their **fertility goals** whether or not they want to have children—when discussing treatments for PCOS with their health care providers. Because some of the more common treatments for PCOS symptoms also prevent pregnancy, it is important that women fully understand their options for treatment and for pregnancy before deciding on a course of therapy. Patients should also discuss the risks of treatments with their health care providers. All treatments have associated risks, some of them serious; some lifestyle factors, such as smoking, can increase these risks.

Some **common treatments for women with PCOS** who want to reduce the effects of high androgen levels (for example, those with irregular periods, acne, or hirsutism) include the following:

- **Oral contraceptives**—Usually the primary treatment for women with PCOS who do not wish to become pregnant, oral contraceptives involve a combination of hormones that:
 - Regulates menstrual periods and ovulation
 - Reduces hirsutism and acne
 - Lowers androgen levels or lowers the body's androgen production, which sometimes improves fertility



Oral contraceptives are also associated with a lower risk of certain kinds of cancers. Currently, no single oral contraceptive is "best" for treating PCOS.¹⁴ However, certain types—ones that do not have properties of androgens—are more effective at treating the hirsutism and acne associated with PCOS.^{9,19}

- **Insulin-sensitizing agents**—These medications make the body more sensitive to the available insulin as a way to help cells better use blood glucose. Studies show that short-term use of insulin sensitizers effectively:¹³
 - Regulates menstrual periods and ovulation
 - Reduces infertility associated with PCOS
 - Minimizes the signs of hirsutism¹⁹
 - Reduces acne

Better use of insulin in the body also reduces the risk of cardiovascular disease and diabetes, which both occur in higher than normal numbers of women with PCOS.²⁰ Currently, the U.S. Food and Drug Administration (FDA) has not approved these medications specifically for the treatment of PCOS symptoms. However, your health care provider may still use these agents to treat symptoms of PCOS; discuss any concerns you have about these treatments with your health care provider.

PCOS Treatments

- **Antiandrogens**—These medications either prevent the body from making androgens, or they limit the activities or effects of androgens. Treatment with antiandrogens:
 - Lowers androgen levels
 - Reduces the signs of hirsutism⁹
 - Treats acne and baldness

Antiandrogens can cause birth defects, so they are often taken with oral contraceptives to prevent pregnancy. As with insulinsensitizing medications, antiandrogens are not FDA-approved for the treatment of PCOS. The "best" type of antiandrogen for treating PCOS symptoms is not known. One antiandrogen—finasteride—is FDAapproved for the treatment of baldness, but is associated with a high risk of birth defects.⁸ Women who want to use this drug should be cautious and should discuss all aspects of the treatment with their health care provider.

The number-one recommendation of health care providers for women with PCOS is lifestyle changes, such as eating a lower calorie diet, losing weight, and getting more physical activity.



• Eflornithine (pronounced EE-floor-nih-theen)—This cream is used to slow growth of unwanted hair, especially on the face. The drug works by blocking an enzyme needed for hair to grow. If the patient stops using the cream, the hair will grow back, so a long-term management plan is needed. Eflornithine is FDA-approved for the treatment of facial hirsutism and is considered safe to use during pregnancy. Although it is known to work successfully in women with facial hirsutism, its specific effectiveness at treating women with PCOS is currently unknown.⁹

- **Cosmetic means of removing or hiding unwanted hair** Women with PCOS can also try other ways to minimize the appearance of unwanted hair, instead of or in combination with medications.^{21,22}
 - Shaving, bleaching, plucking, hair removal creams (called cream depilatories), and waxing are some of the more common ways to remove or hide unwanted hair. Some of these methods, such as shaving and plucking, are associated with skin irritation and ingrown hairs.
 - Electrolysis, intense pulse light therapy, and laser hair removal are other options, but these are often expensive and require multiple treatments.



Women should discuss the risks of these treatments with their health care providers.

• **Retinoids** (pronounced rett-tin-OYDS), **antibacterial agents, and antibiotics for the treatment** of **acne**—These medications reduce inflammation, levels of bacteria in the pores, and oil production to minimize or eliminate acne. Retinoids and antibiotics can be used in cream or pill form; antibacterial agents are only available in cream form. The specific treatment depends on the severity of the acne and how long the acne has been visible.²⁰

PCOS Treatments

What are the treatment options for women with PCOS who want to have a baby?

Even though PCOS is one of the leading causes of female infertility, infertility related to PCOS is treatable in the majority of cases. Women with PCOS can and do still get pregnant—sometimes naturally, sometimes with help.

Lifestyle changes, such as losing weight, can trigger body changes that improve pregnancy rates. For many women with PCOS who want to get pregnant, health care providers will recommend weight loss and other lifestyle changes before adding medications to see if fertility returns and pregnancy occurs naturally. In one study, lifestyle changes alone restored ovulation and improved pregnancy rates.⁷

Sometimes PCOS is not the cause of the infertility. Instead, it results from other factors, such as fallopian tube blockage or a low concentration of sperm in male partners.²³ Women with PCOS and their partners may want to talk to their health care providers about being screened for non-PCOS infertility factors before starting treatment.

Health care providers may prescribe one of the following medications to help women with PCOS get pregnant:

- **Clomiphene** (pronounced KLOM-if-een), or clomiphene citrate, is the most common treatment for infertility in women with PCOS. Women who received this treatment were six times more likely to get pregnant than women who didn't get the treatment.⁶ Women treated with clomiphene were also more likely to have multiple pregnancies (twins, triplets, etc.).⁷ ACOG recommends the use of clomiphene for treating infertility in women with PCOS.¹⁴
- Health care providers are also using **metformin**, an insulin-sensitizing drug currently used to treat diabetes, to treat infertility associated with PCOS. The treatment successfully restarted ovulation in significantly higher numbers of women with PCOS than among those who didn't get the treatment.⁷ But metformin alone did not increase the rate of pregnancy. Metformin is not currently approved by the FDA for the treatment of PCOS-related infertility.
- A combination of metformin and clomiphene may also be used to treat infertility associated with PCOS, particularly in those women who do not respond to clomiphene alone.²³ In studies, use of the combination had only slightly better results than clomiphene alone. However, the combination therapy reduced the number of multiple pregnancies when compared to women treated with clomiphene alone.

• **Gonadotropins** (pronounced go-nadd-ih-TROPE-ins), a category of hormones, are used to treat infertility in women with PCOS who do not respond to metformin or clomiphene.⁷ Low-dosage treatments have a high success rate and show fewer associated problems.

Women considering any of these treatments should discuss risks and benefits with their health care providers.

Women with PCOS can also try other forms of assistive reproductive technology, such as egg donation and *in vitro* fertilization. There are currently few studies of the effectiveness of these methods in women with PCOS.

A surgical procedure—called ovarian drilling—was sometimes used in the past to start regular ovulation or to increase the likelihood of pregnancy. However, it is not clear that such a procedure is actually more successful than medication for treating infertility in women with PCOS. ACOG does not currently recommend ovarian drilling as a treatment for PCOS infertility.⁶

Are women with PCOS at greater risk for certain pregnancy complications?

Yes, women with PCOS who do get pregnant are at higher risk for a variety of pregnancy complications.^{22,24,25} Many of these complications are similar to those common in women with diabetes, probably because of the higher occurrence of diabetes in women with PCOS. Some of these problems include the following:

• **Miscarriage or early pregnancy loss**—The exact reason women with PCOS are at higher risk for miscarriage is uncertain. Obesity is an independent risk factor for miscarriage, so it is not clear whether it is the PCOS or the obesity common in women with PCOS that contributes to miscarriage. Because many women who are obese are also insulin resistant, researchers are exploring whether or not reducing insulin resistance can improve pregnancy outcomes. NICHD-supported research has shown that treatment with the insulin-sensitizing drug metformin can significantly reduce the risk of miscarriage in pregnant women with PCOS.²⁶



PCOS Treatments

• **Gestational diabetes**—This condition is a type of diabetes that only pregnant women get. Pregnancy is usually associated with some degree of insulin resistance, but the body can usually make up for it and function normally. In gestational diabetes, the body can't make up for the insulin resistance, and the woman gets diabetes while she is pregnant. If controlled, gestational diabetes does not usually result in immediate problems for the mother or the fetus. In most cases, the diabetes goes away after the baby is born. Women who have had gestational diabetes and their children are at higher lifetime risk for type 2 diabetes.²⁷



- Preeclampsia This syndrome is marked by a sudden increase in blood pressure after the 20th week of pregnancy.²⁸ Preeclampsia can affect the mother's kidney, liver, and brain. If left untreated, the condition can be fatal for the mother or the fetus. Preeclampsia can lead to eclampsia, a more severe form that can cause seizures and coma in the mother. Daily or weekly blood pressure checks may be useful in detecting sudden changes in blood pressure. Currently, the only cure for preeclampsia is delivering the fetus. If a woman gets preeclampsia, the health care provider may develop a plan to try to prolong the pregnancy to give the fetus more time to grow and mature. This plan may include giving the mother medications to help prevent seizures and maintain blood pressure levels within a normal range. At the same time, the health care provider will closely watch the health of the mother for signs that the fetus needs to be delivered right away, even prematurely if necessary.
- **Pregnancy-induced high blood pressure**—Unlike preeclampsia, pregnancy-induced high blood pressure is a general increase in blood pressure that may begin before the 20th week of pregnancy. If not treated, the condition could lead to preeclampsia. Having high blood pressure can impact delivery of the baby in that surgical delivery (cesarean delivery) may be safer for both mother and baby.

Women with PCOS who do get pregnant should work with their health care providers to plan for ways to promote a healthy pregnancy and delivery.

- **Preterm birth**—Preterm birth is defined as delivery before 37 weeks of gestation. Many researchers believe that the higher risk of preterm birth is the result of more pregnant women with PCOS having preeclampsia.²⁵ Preterm infants are at risk for a number of health problems, including low birthweight and underdeveloped lungs, to name a few.
- **Cesarean delivery**—This surgical type of delivery may be more common among women with PCOS because they are more likely to deliver preterm, they are more likely to be obese (sometimes a reason for this type of delivery), and they are more likely to have pregnancy-induced high blood pressure.²⁵ Because it is a surgical procedure, recovery from cesarean delivery can take longer than recovery from vaginal birth.



Women with PCOS who do get pregnant should work with their health care providers to plan for ways to promote a healthy pregnancy and delivery.

More PCOS Information

What research is being done to learn more about PCOS?

The NICHD has been studying PCOS and its effects for decades. Through its **Reproductive Sciences Branch (RSB)**, within the NICHD Center for Population Research, the Institute is exploring the following PCOS research topics:

- Genetic causes of PCOS—Although mutated genes are not the sole cause of PCOS, some cases of the condition are caused, at least in part, by mutated genes. RSB-supported scientists are working to understand what genes and mutations of these genes play a role in causing PCOS and some of its symptoms.
- Precursors or predictors of PCOS in adolescents — Research suggests that PCOS may be detectable in girls as early as their first menstrual periods, or even before.²⁹ The RSB is supporting studies to determine how early PCOS symptoms are present as a way to better diagnose the condition and to



improve care and outcomes. Researchers are also working, with RSB support, to understand the relationship among obesity, high androgen levels, and PCOS in adolescents and women to determine the best ways to prevent PCOS.

• **Development of animal models to study PCOS**—By creating animal models that mirror PCOS in humans, researchers may be able to pinpoint the mechanisms responsible for the condition.

New treatment strategies for PCOS—As scientists learn more about PCOS and its associated disorders, researchers supported by the RSB are seeking new strategies for treating the condition. For instance, RSB-funded investigators are studying the use of metformin in pregnant women who have PCOS to explore its use in reducing miscarriage. Another group of RSB-supported scientists have been comparing the effects of different medications on treating infertility in women with PCOS.

In addition, the NICHD's **Division of Epidemiology, Statistics, and Prevention Research (DESPR)** is exploring early signs of PCOS in teenage girls. Some research suggests that certain signs of PCOS are present at or before puberty. The DESPR research study is examining the relationships among ovarian shape and size, obesity around the waist, and biomarkers of insulin resistance as signs of PCOS in girls who have not yet reached puberty. For more information on this study, visit <u>http://www.nichd.nih.gov/about/org/despr/studies/growdev/pcos.cfm</u>. DESPR researchers are also investigating the relationship between exposure to environmental chemicals and gynecologic diseases, including PCOS. For more information on this study, visit <u>http://www.nichd.nih.gov/about/org/despr/studies/fecunfert/PCBendo.cfm</u>.

Where can I get more information about PCOS?

The Eunice Kennedy Shriver National Institute of Child Health and Human Development

(NICHD) supports and conducts research on topics related to the health of children, adults, families, and populations, including PCOS. The mission of the NICHD is to ensure that all children are born healthy and wanted, that women suffer no harmful effects from the reproductive process, and that all children have the chance to fulfill their potential for a healthy and productive life, free from disease or disability, and to ensure the health, well-being, productivity, and independence of all people through optimal rehabilitation. You can contact the NICHD at:

NICHD Information Resource Center

Phone: 1-800-370-2943 (TTY: 1-888-320-6942) Mail: P.O. Box 3006, Rockville, MD 20847 Fax: (301) 984-1473 E-mail: <u>NICHDInformationResourceCenter@mail.nih.gov</u> Internet: <u>http://www.nichd.nih.gov</u>



More PCOS Information

A number of other organizations provide information about PCOS and offer support to women and families affected by the condition. Some of these organizations are listed here alphabetically.

The **American College of Obstetricians and Gynecologists (ACOG)** is the nation's leading group of professionals providing health care to women. You can find an OB/GYN using its Web site. You can contact ACOG at:

Phone: (202) 863-2518 Mail: 409 12th Street, SW, Washington, DC 20024-2188 Fax: (202) 484-1595 E-mail: <u>resources@acog.org</u> Internet: <u>http://www.acog.org</u>

The **American Society for Reproductive Medicine (ASRM)** is an organization devoted to advancing knowledge and expertise in reproductive medicine and biology. You can contact the ASRM at:

Phone: (205) 978-5000 Mail: 1209 Montgomery Highway, Birmingham, AL 35216-2809 Fax: (205) 978-5005 E-mail: <u>asrm@asrm.org</u> Internet: <u>http://www.asrm.org</u>

The **Hormone Foundation** is the public education partner of the **Endocrine Society**—a professional organization dedicated to advancing excellence in endocrinology (the study of hormones) and promoting its essential role as an integrative force in scientific research and medical practice. The Hormone Foundation is a leading source of hormone-related health information for the public, health care providers, and the media. Its mission is to serve as a resource for the public by promoting the prevention, treatment, and cure of hormone-related conditions through outreach and education. You can contact the Hormone Foundation at:

Phone: 1-800-HORMONE (1-800-467-6663)
Mail: 8401 Connecticut Avenue, Suite 900, Chevy Chase, MD 20815
Fax: (301) 941-0259
E-mail: <u>hormone@endo-society.org</u>
Internet: <u>http://www.hormone.org</u>

The International Council on Infertility Information

Dissemination, Inc. (INCIID, pronounced "inside") is a nonprofit organization that helps individuals and couples explore their family-building options. INCIID provides current information and immediate support related to the diagnosis, treatment, and prevention of infertility and pregnancy loss and offers guidance to those considering adoption or childfree lifestyles. You can contact INCIID at:

Phone: (703) 379-9178 Mail: P.O. Box 6836, Arlington, VA 22206 Fax: (703) 379-1593 Internet: <u>http://www.inciid.org/</u>

The Polycystic Ovarian Syndrome Association (PCOSA)

is a nonprofit organization that provides comprehensive information, support, and advocacy for women and girls with PCOS. The Web site includes contact information for "Professional Members"—health care providers with an interest in or who specialize in PCOS. You can contact the PCOSA at:

Phone: 1-877-775-PCOS (7267) Mail: P.O. Box 3403, Englewood, CO 80111 E-mail: info@pcosupport.org Internet: <u>http://www.pcosupport.org/</u>

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