POLYCYSTIC OVARY SYNDROME

by Walter Futterweit, M.D.

Polycystic ovary syndrome (PCOS) is a disorder characterized by high levels of male hormones (androgens) and chronic anovulation, or failure to ovulate. In addition, PCOS is associated with insulin resistance, the key problem underlying Type 2 diabetes. (In insulin resistance, body tissues, particularly muscle, fat and liver cells, do not respond properly to insulin. As a result, more insulin that normal is needed to keep a person's blood sugar level in the normal range.)

The effects of the hormone imbalances that occur in PCOS vary somewhat from woman to woman, but typically they cause menstrual irregularities, infertility, acne, increased body hair, and thickening of scalp hair. Having PCOS also raises a woman's risk of developing endometrial cancer (cancer of the lining of the uterus), Type 2 diabetes, and some of the macrovascular complications associated with Type 2 diabetes, including heart disease.

PCOS appears to affect anywhere from 5% to 7.5% of all women of reproductive age (including adolescents) and as many as 25% to 50% women of reproductive age who have Type 2 diabetes. Diabetes develops in about one-third of all women with PCOS.

In spite of the large numbers of women affected by PCOS and its potentially serious consequences, many women have never heard of it. That's unfortunate, because effective treatments are available, and early diagnosis gives a woman the best chance of avoiding long-term complications.

Symptoms

Symptoms of PCOS typically develop during puberty and progress slowly. Some of the more common symptoms include the following:

- Increased body hair (called hirsutism) on the face, trunk, lower abdomen, arms, and legs
- Thinning of scalp hair (called alopecia)
- Persistent, sometimes severe, acne that may last into a woman's 30's
- Erratic menstrual cycles, occurring two to six times a year
- Heavy menstrual bleeding, the formation of blood clots, and the tendency to have several menstrual bleeding episodes a month
- Obesity (although not all women with PCOS are obese)
- Symptoms of low blood sugar after eating significant amounts of carbohydrate
- Difficulty with conceiving

Women who experience these symptoms should have them checked out by a physician, both to rule out other causes and to start treatment for PCOS, if diagnosed, as soon as possible.

Associated Risks

PCOS carries with it an increased risk of early cardiovascular problems, which may include high blood pressure, lipid disorders (high LDL cholesterol, high triglycerides, and low LDL cholesterol), and an increased tendency to develop blood clots. Women with PCOS are at a much higher risk of diabetes than the general population.

There is an increased incidence of endometrial cancer among women with PCOS, and it may occur at a relatively younger age in women who have PCOS than in those who don't. Some 5% to 10% of women who have PCOS develop ovarian tumors. Most of these tumors are benign, but some reach a large size with a tendency to rupture. Frequent expert ultrasonographic studies of the pelvis should be performed to follow not only the endometrium of the uterus, but also the early formation of these tumors, which should be surgically removed.

Genetic studies of families in which one woman has PCOS indicate that a significant number of these women have sisters who may also be affected with PCOS. Male siblings may have an increased tendency to premature balding and lipid abnormalities, particularly high triglycerides. So when a woman is diagnosed with PCOS, family members may also want to get a checkup.

Diagnosis

To diagnose PCOS, a doctor must rule out certain other diseases that can mimic the symptoms of PCOS, such as thyroid disease, diseases of the adrenal glands, prolactin disorders involving an increase in a pituitary hormone called prolactin, and adrenal or ovarian masculinizing tumors (adenomas).

The following laboratory studies are useful in diagnosing PCOS:

- Serum testosterone and active free testosterone
- Serum adrenal hormone studies of androgens
- Serum dehydroepiandrosterone sulfate (DHEAS)
- Serum 17-hydroxyprogesterone (17-OHP)

- Serum Prolactin
- Thyroid function tests (T4, TSH)

An ultrasound examination of the pelvis is helpful but not essential in making the diagnosis. A pelvic ultrasound can reveal the presence of polycystic ovaries - ovaries with multiple cysts - for which this syndrome is named. However, an ultrasound exam is not considered diagnostic since nearly 25% of all women of reproductive age may have polycystic ovaries. What's more, the appearance of the ovaries can be altered by treatment with birth control pills and other medicines that affect sex hormone production, so even a woman with PCOS may not have polycystic ovaries.

While ultrasound may not be necessary for diagnosing PCOS, once a diagnosis is made, ultrasound is useful for examining the endometrium for signs of cancer and for detecting ovarian tumors.

The role of insulin In PCOS

One of the major problems in PCOS is insulin resistance. When muscle and fatty tissue are resistant to the actions of insulin, the pancreas has to produce increased amounts of insulin in response to meals. High levels of insulin may produce carbohydrate cravings as well as symptoms of hypoglycemia such as irritability, sweatiness, and palpitations. In time, this high production of insulin may cause a decline in the function of the insulin-producing beta cells of the pancreas, leading to Type 2 diabetes.

It has been demonstrated that insulin stimulates male hormone production in the ovaries in PCOS. The effects of male hormones in the ovaries are a major cause of the formation of multiple ovarian cysts. However, these cysts do not rupture and release an egg, as occurs during normal ovulation, and the results can be infertility.

Treating PCOS

There is no one-size-fits-all treatment for PCOS. Most experts would agree, however, that weight reduction, exercise, and following a low-carbohydrate diet are of value. In fact, weight reduction has been shown to restore normal menstrual cycles, ovulation, and fertility and to decrease hirsutism in some women. Working with a registered dietician who is knowledgeable about the treatment of Type 2 diabetes can be a big help for women with PCOS.

Beyond diet, exercise, and weight loss, treatment should be tailored to a woman's main complaint, whether it's acne, hirsutism, alopecia, uncontrollable appetite and weight gain, or infertility associated with erratic or heavy menses. Other complaints may include nipple discharge, emotional problems such as depression or poor self-image, recurrent miscarriages, and pelvic pain.

The following are three classes of drugs often used to treat the symptoms or effects of PCOS:

Oral contraceptives. For women who have erratic, occasional bleeding, oral contraceptive therapy is a major mainstay of PCOS therapy. The menstrual periods become regular, and excess hormone production by the ovaries is suppressed, which may reduce the severity of acne and hirsutism. Oral contraceptive therapy also reduces the risk of endometrial cancer. Since oral contraceptives also effectively prevent pregnancy, however, it may not be the ideal treatment for women who desire to conceive.

For women who do wish to conceive, the drug clomiphene citrate (brand names Clomid and Serophene) is often used to induce ovulation. However, not all women who ovulate in response to clomiphene become pregnant. And since clomiphene can have some serious side effects, it must be used with care.

Androgen-blocking agents. The skin and hair manifestations of PCOS can be controlled with a combination of androgen-blocking agents and oral contraceptives. The most commonly used antiandrogen in the United States is Spironolactone (Aldactone). The results are quite good for acne and excessive hair growth. Scalp hair loss is more difficult to control, but using maximal doses of spironolactine, up to 200 milligrams a day, together with an oral contraceptive may significantly reduce shedding of scalp hair. Spironolactone has been used for almost 50 years and has been found to be useful in the treatment of these symptoms, which can cause significant emotional distress.

Another option for controlling facial hair growth is the topical drug eflornithine (Vaniqa). Rather than removing hair, eflornithine slows its growth. The cream is generally applied twice a day, and it may take two months to see significant effects. According to the manufacturer, those who see no results in six months should discontinue its use. For those who do see results, eflornithine must be used for life for continued effects.

Insulin-sensitizing agents. Oral insulin-sensitizing agents are the same drugs as those used to treat Type 2 diabetes. Even though these drugs are not approved by the Food and Drug Administration for treatment of PCOS, many endocrinologists, gynecologists, and fertility specialists prescribe Metformin (Glucophage) for women with PCOS. Metformin has been shown to improve menstrual function as well as fertility. It is generally prescribed in gradually increasing dosages up to a maximum of 2000 milligrams daily in divided doses.

Both women who are obese and women of normal weight improve menstrual cycles, particularly if they show signs of elevated plasma insulin levels. Not only do these agents lower insulin levels, but they also lower male hormone levels.

Other treatments. If oral contraceptives, androgen-blocking agents, and insulin-sensitizing drugs are not effective, more

complicated treatments, including gonadotropins, as well as *in vitro* fertilization and "ovarian drilling," can be tried. Ovarian drilling is a type of laparoscopic surgery in which a small needle is used to make several punctures in the ovary. An electric current is passed through the needle, causing a small portion of the ovary to be destroyed.

Team management helps

There is much that can be done to help a woman with PCOS. Early diagnosis is the key to possible prevention of later complications leading to diabetes, lipid disorders, and possible heart disease. Unfortunately, most women are not diagnosed at an early stage, in part because many are unaware of PCOS and its symptoms. Women who have regular menses alternating with erratic cycles, for example, may not realize anything serious is amiss. The good news is that recent advances in genetics as well as studies of insulin secretion by the pancreas will be useful in diagnosis and treatment.

Just as a team approach works best for treating diabetes, having a health-care team is a good thing for treating PCOS. This life-long condition should be monitored not only by a woman's endocrinologist and gynecologist, but also by her personal physician, dietician, and other professionals who may be able to help her stay healthy and achieve her weight-loss, fitness, child-bearing, or other goals. ☐

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injections with hormone called

MORE ON PCOS

Need to know more? The following resources give more information about PCOS, its diagnosis, clinical features, potential complications, and treatments:

POLYCYSTIC OVARIAN SYNDROME ASSOCIATION (PCOSA)
(877) 775-PCOS (775-7267) www.PCOSupport.org
This Oregon-based nonprofit organization run by women with polycystic ovarian syndrome is a leading source of information and community support for women who have, or believe they may have, PCOS. An advisory board of physicians supports the organization. PCOSA educates women on the symptoms of PCOS and its available treatments and provides links to other organizations and resources. The Web site includes a PCOTeen link, directed to teens with PCOS. It also lists states chapters and local healthcare professionals who support PCOSA.

PCOS PAVILION
www.OBGYN.net/pcos/pcos.asp
A resource for gynecologists and endocrinologists as well as for women with PCOS, OBGYN.net's PCOS Pavilion features articles and interviews written by PCOS professionals. Women can have their individual questions answered by experts; they can also exchange ideas and personal experiences among themselves in three discussion forums. OBGYN.net also provides PCOS fact sheets and links to other reproductive health topics. OBGYN.net is accessible in Spanish and Portuguese.

THE INTERNATIONAL COUNCIL OF INFERTILITY INFORMATION DISSEMINATION (INCIID)
www.inciid.org/faq/pcos.htm
This website offers answers to over 100 Frequently Asked Questions, addressing diverse PCOS-related issues, from cosmetic concerns, to the effects of insulin-sensitizing drugs on egg quality in women who undergo *in vitro* fertilization. The goal of the site is to enable women to have more productive discussions with their healthcare professionals.

BOOKS
The following books are written by well-known authorities in the PCOS field, all of whom contribute to one or more of the Web sites listed above. The books cite medical literature for those who are interested in more detailed information.

PCOS
THE HIDDEN EPIDEMIC
Samuel S. Thatcher, M.D., Ph.D.
Perspectives Press
Indianapolis, Indiana, 2000

LIVING WITH PCOS
Angela Best-Boss and Evelina Weidman Sterling, with Richard S. Legro, M.D. (editor)
Addicus Books, Inc.
Omaha, Nebraska, 2000