<< Return to Previous Page

American Family Physician
A peer reviewed journal of the American Academy of Family Physicians
April 1, 2003 Table of Contents

Practice Guidelines

ACOG Releases Guidelines on Diagnosis and Management of Polycystic Ovary Syndrome

Barrett M. Schroeder

The American College of Obstetricians and Gynecologists (ACOG) recently published a clinical management guideline on the diagnosis and management of polycystic ovary syndrome (PCOS). The guideline appeared in the December 2002 issue of *Obstetrics and Gynecology*.

Polycystic Ovary Syndrome

The ACOG noted that a universally accepted definition of PCOS is lacking. As proposed by the National Institutes of Health (NIH), the diagnostic criteria are chronic anovulation and hyperandrogenism (established by hormone measurements or clinical findings such as acne or hirsutism) in women in whom secondary causes (e.g., hyperprolactinemia, adult-onset congenital adrenal hyperplasia) have been excluded. Although insulin resistance is present in many women with hyperandrogenic chronic anovulation of unknown cause, the NIH did not include it as a diagnostic criterion. Polycystic-appearing ovaries on ultrasound examination are a nonspecific finding in PCOS.

Approximately 4 to 6 percent of women have hyperandrogenic chronic anovulation. Women with PCOS generally present with infertility or menstrual disorders. Ovulation induction in these women is a concern because of the increased risk of ovarian hyperstimulation syndrome, pregnancy loss in the first trimester, and multiple pregnancy. The risk of pregnancy complications, such as hypertension and gestational diabetes, also is increased.

The etiology of PCOS remains unknown, but selective insulin resistance may be a central factor. Conditions associated with insulin resistance, including centripetal distribution of fat, obesity, obesity-related sleep disorders, and acanthosis nigricans, are common in women with PCOS and are risk factors for cardiovascular disease and type 2 diabetes. (Acanthosis nigricans is a condition characterized by velvety, mossy, verrucous, hyperpigmented skin, often noted on the back of the neck, beneath the breasts, in the axillae, or on the vulva.) Furthermore, obesity, chronic anovulation, and hyperinsulinemia with decreased levels of sex hormone binding globulin are associated with endometrial cancer.

Important features of the history are as follows: the onset and duration of signs of androgen excess; the woman's menstrual history, medication use (including exogenous androgens), and lifestyle (e.g., diet, exercise, alcohol use, smoking); and family history of cardiovascular disease and diabetes. Important factors in the physical examination include the following: the presence of acne, balding, or

clitoromegaly; the distribution of body hair; enlargement of the ovaries (based on a pelvic examination); and signs of insulin resistance (e.g., obesity, acanthosis nigricans). In women with acanthosis nigricans, it is important to consider associated insulinoma or malignancy (particularly adenocarcinoma of the stomach).

Causes of androgen excess other than PCOS that need to be excluded include Cushing's syndrome, androgen-secreting tumors of the ovary or adrenal gland, exogenous androgens, nonclassic (late-onset) congenital adrenal hyperplasia, acromegaly, genetic defects in insulin action, primary hypothalamic amenorrhea, primary ovarian failure, thyroid disease, and prolactin disorders. Women with coexisting signs of Cushing's syndrome (e.g., buffalo hump, moon facies, hypertension, abdominal striae, centripetal distribution of fat, easy bruising, or proximal myopathies), should be screened for the disorder. Laboratory tests may include a thyroid-stimulating hormone level (thyroid disease), a prolactin level (hyperprolactinemia), total testosterone or bioavailable or free testosterone levels (ovarian hyperandrogenism), a two-hour oral glucose tolerance test (diabetes), and fasting lipid and lipoprotein levels (dyslipidemia).

Screening for Nonclassic Congenital Adrenal Hyperplasia

Adult women with anovulation and hirsutism may have nonclassic congenital adrenal hyperplasia. In the United States and Europe, this disorder is most common in Ashkenazi Jews, followed by Hispanics, Yugoslavs, Native American Inuits (Alaska), and Italians. The ACOG recommends that all women suspected of having PCOS be screened with a 17-hydroxyprogesterone level (recommendation based on consensus and expert opinion). If the 17-hydroxyprogesterone level is high, an adrenocorticotropic hormone stimulation test should be performed.

Polycystic Ovary Syndrome and Risk of Type 2 Diabetes

The ACOG recommends that because of demonstrated increased risk, all women with PCOS should be screened for type 2 diabetes and glucose intolerance with a fasting glucose level followed by a two-hour glucose level obtained after a 75-g glucose load (recommendation based on good and consistent scientific evidence). The Diabetes Prevention program has found that in women with impaired glucose tolerance, the risk of diabetes can be reduced significantly with the use of lifestyle interventions and metformin (an insulin-sensitizing agent).

Polycystic Ovary Syndrome and Cardiovascular Disease

Women with PCOS have risk factors for cardiovascular disease as well as for diabetes. These women frequently have dyslipidemia, including borderline or high lipid levels and disproportionately elevated low-density lipoprotein (LDL) cholesterol levels. Insulin resistance, a factor in PCOS, has been associated with elevated triglyceride levels, increased levels of small, dense LDL cholesterol, and decreased levels of high-density lipoprotein (HDL) cholesterol.

The ACOG recommends screening for dyslipidemia in all women with PCOS. The fasting lipoprotein profile should include total cholesterol, LDL cholesterol, HDL cholesterol, and triglyceride measurements (recommendation based on good and consistent scientific evidence). The body mass index and waist-hip ratio also should be calculated. Before drug therapy is used, regular exercise and weight control measures should be tried.

Anovulation and Amenorrhea in Women Not Attempting to Conceive

Long-term management of PCOS most often involves the use of combination oral contraceptive pills. Demonstrated benefits include the suppression of androgen secretion by the ovaries and an increase in the level of circulating sex hormone binding globulin. Oral contraceptive pills also reduce the risk of endometrial cancer, but the extent of this effect in women with PCOS is unknown.

Medroxyprogesterone acetate (depot or intermittent oral therapy) suppresses circulating androgen levels and pituitary gonadotropin levels in women with PCOS. The ACOG notes that the optimal progestin and the optimal duration and frequency of treatment to prevent endometrial cancer in women with PCOS is not known.

Women with PCOS also have been treated with drugs that were developed for the management of type 2 diabetes. Termed insulin-sensitizing agents, these drugs include biguanides (metformin) and a number of thiazolidinediones, such as troglitazone (removed from the market because of hepatotoxicity), pioglitazone, and rosiglitazone. Drug class differences exist, with thiazolidinediones tending to increase weight and biguanides tending to decrease weight; risk-benefit ratios and effects for individual agents also differ. Improvements in insulin sensitivity are associated with decreased levels of circulating androgens, better glucose tolerance, and improved ovulation rates. At present, the U.S. Food and Drug Administration (FDA) has not labeled any insulin-sensitizing agent for the treatment of PCOS.

The ACOG notes that interventions to improve insulin sensitivity, such as weight loss and the use of insulin-sensitizing agents, are beneficial in improving the frequency of ovulation in women with PCOS (recommendation based on good and consistent scientific evidence).

Disease Prevention in Women Not Attempting to Conceive

One large study in women with PCOS showed that the androgen suppression that occurs with use of oral contraceptive pills is associated with significant increases in circulating triglyceride and HDL cholesterol levels. However, no evidence suggests that more cardiovascular events occur with oral contraceptive pill use in women who have PCOS compared with the general population.

In women with PCOS who use metformin, glucose tolerance improves or remains steady over time. The role of insulin-sensitizing agents in the primary or secondary prevention of cardiovascular disease in women with PCOS remains unknown.

According to ACOG, interventions that improve insulin sensitivity, including weight loss and the use of metformin or a thiazolidinedione, may have a positive impact on risk factors for diabetes and cardiovascular disease in women who have PCOS (recommendation based on limited or inconsistent scientific evidence).

Ovulation Induction in Women Attempting to Conceive

In women with PCOS who wish to conceive, treatment begins with weight control and a regular exercise program. Then, if needed, medication is used. The ACOG recommends treatment with clomiphene citrate because of its effectiveness (recommendation based on good and consistent scientific evidence). When this agent is used in women with PCOS, about 80 percent ovulate and one half of these patients conceive.

If clomiphene treatment fails, gonadotropins are often used to induce ovulation in women who have PCOS. The ACOG recommends low-dose, rather than high-dose, gonadotropin therapy because low-

dose treatment induces a high rate of monofollicular development with a lower risk of ovarian hyperstimulation (recommendation based on limited or inconsistent scientific evidence).

While metformin and the thiazolidinediones improve the frequency of ovulation, their effects on early pregnancy are not known. Metformin appears to be safe; documentation is poor for the drug's purported effect in reducing the miscarriage rate in early pregnancy.

The ACOG indicates that the benefit and role of surgery (laparoscopic ovarian drilling by laser or diathermy) are undetermined in women who have PCOS.

Weight Loss and Ovarian Function in Polycystic Ovary Syndrome

Changes in body weight (loss of as little as 5 percent of the initial weight) have been shown to improve the metabolic and reproductive abnormalities in PCOS. Weight loss also has been associated with improved ovulation and pregnancy rates in women who have PCOS.

Few studies support the benefits of a high-protein diet for women with PCOS, and there are concerns about the adverse effects that the diet has on renal function and lipids. Although data on the effects of exercise on PCOS are limited, the ACOG notes that it is reasonable to assume that an exercise program (even without weight loss) would have positive effects.

Hirsutism in Polycystic Ovary Syndrome

A primary treatment for hirsutism in PCOS has not been established, and treatment is often palliative rather than curative. Agents that have been used include oral contraceptives, antiandrogen drugs (spironolactone, flutamide, finasteride), insulin-sensitizing agents, and eflornithine. The FDA has labeled only topical eflornithine hydrochloride cream for the treatment of hirsutism; additional benefits or risks for the use of this agent in women with PCOS are unknown.

Combined medical interventions may be the most effective treatment approach to hirsutism. The combination of an antiandrogen and an ovarian suppression agent appears to be effective in women with PCOS, although the best oral contraceptive pill or antiandrogen agent is not known (recommendations based primarily on consensus and expert opinion).

Mechanical removal of hair (e.g., plucking, shaving, waxing), electrolysis, and laser vaporization also are used to manage hirsutism. Electrolysis may be impractical for removing large numbers of hairs. Multiple electrolysis or laser treatments may be needed. Concomitant medical management directed at reducing androgen levels usually is necessary.
