



Polycystic Ovary/Ovarian Syndrome (PCOS)

Underrecognized, Underdiagnosed,
and Understudied

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National Institutes of Health
Office of Research on Women's Health

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Polycystic Ovary/Ovarian Syndrome: Underrecognized, Underdiagnosed, and Understudied



Section I: What is PCOS?

Polycystic ovary/ovarian syndrome (PCOS) is a set of symptoms related to an imbalance of hormones that can affect women and girls of reproductive age.¹⁻⁷ It is defined and diagnosed by a combination of signs and symptoms of androgen excess, ovarian dysfunction, and polycystic ovarian morphology on ultrasound.²

This informational booklet provides guidance for those who are concerned that they may have PCOS and those who have already been diagnosed. There is also information on current efforts to understand and treat PCOS.

At least 70%
of women with PCOS
remain undiagnosed in
primary care*

* Tomlinson, J. A., Pinkney, J. H., Evans, P., Millward, A., & Stenhouse, E. (2013). Screening for diabetes and cardiometabolic disease in women with polycystic ovary syndrome. *The British Journal of Diabetes & Vascular Disease*, 13(3), 115–123. doi:10.1177/1474651413495571



Section II: Defining PCOS through the years

To better understand what PCOS is, it is important to know how PCOS is defined and categorized. Although it is called polycystic ovary/ovarian syndrome, PCOS is not primarily defined by ovarian cysts.⁸ Rather, PCOS is defined by the presence of at least two of three diagnostic criteria. These diagnostic criteria have been defined three separate times—by the National Institutes of Health (NIH) in 1990, by the European Society of Human Reproduction and Embryology (ESHRE) and the American Society for Reproductive Medicine (ASRM) in 2003 (also known as the Rotterdam criteria), and by the Androgen Excess and PCOS Society (AE-PCOS) in 2006. In 2012, NIH endorsed the 2003 Rotterdam criteria for PCOS. See the various definitions below:

Criteria	NIH 1990	ESHRE/ASRM (Rotterdam) 2003	AE-PCOS 2006	NIH 2012 acceptance of Rotterdam 2003
Hyperandrogenism	✓	✓	✓	✓
Ovarian dysfunction	✓	✓	✓	✓
Polycystic ovarian morphology		✓	✓	✓
	2 of 2 required	2 of 3 required	2 of 3 required	2 of 3 required
Exclusion of conditions that mimic PCOS	✓	✓	✓	✓

Specific disorders with signs and symptoms that overlap with those of PCOS must be ruled out for an accurate PCOS diagnosis. These include hyperprolactinemia, non-classic congenital adrenal hyperplasia, and Cushing’s syndrome. Because of the diagnostic challenges involved with PCOS, primary care providers might recommend seeing a gynecologist, which is a doctor who specializes in the health of a woman’s reproductive system, an endocrinologist, which is a doctor who specializes in hormones, or a reproductive endocrinologist, which is a doctor who specializes in a woman’s reproductive system, hormones, and infertility.

Section III: Signs of PCOS

Dermatological Features



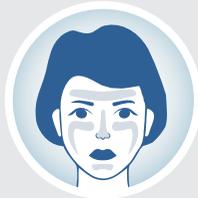
Hirsutism



Balding



Acne



Oily skin



Skin discoloration
(acanthosis nigricans)

High levels of androgens typically lead to various dermatological symptoms.^{9,10} These include hirsutism (coarse and dark hair on the body areas where men typically grow hair—e.g., the face, abdomen, chest, and back), acne, and balding/alopecia. In adolescents, some of the dermatological symptoms may be caused by puberty rather than PCOS.

Menstrual Disorders



Amenorrhea



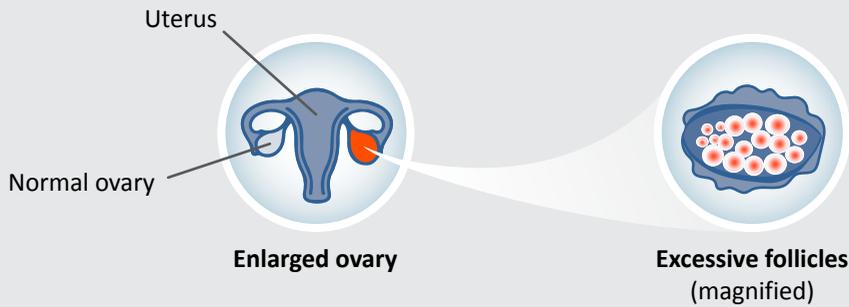
Oligomenorrhea



Menorrhagia

Menstrual disorders may vary, from complete absence of menstruation (amenorrhea) to menstruation delayed to 35 days or more (oligomenorrhea) to heavy bleeding (menorrhagia). Women with irregular menstrual periods have a 91% chance of having PCOS.¹¹ Those with PCOS are 15 times more likely to report infertility.¹²

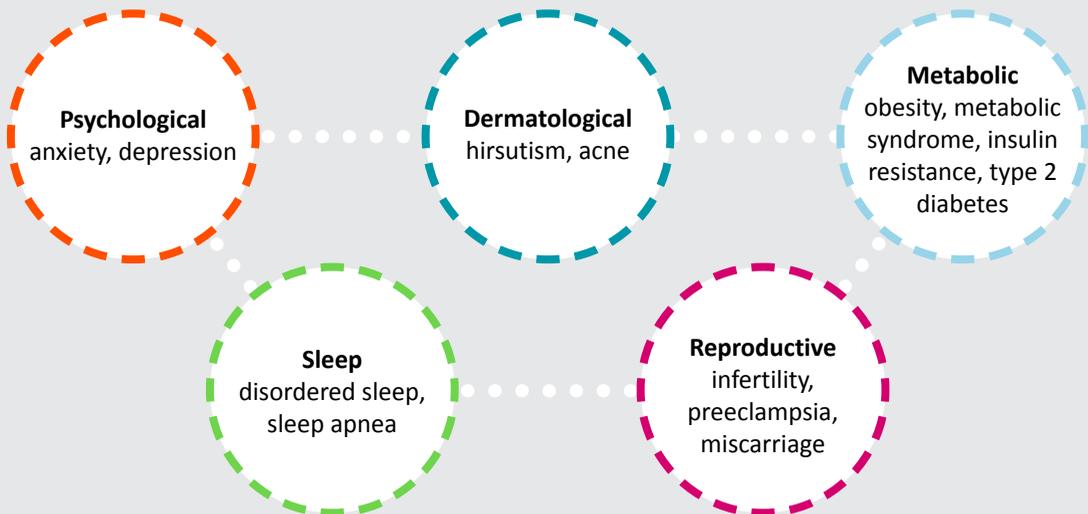
Polycystic Ovaries



Excessive follicles, which is defined as 25 or more follicles that are 2 mm to 10 mm in a single view of a transvaginal ultrasound, may be present in PCOS. Additionally, increased ovarian volume, an ovary that is more than 10 mL, may be present.

a. Health implications

PCOS Affects Many Areas of a Woman's Life



b. An international disease in many forms

Between 5% and 26% of women are affected by PCOS, depending on the diagnostic criteria applied.^{4,13} Women throughout the lifespan are at risk of being affected by PCOS, and women from all regions of the world—including Australia,¹⁴ China,¹⁵ Denmark,¹⁶ Greece,¹⁷ India,¹⁸ the Netherlands,¹⁹ Spain,⁴ the United Kingdom,²⁰ and the U.S.¹—have reported cases of PCOS. There are conflicting results concerning differences in PCOS rates by race, but severity and expression of symptoms may vary based on environmental factors.^{21,22} Understanding differences in symptoms among different racial and ethnic groups can help with the diagnosis:

- Relatively mild in White women
- Higher body mass index (BMI) in White women, especially in North America and Australia
- More severe hirsutism in Middle Eastern, Hispanic, and Mediterranean women
- Increased central adiposity, insulin resistance, diabetes, metabolic risks, and acanthosis nigricans (dark discoloration in body folds and creases) in Southeast Asians and indigenous Australians
- Lower BMI and milder hirsutism in East Asians
- Increased prevalence of metabolic syndrome in Black adolescents and young adults with PCOS compared with their White counterparts²³
- Higher BMI and metabolic features in Africans

c. Across the lifespan

Women who are affected by PCOS are at risk for chronic disease progression, which carries significant public health implications across the lifespan:

Adolescence



Diagnosing PCOS in adolescents is difficult because PCOS and puberty have similar features. These include irregular menstrual cycles and acne. For an accurate diagnosis, adolescents should have all three elements of the Rotterdam criteria for PCOS. Hyperandrogenemia is the main marker for PCOS in adolescents.⁷ Oligomenorrhea or amenorrhea should be present for at least 2 years after the first period. Forty percent of adolescents with menstrual irregularity have polycystic ovaries.

Reproductive age



Fertility issues and hirsutism are the primary issues for women at reproductive ages. Infertility is caused by high levels of androgen and luteinizing hormones, which can lead to irregular menstrual cycles and anovulation, which is an absence of ovulation during a menstrual cycle.²⁴ Women with PCOS have three to four times the rate of pregnancy-induced hypertension and preeclampsia.²⁴ There is also a significantly increased risk of endometrial cancer in women with PCOS.²⁵

Late reproductive to menopausal age



In addition to endometrial cancer, women over 54 years of age with PCOS were found to have a significant risk of ovarian cancer, though the risk for breast cancer is not significantly increased by having PCOS.²⁵ Older women with PCOS have a fourfold to sixfold increase of diabetes compared with women without PCOS.⁷ Older women with PCOS also have more severe hirsutism, in addition to an increased number of metabolic and cardiovascular risk factors.²⁶

d. Obesity and cardiovascular risks

The metabolic abnormalities caused by PCOS, specifically increased abdominal fat and insulin resistance, contribute extensively to increased risk of type 2 diabetes and cardiovascular disease. For women with PCOS, 50–80% have insulin resistance,⁵ 61% are overweight or obese,²⁷ and 50% become prediabetic or diabetic before age 40.²⁸

e. Psychosocial implications

In addition to physical symptoms, women with PCOS are at an increased risk of experiencing mental health issues, including anxiety and depression associated with infertility, obesity, and hirsutism.²⁹

1. **Anxiety.** Anxiety has been found to be significantly higher in women with PCOS compared with controls.^{30–32} PCOS may introduce an additional layer of complexity to the psychological profile and should be considered when evaluating the mental health of women.
2. **Depression.** The prevalence and risk of depression and depressive disorders in women with PCOS are 40–64%, significantly higher than in women without PCOS.^{33,34} Women with PCOS are four times more likely to be at risk for depression compared with women without PCOS.³⁵

f. Coping with worries about having PCOS

If you've been told you have PCOS, you may feel frustrated or sad.³⁶ Also, you may feel relief that there are reasons and possible treatments for the symptoms you have been having such a hard time dealing with—e.g., keeping a healthy weight, hirsutism, acne, or irregular periods. It can be difficult having a diagnosis without an exact cure. However, it's important for women with PCOS to know they are not alone. Finding a support network and a health care provider who knows a lot about PCOS and is someone you feel comfortable talking with is very important. Even though results may take a long time, it is important to keep working on a healthy lifestyle and not let PCOS get you down. Many women with PCOS report that talking with a counselor about their concerns can be helpful.³⁶

Section IV: Risk factors and preventive measures

What factors increase the likelihood of developing PCOS? There are four main risk factors:

a. Genetics

If a close family member, such as a sister or mother, has the condition, you have an increased, but not guaranteed, chance of developing PCOS.^{37,38} Even without a family history of PCOS, there are other risk factors that can lead to its development.



b. Diet

Additionally, diet has been found to be a contributing factor for PCOS. Fats and proteins from one's diet can form advanced glycation end products (AGEs) when exposed to sugar in the bloodstream.³⁹ These compounds are known to contribute to increased bodily stress and inflammation, which have been linked to diabetes and cardiovascular disease.⁴⁰ PCOS patients already have an increased likelihood for metabolic syndrome, cardiovascular issues, and diabetes. *Thus, it's best to limit exposure to AGEs. Animal-derived foods that are high in fat and protein are generally AGE-rich and prone to more AGE formation during cooking.* In contrast, foods that are low on the glycemic index—such as vegetables, fruits, whole grains, and milk—contain relatively few AGEs, even after cooking.⁴⁰



c. Lifestyle

Everyday habits greatly affect the development and severity of PCOS.

- Obesity is widely recognized as aggravating PCOS, so managing a healthy weight, especially abdominal circumference, is recommended.⁴¹
- Exercise helps to reduce many PCOS symptoms, such as depression, inflammation, and excess weight. Aim to incorporate exercise into your lifestyle.⁴¹ The Centers for Disease Control and Prevention (CDC) recommends 150 minutes (2 hours and 30 minutes) of moderate-intensity exercise per week or 75 minutes of high-intensity exercise per week and incorporating strength training 2 days per week.⁴²
- In addition to exercise, increase daily activity by taking the stairs, going on short walks, and stretching throughout the day. No matter the movement, stay consistent and choose an enjoyable activity.
- Women may want to limit inflammatory foods—such as dairy products, foods with gluten, and foods high in glycemic load, such as potatoes, white bread, and sugary desserts—as much as possible.⁴³ But if those foods do not cause bodily aggravation, then there is no need to eliminate them completely.

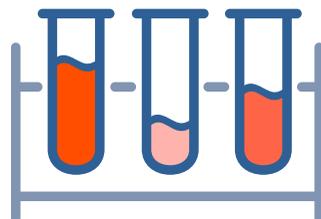
d. Environmental exposure risks

Environmental exposures to endocrine-disrupting chemicals may lead to female reproductive health issues, including PCOS. Research shows that endocrine-disrupting chemicals may pose the greatest risk during prenatal and early postnatal development, when organ systems are developing. Endocrine-disrupting chemicals can be found in many of the everyday products we use, including some plastic bottles and containers, liners of metal food cans, detergents, flame retardants, food, toys, cosmetics, and pesticides. Limiting personal exposure to endocrine-disrupting chemicals may benefit reproductive health.⁴⁴

Long-term medical follow-ups

It's important to follow up regularly with your health care provider and make sure you take all the medications prescribed to regulate your periods and lessen your chances of developing additional chronic diseases. Because women with PCOS have a higher chance of developing diabetes and having other health problems,⁴⁵ your health care provider may suggest having a:

- Blood sugar test once a year
- Hemoglobin A1C test (a test that tells how high your blood sugar has been the past 2–3 months) once a year or a glucose tolerance test every few years
- Vitamin D level test
- Thyroid function test



Section V: Further information for health care providers and researchers

a. Lack of awareness and diagnoses

The existence of multiple diagnostic criteria has made it difficult for health care providers to accurately and consistently diagnose women with PCOS.⁴⁶ This in turn causes patients to be dissatisfied with the diagnostic experience. In an international survey of 1,385 women, only 35% of women were satisfied with their diagnostic experience.⁴⁷ And 84% of women were dissatisfied with the information provided by their health care providers about PCOS and its symptoms.⁴⁷



Some health care providers are less aware of the various diagnostic criteria and phenotypes of PCOS.⁴⁷ Increased awareness of PCOS, its causes, and its symptoms may help the process of diagnosis and bring appropriate subsequent care. As a resource for patients and health care providers, there are international evidence-based guidelines for the assessment and management of PCOS published by researchers at Monash University in Australia. They fully endorse the Rotterdam PCOS diagnostic criteria in adults, which help serve as a PCOS diagnostic tool for medical professionals.²²

b. Possible phenotypes

Phenotypes are the observable characteristics of an individual. Women with PCOS can have any combination of the following phenotypes: excess androgen levels, ovarian dysfunction, and polycystic ovarian morphology. The table below depicts the possible phenotypes from the different combinations³:

Phenotype	Hyperandrogenism	Ovarian dysfunction	Polycystic ovarian morphology
Type A	✓	✓	✓
Type B	✓	✓	
Type C	✓		✓
Type D		✓	✓

Type A is the most severe phenotype, and D is the least severe phenotype. Types A and C are the most prevalent phenotypes.⁴⁸

c. Treatment options

Currently, there is no cure for PCOS, but symptoms can be managed with lifestyle changes and medications. Increasing daily activity—along with eating a high-fiber, low-sugar diet with lots of vegetables, whole grains, and fruits—will help to reduce excess weight and maintain a healthy waist circumference.⁴¹ Also, avoiding or reducing intake of processed foods, trans fats, and saturated fats helps to maintain stable blood sugar levels.⁴⁹ Consider consulting a nutritionist or dietitian. Furthermore, quitting smoking (or never starting) will also improve overall health.

In addition to these lifestyle changes, there are medications that can help with the management of PCOS, which should be tailored to each individual's risk profile, desires, and treatment goals:⁵⁰

- Low-androgen oral contraceptives that contain drospirenone or progestin-only pills, known as minipills⁵¹
- An inositol supplement (myo-inositol, D-chiro-inositol, or a combination of the two), which can help manage PCOS symptoms, such as hirsutism, acne, difficulty conceiving, etc.⁵²
- Metformin
- Lipid-lowering agents for women with lipid abnormalities



Section VI: Economic impact

The cost associated with PCOS derives from treatment of symptoms, including type 2 diabetes (\$1.77 billion), menstrual dysfunction (\$1.35 billion), and hirsutism (\$622 million).⁵³ In comparison, the U.S. health care system spends \$237 billion every year to treat diabetes and \$199 billion on heart disease and stroke.⁵⁴ A team of researchers published a study on the economic impact of PCOS in 2005; see the reference immediately below.** (This was the most up-to-date study on the economic impact at the time of the publication of this booklet.)

\$4.36 billion

**Estimated annual cost of PCOS
to the U.S. health care
system in 2005****

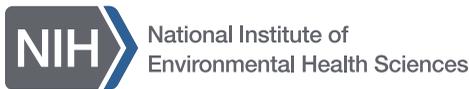
** Azziz, R., Marin, C., Hoq, L., Badamgarav, E., & Song, P. (2005). Health care-related economic burden of the polycystic ovary syndrome during the reproductive life span. *Journal of Clinical Endocrinology and Metabolism*, 90(8), 4650–4658. doi:10.1210/jc.2005-0628

Section VII: How NIH is addressing PCOS



PCOS has been addressed by several institutes across the National Institutes of Health (NIH), including the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD). Through its intramural and extramural organizational units, NICHD

supports and conducts a broad range of research to learn more about the causes of PCOS, its risk factors, and its possible treatments. Though research has demonstrated that PCOS has not just reproductive but also metabolic and mental health manifestations, NICHD funds PCOS research with a particular focus on reproductive health. See more at <https://www.nichd.nih.gov/health/topics/pcos>.



The National Institute of Environmental Health Sciences (NIEHS) has also provided significant contributions in the field of PCOS through its funding support in intramural and extramural research. The studies funded by NIEHS focus on environmental factors that

may play a significant role in the development of PCOS. These include exploring the role of estrogen signaling dysfunction in PCOS development,^{55,56} the origin of theca cells and the effects of irregular differentiation,^{57,58} and environmental factors and genetic predispositions for PCOS through a large multiphase study involving twin sisters.^{59,60} NIEHS efforts focus on causes and origins of PCOS and the development of treatments and preventive measures.



The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) is studying the effects of lifestyle changes on prediabetes metabolic syndrome and insulin resistance, for which PCOS is a risk factor.



On December 21, 2017, the U.S. Senate passed S. Res. 336 by unanimous consent, recognizing the seriousness of PCOS. The resolution encourages States, territories, and local governments to support increasing awareness of PCOS; educate women, girls, health care professionals, and the general public; improve efforts to diagnose and treat PCOS; and improve the quality of life and outcomes for women and girls with PCOS. The resolution also recognizes the need for further research, improved treatment and care options, and a cure for PCOS, acknowledging the struggles affecting all women and girls afflicted with PCOS residing within the U.S.

Section VIII: Conclusion

NIH has conducted valuable research on PCOS. Yet there are critical gaps remaining in the understanding of this disorder, such as the connections of comorbidities to PCOS. Women with PCOS make up the largest group of women at risk for developing type 2 diabetes and cardiovascular disease. They are also at a threefold greater risk for developing uterine cancer. In addition, women with PCOS are at higher risk for mental health disorders—such as anxiety and depression. Because of the serious effects that PCOS can have on many aspects of health, collaborative research efforts will be essential for advancing diagnosis and treatments and reducing the suffering of women with this disorder.

Resources

There are many efforts to address PCOS across the country, including efforts by the American Society for Reproductive Medicine, the American College of Obstetricians and Gynecologists, and the Androgen Excess and PCOS Society. Another noteworthy organization is PCOS Challenge: The National Polycystic Ovary Syndrome Association. It is a 501(c)(3) nonprofit support and advocacy organization for women and girls with polycystic ovary syndrome. PCOS Challenge's mission is to raise public awareness of PCOS and help PCOS patients overcome their symptoms and reduce their risk for life-threatening related diseases, such as diabetes, cardiovascular disease, and cancer. The organization's goal is for PCOS to be treated as a public health priority. Through its national advocacy initiatives, the PCOS Challenge shines light on the need for increased awareness, improved and expanded access to care, and increased funding for PCOS research. It funds efforts to help fight PCOS and organizes the country's largest conference dedicated to education and raising awareness, which typically occurs in mid-September.

The PCOS Awareness Association (PCOSAA) holds another conference around the same time annually. PCOSAA is a worldwide nonprofit dedicated to advocacy for PCOS. The organization and its volunteers are raising awareness of this disorder and providing educational and support services to help people understand what the disorder is, teach people how it can be treated, and decrease the impact of its associated health outcomes.



World PCOS Day is September 1 and marks the start of PCOS Awareness Month. If you see an abundance of teal in September, note that it is the awareness color for the condition.

Section IX: Definitions

The following definitions were taken or adapted from the NCI Dictionary of Cancer Terms, the NCI Dictionary of Genetics Terms, the MedlinePlus Medical Dictionary, or NICHD:

amenorrhea – The absence of a woman’s monthly menstrual period. Occurs when a woman does not get her period by age 16 or when she stops getting her period for at least 3 months and is not pregnant.

androgen – A type of hormone that promotes the development and maintenance of male sex characteristics. Testosterone is one main type of androgen.

cardiovascular disease – A broad term for problems with the heart and blood vessels. These problems are often caused by atherosclerosis and occur when fat and cholesterol are built up in blood vessel (artery) walls.

cyst – A closed, saclike pocket of tissue that can form anywhere in the body. It may be filled with fluid, air, pus, or other material. Most cysts are benign (not cancerous).

dyslipidemia – High levels of lipids (triglycerides or cholesterol) in the blood.

estrogen – A type of hormone that helps the body develop and maintain female sex characteristics and the growth of long bones. Estrogens are made by the body but can also be made in a laboratory. They may be used as a type of birth control and to treat symptoms of menopause, menstrual disorders, osteoporosis, and other conditions.

etiology – The cause or origin of a disease.

follicle – A sac or pouchlike cavity formed by a group of cells. In the ovaries, one follicle contains one egg. In the skin, one follicle contains one hair.

follicle-stimulating hormone (FSH) – A hormone made in the pituitary gland. In females, it acts on the ovaries to make the follicles and eggs grow. In males, it acts on the testes to make sperm. Also called follitropin.

hirsutism – The growth of coarse dark hair above the lips or on the chin, chest, abdomen, or back that resembles male-pattern hair growth.

hyperandrogenism/hyperandrogenemia – Ovarian overproduction of testosterone, leading to the development of male characteristics in a woman.

insulin/insulin resistance (IR) – Insulin is a hormone produced by the pancreas. It is needed to help cells

absorb glucose (sugar) for energy and to control the amount of sugar in the blood. Insulin resistance occurs when cells in key metabolic tissues—liver, muscle, and fat—use insulin less effectively than normal. As a result, a person’s blood sugar level rises above a normal range, placing the person at risk for health problems such as diabetes and kidney, eye, heart, and nerve disease.

luteinizing hormone (LH) – A hormone made in the pituitary gland. In females, it acts on the ovaries to make follicles release their eggs and to make hormones that get the uterus ready for a fertilized egg to be implanted. In males, it acts on the testes to cause cells to grow and make testosterone. Also called interstitial cell–stimulating hormone and lutropin.

menorrhagia – Heavy menstrual periods or excessive bleeding.

oligomenorrhea – Having infrequent menstrual periods—specifically, having periods that occur more than 35 days apart.

perimenopause – The time before menopause that may begin several years before one’s last menstrual period. Signs of perimenopause include more frequent periods at first and then occasional missed periods, periods that are longer or shorter, and/or changes in the amount of menstrual flow.

phenotype – The observable characteristics in an individual resulting from the expression of genes and influences of the environment; the clinical presentation of an individual with a particular genotype.

theca cells – Endocrine cells associated with ovarian follicles that play an important role in fertility by producing the androgen needed for ovarian estrogen production.

type 2 diabetes – The most common form of diabetes, a disease in which the body’s ability to produce or respond to the hormone insulin is impaired, resulting in elevated levels of glucose (sugar) in the blood. Type 2 diabetes is strongly associated with insulin resistance and with subsequent dysfunction in normal pancreatic insulin production. Risk factors for developing type 2 diabetes include obesity, older age, belonging to certain racial or ethnic minority groups, and the presence of other diseases, such as PCOS.

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