Symptoms Associated with Polycystic Ovarian Syndrome (PCOS) [1]

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Polycystic ovarian syndrome or PCOS is one of the most common reproductive conditions in women, and its symptoms include cystic ovaries, menstrual irregularities, and elevated androgen or male sex hormone levels. During the 1930s, Irving Freiler Stein and Michael Leventhal identified the syndrome and its symptoms. Women who experience symptoms of PCOS may also experience secondary symptoms, including infertility and diabetes. Though estimates vary and the causes of the syndrome are not clear as of 2017, PCOS affects approximately ten percent of women of reproductive age. Women who suspect they have symptoms of PCOS should see a doctor, as early treatment may help prevent long-term implications such as infertility, diabetes, and some types of cancers.

Research on PCOS began during the 1930s, when Stein and Leventhal originally investigated the condition, which was then called Stein-Leventhal syndrome. Researchers Stein and Leventhal first identified symptoms associated with what was later called PCOS in a study they published in 1935. The two men found that several of their patients exhibited symptoms of infertility, excess facial and body hair, and menstrual irregularities consisting of either the absence of a menstrual period or an infrequent, sporadic menstrual cycle. When Stein and Leventhal examined women with those symptoms, the researchers observed that the women also had cysts in their ovaries. During those examinations, the two researchers removed the ovaries of some of their patients and discovered that surgically excising ovarian tissue could be therapeutic. The women who had their ovaries excised often found their menstrual periods restored.

In the following decades, researchers and physicians continued to identify novel symptoms that could be used to diagnose women with PCOS. In the 1930s and 1940s, physicians could only diagnose women with PCOS through surgical examination of cysts in the ovaries, one of the main symptoms of PCOS. In 1958, researchers at Harvard Medical School in Boston, Massachusetts, Janet McArthur, Francis Ingersoll, and Jane Worcester documented that women with cystic ovaries also had elevated gonadotropins in their urine. Gonadotropins, hormones secreted by the brain, stimulate hormonal production in the ovaries in women or testes in men. Finding elevated gonadotropins in the urine enabled physicians to diagnose PCOS using a non-surgical method. Physicians commonly used that method during the 1970s and 1980s. However, by the 1990s researchers determined that such a method was unreliable, as women have different amounts of gonadotropins in their urine at different times of their menstrual cycle. In the late 1980s, physicians began using ultrasound technology to diagnose women with PCOS. Ultrasounds reflect ultrasound waves into the abdomen and can show the cysts in the ovaries, a characteristic that is common to the condition. By 1991, a transvaginal ultrasound could reliably detect cystic ovaries, and for this reason the primary means of diagnosis.

As of 2017, physicians look for three primary symptoms to diagnose women with PCOS. Symptoms associated with PCOS can affect women differently depending on a variety of factors, leading to discrepancies in diagnosis of the syndrome. A syndrome functions as a group of symptoms that consistently occur together, though not all symptoms are required to be present for women to receive diagnosis. To receive a diagnosis of PCOS, a woman must exhibit at least two of the three following symptoms: menstrual irregularity, elevated androgens, and/or cystic ovaries. Menstrual irregularity is diagnosed through patient history, meaning that the patient must account for her menstrual cycle over a period of time. Physicians identify elevated androgen levels in a woman with a blood or urine test. Androgens are male sex hormones. Finally, physicians may also identify ovarian cysts in women through a transvaginal pelvic ultrasound. A transvaginal pelvic ultrasound involves the insertion of a thin scoped camera into the vaginal canal to examine the reproductive structures with ultrasound waves. Those three symptoms are the primary symptoms of PCOS and a woman must exhibit at least two of those symptoms to be diagnosed with PCOS. The symptoms used for diagnosis of PCOS are also known as the Rotterdam criteria.

Disruption of menstrual function is one of the three primary symptoms of PCOS. Disruption of menstrual function can include either menstrual absences or menstrual irregularities. When a woman misses her period or experiences sporadic, random menstrual cycles, it means that the glands of the brain, the ovaries, and the uterus are not communicating with one another. In a healthy woman, the uterine lining or endometrium builds up to prepare for a fertilized egg in a cycle that lasts twenty-eight days. The endometrium builds up to provide a hospitable environment for a developing embryo. An egg is ovulated or released by the ovary midway through a woman’s cycle. If sperm does not fertilize the egg by the end of the twenty-eight
day cycle, the endometrium[^11] sheds, which results in a menstrual period during which the woman bleeds. The shedding of the endometrium[^11] lining is a menstrual period and the cycle begins again following a woman’s period. Hormones are directly responsible for the changes in each phase of a woman’s menstrual cycle. Glands in the brain direct those hormones[^4]. Irregularity in that menstrual cycle is the first primary symptom of PCOS.

In addition to menstrual irregularities, women displaying symptoms of PCOS can also experience elevated androgen levels. Androgens are male sex hormones[^9], including dihydrotestosterone, androstenedione, and testosterone. While women generally have low levels of those hormones[^4] in their blood stream, women with PCOS have them in elevated levels. When diagnosing a woman with PCOS, a physician tests a woman’s testosterone levels via a blood test to find evidence that her androgen levels may be increased. The woman’s insulin is typically also tested. Insulin is a hormone[^2] produced by the pancreas to regulate blood glucose and, in women with PCOS, testosterone and insulin tend to both be elevated. That is because women with PCOS also have insulin resistance. Insulin resistance is when the body does not recognize insulin, and is a secondary symptom of PCOS. That process results in a rise in blood glucose and a decrease in sex hormone[^6]-binding globulin. That globulin is responsible for binding to testosterone and for maintaining a healthy level of thirty to ninety-five nanograms of free testosterone per deciliter of blood. When the globulin’s quantity is decreased, regulation[^16] of the production of testosterone decreases, increasing levels of free testosterone, or unbound testosterone. Physicians estimate that sixty to eighty percent of women with PCOS experience elevated androgens[^8]. Though elevated androgens[^8] and menstrual irregularities are critical in diagnosing PCOS, cystic ovaries are also a common primary symptom of the syndrome.

Because, as of 2017, women can only be diagnosed with PCOS through observation of those three primary symptoms, diagnosis can be difficult. One difficulty arises from the fact that women experience the symptoms of PCOS at different times in their lives. Women typically experience the onset of PCOS during adolescence, sometimes at the onset of their first menstrual cycle. For some women, symptoms may not arise until their early twenties. For other women, they do not exhibit any symptoms and do not discover they have PCOS until they seek medical treatment after struggling to get pregnant. Women who delay treatment in PCOS may experience secondary symptoms to a worse degree than those who treat their PCOS early.

Diagnoses of PCOS can also be complicated by secondary symptoms of the syndrome. Secondary symptoms are symptoms that are caused directly or indirectly by the three primary symptoms. Many of the secondary symptoms of PCOS can be a result of another condition. Symptoms like the irregular body hair growth can be caused by medicinal side effects or genetics, or it can be a secondary symptom of PCOS. The secondary symptoms that women with PCOS experience include irregular body and facial hair growth, acne, obesity, insulin resistance and Type II diabetes, depression, and anxiety. Due to the high prevalence of those symptoms in many other conditions, the symptoms of PCOS are often confused with other illnesses, making it difficult to diagnose. Testing to rule out other conditions and observation periods often prolong a diagnosis.

Each primary symptom of PCOS can cause a number of secondary symptoms that can also help in reaching a diagnosis. Increased levels of male sex hormones[^9] can cause a number of secondary symptoms including hair growth irregularities, insulin resistance, and skin conditions. Increased androgen levels can cause acne and hirsutism, or male-pattern hair growth including excess facial and body hair and male-pattern baldness. About sixty percent of women with PCOS experience growth of excess body hair. In addition to acne and male-pattern hair growth, excess androgens[^8] can make it difficult for a woman to ovulate, which may make it difficult for the woman to get pregnant. Cystic ovaries can also cause inovulation. Insulin resistance can further cause Type II diabetes, weight gain and obesity, and a discoloration of the skin to a purple, velvety texture, a condition called Acanthosis nigricans.

Infertility is often the symptom that may lead to the diagnosis of PCOS for some women, despite it being a secondary symptom caused by the primary symptoms of PCOS. Due to a woman’s menstrual and hormonal irregularities associated with PCOS, including elevated androgens[^8], her body may not be capable of ovulating, which is when the ovaries release a mature egg[^13] for fertilization[^17]. Women with PCOS sometimes do not ovulate due to the presence of cysts in their ovaries, a primary symptom in the syndrome. The cysts that are associated with PCOS are not like those that are commonly seen on the surface of the skin. Instead, physicians identify polycystic ovaries as ovaries that are filled with undeveloped eggs trapped inside sacs, which create a type of cyst. A woman can be diagnosed with polycystic ovaries if she has at least twelve cysts in either one or both of her ovaries. Therefore, ovulation[^18] in a woman with cystic ovaries will likely not occur due to the eggs being trapped inside the cysts. Women who experience difficulties getting pregnant with PCOS can be given medications such as clomiphene citrate[^19] or Metformin to help induce ovulation[^18].

As a result of many of the secondary symptoms of PCOS, women with PCOS experience higher rates of depression and anxiety. Over thirty-four percent of women with PCOS deal with depression at some point in their lives compared to seven percent of the healthy female population. Relation of infertility[^3] to inadequacy, undeal body image, and difficulties losing weight can all lead to depression and anxiety in women with PCOS. Women may also develop eating disorders as a result of their weight gain.

Both primary and secondary symptoms of PCOS may build up in women over time to cause other more serious conditions. Such
conditions include obesity, cancer, and other reproductive conditions. Obesity or weight gain can increase the likelihood of a woman to develop sleep apnea, the pause of breathing while asleep, high blood pressure, and high cholesterol. Hormonal imbalances may increase a woman's susceptibility to certain types of cancers, specifically breast and endometrial cancers. Women may also be more prone to heart disease and heart attacks if they become insulin resistant. If a person with PCOS becomes pregnant, she is also more likely to have a miscarriage, or the loss of a pregnancy. PCOS may also occur simultaneously with other diseases, including endometriosis, a disease in which the cells of a woman's uterine lining migrate to other parts of her body and shed with each menstruation. Endometriosis can cause abnormally heavy and painful periods, gastrointestinal symptoms, and infertility.

Women with PCOS treat their symptoms by trying to balance their hormonal production, and the treatment may change depending on whether the woman wishes to become pregnant. Treatment of the symptoms of PCOS include hormonal birth control pills, rings, patches, or injections for women who do not wish to become pregnant. Women who do want to become pregnant can take drugs designed to address infertility by inducing ovulation, Such drugs include clomiphene citrate, a nonsteroidal assisted reproductive technology, medicine designed to induce ovulation in women who cannot ovulate for a known medical reason. In-vitro fertilization may also be used to help women who are unable to ovulate and get pregnant. Physicians recommend women to increase their physical activity and eat a balanced diet to combat the development of insulin resistance, Type II diabetes, and obesity. Treatment and maintenance of the symptoms of PCOS is the primary way for women to avoid unwanted secondary side effects, though there is no single treatment that helps every woman with PCOS, and no cure to the syndrome as a whole.

While some of the primary symptoms of the syndrome directly cause secondary symptoms, physicians and scientist know little about the causes of PCOS. Though the exact causes are unknown as of 2017, research has indicated that there may be a genetic link. Multiple studies have supported the role of genetic factors in PCOS. However, more research is needed. Also, since many of the symptoms seem to cause the other symptoms without any causational pattern, scientists and physicians agree that research has yet to uncover that relationship.

PCOS is estimated to affect eight to seventeen million women between the ages of eighteen and forty-four in the United States. If left untreated, the symptoms of the syndrome may lead to irreversible health conditions that can negatively affect a woman's quality of life. Knowledge of the symptoms, early diagnosis, and developing a suitable treatment plan are all key to managing the symptoms associated with PCOS.

Sources

Metformin increases the ovulatory rate and pregnancy\textsuperscript{[21]} rate from clomiphene citrate\textsuperscript{[19]} in patients with polycystic ovary\textsuperscript{[14]} syndrome who are resistant to clomiphene citrate\textsuperscript{[19]} alone. \textit{Fertility and Sterility} 75 (2001): 310–15.


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Topic
Disorders\textsuperscript{[42]}

Publisher
Arizona State University. School of Life Sciences. Center for Biology and Society. Embryo Project Encyclopedia.

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Format
Articles\textsuperscript{[43]}

Last Modified
Wednesday, July 4, 2018 - 04:40

DC Date Accessed
Tuesday, December 19, 2017 - 21:52

DC Date Available
Tuesday, December 19, 2017 - 21:52

DC Date Created
2017-12-19

DC Date Created Standard
Tuesday, December 19, 2017 - 07:00

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