FEATURE ARTICLE

CE 2.0 Contact Hours

Update on Polycystic Ovary Syndrome

What Dermatology Nurses and Nurse Practitioners Need to Know

Rebecca Carron

ABSTRACT

Purpose: Polycystic ovary syndrome is the most common endocrine disorder in reproductive-aged women. Polycystic ovary syndrome affects approximately 6%–15% of women or about 5–6 million women living in the United States. Dermatology is an entry point in the healthcare system for women with polycystic ovary syndrome. The purpose of this update is to provide dermatology nurses and nurse practitioners with the latest evidence-based guidance for the assessment, diagnosis, and management of polycystic ovary syndrome.

Relevance: Polycystic ovary syndrome occurs worldwide in all ethnic and racial groups. Unfortunately, about 50%–75% of women with the condition are not diagnosed. Dermatology nurses and nurse practitioners are key players in the early diagnosis of polycystic ovary syndrome because of the cutaneous manifestations including acne, hirsutism, and androgenic alopecia.

Essential Points: This update provides clinical information on the following points about polycystic ovary syndrome: epidemiology, pathophysiology, diagnostic criteria, clinical presentation, laboratory testing, comorbidities, management including nonpharmacological and pharmacological interventions, and nursing implications for dermatology nurses and nurse practitioners. This knowledge will help dermatology nurses and nurse practitioners provide expert nursing care for their patients with polycystic ovary syndrome.

Key words: Acne, Hirsutism, Androgenic Alopecia, Dermatology, Nurse Practitioners, Polycystic Ovary Syndrome, PCOS

"GABRIELA" CASE STUDY

Gabriela is a 27-year-old Latina who presents to a dermatology clinic for evaluation of acne occurring on her face and back. She reports to her dermatology nurse practitioner (NP) that her acne has been present "for years." Past providers prescribed oral antibiotics and topical creams. Gabriela reports no improvement in her acne. Gabriela states that her height is 5'5" (165.1 cm) and her weight is 125 pounds (56.8 kg), with a body mass index (BMI) of 20.8 kg/m^2 that is within normal range (http://www.nhlbi.nih.gov/). She denies pregnancy or breastfeeding.

What are the next actions for Gabriela's dermatology NP? Will the NP suggest a trial of another oral antibiotic or a different topical treatment? Or, will the NP assess further to determine if Gabriela's acne might be a sign of an underlying health problem such as polycystic ovary syndrome (PCOS)? Dermatology nurses and NPs are key players in the early diagnosis of PCOS because of the disturbing cutaneous manifestations of PCOS including acne, hirsutism, and androgenic alopecia. These problems bring young women to dermatology clinics for evaluation and treatment.

The purpose of this update is to provide dermatology nurses and NPs with the latest evidence-based guidance for the assessment, diagnosis, and management of PCOS.

Rebecca Carron, PhD, RN, NP-C, *Fay W. Whitney School of Nursing, University of Wyoming, Laramie, WY, and Fort Collins Skin Clinic, Fort Collins, CO.*

The author declares no conflict of interest.

Correspondence concerning this article should be addressed to Rebecca Carron, PhD, RN, NP-C, Fay W. Whitney School of Nursing, Dept. 3065, 1000 East University Avenue, University of Wyoming Laramie, WY 82071-2000.
E-mail: rcarron@uwyo.edu

DOI: 10.1097/JDN.0000000000000259

This knowledge will help dermatology nurses and NPs provide expert nursing care for their patients with PCOS.

EPIDEMIOLOGY

PCOS is the most common endocrine disorder in reproductive-aged women and affects approximately 6%–15% of women (Fauser et al., 2012). Approximately 5–6 million women in the United States or roughly 1 in 10 reproductive-aged women may have PCOS (Futterweit, 2007). The disorder occurs worldwide in all ethnic and racial groups (Fauser et al., 2012). Unfortunately, about 50%–75% of women with PCOS are not diagnosed (Futterweit, 2007). Women may visit several providers before correctly diagnosed. The onset of PCOS is usually at puberty with menstrual irregularity and acne followed by hirsutism (Futterweit, 2007). These symptoms worsen through the young adult years.

Early diagnosis and treatment of PCOS are essential to help prevent the short- and long-term comorbidities associated with the condition. PCOS affects a woman throughout her life (Figure 1). One study reported that PCOS could be responsible for 15.0%–35.6% of cases of type 2 diabetes (T2DM) in White women (Talbott et al., 2007).

The economic burden associated with PCOS in premenopausal women is significant. One analysis reported that the economic burden of PCOS was 4.37 billion dollars (Azziz, Marin, Hoq, Badamgarav, & Song, 2005). In this analysis, 40% of the burden was from PCOS-associated diabetes, whereas only 2.1% of the burden was for the initial evaluation for PCOS. Consequently, the early diagnosis of PCOS in dermatology clinics can help prevent expensive, long-term costs.

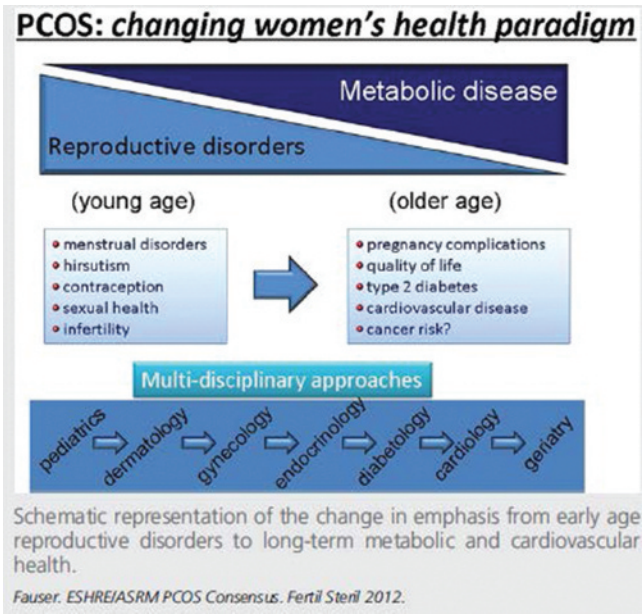

FIGURE 1. Effects of PCOS on the health of women. (Used with permission from Elsevier Science and Technology Journals.)

PCOS occurs in all weight categories from underweight (BMI ≤ 18.9 kg/m^2) to severe obesity (BMI ≥ 40 kg/m^2; Yildiz, Knochenhauer, & Azziz, 2008). Approximately 40%–45% of women with PCOS are not overweight (Futterweit, 2007). Obesity exacerbates insulin resistance and the metabolic and reproductive aspects of PCOS (Fauser et al., 2012). A seminal study showed insulin resistance in nonobese women with PCOS (Dunaif, Segal, Futterweit, & Dobrjansky, 1989). A normal-weight woman with PCOS is at a greater risk for developing T2DM than an overweight woman without PCOS (Wang et al., 2011).

PATHOPHYSIOLOGY

The exact cause of PCOS is unknown. The pathophysiology appears to involve two components: (a) the hypothalamic–pituitary–ovarian axis and (b) insulin metabolism (Ehrmann, 2005). In women with PCOS, the hypothalamus releases gonadotropin-releasing hormone at an increased frequency (Ehrmann, 2005). This appears to cause the anterior pituitary to release more luteinizing hormone (LH) compared with follicle-stimulating hormone (FSH). LH favors the production of testosterone (androgen) by the ovary. Elevated testosterone causes many of the cutaneous signs of PCOS including hirsutism, acne, and androgenic alopecia. Recently, a study reported a genetic disruption in the FSH pathway of women with PCOS that may affect the etiology (Hayes et al., 2015). Adequate FSH is needed to simulate a developing ovarian follicle.

Women with PCOS often have high levels of insulin or insulinemia (Ehrmann, 2005; Futterweit, 2007). Insulin combines with LH and causes the ovary to increase testosterone production. Elevated testosterone prevents the development of ovarian follicles (Futterweit, 2007). A ring of immature ovarian follicles or a "string of pearls" is often visible on an ovarian ultrasound in a woman with PCOS.

Another study found an insulin signaling defect in women with PCOS that could contribute to insulin resistance (Corbould et al., 2005). This intrinsic signaling defect may cause women with PCOS to be at risk for T2DM.

DIAGNOSTIC CRITERIA

PCOS is classified as a syndrome because it is a collection of signs and symptoms without a specific diagnostic test (Azziz et al., 2009). The Rotterdam criteria are most commonly used to diagnose PCOS (Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, 2004). The Rotterdam criteria require two of the three following criteria:

- Ovarian dysfunction expressed as oligo-ovulation or anovulation; women with PCOS often have irregular menstrual cycles, although the cycles can be regular.
- Elevated androgens (hyperandrogenism) expressed as clinical signs (acne, hirsutism, androgenic alopecia)

or biochemical signs (elevated free or total testosterone or elevated dehydroepiandrosterone sulfate [DHEA-S])
- Polycystic ovaries

Polycystic ovaries are classified as 12 or more follicles, 2–9 mm in diameter, in either ovary and/or an ovarian volume greater than 10 ml (Legro et al., 2013). Polycystic ovaries alone are not sufficient for a diagnosis of PCOS because polycystic ovaries are found in approximately 20%–30% of young women (Azziz et al., 2009). PCOS clinicians and researchers are debating a name change for PCOS because of overemphasis on polycystic ovaries, which are not the cause of PCOS (Azziz, 2014). Suggested name changes include "metabolic hyperandrogenic syndrome," "polycystic ovary–hyperandrogenic syndrome," or "polycystic ovary–anovulatory syndrome" (Azziz, 2014, pp. 1144–1145).

A woman with acne and hirsutism (hyperandrogenism) with menstrual cycles occurring every 2–3 months (oligomenorrhea) meets the Rotterdam criteria. Another clinical presentation meeting the Rotterdam criteria is a woman with menstrual irregularity and polycystic ovaries on ultrasound without evidence of hyperandrogenism.

Diagnosing PCOS in adolescent young women can be challenging. The Endocrine Society recommends clinical or biochemical signs of hyperandrogenism with persistent oligomenorrhea for diagnosis (Legro et al., 2013). In adolescents, anovulation or polycystic ovaries do not justify a diagnosis of PCOS as these characteristics may reflect normal development.

DIFFERENTIAL DIAGNOSIS

Related disorders that can mimic PCOS with hyperandrogenism or oligomenorrhea/amenorrhea need to be excluded before determining a PCOS diagnosis (Azziz et al., 2009; Ehrmann, 2005). These disorders include the following:

- Cushing's syndrome
- Hyperprolactinemia or prolactinoma
- Hypothyroidism
- Congenital adrenal hyperplasias
- Androgen secreting tumors

These disorders can be ruled out with appropriate laboratory testing if clinical indicators are present.

CLINICAL PRESENTATION

Women with PCOS often present clinically with a PCOS-related problem, such as acne, without realizing they have an underlying disorder as illustrated in the opening vignette. Women presenting to a dermatology clinic with acne, hirsutism, and/or androgenic alopecia should be screened for PCOS (Futterweit, 2007). Screening suggestions for PCOS are provided in Table 1.

Hirsutism is a distressing symptom of PCOS. Hirsutism is present in approximately 60%–90% of women with PCOS (Practice Committee of the American Society for Reproductive Medicine [ASRM], 2006). Clinicians in dermatology can assess the following body areas for growth of long, coarse terminal hair: upper lip, sideburn area, chin, lower jaw and upper neck, upper and lower back, upper arm, thigh, chest, and upper and lower abdomen (Practice Committee of the ASRM, 2006). Be aware that women from some geographical areas such as eastern Asia may have decreased signs of hirsutism, whereas women from areas such as Brazil may have increased hirsutism (Azziz et al., 2009; Hashimoto et al., 2003).

TABLE 1. Screening Suggestions for Suspected Cases of PCOS

- Acne history and response to treatment
- Growth of terminal, coarse hair on the face, chest (especially in the periareolar area), lower abdomen, medial thighs, and upper or lower back
- Thinning scalp hair in a male pattern
- Menstrual history with age of menarche, frequency of menses; any difficulty, if applicable, conceiving
- Family history of PCOS, particularly in mother or sister

PCOS = polycystic ovary syndrome.

Acne is present in approximately 20%–40% of women with PCOS (Azziz et al., 2009). Assessment includes the typical acne-prone areas of chest, back, shoulders, and face. PCOS-associated acne often is resistant to standard treatment (Futterweit, 2007).

Androgenic alopecia is thinning of the scalp hair in a male distribution pattern. Androgenic alopecia initially can be seen as a widening of the hair part, followed by hair thinning over the crown of the scalp with retention of the frontal hair line (Azziz et al., 2009; Futterweit, 2007). Although numbers vary, androgenic alopecia occurs in approximately 40%–70% women with PCOS (Futterweit, 2007).

Menstrual dysfunction occurs in approximately 50%–90% of women with PCOS and usually presents as oligomenorrhea (irregular menstrual cycles) or amenorrhea (absence of menstruation; Azziz et al., 2009; Practice Committee of the ASRM, 2006). PCOS is the main cause of anovulatory infertility (Futterweit, 2007). Some women with PCOS will report "regular" menstrual cycles. However, women with hirsutism who report regular menstrual cycles often will be found to be anovulatory (Azziz et al., 2009). Ovulatory status can be evaluated with a progesterone level on Days 20–24 of the menstrual cycle. A level of less than 3–4 ng/ml is indicative of anovulation. Menstrual cycles of women with PCOS tend to become more regular as women approach menopause (Fauser et al., 2012).

The Androgen Excess and PCOS Society (AE-PCOS Society) recommends that clinical hyperandrogenism

be manifested as hirsutism; the presence of acne and alopecia alone is not as reliable an indicator of androgen excess as hirsutism (Azziz et al., 2009). If a patient has clinical signs of elevated androgens such as hirsutism and evidence of chronic anovulation, androgen levels or an ovarian ultrasound are not needed for a PCOS diagnosis after the exclusion of related disorders (Legro et al., 2013).

LABORATORY TESTING

Laboratory testing can support a presumed diagnosis of PCOS and aims at detecting excess androgen levels and assessing for oligo-ovulation/anovulation. Measurement of androgen levels should include total and free testosterone and DHEA-S (Practice Committee of the ASRM, 2006). Testosterone is produced primarily from the ovary, and DHEA-S is produced by the adrenal glands. Total testosterone levels can indicate the severity of the androgen excess (Practice Committee of the ASRM, 2006). Free testosterone is unbound to other substances such as sex hormone-binding globulin and is more active (Futterweit, 2007). Increased free testosterone levels are found in approximately 70% of women with PCOS (Azziz et al., 2009). DHEA-S is increased in approximately 25%–35% of women with PCOS (Azziz et al., 2009). Androgen levels are normal in 20%–40% of women with PCOS (Azziz et al., 2009).

Hormonal contraceptives (HCs) can lower androgen levels; patients should be off HCs for at least 6 weeks for accurate results (Futterweit, 2007). Levels should be obtained in the early morning.

The LH-to-FSH ratio is not a reliable indicator of PCOS (Azziz et al., 2009).

The normal LH–FSH ratio is 1:1. FSH levels can be normal or decreased in PCOS. An increased LH–FSH ratio is more frequent in leaner women with PCOS (Azziz et al., 2009). In many obese women with PCOS, the LH–FSH ratio is often normal (Azziz et al., 2009).

COMORBIDITIES ASSOCIATED WITH PCOS

Insulin Resistance

Insulin resistance occurs when usual amounts of insulin cannot transport glucose into cells. The cells are resistant to insulin, so larger amounts of insulin are needed to transport glucose into cells for energy. When the pancreas can no longer compensate with enough insulin, blood sugars begin to rise leading to impaired glucose tolerance (IGT) or prediabetes and T2DM. Approximately 30%–35% of women with PCOS have IGT, and 3%–10% have T2DM (Legro et al., 2013). Women with PCOS are at an increased risk for gestational diabetes (Salley et al., 2007).

The Endocrine Society and the AE-PCOS Society recommend screening all adolescents and women with PCOS with a 2-hour oral glucose tolerance test for IGT and T2DM because of their increased risk (Azziz et al., 2009; Legro et al., 2013). Women with PCOS should be rescreened every 3–5 years or more often as indicated. Management involves lifestyle (diet and exercise) and use of insulin-sensitizing agents such as metformin.

Cardiovascular Disease

Women with PCOS are at risk for cardiovascular disease (CVD) because of multiple risk factors including IGT, the metabolic syndrome (MBS), and dyslipidemia as well as depression, anxiety, and decreased quality of life (Wild et al., 2010). Dyslipidemia is present in approximately 70% of women with PCOS in the United States (Wild et al., 2010). Dyslipidemia can manifest in varying patterns including decreased high-density lipoprotein cholesterol, increased triglycerides, and increased levels of low-density lipoprotein cholesterol.

MBS prevalence in women in the United States with PCOS is approximately 33%–47% which is higher than that in age-matched control women without PCOS (Wild et al., 2010). Central obesity plays a major role in the development of the MBS. The Endocrine Society and the AE-PCOS Society recommend that all women with PCOS should be screened for CVD risk factors including family history, cigarette smoking, glucose intolerance or diabetes, hypertension, dyslipidemia, obstructive sleep apnea, and obesity, especially central obesity (Legro et al., 2013; Wild et al., 2010). The management of CVD and MBS is aimed at modifying and treating risk factors.

Women with PCOS are at risk for increased levels of depressive and anxiety symptoms and decreased health-related quality of life (Fauser et al., 2012). For women with PCOS in the United States, weight is the area of lowest health-related quality of life (McCook, Reame, & Thatcher, 2005). The 3rd PCOS Consensus Workshop concluded that it was not known if it was the syndrome itself or the symptoms and problems of PCOS that resulted in psychological disorders (Fauser et al., 2012).

Endometrial Cancer

Endometrial cancer is a risk for women with PCOS because of risk factors including menstrual dysfunction, T2DM, and obesity (Legro et al., 2013). Regular ultrasound screening in women with PCOS is not recommended (Legro et al., 2013). Combined HCs can help regulate menstrual cycles and decrease the risk for endometrial cancer by regular shedding of the uterine endometrium (Futterweit, 2007).

MANAGEMENT OF PCOS

Management of PCOS will be beyond the scope of practice in most dermatology clinics; nevertheless, nurses and NPs in dermatology clinics need to be able to answer questions about treatment for PCOS, especially

when PCOS is diagnosed in a dermatology practice. Management is aimed at decreasing PCOS symptoms, promoting menstrual regularity, decreasing risk for T2DM and CVD, promoting quality of life, and helping women who desire to conceive (Azziz et al., 2009; Legro et al., 2013). These goals can be achieved with a combination of nonpharmacological and pharmacological interventions, as shown in Table 2.

Nonpharmacological Management

Lifestyle modification with diet and exercise is the first-line treatment for all women with PCOS (Futterweit, 2007). Studies showed that lifestyle intervention (diet, exercise, weight management) in women with PCOS improved body weight and central obesity, decreased testosterone levels, and improved hirsutism and insulin resistance (Moran, Hutchinson, Norman, & Teede, 2011). Exercise goals were approximately 150 minutes per week. The Endocrine Society recommends calorie-restricted diets but does not recommend a particular diet (Legro et al., 2013).

Pharmacological Management

Several medications can help manage PCOS symptoms. Metformin is recommended for women with PCOS who have IGT or T2DM who do not respond to lifestyle interventions or for women who cannot take HCs (Legro et al., 2013; Salley et al., 2007). Metformin is approved by the U.S. Food and Drug Administration (FDA) for T2DM; other uses and benefits are off-label. Metformin can induce ovulation through its antiandrogen properties (Futterweit, 2007), and therefore, women taking metformin should be advised of pregnancy risk.

TABLE 2. Nonpharmacologic and Pharmacologic Treatment for PCOS

Nonpharmacologic treatment
• Lifestyle: diet and exercise: promote weight loss, menstrual regulation, decrease androgen levels, decrease hirsutism, and insulin resistance
Pharmacologic treatment
• Combined hormonal contraceptives (pill, patch, or ring): menstrual regulation, prevent pregnancy, treat acne, hirsutism, and alopecia
• Spironolactone: treat acne, hirsutism, and alopecia
• Metformin: treat impaired glucose tolerance and type 2 diabetes; alternate if women are unable to take combined hormonal contraceptives
• Clomiphene citrate: ovulation induction

PCOS = polycystic ovary syndrome.

Combined HCs (pill, patch, or ring) are the first-line treatment for PCOS (Legro et al., 2013). HCs are FDA approved for birth control; other benefits are additional (http://www.fda.gov/ForConsumers/ByAudience/ForWomen/FreePublications/ucm313215.htm). The progestin lowers LH levels and decreases androgen production, whereas the estrogen increases sex hormone-binding globulin, thereby decreasing androgen levels. HCs are effective for regulating menstrual cycles, improving acne, and hirsutism. Of these contraceptive methods, one has not been found to be more beneficial than the others (Legro et al., 2013).

The diuretic spironolactone (Aldactone) is an effective, off-label, add-on treatment for hirsutism, acne, and alopecia because of its antiandrogen effects (Futterweit, 2007). Spironolactone should not be used by women without adequate contraception because of the increased risk for birth defects. A new study reported that potassium monitoring may not be necessary for healthy women taking spironolactone for acne (Plovanich, Weng, & Mostaghini, 2015). If women were taking other medications that interfered with potassium excretion, monitoring of potassium levels was indicated.

Women with PCOS desiring to conceive often need assistance with advanced reproductive medicine. Clomiphene citrate (Clomid) is a commonly used estrogen modulator that can induce ovulation in women with PCOS (Legro et al., 2013). Clomiphene citrate is FDA approved for ovulation induction. New research indicates that the aromatase inhibitor letrozole, although not FDA approved for ovulation induction, may perform better than clomiphene for live birth rate (Legro et al., 2013).

IMPLICATIONS FOR NURSES AND NPS IN DERMATOLOGY

Nurses and NPs in dermatology settings may encounter women with PCOS who present for evaluation of the cutaneous manifestations of the syndrome. Consequently, nurses and NPs in dermatology need to be up-to-date on the assessment, diagnosis, and management of PCOS. The role of dermatology nurses and NPs in PCOS care is summarized in Table 3. Long-term management of PCOS generally will require referral to a specialist in women's health or endocrinology, depending on the level of women's care provided in each dermatology practice.

We will return to our opening vignette with Gabriela and her NP. Recognizing that acne can be a sign of PCOS, the NP further asked Gabriela about her menstrual cycles and the presence of any excess body hair particularly on her face, periareolar areas, or other areas of her body. Gabriela reported irregular menstrual cycles and that she had problems with dark facial hair on her chin, lower abdomen, thighs, and periareolar areas. Gabriela shaved the excess hair in most body areas, so the NP was only able to note several dark terminal hairs in the periareolar areas. Gabriela had no signs or symptoms of conditions that can mimic PCOS. Gabriela was not on hormonal

TABLE 3. Clinical Pearls for Dermatology Nurses and Nurse Practitioners (NPs)

- PCOS is a common endocrine disorder in reproductive-aged women.
- Dermatology is an entry point in the healthcare system for women with PCOS.
- Nurses and NPs need to screen women with acne, hirsutism, and androgenic alopecia for PCOS.
- Identification of women with PCOS can help women begin treatment for PCOS symptoms sooner and help prevent long-term comorbidities.

PCOS = polycystic ovary syndrome.

HCs. The NP discussed the possibility of a PCOS diagnosis with Gabriela who agreed to be tested for PCOS. The NP ordered the following laboratory tests: total and free testosterone, DHEA-S, and a TSH to assess for thyroid disease. The laboratory tests returned with an elevated free testosterone level, with all other laboratory results normal. The NP referred Gabriela to the local women's health clinic for an OGGT and management with a combined HC and spironolactone. Gabriela was very grateful to her NP for having found the cause of her troubling symptoms. ■

Acknowledgments

The author acknowledges the kind assistance of Drs. Diane Boyle, Pam Clark, Ann Marie Hart, and Sarah Kooienga in the preparation of this manuscript.

REFERENCES

Azziz, R. (2014). Polycystic ovary syndrome: What's in a name? *The Journal of Clinical Endocrinology and Metabolism*, *99*(4), 1142–1145. doi:10.1210/jc.2013-3996

Azziz, R., Carmina, E., Dewailly, D., Diamanti-Kandarakis, E., Escobar-Morreale, H. F., Futterweit, W., … Androgen Excess Society. (2009). Criteria for defining PCOS as a predominantly hyperandrogenic syndrome: An Androgen Excess Society guideline. *The Journal of Clinical Endocrinology and Metabolism*, *91*(11), 4237–4245. doi:10.1210/jc.2006-0178

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. *The Journal of Clinical Endocrinology and Metabolism*, *90*(8), 4650–4658. doi:10.1210/jc.2005-0628

Corbould, A., Kim, Y. B., Youngren, J. F., Pender, C., Kahn, B. B., Lee, A., & Dunaif, A. (2005). Insulin resistance in the skeletal muscle of women with PCOS involves intrinsic and acquired defects in insulin signaling. *American Journal of Physiology—Endocrinology and Metabolism*, *288*, E1047–E1054. doi:10.1152/ajpendo.00361.2004

Dunaif, A., Segal, K. R., Futterweit, W., & Dobrjansky, A. (1989). Profound peripheral insulin resistance, independent of obesity, in polycystic ovary syndrome. *Diabetes*, *38*, 1165–1174.

Ehrmann, D. A. (2005). Polycystic ovary syndrome. *The New England Journal of Medicine*, *352*, 1223–1236.

Fauser, B. C., Tarlatzis, B. C., Rebar, R. W., Legro, R. S., Balen, A. H., Lobo, R., … Barnhart, K. (2012). Consensus on women's health aspects of polycystic ovary syndrome (PCOS): The Amsterdam ESHRE/ASRM-sponsored 3rd PCOS Consensus Workshop Group. *Fertility and Sterility*, *97*(1), 28.e25–38.e25. doi:10.1016/j.fertnstert.2011.09.024

Futterweit, W. (2007). Polycystic ovary syndrome: A common reproductive and metabolic disorder necessitating early recognition and treatment. *Primary Care*, *34*, 761–789. doi:10.1016/j.pop.2007.07.004

Hashimoto, D. M., Schmid, J., Martins, F. M., Fonseca, A. M., Andrade, L. H., Kirchengast, S., & Eggers, S. (2003). The impact of the weight status on subjective symptomatology of the polycystic ovary syndrome: A cross-cultural comparison between Brazilian and Austrian women. *Anthropologischer Anzeiger*, *61*(3), 297–310.

Hayes, M. G., Urbanek, M., Ehrmann, D. A., Armstrong, L. L., Lee, J. Y., Sisk, R., … Dunaif, A. (2015). Genome-wide association of polycystic ovary syndrome implicates alterations in gonadotropin secretion in European ancestry populations. *Nature Communications*, *6*, 7502. doi:10.1038/ncomms88502

Legro, R. S., Arslanian, S. A., Ehrmann, D. A., Hoeger, K. M., Murad, M. H., Pasquali, R., … Endocrine Society. (2013). Diagnosis and treatment of polycystic ovary syndrome: An Endocrine Society clinical practice guideline. *The Journal of Clinical Endocrinology and Metabolism*, *98*(12), 4565–4592. doi:10.1210/jc.2013-2350

McCook, J. G., Reame, N. E., & Thatcher, S. S. (2005). Health-related quality of life issues in women with polycystic ovary syndrome. *Journal of Obstetric, Gynecologic, and Neonatal Nursing*, *34*(1), 12–20. doi:10.1177/0884217504272945

Moran, L. J., Hutchinson, S. K., Norman, R. J., & Teede, H. J. (2011). Lifestyle changes in women with polycystic ovary syndrome. *The Cochrane Database of Systematic Reviews*, (7), CD007506. doi:10.1002/14651858.CD007506.pub3

Plovanich, M., Weng, Q. Y., & Mostaghimi, A. (2015). Low usefulness of potassium monitoring among healthy young women taking spironolactone for acne. *JAMA Dermatology*, *151*(9), 941–944. doi: 10.1001/jamadermatol.2015.34

Practice Committee of the American Society for Reproductive Medicine. (2006). The evaluation and treatment of androgen excess. *Fertility and Sterility*, *86*(5, Suppl. 4), S241–S247. doi:10.1016/j.fertnstert.2006.08.042

Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. (2004). Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). *Human Reproduction*, *19*(1), 41–47. doi:10.1093/humrep/deh098

Salley, K. E., Wickham, E. P., Cheang, K. I., Essah, P. A., Karjane, N. W., & Nestler, J. E. (2007). Glucose intolerance in polycystic ovary syndrome: A position statement of the Androgen Excess Society. *The Journal of Clinical Endocrinology and Metabolism*, *92*(12), 4546–4556. doi:10.1210/jc.2007-1549

Talbott, E. O., Zborowski, J. V., Rager, J. R., Kip, K. E., Xu, X., & Orchard, T. J. (2007). Polycystic ovarian syndrome (PCOS): A significant contributor to the overall burden of type 2 diabetes in women. *Journal of Women's Health*, *16*(2), 191–197. doi:10.1089/jwh.2006.0098

Wang, E. T., Calderon-Margalit, R., Cedars, M. I., Daviglus, M. L., Merkin, S. S., Schreiner, P. J., … Bibbins-Domingo, K. (2011). Polycystic ovary syndrome and risk for long-term diabetes and dyslipidemia. *Obstetrics and Gynecology*, *117*(1), 6–13. doi:10.1097/AOG.0b013e31820209bb

Wild, R. A., Carmina, E., Diamanti-Kandarakis, E., Dokras, A., Escobar-Morreale, H. F., Futterweit, W., … Dumesic, D. A. (2010). Assessment of cardiovascular risk and prevention of cardiovascular disease in women with the polycystic ovary syndrome: A consensus statement by the Androgen Excess and Polycystic Ovary Syndrome (AE-PCOS) Society. *The Journal of Clinical Endocrinology and Metabolism*, *95*(5), 2038–2049. doi:10.1210/jc.2009-2724

Yildiz, B. O., Knochenhauer, E. S., & Azziz, R. (2008). Impact of obesity on the risk for polycystic ovary syndrome. *The Journal of Clinical Endocrinology and Metabolism*, *93*(1), 162–168. doi:10.1210/jc.2007-1834