An Update on Polycystic Ovary Syndrome

Over the past decade, there have been different diagnostic criteria used to evaluate patients with polycystic ovary syndrome (PCOS). Regardless of the diagnostic criteria used, the principal features of PCOS include androgen excess, ovulatory dysfunction, and/or polycystic ovaries.\(^5,6,11\) PCOS is a heterogeneous disorder that is recognized as one of the most common endocrinopathies affecting women. It is critical to note that PCOS is a diagnosis determined by exclusion, such that other disorders of androgen excess or ovulatory dysfunction with clearly defined origins are excluded. These include 21-hydroxylase-deficient non-classic adrenal hyperplasia (NCAH), Cushings syndrome, adrenal tumors, and Cushing’s disease. Ovarian and other adrenal androgen-secreting neoplasms must be ruled out as well. Also, disorders that affect ovulatory dysfunction such as thyroid dysfunction or hyperprolactinemia are often ruled out. However, the prevalence of these abnormalities in patients with apparent hyperandrogenism is low: approximately 2–3%.\(^5,6\)

Obtaining a Diagnosis of the Patient with Possible Polycystic Ovary Syndrome

Whenever attempting to diagnose PCOS, it is important to define the population at high risk for having the syndrome. Women with unwanted hair growth\(^7,8\) or menstrual disturbances\(^9,10\) are highly likely to have PCOS.\(^11,12\) Women with a family history of PCOS should be considered as well. Most importantly, the performance of a thorough history and physical examination in the evaluation of the patient with possible PCOS is critical in arriving at the diagnosis. The four features of the syndrome that should be evaluated include hirsutism, hyperandrogenemia, ovulatory dysfunction, and polycystic ovarian morphology. These findings comprise the cornerstones of the diagnosis, again regardless of the criteria used.

Hirsutism and Polycystic Ovary Syndrome

Hirsutism is the most visible and troubling clinical feature of PCOS. Whereas facial and body hair can be worrisome to patients, only excess terminal hair in a male-type pattern signals androgen excess. Hirsutism most often affects the face, chin, and an area below the umbilicus, which is an extension of pubic hair growth. The modified Ferriman-Gallwey (mFG) score\(^1\) is the most common method of determining the presence of hirsutism. A visual score is assessed based on the method originally reported by Ferriman and Gallwey.\(^13\) Nine body areas are assigned a score of 0–4 based on the density of terminal hairs. A score of 0 represented the absence of terminal hairs and a score of 4 represented extensive terminal-hair growth. Using this approach, cut-off values for defining hirsutism have been reported to be scores of 6–8 or greater.\(^14,15\) Additionally, the prevalence of hirsutism in PCOS can vary according to race and ethnicity. Overall, hirsutism is an important feature of PCOS, affecting approximately 65–75% of non-Asian patients with PCOS.

Hyperandrogenemia and Polycystic Ovary Syndrome

Hyperandrogenemia is a critical component of the PCOS diagnosis. It is defined as supranormal levels of circulating endogenous androgens. The most frequent androgen measured is testosterone (T): total, unbound, or free. Serum T circulates bound to sex-hormone-binding globulin (SHBG), and only the unbound or free T acts on target tissues. Clinicians must be mindful of the limitations and pitfalls inherent in the measurement of T, specifically the highly variable and inaccurate direct assays for total and...
dysfunction.\(^5,6\) Such data clearly indicate that the presence of regular
females diagnosed with PCOS, 65–100% have clinically evident menstrual
following the criteria (new eumenorrhea, although ~5% may demonstrate
episodes of vaginal bleeding is not always indicative of ovulatory cycles,
androgens, including androstenedione and dihydrotestosterone sulfate
improve the use of strict guidelines. Most commonly used today are criteria
measured by a high-quality assay. In addition to an accurate methodology, it is critical that each
ovarian morphology on ultrasonography, depending on the criteria used.\(^4\) It is
impostrated that PCOS is associated with an increased risk of insulin
and type 2 diabetes mellitus.

Ovulatory and Menstrual Function and Polycystic
Ovary Syndrome

Generally, the menstrual dysfunction of PCOS is characterized by irregular,
infrequent, or absent menstrual bleeding. Specifically, 60–85% of patients
on days 20–24 of the cycle; values greater than 3 or 4ng/ml generally
demonstrates the presence of 12 or more follicles measuring 2–9mm in
diameter in each ovary, and/or increased ovarian volume (>10cm\(^3\) or greater than 12 follicles).

Exclusion of Other Disorders of Androgen
Excess or Ovulation

All current definitions of PCOS require that other disorders of androgen
excess or ovulatory function be excluded. Principally, the former includes
21-hydroxylase-deficient non-classic congenital adrenal hyperplasia (NCAH), Cushing’s syndrome, androgen-secreting neoplasms (ASNs), and
drug-induced or iatrogenic hyperandrogenism (IH): the latter includes
thyroid dysfunction and hyperprolactinemia. NCAH is excluded by the
measurement of a follicular phase (pre-ovulatory) basal 17a-
hydroxyprogesterone (17-HP) level, which if >2–4ng/ml mandates an
carcinoma (NCAH), Cushing’s syndrome, androgen-secreting neoplasms (ASNs), and
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excess or Ovulation.\(^\text{13}^{,}\text{19}\) It is important to recognize that the diagnosis of polycystic ovaries by ultrasound
requires the use of strict guidelines. Most commonly used today are criteria
that indicate that polycystic ovaries can be diagnosed when at least one ovary

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<th>Androgen Excess Society (AES) 2006(^\text{1})</th>
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<td>To include all of the following:</td>
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<td>• hyperandrogenism (hirsutism and/or</td>
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<td>• ovarian dysfunction (oligo-anovulation and/or</td>
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<td>polycystic ovaries); and</td>
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<td>• exclusion of related disorders.</td>
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Polycystic Ovaries in Polycystic Ovary Syndrome

Approximately 70–100% of women with PCOS will demonstrate polycystic
ovarian morphology on ultrasonography, depending on the criteria used.\(^4\) It is
important to note that the diagnosis of polycystic ovaries by ultrasound
requires the use of strict guidelines. Most commonly used today are criteria
that indicate that polycystic ovaries can be diagnosed when at least one ovary

It is important to recognize that polycystic ovary syndrome is associated
with an increased risk of insulin resistance, impaired glucose tolerance,
and type 2 diabetes mellitus.
vascular disease, a risk that appears to be worsened by comorbid obesity. All PCOS patients, regardless of weight, should be evaluated for metabolic dysfunction. At a minimum this should consist of a fasting glucose level. However, as most patients with PCOS have good pancreatic β-cell function, although possibly deficient for their degree of insulin resistance, determining the glucose response to a two-hour 75-g oral glucose challenge test (oGTT) is optimum for detecting IGT or DM in these women. Impaired glucose tolerance is diagnosed by a fasting glucose <140 mg/dL and a two-hour glucose level between 140 and 199 mg/dL; type 2 DM is diagnosed if the two-hour glucose during the oGTT is >200 mg/dL. In addition, determination of insulin levels during this test may help in gauging the degree of hyperinsulinemia. A peak insulin level of >300 mIU/L indicates severe hyperinsulinemia, 150–300 mIU/L moderate hyperinsulinemia and 80 or 100–150 mIU/L suggests mild hyperinsulinemia. Finally, while no current recommendations exist, the high prevalence of dyslipidemia and metabolic syndrome in this disorder suggests that most if not all PCOS patients would benefit from an evaluation of their lipid profile.

Conclusions
The evaluation of the patient suspected of having PCOS must consist of a thorough history and physical determining, among other features, the degree of hirsutism as assessed by the mFgS score. This should be followed by a targeted laboratory assessment, which should include, at a minimum, the measurement of a basal 17-HP level in the follicular phase of the cycle to exclude NCAH and possibly TSH and prolactin to exclude thyroid dysfunction and hyperprolactinemia. Androgen levels (total and free T, and DHEAS measured using high-quality assays) should be obtained, as these have the most relevance in patients without overt clinical signs of hyperandrogenism (i.e. without hirsutism). Ovarian morphology determined by transvaginal ultrasound should be assessed when possible. In patients with PCOS, a metabolic assessment is mandated. This should include measuring glucose and insulin levels during a two-hour 75 gram oGTT, and a lipid profile. Overall, the screening and evaluation of patients with possible PCOS is highly cost-effective and represents only 2% of the economic burden of this disorder. PCOS results in serious, long-term morbidities that are associated with a significant impact on quality of life and economic costs. As more and more women are diagnosed with this disorder, it is imperative that research and public awareness continue to increase in order to best treat these patients.

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6. Carmina E, Rosato F, Janni A, et al., Extensive clinical experience: characterization of women with polycystic ovary syndrome in unselected women:28 Impaired glucose tolerance is diagnosed by a fasting glucose level. However, as most patients with PCOS have good pancreatic β-cell function, although possibly deficient for their degree of insulin resistance, determining the glucose response to a two-hour 75-g oral glucose challenge test (oGTT) is optimum for detecting IGT or DM in these women. Impaired glucose tolerance is diagnosed by a fasting glucose <140 mg/dL and a two-hour glucose level between 140 and 199 mg/dL; type 2 DM is diagnosed if the two-hour glucose during the oGTT is >200 mg/dL. In addition, determination of insulin levels during this test may help in gauging the degree of hyperinsulinemia. A peak insulin level of >300 mIU/L indicates severe hyperinsulinemia, 150–300 mIU/L moderate hyperinsulinemia and 80 or 100–150 mIU/L suggests mild hyperinsulinemia. Finally, while no current recommendations exist, the high prevalence of dyslipidemia and metabolic syndrome in this disorder suggests that most if not all PCOS patients would benefit from an evaluation of their lipid profile.

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