Polycystic ovary syndrome, an enigmatic syndrome begging for a name change

More than any other reproductive endocrine disorder, polycystic ovary syndrome (PCOS) has engendered great interest, fascination, passion and controversy. This heterogeneous and enigmatic condition has been the subject of multiple expert consensus conferences, all aiming to unify and/or clarify the PCOS spectrum of clinical and biochemical presentations.

Arguably, PCOS is the most common of all endocrine diseases seen by gynecologists and reproductive endocrinologists (1). Yet, the underlying pathophysiology of this disorder(s) remains inscrutable, so much so that the disorder has defied standardization and/or classification.

Indeed, in 2012 a National Institutes of Health (NIH) consensus panel of experts noted, "We believe the name 'PCOS' is a distraction and an impediment to progress. It causes confusion and is a barrier to effective education of clinicians and communication with the public and research funders." The panel further opined, "It is time to expeditiously assign a name that reflects the complex…interactions that characterize the syndrome—and their reproductive implications" (1). Clearly, as recognized by the NIH panel and many other expert groups, the syndrome represents a spectrum of physical, endocrine and metabolic manifestations that have a profound impact on the lives of our patients.

What is surprising is that even with all of the deliberations and debates, as well as the summaries of experts at consensus conferences, we have not yet agreed on a name or names that satisfactorily represent the anatomic, clinical and metabolic manifestations of this syndrome. Perhaps it is the broad spectrum of etiologies and clinical presentations that have made this task so challenging. Indeed, "clinical heterogeneity is the rule in this disorder," as Lobo (2) so aptly suggested; ovulatory dysfunction occurs in 80% to 100% of women with PCOS, polycystic-appearing ovarian morphology in 70% to 90%, hyperandrogenism in 50% to 100% and metabolic dysfunction in 50% to 70%, depending on the definitions or type of diagnostic methods used by the respective investigators (1). Lobo and others have suggested that hyperandrogenism is the key to this syndrome—due to either ovarian or adrenal sources. Indeed, adrenal markers appear to be elevated in 50% of cases. Thus, he suggested that the syndrome be called hyperandrogenic chronic anovulation (HCA). He emphasized that the anatomic finding of polycystic ovaries, in the absence of hyperandrogenism and anovulation, is not sufficient to be included in the syndrome's description, although he relents to its use for the sake of convention, not necessarily correctness (2).

On the other hand, how should we classify the patient with polycystic ovarian morphology, perhaps better designated as poly-follicular ovarian morphology (PFOM), who does not exhibit hyperandrogenic or clinical manifestation of PCOS (by the Rotterdam Criteria)? These poly-follicular ovarian patients respond to gonadotropins similarly to women with the so-called classical PCOS. Moreover, not only do they exhibit extremely high numbers of follicles, but they also manifest exceedingly high antimüllerian hormone (AMH) levels. Indeed, their risk of developing ovarian hyperstimulation syndrome is similar to that of classical PCOS patients.

More recently, Dunaif and Fauser (3) suggested that there be two names assigned to the PCOS phenotype: Patients with primarily reproductive consequences should continue to be called PCOS, while those with significant metabolic consequences should have a new name. They proposed a "nosological 'two-state solution'" to the conflict: "The endocrine syndrome of hyperandrogenism and chronic anovulation, e.g., the NIH phenotype, should have a new name that acknowledges both its reproductive features and its long-term metabolic risks. The phenotypes diagnosed by ovarian morphology, e.g., the remaining Rotterdam phenotypes, should continue to be known as PCOS" (3).

Dunaif and Fauser (3) made the case for classifying PCOS into two types based on the observation that the NIH phenotype is at high risk for insulin resistance and accompanying features, including metabolic syndrome and type 2 diabetes mellitus. They further underscored the fact that the other phenotypes have a lower incidence of and less severe metabolic abnormalities, especially in women with regular menses. They pointed out that the scientific evidence suggests that the endocrine features of this syndrome, hyperandrogenism and oligo-ovulation, are sufficient for identifying women at high risk for metabolic disorders (3).

It is important to note that while the NIH criteria do not require ovarian morphology, poly-follicular ovarian morphology, indeed, is one of the most common findings in PCOS, occurring in 70% to 80% of women with chronic anovulation and hyperandrogenism. In fact, a recent study by Quinn et al. (4) endeavored to assess whether raising the threshold follicle number for making the diagnosis of PCOS impacts the identification of patients at metabolic risk. Their studied population consisted of women diagnosed as PCOS according to the 2003 Rotterdam Criteria, which requires two of three clinical signs and symptoms to be met: oligomenorrhea or amenorrhea; clinical and/or biochemical signs of hyperandrogenism; or polycystic ovaries on ultrasound, initially defined as ≥ 12 follicles measuring 2 mm to 9 mm or an ovarian volume of >10 ml in at least one ovary. A subgroup of this PCOS population was further identified based on the Androgen Excess and PCOS Society (AE-PCOS) classification, which requires a follicle number of >25 in at least one ovary. Interestingly, utilizing these criteria, only 47 (18.1%) of 259 women were extracted (or excluded) from the Rotterdam Criteria–classified group. These investigators demonstrated that women diagnosed by the less stringent Rotterdam Criteria remain at risk for metabolic dysfunction compared with non-PCOS controls, as they still manifest elevated fasting insulin levels, increased insulin resistance and elevated total cholesterol. Thus, polycystic ovary morphology as defined by the Rotterdam Criteria in the setting of oligomenorrhea or clinical/biochemical hyperandrogenism is associated with metabolic risk. Based on their study, they proposed that the Rotterdam Criteria be retained for the diagnosis of polycystic-appearing ovaries.

Polycystic ovarian syndrome is a common, often under-recognized, highly complex endocrinopathy. Whatever the underlying pathophysiology, whether genetic, metabolic, or endocrine, the finding most often associated with the disorder is a poly-follicular ovarian morphology, characterized by high antral follicle counts and high AMH levels produced by these follicles. Indeed, as recently pointed out by Teede et al. (5), "polycystic ovary" is a misnomer. Histologically, a cyst is an epithelial-lined, fluid-filled sac that is usually >2 cm. In fact, in PCOS, the ovaries contain follicles, typically 2 mm to 9 mm in size that are lined by granulosa cells (5). The term ovarian cyst, for most women, conjures up an image of a neoplastic condition, benign or malignant. Thus, for this and other reasons, this term should be expunged and replaced by the term poly-follicular ovary. As suggested by these authors, the name of a condition should reflect its pathology and convey its meaning to both health professionals and consumers. I concur with their view that the name polycystic ovarian syndrome should reflect the condition's broad clinical features. Upon surveying Australian health care professionals and the public, the authors concluded that an alternative name, i.e. metabolic reproductive syndrome, should be utilized instead (5). Upon reflection, while the term appears inclusive and wide-ranging, it does not seem to reflect the historical observation that this metabolic reproductive syndrome is most often associated with poly-follicular ovaries.

Thus, I propose the following modifications:

1. The term poly-follicular ovarian syndrome (PFOS) should be reserved only for women with poly-follicular ovarian morphology and ovulatory dysfunction, i.e. oligo/amenorrhea.

To accurately and better describe the clinical and metabolic variants of this syndrome, one can further classify these individuals as:

1a. Poly-follicular ovarian syndrome with hyperandrogenic manifestations (PFOS-HM).
1b. Poly-follicular ovarian syndrome with metabolic dysfunction and/or hyperandrogenic manifestations (PFOS-MD and/or -HM).

The term poly-follicular ovaries (PFO) should be reserved for women who exhibit poly-follicular ovarian morphology but have no hyperandrogenic, metabolic or ovulary dysfunction, while the term "metabolic reproductive syndrome" could be reserved for the non–poly-follicular patient who exhibits hyperandrogenic manifestations, oligo-amenorrhea and/or metabolic dysfunction.

Undeniably, there is wide agreement that the term polycystic ovarian syndrome is a misnomer, as it propounds a misleading image of ovarian cysts rather than follicles, as well as excludes the malady's metabolic abnormalities and reproductive dysfunction in its singular description. Thus, this contribution seeks to set forth a meaningful and descriptive name change for the syndrome(s).

Zev Rosenwaks, M.D.
The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medical College, New York, New York

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