Diagnosis, phenotype, and prevalence of polycystic ovary syndrome

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New diagnostic criteria for polycystic ovary syndrome (PCOS) suggested three main phenotypes: classic (hyperandrogenism and anovulation), ovulatory, and normoandrogenic. However, it is unclear whether the normoandrogenic phenotype actually represents PCOS. Overall, 6% to 8% of reproductive-aged women suffer from PCOS, making this disorder one of the most common endocrine abnormalities. (Fertil Steril® 2006;86(Suppl 1):S7–8. ©2006 by American Society for Reproductive Medicine.)

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DIAGNOSIS OF POLYCYSTIC OVARY SYNDROME

To date, there has been little agreement on the criteria on which to base the diagnosis of polycystic ovary syndrome (PCOS), probably a consequence of the heterogeneity of the syndrome and the absence of accepted underlying pathogenetic mechanisms. The proceedings of an expert conference sponsored by the National Institutes of Health (NIH) in April 1990 (1) suggested that the diagnosis of PCOS rested on two main features: hyperandrogenism (either biochemical or clinical) and chronic oligoanovulation (Table 1). Because commercial androgen assays are generally unreliable, clinical signs such as hirsutism are considered sufficient evidence of hyperandrogenism, even in the face of apparently "normal" androgen levels. Secondly, the diagnosis of PCOS depended on the exclusion of a few well characterized hyperandrogenic syndromes (e.g., Cushing's syndrome, androgen-secreting tumors, nonclassic adrenal hyperplasias).

Although referring to its value in suggesting PCOS, the 1990 NIH criteria did not include ovarian sonography as part of the diagnosis of PCOS. More recently, the 1990 NIH diagnostic criteria have come under criticism for being too narrow. In fact, some ovulatory hyperandrogenic women are found to have other clinical, metabolic, and sonographic features similar to those found in 1990 NIH–defined PCOS (2). Theca cells from the ovaries of hyperandrogenic women with polycystic ovaries demonstrate the same steroidogenic abnormalities in vitro, regardless of whether they were ovulatory or not (3).

In addition, many experts, primarily non-US, noting the subjectivity of the hirsutism assessment and the insensitivity of androgen assays, have continued to use ovarian sonography to establish the diagnosis of PCOS. In turn, the non-specificity of polycystic-appearing ovaries has been noted, with as many as 20%–25% of the general young female population demonstrating this finding but with no clinical symptomatology or infertility (4). In addition, patients with hypothalamic-pituitary dysfunction, hyperprolactinemia, and eating disorders and those undergoing the adolescent transition may also demonstrate this ovarian morphology.

Considering these issues, an expert conference sponsored by the European Society for Human Reproduction and Embryology (ESHRE) and the American Society for Reproductive Medicine (ASRM) held in Rotterdam in May 2003 proposed new criteria for the diagnosis of PCOS (5). These proceedings suggested that, after exclusion of the same well characterized but uncommon androgen excess disorders, PCOS could be diagnosed in patients presenting with at least two of three features: clinical or biologic hyperandrogenism, chronic anovulation, and polycystic ovaries (Table 1). However, it is possible that these criteria extended the 1990 NIH criteria too far, including phenotypes that, considering currently available data, cannot be properly considered to form part of the spectrum of PCOS.

PCOS PHENOTYPES

Using the 2003 ESHRE/ASRM criteria, the diagnosis of PCOS may be assigned to patients presenting with three different phenotypes (Table 1):

1. Clinical and/or biochemical hyperandrogenism and chronic oligoanovulation, with or without polycystic ovaries (a.k.a. "classic PCOS", or 1990 NIH criteria).
2. Clinical and/or biochemical hyperandrogenism and polycystic ovaries, but ovulatory cycles (a.k.a. "ovulatory PCOS").
3. Chronic anovulation and polycystic ovaries, but no clinical and/or biochemical hyperandrogenism.

The first two phenotypes appear to be part of the same disorder, with both classic and ovulatory PCOS having hyperandrogenism, polycystic ovaries, insulin resistance, and

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TABLE 1

Possible phenotypes of polycystic ovary syndrome, considering the three principal features of the disorder and the two principal definitions in use today.[a]

	Phenotypes			
	A	B	C	D
Features				
Biochemical and/or clinical hyperandrogenism	√	√	√	
Oligoanovulation	√	√		√
Polycystic ovaries	√		√	√
Definitions				
NIH 1990 (1)	√	√		
Rotterdam 2003 (2)	√	√	√	√

[a] Both these criteria call for the exclusion of more rare, but well characterized and distinct, androgen excess disorders (e.g., Cushing's syndrome, nonclassic adrenal hyperplasia, and androgen-secreting neoplasms).

Carmina and Azziz. Features of PCOS. Fertil Steril 2006.

increased cardiovascular risk factors. However, insulin resistance and the presence of markers for cardiovascular risk are more severely altered in patients with classic PCOS than in patients with ovulatory PCOS. In addition, even among patients with "classic PCOS" the degree of hyperinsulinism appears to vary by subphenotype, with patients having the full syndrome (i.e., hirsutism, hyperandrogenemia, and oligoanovulation) having the more severe degree of metabolic dysfunction (6). In addition, body weight is higher in patients with classic PCOS (2), suggesting that environmental factors may act as modifiers, possibly determining the development of the more severe form of PCOS.

Alternatively, it is unclear whether the third phenotype (oligoanovulation, polycystic ovaries, but no hyperandrogenism) should, at this time, be considered part of PCOS, as patients with these features may have a completely different disorder (6). Consequently, further studies are needed before including some or most of the patients with this phenotype in the spectrum of PCOS.

PREVALENCE OF PCOS

Studies in different populations have suggested that PCOS affects 6% to 8% of the reproductive-age female population, at least using the 1990 NIH criteria (7). A higher prevalence has been suggested in some populations, such as Mexican-Americans, who have a high incidence of insulin resistance (1). The prevalence of the disorder will undoubtedly increase as the full spectrum of PCOS becomes more readily recognized.

CONCLUSIONS

The Rotterdam 2003 criteria expanded the 1990 NIH criteria for PCOS. The 1990 NIH definition signals a form of PCOS that is generally more severely affected than patients with "ovulatory PCOS." Furthermore, the specificity of the phenotype that is defined by the presence of polycystic ovaries and oligoanovulation but the absence of clinical and/or biochemical hyperandrogenism for PCOS remains to be determined. Overall, at least one in fifteen women of reproductive age will be affected by PCOS, making this disorder the most common endocrine abnormality in this age group.

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