

# POSITION STATEMENT: Criteria for Defining Polycystic Ovary Syndrome as a Predominantly Hyperandrogenic Syndrome: An Androgen Excess Society Guideline

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**Objective:** The Androgen Excess Society (AES) charged a task force to review all available data and recommend an evidence-based definition for polycystic ovary syndrome (PCOS), whether already in use or not, to guide clinical diagnosis and future research.

**Participants:** Participants included expert investigators in the field.

**Evidence:** Based on a systematic review of the published peer-reviewed medical literature, by querying MEDLINE databases, we tried to identify studies evaluating the epidemiology or phenotypic aspects of PCOS.

**Consensus Process:** The task force drafted the initial report, following a consensus process via electronic communication, which was then reviewed and critiqued by the AES Board of Directors. No section was finalized until all members were satisfied with the contents and

minority opinions noted. Statements that were not supported by peer-reviewed evidence were not included.

**Conclusions:** Based on the available data, it is the view of the AES Task Force on the Phenotype of PCOS that there should be acceptance of the original 1990 National Institutes of Health criteria with some modifications, taking into consideration the concerns expressed in the proceedings of the 2003 Rotterdam conference. A principal conclusion was that PCOS should be first considered a disorder of androgen excess or hyperandrogenism, although a minority considered the possibility that there may be forms of PCOS without overt evidence of hyperandrogenism but recognized that more data are required before validating this supposition. Finally, the task force recognized, and fully expects, that the definition of this syndrome will evolve over time to incorporate new research findings. (*J Clin Endocrinol Metab* 91: 4237–4245, 2006)

THE DISORDER THAT eventually would be known as the polycystic ovary syndrome (PCOS) was initially described by Stein and Leventhal in 1935 (1). There is little disagreement that PCOS should be considered a syndrome, *i.e.* a collection of signs and features, in which no single test is diagnostic. In essence, the whole (or global assessment) is greater than the sum of the individual features. However, establishing a clear, contemporaneous, and evidence-based definition for this syndrome has important clinical and investigational implications. Nonetheless, the definition of PCOS has continued to generate significant controversy (2–4).

Clinically, diagnosing a woman as having PCOS implies an increased risk for infertility, dysfunctional bleeding, endometrial carcinoma, obesity, type 2 diabetes mellitus, dys-

lipidemia, hypertension, and possibly cardiovascular disease (5). Furthermore, it has important familial implications, principally, but not exclusively, for her sisters and daughters (6–8). Finally, a diagnosis of PCOS may mandate life-long treatments, *e.g.* the use of insulin sensitizers, and may negatively affect her ability to access health care coverage, principally in capitalistic markets. Consequently, the diagnosis of PCOS should not be assigned lightly, and diagnostic criteria should be based on robust data.

A judicious definition of PCOS is also essential to guide current and future research. The inclusion of patients whose definition, characterization, and selection criteria are unclear continues to plague the PCOS scientific literature. This issue is becoming critical as the field moves to the establishment of larger clinical trials and studies of the molecular biology and genetic nature of the disorder. In addition, definitions not based on clear-cut evidence have the potential effect of discouraging future and needed research into the nature of the disorder, its breadth, and its phenotype. Consequently, a contemporaneous definition based on what is currently known will benefit future investigation in this area.

The Androgen Excess Society (AES) is an international organization dedicated to promoting knowledge, and orig-

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Abbreviations: AES, Androgen Excess Society; DHEAS, dehydroepiandrosterone sulfate; IH, idiopathic hirsutism; mFG, modified Ferriman-Gallwey; PCOS, polycystic ovary syndrome; T, testosterone.

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inal clinical and basic research, in every aspect of androgen excess disorders, such as the PCOS, nonclassic adrenal hyperplasia, idiopathic hirsutism, and premature adrenarche. The society was founded in 2000 and currently has more than 200 members principally composed of investigators whose primary focus is the study of androgen excess disorders and PCOS. The Board of Directors of the AES appointed the Task Force on the Phenotype of PCOS and charged it with reviewing all current data concerning the phenotype of PCOS to answer the query: what different component phenotypes (features) constitute PCOS, based on the available published and peer-reviewed data, assuming that long-term morbidity is the anchor? The following summarizes the results of this task force's year-long investigation.

### Process

The Board of Directors of the AES appointed a seven-member task force of experts in the field, intentionally including international investigators. Members of the task force and the board of directors constituted the Writing Committee. No external funding was accepted for this project. The evidence gathered was based on a systematic review of the published peer-reviewed medical literature to identify studies evaluating the epidemiology or phenotypic aspects of PCOS by querying MEDLINE databases. The Medical Subject Headings (MeSH) heading used was polycystic ovary syndrome (C04.182.612.765), with the following limitations: major topic and adolescent (13–18 yr) or adult (19–44 yr) and English and publication date from 1980 to 2005 and core clinical journals and female and humans. A total of 527 articles were initially available for this review, although additional studies (cross-references and those published in 2006) were also considered. Emphasis was placed on those studies that included greater than 100 subjects, although in some areas no studies of this size were available, and the paucity of data was noted. Studies in which epidemiological (e.g. prevalence) data could not be ascertained or calculated or which reported on the same parameter in mostly the same population as a larger study were eliminated from consideration. Unpublished data or personal communications were not included. Although only studies in which the criteria for PCOS were clearly stated were included, we did not define the disorder *a priori* and rather used each individual investigator's own definition. In essence, we allowed PCOS to have a variety of definitions to define more clearly common phenotypes or features irrespective of the definition used.

The task force drafted the initial report, following a consensus process via electronic communication, which was then reviewed and critiqued by the AES Board of Directors. No section was finalized until all members were satisfied with the contents and minority opinions noted. Statements that were not supported by peer-reviewed evidence were not included.

### Current Definitions of PCOS

Currently two definitions of PCOS are in widespread use. The first arose from the proceedings of an expert conference sponsored in part by the National Institute of Child Health and Human Disease of the U.S. National Institutes of Health

(NIH) on April 16–18, 1990. During the meeting, all participants were surveyed regarding their perception of what features formed part of PCOS, and Drs. Zawadzki and Dunaf summarized these findings in the meeting proceedings (9). They concluded that the major criteria for PCOS “should include (in order of importance): 1) hyperandrogenism and/or hyperandrogenemia, 2) oligoovulation, (and the) 3) exclusion of other known disorders.” This survey identified PCOS as an androgen excess disorder of exclusion, with an ovarian etiology and/or consequences.

Another expert conference was convened in Rotterdam, The Netherlands, May 1–3, 2003, sponsored in part by the European Society for Human Reproduction and Embryology and the American Society for Reproductive Medicine (10, 11). The meeting proceedings recommended that PCOS be defined when at least two of the following three features were present: 1) oligo- and/or anovulation, 2) clinical and/or biochemical signs of hyperandrogenism, and 3) polycystic ovaries. These criteria also recognize that other androgen excess or related disorders should be excluded before assigning the diagnosis of PCOS. Whether these definitions are consistent with currently available data and whether they are overly narrow or unjustifiably broad were explored by the task force.

### The Essentials of Defining a Syndrome

The difficulties and intricacies of defining a syndrome are a challenge that many other organizations have and continue to struggle with (12–21). A syndrome may be defined by: 1) historical usage in medical practice and/or literature, 2) expert knowledge and consensus processes, or 3) evidence, via analysis of published data.

One evidence-based approach to establishing the limits of a syndrome is to determine whether the various phenotypes defined by the criteria behave in a manner suggestive that they are part of the same disorder. First, all possible phenotypes generated by the definition of a syndrome are catalogued and examined. Second, a feature not included in the definition (*i.e.* the anchor) is chosen to serve as the common thread (*e.g.* inheritance pattern, morbidities, a response to intervention). Essentially, for the phenotypes to be part of the same syndrome, they should have a common thread above and beyond the commonality of their definition (which in itself may be arbitrary). For example, if the various phenotypes of PCOS have the same overall morbidity (*e.g.* insulin resistance and hyperinsulinism), then we could consider these phenotypes to reflect the same overall syndrome. The task force opted for this latter approach in determining what phenotypes (and hence what criteria) reflected PCOS based on current data.

Essentially, the task force considered that PCOS was defined by all those component phenotypes that potentially signaled an increased risk for insulin resistance and the resulting metabolic abnormalities. This is not to say that all individuals with a component phenotype had to demonstrate metabolic abnormalities but that the phenotype as a group should demonstrate an increased prevalence of markers for metabolic dysfunction. A similar approach has been

taken when defining the limits of the metabolic syndrome (22).

### The Features of PCOS

The task force recognized four key features of PCOS: 1) ovulatory and menstrual dysfunction, 2) hyperandrogenemia, 3) clinical features of hyperandrogenism, and 4) polycystic ovaries. Clinically evident menstrual dysfunction, such as oligomenorrhea or abnormal uterine bleeding, can be observed in a majority of patients with PCOS.

#### Ovulatory and menstrual dysfunction

In large series of patients diagnosed with PCOS, approximately 75% have clinically evident menstrual dysfunction (23–37) (Table 1). Current data also suggest that approximately 20% of women with PCOS will present with a history of apparent eumenorrhea (*i.e.* subclinical oligoanovulation) (23, 25–39) (Table 1). In clinical practice, the presence of anovulation in clinically hyperandrogenic (*i.e.* hirsute) eumenorrheic women may be determined by measuring a serum progesterone level sometime during d 20–24 of the cycle. If anovulation is present, it may be prudent to confirm this finding with a repeat study.

#### Hyperandrogenemia

Elevated circulating androgen levels are observed in approximately 60–80% of PCOS patients (Table 2) (35–37, 40–42). The vast majority of the abnormal values are in the form of free testosterone (T), with the sole measurement of total T adding a limited amount to the diagnosis (36).

The value of also measuring androstenedione is unclear, but it may increase the number of subjects identified as hyperandrogenic by approximately 10% (43). Approximately 25% of patients with PCOS will demonstrate supranormal levels of the androgen metabolite dehydroepiandrosterone sulfate (DHEAS) (44), which may be the sole abnormality in circulating androgens in approximately 10%

of these patients (36, 43). Alternatively, measuring the level of dehydroepiandrosterone, a weak androgen primarily of adrenal origin, has limited diagnostic value.

The task force noted that the measurement of circulating androgen levels, including free T, was to be used only as an adjuvant for the diagnosis of hyperandrogenic disorders and never as the sole criterion for diagnosis or in lieu of the clinical assessment. This recommendation reflects the fact that between 20 and 40% of women with PCOS will have androgen levels within the normal range (36) and that assays for androgens, particularly total T, tend to be highly variable and inaccurate (45–47).

#### Hirsutism, acne, and androgenic alopecia

Clinical features of hyperandrogenism frequently seen in PCOS include hirsutism, acne, and androgenic alopecia. Among women of white, black, southern Asia (Pakistani, Bengali, Gujarati, or Dravidian Indian), Maori, or Pacific Island descent, with PCOS defined by the NIH criteria, approximately 60% are found to be hirsute (Table 2) (24–26, 29–32, 35–37, 40–42, 48–50). We note that the degree of facial and body terminal hair growth in women represents a continuum and that a value as low as 3, using the modified Ferriman-Gallwey (mFG) score, may be considered abnormal (51). However, most investigators have used the 95th percentile of controls as the upper normal limit, which corresponds to an mFG score of 6–8 in the white or black populations studied (51, 52).

Acne affects 15–25% of PCOS patients (38, 39, 53), although it is unclear whether the prevalence of acne is significantly increased in these patients over that observed in the general population (54–58). Finally, androgenic alopecia is a recognized sign of PCOS (39, 40, 59–61), although the prevalence of this abnormality in PCOS is unclear. In one study of 257 patients undergoing treatment for hyperandrogenic symptoms, only 5% complained of hair loss (39). Further studies

**TABLE 1.** Prevalence of menstrual dysfunction in PCOS

Study	Ref.	Total no. PCOS	No. of PCOS patients with oligomenorrhea	PCOS patients with oligomenorrhea (%) <sup>a</sup>	No. of PCOS patients with eumenorrhea	PCOS patients with eumenorrhea (%)
Ferriman and Purdie, 1983	24	280	237	84.6	43	15.4
Conway <i>et al.</i> , 1989	40	556	395	71.0	139	25.0
Kiddy <i>et al.</i> , 1990	48	263	203	77.2	60	22.8
Ardaens <i>et al.</i> , 1991	62	144	105	72.9	39	27.1
Rajkhowa <i>et al.</i> , 1995	49	153	129	84.3		
Balen <i>et al.</i> , 1995	41	1741	1043	59.9	517	29.7
Falsetti and Eleftheriou, 1996	25	240	207	86.3	24	10.0
Khoury <i>et al.</i> , 1996	26	112	112	100.0	0	0.0
Talbott <i>et al.</i> , 1998	29	244	229	93.9	15	6.1
Carmina, 1998	28	332	290	87.3	42	12.7
Alborzi <i>et al.</i> , 2001	30	371	371	100.0	0	0.0
Williamson <i>et al.</i> , 2001	31	162	144	88.9		
Haddad <i>et al.</i> , 2002	33	146	120	82.2	26	17.8
Amer <i>et al.</i> , 2002	32	161	149	92.5	12	7.5
Glueck <i>et al.</i> , 2003	34	138	138	100.0	0	0.0
Orio <i>et al.</i> , 2003	35	100	100	100.0	0	0.0
Chang <i>et al.</i> , 2005	36	316	265	83.9	51	16.1
Hahn <i>et al.</i> , 2005	37	200	200	100.0	0	0.0
Total		5659	4437	78.4	968	18.1

<sup>a</sup> Difference in percentage between patients with oligomenorrhea and eumenorrhea (and anovulation) is composed of patients with polymenorrhea or menometrorrhagia.

**TABLE 2.** Prevalence of hyperandrogenemia and hirsutism in PCOS

Study	Ref.	Total no. PCOS	No. with elevated total T	Elevated total T (%)	No. with elevated free T	Elevated free T (%)	No. with elevated DHEAS	Elevated DHEAS (%)	No. with hirsutism <sup>c</sup>
Ferriman and Purdie, 1983	24	280							230
Conway <i>et al.</i> , 1989	40	556	110	22.3 <sup>a</sup>					320
Kiddy <i>et al.</i> , 1990	48	263							129
Rajkhowa <i>et al.</i> , 1995	49	153							123
Balen <i>et al.</i> , 1995	41	1741	503	28.9					1153
Norman <i>et al.</i> , 1995	50	122							103
Falsetti and Eleftheriou, 1996	25	240							92
Khoury <i>et al.</i> , 1996	26	112							20
Talbott <i>et al.</i> , 1998	29	244							105
Alborzi <i>et al.</i> , 2001	30	371							300
Williamson <i>et al.</i> , 2001	31	162							147
Amer <i>et al.</i> , 2002	32	161							53
Orio <i>et al.</i> , 2003	35	100	33	33.0			27	27.0	100
Chang <i>et al.</i> , 2005	36	316	122	38.6	216	68.4	71	22.5	224
Hahn <i>et al.</i> , 2005	37	200	162	81.0			76	38.0	129
Legro <i>et al.</i> , 2006	42	626	373	60.8 <sup>b</sup>					505
Total		5647	1303	36.8	216	68.4	174	28.2	3228

Subjects included are mostly of white and black race.

<sup>a</sup> Based on the 494 patients who underwent androgen measurements.

<sup>b</sup> Based on the 613 subjects who underwent androgen measurements.

<sup>c</sup> Hirsutism defined variously as mFG scores of 5–9.

are needed to better define the prevalence of acne and androgenic alopecia in PCOS.

#### Polycystic ovaries

Current data suggest that polycystic ovaries detected by transvaginal ultrasonography may be found in approximately 75% of women with a clinical diagnosis of PCOS (25, 26, 30–32, 35, 37, 42, 49, 62–66) (Table 3). However, the task force also recognized that the false-positive rate is relatively high, as evidenced by the high rate of polycystic ovaries in the general population (see above). The task force noted that the diagnosis of polycystic ovaries requires strict criteria (65, 67) and should not be assigned based solely on a polycystic or multicystic appearance of the ovary. The diagnosis of polycystic ovaries has been recently reviewed (68). The most commonly used criteria today are those proposed by Dewailly and colleagues (65) and reaffirmed in the Rotterdam 2003 consensus (10, 11), which indicate that polycystic ova-

ries can be established when at least one ovary demonstrates an ovarian volume of greater than 10 cm<sup>3</sup> (milliliters) or 12 or more follicles measuring 2–9 mm in diameter.

The task force noted that the diagnosis of polycystic ovaries should not be considered more or less objective than that of hirsutism or hyperandrogenemia. Witness the changing definition of polycystic ovaries (67) and the 10–30% of women with PCOS who do not demonstrate polycystic ovaries on ultrasound (68). In addition, there are also technical limitations to this parameter, including the fact that at least 20% of women will refuse transvaginal ultrasonography (69) and that most clinicians (even gynecologists) do not perform their own ovarian ultrasonography, relying instead on the expertise of radiologists who may be less familiar with the diagnosis.

Finally, a number of other features of PCOS have been recognized, including gonadotropic abnormalities, insulin resistance, and obesity. These features have not formed part of any of the recognized definitions to date, and the task force found no evidence to suggest that this should be otherwise.

**TABLE 3.** Prevalence of polycystic ovaries (PCO)<sup>a</sup> by transvaginal ultrasonography in PCOS

Study	Ref.	Total no. PCOS	No. PCOS with PCO	PCOS with PCO (%)
Rajkhowa <i>et al.</i> , 1995	49	153	141	92.2
Falsetti and Eleftheriou, 1996	25	240	180	75.0
Khoury <i>et al.</i> , 1996	26	112	77	68.8 <sup>b</sup>
van Santbrink <i>et al.</i> , 1997	63	198	148	74.7 <sup>b</sup>
Laven <i>et al.</i> , 2001	64	190	154	81.1
Alborzi <i>et al.</i> , 2001	30	371	211	56.9
Williamson <i>et al.</i> , 2001	31	162	161	99.4
Amer <i>et al.</i> , 2002	32	161	93	57.8
Jonard <i>et al.</i> , 2003	65	214	160	74.8
Orio <i>et al.</i> , 2003	35	100	33	33.0
Hahn <i>et al.</i> , 2005	37	200	166	83.0
Legro <i>et al.</i> , 2006	42	626	573	91.5
Total		2727	2097	76.9

<sup>a</sup> Excluding multicystic or multifollicular ovaries.

<sup>b</sup> PCOS defined as oligomenorrhea with increased androgens and/or high LH.

#### PCOS: Exclusion of Other Androgen-Excess and Related Disorders

In addition to PCOS, there are a number of other disorders of androgen excess in women, including adrenal hyperplasias (congenital adrenal hyperplasias), the syndromes of severe insulin resistance, and androgen-secreting neoplasms, that have the appearance of androgen excess (*e.g.* idiopathic hirsutism), or that have not yet been well characterized (*e.g.* idiopathic hyperandrogenism). There are also a number of other disorders that may result in ovulatory dysfunction, including hyperprolactinemia and thyroid abnormalities. These disorders account for approximately 5–10% of all patients with androgen excess (24, 26, 39–42, 60, 70–76) (Table 4) and should be excluded when establishing the diagnosis of PCOS.

Although not a true disorder of androgen excess, idio-

**TABLE 4.** Prevalence of thyroid dysfunction, hyperprolactinemia (Hi-Prl), androgen-secreting neoplasms (ASNs), 21-hydroxylase deficient nonclassic adrenal hyperplasia (NCAH), and Cushing's syndrome (CS) in patients with hyperandrogenism or PCOS

Study	Ref.	Total No. PCOS	No. with thyroid dysfunction	Thyroid dysfunction (%)	No. with Hi-Prl	Hi-Prl (%)	No. NCAH	NCAH (%)	No. CS	CS (%)	No. ASN	ASN (%)
Ferriman and Purdie, 1983	24	467	0	0.0	4 <sup>a</sup>	0.9						
Conway et al., 1989	40	556			58	11.0	10	1.8 <sup>b</sup>				
Luciano et al., 1984	70	150			25	16.7						
O'Driscoll et al., 1994	60	350			1	0.3	3	0.9	0	0.0	2	0.6
Moran et al., 1994	71	250					5	2.0	1	0.40	2	0.80
Balen et al., 1995	41	1871	0	0.0	25	1.3	19	1.0			0	0.00
Khoury et al., 1996	26	112			17	15.2						
Romaguera et al., 2000	72	100					1	1.0				
Azziz et al., 2004	39	873	6	0.7	3	0.3	18	16.5	0	0.00	2	1.83
Escobar-Morreale, 2004	73	109			4	3.7 <sup>c</sup>						
Janssen et al., 2004	74	175	36	20.6 <sup>d</sup>								
Glintborg et al., 2004	75	340			8 <sup>e</sup>	2.3	2	0.6	1	0.29	1	0.29
Carmina et al., 2006	76	950					41	4.3			2	0.21
Legro et al., 2006	42	626	45	7.2								
Total		5353	42	1.2	143	4.3	99	2.3	2	0.14	9	0.21

<sup>a</sup> Four of 467 subjects had amenorrhea and galactorrhea, suggestive of hyperprolactinemia.

<sup>b</sup> Denominator is entire androgen excess population (n = 711).

<sup>c</sup> Another 3.7% also demonstrated macroprolactinemia.

<sup>d</sup> Eleven of 168 controls (6.5%) also had thyroid dysfunction.

<sup>e</sup> Seven of eight hyperprolactinemic PCOS patients demonstrated normalization of prolactin levels during extended follow-up.

pathic hirsutism (IH) should be excluded when assessing a hirsute patient for PCOS. Using the NIH 1990 criteria for PCOS, IH can be strictly defined as hirsutism, in the presence of regular ovulation and the absence of hyperandrogenemia (77), such that approximately 5–7% of hirsute patients will have IH (27, 28, 77). It is possible that these patients may also need to demonstrate normal ovarian morphology on ultrasound, which would reduce their prevalence even further.

#### *A phenotypic approach to defining PCOS: task force recommendations*

The task force considered all data published and summarized above, emphasizing larger epidemiological and phenotypic studies, in arriving to its conclusions and recommendations regarding the phenotype of PCOS. These include the following:

#### *PCOS is a hyperandrogenic disorder*

The task force concluded that PCOS was above all a disorder of androgen excess in women. As such, with currently available evidence, the diagnosis of PCOS cannot be clearly established without evidence of either clinical or biochemical hyperandrogenism. Whereas the exact measures for these may vary, the task force felt that the single most reliable indices of this feature included hirsutism and free T levels. Nonetheless, the task force recognized that the methods for measuring androgens in the circulation were frequently inaccurate and insensitive and that determination of hirsutism using visual scales was subjective, with significant interobserver variation (78), where cutoff level may be unclear (51). Finally, the task force also noted that whereas many patients with PCOS may have evidence of acne or androgenic alopecia, these features could not be used reliably as clinical signs of hyperandrogenism. The task force also noted that support for this criteria is based on the risk for metabolic

morbidity in the disorder, not on whether hyperandrogenism *per se* is present.

#### *The ovarian morphology should be considered when establishing the diagnosis because polycystic ovaries are found in the majority, although not all, women with PCOS*

The task force recognized that approximately 75% of women with PCOS will demonstrate a polycystic ovarian morphology on transvaginal ultrasonography, although they also recognized that the false-positive rate is high, with up to one quarter of unselected reproductive-aged women demonstrating this ovarian morphology. The task force also noted that the diagnosis of polycystic ovaries required the use of clear and strict criteria. Consistent with the recommendation (*PCOS is a hyperandrogenic disorder*) above, the task force felt strongly that in those women with polycystic ovaries but no evidence of clinical or biochemical hyperandrogenism, the diagnosis of PCOS is less certain, regardless of the presence of concomitant ovulatory dysfunction.

#### *Ovulatory dysfunction is a prominent, but not universal, feature of PCOS*

The task force recognized that some patients with PCOS may demonstrate regular ovulation at the time of their evaluation, the so-called ovulatory PCOS (79, 80). However, it was noted that patients with ovulatory PCOS constituted a minority of the PCOS population and had less severe androgenic and metabolic features than anovulatory women with PCOS. It was also recognized that there exist few data regarding the long-term maintenance of ovulation in women with ovulatory PCOS. Nonetheless, the task force recognized that there were persuasive, albeit limited, data to suggest that hyperandrogenic ovulatory women with polycystic ovaries had some degree of metabolic dysfunction and were amenable to the inclusion of this phenotype as a form of PCOS.

*Eumenorrhea in the presence of dermatological features suggestive of hyperandrogenism (e.g. hirsutism) could not reliably be used to establish the presence of normal ovulation*

A history of regular predictable vaginal bleeding in a patient without clinical signs of hyperandrogenism can be used as strong evidence of normal ovulation. Alternatively, a history of regular menstrual cycles in patients who demonstrate hyperandrogenic features (e.g. hirsutism) could not be relied on as evidence of normal ovulation because up to 40% of these women have oligoanovulation when examined more carefully. In these patients, confirmation of ovulatory function by more objective means is required.

*Other well-defined disorders that could result in ovulatory dysfunction, polycystic ovaries, or clinical or biochemical hyperandrogenism had to be excluded*

Although the task force recognized that specific androgen excess or other endocrine disorders needed to be excluded when establishing the diagnosis of PCOS, it also recognized the validity of tailoring testing to reflect the prevalence of these disorders in the population being studied.

#### Recognition of associated abnormalities

The task force noted that the presence of obesity, insulin resistance, and hyperinsulinism and increased LH levels or an LH to FSH ratio, whereas observed in a significant fraction of patients, should not be used as part of the definition of PCOS.

### Minority Report

Notwithstanding the above recommendations, the writing committee acknowledged that two of its members considered the possibility that there are forms of PCOS without overt evidence of hyperandrogenism and that may be associated with metabolic abnormalities and morbidity. However, these investigators also recognized, as did the committee as a whole, that more data are required before validating this supposition. For example, a recent study (81) noted that women with oligoanovulation and polycystic ovaries but without evidence of hyperandrogenism (n = 66) had basal insulin levels, the principal metabolic parameter assessed, similar to controls and lower than patients with hyperandrogenemia and oligoanovulation, with (n = 246) or without (n = 27) polycystic ovaries, or those with hyperandrogen-

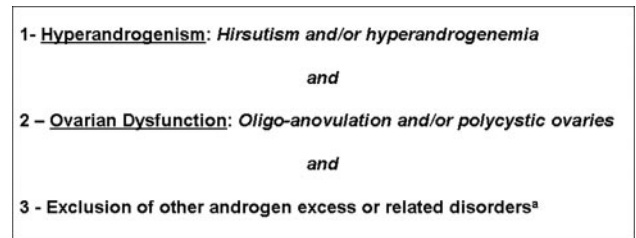


FIG. 1. AES suggested criteria for the diagnosis of PCOS.

<sup>a</sup> Possibly excluding 21-hydroxylase-deficient nonclassic adrenal hyperplasia, androgen-secreting neoplasms, androgenic/anabolic drug use or abuse, Cushing's syndrome, the syndromes of severe insulin resistance, thyroid dysfunction, and hyperprolactinemia.

emia and polycystic ovaries but without oligoanovulation (n = 67).

### Conclusions

Based on the above review of the available data, it is the view of the AES Task Force on the Phenotype of PCOS that there should be acceptance of the original NIH/National Institute of Child Health and Human Disease criteria of 1990 with some modifications, taking into consideration the opinion expressed in the proceedings of the 2003 Rotterdam conference (Fig. 1). Considering the four features of ovulatory dysfunction, hirsutism, hyperandrogenemia, and polycystic ovaries, the task force identified nine different phenotypes that could be considered as being PCOS with currently available evidence (Table 5).

The task force noted that there were ample data to support an increased risk of metabolic dysfunction in women with the following phenotypes: 1) hirsutism and/or hyperandrogenemia, and oligoovulation with and without polycystic ovaries (phenotypes A–F in Table 5) and 2) hyperandrogenemia and/or hirsutism, and normoovulation with polycystic ovaries (phenotype G–I in Table 5) (7, 34, 36, 37, 82–94). Current evidence generally did not support an increased metabolic dysfunction among women with polycystic ovaries only, with or without oligoovulation (phenotype J in Table 5) (95, 96), although not all agreed (97). As expected, the incidence of metabolic dysfunction in PCOS is also significantly increased by the concomitant presence of obesity).

However, the task force recognized that clinical features may not be constant even in a single patient and can be modified by changes in body weight and lifestyle choices and age. In addition, the task force also recognized that there may be a number of women who have features suggestive of

**TABLE 5.** All possible phenotypes based on the presence or absence of oligoanovulation, hyperandrogenemia, hirsutism, and PCOS

Features	Potential phenotypes															
	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P
Hyperandrogenemia	+	+	+	+	–	–	+	–	+	–	+	–	–	–	+	–
Hirsutism	+	+	–	–	+	+	+	+	–	–	+	–	–	+	–	–
Oligoanovulation	+	+	+	+	+	+	–	–	–	+	–	–	+	–	–	–
Polycystic ovaries	+	–	+	–	+	–	+	+	+	+	–	+	–	–	–	–
NIH 1990 criteria	✓	✓	✓	✓	✓	✓										
Rotterdam 2003 criteria	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓						
AES 2006 criteria	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓						

+, Presence; –, absence.

PCOS but who do not fulfill the criteria; clearly these women and their symptoms should be treated accordingly, regardless of whether a diagnosis of PCOS is established.

A principal conclusion of this report is that PCOS should be first considered a disorder of androgen excess or hyperandrogenism. The absence of clinical or biochemical hyperandrogenism in the untreated state, or in women under the age of 40 yr, makes a diagnosis of PCOS less certain, regardless of the presence of ovulatory or menstrual dysfunction or the presence of polycystic ovaries. Overall, at the present time, in the task force's assessment, women with oligomenorrhea and polycystic-appearing ovaries on ultrasonography but no evidence of hyperandrogenism do not have PCOS.

The writing committee also acknowledged that some of its members considered the possibility that there are forms of PCOS without overt evidence of hyperandrogenism but recognized that more data are required before validating this supposition. Alternatively, the diagnosis of PCOS in women who have evidence of hyperandrogenism and polycystic ovaries, in the presence of ovulatory cycles, appears justified based on current data. Finally, whereas the aim of this report was to yield criteria based on currently available data to guide research and clinical diagnosis and future investigations, the task force recognized that the definition of this syndrome will evolve over time to incorporate new research findings.

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