

The history of ESHRE/ASRM sponsored PCOS consensus workshops *(Tarlatzis/Fauser)*

- I **Diagnosis (2003, Rotterdam)**
- II **Infertility treatment (2007, Thessaloniki)**
- III **Women's Health (2010, Amsterdam)**



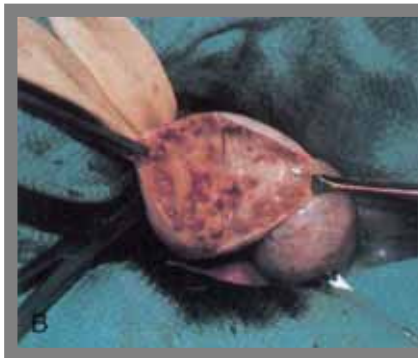
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Morphology 1935 syndrome 1963 endocrinology 1980 ultrasound 1988

metabolic 1990

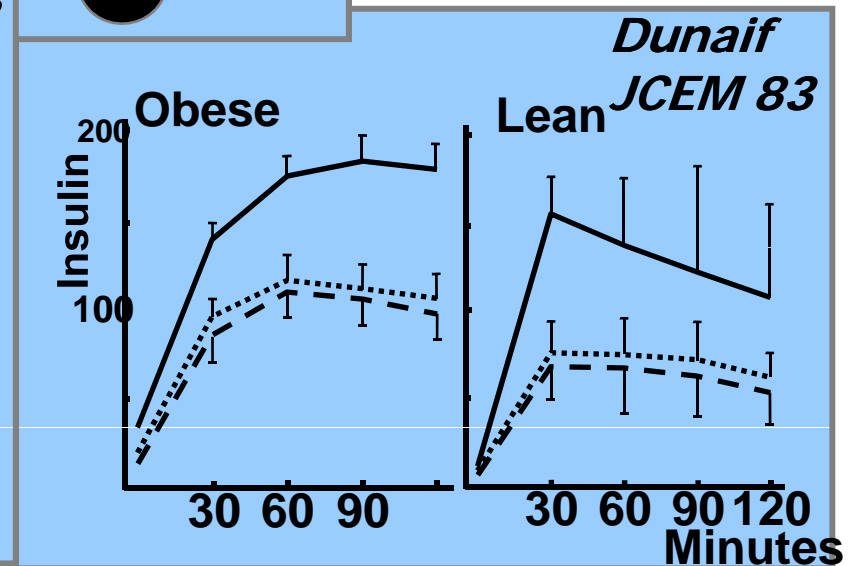
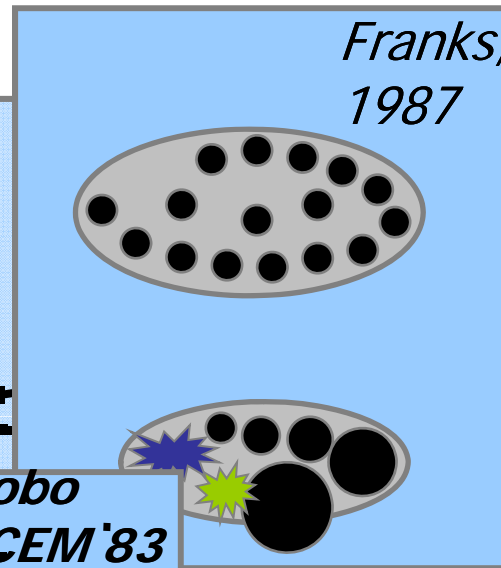
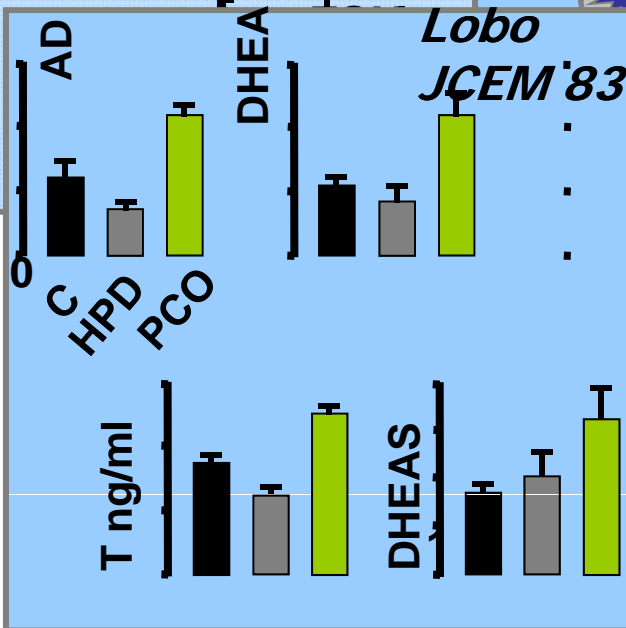
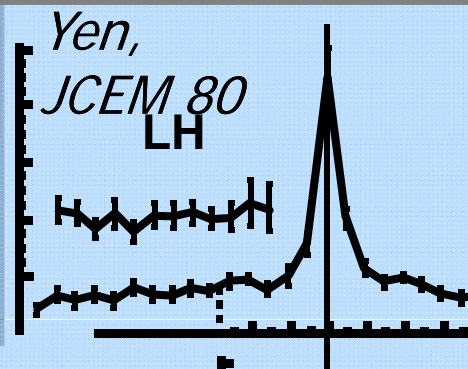


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Stein Leventhal

Axelrod & Goldzieher, 1963
(187 references, 1079 cases)

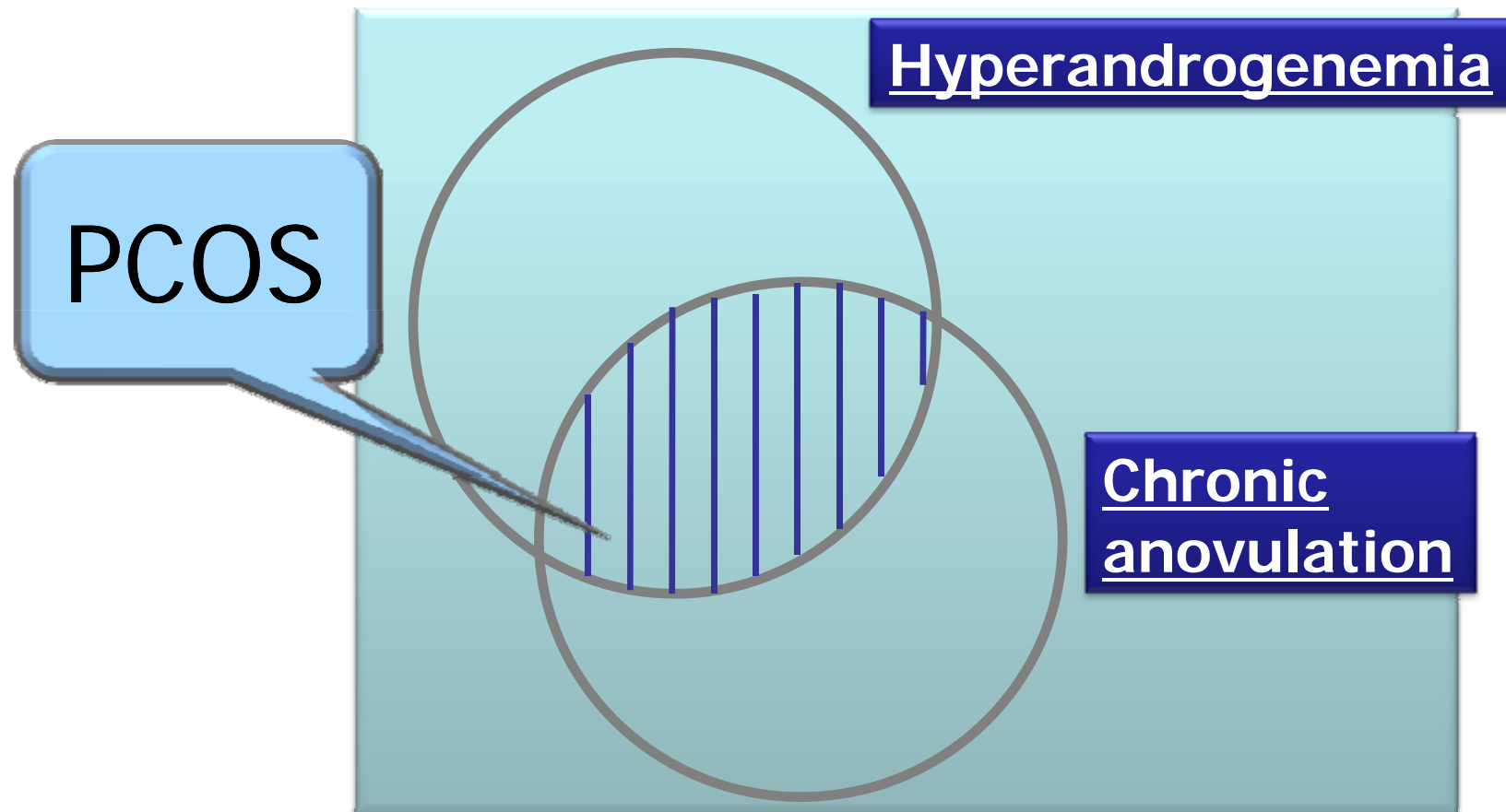


PCOS diagnosis

- 1990 NIH criteria -



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Applied criteria for PCOS diagnosis in the literature



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- Elevated LH
- Elevated androgens
- Ultrasound
- LH + US
- Androgens + US
- LH + Androgens
- LH + Andr + US
- Insulin resistance

Yen, Schoemaker

Lobo, Barbieri, NIH

Jacobs, Franks, Balen

Conway, Risma

Fauser, Norman

Shelly, Ardeans

Eden, Pache

Nestler, Dunaif

(Summary literature 1990-2002)

Rotterdam, Hotel New York - *history meets today*



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Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS)

The Rotterdam ESHRE/ASRM-sponsored PCOS consensus workshop

Correspondence to: Bart C.J.M.Fauser, Center of Reproductive Medicine, Erasmus Medical Center, Netherlands. E-mail: b.fauser@erasmusmc.nl

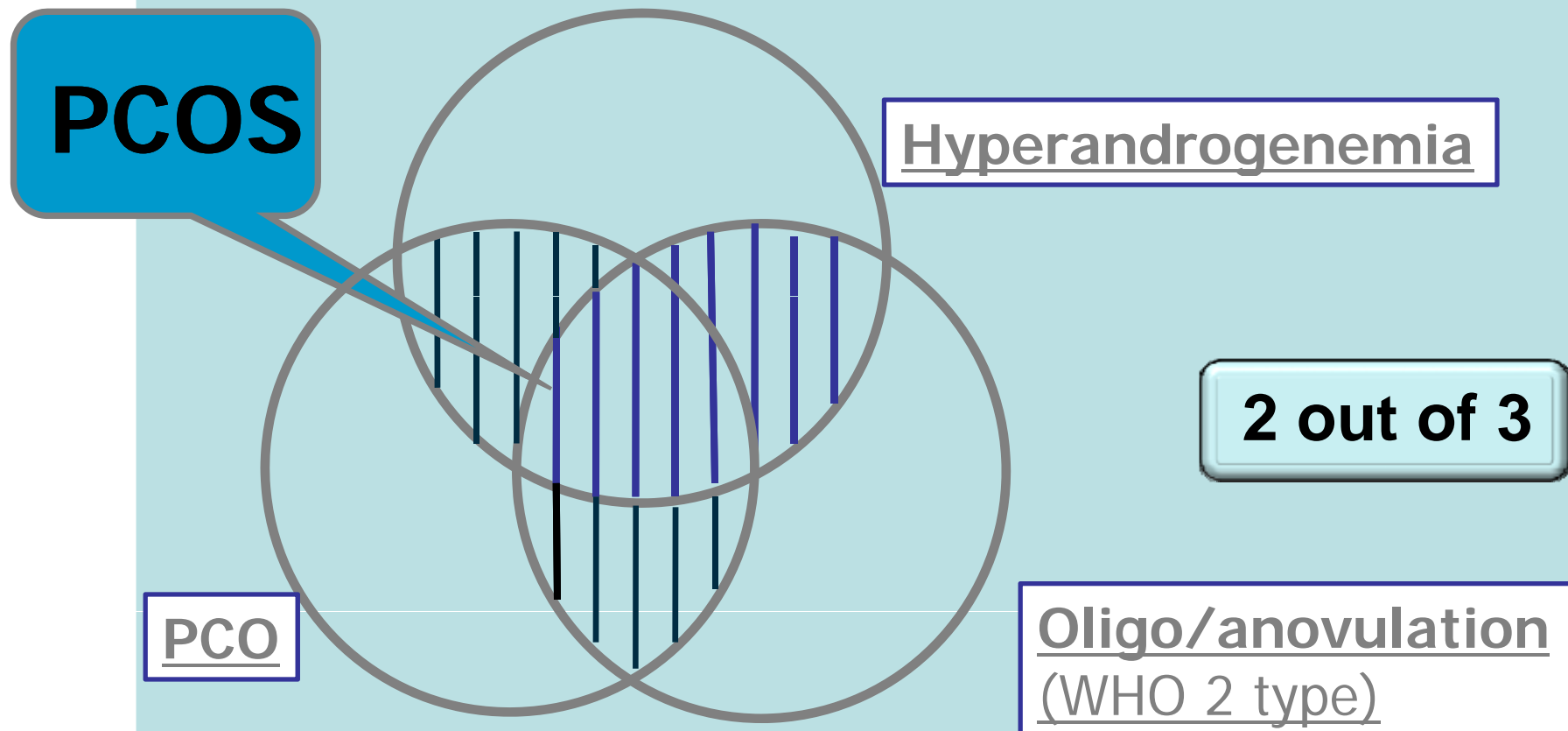
FERTILITY AND STERILITY®
VOL. 81, NO. 1, JANUARY 2004
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CONSENSUS STATEMENT

Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome

The Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group
Rotterdam, The Netherlands

Received October 22,
2003; revised and



PCOS as a complex genetic condition

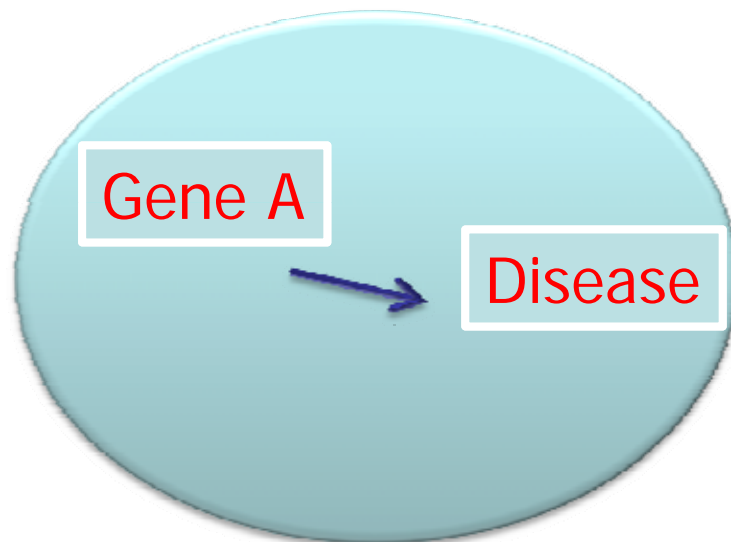


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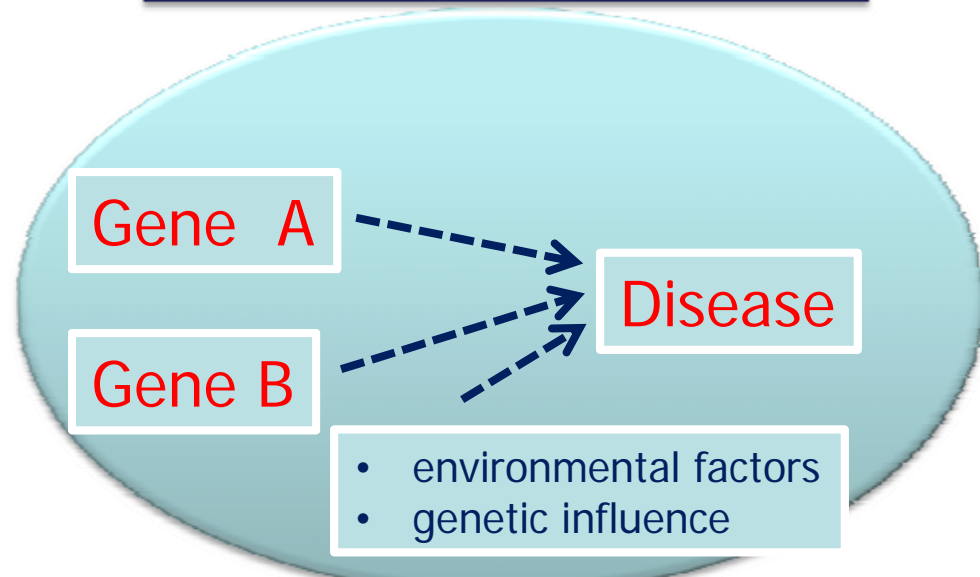
**Monogenic disorders
(mendelian)**
autosomal or X-linked



**Complex, polygenic
condition**
Multi-gene/environment
interaction



(mutation)



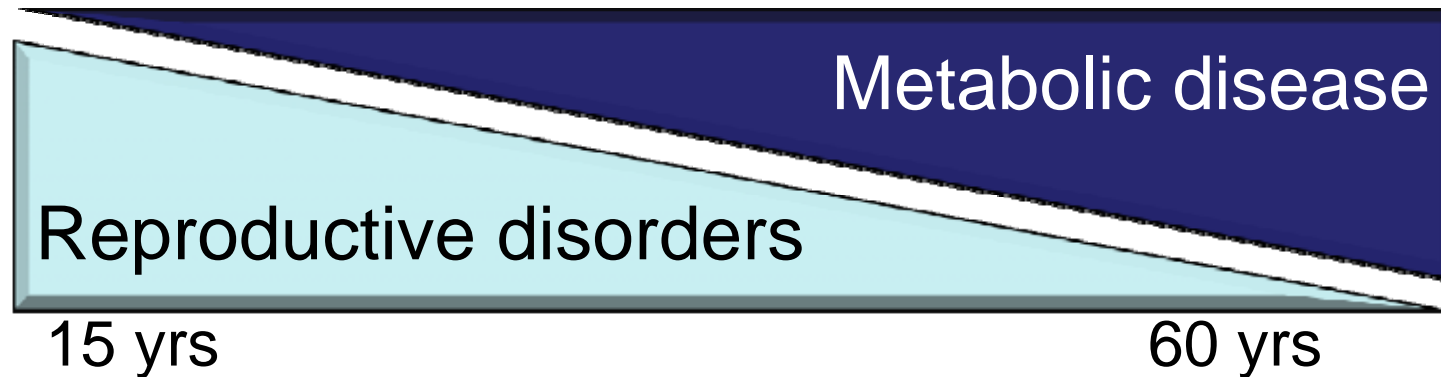
(polymorphism, SNPs)

PCOS

changing paradigms



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- menstrual disorders
- hyperandrogenemia
- infertility



- Pregn complic.
- type 2 diabetes
- cardiovasc disease

Multi-disciplinary approaches



PCOS

- *hyperandrogenemia*



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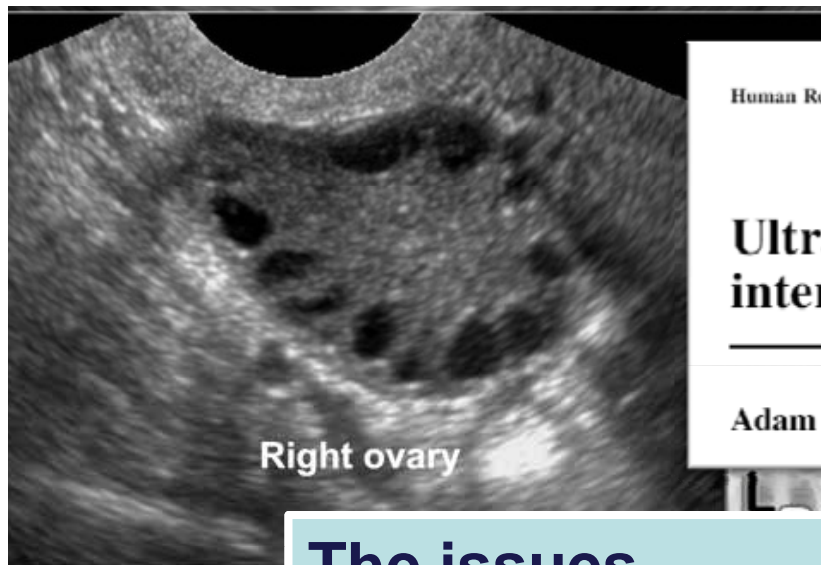
Clinical:

- Acne
- Hirsutism



Biochemical:

- Testosterone
total or free (unbound)
- Free androgen index
($T \times 100 / SHBG$)
- Androstenedione
- Other androgens (DHEAS)
- combination



Ultrasound assessment of the polycystic ovary: international consensus definitions

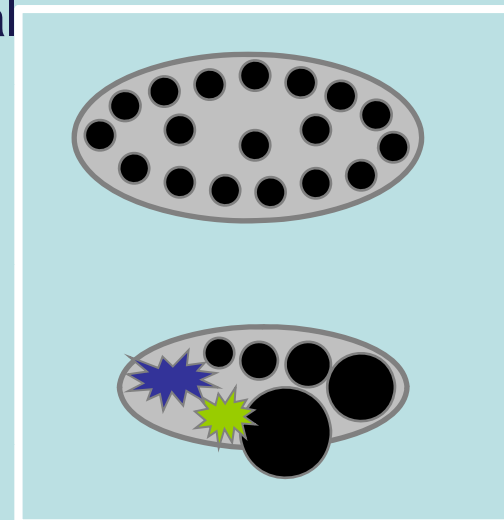
Adam H.Balen^{1,5}, Joop S.E.Laven², Seang-Lin Tan³ and Didier Dewailly⁴

The issues

- Transabdominal versus transvaginal
- Few controlled studies
- Ovarian volume
- Follicle number / size
- Ovarian stroma

Conclusions

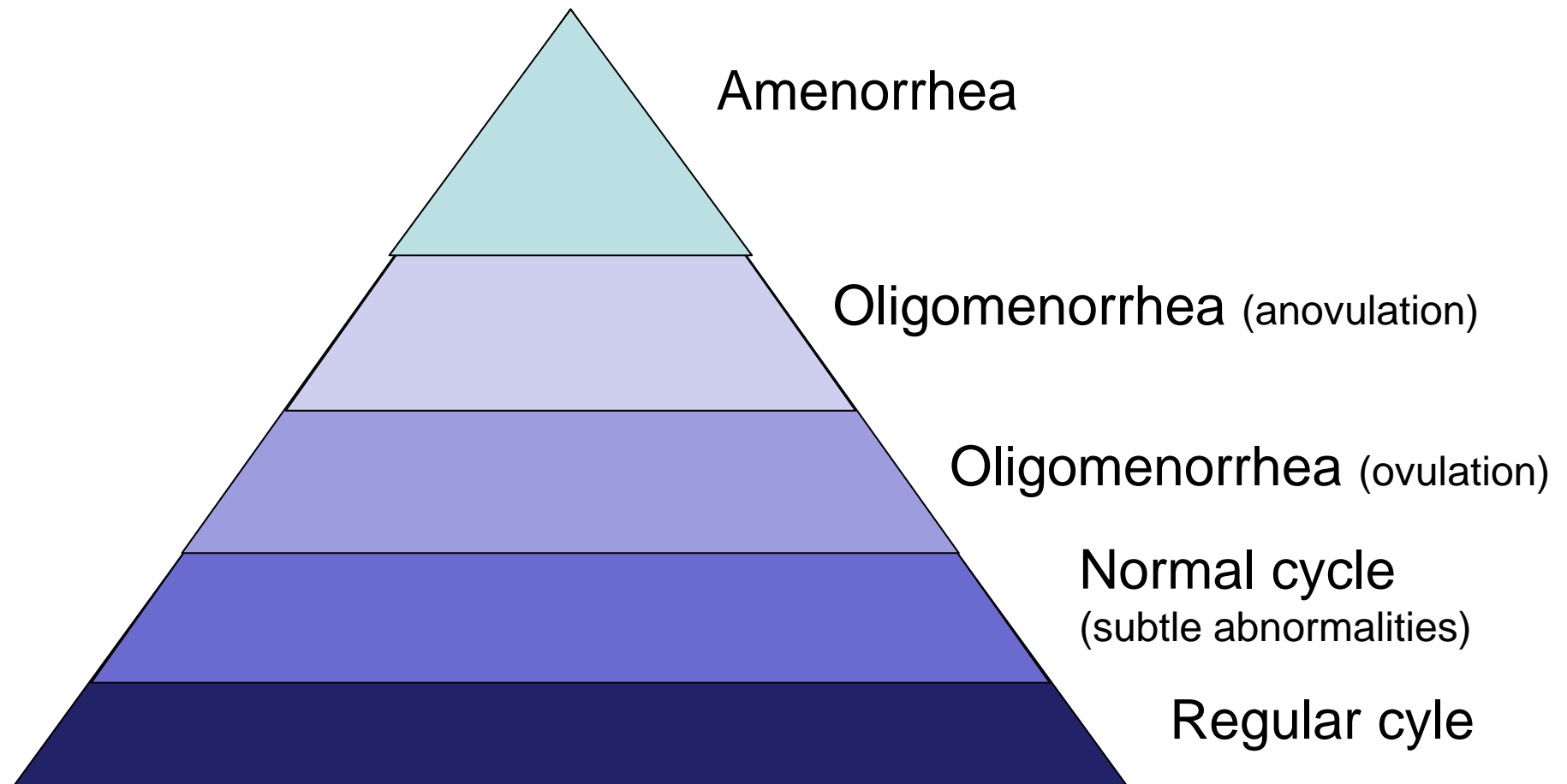
- ≥ 12 follicles (2-9 mm)
- $> 10 \text{ cm}^3$



Oligo-, anovulation



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Commentary

A comment on the European Society of Human Reproduction and Embryology/American Society for Reproductive Medicine consensus of the polycystic ovarian syndrome

Franz Geithövel

Center of Gynecological Endocrinology and Reproductive Medicine Freiburg (CGE and RMF), Kaiser-Joseph-Strasse 168, D-79098 Freiburg, Germany

Correspondence: e-mail: geisthoevel@t-online.de

Abstract

This commentary on the European Society of Human Reproduction and Embryology/American Society for Reproductive Medicine (ESHRE/ASRM) consensus on diagnosis, nomenclature and long-term health risks of the polycystic ovarian syndrome (PCOS) (conference in Rotterdam, Netherlands, March 2003) questions whether the preservation of the term PCOS sufficiently considers the modern aspects of the aetiology and pathogenesis of this complex syndrome. The misleading and simplified term PCOS, which comprises a variety of different entities, carries with it the risk of misinterpretation and under- and overestimation of symptoms, as well as of overlooking contraindications. Additionally, bias in future studies is pre-programmed. In this commentary, it is proposed that the term polycystic should be substituted with polyfollicular, and the term PCOS with functional hyperandrogenism, which is further subdivided into five additional

Outlook

PCOS: a diagnostic challenge



Dr Ricardo Azziz

Ricardo Azziz

Department of Obstetrics and Gynecology, Cedars-Sinai Medical Centre and Department of Obstetrics and Gynecology and Department of Medicine, The David Geffen School of Medicine at UCLA, 8635 West Third Street, Suite 160W, Los Angeles, CA 90048, USA

Correspondence: Tel: +1 310 4237433; Fax: +1 310 4233470; e-mail: azzizr@cshs.org

Dr Azziz is currently Chairman of both the Helping Hand of Los Angeles in Obstetrics and Gynecology, and the Department of Obstetrics and Gynecology at Cedars-Sinai Medical Center, Los Angeles, California, USA. He also holds positions at The David Geffen School of Medicine at UCLA. Dr Azziz is a Fellow of both The American College of Surgeons (FACS) and The American College of Obstetricians and Gynecologists (ACOG). He is a current member of the Reproductive Endocrinology Study Section of the National Institutes of Health. Dr Azziz has published over 200 original articles, book chapters, and reviews. His research interests include the study of the polycystic ovary syndrome (PCOS), the non-classic adrenal hyperplasias (NCAH); the role of the adrenal gland in hyperandrogenic disorders; the genetics of hyperandrogenic disorders; the treatment of hirsutism; the regulation and physiology of adrenal androgens; and operative endoscopy for pelvic reconstruction.

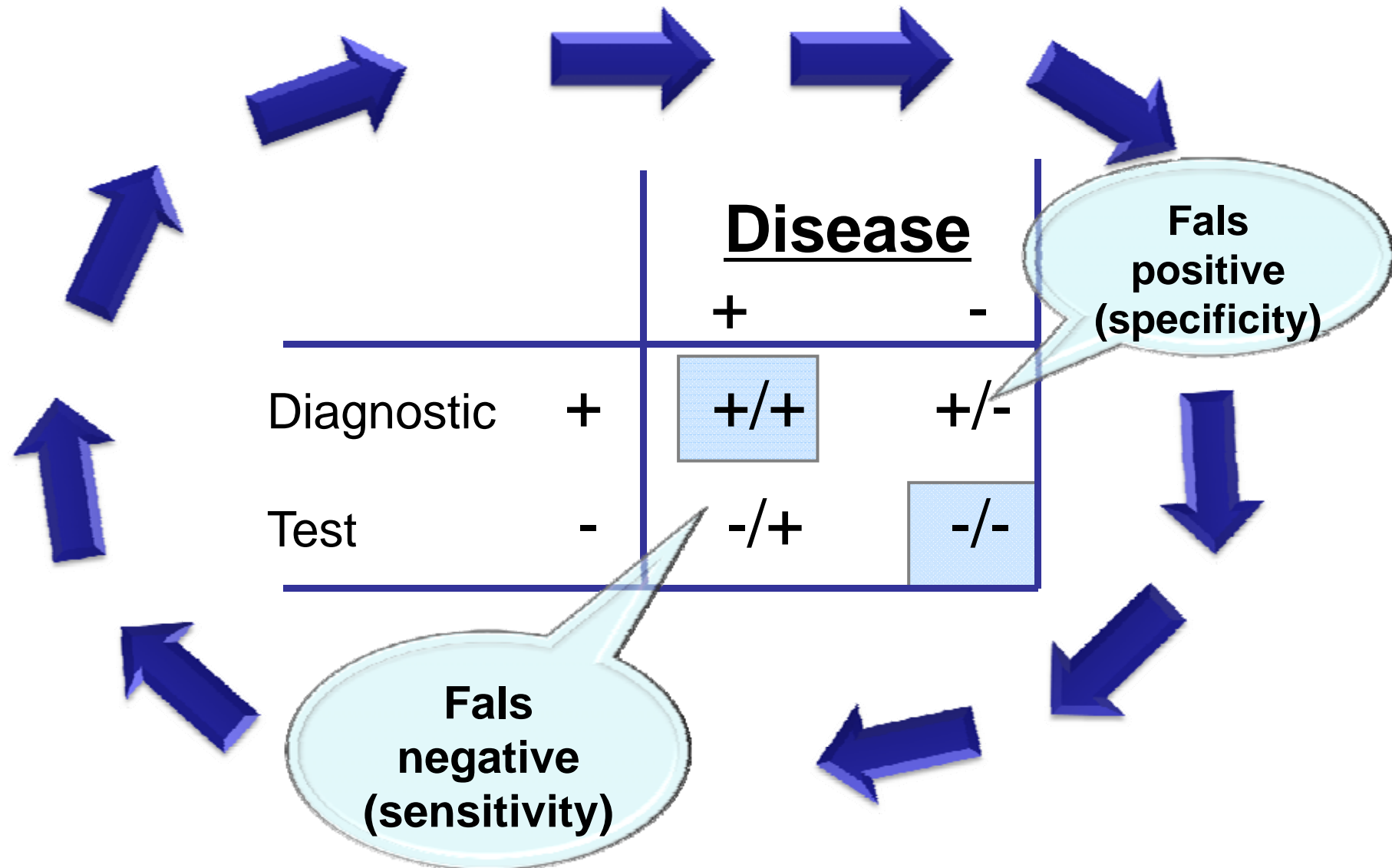
Abstract

Useful research and diagnostic criteria for PCOS arose from a conference in 1990, whereby PCOS could be defined by: (i) clinical and/or biochemical hyperandrogenism, (ii) chronic anovulation, and (iii) exclusion of related disorders. The presence of 'polycystic ovaries' was not included in this definition, which created significant concern since many women with PCOS have polycystic ovaries on ultrasound, and conversely women with this ovarian morphology have a higher prevalence of androgen excess and insulin resistance. More recently, at an expert meeting in 2003 in Rotterdam, it was recommended that PCOS be defined when at least two of the following three features were present, after exclusion of other aetiologies: (i) oligo- or anovulation, (ii) clinical and/or biochemical hyperandrogenism, or (iii) polycystic ovaries. These newer criteria effectively create additional phenotypes of PCOS (e.g. women with hyperandrogenism and polycystic ovaries but normal ovulatory function, and women with ovulatory dysfunction and polycystic ovaries but no clinical or biochemical evidence of hyperandrogenism). It remains to be demonstrated whether these phenotypes actually represent patients with PCOS. Nonetheless, the trend towards the use of uniform diagnostic criteria in studies of PCOS will increase the comparability and potentially the value of published research.

Diagnostic tests and the identification of disease



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The Androgen Excess and PCOS Society criteria for the polycystic ovary syndrome: the complete task force report

Ricardo Azziz, M.D., M.P.H.,^a Enrico Carmina, M.D.,^b Didier Dewailly, M.D.,^c
Evanthia Diamanti-Kandarakis, M.D.,^d Héctor F. Escobar-Morreale, M.D., Ph.D.,^e
Walter Futterweit, M.D.,^f Onno E. Janssen, M.D.,^g Richard S. Legro, M.D.,^h
Robert J. Norman, M.D.,ⁱ Ann E. Taylor,^j and Selma F. Witchel, M.D.,^k (Task Force on the
Phenotype of the Polycystic Ovary Syndrome of The Androgen Excess and PCOS Society*)

Main Outcome Measure(s): A systematic review of the published peer-reviewed medical literature, by querying MEDLINE databases, to identify studies evaluating the epidemiology or phenotypic aspects of PCOS.

Result(s): The Task Force drafted the initial report, following a consensus process via electronic communication, which was then reviewed and critiqued by the Androgen Excess and PCOS (AE-PCOS) Society AE-PCOS Board of Directors. No section was finalized until all members were satisfied with the contents, and minority opinions noted. Statements were not included that were not supported by peer-reviewed evidence.

Conclusion(s): Based on the available data, it is the view of the AE-PCOS Society Task Force that PCOS should be defined by the presence of hyperandrogenism (clinical and/or biochemical), ovarian dysfunction (oligo-anovulation and/or polycystic ovaries), and the exclusion of related disorders. However, 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 def-

All possible phenotypes based on the presence or absence of oligo-anovulation, hyperandrogenemia, hirsutism, and polycystic ovary syndrome (PCOS).

Potential Phenotypes

Features	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P
Hyperandrogenemia	+	+	+	+	-	-	+	-	+	-	+	-	-	-	+	-
Hirsutism	+	+	-	-	+	+	+	+	-	-	+	-	-	+	-	-
Oligo-anovulation	+	+	+	+	+	+	-	-	-	+	-	-	+	-	-	-
Polycystic ovaries	+	-	+	-	+	-	+	+	+	+	-	+	-	-	-	-
NIH 1990 criteria	✓	✓	✓	✓	✓	✓										
Rotterdam 2003 criteria	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓						
AE-PCOS 2006 criteria	✓	✓	✓	✓	✓	✓	✓	✓	✓							



Prevalence of hyperandrogenemia and hirsutism in the polycystic ovary syndrome (PCOS).

Study	Reference	Total No. PCOS	No. with elevated Total T	% with elevated Total T	No. with elevated Free T	% with elevated Free T	No. with elevated DHEAS	% with elevated DHEAS	No. with Hirsutism ^c	% with Hirsutism ^c
Ferriman & Purdie, 1983	83	280							230	82.14%
Conway et al., 1989	84	556	110	22.30% ^a					320	57.55%
Kiddy et al., 1990	85	263							129	49.05%
Rajkhowa et al., 1995	86	153							123	80.39%
Balen et al., 1995	87	1741	503	28.90%					1153	66.23%
Norman et al., 1995	109	122							103	84.43%
Falsetti & Eleftheriou, 1996	88	240							92	38.33%
Khoury et al., 1996	89	112							20	17.86%
Talbott et al., 1998	90	244							105	43.03%
Alborzi et al., 2001	92	371							300	80.86%
Williamson et al., 2001	93	162							147	90.74%
Amer et al., 2002	95	161							53	32.92%
Orio et al., 2003	97	100	33	33.00%			27	27.00%	100	100.00%
Azziz et al., 2004	47	873							517	72.20%
Chang et al., 2005	98	316	122	38.60%	216	68.40%	71	22.50%	224	70.89%
Hahn et al., 2005	99	200	162	81.00%			76	38.00%	129	64.50%
Legro et al., 2006	110	626	373	60.80% ^b					505	80.67%
Diamanti-Kandarakis & Danidis, 2007	100	634	535	84.38%			70	11%	441	69.55%
Total		6281	1839	29.26%	216	3.44%	244	3.88%	4691	74.69%



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The Journal of Clinical Endocrinology & Metabolism 91(3):781-785
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doi: 10.1210/jc.2005-2153

CONTROVERSY IN CLINICAL ENDOCRINOLOGY

Diagnosis of Polycystic Ovarian Syndrome: The Rotterdam Criteria Are Premature

Ricardo Azziz

0021-972X/06/\$15.00/0
Printed in U.S.A.

The Journal of Clinical Endocrinology & Metabolism 91(3):786-789
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doi: 10.1210/jc.2005-2501

CONTROVERSY IN CLINICAL ENDOCRINOLOGY

Diagnosis of Polycystic Ovarian Syndrome: In Defense of the Rotterdam Criteria

Stephen Franks

Diagnostic PCOS criteria

recommendations by various expert groups



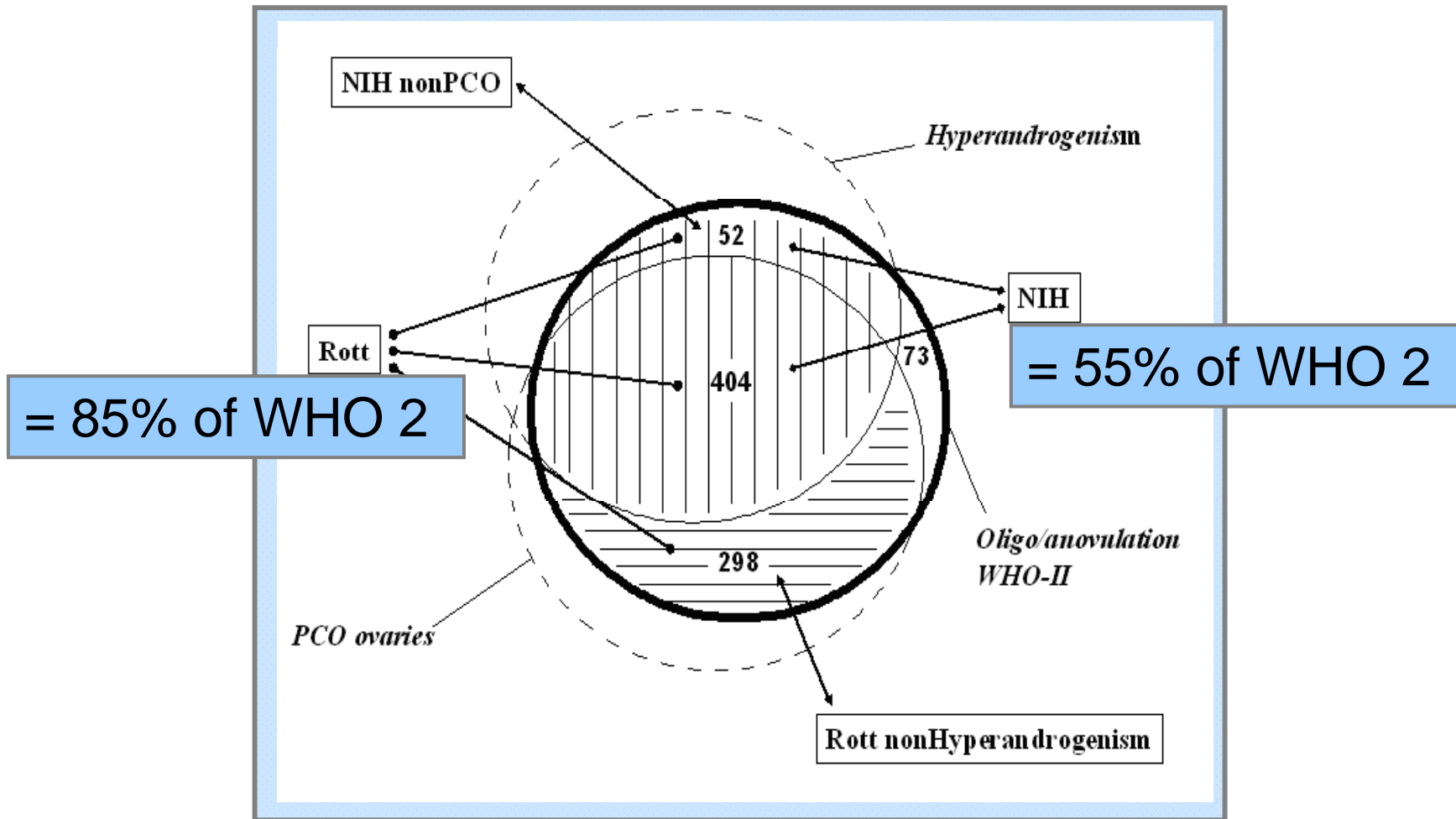
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	NIH (1990)	Rott Cons (2003)	AES (2006)
Hyperandrogenism	+	<u>+</u>	+
Oligo/amenorrhea	+	<u>+</u>	<u>+</u>
PCO (US)		<u>+</u>	<u>+</u>

PCOS according to the Rotterdam consensus criteria: change in prevalence among WHO-II anovulation and association with metabolic factors

BJOG 2006

FJ Broekmans,^a EAH Knauff,^a O Valkenburg,^b JS Laven,^b MJ Eijkemans,^c BCJM Fauser^a



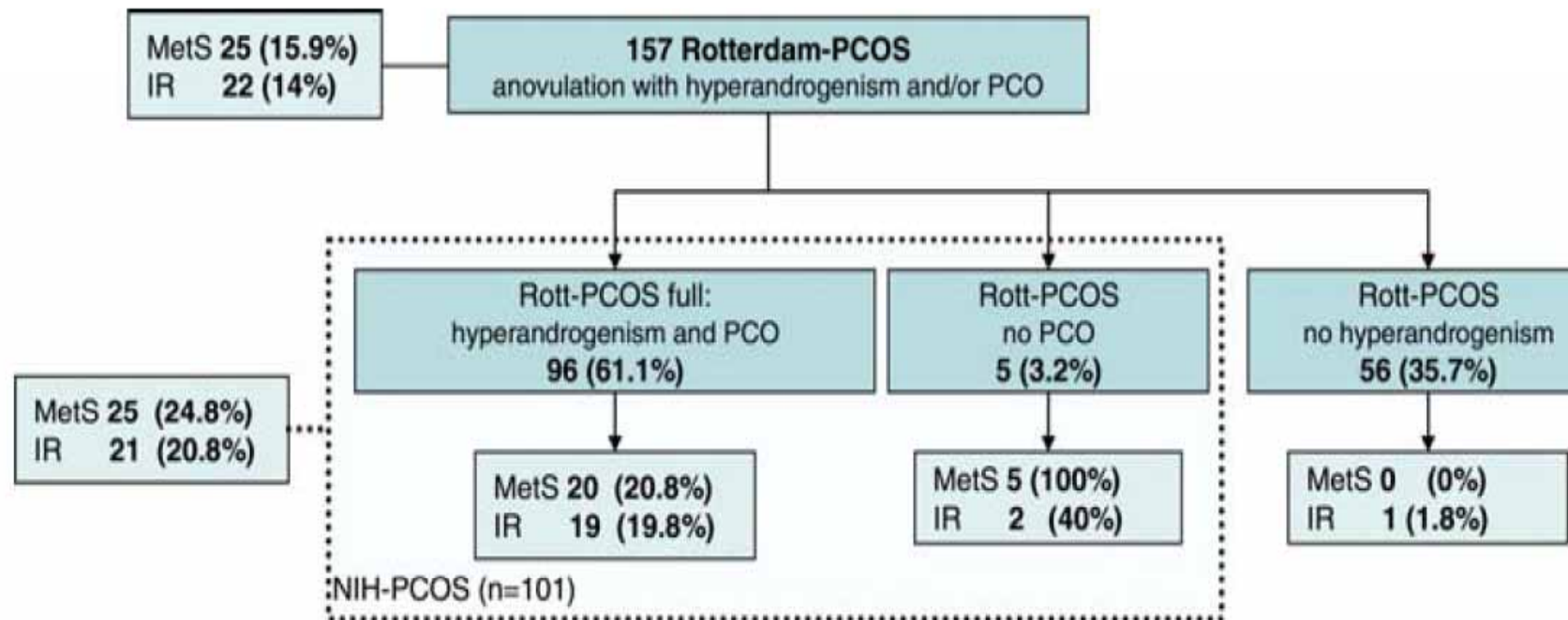
WHO 2, n=827

Indicators for metabolic disturbances in anovulatory women with polycystic ovary syndrome diagnosed according to the Rotterdam consensus criteria



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A.J. Goverde^{1,3}, A.J.B. van Koert¹, M.J. Eijkemans¹, E.A.H. Knauff¹,
H.E. Westerveld², B.C.J.M. Fauser¹, and F.J. Broekmans¹





Human Reproduction

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5th – 6th November 2010
Thessaloniki, Greece

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1. Reproductive Endocrinology:

The Rotterdam ESHRE/ASRM-sponsored PCOS consensus workshop group

Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS)

Hum. Reprod. (2004) 19(1): 41-47 doi:10.1093/humrep/deh098

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2. Environmental effects on reproductive health:

N.E. Skakkebaek, E. Rajpert-De Meyts, and K.M. Main

Testicular dysgenesis syndrome: an increasingly common developmental disorder with environmental aspects: Opinion

Hum. Reprod. (2001) 16(5): 972-978 doi:10.1093/humrep/16.5.972

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3. Andrology:

André C. Van Steirteghem, Zsolt Nagy, Hubert Joris, Jiaen Liu, Catherine Staessen, Johan Smits, Arjoko Wisanto, and Paul Devroey

High fertilization and implantation rates after intracytoplasmic sperm injection

Hum. Reprod. (1993) 8(7): 1061-1066

» [Abstract](#) » [Full Text \(PDF\)](#)

4. Physiology:

M.J. Faddy, R.G. Gosden, A. Gougeon, Sandra J. Richardson, and J.F. Nelson

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The Journal

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1. Article:

Egbert R. te Velde and Peter L. Pearson

The variability of female reproductive ageing

Hum. Reprod. Update (2002) 8(2): 141-154 doi:10.1093/humupd/8.2.141

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2. Embryology:

Adam H. Balen, Joop S.E. Laven, Seang-Lin Tan, and Didier Dewailly

Ultrasound assessment of the polycystic ovary: international consensus definitions

Hum. Reprod. Update (2003) 9(6): 505-514 doi:10.1093/humupd/dmg044

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3. Article:

M. Beato and J. Klug

Steroid hormone receptors: an update

Hum. Reprod. Update (2000) 6(3): 225-236 doi:10.1093/humupd/6.3.225

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4. Review:

F.J. Broekmans, J. Kwee, D.J. Hendriks, B.W. Mol, and C.B. Lambalk

A systematic review of tests predicting ovarian reserve and IVF outcome

Hum. Reprod. Update (November/December 2006) 12(6): 685-718 first published online August 4, 2006 doi:10.1093/humupd/dml034

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5. MONOGRAPH:

Barry D. Bavister

Culture of preimplantation embryos: facts and artifacts

Hum. Reprod. Update (1995) 1(2): 91-148 doi:10.1093/humupd/1.2.91

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- ☐ Sperm morphologic features as a prognostic factor in in vitro fertilization
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The prevalence of polycystic ovary syndrome in a community sample assessed under contrasting diagnostic criteria

Human Reproduction, Vol.25, No.2 pp. 544–551, 2010

Wendy A. March^{1,2}, Vivienne M. Moore², Kristyn J. Willson¹,
David I.W. Phillips³, Robert J. Norman¹, and Michael J. Davies^{1,4}

Background	Prevalence estimate PCOS in community according to NIH, Rotterdam, AES criteria
Design	Retrospective cohort study 728 women (born 1973-1975), single hospital
Results	Estimate prevalence; <ul style="list-style-type: none">● 8.7 NIH● 11.9 Rotterdam● 10.2 AES
Conclusion	Rotterdam and AES prevalence estimated up twice compared to NIH

PCOS diagnosis

- *inclusive or exclusive*

Risks associated with over- or underdiagnosis

- For the patient? (*“to know what’s wrong”*)
- Treatment
- Future health risk assessment
- Health insurance coverage
- Family studies (genetics)

PCOS diagnosis



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