Polycystic Ovary

- International consensus definitions
- The baseline ultrasound scan of the pelvic is best performed in the early follicular phase (day 1-3)
- These criteria include the ovarian volume and the follicle number.
- 12 or more follicles measuring 2-9 mm
- Increased ovarian volume (> 10 cm^3) or >7 ml (Jonard S, 2005).
- Only ovary fitting this definition is sufficient the PCO (Balen AH., Hum Reprod Upd. 2003)

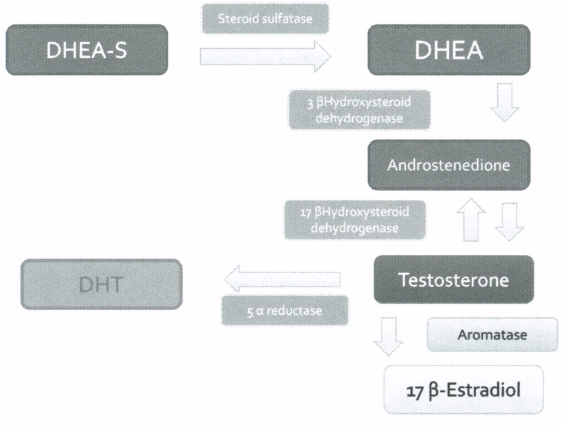
Polycystic Ovary

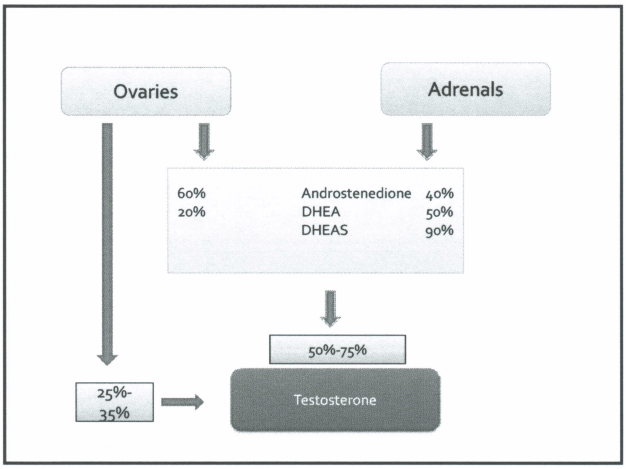
- The prevalence of PCOM has been suggested to be higher than 14-23% both in Western and Asian women (Ho PC, 2005)
- The criteria for the diagnosis PCO by 3D ultrasongrophy need to be defined (Lam, PM, Hum Reprod. 2006)
- PCOM is the most frequently used criterion in PCOS diagnosis (Hsu, 2007).

Androgen Excess

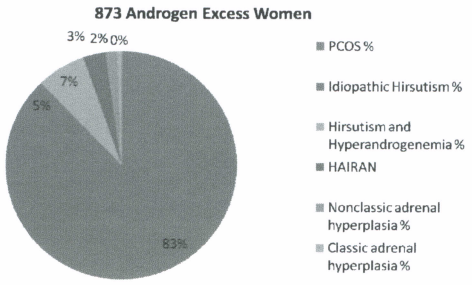
Androgen production in women

- Androgens in circulating
  - Dehydroepiandrosterone sulphate (DHEAS)
  - Dehydroepiandrosterone (DHEA)
  - Androstenedione (A)
  - Testosterone (T)
  - Dihydrotestosterone (DHT)
- Steroidogenic enzymes
  - Steroid sulfatase
  - Type 1 3 β-HSD, type 3 and 5 17 3 β-HSD, 3 α-HSD
  - 5 α–reductase, Aromatase

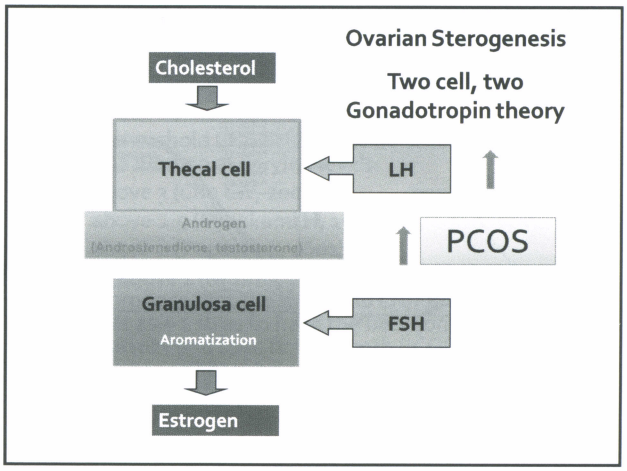




Androgen Excess



Azziz R, JCEM, 2004



Excess androgen

- Excess androgen was defined as clinical and biochemical hyperandrogenism
- Clinical hyperandrogenism:
  - Hirsutism:
  - Acne
  - Alopecia
- Biochemical hyperandrogenism
  - DHEAS, DHEA, Androstenedione, Testosterone, Free androgen index
- The important role of hormones in the pathophysiology of Pilosebaceous Units (PSUs) could be expected. (Deplewski D, 2000).

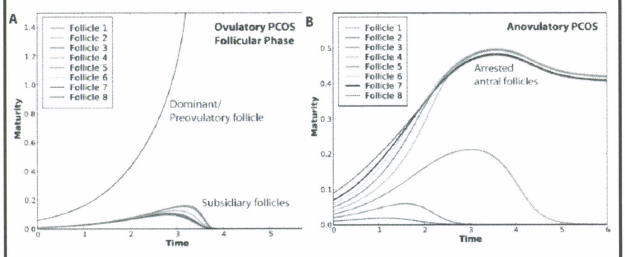
Androgens stimulating sebum production

- Androgens stimulate sebocyte proliferation
- Androgen-insensitive subjects do not produce sebum and do not develop acne
- Androgen-producting tumors are often associated with the development of acne
- Systemic administration of testosterone and DHEAS increases the size and secretion of sebaceous gland
- Severe acne is often associated with elevated serum androgen levels
  - Thiboutot D, Clinics in Dermatology, 2004

Ovulatory Dysfunction

Ovulatory dysfunction

- Ovulatory dysfunction was based on menstrual history during the previous 12 months with oligomenorrhea (<9 cycles of menstruation, i.e., average menstrual interval >45 days) or amenorrhea (absence of menstruation for ≥180 days)



Chavez-Ross, J Math Biol 1997

Inappropriate gonadotropin secretion

Inappropriate gonadotropin secretion in polycystic ovary syndrome

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Objective: To evaluate inappropriate gonadotropin secretion in women with polycystic ovary syndrome (PCOS).
Design: Retrospective study.
Setting: Academic tertiary center.
Patient(s): A total of 373 women were classified into three groups: [1] healthy control women (n = 48); [2] women who were positive for PCOS risk factor; and [3] women with PCOS (n = 251).
Intervention(s): None.
Main Outcome Measure(s): Gonadotropin levels, LH-FSH ratio, body mass index, and clinical and/or biochemical presentations of PCOS.
Result(s): The area under the receiver operating characteristic curve, used to predict PCOS for the LH-FSH ratio, showed similar diagnostic performance to total T and average ovarian volume. The LH-FSH ratio exhibits greater observed accuracy than total T and average ovarian volume for evaluation of women with oligomenorrhea or anovulation. An LH-FSH ratio of >1 presented the best combination of sensitivity and specificity. Body mass index was positively correlated with total T in non-PCOS and PCOS groups; however, body mass index was negatively correlated with LH in PCOS but showed no correlation in non-PCOS subjects.
Conclusion(s): The LH-FSH ratio is a valuable diagnostic tool in evaluating women with PCOS and oligomenorrhea or anovulation, and an LH-FSH ratio of >1 may be used as a decision threshold. The link between body mass index and LH may provide clues for further understanding the pathological milieu of PCOS. (Fertil Steril® 2009;91: 1168–74. ©2009 by American Society for Reproductive Medicine.)

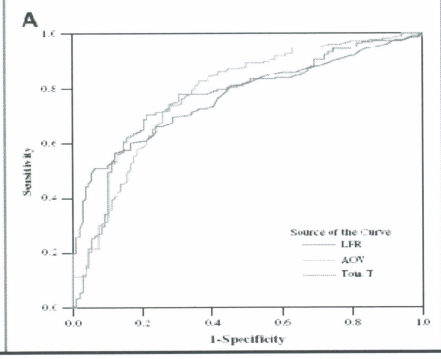
Key Words: PCOS, gonadotropin, LH, LH to FSH ratio, oligomenorrhea, obesity, diagnosis

Inappropriate gonadotropin secretion

- The mechanisms underlying the increased LH/FSH ratio in PCOS include an increased frequency of GnRH secretion.
- Decreased sensitivity to progesterone negative feedback on the GnRH pulse generator may play a role in this neuroendocrine defect.
- Increased hypothalamic GnRH, which at increased pulsatile frequency favors LHß gene expression at the expense of the FSHß gene.

FIGURE 1

Receiver operating characteristic plots of LH-FSH ratio (LFR), average ovarian volume (AOV), and total T for evaluation of women (**A**) with PCOS and (**B**) with Oligo-An.



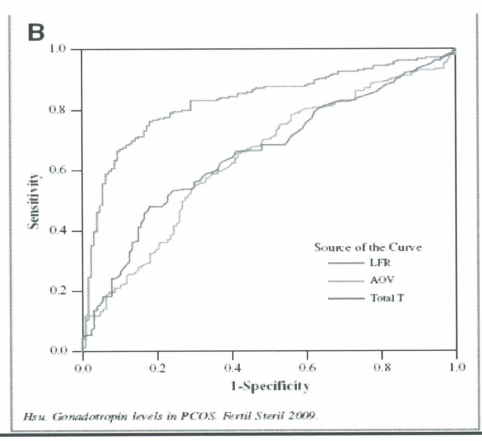


TABLE 2

Sensitivity and specificity in decision thresholds of LH-FSH ratio (LFR) for evaluation of PCOS and oligomenorrhea or anovulation.

	PCOS		Oligomenorrhea or anovulation	
Decision threshold for LFR	Sensitivity	Specificity	Sensitivity	Specificity
>0.8	74	72	80	74
>0.9	71	76	77	78
>1	69	80	75	83
>1.1	65	80	71	83
>1.5	52	89	58	94
>2	35	90	41	96
>2.5	23	94	27	98
>3	13	96	15	98

Note: All data are percentages.

Ibu. Gonadotropin levels in PCOS. Fertil Steril 2009.

LH/FSH ratio

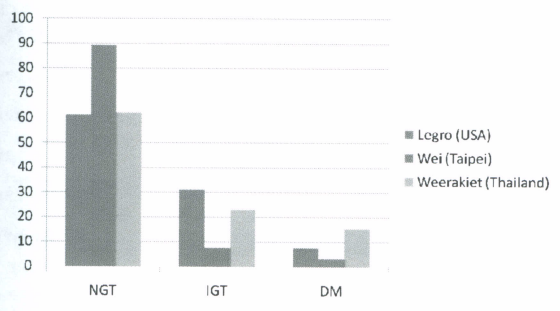
- The threshold LH/FSH ratio to be used in identifying PCOS women at varying levels:
  - above 3 (Cho LW, 2006),
  - above 2.5 (Minakami H, 1988),
  - above 2 (Papaleo E, 2001)
  - or above 1 (Iwasa T, 2006).
- We propose that the threshold LH/FSH ratio could be set as > 1 so as to have the best combination of sensitivity and specificity in both PCOS and oligomenorrhea/Anovulation diagnosis.

Insulin Resistance

Prevalence of Insulin Resistance

- Insulin Resistance: 50-70% among women with PCOS (Legro RS, 2004)
- Insulin resistance was detected in approximately 80% of women with PCOS, and in 95% of obese women. The detection of IR is superior using the calculated indices HOMA and QUICKI (Carmina E, Fertil Steril. 2004)
- The prevalence of IR in Chinese women with PCOS was 43.2%. Obese PCOS (82.8%) and Non-obese PCOS (20.5%). (Lin JF, Zhonghua Fu Chan Ke Za Zhi. 2006)

Prevalence of IGT and DM



Obesity and PCOS

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Clinical and biochemical presentations of polycystic ovary syndrome among obese and nonobese women

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Objective: To study the differences in clinical and biochemical characteristics between obese and nonobese women with polycystic ovary syndrome (PCOS).
Design: Retrospective study.
Setting: University teaching hospital.
Patient(s): Four hundred sixty-four Taiwan Chinese women, among whom 295 were diagnosed with PCOS and 169 were non-PCOS controls.
Main Outcome Measure(s): Body mass index, average menstrual interval, modified Ferriman-Gallwey score, acne, total T, and waist-to-hip ratio.
Result(s): Obese women with polycystic ovary morphology (PCOM) had a greater risk of developing of PCOS (odds ratio [OR], 2.5; 95% confidence interval [CI], 1.5–10.4) than nonobese women with PCOM. Obese women with PCOM had a higher incidence oligomenorrhea (OR, 2.6; 95% CI, 1.6–4.1) and biochemical hyperandrogenemia (OR, 2.5; 95% CI, 1.6–4.0) than nonobese women with PCOM. Obese subjects with PCOS had a higher risk of developing oligomenorrhea (OR, 2.2; 95% CI, 1.3–3.7) and biochemical hyperandrogenemia (OR, 2.6; 95% CI, 1.6–4.2) than nonobese women with PCOS. Moreover, obese women with PCOS had significantly higher serum total T levels and more prolonged menstrual intervals than nonobese women with PCOS. Notably, the obese women with PCOS presented less acne than the nonobese subjects (OR, 0.5; 95% CI, 0.3–0.9).
Conclusion(s): Obese women with PCOS had more severe ovulatory dysfunction and higher serum total T levels than nonobese subjects. Moreover, obese women with PCOS had a significantly lower frequency of acne than nonobese subjects. (Fertil Steril® 2008;■■:■■–■■. ©2008 by American Society for Reproductive Medicine.)

Keywords: Polycystic ovary syndrome, polycystic ovaries, obese, hyperandrogenism, hirsutism, acne

Obesity

- Negatively correlated with
  - SHBG
  - HDL-C
  - AMH
  - LH in PCOS
- Postively correlated with
  - LDL-C
  - CRP
  - insulin resistance
  - total testosterone
  - menstrual distubrance

TABLE 1
Clinical and biochemical presentation of obesity and nonobesity in the PCOS and non-PCOS groups.

	PCOS				Non-PCOS			
	Total	Obesity	Nonobesity	*P*	Total	Obesity	Nonobesity	
No. of cases (%)	295	115 (39)	180 (61)		169	38 (23)	131 (77)	
Age, years	26.7 ± 5.4	27.6 ± 5.5	26.2 ± 5.2	.027	29.8 ± 5.9	29.2 ± 6.6	30.0 ± 5.7	
Polycystic ovaries, %	93	90	95	NS	33	29	34	
Oligomenorrhea, %	64	75	57	.002	7	18	3	
Amenorrhea, %	9	13	6	.041	2	3	2	
Hyperandrogenemia, %	46	61	37	<.001	12	18	11	
Hirsutism and/or acne, %	57	49	63	.017	20	21	19	
Hirsutism, %	28	25	30	NS	6	16	3	
Acne, %	48	38	54	.009	18	16	18	
LH/FSH > 1, %	71	67	74	NS	25	35	23	
mF-G score	3.1 ± 3.5	3.1 ± 3.8	3.1 ± 3.3	NS	1.0 ± 2.2	1.7 ± 2.7	0.8 ± 1.0	
Total T, mmol/L	3.0 ± 1.4	3.5 ± 1.5	2.7 ± 1.2	<.001	1.9 ± 0.8	2.3 ± 0.8	1.8 ± 0.8	
Interval[a]	80.7 ± 62.3	95.2 ± 65.9	71.3 ± 59.2	.001	37.7 ± 33.2	46.5 ± 33.3	35.3 ± 33.0	
PRL, mIU/mL	13.7 ± 5.0	13.3 ± 4.9	13.9 ± 5.1	NS	14.3 ± 5.4	14.1 ± 5.8	14.3 ± 5.3	
FSH, mIU/mL	5.9 ± 1.9	6.0 ± 2.0	5.9 ± 1.9	NS	6.9 ± 2.6	6.4 ± 2.4	7.1 ± 2.6	
LH, mIU/mL	10.2 ± 7.0	8.6 ± 5.8	11.3 ± 7.5	.005	6.01 ± 6.17	5.58 ± 3.82	6.12 ± 6.68	
LH to FSH ratio	1.8 ± 1.2	1.5 ± 1.1	2.0 ± 1.3	.003	1.0 ± 1.0	1.0 ± 0.7	0.9 ± 1.0	
BMI, kg/m^2	24.5 ± 6.2	31.2 ± 4.4	20.3 ± 2.1	<.001	22.5 ± 5.0	30.4 ± 3.8	20.2 ± 2.2	
Waist, cm	73.8 ± 16.2	89.9 ± 14.1	63.9 ± 6.6	<.001	68.0 ± 11.6	85.3 ± 10.2	63.2 ± 6.0	
WHR	0.80 ± 0.10	0.86 ± 0.10	0.76 ± 0.07	<.001	0.77 ± 0.07	0.83 ± 0.06	0.75 ± 0.06	

Note: NS = nonsignificant.
[a] Obesity: BMI ≥ 25. Nonobesity: BMI ≤ 25. *Interval*: 365/the number of menstrual cycle in previous 12 months.

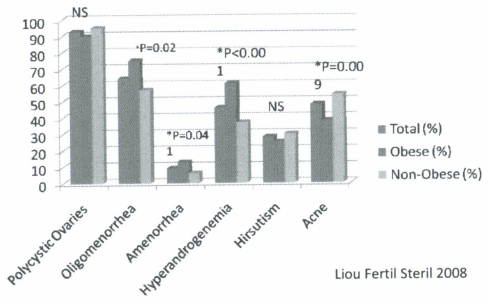
Liou. Obesity and PCOS. Fertil Steril 2008.

TABLE 2
Pearson correlation between BMI and clinical and biochemical presentation in patients with and without PCOS.

	Total (N = 464)		PCOS (n = 295)		Non-PCOS (n = 169)	
	Correlation	*P*	Correlation	*P*	Correlation	*P*
Age, years	0.053	NS	0.104	NS	0.094	NS
mF-G score	0.079	NS	0.013	NS	0.091	NS
Total T, ng/dL	0.345*	<0.001	0.330*	<0.001	0.243*	.001
Interval[a]	0.221*	<0.001	0.180*	.002	0.144	NS
PRL, mIU/mL	−0.088	NS	−0.091	NS	−0.060	NS
FSH, mIU/mL	−0.047	NS	0.027	NS	−0.053	NS
LH, mIU/mL	−0.099	NS	−0.189*	.005	−0.118	NS
LH/FSH	−0.063	NS	−0.173*	.010	−0.057	NS
Average ovaries volume, mL	0.098*	.041	0.085	NS	−0.105	NS
Waist	0.923*	<0.001	0.918*	<0.001	0.935*	<0.001
Waist/hip	0.606*	<0.001	0.598*	<0.001	0.598*	<0.001

* $P<0.05$.
[a] Interval: 365/the number of menstrual cycle in previous 12 months.

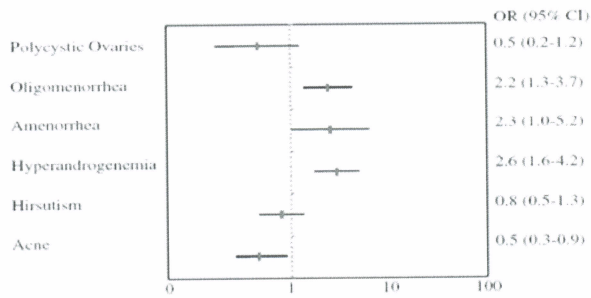
Obesity vs Non-obesity in PCOS



Liou Fertil Steril 2008

FIGURE 1

OR for the incidence of some clinical manifestations in obese versus nonobese women with PCOS.



Liou. Obesity and PCOS. Fertil Steril 2008.

PCOS and IR

- Women with PCOS defined by oligo-anovulation and hyperandrogenism had both higher BMIs and increased insulin levels among three of the phenotypes of PCOS (Welt CK, 2006).
- Women diagnosed with PCOS without hyperandrogenism had both lower BMI and insulin levels among the four phenotypes of PCOS (Shroff R, 2007).

PCOS and IR

- Insulin resistance in women with PCOS was measured by a continuous infusion of glucose with model assessment, and demonstrated that BMI, not testosterone, was independently associated with insulin sensitivity (Spranger J, 2004).

Various Phenotypes of PCOS

	Control	A+O+P	A+O	A+P	O+P	P-value
Cases	40	125	25	37	46	
Age	27.2	26.6	26.4	27.1	27.4	NS
BMI	24.3	24.9	25.2	25.0	25.1	NS
Obesity %	40	40	40	41	39	NS
Menarche	12.1	12.5	12.4	11.9	13.1	NS
Weight	62.9	64.4	65.1	64.2	65.3	NS
Height	160.8	160.7	161.0	160.4	161.1	NS
Waist	71.3	74.4	73.5	73.1	73.2	NS
Hip	92.0	93.1	92.3	92.9	92.4	NS
WHR	0.77	0.79	0.79	0.78	0.79	NS

Various Phenotypes of PCOS

	Control	A+O+P	A+O	A+P	O+P	P-value
Cases	40	125	25	37	46	
BMI	24.3	24.9	25.2	25.0	25.1	NS
Insulin	7.96	9.80	7.61	8.30	9.81	NS
Glucose	92.3	93.2	91.0	91.8	94.7	NS
GIR	22.5	18.7	21.7	25.4	19.4	NS
HOMA-IR	1.88	2.36	1.75	1.92	2.39	NS
QUICKI	0.38	0.36	0.38	0.38	0.36	NS
IR-GIR %	28	42	40	24	28	NS
IR-HOMA	23	38	32	24	30	NS
IR-QUICKI	25	38	32	24	30	NS

Obese and Non-obese in PCOS

	Non-Obese			Obese		
	Control	PCOS	P-value			
Cases	24	140		16	93	
Age	26.8	25.6	NS	27.9	28.7	NS
BMI	21.4	21.0	NS	28.8	30.9	NS
Menarche	12.8	12.9	NS	11.2	11.9	NS
Weight	55.3	54.4	NS	74.3	80.0	NS
Hip	86.8	86.3	NS	99.3	103.0	NS
Waist	64.4	64.9	NS	81.0	87.7	0.027
WHR	0.74	0.75	NS	0.82	0.85	0.049
Interval	34.9	85.0	<0.001	31.2	113.6	0.043
AOV	6.5	11.1	<0.001	7.3	12.2	0.003

Obese and Non-obese in PCOS

	Non-Obese			Obese		
	Control	PCOS	P-value			
Cases	24	140		16	93	
BMI	21.4	21.0	NS	28.8	30.9	NS
Insulin	5.0	5.7	NS	12.4	14.8	NS
Glucose	91.4	90.0	NS	93.6	97.6	NS
GIR	28.1	26.7	NS	14.2	10.5	NS
HOMA	1.1	1.3	NS	3.0	3.7	NS
QUICKI	0.40	0.39	NS	0.35	0.33	NS
IR-GIR	8	16	NS	56	68	NS
IR-HOMA	8	11	NS	44	67	NS
IR-QUICKI	8	11	NS	50	67	NS

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Polycystic ovary syndrome

PCOS

- Diagnostic criteria
  - Polycystic ovary morphology
  - Androgen excess
  - Ovulatory dysfunction
- Clinical and biochemical presentation
- Inappropriate gonadotropin secretion
- Insulin Resistance
- Obesity
- Special treatment

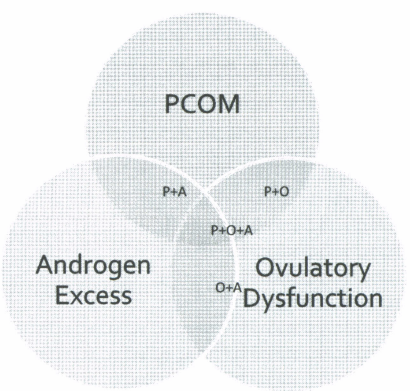
Diagnosis

How to diagnose PCOS

- Women without any PCOS related syndrome
- PCOS risk factor positive women
- Women with PCOS
  - PCOS without androgen excess
  - Rotterdam criteria
  - NIH criteria

Diagnostic criteria of PCOS

- NIH 1990
  - Chronic anovulation
  - Clinical and/or hyperandrogenism
- Rotterdam 2003
  - Chronic anovulation
  - Clinical and/or hyperandrogenism
  - Polycystic ovaries



Diagnostic criteria for polycystic ovary syndrome in Taiwanese Chinese women: comparison between Rotterdam 2003 and NIH 1990

Roughly 61% of patients diagnosed with polycystic ovary syndrome (PCOS) using the 2003 Rotterdam criteria fulfilled the 1990 National Institutes of Health (NIH) criteria. Patients meeting the 1990 NIH diagnostic criteria have more severe clinical and biochemical PCOS symptoms than those who did not. (Fertil Steril® 2007; 88:727–9. ©2007 by American Society for Reproductive Medicine.)

TABLE 1

Clinical and biochemical presentation in various phenotypes of PCOS.

Diagnosis	Number (%)	Interval[a]	T[b]	mFG Score	Hirsutism (%)	Acne (%)	LH (mIU/mL)	LH/FSH	BMI	WHR
PCOS all	170 (100%)	81.5 ± 58.7	3.44 ± 1.60	3.70 ± 3.97	50%	41%	11.21 ± 6.50	1.98 ± 1.20	24.4 ± 6.0	0.81 ± 0.07
Control	45	30.3 ± 3.0	1.42 ± 0.45	0.42 ± 0.72	0	0	3.92 ± 1.94	0.61 ± 0.38	21.2 ± 3.1	0.74 ± 0.04
Non-NIH	67 (39%)	58.1 ± 46.9	2.71 ± 1.42	2.99 ± 3.44	22%	30%	9.26 ± 5.40	1.69 ± 1.01	23.3 ± 5.6	0.80 ± 0.05
O+P	31 (18%)	87.7 ± 59.6	1.91 ± 0.56	1.23 ± 1.50	0	0	10.44 ± 4.34	1.90 ± 1.01	23.5 ± 6.0	0.79 ± 0.05
A+P	36 (21%)	32.5 ± 4.8	3.37 ± 1.60	4.50 ± 3.92	42%	56%	8.25 ± 6.05	1.50 ± 0.98	23.2 ± 5.3	0.80 ± 0.05
NIH	103 (61%)	96.7 ± 59.5	3.92 ± 1.53	4.20 ± 4.23	35%	48%	12.48 ± 6.85	2.17 ± 1.28	25.7 ± 6.1	0.82 ± 0.07
A+O	15 (9%)	81.3 ± 47.2	3.57 ± 1.74	2.93 ± 2.66	27%	46%	9.47 ± 6.04	1.79 ± 1.27	24.9 ± 6.8	0.82 ± 0.06
A+O+P	88 (52%)	99.3 ± 61.5	3.99 ± 1.49	4.42 ± 4.42	36%	48%	13.0 ± 6.88	2.23 ± 1.27	25.8 ± 6.0	0.82 ± 0.07
P value										
NIH vs. non-NIH		.000	.000	NS	NS	.020	.001	.010	.013	.012
O+P vs. control		.000	.002	NS	NS	NS	.000	.000	NS	.000
A+P vs. control		NS	.000	.000	.000	.000	.002	.000	NS	.000
A+O vs. control		.006	.002	.024	NS	.032	.029	.027	NS	.001
A+O+P vs. control		.000	.000	.000	.000	.000	.000	.000	.000	.000

Note: Data presented as mean ± SD or as %; A/P value of < .05 was considered to be significant; Comparison between control vs. (O+P), (A+P), (A+O), and (A+O+P) using multiple comparisons of post hoc test; A = androgen excess; BMI = body mass index (kg/m²); mFG = modified Ferriman-Gallwey score; NIH = PCOS according to NIH 1990 criteria (androgen excess and ovulatory dysfunction); non-NIH = PCOS without androgen excess or PCOS without ovulatory dysfunction, according to Rotterdam 2003 criteria; NS = not significant; O = ovulatory dysfunction; P = polycystic ovaries; WHR waist-to-hip ratio.

[a] Average menstrual interval; 365 days/no. of menstrual cycles in the previous 12 months.

[b] T = Total testosterone (nmol/L; 1 ng/mL = 3.47 nmol/L.

Yin. Diagnostic criteria for PCOS in Taiwanese Chinese women. Fertil Steril 2007.

Phenotypes

Ethinicity	Author	Total Case	A+O+P%	O+P%	A+O%	A+P%
Taiwan	Hsu	171	51.8	18.2	8.8	21.2
Korean	Chae	166	52.4	31.3	13.9	2.4
USA	Shroff	258	58.1	14.3	14.3	13.2
USA	Welt	418	71.3	8.6	1.7	18.4
France	Dewailly	406	60.6	16.3	6.7	16.5
UK	Barber	309	61.8	13.6	0	24.6
Italy	Belosi	345	73.6	13.3	7.5	5.5
Total		2073	63.4	15	6.5	15.1

Clinical Presentation

	Location	Criteria	Cases	Age	BMI	Acne	Hirsutism	Obesity
Hsu	Taiwan	2003	251	27.2	24.7	43%	30%	40%
Li L	China	1990	273	24.8	22.2	45%	35%	30%
Azziz	USA	1990	716	27.6	33.4	14.5%	72.2%	60%
Welt	Iceland	1990	305	28.7	32.0			
DeUgarte	Alabma	1990	271	27.4	36.4	29.2%	77%	

TABLE 1

Clinical and biochemical characteristics of healthy control, PCOS risk factor positive, and PCOS groups.

Parameter	n	Age (y)	PCOM	Oligo-An	HA	Amen	Hand	Hirs	Acne	LF>1	Obese
Subject group											
All subjects	373	27.6 ± 5.5	73	63	54	28	36	22	31	55	34
Control	48	29.2 ± 5.0	0	0	0	0	0	0	0	17	13
PCOSrf	74	28.1 ± 5.6	49	30	22	12	11	9	12	27	29
PCOS	251	27.2 ± 5.5	94	85	74	39	50	30	43	70	40
P values											
Control vs. PCOSrf		NS	.000	.000	.008	.013	.023	.042	.013	NS	NS
Control vs. PCOS		NS	.000	.000	.000	.000	.000	.000	.000	.000	.000
PCOS vs. PCOSrf		NS	.000	.000	.000	.000	.000	.000	.000	.000	NS

Note: Data are either mean ± SD or are percentages, unless otherwise indicated. Amen = amenorrhea; Hand = hyperandrogenemia; Hirs = hirsutism; LF>1 = LH-FSH ratio of >1; Interval = average menstrual interval, that is, 365 d/number of menstrual cycles in previous 12 mo; LFR = LH-FSH ratio; FG score = modified Ferriman-Gallwey score; AOV = average ovarian volume; NS = not significant.

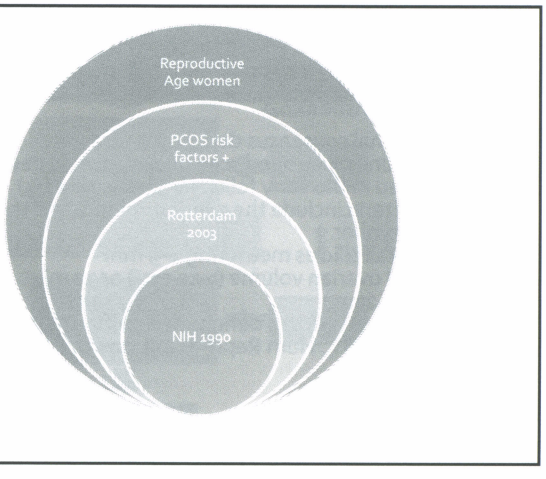
Hsu. Gonadotropin levels in PCOS. Fertil Steril 2009.

Diagnostic Criteria of PCOS in East Asia

- About 70% of PCOS fulfilled 1990 NIH criteria, phenotypes were similar
- NIH criteria diagnosed PCOS might present more severe form PCOS (Hsu MI, 2007, Lam PM, 2008)
- Women fulfilling the NIH criteria have higher metabolic risk than those who do not. (Lam PM, 2008)
- PCOM is the most commonly used criteria (Hsu MI, 2007)
- PCOS without androgen excess has least clinical significant (Hsu MI, 2007, Chae SJ, 2008)
- PCOS-risk factor positive women might be in sub-abnormal condition ((Hsu MI, 2008)

Metabolic Component

	City	Criteria	Cases	Age	BMI	Fin	Flu	G/I	HOMA
Shi	Shandong	2003	1040	28.3	24.8	9.92	88.6		
Li L	Guangdong	1990	273	24.8	22.2	12.1	91.8	11.7	2.76
Azziz	Mexico	1990	716	27.6	33.4	21.1	89.5	72.2%	4.70 (IR)
Welt	Iceland	1990	305	28.7	32.0	11.7	87.5		2.62
DeUgarte	Alabma	1990	271	27.4	36.4	28.0	87.8		4.8 (IR)

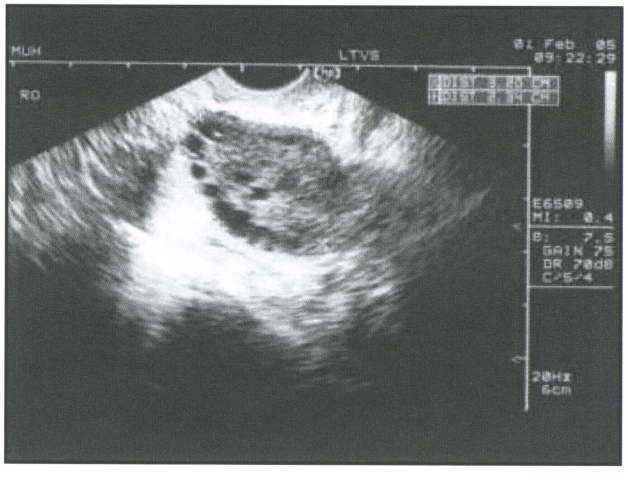


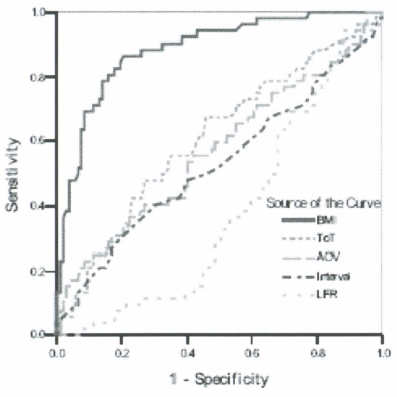
Prevalence

The prevalence of PCOS

- 400 unselected consecutive premenopausal women seeking a preemployment physical at the University of Alabama at Birmingham were studied
- PCOS was diagnosed by NIH criteria
- The cumulative prevalence of PCOS in the population was 6.6% (26.5 of 400).
- The prevalence rates of PCOS for Black and White women were 8.0 and 4.8%, respectively, not significantly different.
  - Azziz R, JCEM, 2004

PCO





The odds ratios of IR

- Obese vs. Non-Obese:
  - 63% vs. 11%, OR = 14.0, 95% CI 7.5–26.2
- Hyperandrogenemia vs. Non-Hyperandrogenemia
  - 42% vs. 25%, OR = 2.1, CI 1.3–3.6
- Oligo/amenorrhea vs. Non-Oligo/amenorrhea
  - 35% vs. 23%, OR = 1.8, CI 1.0–3.3
- PCOM vs. Non PCOM
  - 34% vs. 26%, OR = 1.4, CI 0.8–2.7

Obese and hyperandrogenism

- There is a Positive correlation between total testosterone and BMI (Hsu 2008, Holte J,1994, Cupisti S, 2007)
- There is a Negative correlation between SHBG and BMI (Cupisti S, 2007, Franks S,1991, Holte J,1994).
- Obese women must have high free androgen indexes owing to their having greater total testosterone and lower SHBG than non-obese women. (Cupisti S,2007, Franks S,1991, Holte J,1994, Bernasconi D,1996).

Table 1: Acne vs. Non-Acne

	Total	Acne	Non-Acne	P-value
Case Number	627	240	387	
Age	27.8	26.6	28.6	<0.001
Obesity %	34	27	38	
PCOS %	55	70	45	
Hirsutism %	19	30	12	
Hyperandrogenemia %	33	38	30	
Oligomenorrhea %	50	43	54	0.007
Total testosterone (ng/dL)	2.27	2.48	2.15	
M-FG score	2.33	3.25	1.76	<0.001
BMI	23.8	23.0	24.3	

Hsu MI, ASRM 2008

Table-2: Obesity vs. Non-obesity

	Total	Obesity	Non-Obesity	P-value
Case Number	627	213	414	
Age	27.8	27.8	27.8	NS
Acne %	38	31	42	
PCOS %	55	64	51	
Hirsutism %	19	22	18	
Hyperandrogenemia %	33	51	25	
Oligomenorrhea %	50	69	40	<0.001
Total testosterone (ng/dL)	2.27	2.83	1.99	
M-FG score	2.33	2.75	2.12	0.019
BMI	23.8	30.7	20.3	<0.001

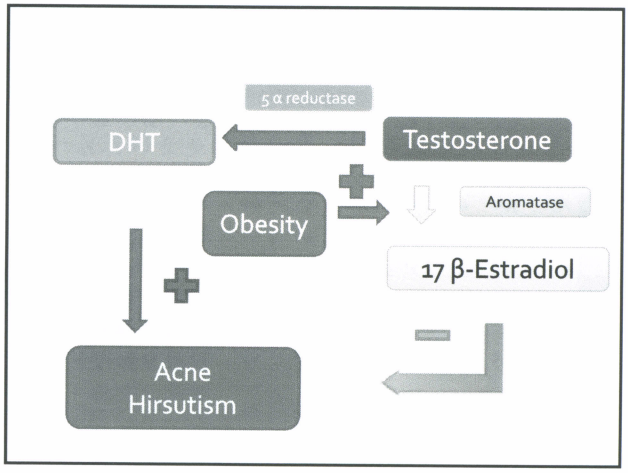
Hsu MI, ASRM 2008

Acne/Hirsutism

- The prevalence of acne seems to be more profoundly decreased than hirsutism in obese women in the study.
- Previous studies showed the severity of acne or hirsutism is quite different for a given degree of androgen excess (Deplewski D, 2000).
- The onset of acne and hirsutism had been purposed as two different pathogenetic mechanisms (Falsetti L, Gynecol Endocrinol. 2002)

Aromatase and Obesity

- Aromatase is the enzyme that converts testosterone to estradiol(Chen W, 2002).
- The increase in adipose tissue is associated with an increase in the enzyme aromatase (Cohen PG., 2001),
- Generalized obesity (BMI) was associated with increased subcutaneous measured mRNAs for aromatase (Wake DJ, 2007).

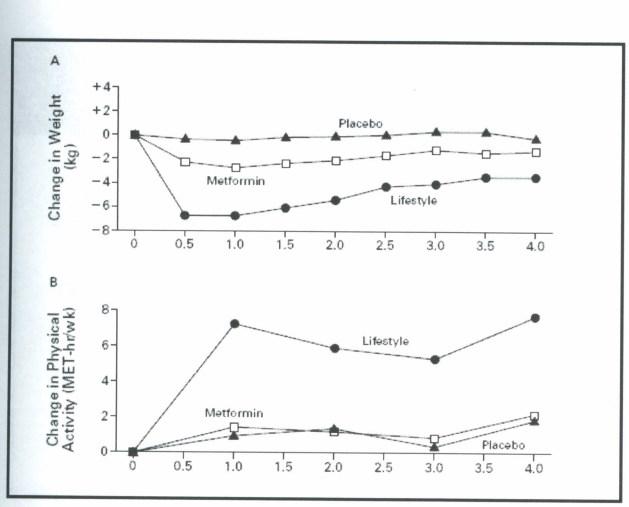


Metformin

- In IVF, metformin led to fewer cases of ovarian hyperstimulation syndrome (OHSS) (RR 0.33; 95% CI 0.13-0.80).
- This meta-analysis demonstrates that CC is still first choice therapy for women with therapy naïve PCOS.
- In CC-resistant women, the combination of CC plus metformin is the preferred treatment option before starting with LOD or FSH.
- At present, there is no evidence of an improvement in live birth when adding metformin to LOD or FSH. In IVF, metformin leads to a reduced risk of OHSS.
  - Moll E, Hum Reprod Update. 2007

Metformin as DM preventation

- 3234 nondiabetic persons with elevated fasting and post-load plasma glucose concentrations
  - 1082 in placebo
  - 1073 in Metformin
    - 850 mg Bid
  - 1079 in Lifestyle (diet and exercise)
    - Diet, exercise, 7% weight reduction
- Average follow-up 2.8 years
- Incidence od diabetes was reduced by 58% in lifestyle and 31 % in metformin intervention



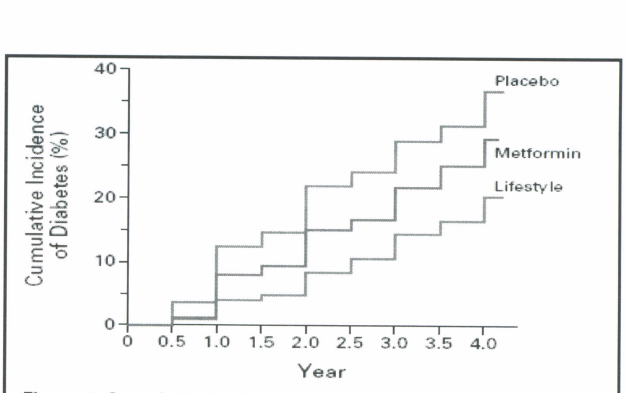


Figure 2. Cumulative Incidence of Diabetes According to Study Group.

The diagnosis of diabetes was based on the criteria of the American Diabetes Association.[11] The incidence of diabetes differed significantly among the three groups ($P<0.001$ for each comparison).

	Case Number	Age	Inftility Duration	hCG day E2	Oocyte Number	Fertilized egg	ET	Prregnancy Rate %	Abortion Rate %	Implantation Rate %	Fertilization Rate %
Endometriosis	969	35.1	4.0	639	7.4	4.8	3.1	31	20	12	70
Male	705	34.0	4.1	828	8.8	5.2	3.4	26	28	9.6	62
PCOS	105	33.1	3.5	2166	15.3	9.3	4.0	50	23	19	62
Tubal	594	34.5	3.7	1885	8.8	6.0	3.3	29	21	11	72
Unexplain	109	36.6	3.9	690	7.5	4.9	3.2	18	35	6.0	70
Combined	259	34.6	4.1	720	7.9	4.7	3.3	32	22	12.2	63
Other	117	38.3	3.8	638	7.1	5.0	3.0	17	10	7.1	76
Total	2858	34.8	3.9	985	8.4	5.3	3.3	29	23	11.2	68

IVF in TMUH

	Case Number	Age	Duration	E2	Oocyte	Fertilized egg	PR %	AR %	IR %	Fertilization Rate %	OHSS
Total	2858	34.8	3.9	985	8.4	5.3	29	23	11.2	68	.0067
PCOS	105	33.1	3.5	2166	15.3	9.3	50	23	19	62	.0097
Non PCOS	2753	34.8	3.9	1297	8.1	5.2	28	23	10.8	68	.0066
P value		0.000	NS	0.000	0.000	0.000	0.000	NS	0.000	0.008	NS

	Case Number	Age	Duration	hCG day E2	PR %	AR %	OHSS%
Endometriosis	1692	33.6	3.3	901	22	18	0.02
Male	294	32.6	2.9	1235	18	15	0.01
PCOS	467	32.3	3.1	1258	29	26	0.01
Tubal	214	33.1	3.0	1002	18	38	0
Unexplain	763	33.2	2.9	1763	24	32	0.1
Combined	64	33.5	2.8	900	28	28	0
Other	630	35.5	2.8	709	19	24	0
Total	4124	33.6	3.0	1108	22	23	0.1

IUI in TMUH

	Case Number	Age	hCG day E2	PR %	AR %	Mutiple P %	OHSS %
Total	4124	33.6	1108	22	23	10	0.1
NPCOS	3657	33.7	1089	21	23	7	0.01
PCOS	467	32.3	1258	29	26	11	0.01
P value		0.000	NS	0.000	NS	NS	NS

Treatment of infertility

- The recommended first-line treatment for ovulation induction remains the anti-estrogen CC.
- Recommended second-line intervention should CC fail to result in pregnancy is either exogenous gonadotrophins or LOS.
- The use of exogenous gonadotrophins is associated with increased chances for multiple pregnancy and intense monitoring of ovarian response is therefore required. LOS is usually effective in <50% of women and additional ovulation induction is required under those circumstances.

Treatment of infertility

- Overall, ovulation induction (representing the CC, gonadotrophin paradigm) is reported to be highly effective with a cumulative singleton live birth rate of 72%.
- Recommended third-line treatment is IVF, because this treatment is effective in women with PCOS. Data concerning the use of single ET in (young) women with PCOS undergoing IVF, significantly reducing chances of multiple pregnancies, are awaited.

北萬研究計畫（98TMU-WFH-05）

- 多囊性卵巢症候群與卵巢型態
  - 許淳森副院長-護理學系陳靜敏教授
- 多囊性卵巢症候群與肥胖
  - 復健科劉燦宏醫師-護理學系 李碧霞副教授
- 多囊性卵巢症候群與心血管疾病
  - 心臟內科陳亦仁主任-護理學系蔡仁貞教授
- 多囊性卵巢症候群與生殖內分泌異常
  - 婦產科徐明義醫師-營養保健學系邱琬淳助理教授

國科會研究計畫(NSC 98-2629-B-038-001-MY3)

- 台灣婦女多囊性卵巢症候群肥胖與心血管疾病之研究
- 主持人
  - 徐明義醫師
- 共同主持人
  - 許淳森教授
  - 曾啟瑞教授
  - 劉燦宏醫師
  - 陳亦仁主任

台北醫學大學保健營養系

- 黃士懿教授實驗室
- 透過PCOS基因多型性資料與複合檢測模式的使用，以了解並提供PCOS進一步分型的依據。
- 檢測項目：
- 1.IL-6
- 2.TNF-α
- 3.荷爾蒙代謝基因（Androgen, Estrogen, Prolactin, Insulin, Insulin Recsptor, fatty acids profile and PPAR-r）
- 4.Genetic polymorphism of Glucose transporter-1 and 4
- 5.Fatty acids profile of plasma and RBC

皮膚科

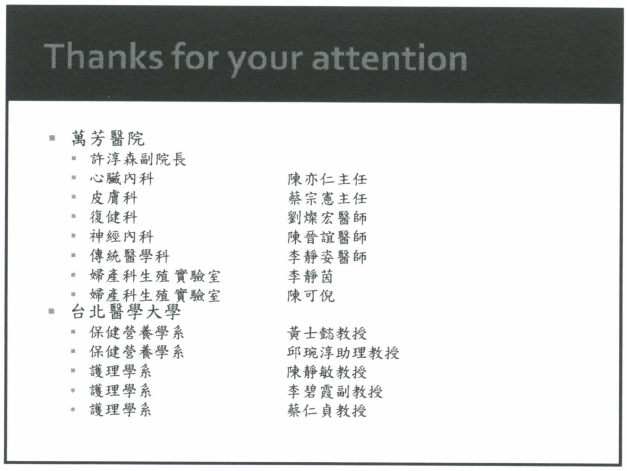
- 蔡宗憲主任
- 青春痘與多毛症與婦女雄性素的關聯性
- 台灣婦女雄性素增加的臨床表現
- 肥胖對雄性素增高的臨床表現的影響

神經內科

- 陳晉誼醫師　鄧浩文醫師
- 執行內容：研究國人多囊性卵巢患者的早發性動脈硬化。利用非侵入性頸動脈超音波檢查頸動脈內膜厚度，評估多囊性卵巢患者的早發性動脈硬化以及其背後的相關因子。
- 檢測項目：
- 1.Intima-media thickness
- 2.Plaque index

傳統醫學科

- 李靜姿醫師
- 執行內容：以問卷評估方式將多囊性卵巢症候群婦女在傳統醫學上作一診斷分類，以期能於未來以此分類依據在治療多囊性卵巢婦女成為一可靠的治療指標。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Thanks for your attentation