

# 청소년 다낭성 난소증후군 환자의 진단 및 관리 업데이트

서울대병원 강남센터  
김진주



# 청소년

---

- '청소년'
  - 만 13세 이상 19세 미만

# 국내 현황

<지난 5년간 연령대별 다낭성난소증후군 환자 현황>

구분	2012년 (명)	2013년 (명)	2014년 (명)	2015년 (명)	2016년 (명)	전체 (명)	증감 (12년 대비 '16년)
계	23,584	24,861	28,045	30,886	35,316	142,692	50%
19세이하	2,337	2,614	3,011	3,172	3,601	14,735	54.1%
20-24세	5,945	6,449	7,724	8,744	10,125	38,987	70.3%
25-29세	6,812	6,958	7,887	8,734	10,302	40,693	51.2%
30-34세	5,895	6,111	6,479	6,517	6,933	31,935	17.6%
35-39세	1,875	1,852	2,100	2,459	2,753	11,039	46.8%
40-44세	529	593	609	766	836	3,333	58%
45-49세	130	203	173	347	489	1,342	276.2%
50세이상	61	81	62	147	277	628	354.1%

# 가이드라인

- **An Endocrine Society Clinical Practice Guideline (2013)**
- **American Association of Clinical Endocrinologists, American College of Endocrinology, and Androgen Excess and PCOS society (2015)**

# An International Consortium Update (2017.11)

---

**HORMONE  
RESEARCH IN  
PÆDIATRICS**

## Clinical Practice

---

Horm Res Paediatr 2017;88:371–395  
DOI: 10.1159/000479371

Received: May 22, 2017  
Accepted: July 10, 2017  
Published online: November 13, 2017

---

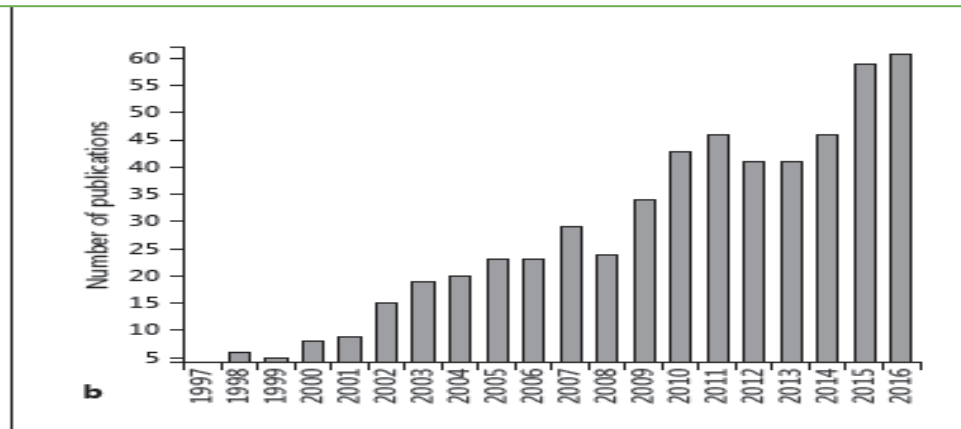
## **An International Consortium Update: Pathophysiology, Diagnosis, and Treatment of Polycystic Ovarian Syndrome in Adolescence**

Lourdes Ibáñez<sup>a,b</sup> Sharon E. Oberfield<sup>c</sup> Selma F. Witchel<sup>d</sup> Richard J. Auchus<sup>e</sup> R. Jeffrey Chang<sup>f</sup>  
Ethel Codner<sup>g</sup> Preeti Dabadghao<sup>h</sup> Feyza Darendeliler<sup>i</sup> Nancy Samir Elbarbary<sup>j</sup>  
Alessandra Gambineri<sup>k</sup> Cecilia Garcia Rudaz<sup>l</sup> Kathleen M. Hoeger<sup>m</sup> Abel López-Bermejo<sup>n</sup>  
Ken Ong<sup>o</sup> Alexia S. Peña<sup>p</sup> Thomas Reinehr<sup>q</sup> Nicola Santoro<sup>r</sup> Manuel Tena-Sempere<sup>s</sup>  
Rachel Tao<sup>t</sup> Bulent O. Yildiz<sup>u</sup> Haya Alkhayyat<sup>v</sup> Asma Deeb<sup>w</sup> Dipesalema Joel<sup>x</sup>  
Reiko Horikawa<sup>y</sup> Francis de Zegher<sup>z</sup> Peter A. Lee<sup>A</sup>

First global update on adolescent PCOS

# Levels of evidence and Grades of recommendations

A:	There is good research-based evidence to support the recommendation.
B:	There is fair research-based evidence to support the recommendation.
C:	The recommendation is based on expert opinion and panel consensus.



**Fig. 1. a** Annual number of citations for “adolescent PCOS” over the past 2 decades. **b** Annual number of publications for “adolescent PCOS” over the past 2 decades. Web of Science, Thomson Reuters, 2017.

# 청소년 다낭성 난소증후군

Is it important to differentiate PCOS at this stage?  
Or is it acceptable to delay diagnosis until adulthood?



# PCOS 진단기준

**Criteria for the Diagnosis of Polycystic Ovary Syndrome**  
(Other Hormonal or Androgen Excess Conditions Being Previously Excluded)<sup>a</sup>

<b>NIH/NICHD</b> (must meet both criteria)	<b>ESHRE/ASRM</b> (Rotterdam criteria) 2004	<b>Androgen Excess Society 2006</b>
Includes all of the following:	Includes two of the following:	Includes all of the following:
• Clinical and/or biochemical hyperandrogenism	• Clinical and/or biochemical hyperandrogenism	• Clinical and/or biochemical hyperandrogenism
• Menstrual dysfunction	• Oligo-ovulation or anovulation • Polycystic ovaries	• Ovarian dysfunction and/or polycystic ovaries



# 청소년 PCOS 진단

- IM + PCO are not sufficient to make a diagnosis in adolescents because they may be evident in normal stages in reproductive maturation.

## Diagnostic criteria for polycystic ovary syndrome in adolescents

Criterion	Hyperandrogenism <sup>a</sup>	Chronic anovulation <sup>b</sup>	Polycystic ovaries <sup>c</sup>
Diagnosis of PCOS	+	+	+
Diagnosis of PCOS probable but not confirmed	+	+	—
Diagnosis of PCOS not possible during adolescence	+	—	+
Diagnosis of PCOS not possible during adolescence	—	+	+
Not PCOS	+	—	—
Not PCOS	—	+	—
Not PCOS	—	—	+

PCOS, polycystic ovary syndrome.

<sup>a</sup> Hyperandrogenemia is primary criterion—acne and alopecia are not considered as evidence for hyperandrogenism—hirsutism may be considered sign of hyperandrogenism only when it has been documented to be progressive; <sup>b</sup> Oligoamenorrhea (or documented anovulation) has to be present for at least 2 years; <sup>c</sup> Diagnosis of polycystic ovaries by abdominal ultrasound has to include increased ovarian size ( $>10 \text{ cm}^3$ ).

Carmina. The diagnosis of PCOS in adolescents. *Am J Obstet Gynecol* 2010.

# Diagnosis in adolescents

- Hyperandrogenism is central in adolescents (2013 미국내분비학회)
  - Clinical and/or biochemical evidence of hyperandrogenism in the presence of persistent oligomenorrhea

# Suggested criteria 2017

Required	Optional <sup>a</sup>	Not recommended <sup>b</sup>	Comments
1. Irregular menses/ oligomenorrhea 2. Evidence of hyperandrogenism: a. Biochemical b. Clinical (e.g., progressive hirsutism)	1. PCOM 2. Severe cystic acne	1. Obesity 2. Insulin resistance 3. Hyperinsulinemia 4. Biomarkers (e.g., AMH, T/DHT ratio) 5. Acanthosis nigricans	1. Must generally be 2 years post-menarche 2. Must rule out other disorders of hyperandrogenism (e.g., NC-CAH, Cushing syndrome)

<sup>a</sup> Often used in concert with the required criteria, but should not be used independently as diagnostic features

# Suggested criteria 2017

- Persistent menstrual disturbances beyond 2 years after menarche or primary amenorrhea in girls with completed puberty may suggest androgen excess (**Level B**).
- 초경 후 5년까지 불규칙한 월경은 가능하나 대개 2년이면 21-35일 주기가 확립됨.
- 무배란은 AUB 양상으로 나타날 수 있음

# Suggested criteria 2017

Required	Optional <sup>a</sup>	Not recommended <sup>b</sup>	Comments
1. Irregular menses/ oligomenorrhea 2. Evidence of hyperandrogenism: a. Biochemical b. Clinical (e.g., progressive hirsutism)	1. PCOM 2. Severe cystic acne	1. Obesity 2. Insulin resistance 3. Hyperinsulinemia 4. Biomarkers (e.g., AMH, T/DHT ratio) 5. Acanthosis nigricans	1. Must generally be 2 years post-menarche 2. Must rule out other disorders of hyperandrogenism (e.g., NC-CAH, Cushing syndrome)

# Suggested criteria 2017

- Biochemical hyperandrogenism
  - Should be defined based on the methodology used (Level A).
  - Testosterone measured in a reliable methods\* documents hyperandrogenemia in a symptomatic adolescent (Level B).
- FAI (2013 미국내분비학회, 2015 AE-PCOS)

\* Liquid chromatography/tandem mass spectrometry (LC-MS/MS)  
High-quality RIA with extraction and chromatography

# Suggested criteria 2017

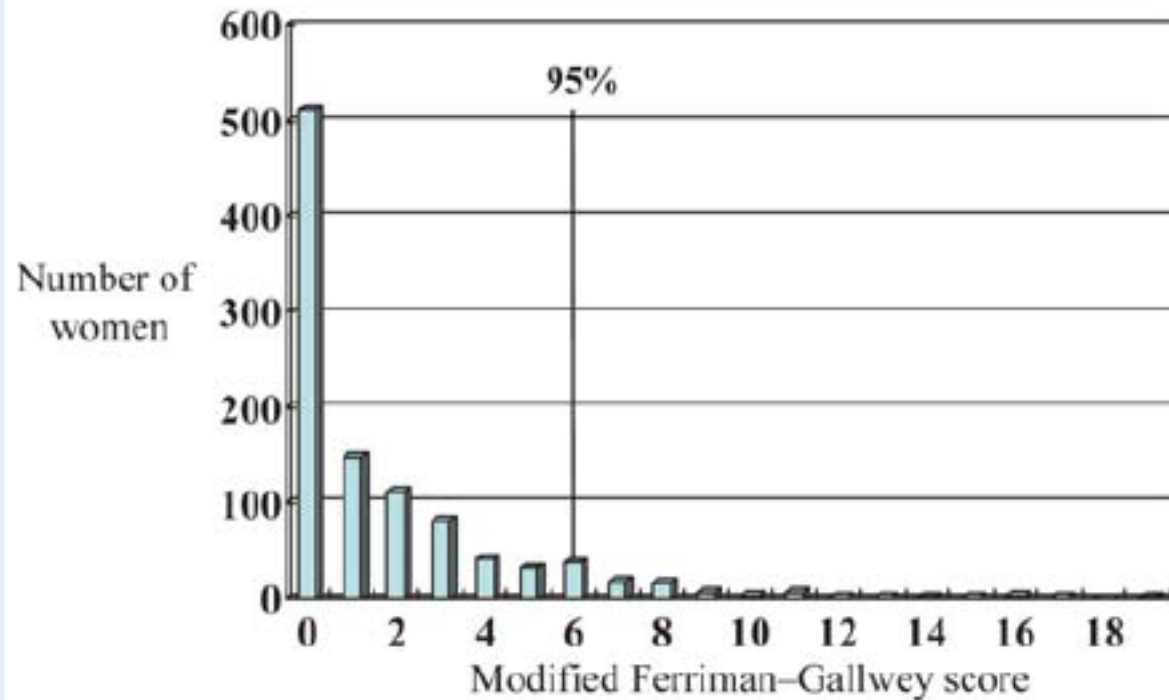
- Moderate to severe hirsutism constitutes clinical evidence of androgen excess (**Level B**).
- Mild\* hirsutism may be a sign when associated with menstrual irregularities (**Level C**).
- Isolated acne should not be considered diagnostic criteria for PCOS in adolescence (**Level C**).
- Moderate or severe inflammatory acne unresponsive to topical therapy may require investigation of androgen excess (**Level C**).

\* H-score 8-15 (백인여성)

Ethnic and racial variation

Alopecia is rare and not well studied in adolescents





**Figure 1** Distribution of the mF-Gs in 1010 random Korean women.

domly  
ing  
-up

ik Hwang<sup>4</sup>,  
Yong Moon<sup>3</sup>

ital, Seoul, South Korea  
ics and Gynecology,  
ge of Medicine, 28  
of Medicine, Inha  
Seoul, South Korea

Adult terminal hair distribution is usually achieved by 2 years after menarche  
H-score included females starting from 15 years

# Suggested criteria 2017

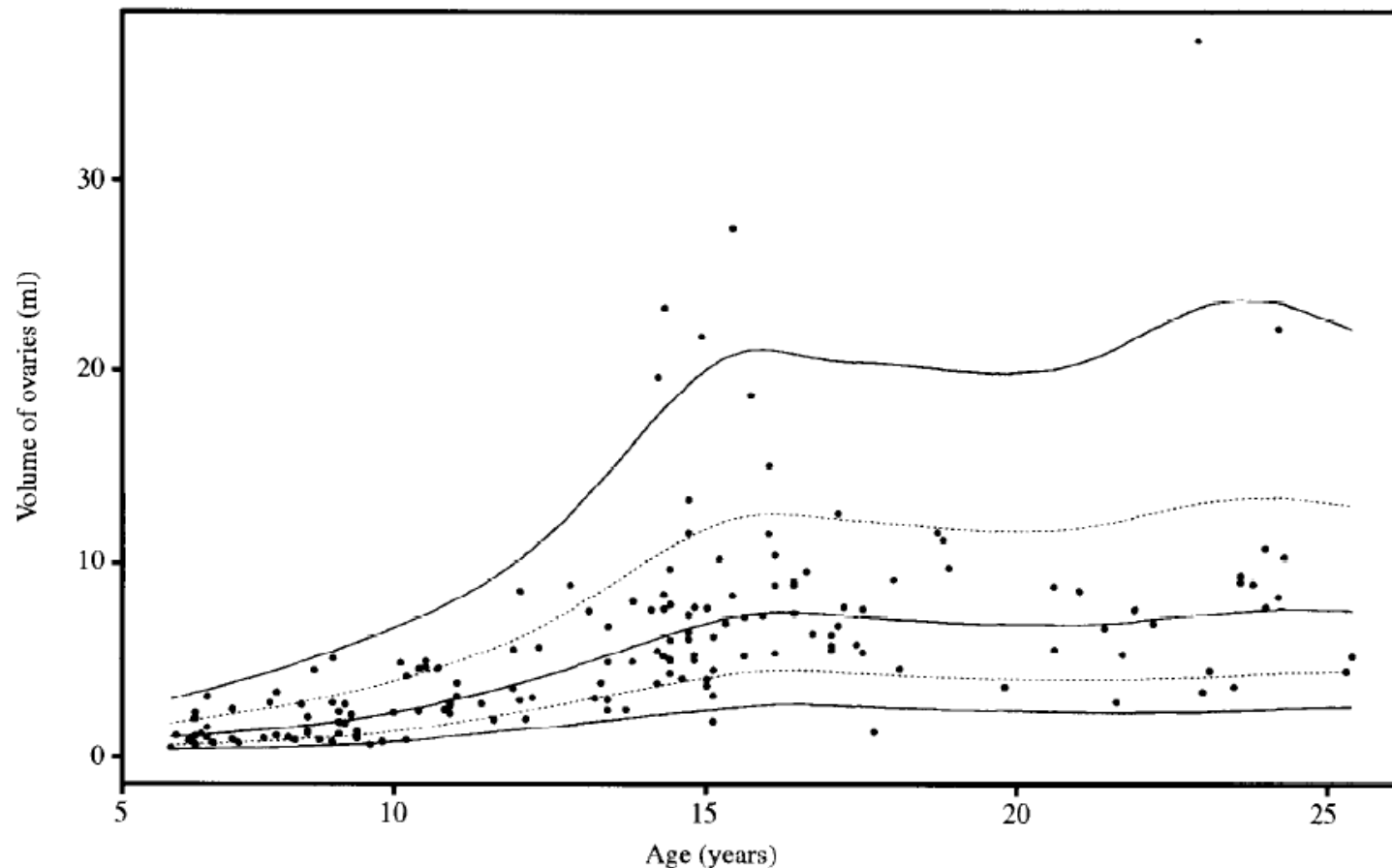
Required	Optional <sup>a</sup>	Not recommended <sup>b</sup>	Comments
1. Irregular menses/ oligomenorrhea 2. Evidence of hyperandrogenism: a. Biochemical b. Clinical (e.g., progressive hirsutism)	<div>1. PCOM</div> 2. Severe cystic acne	1. Obesity 2. Insulin resistance 3. Hyperinsulinemia 4. Biomarkers (e.g., AMH, T/DHT ratio) 5. Acanthosis nigricans	1. Must generally be 2 years post-menarche 2. Must rule out other disorders of hyperandrogenism (e.g., NC-CAH, Cushing syndrome)

# Suggested criteria 2017

---

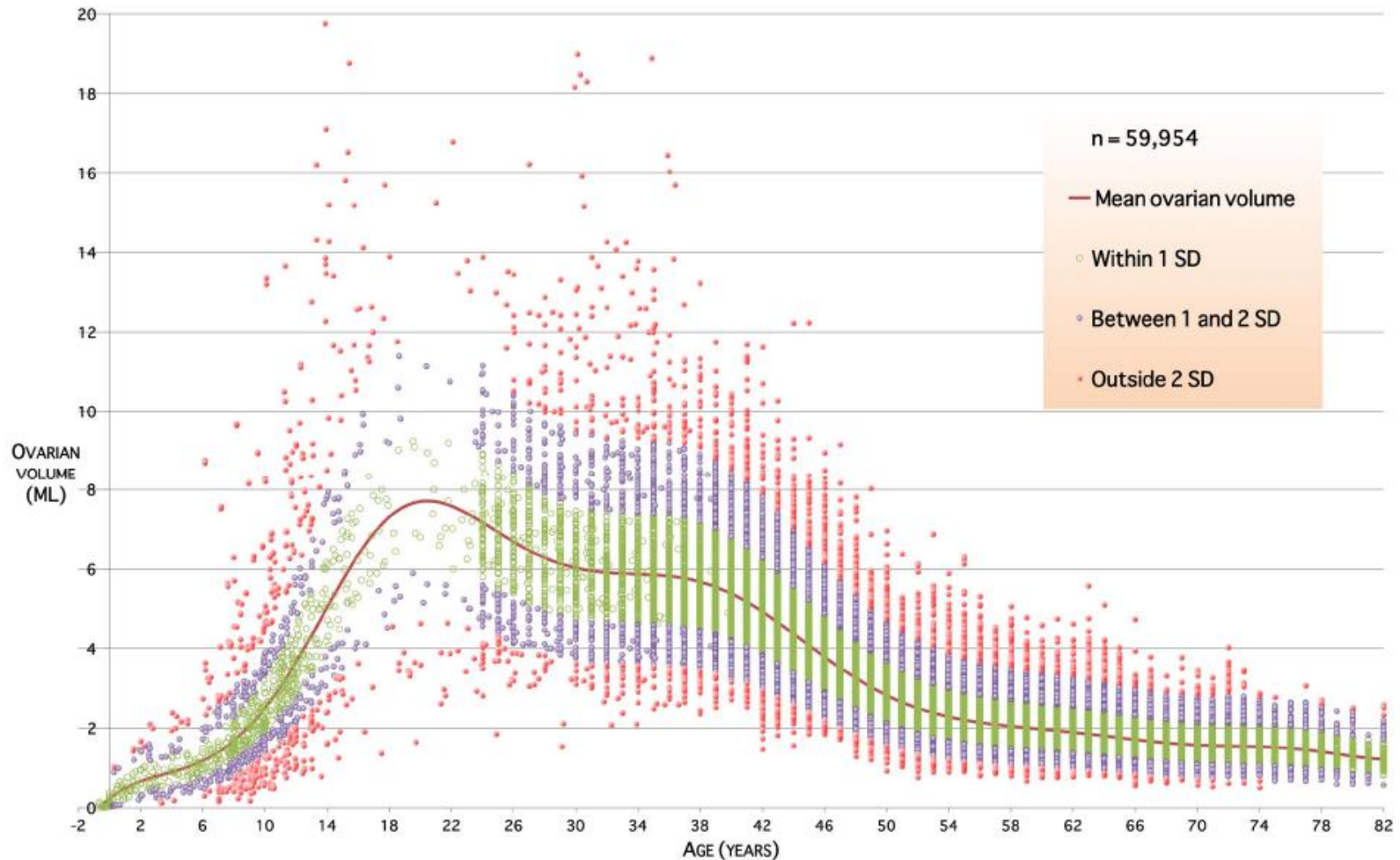
- 30–40%: prevalence of PCO based on follicle count in adolescent girls
  - Non-obese, nonhirsute girls with regular menstrual cycles, PCO is not associated with hyperandrogenism or IR.
- PCO in an adolescent who does not have hyperandrogenism/oligo-anovulation does not indicate a diagnosis of PCOS (**Level A**).

# Average ovarian volume in girls



**Figure 4** Average volume of both ovaries in 165 girls related to age. Curves represent +2 SD, +1 SD, mean, -1 SD, -2 SD. The five largest ovaries correspond to the five follicles of 30 mm or more seen in Figure 6

# Average ovarian volume throughout life



**Figure 4. The normative validated model of ovarian volume throughout life.** The red line is predicted mean ovarian volume in millilitres for any age. Colour bands indicate ranges within  $\pm 1$  standard deviation from mean, within  $\pm 1$  and  $\pm 2$  standard deviations, and outside 2 standard deviations.

doi:10.1371/journal.pone.0071465.g004

# Suggested criteria 2017

---

Volume is better than AFC

- 10mL: The Androgen Excess and PCOS Society, 2009
- 12mL: Androgen Excess and Polycystic Ovary Syndrome Society, 2015

Persistence of enlarged ovaries and menstrual irregularities may foretell the future PCOS

Azziz et al. Fertil Steril 2009; 91: 456–488; Dewailly et al. Hum Reprod Update 2014; 20: 334–352; Venturoli et al. J Clin Endocrinol Metab 1992; 74: 836–841; Mortensen et al. J Clin Endocrinol Metab 2009; 94: 1579–1586.

# Suggested criteria 2017

---

- The use of AMH has not been validated in adolescents (Level C).
- Insulin resistance or obesity should not be considered as diagnostic criteria for PCOS in adolescents (Level A).

# 청소년 다낭성 난소증후군

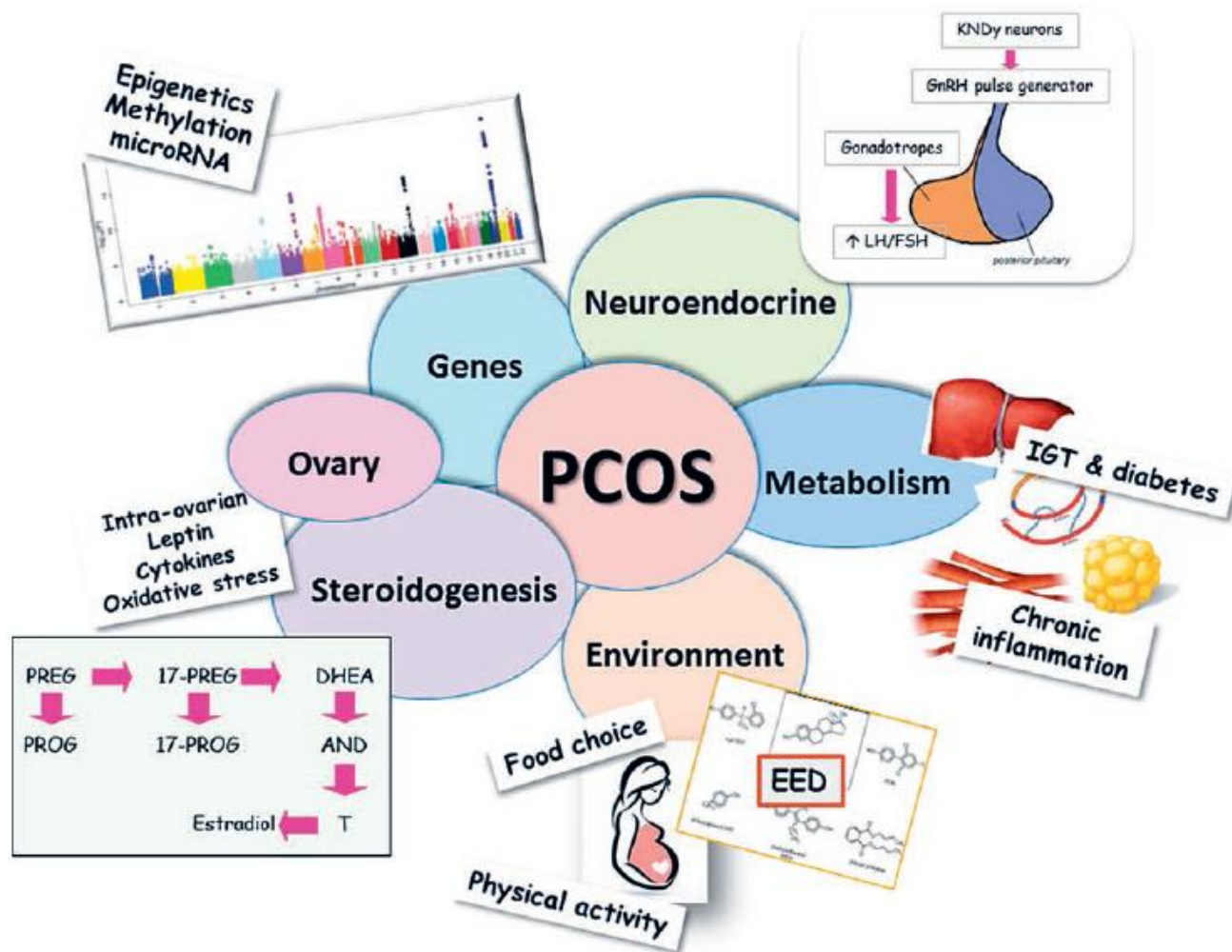
---

어떻게 관리? 예방?



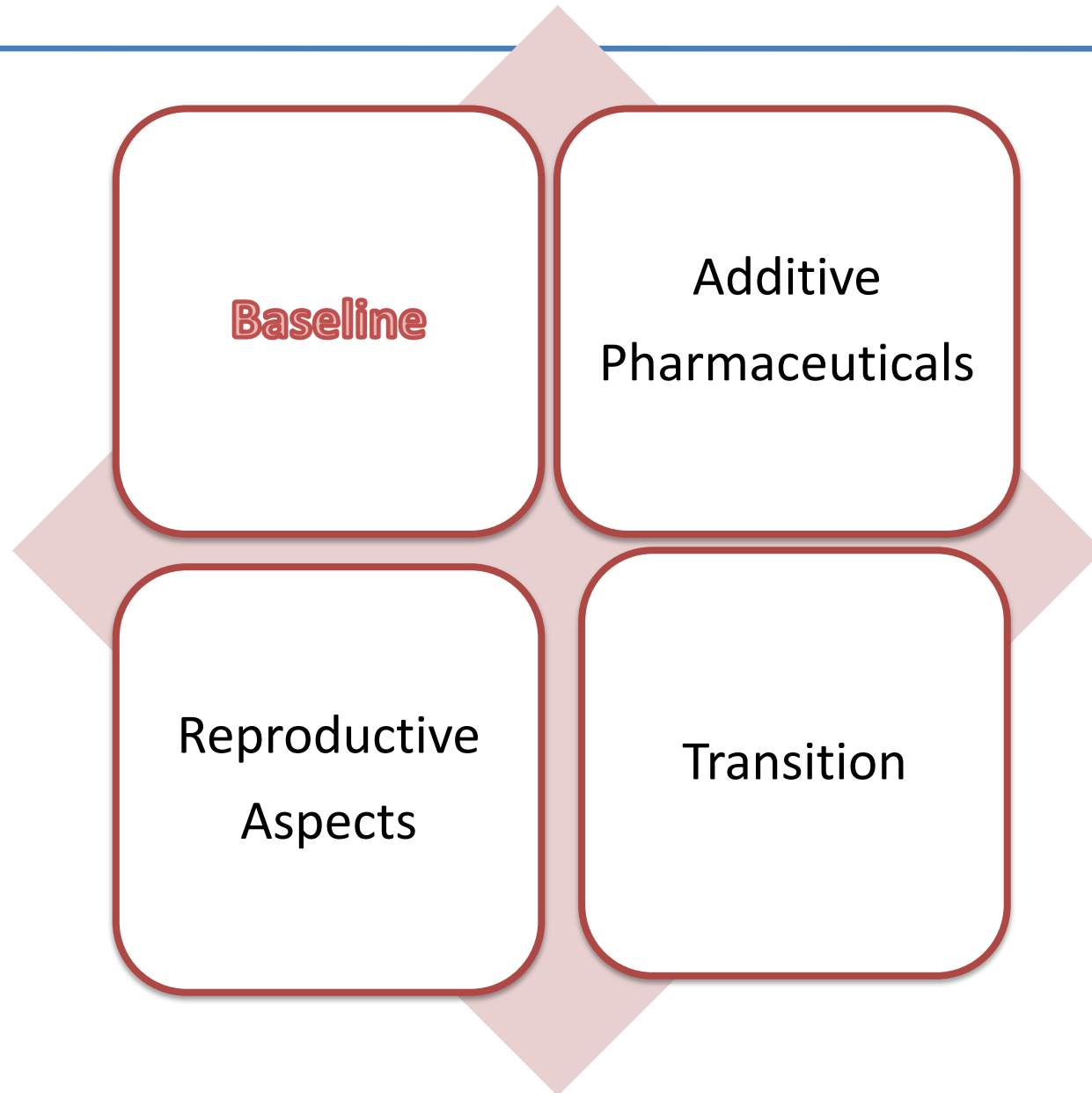


# Back to the pathophysiology of PCOS

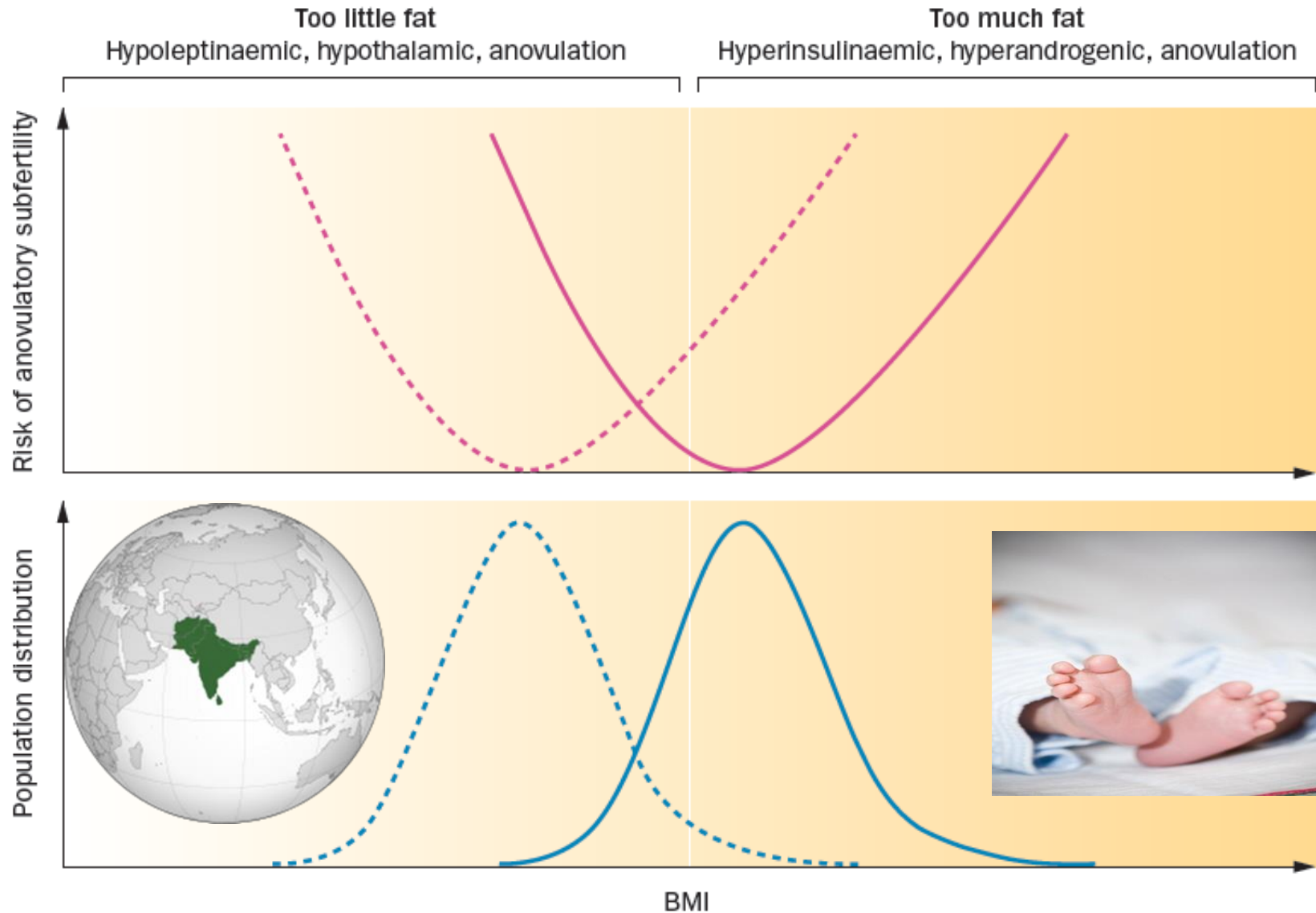


# Treatment

---



# BMI and the risk of anovulatory subfertility



# Baseline treatment - Lifestyle Intervention

---

- Combined weight loss and physical exercise are the first-line therapy in **overweight and obese** girls (**Level C**).
  - Combined with calorie-restricted diet
  - Decrease androgen levels, normalize menstrual cycles (**Level A**)
  - Improve cardiometabolic markers (**Level B**).
- Decreasing sedentary behavior is at least as important as increasing physical activity.
- Family treatment is essential: parents' readiness to change habits affects the outcome

# Baseline treatment - Lifestyle Intervention

---

- Extremely obese adolescents respond poorly (Level B).
- Normal-weight girls
  - Increasing physical activity is effective in reducing the development of metabolic syndrome (Level C).
  - Benefits of exclusive weight loss are not supported by RCTs (Level C).

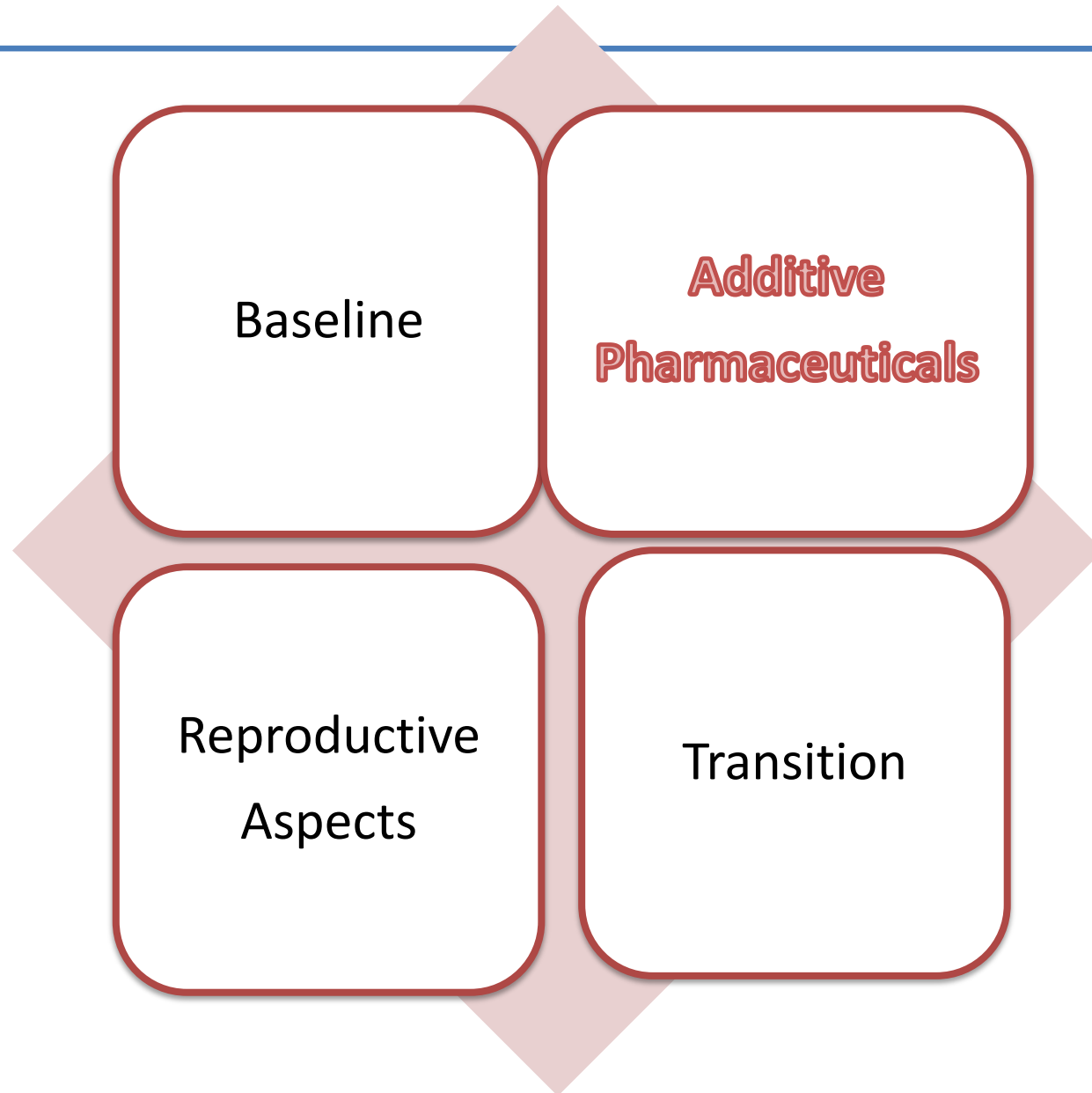
# Baseline treatment - Cosmetics

---

- Photoepilation is the first-line management of localized hirsutism in PCOS (Level B).
  - Diode and alexandrite lasers are preferred (Level C).
  - The alexandrite laser is superior to IPL (Level B)
- Eflornithine cream is recommended as an adjuvant or monotherapy (Level A).

Most effective in dark hair on light-skinned people

# Treatment



# Additive Pharmaceuticals: Oral Contraceptive Pills

---

## Mainstay of therapy

- There are no high-quality RCTs of specific OCP for adolescents with PCOS (**Level B**).
  - No specific formulation can be recommended over another

Majority of girls aged 14–17 years are not sexually active

Long-term intake

- Tends to be accompanied by a gain in fat mass and a loss of lean mass
  - Aggravation of body adiposity that is masked by an absence of substantial weight
  - Mediated by a rise in circulating levels of follistatin



# Additive Pharmaceuticals: Metformin

---

- Beneficial effects\* in **overweight or obese** adolescents with PCOS, but only short-term data are available (**Level A**).
- In **non-obese** adolescents with PCOS **and hyperinsulinemia**, metformin improves ovulation and testosterone levels (850mg) (**Level B**).\*\*

\* BMI and menstrual cycle

\*\* Most studies showed no improvement in hirsutism

# Additive Pharmaceuticals: Metformin

---

- OCP and metformin are the treatment options in adolescents (2013, 미국내분비학회)
- Commonly used as first-line monotherapy (2015, AE-PCOS)

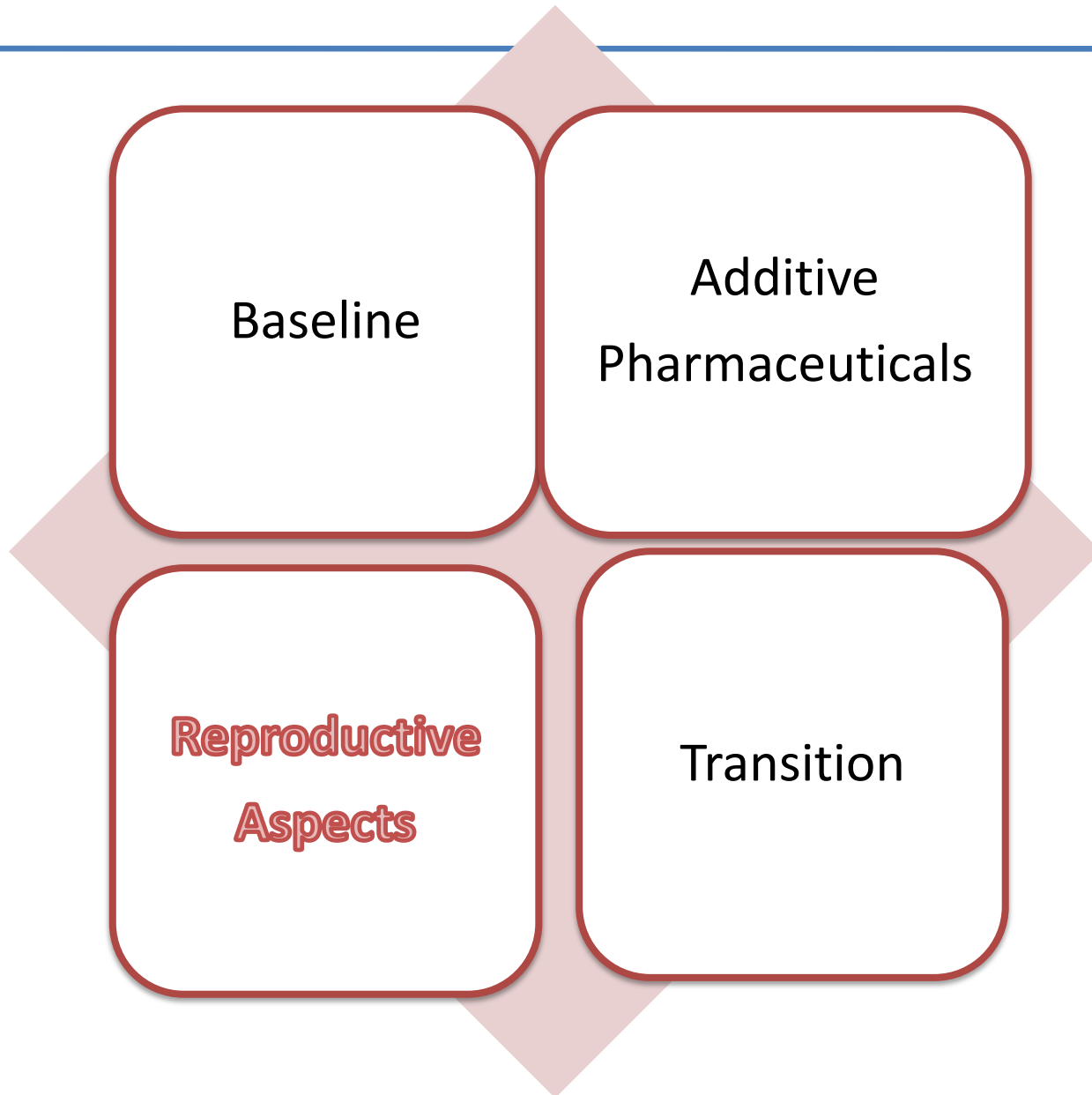
# Additive Pharmaceuticals: Anti-Androgens

---

- Spironolactone is the most commonly used (Level C).
  - Safe and widely used
  - Should only be used when contraceptive measures are guaranteed.

# Treatment

---



# Reproductive Aspects - Ovulation

---

- Normal ovulatory function may emerge with time in some adolescent PCOS (**Level A**).

Early postmenarchal adolescents (<3 years) with irregular menstruation and elevated androgen levels were followed for 3 years

- Group 1 (n=7): high LH
- Group 2 (n = 6) : normal LH
- Controls (n=7)

Gonadotropin concentrations were measured at 10-min intervals for 8 h on day 4 of the cycle at baseline and 40 months later.

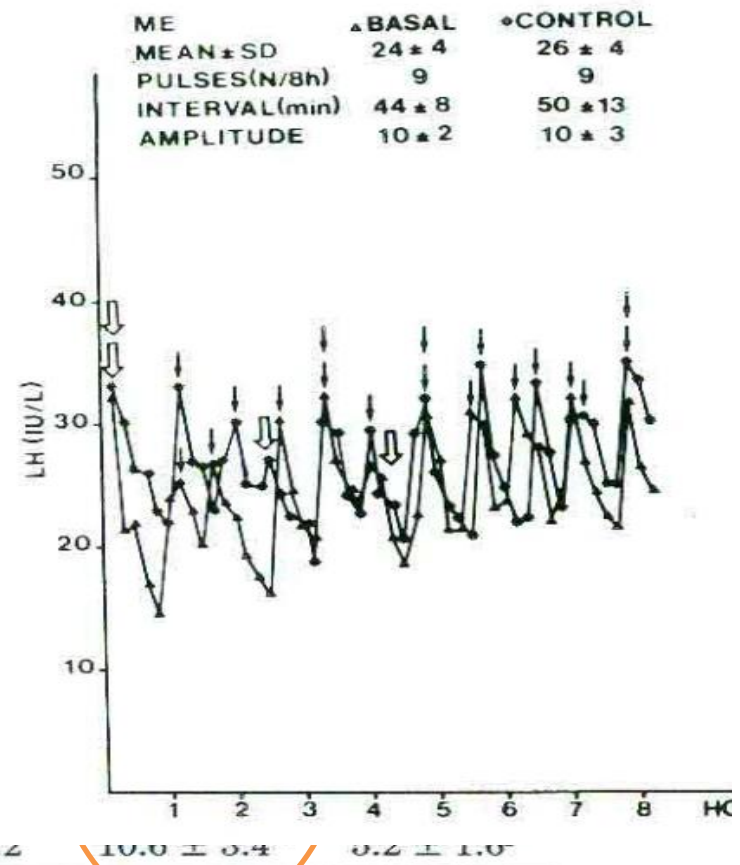
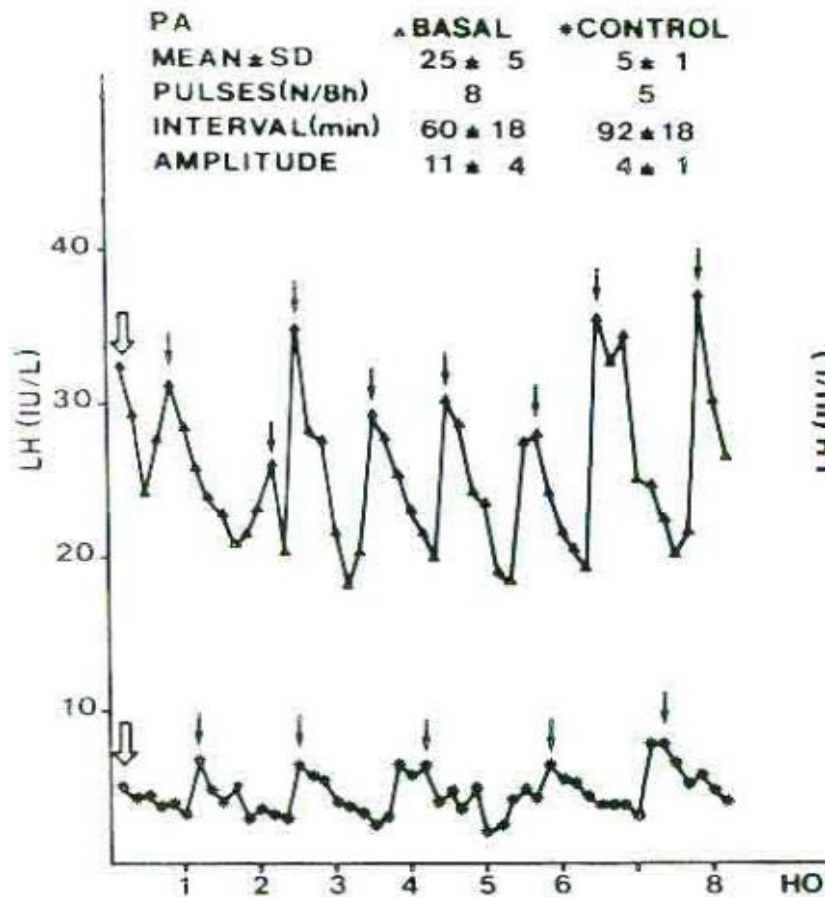
# Reproductive Aspects - Ovulation

TABLE 1. Basal plasma LH characteristics in the control and DETECT methods)

7/7 ovulatory

3/7 ovulatory

5/6 ovulatory

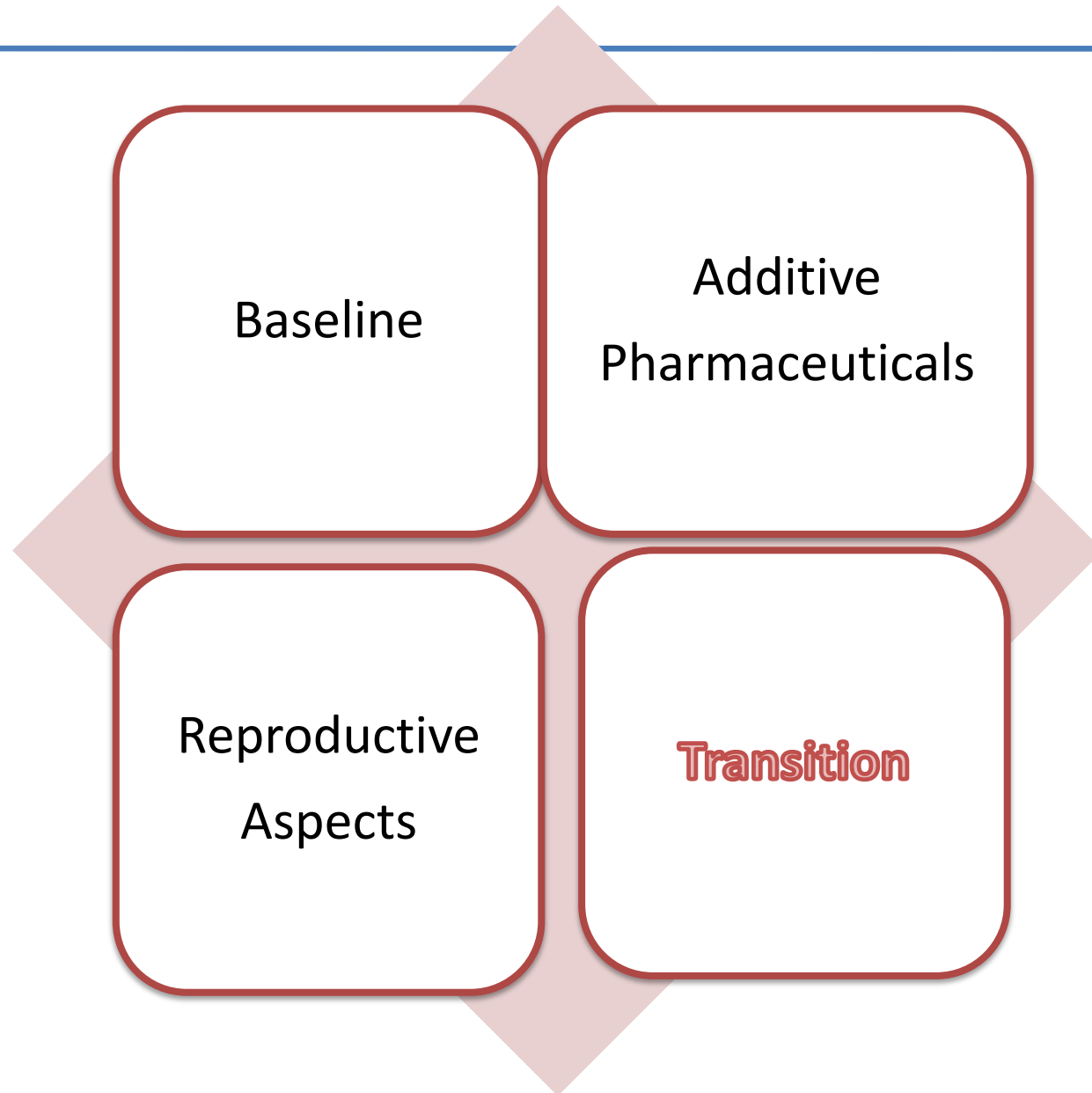


# Reproductive Aspects - Contraception

---

- No evidence to suggest a decreased pregnancy risk in adolescents with PCOS compared to adult PCOS.
- OCP as a first-line therapy consistent with published guidelines
- Progestin-only contraception, such as depot MPA
  - Weight gain and possibly bone loss, although recoverable

# Treatment





# PCOS management in adolescence

---

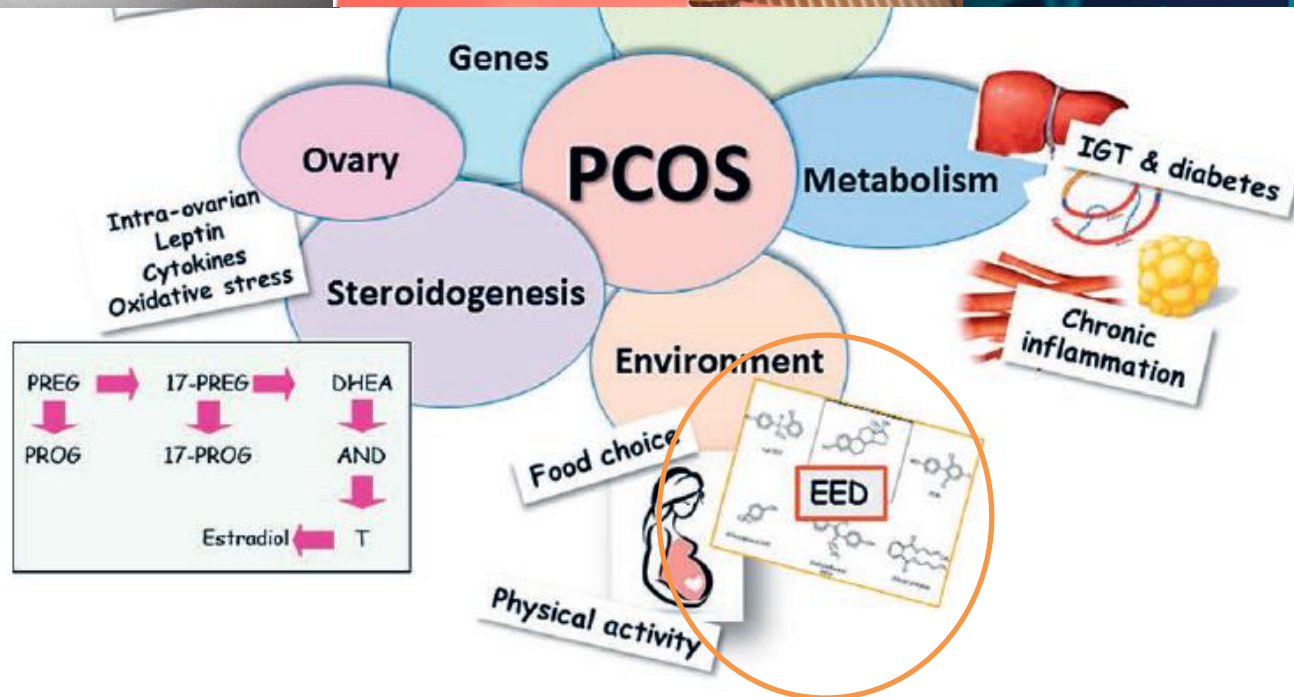
- Should focus on
  - Appropriate diagnosis
  - Reduction of symptoms
  - Improvement of post-treatment health in adulthood
    - Decreasing hepato-visceral adiposity, enhancing central fat loss (**Level B**).

# 예방?

---

- Early weight control?
- Early metformin therapy for 4 years (8-12 years) with low birthweight and precocious pubarche
  - At age 18 years, prevalence of PCOS was 5% in treated group, 52% in no treatment group.

10



# 감사합니다

