

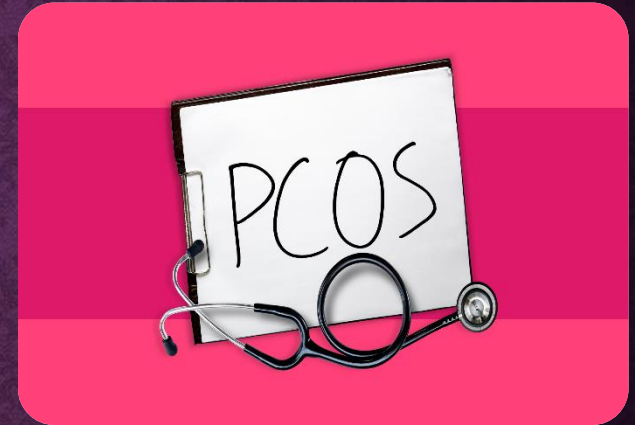
**IN THE NAME
OF
GOD**



POLYCYSTIC OVARY SYNDROME

METABOLIC DERANGEMENTS IN

ADOLESCENCE



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References:

1. Williams Textbook of Endocrinology 2020
2. BMC Guidelines 2020

POLYCYSTIC OVARY SYNDROME (PCOS)

**Most common endocrine disease
of reproductive age women**

- Prevalence : 10%
- Inheritance:
 - Polygenic fashion, multifactorial
- At risk for future PCOS
 - Premature adrenarche
 - Small for Gestational Age
 - Obese girls

**STILL
NOT COMPLETELY
UNDERSTOOD**

SIGNS, SYMPTOMS, MORBIDITY

- **A lifelong disorder**
- May present at any age
- Ovulatory dysfunction
 - amenorrhea, oligomenorrhea, ...
- Hirsutism, Seborrhea, Acne, Alopecia, Clitoromegaly
- Infertility, Increased pregnancy loss
- Obesity (?), insulin resistance, Type 2 diabetes, hyperlipidemia
- ↑ risk of endometrial cancer
- ↑ metabolic and cardiovascular risk factors



POLYCYSTIC OVARY SYNDROME (PCOS)

- **Hallmarks:**

(some may display none of these)

- Hyperandrogenism
 - Clinical (Hirsutism,...)
 - Biochemical
- Anovulation
 - Irregular menstruation: Amenorrhea, oligomenorrhea,...
- Insulin resistance → metabolic sequelae

❖ Obesity is present in **50%** of women with PCOS

OBESITY, INSULIN RESISTANCE AND ANOVULATION

- Insulin →
 - ↑ Ovarian androgen production
 - ↓ Sex hormone binding globulin → ↑ free testosterone
- Android obesity (↑ waist-to-hip ratio):
 - A **more specific** risk factor for PCOS
 - This type of fat is:
 - ↑ sensitivity to catecholamines
 - ↓ sensitivity to insulin
 - More active metabolically
 - Associated with
 - Cardiovascular risk factors (HTN, Dyslipidemia)
 - Poor-prognosis breast cancer



POLYCYSTIC OVARIES

- ≥ 12 follicles in 1 ovary and/or ovarian volume $> 10 \text{ mm}^3$
- Polycystic ovaries ? (a result of any state of anovulation)
- Polycystic ovarian morphology
 - May be a marker of PCOS
 - May be normal in young women



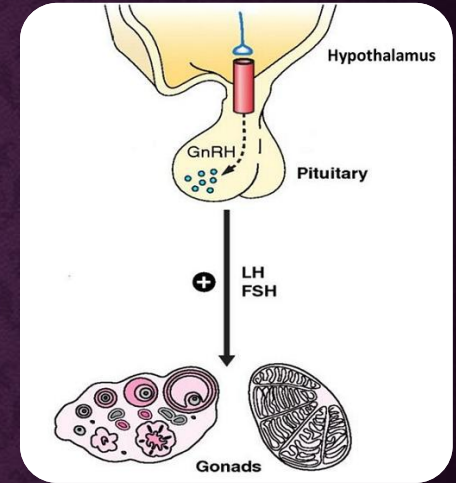
PELVIC ULTRASOUND



- **Not** indicated for PCOS diagnosis in **adolescents**
- Can be used to investigate other possible uterine or ovarian abnormalities in adolescent girls
- Use of pelvic ultrasound: ↑ risk of PCOS **over-diagnosis** during adolescence

GUIDELINE RECOMMENDATION

- Physiological maturation of the hypothalamic–pituitary–ovarian axis occurs over the years
- Ovulation/menstrual cycles in adolescents may **not** match those of women in reproductive age



- The term 'adolescents' can be avoided and be replaced by the terms '**gynecological age**' or '**time post menarche**'
- A gynecological age of < 8 years as the cut-off was chosen (maximum ovarian volume is reached at age 20)

DEFINITION OF IRREGULAR MENSTRUAL CYCLES

Time post menarche	Definition of irregular menstrual cycles
<1 year	Irregular menstrual cycles are normal pubertal transition
>1 to <3 years	<21 or >45 days
>3 years	<21 or >35 days or <8 cycles / year
More than 1 year	>90 days for any one cycle
	Primary amenorrhea by age 15 years or >3 years post thelarche

CRITERIA FOR DEFINITION

- Two of the following: (Rotterdam, 2003)
(Characteristic **triad** for diagnosis)
 - Androgen excess
 - Ovulatory dysfunction
 - Polycystic ovaries
- All of the following: (Androgen Excess Society, 2006)
 - Hyperandrogenism
 - Ovarian Dysfunction
 - Exclusion of other androgen excess or related disorders

DIFFERENTIAL DIAGNOSIS

Diagnosis of PCOS is made by **excluding**:

1. Nonclassic congenital adrenal hyperplasia
2. Androgen-secreting tumors
3. Hyperprolactinemia
4. Hypothyroidism
5. Cushing syndrome
6. Glucocorticoid resistance

LABORATORY FINDINGS

- ↑ LH/FSH, ↑ Estradiol
- ↑ DHEAS, ↑ Androstenedione, ↑ Testosterone
- Fasting Blood Sugar, Glucose Tolerance Test (↑/ NL)
- Lipid profile (↑/ NL)
- T4, TSH, Prolactin (NL)
- 17 OH Progesterone (NL)
- Cortisol level (LDDST) 8am, and 4 pm (NL)
- ↑ Anti Mullerian Hormone (?)

❖ LH/FSH ratio

- Normal in obesity
- Supports the diagnosis if increased
- Not a diagnostic criteria



TREATMENT

- Lifestyle Modification : The **Primary Approach**
 - Success is achievable
 - Failure is substantial
 - Should be permanent
- ↓ Insulin resistance, ↓ androgen excess and ↓ diastolic blood pressure by:
 - ✓ ↓ Daily food intake by 500 kcal
 - ✓ Exercise 30 mins/day for 6 months
 - ✓ 5% Weight reduction
- Significant weight loss has resulted in **pregnancy**

TREATMENT

UNOPPOSED ESTROGEN EFFECT

- Absence of progesterone causes:
 - Irregular uterine bleeding
 - Amenorrhea
 - Infertility
 - ↑risk of endometrial cancer
- Duration : critical risk factor
- If untreated: (after pregnancy ruled out)
 - Periodic endometrial bx

TREATMENT

ORAL CONTRACEPTIVES

- Simplest, most effective way to administer progestin
- **First line** of therapy for:
 - Adults not desiring fertility
 - Adolescents
- Avoids hyperplastic endometrial state
- Manages abnormal uterine bleeding
- Suppress LH and stimulate SHBG →
 - ↓ Circulating androgens, ↓ DHEAS and ↓ hirsutism

TREATMENT

ORAL CONTRACEPTIVES

- Less-androgenic progestational components (drospirenone, desogestrel) → better relief from androgenic symptoms
- Recommended for women with PCOS + Hirsutism
 - **LD OCP + 100 mg/day Spironolactone**
- Severe androgen excess:
 - GnRH agonists may be needed

TREATMENT

PROGESTIN ALONE

- Anovulatory with **no hirsutism** →
 - Progestin alone
- Does **not** decrease androgen excess
- Does **not** provide contraception
- Norethindrone acetate (5 mg/day) or medroxyprogesterone acetate (10 mg/day) for a 12 day course every other month

TREATMENT

INSULIN RESISTANCE

- Biguanides (Metformin)
 - ↓ Hepatic glucose output → ↓ insulin → ↓ androgen production
 - 500 mg 3 times/day
 - Effective in prevention for high risk groups
 - Benefits present only during therapy
 - Improves: Insulin and testosterone level, BP, LDL
 - Metformin + OCP → weight loss
- Thiazolidinediones **not** recommended
 - Hepatotoxic, teratogen, heart failure, stroke

TREATMENT

ANTIANDROGENS

- Alone or in combination with other medication
- Cyproterone (highly active androgen antagonist and progestin) : alone or + ethinyl estradiol
- Spironolactone (androgen antagonist and impairs androgen synthesis): 100-200 mg/day
- Lack of evidence → rarely used:
 - Finasteride (5-alpha-reductase inhibitor)
 - Flutamide (androgen receptor antagonist)
 - Potential hepatotoxicity

TREATMENT

OVULATION INDUCTION

- Clomiphene citrate
 - 50 mg/day started on day 3 of the cycle
 - Continued for 5 days
- Aromatase inhibitors
 - Letrozole 2.5 mg/day
 - Anastrozole 1 mg/day
- Clomiphene + metformin
- Low Dose Gonadotropin Therapy

PREVENTIVE MEASURES

- Age at onset of NIDDM is significantly earlier
- More likely to experience Gestational DM
- Periodic Glucose Tolerance Test
- ? Long term metformin
- One half of first-degree relatives/ sisters are affected:
 - Higher risk for CVD

NIDDM: Non Insulin Dependent Diabetes Mellitus
CVD: Cardio Vascular Diseases

**THANK YOU FOR YOUR
ATTENTION**

