



From PCOS to PMOS: Rethinking a Multisystem Endocrine-Metabolic Disorder

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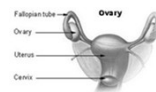
Objectives

- Explain the rationale for transitioning from PCOS to PMOS.
- Apply current diagnostic criteria and identify important differential diagnoses.
- Recognize the reproductive, metabolic, and psychological impacts across the lifespan.
- Summarize recommended metabolic screening and management strategies.

Epidemiology and impact

- PMOS is common affecting 8-13% of reproductive age women (up to 1 in 8, variance depending on definition used and ethnicity)
- This is the most common endocrinology condition in this population
- PMOS is lifelong and chronic
- PCOS can be accompanied by metabolic, reproductive and psychological complications that significantly affects patient quality of life and morbidity.
- The economic impact of PCOS is also significant but health care funding for this condition is not proportionally allocated.

History: Stein Leventhal Syndrome (1935)



- Described 7 cases of females presenting with **amenorrhea and fertility issues** for which they completed ovarian wedge resections after failed medical therapy.
- There was resumption of monthly cycles in all cases and 1 of the 6 had pregnancy after surgery.
- Proposed that the ovarian changes occurred due to hormonal stimulation.

Images: Ovaries (Ovary.nih - File:Ovary.nih.jpg - Wikimedia Commons)

NIH 1990	Rotterdam 2003	AE-PCOS Society 2006
Anovulation Hyperandrogenism * Both criteria needed	Ovulatory dysfunction/irregular menses Hyperandrogenism PCO morphology (or elevated AMH 2023) * 2/3 criteria needed	Irregular menses and/or polycystic ovarian morphology Hyperandrogenism * Both criteria needed

*Exclude other causes.

2023 International PCOS Network

- 39 national and international collaborating societies (71 countries)
- More than 100 global PCOS clinicians, researchers and lived-experiences.
- Guidelines are proposed to promote a consistent message to healthcare providers and to ensure a model for care.
- Reinforced 2 out of 3 Rotterdam Criteria to make the diagnosis.
- Goals are to improve quality of care and quality of life.
- Proposed a mix of evidence-based data, clinical expertise and patient preference approach.
- Medications are still used "off label" based on symptom management and aim of treatment.

Polycystic Ovary Syndrome to Polyendocrine Metabolic Ovarian Syndrome (2026)

- What: Moving forward with a name transition to better represent this condition. There will be an overlap time of dual terminology.
- When: 2026 global consensus reached after 11-year process
- Who: Multistep global consensus with 56 organization and > 14,000 respondents, included patient organizations with > 80% endorsing a new name
- Why: Improve delays in diagnosis and recognition and avoid the gynecologic only focus.

Knowledge gaps

- 55% of OB-GYN residents identified all 3 Rotterdam criteria (1)
- 70% used Rotterdam criteria, 23% didn't know what criteria to use (Northern European survey of OB-GYN, REI and ME) (2)
- OCPs used more in GYN vs TLC/metformin in ME (2)
- ASRM/ACOG survey (REI&OB/GYN): in total, almost 30% did not know what criteria they used to diagnose PCOS or used criteria not listed in any of the guidelines (3)
 - -68% of REI and 41% of OB-GYN applied Rotterdam criteria
 - -Good recognition of cardiometabolic complications but less so for pregnancy related and psychosocial complications
- Delay in diagnosis is frustrating for patients.

1. Chemerinski A, Cooney L, Shah D et al. Gynecol Endocrinol. 2020 Apr 6:1-6
 2. Pittonen TT, Ruokojärvi et al. PLoS One. 2019 Dec 26;14(12)
 3. Dokras et al. Fertil Steril. 2017 Jun;107(6):1380-1386.

Moving away from “polycystic”

- Cysts seen in these patients are not truly cysts or pathologic.
- There is a pattern of immature small follicles that *may* be seen in some but not all women with this syndrome.
- Moving instead to the emphasis on:
 - Complex pathophysiology
 - Complex endocrine dysregulation
 - Impacts on ovulation and menstrual cycle

Polyendocrine Metabolic Ovarian Syndrome (PMOS)

- Polyendocrine: emphasis on multiple hormonal interactions
- Metabolic: insulin resistance highlighted with the cardiometabolic risks emphasized
- Ovarian: ovarian dysfunction manifested as irregular cycles and anovulation are still recognized
- **No change in diagnostic criteria**
- **No new treatments approved**

PMOS: Diagnostic challenges

- The psychosocial stress to affected patients may limit their seeking care and evaluation.
- Heterogenous presentation impairs diagnosis.
- Misnamed condition – not “ovarian cysts”
- Not just a gynecological issue
- Complex, under recognized or misdiagnosed, under researched and underfunded condition
- Includes psychological/quality of life, metabolic and reproductive impact.

Differential diagnoses for PMOS

- Physiologic anovulation of adolescence
- Pregnancy
- Hypothalamic amenorrhea
- Thyroid disorder
- Hyperprolactinemia, prolactinoma
- Congenital adrenal hyperplasia
- Androgen secreting tumor
- Obesity related anovulatory bleeding

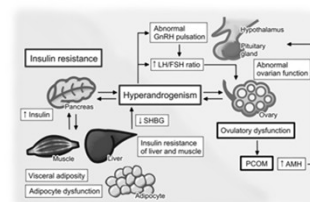
Differential			Distinguishing features	
Condition	Hyperandrogenic	Irregular menses	Clinical	Hormonal
Nonclassical 21-hydroxylase CAH	yes	likely	Ethnicity?	17-OHP elevated
Hypercortisolemia	yes	possible	High glucose or BP, striae, bruising, etc	LNSC, 24 hr urine cortisol, 1mg DST
Hyperprolactinemia	no	likely	Headaches, galactorrhea	Prolactin elevated
Hypothyroidism	no	possible	Family history, goiter?	Elevated TSH
Acromegaly	possible	likely	Physical exam	Elevated IGF-1
Primary ovarian insufficiency	no	yes	Autoimmune history	FSH/E2 in postmenopausal ranges, low AMH
Obesity/weight change	possible	possible	Based on history/eval	Exclusion by other eval/labs
Androgen producing tumor	yes	yes	Rapid, more virilization, more alopecia	Androgens very elevated
Medications	possible	possible	History	none

Condition	Test
Pregnancy	Serum or urine hCG
Thyroid disease	TSH
Prolactin excess	Serum prolactin
Congenital adrenal hyperplasia	Serum 17-OHP
Hypothalamic amenorrhea	LH, FSH, estradiol
Primary ovarian insufficiency	FSH, estradiol
Androgen secreting tumor	Testosterone, DHEA-s (ultrasound, MRI adrenals)
Cushing's syndrome	24 hr urine cortisol, late night salivary cortisol, DST
Acromegaly	IGF-1

Multifactorial pathophysiology

- Polygenic inheritance
 - Increased risk for child born to women with PMOS to develop the same condition
 - Non-Mendelian inheritance similar (like type 2 diabetes or obesity)
 - Susceptibility genes + environmental factors
- Preantral androgen exposure
- GnRH aberrancy
- Ovarian dysfunction
- Hyperandrogenism
- Insulin resistance

Pathophysiology of polycystic ovary syndrome revisited: Current understanding and perspectives regarding future research



“Vicious cycle”
 Abnormal GnRH pulsation altering LH/FSH ratio
 → Ovulatory dysfunction → androgens
 → PCO morphology (AMH elevation)

Hyperandrogenism + Insulin resistance

Synergy and individual variances → heterogenous condition

Harada M. Pathophysiology of polycystic ovary syndrome revisited: Current understanding and perspectives regarding future research. Reprod Med Biol. 2022 Oct 8;21(1):e12487. doi: 10.1002/rmb2.12487. PMID: 36310656; PMCID: PMC9601867.

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Diagnosis of PMOS (2023 guidelines)

- Irregular menses: < 21 days or > 35 days or < 8/yr
- Hyperandrogenism
 - Hirsutism emphasized over balding/acne in isolation
 - Biochemical measurement – Total or free testosterone
 - May be exacerbated by obesity.
- PCO Morphology: For adults, if above 2 cannot be established, you can use PCO morphology (ultrasound with antral follicular count/ovarian volume or *elevated AMH*)

Teele HJ, et al. Eur J Endocrinol. 2023 Aug 2;189(2):G43-G64. doi: 10.1093/ajendo/ivad096. PMID: 37580861.

Hirsutism defined

- Excessive growth of androgen-dependent terminal hair (thicker, pigmented hair, 5mm) typically appearing in a male growth pattern in females
- *Hypertrichosis: any excess hair growth (vellus or terminal) that can occur all over the body (hereditary or medication side effect).*
- Ferriman-Gallwey score- score may underrepresent severity as patient have already treated themselves prior to initial evaluation and there is ethnic variation. (Patient self assessment tool: [Ferriman-Gallwey Score: Chart, Cut-Offs & Free Calculator](#))

PMOS: Hirsutism management

- **Combined oral contraceptive pills (COCs) are first-line pharmacological therapy.** No specific preparation is recommended. Preference for progestins with fewer androgenic side effect.
- **Anti-androgens are reserved for suboptimal response after a minimum of 6 months of COC and/or cosmetic therapy.** (*Counsel on contraception due to teratogenicity.*)
 - **Spironolactone** has the lowest risk of adverse effects. Doses typically are lower for acne only and higher to impact hirsutism.
 - **Finasteride** carries increased liver toxicity risk, rare may see used for hirsutism.

PMOS: Metabolic impacts and comorbidities

- Insulin resistance, impaired glucose tolerance → type 2 diabetes
 - Insulin resistance also reduces SHBG making more testosterone available
- Dyslipidemia that is atherogenic, thus PMOS is a CVD risk enhancing factor
 - Early aggressive therapy with lifestyle and pharmacologic intervention
- OSA
- MASLD – not specified in guidelines but there is clear overlap

PMOS: Metabolic screening

- Glycemic status: Evaluate every 1-3 years based on risk.
 - 75 gram OGTT is most accurate and preferred (especially if preconception discussion); second line is fasting glucose/A1c
- Lipids: Assess total cholesterol, LDL, HDL and triglycerides at diagnosis (all BMI) and reassess based on CV risk
- Blood pressure: measure annually
- CV risk assessment: ensure PMOS is added as an independent risk factor when estimating CVD and diabetes risk
- OSA screening recommended if any symptoms (snoring and fatigue/daytime sleepiness/awakening unrefreshed)

BMI independent

PMOS: Treatment of metabolic features

- Lifestyle:
 - No single diet or exercise type is superior.
 - Goal is for a sustainable, individualized approach to support prevention of weight gain and benefit even without weight loss.
- Pharmacologic therapy: Metformin
- Supplements: Inositol considered 2nd line and less effective
- Anti-obesity medications and/or weight loss surgery: Follow the same evidence-based weight-management approach recommended for the general population.

Psychological Health

- Anxiety
- Depression
- Disordered eating
- Body image distress
- Psychosexual dysfunction
- Reduced quality of life

Highlights the importance of a multispecialty collaborative team

Key points:

- Lifespan impact: PMOS affects women throughout life, with clinical manifestations varying by age and shifting from reproductive symptoms toward greater metabolic complications.
- Multisystem approach: The name change from PCOS to PMOS emphasizes a broader endocrine-metabolic disorder.
- Proactive screening: The guidelines and name change highlight the importance of screening for metabolic, cardiovascular, gynecologic, and psychological complications.
- Research and funding: Current treatments and research are lacking. The name change may help advance research and increase funding opportunities.



Polyendocrine Metabolic Ovary Syndrome – Gynecologic Impacts

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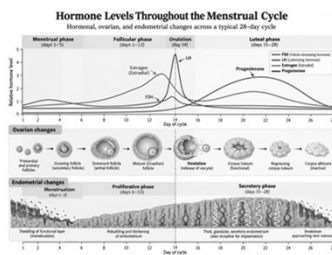
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Learning Objectives

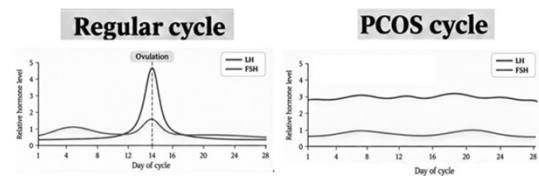
- Describe the pathophysiology of PMOS from a gynecologic standpoint
- Review diagnostic criteria
- Formulate individualized management plans and assess for comorbidities

PMOS and the Menstrual Cycle

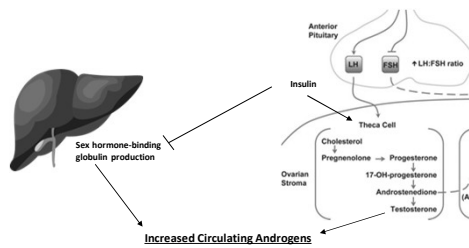
- Anterior Pituitary releases FSH
- FSH promotes estradiol production within the ovary
- Estradiol suppresses FSH and LH production
- Dominant follicle produces enough estradiol to switch the feedback loop from negative to positive and promote an LH surge
- Peak LH triggers ovulation
- Ovulation results in corpus luteal formation and progesterone production
- In the absence of pregnancy, the corpus luteal involutes and progesterone concentration decreases



PMOS and the Menstrual Cycle cont.



Hyperandrogenism



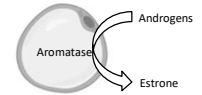
Obesity

Comorbidity that may amplify effects of PMOS

Not a diagnostic criteria for PCOS (20% of PCOS patients are not obese)

Adipose tissue contains aromatase

- Androgens from the ovary are aromatized to weak estrogens (estrone)
- Estrone provides further negative feedback on anterior pituitary
- Propagates further decrease in FSH production



Gynecologic Impacts of PMOS

Irregular periods

Infertility

Endometrial proliferation → endometrial hyperplasia/malignancy

PMOS Diagnosis

NIH 1990	Rotterdam 2003	AE-PCOS Society 2006
<ul style="list-style-type: none"> • Chronic anovulation • Clinical and/or biochemical signs of hyperandrogenism (Both criteria needed) 	<ul style="list-style-type: none"> • Oligo- and/or anovulation • Clinical and/or biochemical signs of hyperandrogenism • Polycystic ovaries (Two of three criteria needed) 	<ul style="list-style-type: none"> • Clinical and/or biochemical signs of hyperandrogenism • Ovarian dysfunction (Oligo-anovulation and/or polycystic ovarian morphology) (Both criteria needed)

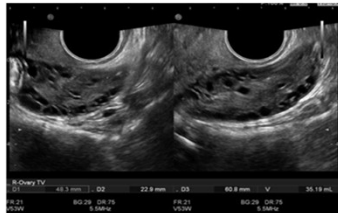
PMOS Diagnosis - ultrasound

PMOS morphology

*Follicle number per ovary ≥ 20 in at least one ovary

Ovarian volume ≥ 10 mL in at least one ovary

Follicle number per cross-section ≥ 10 in at least one ovary



Pre-antral follicles are 2-9mm in diameter. If a dominant follicle > 10mm in diameter is present, U/S should be repeated at a time of ovarian quiescence

PMOS Diagnosis cont.

Pelvic Ultrasound

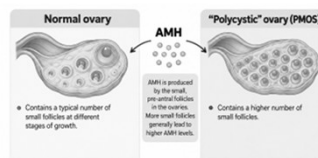
Labs can vary by phenotype

- FSH
- TSH
- Prolactin
- Testosterone
- 17-hydroxyprogesterone
- DHEAS
- Cortisol
- AMH
- + metabolic screening

Anti-Müllerian Hormone (AMH)

Elevated AMH can be used as a diagnostic marker of PMOS as an adjuvant to existing diagnostic criteria, but is not used alone

Factors that affect AMH:
 Age (peaks 20-25 years)
 Hormonal contraception use, ovarian surgery
 Smoking
 BMI (higher BMI may lower AMH)
 Ethnicity
 *can be measured at any time of the cycle



*No clear AMH cut off value, assay variability

PMOS Treatment

Trying to conceive vs not trying to conceive

- Menstrual management/endometrial protection
- Ovulation support/induction

Menstrual Management/Endometrial Protection

Combined oral contraceptive pills are first-line

- Suppression of pituitary LH secretion
- Suppression of ovarian androgen secretion
- Increased circulating SHBG

There is no specific recommended formulation

- Consider anti- or less-androgenic progestin

Consider Slynd (drospirenone) for patients who are not estrogen candidates

Levonorgestrel	High
Norgestrel	
Norethindrone	Medium
Norethindrone acetate	
Norgestimate	Low
Desogestrel	
Drospirenone	Anti

Menstrual Management/Endometrial Protection Cont.

Progestins: effective for endometrial protection, no data on hirsutism management

- Cyclic medroxyprogesterone* to induce withdrawal bleed at least once every 3 months
- Depo Provera
- Levonorgestrel IUD

*Not effective for contraception

Metformin and Inositol can induce spontaneous ovulation

- Metformin indicated for insulin insensitivity or BMI $\geq$ 25 without insulin insensitivity in PMOS (off-label)
- Improved insulin sensitivity $\rightarrow$ decreased circulating androgens, improved ovulation rates

Endometrial Evaluation

Endometrial evaluation should be considered for patient's who are at high risk of endometrial hyperplasia/malignancy

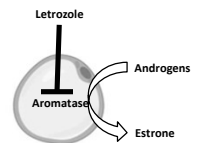
Risk factors:

- Prolonged anovulation
- BMI $>$ 30
- Family history
- Non-response to medical treatment
- Age $>$ 45

Ovulation Induction

Letrozole

- Aromatase inhibitor
- Blocks conversion of androgens to estrogen
- Allows increased anterior pituitary secretion of FSH to stimulate ovarian follicle maturity
- If unable to achieve ovulation with 2 dose increases, will need Infertility specialist for likely IVF



Key Concepts

Underlying insulin resistance and gonadotropin dysregulation

Insufficient FSH to promote follicle growth beyond preovulatory stage

Excessive production of androgens from the ovary and aromatized from adipose tissue

Treatment is individualized to the patient's goals and symptoms

Menstrual management includes endometrial protection and possible evaluation

Patients may need ovulation support to conceive