Polycystic Ovarian Syndrome (PCOS)
for the Family Physician

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Important references for PCOS


35 year old obese woman

- 285 lbs, 5’3”, 148/90.
- Excessive hair on forearms, chin and legs; acne always been a problem.
- Always oligomenorrheic (4 periods a year) until 6 months ago when stopped menstruating.
- “Infertile” since attempting pregnancy age 21.
- Never been evaluated for PCOS.

PCOS: Add up the Risk Factors

- Up to 5-10% of premenopausal women may be affected.
  - Menstrual dysfunction
  - Anovulation
  - Androgen excess
  - Obesity
  - Infertility

PCOS: There is something for everyone

- The clinical scenario varies depending on the specialist consulted.
  - Dermatologist: severe acne, hirsutism.
  - Gynecologist: irregular menses, infertility.
  - Internist: obesity, diabetes, hypertension.
  - Psychiatrist: depression or body image.
  - Family physician: all of the above!

Fast facts on diagnosis of PCOS

- Hirsutism is common; virilization is rare.
- 7% of reproductive women have hyperandrogenic anovulation.
- Differential diagnosis includes a spectrum of causes of androgen excess, abnormal uterine bleeding, polycystic ovaries and other endocrine diseases.
- What is not PCOS?
  - androgen-secreting tumor, Cushing syndrome
Differential diagnosis of PCOS (need to exclude)

- Androgen-secreting tumors.
- Exogenous androgens
- Congenital adrenal hyperplasia.
- Type 2 diabetes.
- Hyperprolactinemia.
- Thyroid disease.
- Cushing syndrome.

PCOS is not a distinct disorder

- Diagnostic criteria differ. Endocrine Soc Guidelines use Rotterdam criteria.
- Common pathway of an undetermined number of dysfunctional endocrine processes.
  - One sign or symptom should prompt a search for others.

Diagnostic criteria based on Rotterdam Endocrine Society Guidelines

- Allows physicians to make the diagnosis of PCOS if clear symptoms are present based on hyperandrogenism and anovulation.
- Avoids resorting to universal hormone tests or ultrasounds if patients already meet 2/3 criteria clinically.

How the PCOS evidence-based guideline works

- Woman must have at least 2/3 of the following:
  - Excess androgen
  - Ovulatory dysfunction (oligomenorrhea or amenorrhea).
  - Polycystic ovaries.
  - Rule out other androgen-excess disorders.
  - Terminal hair growth (sideburns, full neck, back), androgenic alopecia, acanthosis nigricans, clitoromegaly

Table 1. Recommended Diagnostic Schemes for Polycystic Ovary Syndrome by Varying Expert Groups

Table 1. Summary of Proposed Diagnostic Criteria for PCOS in Adults

Clinical or biochemical hyperandrogenism for PCOS

- Included as one criterion in all classification systems.
- If androgen signs are present without virilization, serum androgens are unnecessary for the diagnosis.
- If a patient has signs of hyperandrogenism and ovulatory dysfunction, ovarian ultrasound is unnecessary.


Making the diagnosis
3 basic approaches

- Clinical findings: symptoms, physical exam.
- Anatomy: transvaginal ultrasound
- Biochemical parameters: lab testing.

- Rule out other diagnoses and then diagnose PCOS.

Virilization

- Male pattern androgenic alopecia.
- Change in voice.
- Clitoromegaly.
- Terminal hair on sideburn area, neck, back, inner thighs.
- Usually rapid onset.
- Total testosterone, DHEAS markedly elevated.

PCOS: Anatomic findings

- **Ovarian morphology**
  - TVUS: Cysts found on peripheral subcortical ring “string of pearls”.
  - Must have >12 follicles, 2-9 mm or ovarian volume >10mm.
  - One or both ovaries can be enlarged.
- **Caution:** Polycystic ovaries can be seen in women with hyperprolactinemia (50%), hyperthyroidism (36%), hypothalamic hypogonadism (24%).

Be careful about biochemical levels!
No one lab defines PCOS

- Results may be only “upper limits of normal”, showing “tendency” for abnormality.
- Any level twice upper or lower limit of normal is very important and is probably not PCOS.

- **Total testosterone** (rather than free T).
  - > 60 ng/dL is 2 standard deviations above the mean.
  - 2-3x elevation: r/o ovarian tumor with CT.
- **DHEAS** to evaluate adrenal androgen component.
- **17-hydroxyprogesterone** to exclude 21-hydroxylase deficiency (obtain in follicular phase between 7-9AM)

PCOS: Menstrual disorders

- **Adolescents.**
  - Menarche occurs at normal age unless obesity present (earlier).
  - Oligomenorrhea in early adolescence is very common in PCOS.
  - May have amenorrhea or spotting only.
  - Cycles tend to normalize over time after adolescence if PCOS absent.
  - OCPs may mask symptoms of PCOS.
Evidence for adolescents
- Diagnosis made on presence of clinical and/or biochemical parameters of androgen excess in presence of oligomenorrhea.
- Anovulation symptoms and PCOS morphology are insufficient to make a diagnosis.
- Mid-luteal progesterone may aid in diagnosis if bleeding suggests regular ovulation.

PCOS: Menstrual disorders
- Suspect PCOS in any women older than age 35 years with cycle length of more than 35 days.

Benefits of OCP’s
- Regular menses occur more frequently with OCP’s than with metformin.
- More reduction in hirsutism than metformin.
- Reduces risk of endometrial cancer.
- Primary prevention of ovarian cancer.
  - Significant duration-response relationship between OCP use and ovarian cancer incidence.
  - 50% reduction if used for ≥10 years.
  

PCOS: Hair and skin problems
- Skin manifestations of PCOS are more common than menstrual irregularity or obesity.
- Why?
  - Absolute increase in androgen levels.
  - Exaggerated response of the skin to even relatively normal levels of androgens.
  - Hair follicles are sensitized to androgens.

Hirsutism
Increase in amount or coarseness of hair
- Excessive may not be evident due to cosmesis.
- Male-pattern hair growth (not moustache or hairs on breasts!).
  - Sideburns.
  - Lower neck and back.
  - Inner thighs.
  - Alopecia (most distressing of hyperandrogenic skin disorders): vertex hair loss most common.

Treating hirsutism
- Counsel that response to therapy will be slow and subtle (may not show for 6 months).
- There is no accepted method for assessing response to therapy (women camouflage hair growth). ASK: Are you shaving less?
- Goal is reduction of androgen levels.
Spironolactone is an antiandrogen

- Spironolactone: inhibit androgens from binding to the androgen receptor (moderate antiandrogenic effects when used in high doses).
  - Start at 50mg and increase every 4 weeks by 25 mg to 150-200mg daily.
- Spironolactone and OCPs are synergistic.
  - Combo with OCPs to increase SHBG.

Hirsutism: medical treatments

- Finasteride (5-a reductase inhibitor): 1-5mg/d.
  - Teratogenic!
  - Less effective than spironolactone.
- Eflornithine (Vaniqua) 13.9% topical bid.
  - Only for face: improvement noted after 8-24 weeks (stop if not effective after 24 months).
  - 60% of women showed significant improvement.

Hirsutism: mechanical treatments

- Electrolysis: costly and painful; multiple treatments.
- Laser: destroys pigmented hairs; costly, multiple treatments (less than electrolysis).
  - Most effective on lighter skin and dark hairs.
  - Swelling gone in 48 hours; minimal erythema.
  - Replaced electrolysis.

Evidence: treatment of hirsutism

- OCP’s, patch or vaginal ring recommended as first line management for hirsutism or acne.
- Screen for contraindications per MEC.
- One formulation of OCPs is not recommended over another.

Obesity of PCOS

- Obesity is a co-morbidity that may amplify the effects of PCOS.
  - 20% of women with PCOS are not obese.
- Metabolic syndrome is common among women with PCOS, 33% affected.
- Reduction in body weight is associated with improved pregnancy rates, decreased hirsutism and improvements in glucose and lipid levels.

Box 1: Suggested Evaluation for Patients With Polycystic Ovary Syndrome (continued)

Laboratory (continued)

- Evaluation for metabolic abnormalities
  - 2-hour oral glucose tolerance test (fasting glucose less than 110 mg/dL = normal, 110-125 mg/dL = impaired, greater than 126 mg/dL = type 2 diabetes followed by 75 g oral glucose ingestion and then 2-hour glucose level (less than 140 mg/dL = normal glucose tolerance, 140-199 mg/dL = impaired glucose tolerance, greater than 200 mg/dL = type 2 diabetes)
- Fasting lipid and lipoprotein level (total cholesterol, high density lipoproteins less than 50 mg/dL abnormal, triglycerides greater than 150 mg/dL abnormal, [low density lipoproteins usually calculated by Friedewald equation])

ACOG 2009
**Evidence: Weight loss PCOS**
- Weight loss can improve the endocrine syndrome of PCOS.
- Lowers androgen levels and causes spontaneous resumption of menses.
- Morbidly obese women with PCOS who undergo gastric bypass surgery experience near normalization of their reproductive and metabolic abnormalities.
- Reported with loss as little as 5% of initial wt.


**Evidence: Metformin therapy**
- Not recommended for treatment of acne and/or hirsutism, obesity or prevention of pregnancy complications.
- Recommended for women with PCOS who fail lifestyle modifications.
- Can be used as second-line therapy in women with menstrual irregularity who do not respond to hormonal contraception.
- Pregnancy Cat. B (appears safe in pregnancy)

**PCOS women with infertility**
- Overweight-obese infertile women with PCOS.
- Show significant benefit from preconception lifestyle modifications and weight loss program before undergoing fertility treatment.
- Delayed use of clomiphene after implementation of lifestyle modifications resulted in significant improvement in ovulation and live birth rates.


**My favorite solution**
- Weight loss.
  - As little as 5% can lower androgen levels and resume regular menses and ovulation.

**Evidence-based treatment algorithm for PCOS**

- **menstrual**
  - OCP
  - progestin
  - weight loss
  - metformin

- **Hirsutism/acne**
  - OCP
  - Spironolactone
  - Eflornithine
  - Laser
  - Weight loss

- **infertility**
  - Weight loss
  - clomiphene

- **General health issues**
  - weight loss

**Thanks!**