IN THE CLINIC

THE POLYCYSTIC OVARY SYNDROME (PCOS) IN ADOLESCENTS

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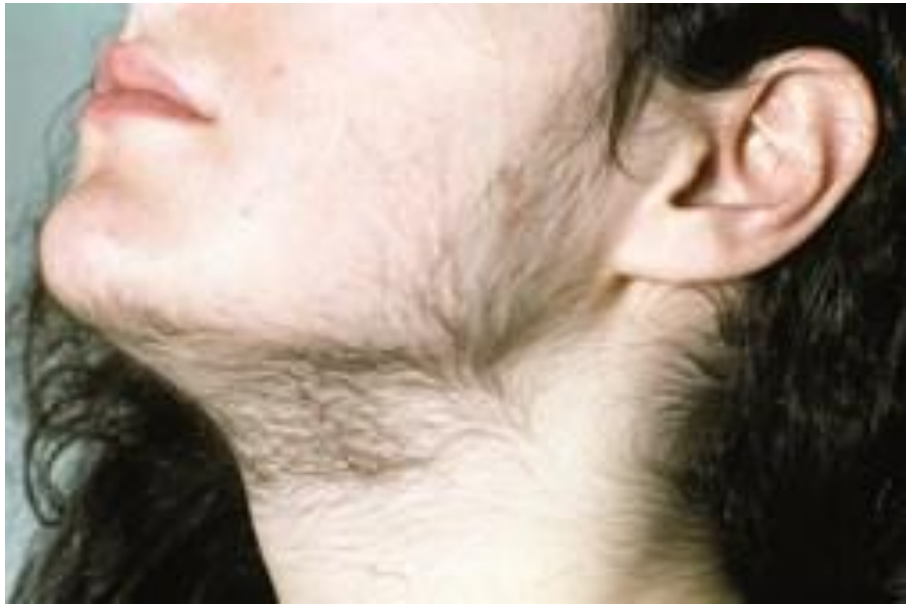
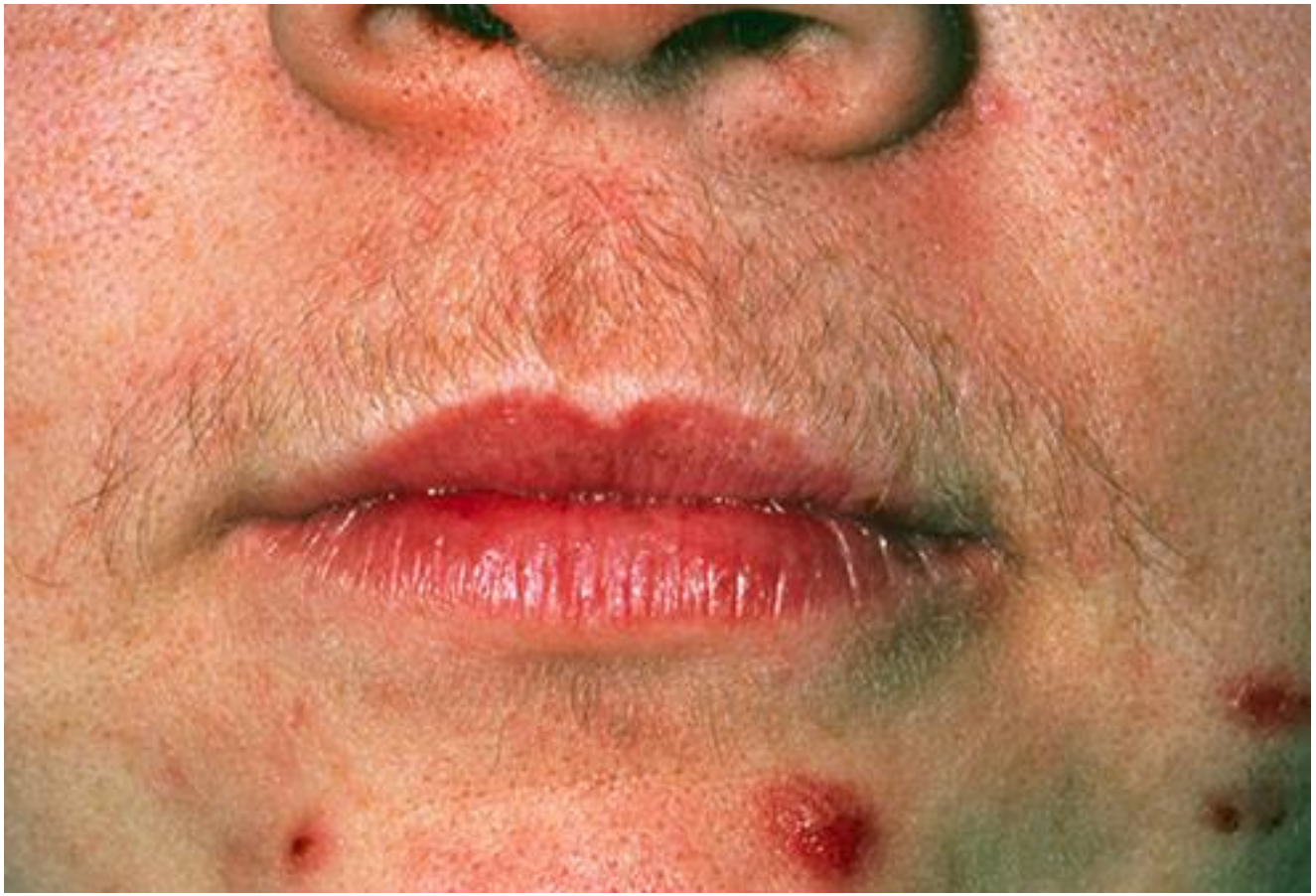
PCOS in Adolescents: Objectives

1. Recognize patients with PCOS
2. Be able to diagnose PCOS using evidence-based criteria
3. Understand and evaluate clinical conditions associated with PCOS
4. Help patients choose treatment options

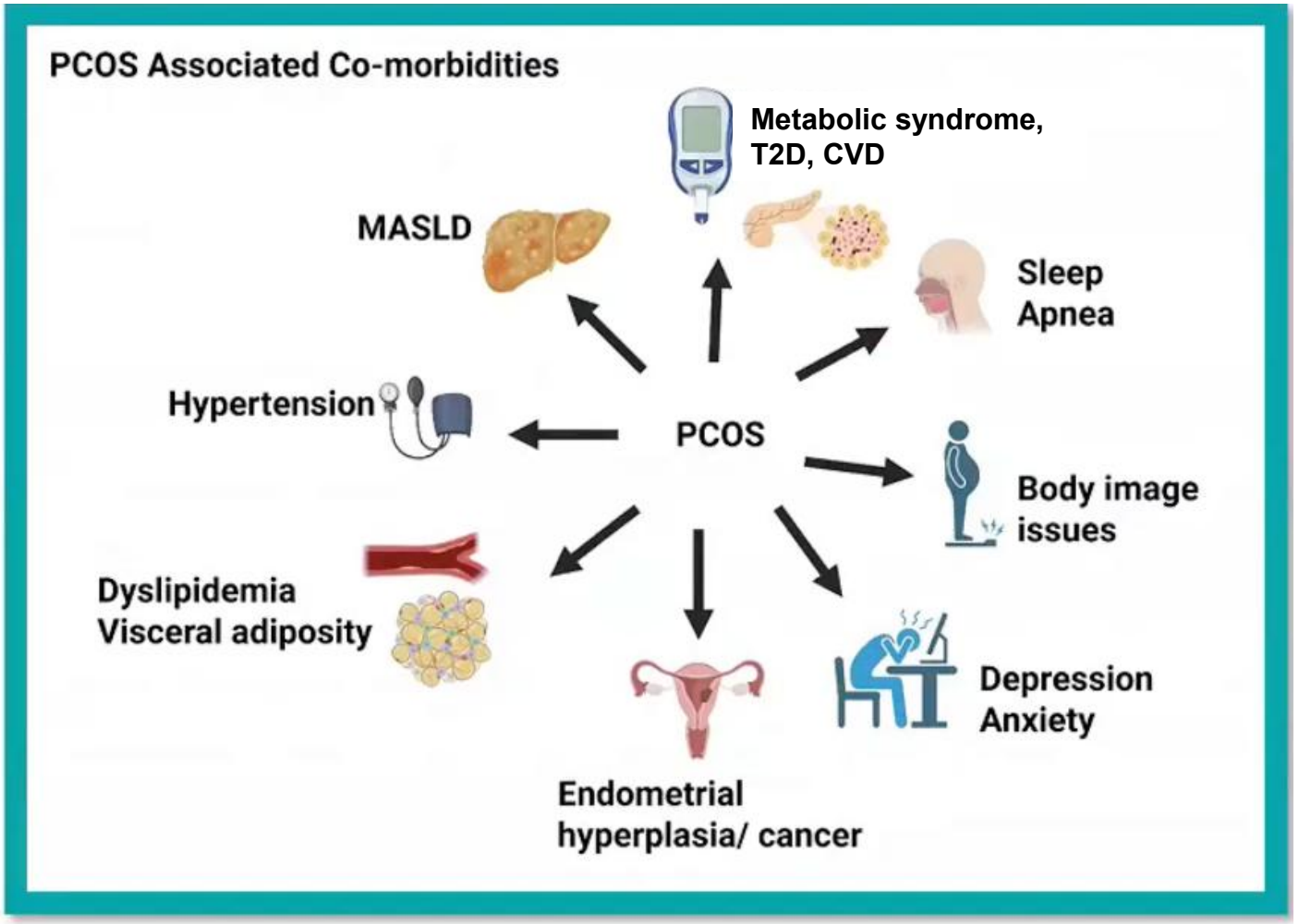




PCOS: What is it?

- Most common endocrinopathy in reproductive-aged women
- Genetic and environmental factors interact; heritability 70%
- Characterized by insulin resistance and hypothalamic-pituitary-ovarian axis dysfunction resulting in:
  - **Ovulatory dysfunction**
  - **Androgen excess**
  - **“Polycystic” appearance of ovaries**
- Linked to multiple comorbidities

Comorbidities



Tfayli H, et al. Reproduction 2025. 170(6) e250115. PMID:411758561

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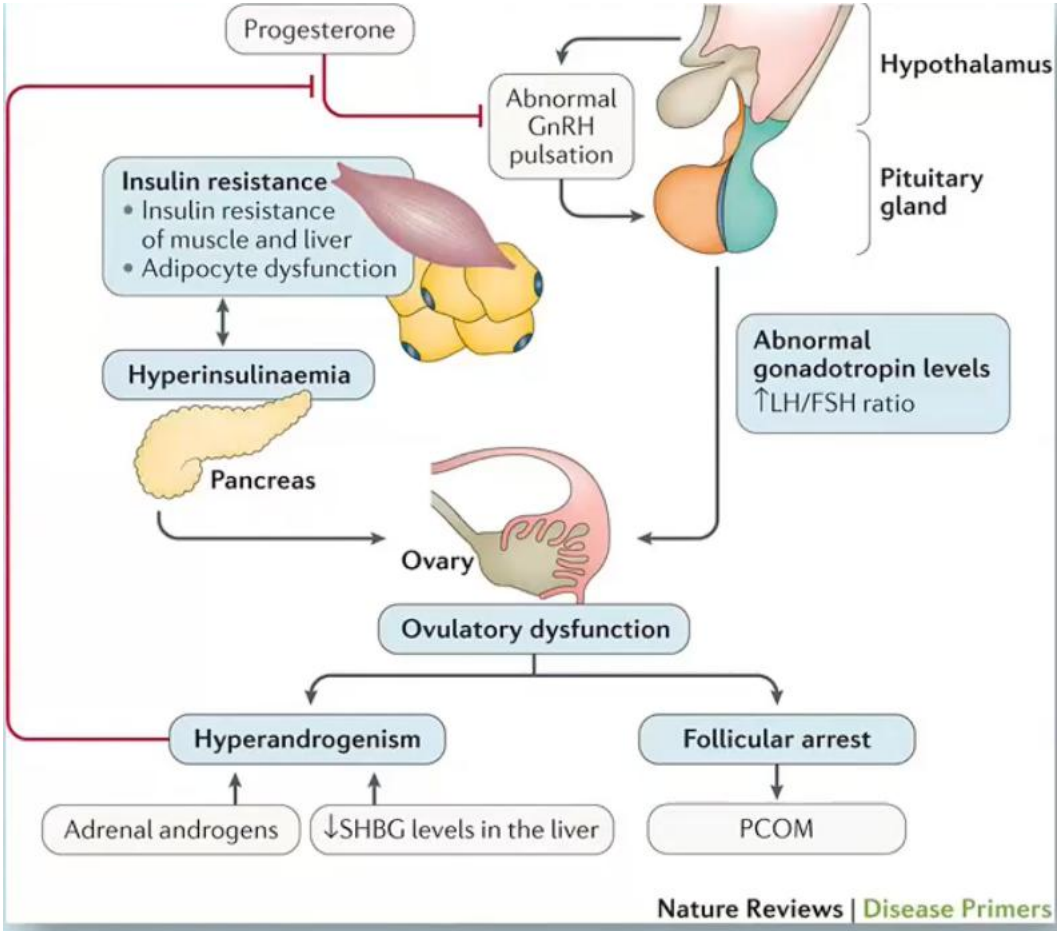
Pathophysiology



Azziz A, et al. *Nature Reviews Disease Primers* **volume 2**, Article number: 16057 (2016)

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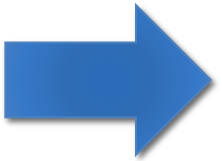
What happens to hormone levels in PCOS?

- PCOS is a normoestrogenic but hyperandrogenic state
- Because PCOS women are oligo- or anovulatory, they don't make the progesterone that comes from the luteal phase of the cycle

Bottom line:

- Without cyclic progesterone, the uterus is at risk for:
  - Heavy bleeding
  - Endometrial hyperplasia  endometrial cancer

Obesity, early menarche and Type 2 diabetes are additional risk factors for endometrial cancer

PCOS: A LIFELONG HEALTH CONCERN

GOAL: IMPROVE PATIENT EXPERIENCES AND HEALTH OUTCOMES

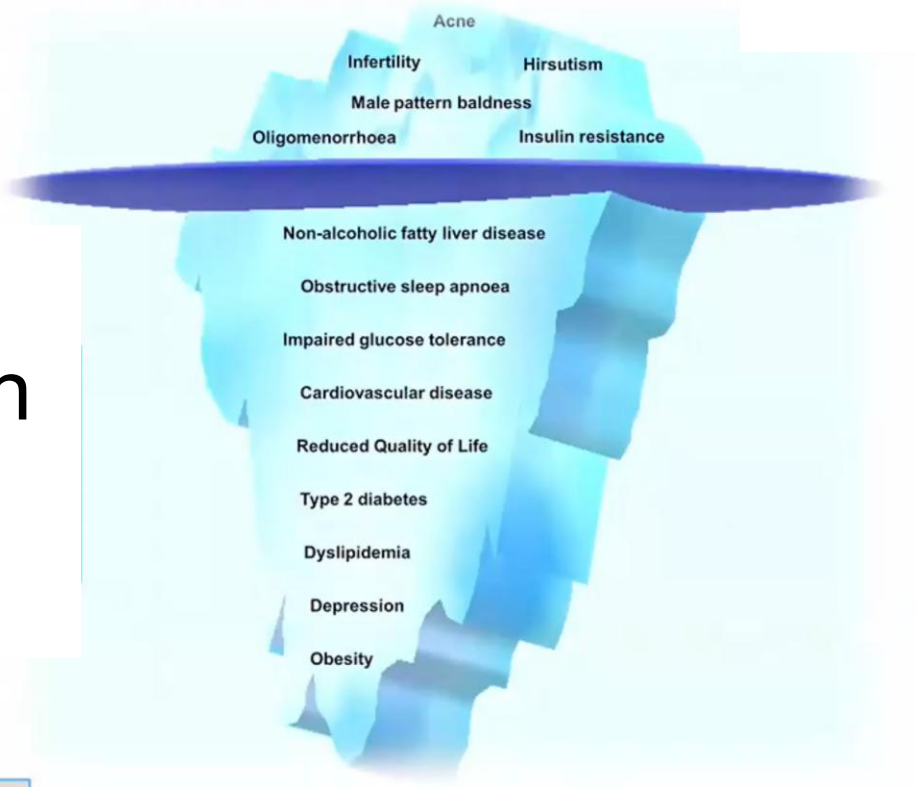
PCOS: Why is a diagnosis important ?

Gynecologic issues

- Infertility
- Abnormal uterine bleeding
- Endometrial carcinoma

Increased risk for comorbidities

PCOS Presentation is the Tip of the Iceberg



Kempegowda P, et al. Implicating androgen excess in propagating metabolic disease in polycystic ovary syndrome. Ther Adv Endocrinol Metab. June 2020

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PCOS: Who is at risk?

- Latinas > White, African-American women
- + Family history of PCOS, metabolic/CV disease
- Prenatal androgen exposure
- Poor fetal growth
- A history of premature adrenarche
- T1D, T2D, gestational diabetes
- BMI >30 kg/m^2

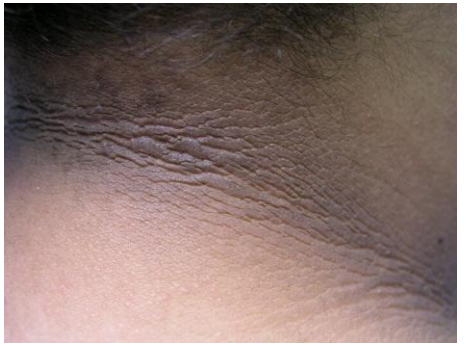
  50% of women with PCOS are obese

Consider PCOS in Any Adolescent with:

1. Cutaneous signs of hyperandrogenemia
   - Hirsutism
   - Acne
   - Also seborrhea, hyperhidrosis, hidradenitis, male or female pattern hair loss (unusual)
2. Menstrual irregularity
   - Even primary amenorrhea!

Consider PCOS, cont.

- 3. Signs related to insulin resistance/obesity
  - Acanthosis nigricans
  - Elements of metabolic syndrome
  - Sleep disordered breathing
  - MASLD



- 4. + Polycystic ovaries (one or both)

HOWEVER:

- No definitive criteria to define PCO morphology in adolescents
- Ultrasound not recommended routinely in adolescents

Can’t Make Diagnosis Unless Patient Meets These Criteria:

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International Consensus Diagnostic Criteria for PCOS in Adolescents

Otherwise unexplained combination of:

1. Abnormal menstrual pattern as evidence of ovulatory dysfunction
   - Abnormal for (gynecologic) age
   - Persistent for 1-2 years

- Clinical or biochemical evidence of hyperandrogenism
  - Hirsutism, especially if moderate or severe (clinical)
  - Elevation of free or total testosterone by a specialty reference assay (biochemical)

Pediatrics, Vol 136, Pages 1154-65, Copyright © 2015 by the AAP. Updated with information from:
Rosenfield RL. Perspectives on the International Recommendations for the Diagnosis and Treatment of Polycystic Ovary Syndrome in Adolescence. J Pediatr Adolesc Gynecol 2020; S1083.

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Abnormal Uterine Bleeding in Adolescents

Symptom	Definition
Primary amenorrhea	Lack of menarche by 15 years of age or by 3 years after the onset of breast development*
Secondary amenorrhea	More than 90 days without a menstrual period, after previously menstruating
Oligomenorrhea (infrequent abnormal uterine bleeding)	▪ Year 0 to <1 post-menarche – Average cycle length >60 days (fewer than 6 periods per year) ▪ Year 1 to <3 post-menarche – Average cycle length >45 days (fewer than 8 periods per year) ▪ Year 3 post-menarche to perimenopause – Average cycle length >38 days (fewer than 9 periods per year)
Excessive uterine bleeding¶	Menstrual bleeding that is more frequent than every 21 days (or 19 days in year 1 post-menarche) or prolonged (lasts more than 7 days) or heavy (soaking pads or tampons sufficiently to interfere with quality of life)

From UpToDate 2024: Definition, clinical features, and differential diagnosis of polycystic ovary syndrome (PCOS) in adolescents

Difficulties in Diagnosis - Adolescents

- Menstrual irregularity is common in first one to 2 years after menarche
- Hirsutism can be mild early in sexual development
- Acne is common
- Testosterone levels in this age group problematic
- Polycystic ovary morphology by adult standards common

∴ *Overlap between normal puberty and PCOS*

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Difficulties, cont.

SO:

- For those with PCOS features within 1-2 years after menarche or without all the features, assign a provisional dx of “at risk for PCOS”, treat, and reevaluate on reaching gynecologic maturity

  (5-8 years p/menarche); i.e., *refer to Gyn or Adult Endocrinology!*

What else is in differential diagnosis?

- Late-onset congenital adrenal hyperplasia
- Androgen-producing neoplasms
- Cushing syndrome
- Hyperprolactinemia
- Pregnancy
- Hypothyroidism
- Acromegaly

Making the Diagnosis

History and Physical

History

- Age of menarche
- Menstrual pattern
- Timing and tempo of progression of signs/symptoms
- Family history
- Medications

Physical Exam

- Obesity
- Acanthosis
- Hirsutism
- Acne
- Genital exam

Initial Lab Testing for Adolescents

- Total and free testosterone (morning best)
  - Total T – tandem mass spec (LC-MS/MS); Quest and Labcorp ✅
  - Free T – calculation, FAI, equilibrium dialysis, or ammonium sulfate precipitation
  - Do not use direct immunoassays for either T or free T
  - Serum AMH should not yet be used in adolescents
  - Patient should be off COC 3 months before testing
- With menstrual abnormalities:
  - βhCG, prolactin, TSH, CBC, LH and FSH
  - Chronic disease screening as indicated (CBC, ESR, CMP)
- In all patients:
  - Fasting lipids, FBS, HBA1c, LFTs – ANNUALLY

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Lab testing, cont.

- If total and/or free T high, then look at:
  - DHEAS (to R/O adrenal neoplasm, significant if > 700 mcg/dL)
    - Also helpful if total or free T not elevated and patient hirsute
  - 17 OH Progesterone at 8 AM (significant if > 170 ng/dL)
    Rules out classical form of congenital
    adrenal hyperplasia
  - 24 hour urine free cortisol if central obesity
  - IGF1 if acromegalic features

Virilization is Not PCOS

- Rapid onset or progression of hirsutism
- Increased muscle bulk
- Voice deepening
- Onset of clitoromegaly

Above indicate **FRANK VIRILIZATION**.

T level > 150 should prompt evaluation for ovarian or adrenal neoplasm

Additional Workup

- If snores/apneic while sleeping:
  - Sleep study
- If mental health issues suspected:
  - Screen for depression, anxiety, eating disorders

Another, great, "functional" test:

Progestin challenge if no period ≥ 3 months

- Prometrium (micronized progesterone)
  - 100-200 mg orally at bedtime for 7-10 days
- Provera (Medroxyprogesterone acetate)
  - 5-10 mg orally at bedtime for 7-10 days
  - Period should occur within a few days before up to a week after stopping medication

Withdrawal bleeding confirms the diagnosis of PCOS and readies the endometrium for therapy

TREATMENT MODALITIES

Go by what is most important to the patient and also addresses major health issues!

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Best Treatment for Menstrual Irregularity and Hirsutism/Acne

Combined oral contraceptives (COC)- 1st line therapy

- All COCs are effective for acne and hirsutism
  - Contraindicated in patients with venous thrombosis, uncontrolled HTN, migraine with aura
  - Combined estrogen-progestin contraceptive vaginal ring or transdermal patch are acceptable alternatives
- 30-35 mcg ethinyl estradiol COCs preferable
  - Try not to use 20 mcg pills in adolescents: less desirable for both irregular uterine bleeding and bone accrual

Limitations of COC

- 4 fold ↑ risk of venous thromboembolism
- COC's containing 30-40 mcg ethinyl estradiol carry a small ↑ risk of stroke and MI
- In adolescent who is still growing, the risk of growth inhibition by estrogen must be considered
- Can raise BP

Best Treatment if Menstrual Irregularity the Biggest Issue and COCs not a consideration

Progestin only (oral)

- Prometrium (micronized progesterone)
  - 100-200 mg orally at bedtime for 7-10 days
- Provera (Medroxyprogesterone acetate)
  - 10 mg orally at bedtime for 7-10 days
- Norethindrone acetate 2.5-10 mg for 7-10 days

- Period should occur within a few days of end of course

- Can use either drug at 2 month intervals which allows detection of spontaneous menses

- Side effects – breast soreness, mood sx, bloating, HA

- Not a means of contraception; **no** help with hirsutism

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Other Treatments for Menstrual Irregularity

- **Progestins that provide contraception**:
  - POPs (Progestin-only pills) – taken every day
    - norethindrone 0.35 mg, drospirenone 4 mg
    - Easily reversible
    - Easiest to manage BTB
  - IM Depot-Provera every 3 months
    - Mild, reversible loss in BMD
  - Mirena IUD (levonorgesterel)
  - Nexplanon implant (etonogestrel)
- **Insulin-sensitizing drugs** (metformin)
- **Weight loss**

PCOS Treatment: Metformin

- Metformin – off-label for PCOS
  - Consider in patients who also have glucose intolerance and/or dyslipidemia
  - Anorexic effect – only works if + weight loss
  - ↓ insulin, ↓ androgens
  - **Restores menstrual cyclicity & ovulatory** menses in approx 30-50% of PCOS women
  - Since can restore fertility, use with contraception as needed
  - **NO** impact on hirsutism

Metformin, cont.

- Contraindicated with:
  - Impaired hepatic or renal function
  - Alcoholism
  - Cardiopulmonary insufficiency
- Start low & go slow: initial dose 250-500 mg with meal, ↑ gradually to max of 2000 mg total daily dose
- If GI upset, give extended release, liquid form or divide doses; use with food
- Check yearly CBC, creatinine, and B12

PCOS Treatment: Obesity

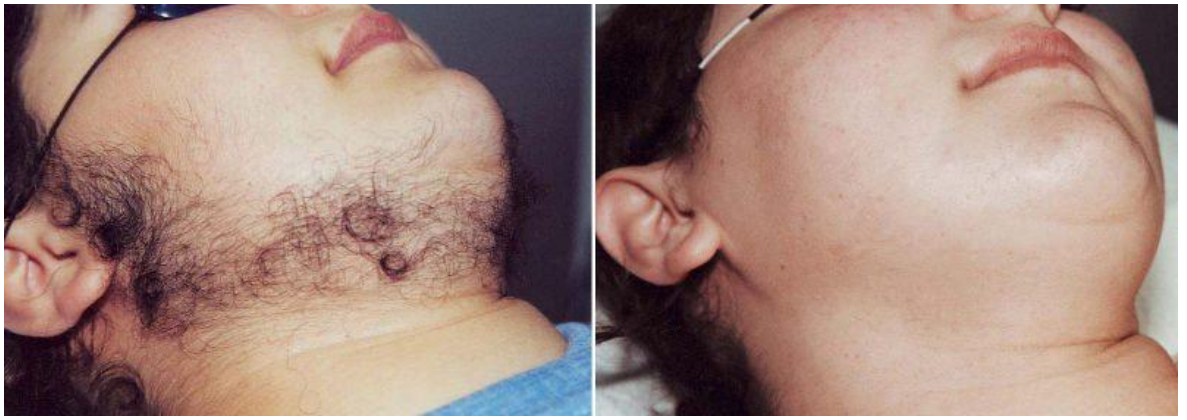
- Lifestyle Changes
  - 60 minutes exercise daily
  - Nutrition plan – no evidence for one diet over another
- Medications
  - Liraglutide
  - Semaglutide

  GLP-1 agonists, approved ≥ 12 yr
- Bariatric surgery
  - For adolescents, should only be recommended after a comprehensive multidisciplinary weight loss program

PCOS Treatment: Cosmetic Therapy for Hirsutism

First line: Shaving/Waxing/Chemical depilation/Bleach

Second line (after 6 months): Physical hair removal by laser therapy (including intense pulsed light) or electrolysis



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Additional Treatment for Patients with Severe Hirsutism

Antiandrogen – if no improvement after 6 months of COC or if COC contraindicated, poorly tolerated

- Spironolactone
  - only use with contraception 2º adverse effects on fetus
  - May take 9-12 months for results

Consult endocrinology

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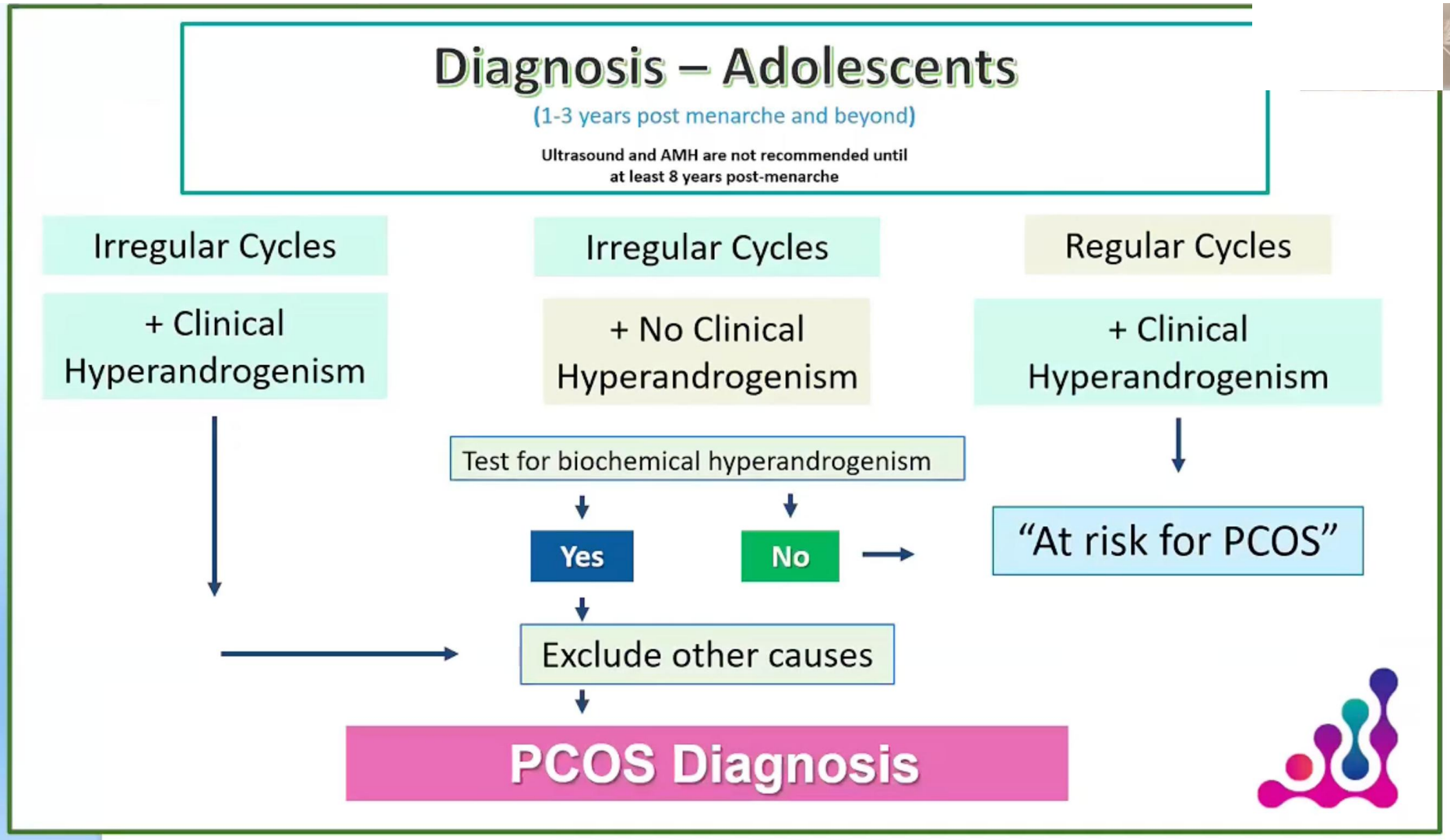
Length of Treatment

- Little is known re: natural history of PCOS in adolescents
- Optimal duration of treatment not determined
  - Continue until patient gynecologically mature (5-8 years p/menarche)

  And/or
  - Obese patient has lost substantial weight



Witchel SF, Teede HJ, Peña AS Pediatr Res. 2019 Oct 18.
Chua SJ, et al. Clin Endocrinol (Oxf). 2025 Jun 24. doi: 10.1111/cen.15294

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Summary

- Overlap between normal pubertal development and characteristic features of PCOS
- Look for **hirsutism** (equivalents) and persistent **menstrual abnormalities ≥ 2 years**
- Perform lab evaluation: **Fasting 8a if possible**:

  Total and free T, pregnancy test, prolactin, TSH, CBC, LH, FSH, lipids, plasma glucose, HBA1c, LFTs, DHEAS, 17 OH progesterone, IGF-1, 24 hour urine free cortisol
- Defer diagnostic labeling and reevaluate those considered to be "at risk" for PCOS to avoid overdiagnosis and unnecessary treatment

Summary, cont.

- Share decision making
- COC first line treatment for menstrual abnormalities and cutaneous signs of PCOS
- Lifestyle interventions - always
- Screening and intervention for depression
- Identify and monitor for comorbidities
- Consider evaluation of at-risk family members (men, too)
- Followup

Information for Patients

https://www.askpcos.org/

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Additional References

1. Recommendations From the 2023 International Evidence-based Guideline for the Assessment and Management of Polycystic Ovary Syndrome Helena J Teede , et al. J Clin Endocrinol Metab 2023 Sep 18;108(10):2447-2469.doi: 10.1210/clinem/dgad463.

2. UpToDate chapters: 1) Definition, clinical features, and differential diagnosis of polycystic ovary syndrome (PCOS) in adolescents; 2) Diagnostic evaluation of polycystic ovary syndrome (PCOS) in adolescents; 3) Treatment of polycystic ovary syndrome (PCOS) in adolescents

3. Update on diagnosis of polycystic ovary syndrome during Adolescence. Alexia Sophie Peña, Ph.D. , Selma Feldman Witchel, M.D. Fertil. Steril. Volume 124, Issue 5, P956-961. November 15, 2025

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MAVEN Case

- 14 year old Latina patient with profound hirsutism with long coarse hair on her chin.

I did not meet family as they remained in car because of COVID
Menarche was age 12, somewhat irregular.

- Ht: 66", Wt: 135#, BMI 21, stable on growth curve. She had dark finer hair in sideburns even finer on upper lip. Chin hair was course and curly up to an inch long, she's happy to wear her mask! She has not had genital exam, no balding or acanthosis. Not hairy on back or abdomen.
- Labs she had drawn this June at another facility before starting Yaz, not sure what day of cycle:

LH 25.9, FSH 6.3, TSH 1.7, prolactin 22.7, testosterone 27.09 (wnl), insulin 10.2, 17 OH progesterone 111
A1c 5.3%
SHBG 27.09 (Female premenopause 21-60 years = 10.84 ->180)
Bioavailable testosterone 1.93mol/L (0.24-1.35) 
FAI 7.1 (Female premenopause 21-60 years= 0.27-7.64)

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Case, cont.

Question: PCP started her on low androgenic ocps two months ago. Will labs be helpful while on Yaz?
A: You can check free testosterone while on placebo pills of 3rd month or later to assess if testosterone is suppressed on Yaz. However, not necessary to do this if clinical response apparent. Can add DHEAS since not done before Yaz started.

Q: What additional questions would you ask patient?
A: What is FH PCOS, hirsutism, comorbidities?

Q: What other part of physical exam does she need?
A: Genital exam

Case, cont.

Q: If she has little response to Yaz after 6 months, what would you recommend?
A: Consider antiandrogen, like spironolactone. May refer to endocrine at that point

Q: What labs would you suggest annually?
A: Lipids, A1c, FBS

Other suggestions: cosmetic treatments

Another case

Patient 1: 12 yo girl with BMI 24.7 kg/m^2 (~95th percentile) and irregular menses. She had onset of pubic hair development at age 7 yrs. Breast budding started at age 9 yrs and menarche was at age 11 yrs. Exam shows mild acanthosis nigricans about her neck and increased terminal hairs on her face, lower abdomen, and lower back (mFG=6). Tanner 5 breast and pubic hair development.

Laboratory testing:
hCG negative
17 hydroxyprogesterone = 115 ng/dL (Nl < 100 ng/dl)
DHEAS =220 mcg/dL (44-248 mcg/dl)
Total testosterone =55 ng/dL (Nl <39 ng/dl)
LH =6.6 mIU/mL and FSH =5.5 mIU/mL
Normal thyroid function studies
Prolactin 14 ng/ml
Hemoglobin A1C 6.1% (Nl <6.3%)

Irregular menses
Elevated testosterone
But, less than 2 years post-menarche

Another case

Patient 1: 12 yo girl with BMI at 95th percentile and irregular menses. She had onset of pubic hair development at age 7 yrs. Breast budding started at age 9 yrs and menarche was at age 11 yrs. Exam shows mild acanthosis nigricans about her neck and increased terminal hairs on her face, lo[illegible]men, and lower back (mFG=6). Tanner 5 breast and pubic h[illegible]

"At risk for PCOS"

Laboratory testing:
hCG negative
17 hydroxyprogesterone = 115 ng/dL (N[illegible]
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Questions?