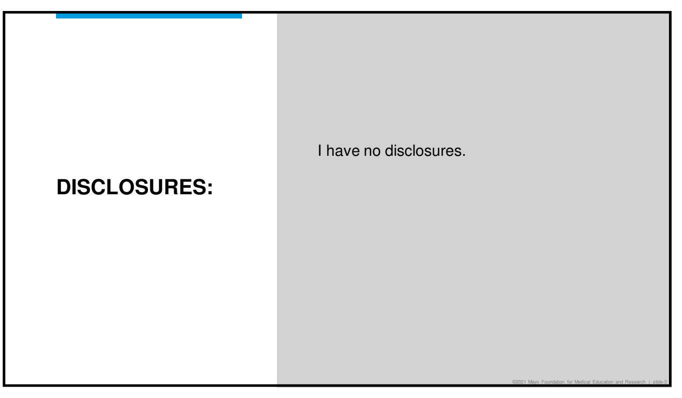
1

LEARNING OBJECTIVES:

1. Understand the criteria for diagnosing PCOS.
2. Understand the challenges in diagnosis PCOS in Adolescents.
3. Review the recommendations from the 2023 International evidence-based guidelines for the management of PCOS.

2



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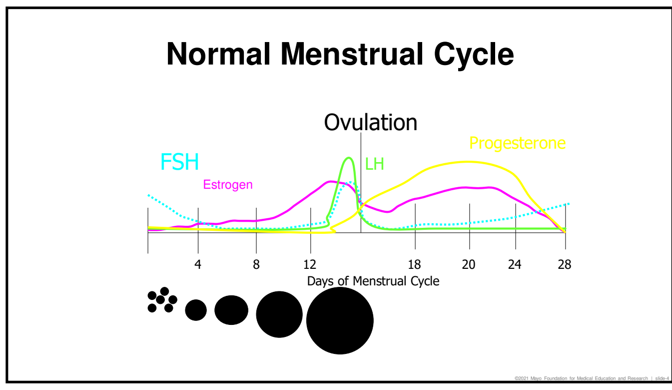

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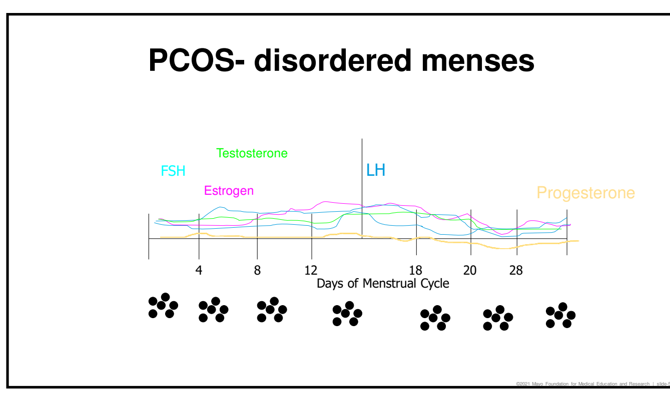

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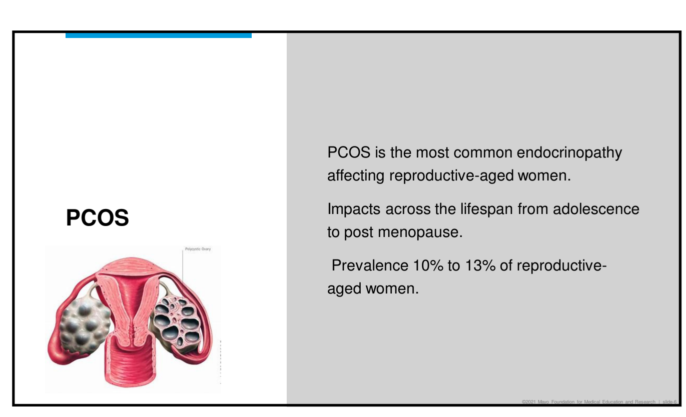

6

PCOS

Recommendations From the 2023 International Evidence-based Guideline for the Assessment and Management of Polycystic Ovary Syndrome*

• Helena J. Teede,1,2 Chau Thien Tay,1,2 Joop J. E. Laven,2,3 Anuja Dokras,4 Lisa J. Moran,1,2 Terhi T. Piltonen,5 Michael F. Costello,2,6 Jacky Boivin,7 Leanne M. Redman,8 Jacqueline A. Boyle,2,9 Robert J. Norman,2,10 Aya Mousa,1 and Anju E. Joham;1,2 on behalf of the International PCOS Network†

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7

2023 INTERNATIONAL PCOS GUIDELINES

GOOD NEWS: Assessment and management of PCOS has generally improved in the past 5 years.

Recommendations are strengthened and evidence improved, but more research needed.

i) Screening, diagnostic, and risk assessment
ii) Psychological features and models of care
iii) Lifestyle management
iv) Management of nonfertility features
v) Assessment and management of infertility

8

PCOS- Diagnostic Criteria
2 of the following 3*

1. Irregular menstrual cycles (history)
2. Hyperandrogenism
   - Either skin manifestations (acne, hirsutism)
   - Elevated serum androgens
3. Polycystic appearing ovaries by ultrasound

AND

*__Exclusion of phenotypically disorders__

*2003 Rotterdam Consensus Conference

9

Algorithm 1: Diagnostic algorithm for polycystic ovary syndrome (PCOS)

Step 1: Irregular cycles + clinical hyperandrogenism

(exclude other causes)* = diagnosis

Step 2: If no clinical hyperandrogenism

Test for biochemical hyperandrogenism (exclude other causes)* = diagnosis

Step 3: If ONLY irregular cycles OR hyperandrogenism

Adolescents ultrasound is not indicated = consider at risk of PCOS and reassess later

Adults - **request ultrasound for PCOM***, if positive (exclude other causes)* = diagnosis

10

DEFINITION OF IRREGULAR MENSTRUAL CYCLES

- **Irregular cycles are normal in the first-year post menarche as part of normal puberty.**
- **1 to 3 years after menarche:**
  - <21 days or > 45 days
  - Or > 90 days for any one cycle
- **3 years + after menarche to perimenopause:**
  - <21 days or > 35 days
  - Or > 90 days for any one cycle

11

OTHER OVULATORY DYSFUNCTION

- Primary amenorrhea– No cycles by age 15 or >3 years after breast development.
- Anovulation can occur with regular cycles. Check midluteal progesterone to confirm ovulatory dysfunction.
- If Progesterone < 2.5, ovulation has not occurred.

12

EXCLUDE OTHER HORMONE DISORDERS

- **TSH**
- **Prolactin**
- **FSH, LH, estradiol**
- **17-hydroxyprogesteone (17-OHP)**
  - **rule out non-classical Congenital Adrenal Hyperplasia**
- **Total testosterone and Free testosterone**
- **DHEA-S and androstenedione**
- **Comprehensive metabolic panel, cholesterol panel, HgbA1c**
- **New in 2023 *** AMH can now be used instead of ultrasound******

13

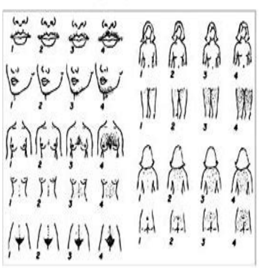
BIOCHEMICAL HYPERANDROGENISM

- Total and free testosterone to assess biochemical hyperandrogenism.
- Androstenedione and DHEAS have poorer specificity.
- If patient is already on combined ocps, need a 3-month wash-out.
- Androgens reach adult levels by age 12-15.
- No role for repeating androgens.
- No upper value given by 2023 consensus to consider other diagnosis (ovarian/adrenal tumors).
- General rule. DHEAS> 700, Total Testosterone > 150, or signs of virilization need further evaluation

14

HIRSUTISM

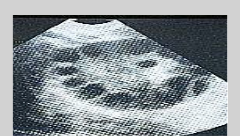
- The presence of Hirsutism is considered hyperandrogenism in adults.
- Modified Ferriman-Gallwey score of 4-6.

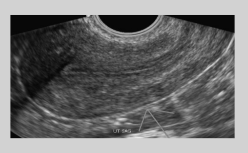


15

PCOS- ULTRASOUND FINDINGS

- **Vaginal Ultrasound**
- **Follicle number per ovary (FNPO) most effective ultrasound marker to detect PCOS in adults.**
- **20 or more follicles in one ovary in adults.**
- **Early follicular phase: Day 2—4 of cycle.**
- **Examine the uterine lining for thickness < 6mm.**
- **No definitive criteria to define PCOS in adolescents; hence, TV USN is not recommended in adolescents.**





16

ANTIMULLERIAN HORMONE (AMH)

- Serum AMH peaks between the ages of 20-25.
- AMH is lower in those with higher BMI.
- AMH may be suppressed by current or recent COCP use.
- AMH may vary across the menstrual cycle.
- Should not be used in adolescents.
- Cut off for PCOS dx not given in the 2023 Consensus (AMH > 10 is consistent with PCOS in most labs).
- Should not be used as sole criteria for PCOS dx.

17

PCOS- WHAT ARE THE OTHER RISKS?

- HTH, heart disease, and high cholesterol
  - All women with PCOS should have annual BP check
  - Chol panel initially and then as indicated
- **Non-alcoholic fatty liver disease (NAFLD)**

18

PCOS- RISKS

Obesity

Weight loss (as little as 5-10 lbs)

Improved menstrual regularity

Lower insulin levels

Lower testosterone levels

19

PCOS- RISKS

- Type II DM
  - All women and adolescents with PCOS should be screened for Type II DM every 1-3 years.
  - 75 GM Oral GTT is recommended.
  - HgbA1c can be used though not as accurate
  - Insulin levels have limited clinical relevance and are not recommended.
  - Pregnant women with PCOS- 3H GTT at first prenatal visit and at 24-28 wks.

20

PCOS- WHAT ARE THE OTHER RISKS?

Endometrial hyperplasia and endometrial cancer.
- More common than people realize.
- Hyperplasia can start in the teens. Cancer in 20s
- Maintain regular cycles.
- Birth control pills, Mirena IUD, Cyclic Prometrium, etc.
- If no hormonal suppression, need a minimum of 4 menstrual cycles per year.
- **When excessive endometrial thickness is detected, consider endo Bx (Day 3 endo lining < 7 mm).**

21

PCOS- WHAT ARE THE OTHER RISKS?

- Anxiety/Depression
  - Screening, support, and treatment when indicated.
- Eating disorders
  - Screening, support, and treatment when indicated.
- Sleep Apnea
  - Consider sleep study in appropriate patients.

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22

TREATMENT: LIFESTYLE MANAGEMENT

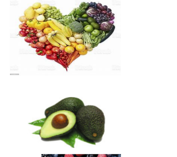
- Fitness tracking device.
- Exercise- any is better than none.
  - Minimum 30 min of mod exercise 5 days/ wk to maintain weight
  - Minimum 50 min of mod-intense exercise 5 days/wk to lose weight with Weights/resistance training twice/ wk.
- Healthy diet
  - No specific dietary guidelines in 2023 guidelines.
  - Higher protein/ lower processed carbs.

23

NUTRITION

Consider nutrition consult

- In Genera, eat a healthy (Try to eat a rainbow everyday)
  - 5-7 vegetables and fruits per day
  - Green leafy vegetables, berries, fruits
  - Chose vegetables for snacks
  - Healthy fats- avocado, nuts, olives
  - Chose Whole grain foods and Lean meats
  - Eliminate empty calories (sodas, sugary snacks)
  - Avoid highly processed foods
  - Vegetarian /Vegan eating plans are fine
  - During fertility treatments, avoid Ketosis plans
  - Programs that have been shown to help with weight loss
  - Weight Watchers, 21-Day Fix , Noom



24

TREATMENT: COMBINED ORAL CONTRACEPTION

- Combined Oral Contraceptives- (20-30mcg EE or oestradiol) to treat irreg cycles/ hirsutism.
- No specific brand recommended.
- Avoid 35 mcg and higher.
- Progesterone only pills for women with contraindications to estrogen.

Avoid Depot Provera with PCOS due to unwanted side effects

25

TREATMENT: METFORMIN

- Treatment of adults with BMI > 25 or for cycle regulation.
- Treatment of adolescents for cycle regulation.
- Start 500 mg XR with supper for 1-2 wks and gradually increase by 500 mg.
- Max dose: 2000 adolescents. 2500 adults.
- Risk of Vit B 12 def in certain populations- DM, post-bariatric surgery, pernicious anemia, Vegan diet.
- Not FDA approved to treat PCOS.

26

TREATMENT:

- Consider Anti-obesity medications, including liraglutide, semaglutide, and both glucagon-like peptide-1 (GLP-1) receptor agonists and orlistat.
- Intervention, for the management of higher weight in adults with PCOS as per general population guidelines.
- Not Safe in pregnancy. Utilize contraception.

27

TREATMENT

- Spironolactone at 25-100 mg/day appears to have lower risks of adverse effects.
- Cyproterone acetate at doses ≥ 10 mg is not advised due to an increased risk including for meningioma.
- Inositol (in any form) has limited harm, potential for improvement in metabolic measures, yet limited clinical benefits.

28

TREATMENT

- Mechanical laser and light therapies should be considered for reducing facial hirsutism and for related depression, anxiety, and quality of life in women with PCOS.
- Laser is relatively ineffective in women with blond, grey, or white hair.
- The addition of combined oral contraceptive pills (COCP), with or without anti-androgens, to laser treatment may provide greater hair reduction and maintenance compared to laser alone.
- Low- and high-fluence lasers appear to have similar efficacy in reducing facial hair, while low-fluence laser has reduced associated pain.

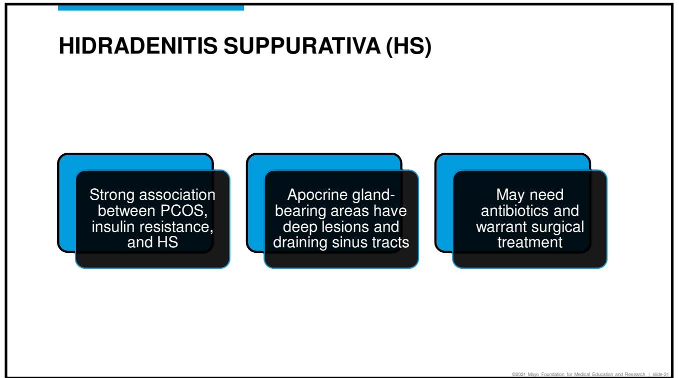
29

TREATMENT: BARIATRIC SURGERY

- Bariatric/metabolic surgery could be considered to improve weight loss, hypertension, diabetes (prevention and treatment), hirsutism, irregular menstrual cycles, ovulation, and pregnancy rates in women with PCOS.
- Rapid return of fertility and the need to commit to effective contraception. Even when pregnancy is desired, contraception should be continued until a stable weight is achieved, usually after 1 year, to avoid significantly increased risk of growth restriction, prematurity, small for gestational age, pregnancy complications, and prolonged hospitalization of the infant.

30

HIDRADENITIS SUPPURATIVA (HS)



31

HIRSUTISM

Treatment:

OCPs

Similar benefits in adding Metformin to OCPs for those in the overweight category.

May take 6 months to see improvement.

Spironolactone 50 mg qd, can increase to bid.
- Blocks androgen action.
- Very useful for women with contraindications to ocps.
- Must have contraception. Risks of birth defects.

32

ACANTHOSIS NIGRICANS

- Treatment
- Metformin
- OCPS
- Topical treatments: Tretinoin
- Fish oil
- Dermabrasion/ laser therapy in severe cases

33

FERTILITY

- Women with PCOS have:
  - Lower oocyte quality
  - Abnormal endometrium
  - Hyperinsulinemia effects
- Medications such as letrozole are very effective with BMI < 40. When BMI > 42, women are less likely to become ovulatory and are more resistant to fertility medications.

34

OBESITY AND PREGNANCY

- Risks to Mom:
  - *50% greater odds of developing:
    - Diabetes, Chronic hypertension, Cardiovascular disease.
  - *35% increased risk of premature mortality.
- Risk of pregnancy loss and stillbirth are increased with BMI > 30.
- Reduced fertility treatment success with BMI > 35.

- **Risks to the Baby**:
- Increased risk of Macrosomia
- Increased risk of Stillbirth and neonatal death (Kalliala et al. 2017)
- For children who are large for gestational age (LGA)
- 2- to 5-fold higher risk of childhood and adult obesity
- Increased risk of cardiovascular risk factors in young adulthood
- Glucose intolerance
- Insulin resistance
- Hypertension
- Dyslipidemia

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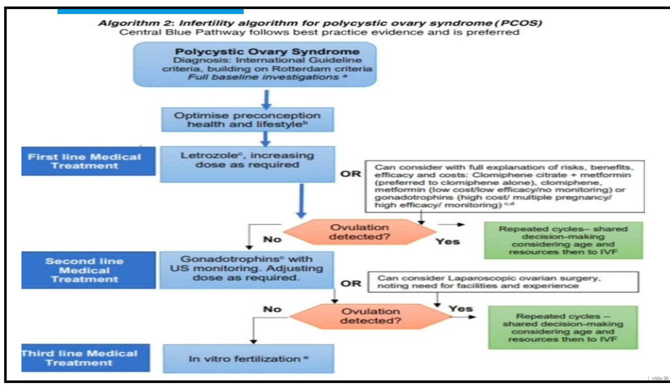

36

TREATMENT: FERTILITY

- The use of letrozole and metformin is off-label for ovulation induction.
- Letrozole should be the first-line pharmacological treatment for ovulation induction in infertile anovulatory women with PCOS.
- Letrozole should not be given if there is any possibility of a pre-existing pregnancy.
- Metformin alone is not as effective as letrozole or clomid.
- Clomid alone is not as effective as clomid with metformin.
- No evidence of increased risks of birth defects with clomid or letrozole compared to naturally conceived pregnancies.

37

- **Must** have a negative pregnancy test before starting med each cycle.
- Start med cycle day 3-5.
- Typically 1-3 tablets (2.5 to 7.5 mg) per day.
- Usually 5-10 days of medication.
- Follow up ultrasound.
- Often used with Ovidrel to trigger ovulation.
- Increased chance of twins (rarely triplets).
- Side effects: Hot flashes, nausea, headaches, irritability, breast tenderness.
- FDA Approved for breast cancer treatment.
- Can be utilized with timed intercourse or Intra-uterine insemination (IUI).

38

TREATMENT: INFERTILITY

- Gonadotropins. Expensive. Frequent monitoring. High risk of high order multiples
- IVF with freeze all embryo cycle and future transfer of a single embryo.

In Vitro Fertilization
① egg production stimulated by hormone therapy
② eggs retrieved from ovary
③ sperm sample provided
④ eggs and sperm combined to allow fertilization
⑤ fertilized eggs introduced into uterus
Infographic: FDA/Renée Gordon

39

IMPACT OF WEIGHT ON FERTILITY

- BMI is a predictor of successful pregnancy and childbirth.
- Extremes of weight adversely impact egg quality.
- Risk of pregnancy loss and stillbirth are increased with BMI > 30.
- Reduced fertility treatment success with BMI > 35 and < 18.

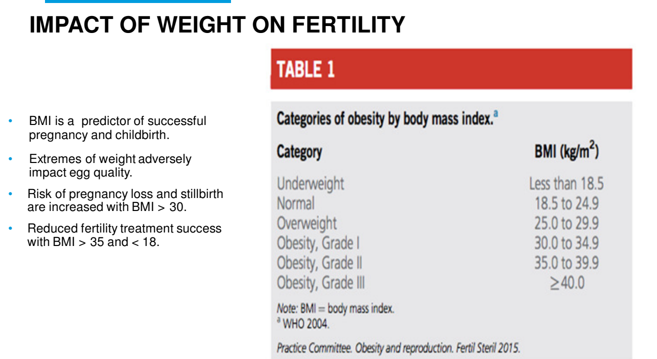

TABLE 1

Categories of obesity by body mass index.[a]

Category	BMI (kg/m^2)
Underweight	Less than 18.5
Normal	18.5 to 24.9
Overweight	25.0 to 29.9
Obesity, Grade I	30.0 to 34.9
Obesity, Grade II	35.0 to 39.9
Obesity, Grade III	$\geq$40.0

Note: BMI = body mass index.
[a] WHO 2004.

Practice Committee. Obesity and reproduction. Fertil Steril 2015.

40