PCOS for the Primary Care Provider

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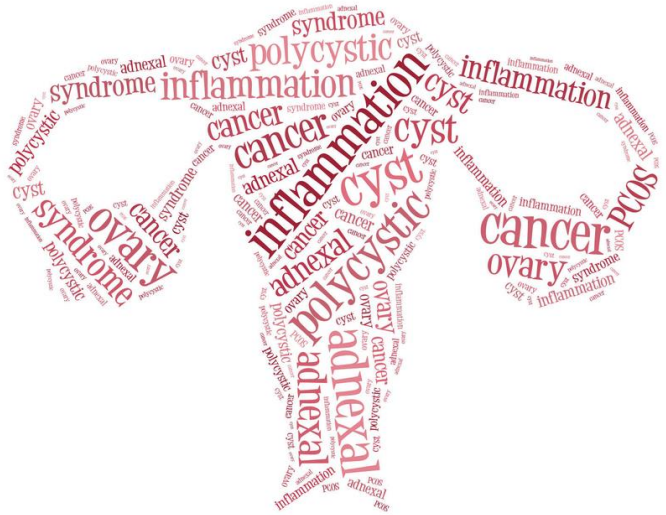
No Disclosures

Objectives

At the end of this presentation, audience members will be able to:

- Explain the etiology, risks factors and pathophysiology of PCOS.
- Describe PCOS symptom presentation and diagnosis.
- Compare and contrast the various pathologic conditions related to PCOS.
- Summarize physical exam findings, diagnostic evaluation and treatment for PCOS.
- Summarize patient care recommendations for polycystic ovarian syndrome (PCOS).
- Apply evidence-based medicine to case-based learning scenarios.

What is PCOS?



- Polycystic Ovary Syndrome
  - Most common endocrine reproductive disorder
  - Globally 5-15% of adult females; 6% adolescent girls
  - Affects females 18-44
  - Hormonal imbalance leads to numerous cysts and irregular menstrual periods which causes infertility
  - Syndrome is clinical and biochemical and encompasses a spectrum of features from mild to severe symptoms

- Reproductive – Metabolic – Psychologic

What is PCOS?

- Exact etiology is unknown
- PCOS involves interaction of hormones that can lead to an ↑ in LH and normal or ↓ FSH which equals ↑ production of testosterone compared to estradiol
- High levels of insulin; Insulin resistance
- Genetics

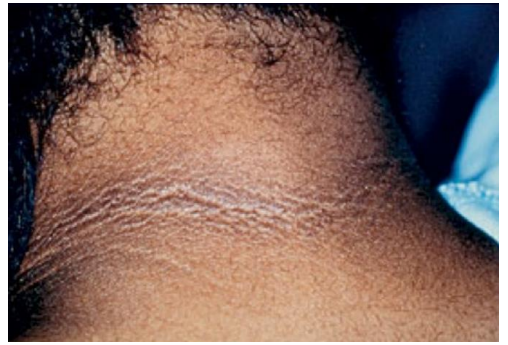
Risk Factors

- Genetic and Environmental
  - Environmental
    - Obesity
    - Diet - Sedentary lifestyle
    - Infectious mediators
    - Chemicals (endocrine disruptors)
  - Genetic factors
    - Family history
    - 241 gene variations questioned
      - CAPN10, Cytochrome family p450, Insulin gene, AR, FTO, FSHR, etc

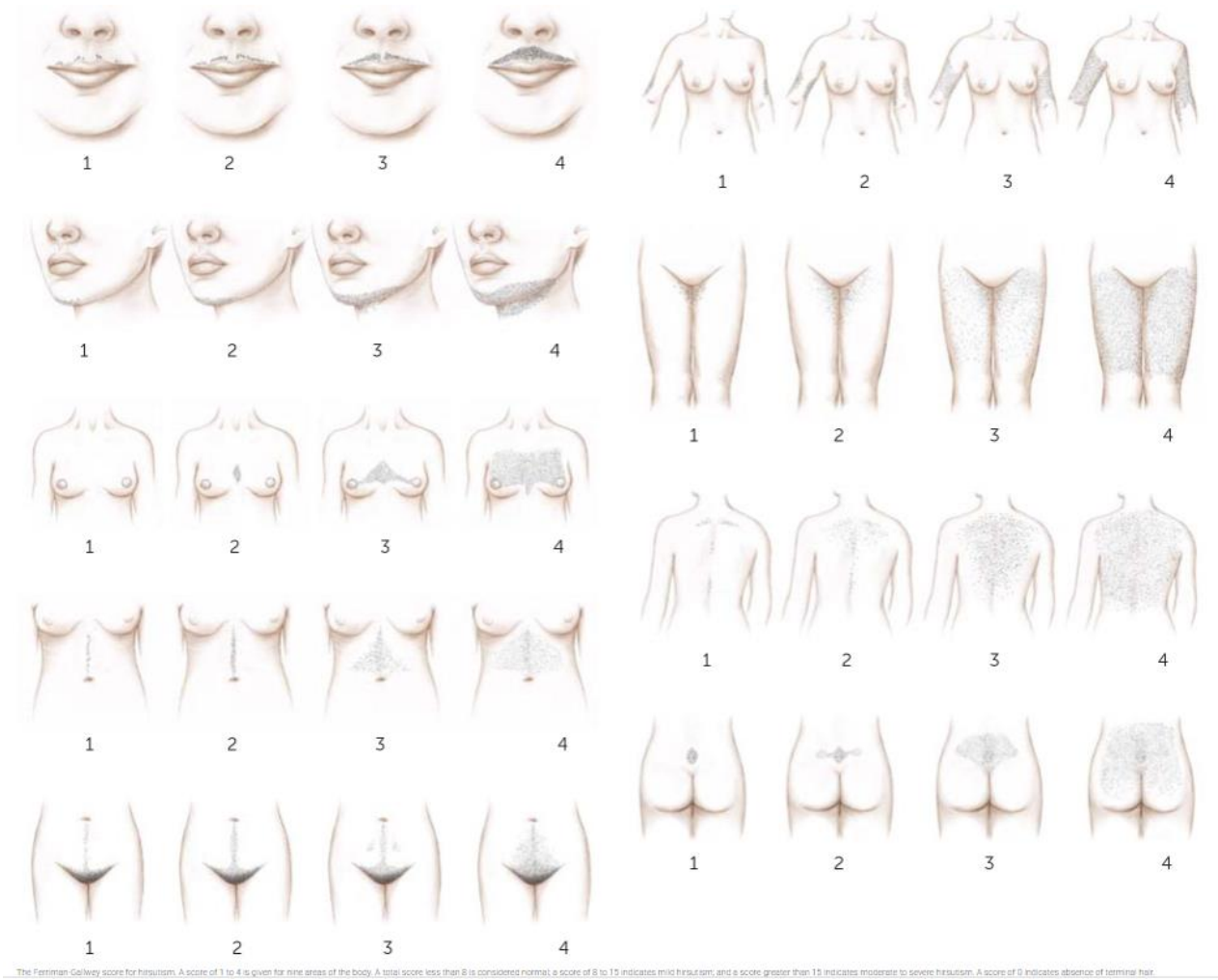
Symptom Presentation

- Begins around puberty; gradually progress
- Symptoms after 30+ or progress rapidly may indicate other causes

- ↑ androgen
  - Clinical: acne, hirsutism, androgenic alopecia **OR**
  - Biochemical: elevated free testosterone, total testosterone or DHEA
- Oligomenorrhea (<10 menstrual cycles per year or anovulation, >45 days, >90 days for any one cycle)
- ↑ insulin resistance causes obesity
  - Acanthosis nigricans; skin tags
- Infertility (70%)

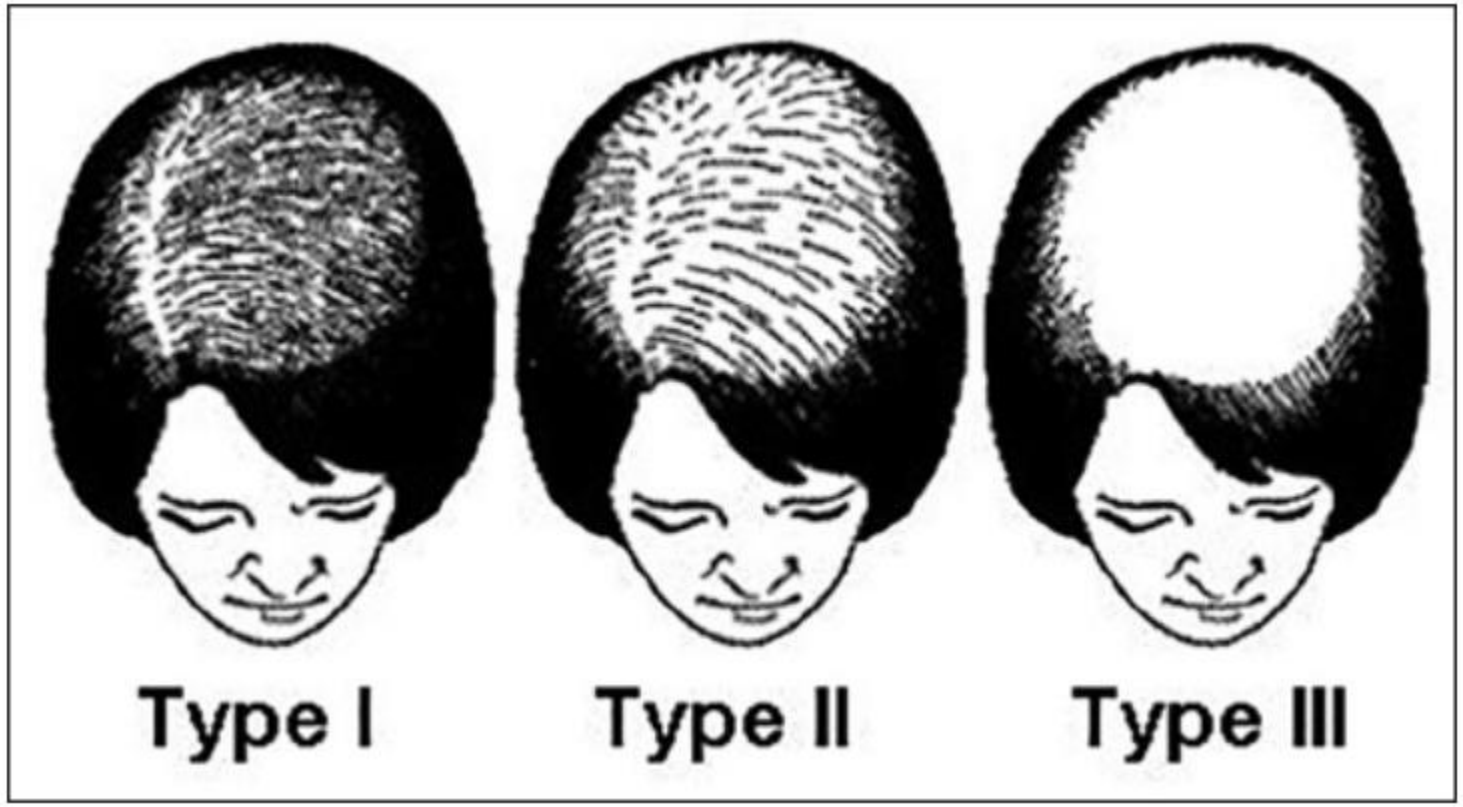


Physical Exam Findings

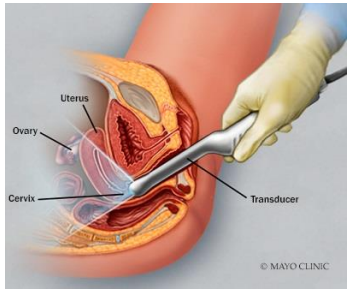


The Ferriman-Gallwey score for hirsutism. A score of 1 to 4 is given for nine areas of the body. A total score less than 8 is considered normal; a score of 8 to 15 indicates mild hirsutism; and a score greater than 15 indicates moderate to severe hirsutism. A score of 0 indicates absence of terminal hair.

Physical Exam Findings



Diagnosis



- Diagnosis of exclusion; exclude all other causes of hyperandrogenism
  - ***Rotterdam criteria (2003) - ADULTS - irregular menstrual cycle, elevated androgen level, presence of cysts
    - Require 2 out of 3 criteria *ultrasound is **NOT** necessary for diagnosis
      - Androgen excess (clinical or biochemical)
      - Ovulatory dysfunction (oligomenorrhea or amenorrhea)
      - Polycystic ovary morphology by ultrasound (preferably transvaginal)
        - Follicle count: ≥25 with a diameter of 2-9 mm in one or both ovaries
        - Ovarian volume: one or both ovaries >10 cc (with no follicle >10 mm and volume used only when follicles cannot be reliably counted)
  - AE-PCOS Society (2006) - ADOLESCENTS - Biochemical and clinical evidence of hyperandrogenism and dysfunctional ovaries
    - Excludes polycystic ovarian morphology as this is not often present in adolescents

Diagnosis

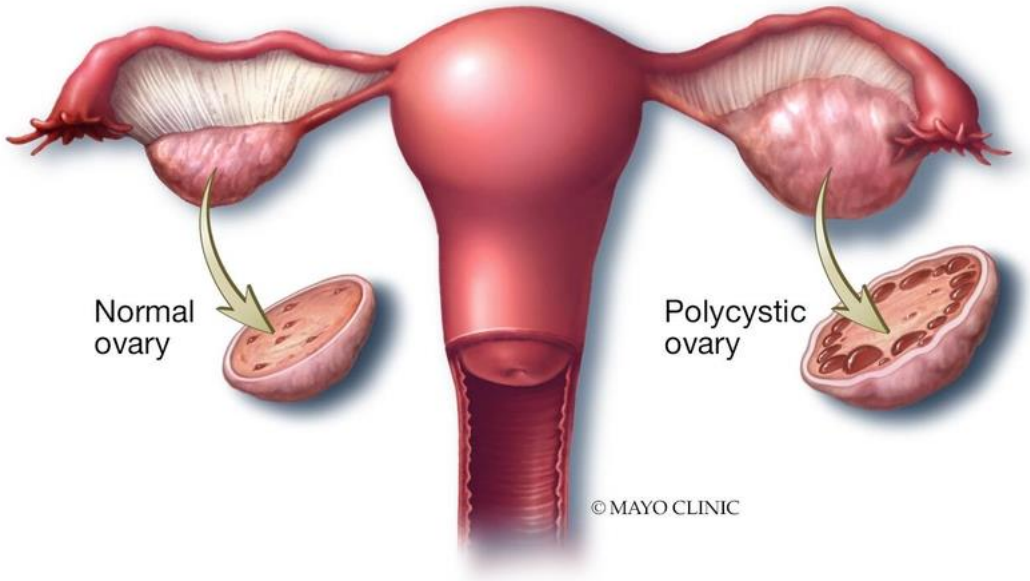
- Exclude other causes
  - Ovulatory dysfunction
    - Pregnancy: Pregnancy test
    - Thyroid disorder: TSH
    - Hyperprolactinemia (galactorrhea/milky discharge): Prolactin
    - Ovarian failure (menopause symptoms): Estradiol
    - Hypothalamic dysfunction (amenorrhea): A progesterone challenge (10 days of oral progesterone, should expect a withdrawal bleed a few days after stopping); if no withdrawal bleed check FSH and LH
      - FSH low/normal and LH high in PCOS
      - FSH and LH both low in hypothalamic dysfunction
  - Hyperandrogenism
    - Congenital adrenal hyperplasia (RARE): Basal serum 17- hydroxyprogesterone level (early morning, before 8 AM)
    - Androgen producing tumor (moderate to serve hirsutism or rapid onset): Total testosterone and DHEAS
    - Cushings Disease: (abd striae, dorsocervical fat, proximal myopathy, easy bruising): 24 hr urinary free cortisol or an overnight dexamethasone suppression test

Diagnosis

- Laboratory tests may include:
  - Total and bioavailable testosterone
  - Dehydroepiandrosterone (DHEA) sulfate
  - 17-hydroxyprogesterone

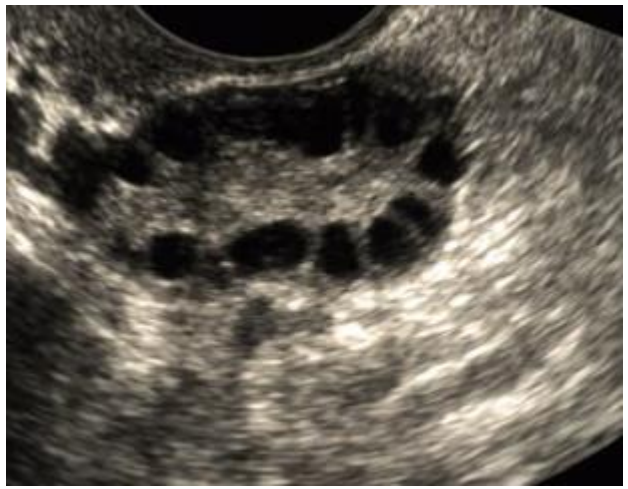
- If indicated, other tests may include:
  - Androstenedione
  - Screening for Cushing syndrome
  - LH and FSH
  - Prolactin
  - Anti-Müllerian hormone (not YET adequate for PCOS dx)

- Testing for metabolic complications should be done periodically:
  - Fasting glucose
  - HbA1c
  - Lipids
  - Liver enzymes



Diagnosis

- Oral contraceptives interfere with androgen assessment and may minimize hirsutism, acne and can affect biochemical testing
- PCOS can exist WITHOUT multiple cysts in the ovaries; Multiple ovarian cysts WITHOUT hyperandrogenism/ovulatory dysfunction does NOT confirm PCOS



Associated Comorbidities

- Reproductive
  - Hyperandrogenism (acne; alopecia)
  - Irregular menses
  - Infertility
  - Pregnancy complications
    - Higher rates of miscarriage, GDM preeclampsia, C-section
  - Endometrial cancer
- Metabolic
  - Obesity
    - OSA, nonalcoholic fatty liver disease, acanthosis nigricans, skin tags
  - Impaired fasting glucose & DM type 2
  - CV disease
    - Dyslipidemia, hypertension
- Psychological
  - Depression
  - Anxiety
  - Low self-esteem
  - Eating Disorders
  - Psychosexual dysfunction
  - Poor quality of life

Treatment - Acute

- 1st line – education, exercise and healthy eating
  - For overweight patients losing 5% of body weight can improve metabolic parameters, improve hyperandrogenism and restore ovulation
  - For normal weight patients exercise and healthy eating can improve insulin resistance and other metabolic characteristics
- Assess for emotional wellbeing
- Treatment otherwise guided by the **MOST** concerning symptoms

Treatment - Acute

- Hyperandrogenism
  - Oral contraceptives (especially those with drospirenone as the progestin)
    - ↑VTE risk
  - Spironolactone (for hirsutism and acne)
    - Titration to a higher dose of 150-200m mg/day is often required
    - Requires reliable contraception
    - Effects may be delayed 6 months
    - Periodic K+ monitoring is needed
  - Topical cosmetics (laser therapy, electrolysis, shaving); Finasteride 5 mg daily; local eflornithine hydrochloride cream 13.9% (for hirsutism; slows growth)
- Irregular menstrual periods
  - Combined hormonal contraceptives (pills, patch, ring); IUC

Treatment – Acute

- Infertility
  - Metformin
  - Weight loss – 10% weight loss can restore menses
  - Clomiphene
  - *Letrozole
  - Gonadotropins (2nd line)
  - In Vitro (3rd line)
- Metabolic abnormalities
  - Lifestyle intervention
  - Metformin, titrate up to 2,000 mg/day
  - Statin (if not planning on becoming pregnant)
    - Needs reliable birth control
  - In selected cases, glucagon-like peptide 1 (GLP-1) receptor agonists

Follow-up – Long Term

- Assessment for amenorrhea or oligomenorrhea and need for endometrial protection to prevent endometrial hyperplasia
  - 2-6-fold increased risk of endometrial cancer (often present before menopause)
  - Risks: obesity, no menses for >3 months, endometrial thickness > 12 mm
  - If patient is not trying to get pregnant
    - Oral contraceptives, cyclic or continuous
    - Provera 10 mg PO for the first 10 calendar days of every month
    - Progesterone IUC
    - Subdermal contraceptive
    - Depo-Provera

Follow-up – Long Term

- Warrants periodic screening for metabolic complications
  - Glucose
    - ↑ prevalence of GD, impaired glucose tolerance and DM2 (5-fold in Asia, 4-fold in America and 3-fold in Europe)
    - Baseline and every 1-3 years depending on risk factors
    - Yearly for those with IGT
  - Lipids
  - Weight
  - Blood pressure
  - OSA ONLY if symptoms
  - ↑ risk of coronary calcifications
  - ↑ risk of venous thromboembolic disease (1.5X)
    - PCOS and on a OCP have a 3.7X

Follow-up – Long Term

- Psychologic
  - High prevalence of anxiety and depression
    - PCOS quality of life tool (PCOSQ) or the modified PCOSQ
      - 26 items on a 7-point Likert-type scale
      - Focuses on 5 domains: emotions, body hair, weight, infertility, and menstrual
    - PHQ-9/PHQ-2
    - Other appropriate tools
  - If necessary, consider therapy and/or pharmacologic treatment
    - Caution for use of agents that can exacerbate weight gain
  - Increased psychosexual function
  - Negative body image/eating disorders

Prevention and Lifestyle Improvements

- Prevention of excess weight gain - **1° intervention**
  - Healthy eating
    - Variety of acceptable approaches
    - Should be based on dietary restrictions and cultural food preferences
  - Regular physical activity
    - Minimum of 150 min/week of moderate intensity OR 75 min/week of vigorous intensity
    - Include muscle strengthening activities on 2 non-consecutive days/week
    - Aim at 30 minutes most days
    - Aim at 10,000 steps per day
  - Behavioral strategies

  - Dietician or obesity specialist
  - Health/wellness coach
  - Personal trainer
  - Cognitive behavioral therapy specialist
  - Dietary/Fitness tracking

Complications

- Infertility
- ↑ risk of endometrial cancer
- Acne scarring; worsening hirsutism; Alopecia
- Metabolic complications
  - DM
  - Hypertension
  - Hyperlipidemia
  - OSA
  - Cardiovascular risks
- ↑ mental health symptoms

Case 1

- A 30-year-old female presents for infertility evaluation. She is an avid runner and completes 1-2 marathons per year. She reports stopping her OCP when she got married 2 years ago but she has not had a regular period since. She reports her periods were regular on her OCP but since stopping she has only had 2 periods. Her and her husband have been trying to conceive but without periods to guide timing they have been unsuccessful. Her past medical history includes exercise induced asthma with use of prn albuterol and acne requiring Isotretinoin as a teenager and OCPs as an adult. She denies hirsutism and alopecia. Her BMI is normal, and her last screening glucose was 82. The rest of her review of systems is unremarkable.

Case 1

- It sounds like PCOS…..does she meet diagnostic criteria? How would you diagnose?

Yes, but make sure you have excluded other causes before!

Pregnancy test; TSH

- Rotterdam criteria (2003) - ADULTS - irregular menstrual cycle, elevated androgen level, presence of cysts
  - **Require 2 out of 3 criteria** *ultrasound is not necessary for diagnosis
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Case 2

- A 37-year-old G2P2 female presents to the primary care office for her scheduled Pap smear. Her past medical history is only significant for PCOS in which she required ovulation induction for with both of her pregnancies. She reports since giving birth to her last child 3 years ago she has only had a handful of periods. She does not desire future pregnancy but has declined birth control as her husband had a vasectomy. She has no concerns with acne, hirsutism or alopecia. How would you manage her PCOS going forward?

Case 2

- Endometrial protection
- Periodic metabolic screening
- Assess mental health
- Associated condition screening
- Continued exercise and healthy eating
- Optimize weight
- Patient education and prevention!

Summary

- Recognize the criteria appropriate to diagnose PCOS
- Before diagnosis, rule out possible causes
- PCOS is complex and symptoms can be mild or severe and comorbidities exist
  - Screening for comorbidities is important
- Don’t forget long term follow-up
- Women with PCOS who have irregular periods need endometrial protection

Questions

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