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Irregular Menses: When is it PCOS?

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Disclosures

I have no conflict of interest of any kind related to this presentation.

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Objectives

- Describe abnormal menstrual patterns in adolescents

- List the diagnostic criteria and evaluation indicated for diagnosis of PCOS in adolescents

- Generate an evidence-based, patient-centered treatment approach to reduce symptoms and mitigate disease-associated long-term sequelae

Case #1

14 yo presents for WCC. She reports menarche was at age 12 years. She reports her period was irregular during her first year after menarche but seems to be more regular this year.

Is this normal?

She reports her periods last 3-5 days and she uses 3 pads per day at their heaviest. She has mild cramping on the first day. The longest between menstrual periods was 3 months. This only occurred once in the past year.

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Can we reassure this patient that her menstrual patterns are normal?

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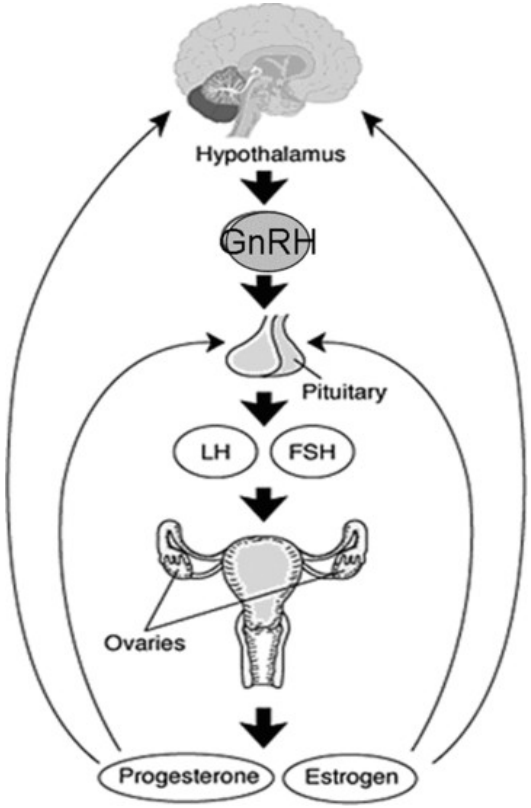
Menstrual Patterns in Adolescents

"It's normal to have irregular periods in the first few years."

- Puberty initiated by pulsatile GnRH that triggers LH and FSH secretion
- Hypothalamic-pituitary-ovarian (HPO) axis matures throughout adolescence
- Variability in menstrual patterns result from anovulation associated with immature HPO axis



What is abnormal?

TECHNICAL REPORT

for the

INTERNATIONAL EVIDENCE-BASED GUIDELINE FOR THE ASSESSMENT AND MANAGEMENT OF POLYCYSTIC OVARY SYNDROME

2023 UPDATE

MONASH University

European Society of Endocrinology
The voice for endocrinology

asrm
American Society for Reproductive Medicine

CREWHiRL
Centre for Research Excellence in Women's Health in Reproductive Life

eshre
SCIENCE MOVING PEOPLE MOVING SCIENCE

ENDOCRINE SOCIETY

CREPCOS
Centre for Research Excellence in Polycystic Ovary Syndrome

Menstrual Patterns in Adolescents

- First post-menarcheal year
  - Approx 50% of cycles are anovulatory
  - 80% of cycles occur in a predicatable range of 21-45 days with bleeding lasting 2-7 days
- Third post-menarcheal year
  - 95% in 21-45 day range
- Earlier onset associated with early onset of regular ovulatory cycles

What is abnormal?

- No menses by age 15 or
  > 3 years post thelarche
- > 1 year post menarche experiencing > 90 days for any one cycle (interval between periods)
- > 1 to < 3 years post menarche experiencing < 21 days or > 45 days between periods
- > 3 years post menarche experiencing < 21 days or > 35 days or < 8 cycles per year

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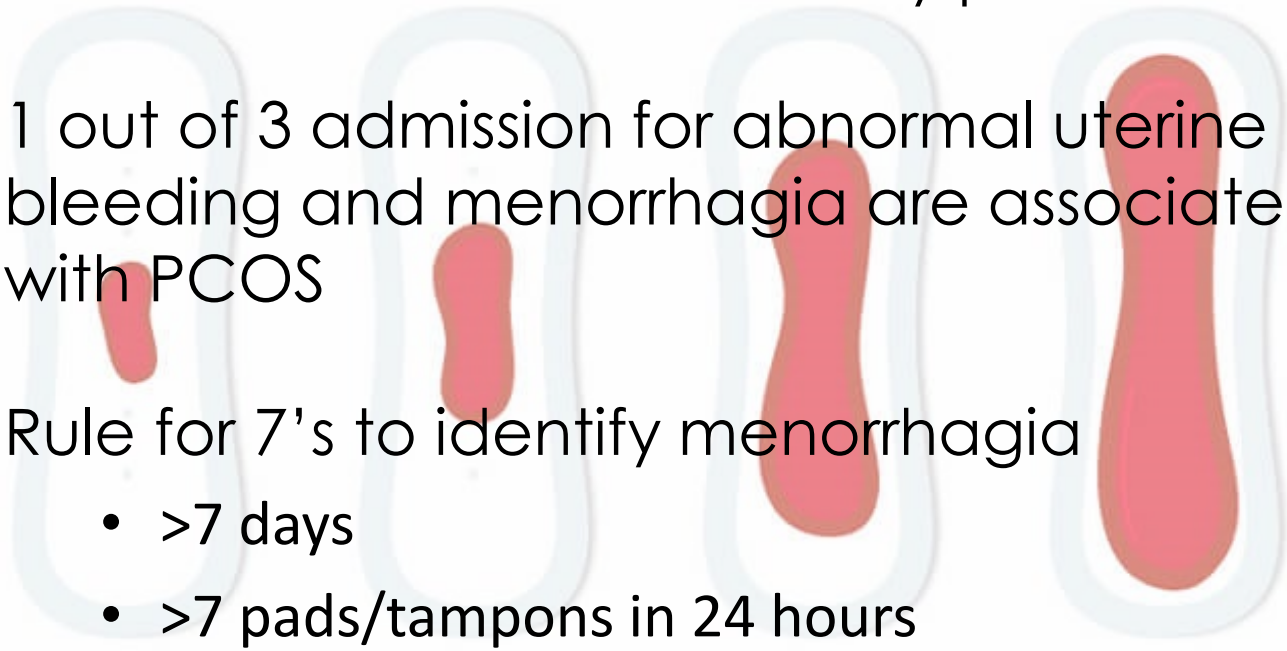
What is abnormal?

- Anovulation can cause heavy periods too
- 1 out of 3 admission for abnormal uterine bleeding and menorrhagia are associated with PCOS
- Rule for 7's to identify menorrhagia
  - >7 days
  - >7 pads/tampons in 24 hours



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In addition to menstrual irregularity which of the following are criteria for diagnosis of PCOS?

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Evolution of Diagnostic Criteria

Table 1 PCOS phenotypes included in specific diagnostic criteria

Diagnostic criteria	PCOS phenotype			
	AE + OD	AE + PCOM	PCOM + OD	AE + PCOM + OD
NIH 1990	+			
Rotterdam 2003/2006	+	+	+	+
AE-PCOS society 2006	+	+		+
NIH 2012	+	+	+	+

All criteria recommend exclusion of other causes. AE, androgen excess; OD, ovulatory dysfunction; PCOM, polycystic ovary morphology; PCOS, polycystic ovary syndrome.

- Challenged by menstrual irregularity and hyperandrogen symptoms typical of adolescence
- Poorly defined testosterone norms
- Normal adolescents can have polycystic ovarian morphology

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PCOS Diagnostic Criteria (2023)

- ☑ Ovulatory dysfunction
- Evidence of androgen excess
- Exclusion of other diagnoses

Evidence of Androgen Excess

- Clinical Evidence
  - Moderate to severe hirsutism
  - Severe or persistent acne
- Biochemical Evidence
  - Elevated total and/or free testosterone*

*Best evidence to indicate androgen excess

Hirsutism

- Defined as male pattern hair growth
- Terminal hairs instead of vellus hairs
- Recommend asking about hair removal and/or use visual aid
- Defer to patient level of concern

Ferriman-Gallwey Scoring

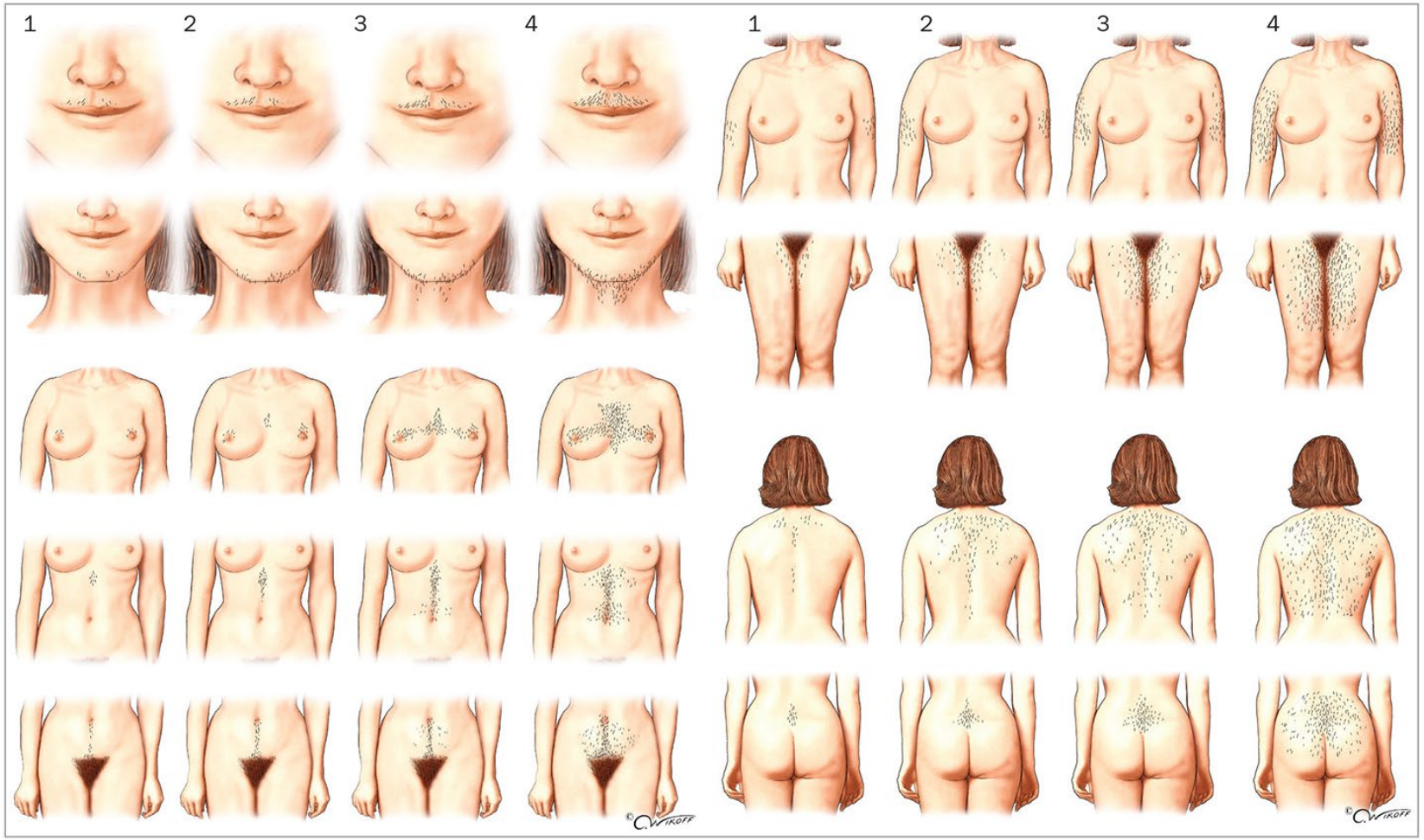

Figure 2. Modified Ferriman–Gallwey scoring system for hirsutism. Nine body areas (upper lip, chin, chest, upper abdomen, lower abdomen, arms, thighs, upper back and lower back) are scored from 1 (minimal terminal hairs present) to 4 (equivalent to a hairy man). If no terminal hairs are observed in the body area being examined the score is zero (left blank). Clinically, terminal hairs can be distinguished from vellus hairs primarily by their length (i.e. 0.5 cm) and the fact that they are usually pigmented. A score above 4 to 6 indicates hirsutism.

https://medicinetoday.com.au/mt/2024/jan-feb/feature-article/management-polycystic-ovary-syndrome-role-primary-care

Acne

- Varying definitions regarding severity
  - Defer to patient perception
- Refractory to treatment
  - Topical retinoid
  - Topical or oral antibiotic
- Hormonal distribution
  - Lower face/jawline
  - Back/chest

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Androgen Excess

- Elevated total and/or free testosterone
  - Total testosterone >55 ng/dL
- Free testosterone calculation
  - SHBG, albumin, total testosterone
- Free Androgen Index (FAI)
  - Total testosterone (nmol/L)/SHBG (nmol/L) x 100
  - Normal = 7-10

PCOS Diagnostic Criteria

- [x] Ovulatory dysfunction
- [x] Androgen excess
- [ ] Exclusion of other diagnoses

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What is the differential diagnosis for irregular menses and/or hyperandrogenism?

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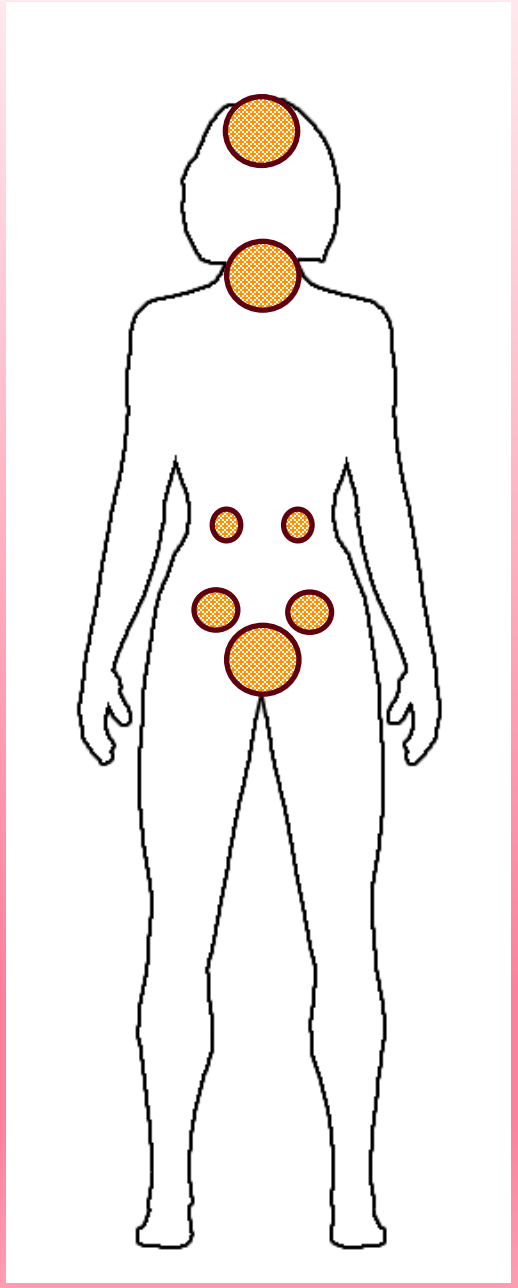
Differential Diagnosis

- Hypothalamic Suppression
- Pituitary Disorder
- Thyroid Disorder
- Adrenal Disorders
- Ovarian Disorders
- Pregnancy
- Anatomic Abnormality
- Idiopathic hirsutism
- Medications



Laboratory Studies

- Pregnancy test
- LH/FSH
- Prolactin*
- TSH/FT4 (Thyroid-stimulating hormone/free thyroxine)
- Total/Free Testosterone*
- DHEA-S (dehydroepiandrosterone sulfate)*
- 17-OHP (17-hydroxyprogesterone)*
- Androstenedione*

*First morning values more accurate

PCOS Diagnostic Criteria

- ☑ Ovulatory dysfunction
- ☑ Androgen excess
- ☑ Exclusion of other diagnoses

- What about ultrasound findings?

Case #2

17 yo with intervals between periods averaging 32 days. Menarche was at age 13 yrs. Each period lasts 5-6 days. The first 2 days of her periods are heavy and very painful. Her mother and maternal aunt have PCOS and they are concerned that she also has PCOS. She has scattered papules and pustules on her forehead and scores a 6 on the Modified Ferriman-Gallwey scale.

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What would be the best next step for evaluation and/or management of this patient?

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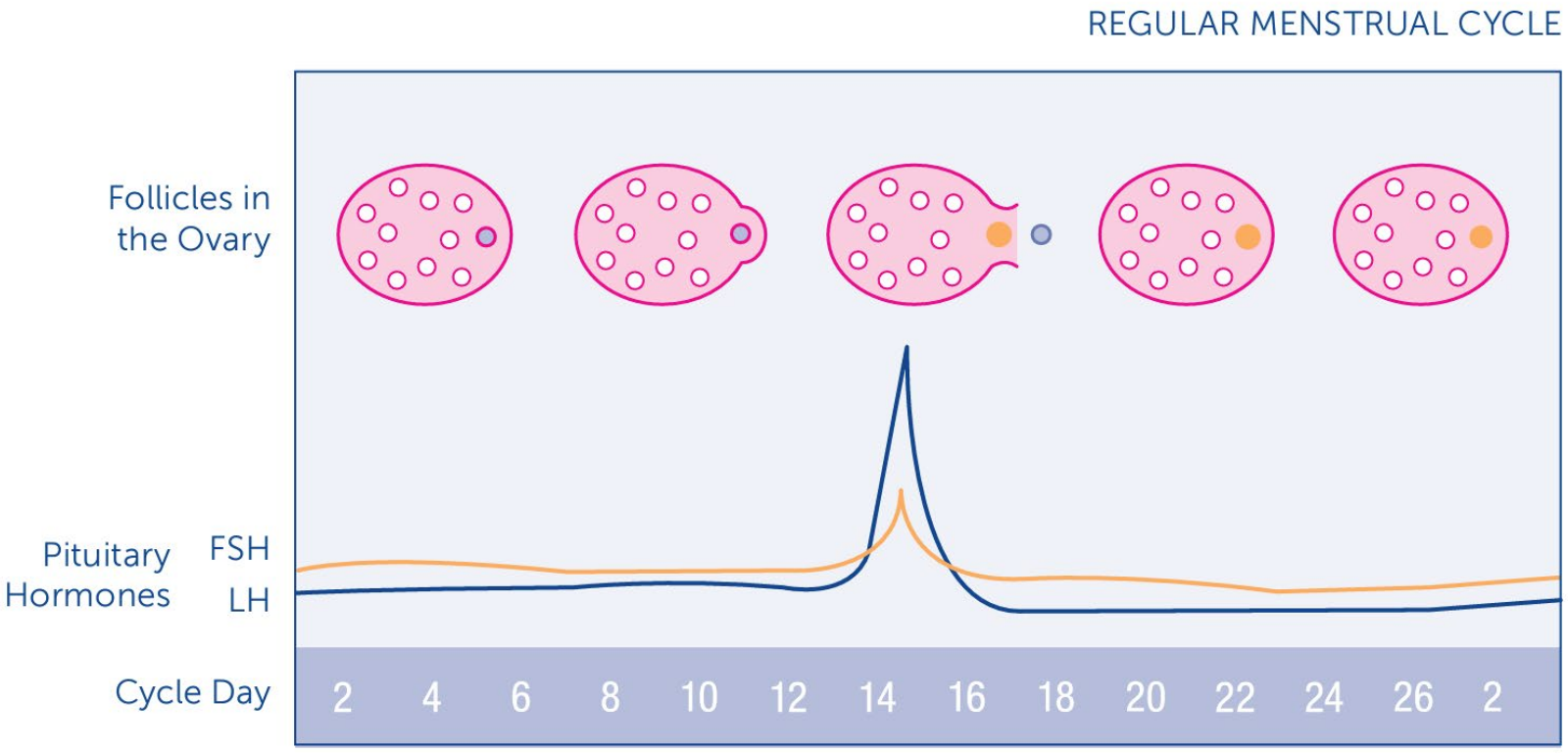
Polycystic Ovarian Morphology



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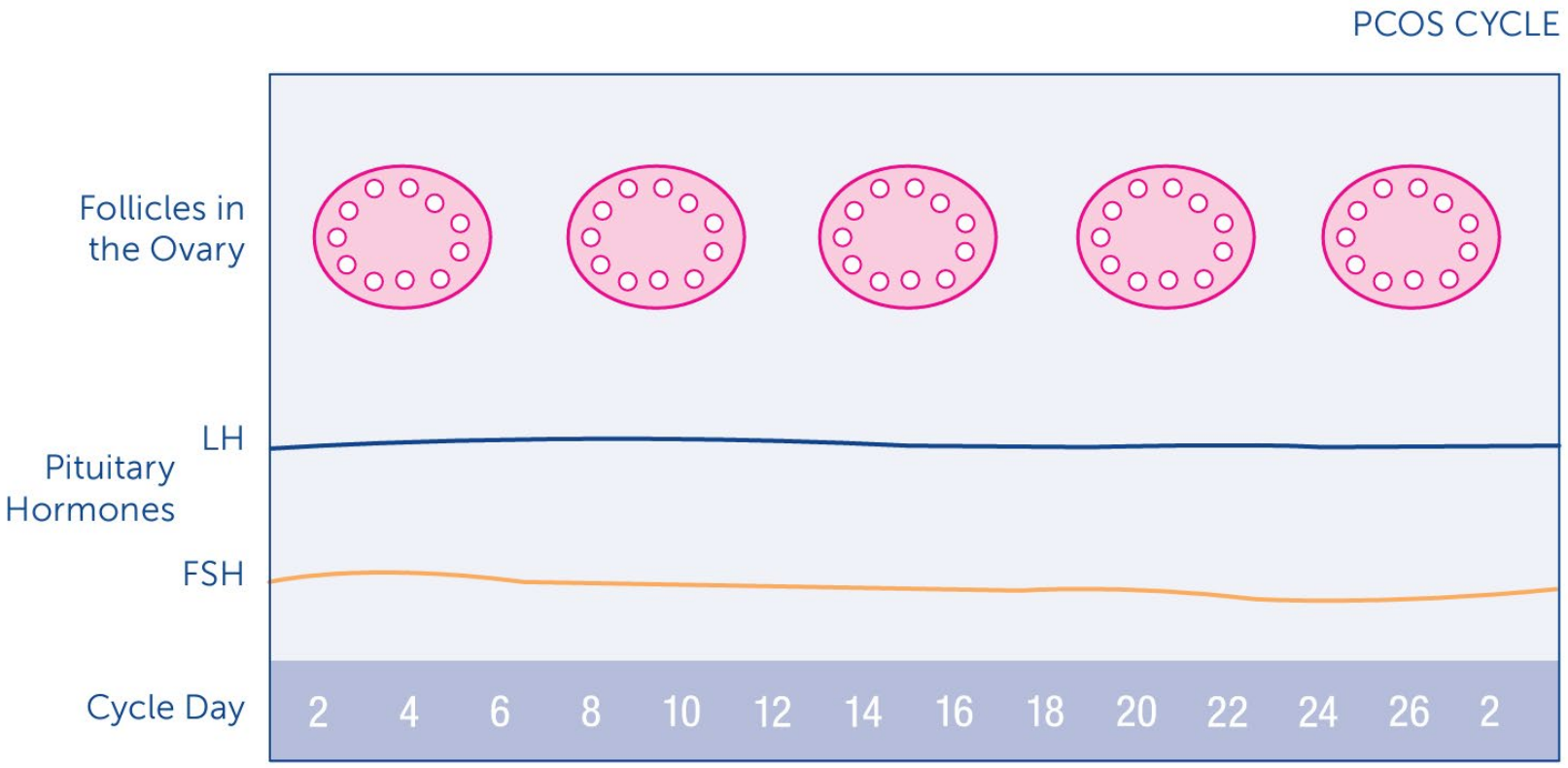
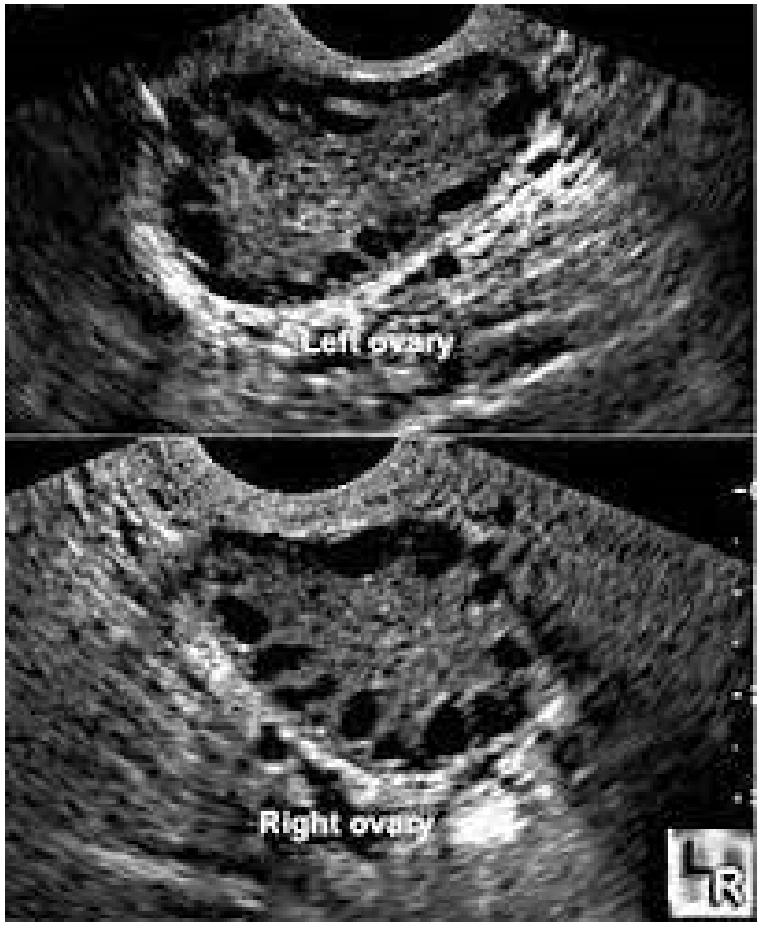
Polycystic Ovarian Morphology



Polycystic Ovaries

- >/= 20 antral follicles (2-9mm)
- Enlarged ovaries >10cm^3

- 30-40% adolescents have PCOM on ultrasound without associated hormonal or menstrual abnormalities



When They Don't Meet Criteria

"At Risk of PCOS"

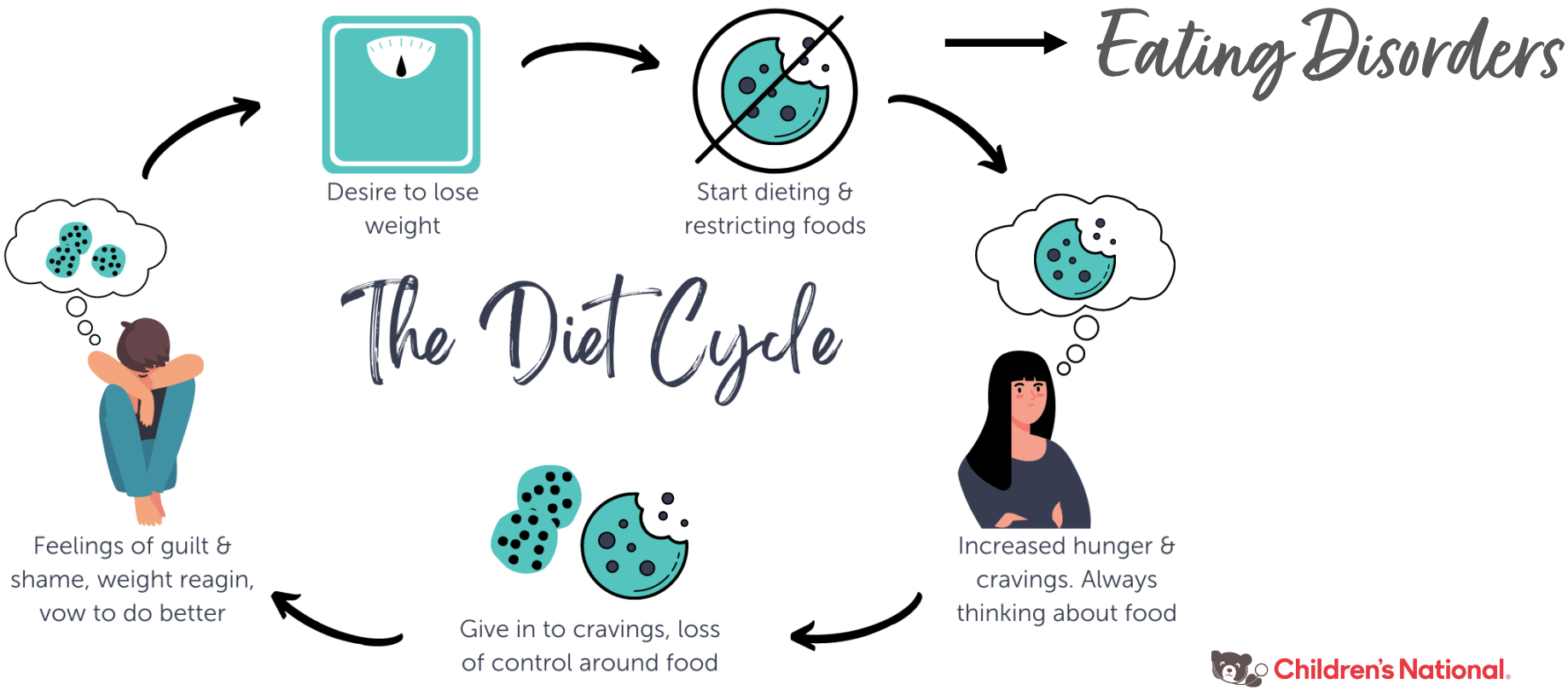
- Treatment of symptoms can occur without definitive diagnosis
- Monitor symptoms and reassess signs and symptoms over time
- Elevated BMI and insulin resistance associated with PCOS but not appropriate for diagnostic purposes

Treatment Options

- Treatment Goals:
  - Improved quality of life
  - Reduced symptoms and comorbidity risk
- First line recommendation → lifestyle modification
- Proceed with caution!
- Refer to knowledgeable dietitian

- Physicians report lack of training and low confidence in nutrition knowledge, dedicating 2-3 minutes per visit to nutrition counseling
- Only ¼ of medical schools offer the recommended 25 hours of nutrition training
- Only 20% of physicians report meeting the recommended 5 a day fruit/veggie intake per day themselves
- Weight loss often recommended to address physiological complications occurring largely due to factors beyond individual control
- Weight loss attempts following medical visits are often self-directed by patient

Dieting & Self-Directed Weight Loss: The Consequences



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Medications

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Combined Hormonal Contraceptives (CHC)

- Mechanism of Action
  - Suppress HPO axis reducing ovarian androgen production
  - Increase sex hormone binding globulin decreasing circulating androgens

- Clinical Effects
  - Menstrual regulation
  - Reduction of acne and hirsutism
  - Decreased endometrial hyperplasia

Hormonal Contraceptives

- Start with 20 mCg ethinyl estradiol combined pill with a progestin of your choice or patch or ring
- If ethinyl estradiol is contraindicated, progestin only option will:
    - Improve menstrual patterns
    - Prevent/reduce endometrial hyperplasia
- Progestin Only Pill Options
    - Drospirenone*
    - Norethindrone
    - Norgestrel
- Implant, IUD or Injection

Metformin

- Initiate if Type 2 DM or evidence of insulin resistance
- Associated with improved weight reduction, glycemic regulation and reduced hirsutism
- Take with food and MVI

- Extended Release (XR) Regimen
  - 500 mg daily x 2 weeks
  - 1000 mg daily x 2 weeks
  - 1500 mg daily

- Baseline labs: CBC, BUN/Cr, AST/ALT

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Spironolactone

- Aldosterone antagonist with antiandrogenic effects
- Teratogenic → consider contraceptive
- Metformin PLUS spironolactone better than either solo
  - Decreased menstrual irregularity, hirsutism, testosterone levels and insulin resistance

- Regimen
  - 50 mg daily x 1 week
  - 100 mg daily x 1 week
  - 100 mg BID

- Baseline labs: Consider BMP

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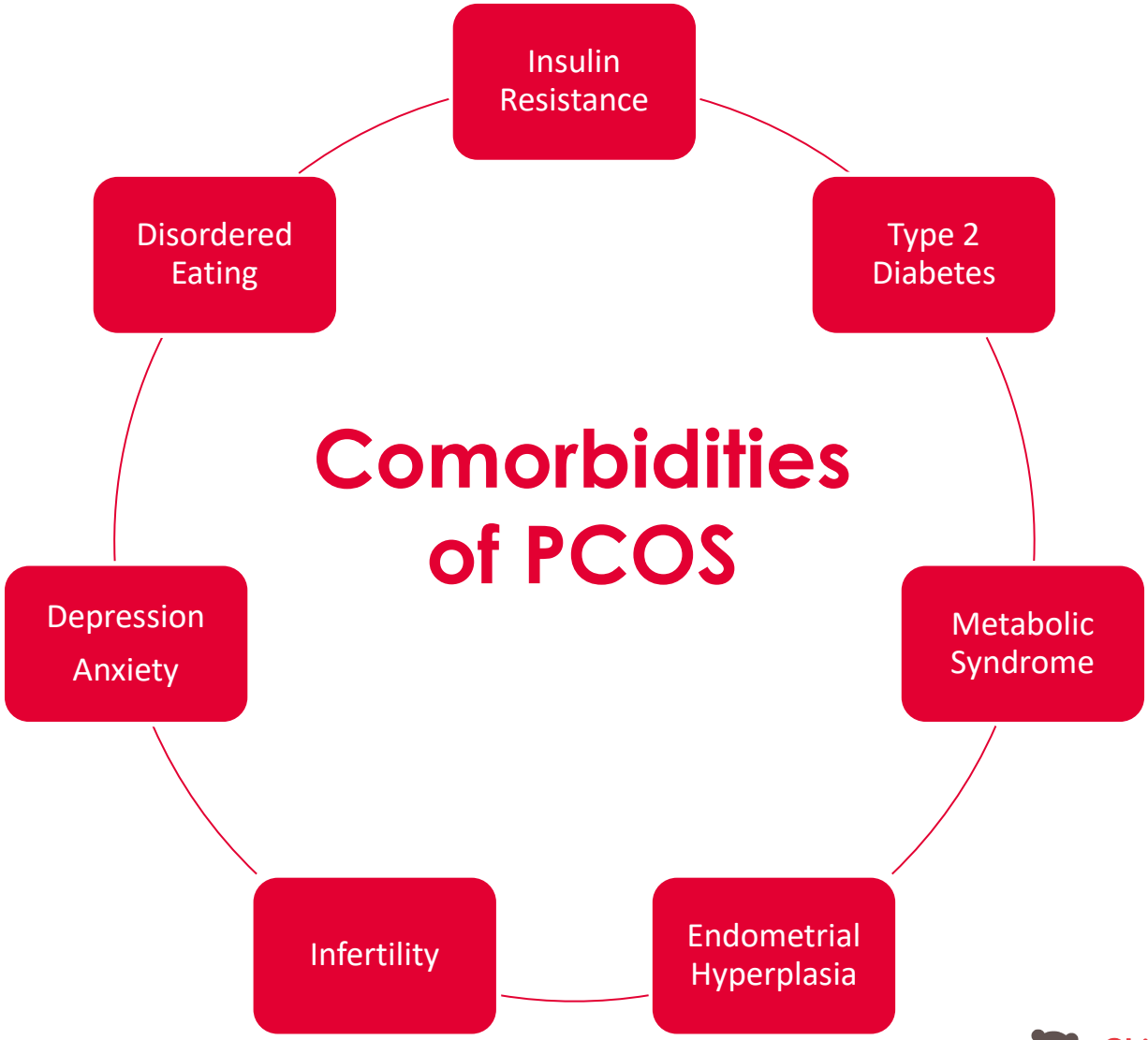
Hair Removal Options

- Eflornithine cream
- Electrolysis, laser, depilatories, plucking, waxing, shaving, bleaching



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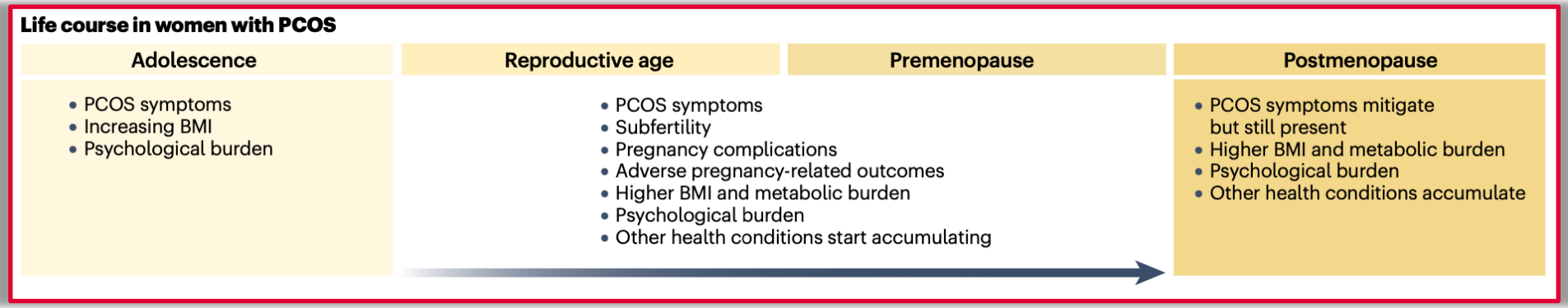
Life Course



Early Identification & Treatment

+

Ongoing Monitoring & Screening

=

Improved Quality of Life & Health Outcomes

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Ongoing Follow-Up

- Fasting lipid panel
- Fasting glucose/insulin or Hgb A1C
- Consider 2 hour glucose tolerance test
- Screening for depression and anxiety
    - PHQ-9 and GAD-7
- Screening for eating disorders
    - SCOFF
- Can repeat testosterone levels after 3+ months of treatment
- Trial off medications 1+ years after treatment initiation

PCOS Take Aways

- Refined definition of menstrual irregularity
- Clarification of diagnostic criteria
- Treatment and monitoring recommendations

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Audience Q&A Session

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Resources

https://youngwomenshealth.org/

Center for Young Women's Health

- PCOS (Polycystic Ovary Syndrome): General Information
- PCOS: Insulin and Metformin
- PCOS: Nutrition Basics
- PCOS: PCOS-Friendly Foods, Snacks, and Grocery Shopping Tips
- PCOS: Preparing for Your Oral Glucose Tolerance Test
- PCOS: Quiz
- PCOS: Sample Menus and Recipes
- PCOS: Spironolactone
- PCOS: The Oral Contraceptive Pill
- PCOS: Worksheets

Ask PCOS

https://www.askpcos.org/

2023 IntNal Guidance: https://www.monash.edu/medicine/mchri/pcos/guideline

Testosterone calculator: https://www.issam.ch/freetesto.htm

Eating Disorder Screener: https://eatingdisorderscreener.org/

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