

Reproductive Endocrinology for the Internist

A. Common/important causes of irregular menses:

Condition	Diagnostic clues
Associated with hirsutism:	
Polycystic ovary syndrome	Chronic anovulation (irregular menses, often since puberty) + elevated circulating androgens +/- polycystic ovaries on U/S
Congenital adrenal hyperplasia (non-classic)	Elevated 17-OH progesterone level* (in most common form of CAH): Basal > 6 nmol/L Stimulated > 30 nmol/L * test in follicular phase (days 3-8 of cycle or when serum progesterone < 8 nmol/L)
Cushing's syndrome	Clinical features of Cushing's + elevated 24-hour urine free cortisol (> 135 nmol/24 hrs)
Adrenal adenoma or carcinoma	Rapid onset or progression of symptoms + DHEA-S > 16 μ mol/L
Ovarian tumor	Rapid onset or progression of symptoms + testosterone > 6 nmol/L
Not associated with hirsutism:	
Prolactinoma	Presents with irregular menses or infertility, galactorrhea, sometimes headache or vision change
Hypothyroidism	Presents with weight gain, cold intolerance etc. + high TSH

B. Approach to patient with irregular menses:

- history:
 - symptoms of hyperandrogenism (acne, oily skin, hirsutism, oligomenorrhea or amenorrhea)
 - onset and rate of progression of symptoms
 - medications

- family history
- physical examination:
 - blood pressure (increased in Cushing's & one form of CAH – 11-hydroxylase deficiency)
 - degree & extent of terminal hair growth
 - skin: acne, acanthosis nigricans, striae, fat pads
 - consider pelvic ultrasound
- labs:
 - free testosterone, DHEA-S
 - prolactin, TSH
 - 17-OH progesterone
 - fasting glucose, lipids
 - 24-hour urine free cortisol or overnight dexamethasone suppression test if signs of Cushing's

C. Treatment of PCOS:

- tailor to goals of patient (eg. fertility, control of acne/hirsutism, avoidance of long-term health consequences etc)
- ovulation induction:
 - eg. clomiphene, GnRH
 - ? metformin
- treatment of acne/hirsutism:
 - suppress ovarian androgen production:
 - oral contraceptives, estrogen or progesterone alone, GnRH
 - ? metformin
 - suppress adrenal androgen production:
 - glucocorticoids (used for CAH)
 - inhibit androgen action:
 - spironolactone, cyproterone acetate, flutamide (competitively bind androgen receptor)
 - finasteride (5 α -reductase inhibitor)
 - modify cardiovascular risk factors:
 - screen for diabetes or atherogenic lipid profile
 - lifestyle modification

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Clinical Scenario

Ms. T. J.

ID: 21 year-old student

CC: hirsutism and irregular menses

HPI:

- ?? irregular menses since menarche at age 13
- ?? acne & excessive hair growth on face, neck & lower back for 6 years
- ?? electrolysis -some effect
- ?? no desire for fertility at present

PMH:

Healthy

meds: none

Family History: sister - similar symptoms, required treatment for infertility
maternal uncle and grandmother - type 2 diabetes

Physical Examination:

Moderately obese
BP 140/90
moderately severe acne on face & back
terminal hair growth on chin, neck, lower back, abdomen
acanthosis nigricans at nape of neck
cardiovascular and respiratory exams normal
abdomen - normal, no striae

Labs:

testosterone	3.2 nmo/L (< 3.0)
DHEA-S	11.0 umol/L (< 11.0)
17-OH progesterone	3.0 nmo/L
fasting glucose	6.2 mmol/L
prolactin	26 (<20)
TSH	2.4