

Hirsutism

Background

1. Definition
 - Increase in androgen-dependent terminal hairs in women
2. General information
 - Increased androgen production causes terminal hair growth in parts of the body normally specific to men
 - Areolae, chest, back, anterior thighs
 - Virilization (caused by high levels of androgen)
 - Frontal balding, deepening of voice, increased muscle mass
 - Breast atrophy, clitoromegaly, hirsutism, infrequent or absent menses, loss of normal female body contour
 - Acne, increased libido
 - Normal variant depending on race and ethnicity should be considered

Pathophysiology

1. Pathology
 - Idiopathic
 - Medication-induced
 - Anabolic steroids, metoclopramide, phenothiazines, testosterone, progestins, danazol
 - Polycystic ovary syndrome
 - Most common cause
 - Presents around puberty
 - Symptoms gradually worsen with age
 - Congenital adrenal hyperplasia
 - Inherited disorder causing decreased cortisol production
 - Defects in 21-hydroxylase (95% cases), 11-beta-hydroxylase (5% cases), and other rare causes, shift adrenal steroidogenesis toward androgen overproduction
 - Ovarian cancer or adrenal neoplasm
 - May produce androgens
 - Characterized by rapid progression and virilization
 - Serum testosterone usually > 150-200 ng/dl
 - Cushing's syndrome
 - Hypercortisolism
 - Usually see abdominal striae, posterior neck fat pad, or proximal muscle weakness
 - Hyperthecosis
 - Severe insulin resistance syndromes
 - Hyperinsulinemia causes increased ovarian androgens and decreased sex hormone-binding globulin allowing for increased free testosterone
2. Incidence, prevalence
 - Up to 8% of women

3. Risk factors
 - Obesity
 - Screen for insulin resistance and risk factors for CAD
 - Family history
 - Up to 50% of women with hirsutism have family history of the disorder
 - Androgenic medications
4. Morbidity/ mortality
 - All secondary to underlying disease
 - Can cause significant quality-of-life issues

Diagnosics

1. History
 - Complete review of symptoms
 - Onset: rapid vs slow progression
 - Rapid progression suggests malignant/neoplastic process
 - Severity
 - Family history of hirsutism
 - Medication use
 - Abnormalities associated with hirsutism
 - Acne, alopecia, android obesity, cardiovascular disease, dyslipidemia, glucose intolerance/insulin resistance, hirsutism, hypertension, infertility, menstrual dysfunction
2. Physical exam
 - Hair mapping
 - Ferriman–Gallwey Scoring System for Hirsutism ¹
 - Evaluates extent of hair growth (score 0-4) in 9 areas
 - Score 8-15 is mild, score >15 is moderate/severe ²
 - Difficult to assess as most individuals use some method of hair removal at time of evaluation
 - Does not correlate well with androgen levels
 - May be helpful in determining response to treatment
 - Evidence of virilization
 - Indication for further evaluation
 - Evidence of adrenal or ovarian masses
 - Acanthosis nigricans
 - Marker for insulin resistance
3. Diagnostic testing
 - Laboratory
 - Indicated if history or physical exam suggests significant pathology (rapid progression, virilization, mass, etc)
 - Early AM total testosterone
 - Indicated for infertility, irregular menses, moderate hirsutism, sudden onset, rapid progression, virilization
 - Total and/or free testosterone levels completed in specialty lab
 - Should be performed if normal total testosterone with progression of symptoms despite treatment
 - High levels may indicate malignancy (>200 ng/dl)

- DHEA-S
 - Derived mostly from adrenals
 - If elevated, may need to do exclude adrenal tumor with a CT scan and ACTH stimulation test Prolactin level
 - Indicated if galactorrhea or other concern for pituitary tumor
 - CAH screening (early morning 17-hydroxyprogesterone)
 - If elevated obtain ACTH stimulation test
 - Glucose
 - Indicated if concern for insulin resistance or diabetes
 - Imaging
 - Pelvic ultrasound to exclude ovarian malignancy
 - CT/MRI abdomen if concern for adrenal tumor
 - If elevated, consider CT scan to exclude adrenal tumor
- 4. Diagnostic criteria
 - Increased male pattern hair growth

Differential Diagnosis

1. Congenital adrenal hyperplasia
2. Adrenal tumor
3. Polycystic ovary syndrome
4. Ovarian tumor
5. Medications
6. Family condition
7. Hypertrichosis
8. Cushing's syndrome
9. Thyroid dysfunction
10. Hyperprolactinemia

Therapeutics

1. All medical therapies require minimum 8 wk before noticeable results
2. Hormonal contraceptive pills
 - Decrease free testosterone levels by increasing sex hormone binding globulin
 - May want to avoid pills with androgenic progestins
 - Non-androgenic progestones: drospirenone, cyproterone
 - Well tolerated and inexpensive
 - Usual dose: 30-35 mcg/d ethinyl estradiol
3. Spironolactone
 - Inhibits testosterone from binding to receptors
 - More effective than placebo at reducing Ferriman-Gallwey scores³
 - Usual dose: 100 mg BID
4. Finasteride
 - 5-alpha reductase inhibitor
 - Less effective than Spironolactone⁴
 - Usual dose: 5 mg/d

5. Flutamide
 - Androgen-receptor blocker
 - GI side effects, including significant hepatotoxicity
6. Topical Eflornithine
 - Inhibits ornithine decarboxylase
 - Removes unwanted facial hair
 - Expensive and usually not covered by insurance
7. Weight loss
 - Decreases levels of sex hormone binding globulin
8. Cosmetic measures
 - Depilation- removes hair shaft from the surface
 - Shaving, creams
 - Epilation- extraction of hairs to above the bulb
 - Plucking, waxing
 - Bleaching
 - "Permanent" hair reduction
 - Electrolysis
 - Photoepilation (laser and intense pulsed light)
 - Hair regrowth common because of continued stimulation by androgen
9. Long term treatment
 - Unwanted hair growth will usually return after discontinuing treatment
 - Women choosing direct methods of hair removal are suggested to continue pharmacotherapy to minimize regrowth of hair⁵
 - Women on antiandrogen therapy should have appropriate contraception secondary to potential teratogenic effects⁶
10. Recommendations
 - Pharmacotherapy or direct hair removal methods are suggested for patient-important hirsutism⁷
 - Oral contraceptives are the suggested initial pharmacotherapy for most hirsute women⁸
 - Cyprotenone acetate appears to be as effective as other medications for hirsutism caused by excessive androgen production by the ovaries
 - Flutamide is not suggested for routine use¹⁰
 - Secondary to potential hepatotoxicity and expense
 - Suggested interval of 6 months before altering medication regimen or dosage¹¹

Follow-Up

1. As needed

Prognosis

1. Medical treatments effective in majority of individuals
2. Manual hair removal strategies are all effective
3. Can have significant adverse effects on psychological well-being

Prevention

1. Avoidance of risk factors (increased weight) and androgenic medications

Patient Education

1. Pri-Med Patient Information Center- Hirsutism:
<http://www.patientedu.org/asp/HealthELibrary/HealthETopic.aspx?cid=211213>
2. AAFP Hirsutism patient information:
<http://www.aafp.org/afp/2002/1115/p1913.html>
3. Familydoctor.org patient information- Hirsutism:
<http://familydoctor.org/online/famdocen/home/common/hormone/210.html>

Reference

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3. Swiglo BA, et al. Antiandrogens for the Treatment of Hirsutism: A Systematic Review and Metaanalyses of Randomized Controlled Trials. *J Clin Endocrinol Metab* 2008; 93(4): 1156.
4. Brown J, Farquhar C, Lee O, Toomath R, Jepson RG. Spironolactone versus placebo or in combination with steroids for hirsutism and/or acne. *Cochrane Database of Systematic Reviews* 2009, Issue 2. Art. No.: CD000194. DOI: 10.1002/14651858.CD000194.pub2.
5. Martin, KA, Chang, RJ, Ehrmann, DA, et al. Evaluation and treatment of hirsutism in premenopausal women: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab* 2008; 93(4):1114.
6. Van der Spuy ZM, Le Roux PA, Matjila MJ. Cyproterone acetate for hirsutism. *Cochrane Database of Systematic Reviews* 2003, Issue 4. Art. No.: CD001125. DOI: 10.1002/14651858.CD001125.

Evidence-Based Medicine

1. What is the best approach to the evaluation of hirsutism?
2. What treatments are effective for idiopathic hirsutism among women?

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