

# **HIRSUTISM**

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## **General Considerations**

- Excess hair growth is a common complaint but only rarely is due to serious disease such as ovarian or adrenal neoplasm
- The central issue is to distinguish the rare patient with a serious underlying cause of hirsutism from the majority of hirsute women in whom excess hair growth is a cosmetic problem
- Cosmetic concerns should not be taken lightly; a variety of local as well as pharmacologic remedies are available
- History is critical; hair growth which “has always been there” and is slowly progressive is less likely to be due to tumor than recent onset, rapidly progressive hair growth
- Coarse dark hair growth (“terminal” hair) is normal in women in the axillary and pubic regions; 80% of women will have some dark hair over the legs and forearms but will have little facial hair. About 1/3 of women will have some hair on the chest and extending along the linea alba on the abdomen

## **Factors Controlling Hair Growth**

### **Endocrine Factors:**

- Androgens are the major determinants of hair distribution
  - Dehydroepiandrosterone (adrenal)
  - Androstenedione (adrenal and ovary)
  - Testosterone (adrenal, ovary; also converted by extraglandular tissue)
- Androgens must be converted to testosterone (or dihydrotestosterone) before binding to the androgen receptor of the hair follicle

### **Genetic Factors:**

- Dark-haired, darkly pigmented women tend to be more hirsute
- Orientals, American Indians, and blacks are less hirsute than whites
- Inheritance of hair patterns is polygenic

### **Aging:**

- Menopause decreases hair in the pubic region, axillae and extremities but increases hair growth on the face

### **Pathologic Hair Growth**

- Key to determining if excess hair growth is pathologic is whether signs of virilization are present. Such signs indicate androgen excess.

### **Clinical Signs of Virilization**

<b>Signs of Virilization</b>
Frontotemporal balding
Acne
Decrease in breast size
Increase in muscle mass
Clitoromegaly (>2 cm)
Coarsening of the voice
Amenorrhea or oligomenorrhea

- Remember, signs of virilization may not necessarily imply active disease as changes may have occurred during a previous phase of the patient's life.
- Also, marked increase in androgens may occur without signs of virilization.

### **Possible Etiologies**

#### **1. Simple Hirsutism**

- Excess body hair without signs of virilization can be an early sign of a virilizing syndrome but is most often idiopathic
- Prevalence is 10% in the USA
- Family history is common
- Begins with menarche and is slowly progressive
- Normal menses, normal sized ovaries
- May be slight elevations of plasma androstenedione and testosterone

## 2. Iatrogenic

- Drugs which increase hair growth but do not produce virilization
  - diazoxide
  - cyclosporin
  - minoxidil
  - dilantin
- Drugs which increase androgenic activity
  - Danazol
  - Testosterone-containing creams
  - Oral contraceptives that contain androgenic progestins like norgestrel

## 3. Adrenal /Endocrine

- Congenital adrenal hyperplasia: inherited cause of defects in adrenal steroidogenesis which usually manifest in childhood although a variant can present in adulthood; mimics PCOS
  - Deficiency in 21-hydroxylase is the most common
  - Deficiency in 11 beta-hydroxylase
  - Deficiency in 3 beta-hydroxy steroid dehydrogenase isomerase
- Androgen-secreting tumor
- Cushing's
- Hyperprolactinemia- suggest pituitary tumor or hypothalamic disease.

## 4. Ovary

- Polycystic Ovary Syndrome (PCOS): combination of hirsutism, obesity, acne, amenorrhea and polycystic ovaries although now it is believed that this combination is present in < 50% of patients with this disease
  - Insulin resistance and compensatory hyperinsulinemia are intrinsic features; fasting glucose-insulin ratio < 4.5
  - Hypersinsulinemia may be the cause of ovarian hyperandrogenism
- Androgen-secreting tumors of the ovary (arrhenoblastoma)
- Krukenberg tumors of the ovary which stimulate ovarian stromal tissue to produce androgens

## Diagnosis

### • History:

- Vellus (fine hair) vs terminal (coarse, dark) hair
- Age of onset
- Rate of progression
- Medication usage which increases androgenic activity (see above)
- Type of hair removal method (shaving, depilatory and how often)
- Menstrual history and its relation to onset of hirsutism
- Family history

- Weight history-obese women have increased androgen production
- **Physical Examination:**
  - Extent and distribution of hair growth (see Figure 1 for Ferriman-Gallwey diagram). Look particularly for male-type escutcheon with hairs extending from the pubic region up to the umbilicus. Also, hoar growth on the upper abdomen, sternum or back suggests a more serious etiology. Most clinicians use a score of  $\geq 8$  to define hirsutism.
  - Body Habitus
  - Signs of virilization
    - increased muscle mass
    - decreased subcutaneous fat in the hips and breasts
    - clitoral enlargement  $> 2.0\text{cm}$
    - deepening of the voice
    - male pattern baldness
    - Galactorrhea-spontaneous vs. expressible
  - Pelvic examination for palpable ovarian or adrenal mass
- **Clinical Findings that suggest Rare Cause of Hirsutism**
  - Abrupt onset, short duration less than year, or progressive worsening of hirsutism
  - Onset in third decade of life
  - Signs of virilization
  - If has above look for adrenal/ovarian causes
- **Laboratory Evaluation:**
  - Some clinicians feel that hormonal evaluation is unnecessary prior to initiating treatment in the patient with regular menses, a long history of mild hirsutism, and no evidence of virilization.
  - In the patient with abnormal menses, recent onset or rapid progression of hirsutism, virilizing signs, abnormalities on physical examination or resistance to therapy, hormonal evaluation is essential (see Figure 2)
  - ✓ Total testosterone
    - If  $> 200\text{ng/dL}$  in a premenopausal woman, suggests ovarian neoplasm or hyperthecosis. Endovaginal ultrasonography of ovaries and referral to a gynecologist is suggested.
    - If  $> 100\text{ ng/dL}$  in a postmenopausal woman, suggests ovarian neoplasm. Endovaginal ultrasonography of ovaries and referral to a gynecologist is suggested.
    - If  $100\text{-}200\text{ ng/dL}$ , suggest Polycystic Ovary Syndrome (PCOS); order fasting glucose and insulin. If the fasting glucose-insulin ratio is  $< 4.5$ , suggests PCOS.
    - If  $< 100$ , look for an adrenal source of androgens such as androstenedione by checking DHEA-S; if elevated, image the adrenals with CT scan and refer to an endocrinologist for evaluation of primary adrenal tumor

- Pts with normal total testosterone may have increased levels of free testosterone due to reduced sex hormone-binding globulin or may have increased sensitivity of hair follicles to testosterone.
- Serum prolactin- increased level associated with hypothalamic disease or pituitary tumor.

## TREATMENT

- Stop drug or remove tumor
- If adrenal steroidogenic defects are identified, glucocorticoids may suppress ACTH
- For POS, cosmetic treatment as well as suppression of androgens is advised.
- Hormone therapy arrests or slows the rate of hair growth but local therapy is necessary to remove existing hair growth
  - Bleaching
  - Waxing
  - Shaving, plucking
  - Depilatories
  - Electrolysis
- New topical cream, eflornithine hydrochloride 13.9% (Vaniqa ® made by Bristol-Myers-Squibb) is safe and modestly effective in some women in reducing unwanted facial hair. Slows the rate of hair growth and hair becomes finer and lighter, 20-40% of women report improvement. Benefit lasts only as long as active treatment. Cost: approximately \$42 for 30 gm tube.
- Medical therapy takes 6-8 months before androgen excess is eliminated; caution patients to not expect quick results
  - Oral contraceptives: estrogen in the OC's decreases ovarian androgen production, increases plasma sex hormone binding globulin and reduces free testosterone. Use a less androgenic OC such as Orthocyclen or OrthoTriCyclen
  - Spironolactone: blocks androgen receptor and inhibits androgen production; 100 mg bid; watch K +
  - Metformin can be used to treat PCOS but its effect on hirsutism is not dramatic

## SPECIAL COMMENTS FOR THE STUDENT HEALTH PATIENT POPULATION

- Please be cost-effective in your workup. ONE endocrine test can consume the ENTIRE annual health fee for a student!
- Because our population is sexually active and unwanted pregnancy is usually a concern, if medical Rx of hirsutism is desired, we most commonly use oral contraceptives. OC's can be started if the student has had an appropriate gynecological evaluation (recent PAP smear) but students with the presumptive diagnosis of PCOS should be advised that fertility may be an issue in the future. Also advise them that oligomenorrhea may be masked by taking OC's.

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