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Hirsutism

Shibani Kanungo  
*University of Kentucky*

Hatim A. Omar  
*University of Kentucky*, hatim.omar@uky.edu

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**HIRSUTISM**

Shibani Kanungo, MD, MPH
Hatim A. Omar, MD

**BASICS**

**DESCRIPTION**
- From the Latin, *hirsutus* = hairy
- Symptom associated with male pattern of pigmented terminal hair growth
- Locations are assessed for research purposes in Ferriman-Gallwey score.
- Often associated with acne, irregular menstrual periods, galactorrhea, dark velvety patches of skin, central obesity, infertility

**Pediatric Considerations**
- Infancy: 10% of women, of which 20% have idiopathic hirsutism
- Adolescence: Associated with PCOS, late-onset CAH, HAIR-AN syndrome, steroid use, depression, pregnancy, or drug-induced
- Adolescence: Associated with PCOS, HAIR-AN syndrome, hyperprolactinemia, ovarian tumor, menopause, depression, or drug-induced

**EPIDEMIOLOGY**
- 5-10% of women, of which 20% have idiopathic hirsutism

**RISK FACTORS**
- Ethnicity (Mediterranean, Middle Eastern, South Asian)
- Family history
- Infertility
- Obesity

**Genetics**
- Can be familial or multifactorial
- Seen with:
  - Polymorphism of 5 α-reductase (SRD5A1 and SRD5A2) isomers
  - CYP21 gene mutation
  - NIPBL mutation associated with Cornelia de Lange syndrome

**PATHOPHYSIOLOGY**
- Caused by increased:
  - Levels of androgen secretion (DHEA, DHEAS, androstenedione and testosterone)
  - Peripheral conversion of testosterone to potent DHT
  - Sensitivity of hair follicles to androgens regulated by 5 α-reductase, which transforms testosterone or androstenedione to DHT
- Caused by decreased:
  - SHBG concentration with resultant increased free androgen

**ASSOCIATED CONDITIONS**
- Idiopathic hirsutism
- PCOS
- HAIR-AN syndrome
- CAH
- Cushing disease
- Hyperthyroidism
- Hyperprolactinemia
- Adrenocortical tumors
- Ovarian tumors
- Cornelia de Lange syndrome
- Fetal alcohol syndrome
- Drugs: Corticosteroids, anabolic steroids, phenytoin, valproate, danazol, diazoxide, minoxidil
- Pregnancy
- Stress
- Male pseudohermaphroditism
- Depression

**DIAGNOSIS**

**SIGNS AND SYMPTOMS**
- Based on the Ferriman-Gallwey score of hair growth level on 9 different locations of the body:
  - Upper lip, chin, chest, upper back, lower back, upper abdomen, lower abdomen, upper arms, and thighs
  - Hair growth is rated from 0-4, where 0 is virtually no hair at all, and 4 is completely covered with hair. The maximum score is 36. Commonly used research scale in US
  - Normal: ≤8
  - Light hirsutism: 8–16
  - Moderate hirsutism: 17–25
  - Severe hirsutism: >26
  - The scale may vary for different ethnic groups with different levels of expected hair growth.

**History**
- Age of onset
- Duration
- Location
- Rate of progression
- Skin changes
- Associated symptoms of virilization
- Medication use
- Ethnic background
- Medical history
- Puberty/Menstrual history
- Family history of females with hirsutism, males with early balding
- Psychosocial history/stress, depression

**Review of Systems**
- Other associated signs and symptoms:
  - Acne
  - Irregular menstrual periods
  - Dark velvety patches of skin (acanthosis nigricans)
  - Breast discharge
  - Central obesity
  - Deepening of the voice
  - Increased muscle mass
  - Infertility

**Physical Exam**
- Vital signs: Increased BMI, high BP, waist circumference >30 inches
- General: Central obesity, BMI, dysmorphism, deepening of voice, male habitus
- Skin: Acne, male pattern hair, seborrhea
- HEENT: Tonsillar enlargement, thyromegaly, acanthosis nigricans, cervical fat pad, temporal balding
- Chest: Breast tenderness, galactorrhea, truncal obesity, buffalo hump
- Abdomen: Striae, tenderness
- GU: Clitoromegaly, ovarian mass

**TESTS**
- Ferriman-Gallwey scoring for research purposes

** Labs**
- Testing as clinically appropriate for:
  - DHEA-S
  - Total testosterone
  - Free testosterone
  - Fasting insulin and glucose
  - IGF-1
  - TSH
  - Free T4
  - 17 OH progesterone
  - Prolactin
  - LH
  - FSH
  - ACTH
  - Cortisol
  - 24-hour urine cortisol

**Imaging**
- Pelvic ultrasound if ovarian mass suspected
- CT abdomen and pelvis if adrenal mass suspected
- MRI head if pituitary abnormality suspected

**DIFFERENTIAL DIAGNOSIS**
- Hypertrichosis: Excessive androgen-independent fine and soft total body hair growth in both men and women
- Idiopathic hirsutism
MEDICATION (DRUGS)
Aimed at primary cause of hirsutism:
- OCP reduces circulating androgen levels through suppression of circulating LH, stimulation of SHBG levels with resultant decreases in free androgens, and reduction of 5α-reductase activity
- Clomiphene induces ovulation
- Metformin promotes ovulation and reduces insulin resistance of peripheral tissue.
- Gonadotropins: Leuprolide
- Cyproterone competes with DHT for binding to the androgen receptor.
- Spironolactone competes with DHT for binding to the androgen receptor.
- Flutamide is a pure androgen receptor blocker.
- Ketoconazole reduces levels of concentration of circulating androgens.
- Finasteride inhibits activity of 5α-reductase,

SURGERY
- Hair removal with intense pulsed light irradiation system (IPL) or normal-mode ruby laser for idiopathic or familial hirsutism
- Surgery can be aimed at underlying pathology:
  - Adrenal/Ovarian tumor resection
  - Oophorectomy for androgen-producing ovarian tumor
  - Ovarian wedge resection/ovarian drilling in PCOS

FOLLOW-UP
Depends on cause or associated condition

DIAGNOSIS
Issues for Referral
- Endocrinology or gynecology or genetics or surgery for hormonal or syndromic or tumor etiology
- Dermatology or cosmetology for idiopathic or familial hirsutism only

PROGNOSIS
Dependent on cause and intervention or therapy

PATIENT MONITORING
- Endocrinology or gynecology or genetics or surgery for hormonal or syndromic or tumor etiology
- Dermatology or cosmetology for idiopathic or familial hirsutism only

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Goodwin MO, et al. Variants in the 5α-reductase type 1 and type 2 genes are associated with polycystic ovary syndrome and the severity of hirsutism in affected women. J Clin Endocrinol Metab. 2006; 91(10):4085–4091.

MICROBIAL
Virilization indicates more severe androgen effect including breast atrophy, ditoromegaly, temporal balding

CLINICAL PEARLS
- Hirsutism without menstrual irregularities or weight gain is most likely idiopathic or familial.
- Adolescents with hirsutism and early-onset, severe, and refractory acne are likely to have PCOS, OCPs can benefit self-esteem and prevent scarring from acne.
- Hirsutism can be the only clinical presentation of depression or stress in adolescents; warrants psychosocial workup.

ABBREVIATIONS
- ACTH—Adrenocorticotropic hormone
- CAH—Congenital adrenal hyperplasia
- DHEA/DHEAS—Dehydroepiandrosterone-DHEAS sulfate
- DHT—5α-dihydrotestosterone
- FAS—Fetal alcohol syndrome
- FSH—Follicular stimulating hormone
- HCGT—Head, eyes, ears, nose, throat exam
- IGF—Insulin-like growth factor
- LH—Luteinizing hormone
- OCP—Oral contraceptive pill
- PCOS—Polycystic ovarian syndrome
- SHBG—Sex hormone binding globulin
- TSH—Thyroid stimulating hormone

CODES
ICD9-CM
704.1 Hirsutism

PATIENT TEACHING
- Diagnosis of idiopathic hirsutism or familial hirsutism should be considered after a thorough workup for all other causes such as hormonal, oncologic, and syndromic agents have been ruled out.
- Current medical therapies have their pros and cons. No drug is yet FDA approved. Cosmetic remediation or counseling and education may also be helpful.

PREVENTION
- Exercise for weight control and stress reduction may improve PCOS.
- Careful use of medication such as steroids, antiepileptics, vasodilators with awareness of hirsutism as side effect.