بسم الله الرحمن الرحيم

الموسم

الشعر

لهجت

الفصاحة

نشر

يحيى بن سهل

المصري

بسم الله الرحمن الرحيم
Hirsutism
(Clinical features and Diagnosis)
- **Hirsutism** is excessive growth of *terminal hairs* in a "male pattern" in a *female* patient.

- **Hypertrichosis** represents the growth of hair in an excessive amount that may be generalized or localized.
-Hirsutism is related to hormonal factors, in particular an increase in circulating androgen levels or enhanced end-organ sensitivity to androgens.

However, not all women with greater amounts of secondary sexual hair will have abnormal androgens.
Perception of hirsutism is by definition subjective, and women present with a wide variation in severity.

-Both the severity of the hirsutism and the degree of its acceptance are dependent on racial, cultural and social factors.
In clinical practice, it has often been suggested that 'real' hirsutism is simply that which the woman in question thinks is excessive.

Even the criteria for the definition of hirsutism used by physicians vary widely.
-The standard grading system, defined hirsutism purely on quantitative grounds is the **Ferriman and Gallwey scale**.

-Scoring is on a *global* basis assessing **9** body sites.

-**Hirsutism** is defined by a score of **>8** on the Ferriman and Gallwey scale.
The Ferriman and Gallwey score reflects:

**Functional hirsutism**: the score is **9-14**

**Organic hirsutism**: the score is **greater than 15**.
Abraham's classification of hirsutism is also used to assess degree of severity.

<table>
<thead>
<tr>
<th>Score</th>
<th>Classification</th>
</tr>
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<tbody>
<tr>
<td>&lt;8</td>
<td>Normal</td>
</tr>
<tr>
<td>8–16</td>
<td>Discrete</td>
</tr>
<tr>
<td>17–25</td>
<td>Moderate</td>
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<tr>
<td>&gt;25</td>
<td>Important</td>
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Epidemiology:

It affects approximately 5% of women of reproductive age in the general population.
Hirsutism may be accompanied by seborrhea, acne and androgenetic alopecia (SAHA syndrome) that are the result of the actions of androgens on target tissues.

SAHA syndrome can be isolated with minimal or no hormonal abnormalities or associated with other disorder of androgen excess like polycystic ovary syndrome (PCOS)
CLASSIFICATION OF TYPES OF HIRSUTISM:

- CONSTITUTIONAL (minimal or no hormonal abnormality)

- ENDOCRINE ORGAN-BASED

- ECTOPIC HORMONE PRODUCTION

- DRUGS (IATROGENIC)
Constitutional hirsutism:

- Familial
  (normal hormonal tests)
- Adrenal SAHA syn
  (mild increase in DHEA-S)
- Ovarian SAHA syn
  (mild increase in free testestrone)
- SAHA syn with hyperprolactinemia
  (mild increase in prolactine)
Endocrine organ based hirsutism:

- Adrenal hirsutism:
  1. congenital adrenal hyperplasia (17OH Prog, DHEA-S, ACTH): ↑
  2. hypercorticism (cushing's syndrome) (cortisol, DHEA-s, free testosterone), (ACTH): ↑

  ↓
Glucocorticoids (e.g., cortisol)
Mineralocorticoids (e.g., aldosterone)
Sex steroids (e.g., testosterone)

Epinephrine
Norepinephrine

Cortex
Medulla

Adrenal gland
Kidney
Endocrine organ based hirsutism

-Ovarian hirsutism

1-polycystic ovary syndrome
(FSH,SHBG): ↑  (LH,estrone): ↓

2-Hyperthecosis
(normal FSH,LH)  (estrone): ↑

3-Ovarian tumor
Free testosterone: ↑
Endocrine organ based hirsutism

- Pituitary hirsutism
  1- Cushing disease
  2- Prolactin secreting adenoma
  3- Psychogenic drugs that cause hyperprolactinemia
Ectopic hormone production

- ACTH (lung cancer, carcinoeoid)
- HCG (choriocarcinoma)
Drugs (iatrogenic)

- Anabolic steroids
Clinical findings:

Familial constitutional hirsutism: normal hormonal tests

Generally facial with prolongation of preauricular hair implantation line
Clinical findings:

Adrenal SAHA Syn: mild increase in DHEA-S

- Usually a stressful young woman
- Predominantly central hirsutism (anterior neck, upper pubic area)
- Intense seborrhea, nodulocystic acne, FAGA I-II, oligomenorrhea
Clinical findings:

Ovarian SAHA Syn: mild increase in free testestrone

Young women; tend to be obese; mild lateral facial and mammary hirsutism; intense seborrhea, papulopustular acne, FAGA I , normal menses or polymenorrhea
Clinical findings:

SAHA Syn with hyperprolactinemia:

Slight increase prolactin

Central and lateral hirsutism; sometimes seborrhea, acne, FAGA I; oligomenorrhea; occasionally galactorrhea
Clinical findings:

Adrenal hirsutism:
In a patient of any age presenting with obvious central hirsutism (i.e. anterior neck to upper pubic area), female androgenetic alopecia (FAGA; Ludwig I-III) or male pattern androgenetic alopecia, signs of virilization, and a thin body habitus.

1 - Congenital adrenal hyperplasia (CAH) is due to a congenital deficiency of one of the enzymes involved in the synthesis of adrenal steroids.

This leads to an accumulation of the intermediate product that are not recognized by the pituitary so that the negative feedback mechanism is not initiated, resulting in very high level of ACTH level.
Cholesterol is metabolized in the adrenal cortex, via a complex pathway, into aldosterone, cortisol, androgens and oestrogens.

In approximately 95% of cases, 21-hydroxylation is impaired so that 17-hydroxyprogesterone (17-OHP) is not converted to 11-deoxycortisol resulting in overproduction of 17-OHP.

This causes excessive production of androgens, resulting in virilization.
SYNTHESIS OF GLUCOCORTICOIDS AND ANDROGENS

Cholesterol

20-22 Desmolase

Pregnenolone

3βHSD

17-20 Desmolase

Dehydroepiandrosterone

17-Ketosteroid reductase

Androstanediol

3βHSD

Aromatase

Testosterone

5αR

Dihydrotestosterone

3αHSD

Androstanediol

5αR

Androsterone

3αHSD

Androstenedione

5αR

Androstenedione

female pathway

17-Ketosteroid reductase

17-Ketosteroid reductase

17-Ketosteroid reductase

17-Ketosteroid reductase

17-20 Desmolase

17-OH-Pregnenolone

17-Hydroxylase

17-OH-Progesterone

3βHSD

21βOH

11βOH

11βOH

Desoxycorticosterone

Corticosterone

Cortisol

Metabolism of androgens in skin
21-Hydroxylase deficiency is responsible for 95% of all cases of CAH.

These salt wasting patients, as well as individuals with less severe forms of classic CAH, show premature growth of axillary and pubic hair during early childhood (precocious puberty), which is soon followed by hirsutism accompanied by acne and the onset of patterned alopecia. Virilization is often observed.
Late-onset CAH (attenuated CAH): is due to partial enzyme deficiencies (e.g. of 21-hydroxylase), and it becomes clinically apparent when demand for steroids increases at puberty or thereafter.

Virilization is again a clinical feature; however, 40% of patients only have hirsutism.
-The diagnosis of non-classical late-onset CAH (LO-CAH) cannot be made clinically, and dynamic endocrine investigations are required to differentiate between it, PCOS and constitutional hirsutism.

-These women may have only mild degrees of hirsutism, normal physique, normal menses, no metabolic sequelae on cortisol pathway. However, approximately 80% will have polycystic ovaries.
Adrenal hirsutism

2-Hypercortisolism (Cushing's syndrome)

All patients have an increase in plasma cortisol, which is the cause of the major clinical features, e.g. central obesity with "moon facies" and "buffalo hump", hypertension, glucose intolerance, purple striae, and ecchymoses.
Hypercortisolism (Cushing syn):
- Primary nodular hyperplasia
- Adrenal adenoma
- Adrenal carcinoma

Hyperplasia or adrenal adenomas typically have an insidious onset of symptoms, but with an adrenal carcinoma or ectopic ACTH production by a malignant tumor, manifestations appear more rapidly.
-congenital adrenal hyperplasia
(17OH Prog, DHEA-S, ACTH): ↑
-hypercorticism (cushing's syndrome)
(cortisol, DHEA-s, free Testestrone): ↑
(ACTH): ↓
Ovarian hirsutism:

1-**Polycystic ovary syndrome**

Presence of 2 of the following Rotterdam criteria:

- Oligo or amenorrhea
- Elevated circulatory androgens (e.g. total or free testosterone) or clinical signs of androgen excess (e.g. hirsutism, androgenic alopecia, acne)
- Polycystic ovaries on ultrasound
PCO

- It is necessary to exclude other specific disorders such as non-classical adrenal 21-hydroxylase deficiency, Cushing's syndrome, hyperprolactinaemia and androgen-producing Tumours

- It is primarily caused by an ovarian abnormality with excess androgen secretion, inappropriate gonadotrophin secretion with abnormal LH pulses.
PCO

The associated hirsutism is usually lateral, i.e. on the breasts, lateral aspects of the face and neck, as well as on the abdomen.

At least 50% of patients are obese, and some develop acanthosis nigricans.
Women with PCOS have a higher prevalence of insulin resistance, dyslipidemia and hypertension, as well as obesity, components of the "metabolic syndrome" that confer an increased risk of atherosclerotic cardiovascular disease.
1-polycystic ovary syndrome

(FSH, SHBG,): ↓

(LH, estrone, Testosterone): ↑

FSH/LH < 3

- FSH and LH best measured during days 1-3 of a menstrual bleed; If oligo-/amenorrhoeic then random samples are taken
2-Ovarian hyperthecosis:
This is similar to PCOS, but with greater production of androgens, especially testosterone. The patients present with signs of virilization, hirsutism, and even androgenic alopecia. Serum levels of LH and FSH are normal, but estrone levels are greatly elevated.
3-Tumoral ovarian hirsutism

Hirsutism is an almost universal feature in virilizing ovarian tumors; however, functioning tumors that cause virilization represent approximately 1% of ovarian tumors.

Amenorrhoea or oligomenorrhoea develop in all premenopausal patients, and alopecia, clitororomegaly, deepening of the voice and a male habitus develop in approximately half of the patients.
Pituitary hirsutism

This type of hirsutism is due to the secretion of hormones from the anterior pituitary, particularly ACTH and prolactin.

There are a number of etiologies of hyperprolactinemia, although pituitary adenomas and drugs are the major causes. Clinical features are the "amenorrhea-galactorrhea syndrome“ and infertility.

Usually, women are younger than 50 years of age and present with FAGA, acne, seborrhea, and hirsutism; the latter is both central and lateral, with a slight predominance of central hirsutism. There are signs of virilization.
Iatrogenic hirsutism:
This type of hirsutism tends to be localized to the lateral aspects of the face and back. Anabolic steroids (e.g. danazol) and oral contraceptives of the nonsteroidal progestogen type have been reported to cause hirsutism.
Once the anabolic steroids are discontinued, there are no associated laboratory abnormalities and the hirsutism improves or resolves.
Hirsutism due to ectopic hormones

Patients develop central or lateral hirsutism, depending on the hormone produced by the tumor.
Diagnostic approach to the hirsute woman:

- Although there are scoring systems, these are mainly of scientific interest or as a means of monitoring response to treatment.

  The presence or absence of terminal hair at specific sites is important to document. This can be supplemented by an approximation of how dense the growth is ranging from a few scattered hairs to confluence.

- Other features of androgenization to be noted are acne, androgenetic alopecia, acanthosis nigricans and obesity. Malignant androgen-secreting tumours may also lead to clitoromegaly, increased muscle bulk and a deeper voice.
-Menstrual regularity is a further important detail, where lifelong menstrual disturbance suggests PCOs, recent marked alteration suggests a new evolving diagnosis, and the absence of any menstrual problem is likely to mean that there is no hormonal basis to the hirsutism

-Drug history
Clarifying the diagnosis of PCOS may be Appropriate.

Pursuing the diagnosis of LO-CAH is controversial. In some hands the diagnosis will not alter management.
The first step in laboratory evaluating a woman with hirsutism is to determine the source of the androgens, i.e. adrenal cortex or ovaries.

- The marker for adrenal gland androgens is DHEA-S.

- The marker for the ovarian androgen is androstenedione.
As a general rule, "whenever there is hirsutism which appears abruptly and quickly, one must first suspect that there is an ovarian, adrenal or pituitary tumor".
**Ovarian origin:** hirsutism is mainly localized on the areola and the lateral surfaces of the face and neck.

**Adrenal origin:** the location is central, with a distribution from the pubic triangle to the upper abdominal area and from the presternal region to the neck and the chin.

**Iatrogenic:** When there is only hair on the lateral aspect of the face and on the back.

With time, however, the distribution can evolve to include both central and lateral involvement.
After the patient has been examined for clinical signs that suggest a particular diagnosis; a **biochemical evaluation** should be initiated.

- Total and free testosterone
- DHEA-S
- Prolactin
- SHBG
- Androstenedione

Depending on the results of these tests, the laboratory evaluation can be expanded. If substantial abnormalities are detected, referral to an endocrinologist is usually indicated.
Testosterone (20-90 ng/dl):

- Normal  →  constitutional hirsutism
- 100-200 ng/dl  →  PCO, CAH, Cushing syn
- >200 ng/dl  →  Adrenal or Ovarian Tumor
Hirsutism in pregnancy

-Hirsutism has only rarely been reported to develop during pregnancy; it may be caused by the development of PCOs or a virilizing tumour.

-PCOs has been reported to present with virilization during the first or third trimester and may regress postpartum.

-Androgens freely cross the placenta and virilization of a female fetus may occur
Thank you for your attention