



A close-up photograph of a woman's face, focusing on her chin and upper lip. She has a significant amount of dark, coarse hair (hirsutism) on her chin and upper lip. The background is a soft, out-of-focus light blue.

Hirsutism

**(Diagnostic Approach
& Lines of Treatment)**

By

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Definitions:

■ Hirsutism:

- Is the presence of terminal hair in androgen-dependent sites where hair does not normally grow in women.
- This hair growth is located predominantly on midline portions of the body, including the face, chest abdomen, and inner thigh.

- **hypertrichosis:** which simply indicates generalized increase body hair (nonsexual hair). It can be seen in anorexia nervosa, porphyria cutanae tarda, and underlying malignancy and is caused by certain drugs (e.g. ciclosporin, minoxidil)

Virilization:

- Is hirsutism associated with other signs of hyperandrogenism, such as increased muscle mass, clitorimegaly, temporal balding, voice deepening, and increased libido.
- It can also be associated with signs of defeminization, such as decreased breast size and loss of vaginal lubrication.

Hair Growth Cycle

1. Growth phase: **Anagen**.
2. Rapid involution and shedding phase: **Catagen**.
3. Quiescent phase: **Telagen**.
 - The length of the hair is determined by the duration of anagen.
 - This is longest in scalp hair (3 years) and shortest in forearm hair.

Types of Hair

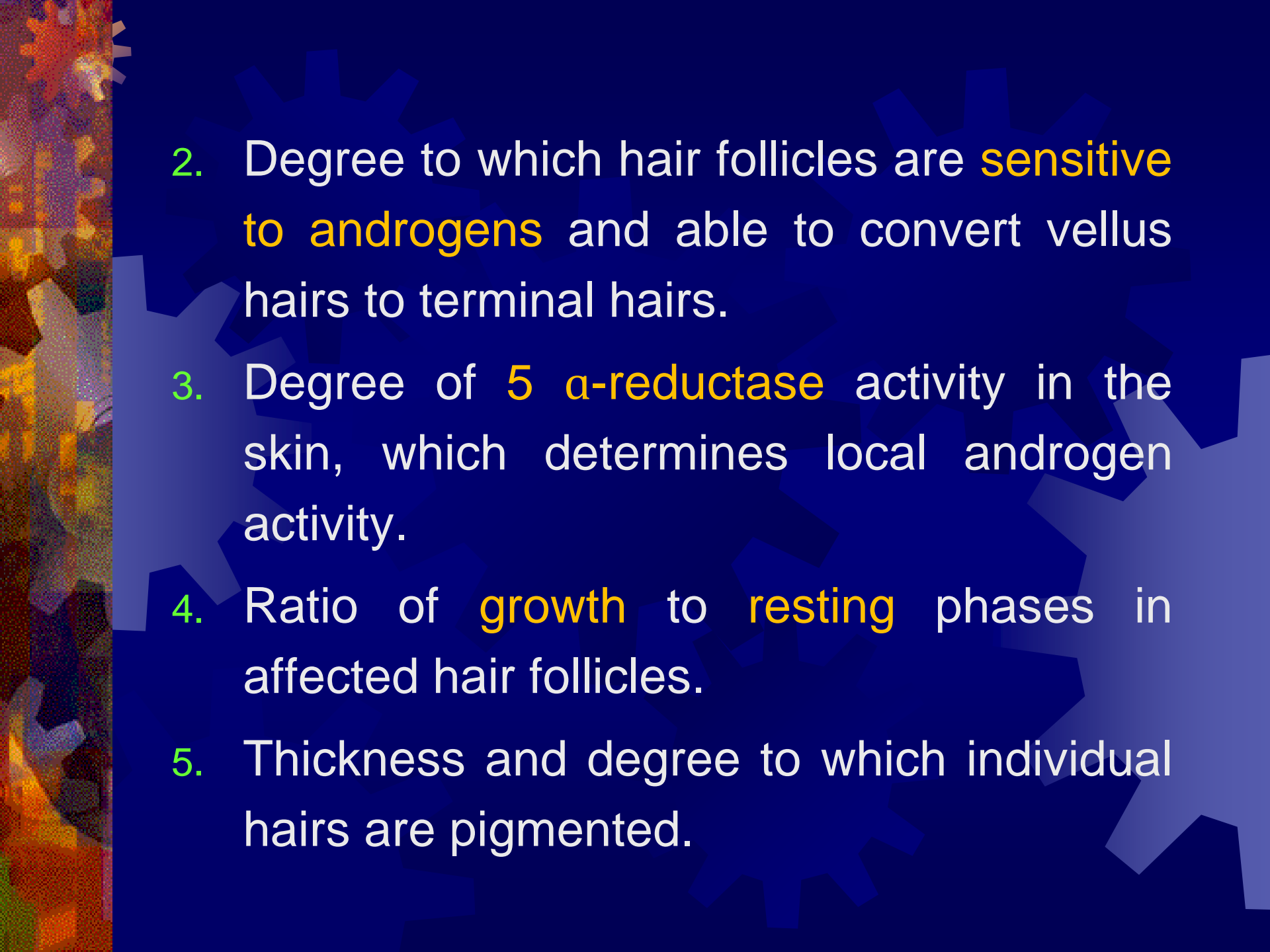
1. **Lanugo hair:** It is soft, short hair covering the fetus that is shed in late gestation and during the neonatal period.
2. **Vellus hair:** It is soft, fine, unpigmented hair that covers apparently hairless areas of the body.
3. **Terminal hair:** It may be: **sex hormone dependent** hair as the long, coarse, pigmented hair that may grow in response to sex hormones (e.g., over the chin and abdomen of men) or may be **sex hormone-independent** as eyebrows and eyelashes.

Factors affecting hair growth:

- Hair growth, and thus hirsutism, is regulated by:

1. Number and concentration of hair follicles.

- This varies according to racial and ethnic back-ground but not gender.
- For example, Asian women generally have low concentrations of hair follicles, and hirsutism is rarely seen in these individuals.

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2. Degree to which hair follicles are **sensitive to androgens** and able to convert vellus hairs to terminal hairs.
 3. Degree of **5 α -reductase** activity in the skin, which determines local androgen activity.
 4. Ratio of **growth** to **resting** phases in affected hair follicles.
 5. Thickness and degree to which individual hairs are pigmented.

Pathophysiology of Hirsutism

- A combination of the following factors results in hirsutism:
 1. Increased concentration of serum androgens, especially free testosterone.
 2. Decreased levels of SHBG, resulting in increased bioavailable androgen.
 3. Increased activity of 5 α -reductase.

Sources of androgens in females:

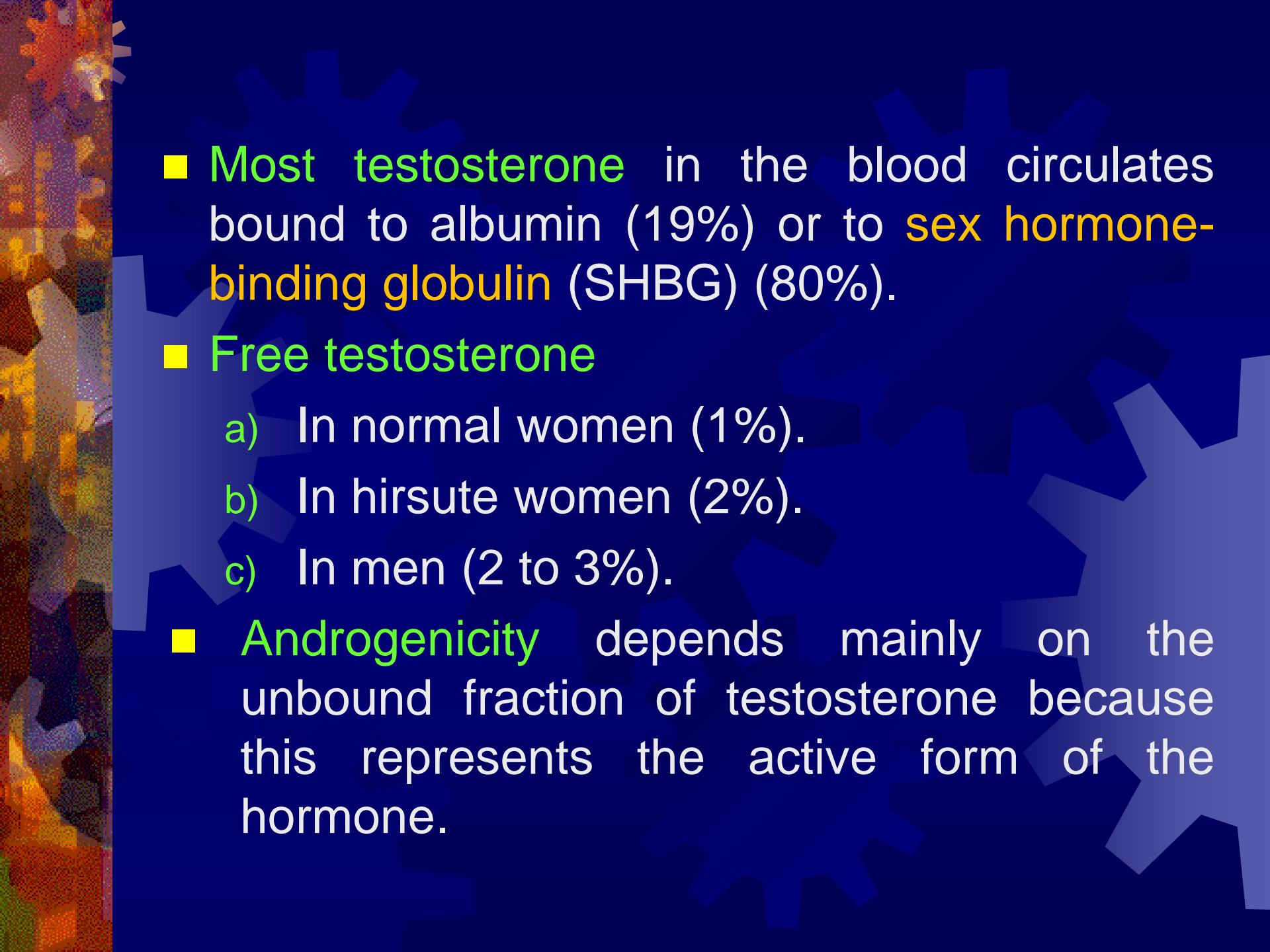
- In women, androgens are mainly produced by:
 1. The adrenal gland.
 2. The ovary.
 3. Peripheral transformation.

Type of androgens are:

1. Testosterone is the **most potent** androgen.
2. Androstenedione.
3. Dehydroepiandrosterone (DHEA).
4. DHEA sulfate (DHEAS).

I- Testosterone

- **Total testosterone:** Levels in women are usually less than 70 ng/dL.
- **Sources:**
 - a) Ovarian 25% (in stroma and follicles).
 - b) Adrenal origin 25%.
 - c) Peripheral transformation of androstenedione to testosterone 50%.

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- **Most testosterone** in the blood circulates bound to albumin (19%) or to **sex hormone-binding globulin** (SHBG) (80%).
 - **Free testosterone**
 - a) In normal women (1%).
 - b) In hirsute women (2%).
 - c) In men (2 to 3%).
 - **Androgenicity** depends mainly on the unbound fraction of testosterone because this represents the active form of the hormone.

II- Sex Hormone-Binding Globulin (SHBG)

A. Factors that decrease plasma SHBG

1. Obesity.
2. Increased androgen production.
3. Hyperinsulinemia.
4. Hyperprolactinaemia.
5. Corticosteroid therapy.
6. Hypothyroidism.
7. Acromegaly.



B. Factors that increase plasma SHBG

1. Estrogen therapy.
 2. Pregnancy.
 3. Hyperthyroidism.
 4. Liver cirrhosis.
- In general, hirsute women have reduced serum concentrations of SHBG.

III- 5 α -Reductase

- 5 α -Reductase converts testosterone to **dihydrotestosterone** (DHT) in androgen-sensitive tissues such as hair follicles and skin.
- Levels of this enzyme are significantly elevated in the skin of hirsuted women compared with non hirsuted.
- The enzyme activity is partly stimulated by elevated circulating testosterone levels.
- Dihydrotestosterone is responsible for stimulating hair growth and is two to three times as potent as testosterone.

Causes of Hirsutism

- ★ PCOS 75%
- ★ Idiopathic hirsutism 15%
- ★ Adrenal hyperplasia 3%
- ★ Cushing's disease 1%
- ★ Hyperprolactinemia 1%
- ★ Tumor of the ovary 1%
- ★ Tumor of the adrenal 0,1%
- ★ Medications 1%



The background is a dark blue field filled with various sizes of gear silhouettes in shades of blue and grey. On the left side, there is a vertical strip containing a detailed, colorful image of interlocking gears in shades of orange, red, and brown.

Diagnosis of Hirsutism

History:

1) Onset of hirsutism

- **Gradual onset** of hirsutism which is associated with acne, oily skin, weight gain, and irregular menstrual cycles. This suggests an underlying endocrine condition, such as polycystic ovary syndrome (**PCOS**).
- **Abrupt onset** or rapidly worsening hirsutism with signs of virilization should direct concern for an androgen-producing tumors.

The background features a dark blue field with several large, semi-transparent gears of various sizes. On the left side, there is a vertical strip with a colorful, abstract, and somewhat pixelated texture in shades of orange, red, and brown.

2) Presence or absence of virilization.

3) Drug ingestion.

- Drugs are usually associated with hypertrichosis, but androgenic drugs (e.g., steroids and phenytoin) may cause hirsutism.

4) Family history.

- A family history of hirsutism may indicate an inherited disorder (i.e., familial hypertrichosis).



5) **Ethnic background.**

- The pattern of hair growth is genetically predetermined and is associated with differences in 5 α -reductase activity at hair follicles.

6) **Local trauma.** Changes in skin and hair growth may occur.

7) **Regularity of menstrual cycles.**

- Patients with regular menstrual cycles and hirsutism often have idiopathic, ethnic, or familial hirsutism.

8) **History of infertility.**



Differential Diagnosis of Hirsutism

1- Polycystic ovary syndrome:

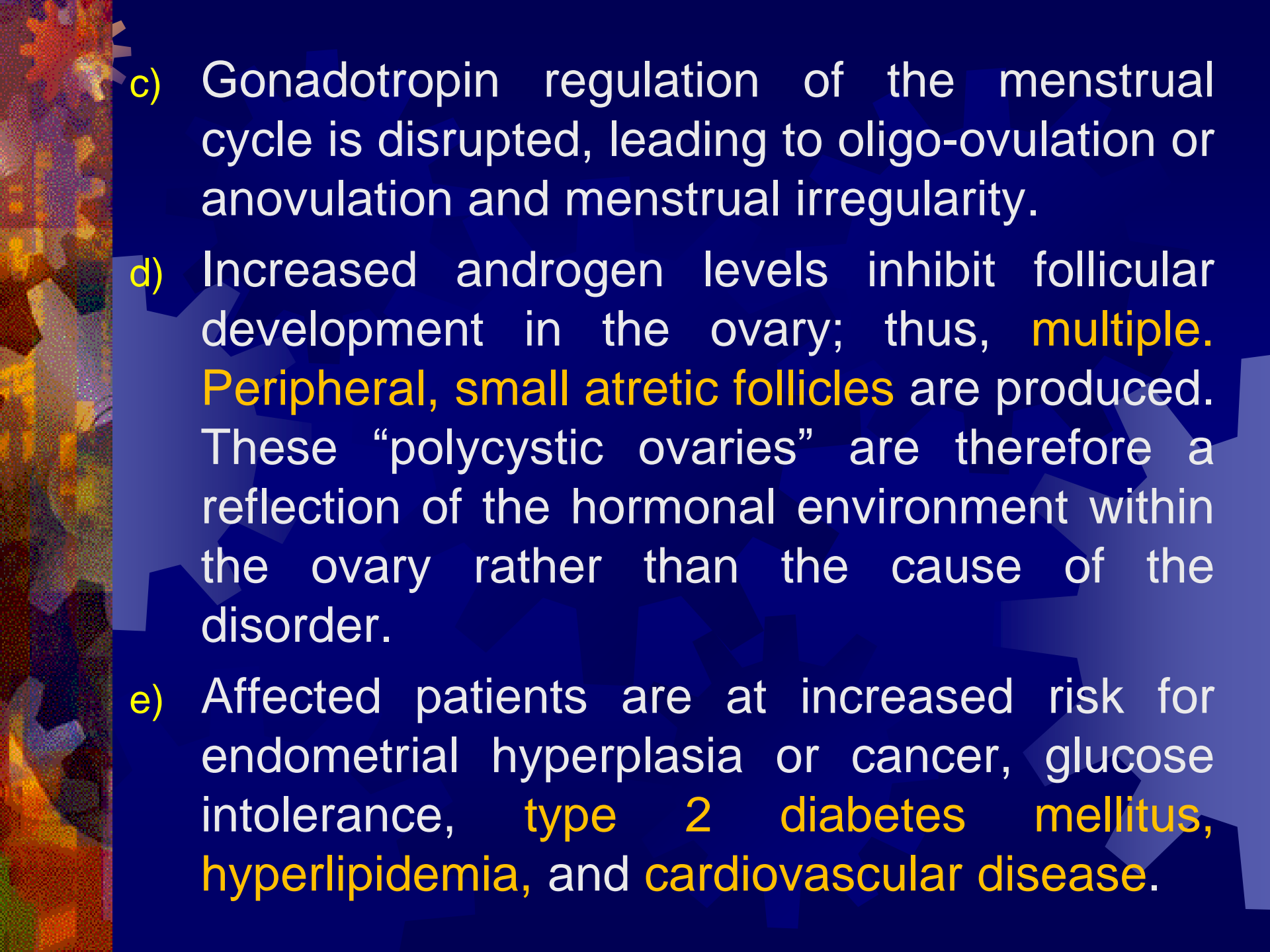
- This heterogeneous **endocrine, metabolic, and genetic** disorder is seen in 5 to 10% of the general population and is the cause of androgen excess in 65 to 85% of hirsute patients. This syndrome is characterized by hyperandrogenism, oligomenorrhea or amenorrhea (caused by chronic anovulation), and obesity.
- It is associated with **insulin resistance**. Patients usually present with hirsutim, menstrual irregularity and infertility.



a) The fundamental pathophysiologic defect is not known.

b) Increased production of androgens may result from:

- Increased secretion of luteinizing hormone (LH) from the anterior pituitary, leading to increased ovarian androgen production.
- Insulin resistance and compensatory hyperinsulinemia, stimulate ovarian and adrenal androgen production by direct and indirect mechanisms.

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- c) Gonadotropin regulation of the menstrual cycle is disrupted, leading to oligo-ovulation or anovulation and menstrual irregularity.
 - d) Increased androgen levels inhibit follicular development in the ovary; thus, **multiple. Peripheral, small atretic follicles** are produced. These “polycystic ovaries” are therefore a reflection of the hormonal environment within the ovary rather than the cause of the disorder.
 - e) Affected patients are at increased risk for endometrial hyperplasia or cancer, glucose intolerance, **type 2 diabetes mellitus, hyperlipidemia,** and **cardiovascular disease.**

2- Idiopathic hirsutism:

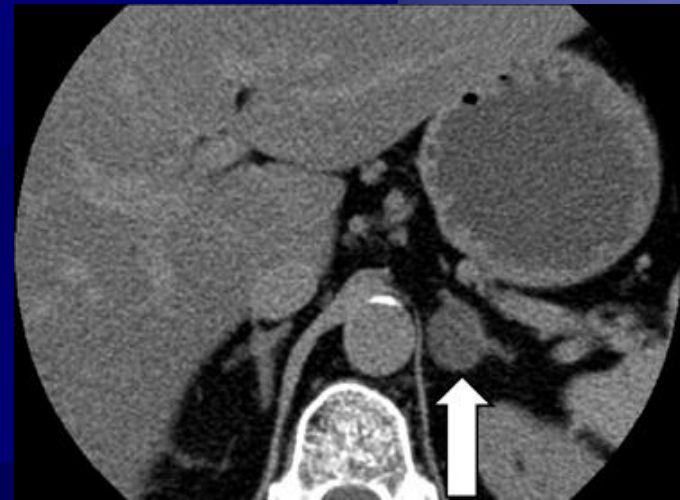
- This condition, accounts for 15 to 30% of hirsute women.
- It is caused by end-organ (skin) hypersensitivity to androgens.
- It is characterized by:
 - a. Regular ovulatory menstrual cycles.
 - b. Normal circulating androgen levels.
 - c. Increased peripheral conversion of androgens caused by increased skin 5 α -reductase activity.

3- Non classical (adult-onset) adrenal hyperplasia:

- This condition is present in approximately 1% of hyperandrogenic women.
- There is deficiency in activity of adrenal enzymes and thus formation of excess cortisol precursors (e.g., 17-hydroxyprogesterone and androstenedione) which leads to increased production of androgens. The most common enzyme deficiency is **21-hydroxylase**.
- Inheritance is **autosomal recessive**, and occurrence is increased in Ashkenazi Jews.

4- Cushing syndrome:

- Adrenocortical hyperfunction leads to:
 - a. Excess production of corticosteroids.
 - b. Hyperandrogenism.
 - c. Menstrual irregularities.
 - d. Glucose intolerance.
 - e. Obesity.



5- Androgen-producing tumors:

- These are associated with:
 - a. **Sudden-onset** hyperandrogenic state.
 - b. Rapid progression.
 - c. Frank virilization.
- Types are:
 - a. Ovarian tumors (e.g., Sertoli-Leydig cell tumor, thecoma, luteoma of pregnancy).
 - b. Adrenal tumors.



6- Disorders of pituitary origin

- Hyperprolactinemia.
- Acromegaly.

7- Androgenic drug exposure

- Without virilization: phenytoin, diazoxide, corticosteroids, cyclosporine.
- With potential virilization: anabolic steroids, androgen therapy.

8- Y-containing mosaic and incomplete androgen insensitivity.

- These patients show signs of androgen stimulation at puberty.

9- HAIR-AN Syndrome:

- There is hyperandrogenism, insulin resistance, and acanthosis nigricans syndrome.
- This condition is similar to PCOS, but patients have a greater degree of insulin resistance and hyperinsulinemia.
- This disorder is often inherited.



Laboratory Evaluation of Hirsutism

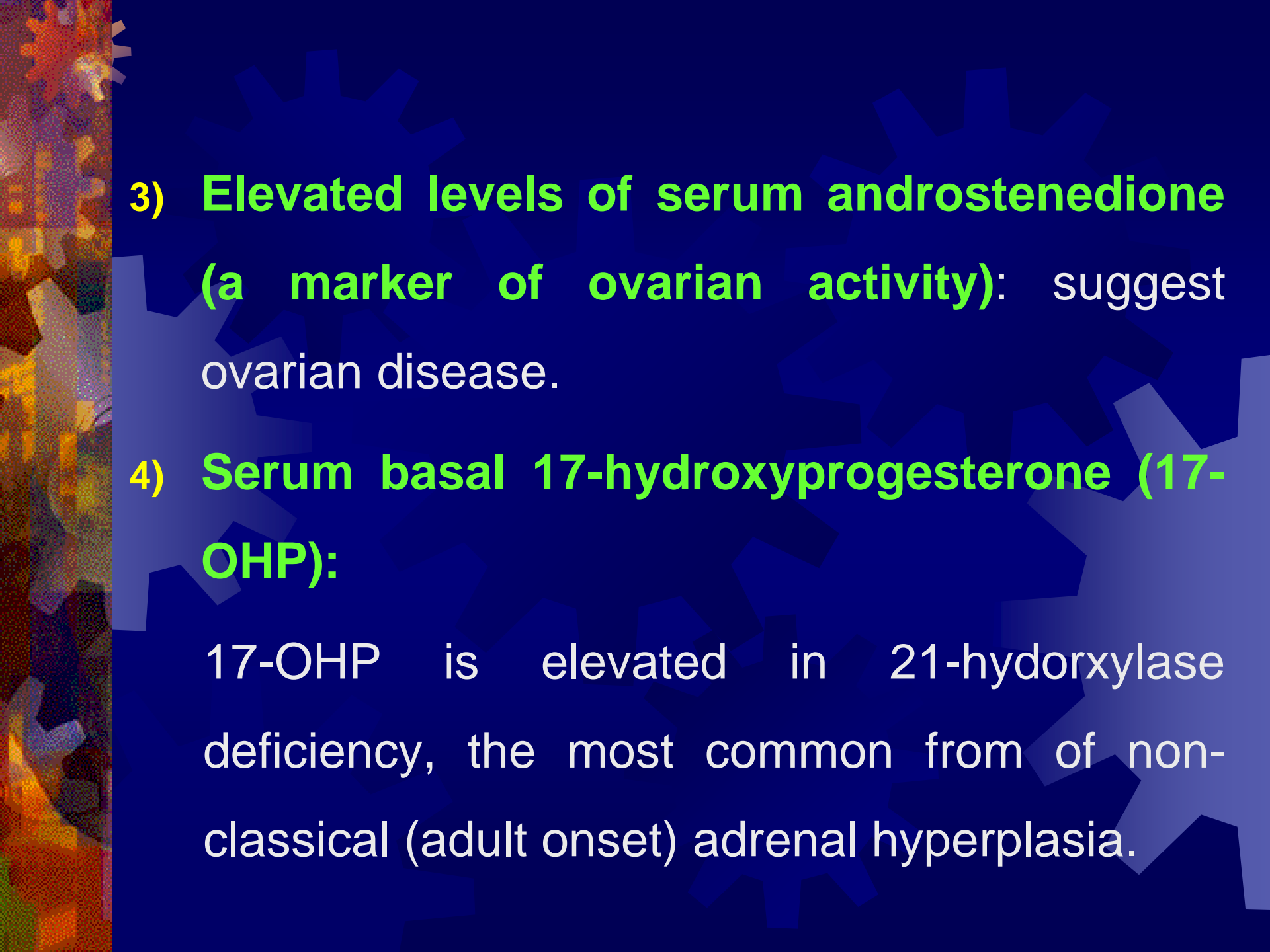
1) Serum total testosterone:

- It is a marker of ovarian and adrenal activity.
- Total testosterone levels greater than 200 ng/dL:
 - This suggest **androgen-producing tumor**.
 - In this condition, **imaging** is indicated:
 - a. Pelvic ultrasound is best to provide and image of the ovaries.
 - b. CT or MRI views the adrenal glands.
- **Total testosterone levels less than 200 ng/dL** are associated with anovulation and hirsutism. The most likely diagnosis is PCOS.

2) Serum DHEAS (a marker of adrenal activity):

It is almost exclusively produced by adrenal glands and reflects adrenal androgen activity.

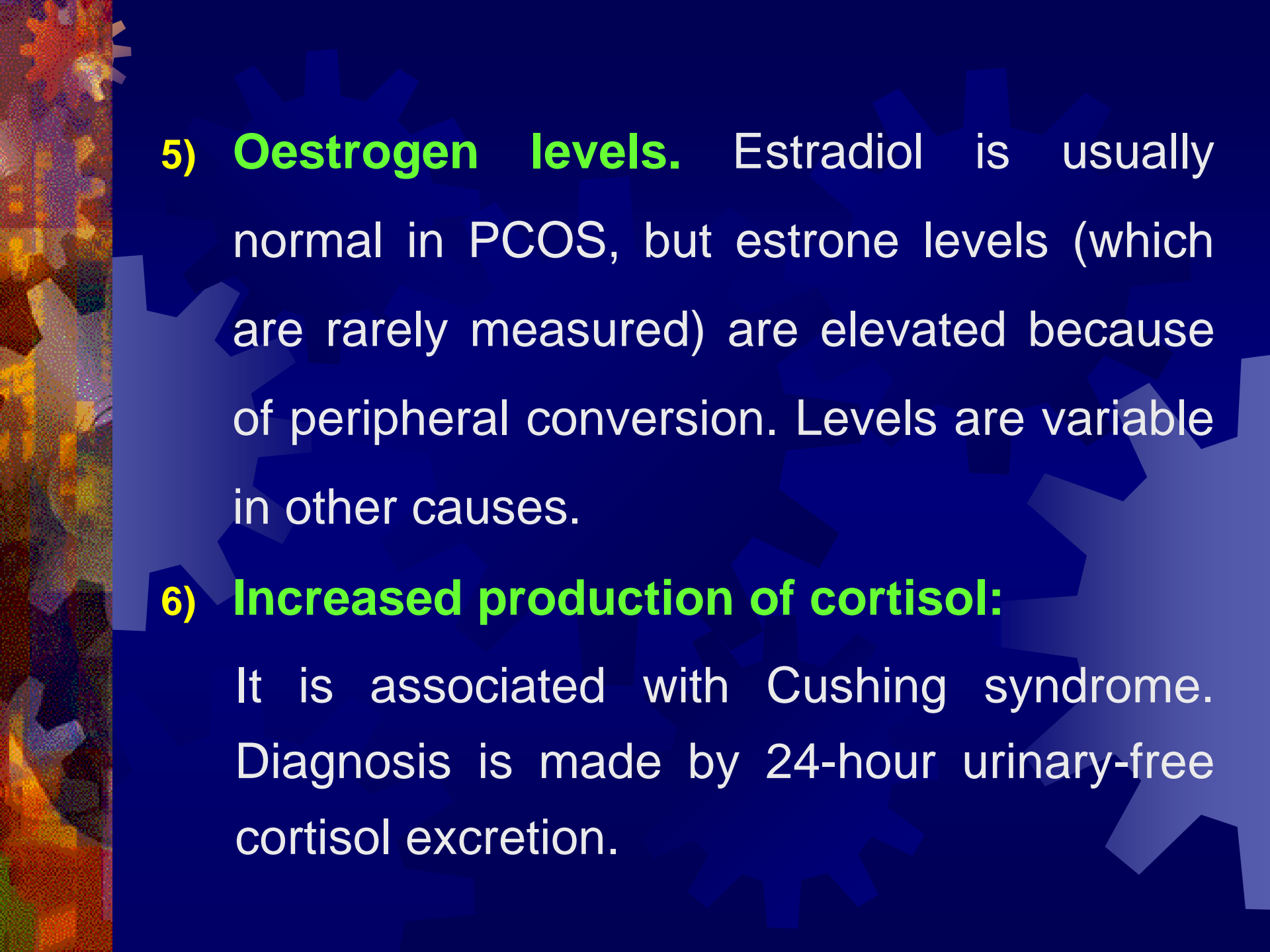
- High level suggest an adrenal tumor.
- Moderately elevated DHEAS levels may occur with anovulation , PCOS, or adrenal hyperplasia.
- Normal DHEAS levels indicate that adrenal disease is less probable and that ovarian androgen production is more likely.



3) Elevated levels of serum androstenedione (a marker of ovarian activity): suggest ovarian disease.

4) Serum basal 17-hydroxyprogesterone (17-OHP):

17-OHP is elevated in 21-hydroxylase deficiency, the most common form of non-classical (adult onset) adrenal hyperplasia.

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5) Oestrogen levels. Estradiol is usually normal in PCOS, but estrone levels (which are rarely measured) are elevated because of peripheral conversion. Levels are variable in other causes.

6) Increased production of cortisol:

It is associated with Cushing syndrome. Diagnosis is made by 24-hour urinary-free cortisol excretion.

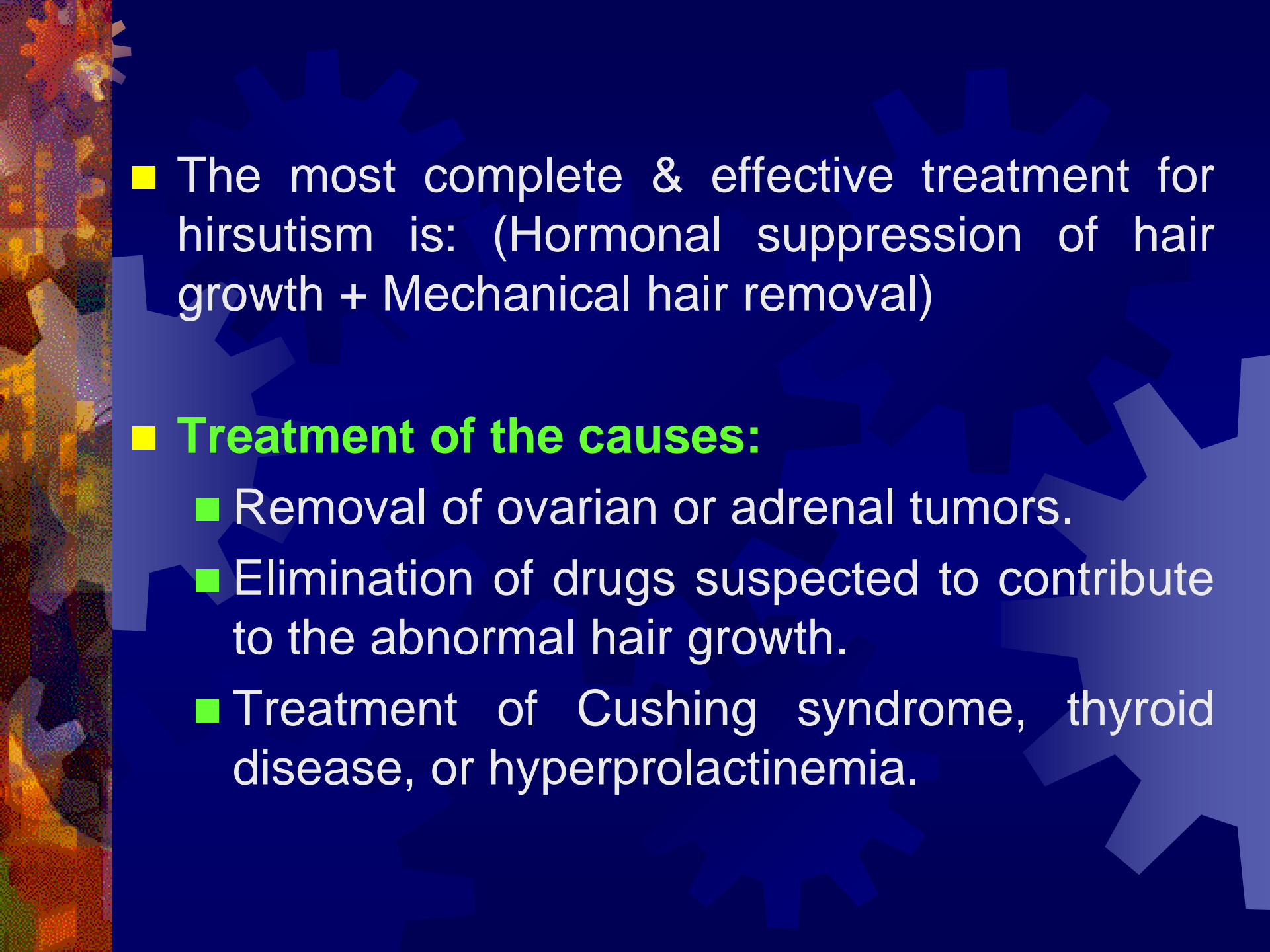
7) **Gonadotropins:**

- An elevated LH: FSH ratio suggests PCOS.
- However, this finding is not present in approximately 40% of patients with PCOS.

8) **Thyroid-stimulating hormone and prolactin.**

The background is a dark blue field filled with various sizes of gear silhouettes in lighter shades of blue. On the left side, there is a vertical strip with a complex, textured pattern of warm colors like orange, red, and brown, resembling a microscopic or geological surface.

Treatment

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- The most complete & effective treatment for hirsutism is: (Hormonal suppression of hair growth + Mechanical hair removal)
 - **Treatment of the causes:**
 - Removal of ovarian or adrenal tumors.
 - Elimination of drugs suspected to contribute to the abnormal hair growth.
 - Treatment of Cushing syndrome, thyroid disease, or hyperprolactinemia.



■ **Suppression of androgen synthesis:**

1. **Combined oral contraceptives:**

- **Dose:** Low-dose formulations 20µg preparations.
- **Action:**
 - **Estrogen & progestin:** ↓ gonadotropin → ↓ ovarian androgen.
 - **Estrogen:** (++) ↑ SHBG.
 - **Progestin:** Displace active androgens at the hair follicle + (--) 5α-reductase activity.
- **Results:** results within 1 to 3 months

2. Medroxyprogesterone acetate:

- Dose: 150 mg intramuscularly every 3 months.
- Action: → Progestin: as above (when COCs are contraindicated)

3. Gonadotropin-releasing hormone (GnRH) agonists:

- Action: (--) hypothalamic-pituitary-ovarian axis
→ ↓ ovarian steroidogenesis.
- Indications: → severely androgenized patients refractory to other therapies.

4. Corticosteroids:

- Indications: severe cases of adrenal hyperplasia (CAH).

■ **Androgen-receptor blockers:**

- Action: (--) binding of DHT to androgen receptor.

■ Types:

- Spironolactone (aldosterone antagonist)
- Flutamide.
- Cyproterone acetate.

■ **Others:**

- Cimetidine: androgen receptor blocker.
- Ketoconazole: (--) adrenal & ovarian androgen synthesis.
- Insulin-sensitizing agents: e.g, metformin
- 5 α -reductase inhibitors.

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■ Supportive measures:

- Shaving, tweezing, waxing, and use of depilatories → temporary measures, which may need to be repeated daily.
- Bleaching is effective for mild hair growth.
- Electolysis: permanent destruction of hair follicles: Multiple treatment are needed.
- Laser epilation: provides directed damage to hair follicles, which temporarily or permanently remove terminal hair, can be used over a larger area.

**Thank
You**

