Hirsutism

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Hirsutism is defined as the development of a malelike pattern of excess hair especially in women. Hirsutism often results from raised androgen levels in the body and may indicate the existence of a serious underlying endocrine condition, such as polycystic ovary syndrome (PCOS). Treatment of hirsutism may require both medical and cosmetic actions. Medical therapy aims to counteract any suspected hormonal imbalance and can include administration of oral contraceptives and antiandrogens. Cosmetic treatment directly addresses excess hair and seeks to either remove the hair or diminish its appearance. Cosmetic options range from conventional methods, such as shaving and waxing, to modern techniques, such as laser photoepilation.

Hirsutism refers to the growth of coarse terminal hair in females that follows a malelike pattern, most commonly in the upper lip area, beard area, abdomen, or chest. The amount of hair that is considered normal is subjective. In some cultures, women are disturbed by even a small amount of excess hair, while in other cultures, larger amounts may be tolerated and considered normal. The perception of excess hair has an associated psychosocial stigma that affects the lives of afflicted women considerably.[1,2]

ETIOLOGY AND PATHOPHYSIOLOGY

There is a wide variety of conditions that can cause hirsutism. Most of these conditions are associated with raised levels of androgens in the body, which often stem from a dysfunction in the ovulatory process. Idiopathic hirsutism, on the other hand, refers to hair growth that occurs despite normal androgen levels and normal ovulatory function.

To comprehend the underlying mechanism of hirsutism, it is necessary to understand the physiology of hair growth. There are 2 types of hair: fine, nonpigmented vellus hair and coarse, pigmented terminal hair. Both of these hair types originate from the same pilosebaceous unit in the skin. Development of terminal hair mainly is dependent on stimulation of the pilosebaceous unit by androgens. Overstimulation of pilosebaceous units leads to growth of terminal hair in atypical areas of the body, which causes hirsutism. Some important factors that influence the follicle stimulation process are: the quantity of androgens secreted by the adrenal glands and the ovaries; the amount of free androgens circulating in the blood; the metabolic clearance rate; and the degree of sensitivity of hair follicles to androgens. Peripheral conversion of testosterone to dihydrotestosterone mediated by 5α-reductase, particularly type 1 isoform[3,4] and the metabolism of dihydrotestosterone by 3α-hydroxysteroid dehydrogenase,[5,6] plays a major role in determining the degree of sensitivity of hair follicles to androgens (Figure). Activity of 5α-reductase mainly is controlled by androgen levels, but studies have shown that insulinlike growth factor 1,[7] transforming growth factor-β, epidermal growth factor, and inhibin and activin[8] also regulate its activity.

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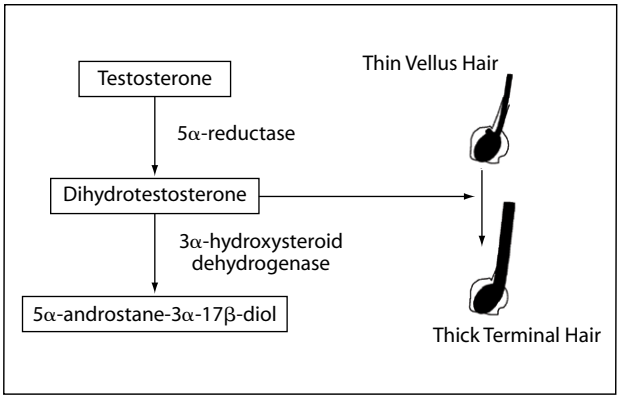

Androgens and the terminalization of hair follicles.

Hirsutism may be considered a clinical presentation of many different conditions rather than a specific disease entity unto itself. Hirsutism is associated with conditions such as polycystic ovary syndrome (PCOS), ovarian neoplasm, congenital adrenal hyperplasia, Cushing syndrome, adrenal neoplasm, obesity, hyperinsulinism, hyperprolactinemia, excess growth hormone, and hypothyroidism (Table 1).

TREATMENT

Hirsutism treatment options may be divided into 2 main categories: those that treat the underlying disorder and androgenic dysfunction, and those that simply remove unwanted hair. The aspect of therapy that addresses androgenic dysfunction mostly consists of medical treatment, while procedures for hair removal have evolved to include a wide spectrum of options ranging from conventional methods, such as shaving, to more modern processes, such as laser and intense pulsed light therapies.

Medical Therapy

Pharmacologic therapy is aimed at either lowering the free androgen level or reducing the sensitivity of hair follicles to androgens. These aims can be accomplished by drugs that suppress androgen secretion, androgen receptor inhibitors, 5α-reductase inhibitors, or insulin sensitizers. Oral contraceptives suppress androgen production and increase sex hormone–binding globulin, which effectively decreases free androgen quantities.[11]

Oral Contraceptives—Oral contraceptives suppress pituitary production of luteinizing and follicle-stimulating hormones, thereby reducing ovarian androgen output. Oral contraceptives are particularly useful in situations where hirsutism is caused by an overproduction of androgens by the ovaries, as in cases of PCOS. Oral contraceptive pills used for treating hirsutism contain ethynyl estradiol in combination with a nonandrogenic progestin such as norgestimate or norethindrone. Progestins with antiandrogenic activity such as cyproterone acetate and drospirenone also can be used in combination with ethynyl estradiol.[12,13]

Antiandrogens—This category includes cyproterone acetate, spironolactone, and flutamide, which inhibit the binding of androgens to the peripheral androgen receptors. Flutamide, unlike cyproterone acetate or spironolactone, is a nonsteroidal drug. Antiandrogens may be used alone or as an adjunct to contraceptives. Recent data, however, suggest that antiandrogens do not provide substantial benefits.[14]

TABLE 1

Causes of Hirsutism

Idiopathic hirsutism
Ovarian causes
Polycystic ovaries
Hyperreactio luteinalis[9,10]
Ovarian tumors
Luteoma of pregnancy
Arrhenoblastomas
Leydig cell tumors
Hilar cell tumors
Thecal cell tumors
Adrenal causes
Congenital adrenal hyperplasia
Cushing syndrome
Adrenal neoplasm
3β-hydroxysteroid dehydrogenase
11β-hydroxylase deficiency
Hypothyroidism
Insulin resistance and hyperinsulinemia
Anorexia nervosa
Acromegaly
Porphyria
Hyperprolactinemia
Drugs
Oral contraceptives
Phenytoin
Minoxidil
Diazoxide
Anabolic steroids

α-Reductase Inhibitors—5α-Reductase type 2 is responsible for the conversion of testosterone to dihydrotestosterone in peripheral tissues, including the hair follicles found in the skin. Inhibitors of this enzyme, such as finasteride can be effective in treating hirsutism.[15,16]

Insulin-Sensitizing Drugs—Hyperinsulinism and insulin resistance contribute substantially to the hyperandrogenism associated with PCOS, which may be the most common cause of hirsutism.[17] Metformin, an insulin sensitizer, has come to be regarded as first-line therapy for PCOS. Some studies have shown insulin sensitizers to be effective in treating hirsutism, especially hirsutism associated with PCOS[18,19]; recent analyses, however, have shown that insulin sensitizers produce inconsistent results.[20,21]

Removal of Unwanted Hair

Removal of unwanted hair is a central aspect of hirsutism treatment. Although mild forms of hirsutism may be controlled by the aforementioned medical procedures, severe forms of hirsutism usually require removal of terminalized hair follicles in addition to medical therapy. The different methods of hair removal include shaving, waxing, plucking, threading, depilatory creams, bleaching, eflornithine cream, electrolysis, lasers, and intense pulsed light–assisted hair removal.

Temporary Methods—Several of the hair removal methods are classified as temporary because their effects usually only last for a few days or weeks (Table 2). These methods do not impede the permanent growth of hair and therefore must be repeated as hair reappears.

TABLE 2

Temporary Methods of Hair Removal

	Mechanism	Advantages	Disadvantages
Shaving	Manual or electric razor is used. Hair is cut at or just below the skin surface	Easy and inexpensive	Cuts may occur; effective only for a few days or weeks; hair regrowth appears thicker
Waxing	Hot or cold wax is applied and then ripped off using a piece of paper or cloth	Hair is removed at or near the base; effects usually last longer than shaving	Patient discomfort; may result in irritation and scarring; an experienced person is needed to perform the procedure
Plucking and threading	Tweezers or twisted thread is used	Hair is removed above the hair bulb	May cause discomfort and folliculitis
Depilatory cream	Usually contains calcium thioglycolate, which breaks down disulfide bonds in keratin of hair, which is then easily scraped off	Ease of application; can be used at home; quick results	Sulfur compounds may lead to irritation and pruritus; bad odor; hair grows back within a few days
Bleaching agent	Usually contains hydrogen peroxide	Masks dark hair	Does not remove hair; may cause irritation, pruritus, skin discoloration

Eflornithine—Eflornithine initially was developed as an anticancer drug. It later was discovered that one of the side effects of eflornithine is hair loss. Eflornithine is used in a cream formulation to treat hirsutism.[22] By prolonging the anagen phase of the hair growth cycle through the inhibition of ornithine decarboxylase activity, eflornithine makes hair appear fine and less noticeable and delays the return of the hair growth.[23] Eflornithine may best be used in combination with laser treatment. In recent studies, combination treatment demonstrated more favorable results than either mode of treatment alone.[24]

Permanent Hair Reduction—Permanent hair reduction as defined by the US Food and Drug Administration refers to long-term, stable reduction in the number of hairs that regenerate after a treatment regime that includes several sessions. The number of hairs that reappear must remain stable over a time period greater than the duration of a complete growth cycle of the hair follicles, which varies from 4 to 12 months depending on where the hair is situated. Permanent hair removal does not refer to complete removal of all hair from a specific area; therefore, some hair growth may occur even though treatment has been completed successfully. Permanent hair reduction can be achieved by electrolysis or by photoepilation, which include both laser and intense pulsed light methods.

Electrolysis—Electrolysis is a popular method of permanent hair reduction whereby an electric current passes through a probe that has been inserted into the skin, destroying the hair follicle. The process is slow and multiple treatment sessions often are necessary. The success of the procedure is operator-dependent because complete destruction of the follicular isthmus and hair bulb is needed to prevent the regrowth of hair.[25] The adverse effects of electrolysis include pain and erythema. Scarring and keloid formation also may occur in susceptible individuals.

Photoepilation—Photoepilation operates on the principle of selective photothermolysis. Selective photothermolysis occurs when melanin in hair follicles absorbs a selected wavelength and pulse duration of light from a laser before the light's heat dissipates into surrounding tissue. This results in the destruction of hair follicles while leaving neighboring skin unaffected. This technique has proved to be superior to conventional hair removal treatment (shaving, waxing, depilatory creams).

The efficacy of laser treatment, as well as the severity of its side effects, are influenced by a number of factors, including laser wavelength, pulse width, spot size, epidermal-cooling mechanisms, and treatment regimen.

Several wavelengths of light, ranging from the visible to the infrared spectrum, are used in laser treatment. These include the ruby laser (694 nm), alexandrite laser (755 nm), diode laser (810 nm), and Nd:YAG laser (1064 nm). One study concluded that the alexandrite laser achieved the most effective and long-lasting reduction, removing, on average, 50% of hair for up to 6 months.[26] Rotational therapy between the various wavelengths has been found to be both more or less effective than consistent use of a single wavelength depending on the study.[27]

It has been reported that patient discomfort varies depending on the wavelength used. Nd:YAG laser was found to be the least comfortable of all lasers, while alexandrite and diode lasers were identified as the least painful options.[28]

Skin tone has been well-documented in its influence on the efficacy, discomfort, and side effects of laser treatment. The additional melanin that is present in darker skin (specifically, skin phototypes IV, V, and VI[29]) can act as a chromophore, absorbing energy. This puts the patient at a greater risk of skin damage. The usual side effects associated with photoepilation are folliculitis, pigmentary changes, blisters, and crusting.[30]

Long-pulsed Nd:YAG wavelength–based laser systems are best suited to reduce the risk of side effects in treating darker-skinned patients. Modern cooling devices also reduce the risk of side effects.[30] Additionally, darker-skinned patients have been found to experience higher levels of discomfort during laser treatment because more heat is absorbed by the skin. This issue is compounded by the increased pulse duration and wavelength often used in treating darker-skinned patients. However, discomfort is substantially reduced when laser treatment is combined with pneumatic skin flattening.[31] The increased heat absorbance by the skin of patients of dark complexion also may reduce the efficacy of laser treatment because less heat is absorbed by the hair follicle. One study[32] found alexandrite laser therapy to be most effective in treating darker-skinned patients and concluded that diode lasers were best for lighter-skinned patients. However, the higher fluence necessary to treat darker-skinned patients increases the risk of complications particularly blistering and postinflammatory pigmentation.[32,33]

Another variable that has been found to influence the outcome of laser hair removal treatment is hair type. Treatment has been shown to be most effective in darker-haired patients. This phenomenon can be understood because of the concept of selective photothermolysis; darker hair readily absorbs light and thus incurs greater damage than light hair.[34]

Caution to Patients—It is important to ensure that patients undergoing laser hair removal treatment have realistic expectations. Patients seeking hair removal often

are misled by advertisements promising permanent hair reduction, which does not necessarily entail permanent removal of all hair. As stated above, according to the US Food and Drug Administration, permanent hair reduction is defined as a long-term, stable reduction in hair growth, following a treatment regimen that includes several sessions, with hair growth being impeded over a time period greater than the duration of a complete growth cycle of hair follicles for that area.[26] Permanent hair reduction does not refer to complete, lifetime elimination of all hair from a specific area.

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