REVIEW

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Update on the management of hirsutism

■ ABSTRACT

Hirsutism is a source of significant anxiety in women. While polycystic ovary syndrome or other endocrine conditions are responsible for excess androgen in many patients, other patients have normal menses and normal androgen levels ("idiopathic" hirsutism). The goal of the evaluation is to rule out any underlying pathology. The goals of therapy are to treat any underlying condition and to remove the excess hair. Current options for hair removal are discussed. Educating patients so they have reasonable treatment expectations is essential, as significant improvement may take weeks or months, and treatment may need to be repeated on an ongoing basis.

■ KEY POINTS

The finding of polycystic ovaries is not required for the diagnosis of polycystic ovary syndrome, nor does their presence prove the diagnosis. Gonadotropin-dependent functional ovarian hyperandrogenism is believed to cause this syndrome; however, mild adrenocorticotropic-dependent functional adrenal hyperandrogenism also is a feature in many cases.

Even women with mild hirsutism with subtle symptoms and signs of hyperandrogenism can have elevated androgen levels, and thus, they deserve a laboratory evaluation.

Laser treatment does not result in complete, permanent hair reduction, but it is more effective than shaving, waxing, and electrolysis, producing partial hair reduction for up to 6 months.

HIRSUTISM CAUSES SIGNIFICANT anxiety and lack of self-esteem in women. Although it is itself a benign condition, it is often the sign of an underlying and possibly serious endocrine condition.

As we will discuss, the diagnosis begins with a detailed history and physical examination, with laboratory testing and imaging as needed to confirm or rule out underlying causes. Management begins with patient education and support and includes hair removal and drug treatment of any underlying metabolic derangement.

■ PREVALENCE AND IMPACT

Hirsutism is a common disorder of excess growth of terminal hair in an androgen-dependent male distribution in women, including the chin, upper lip, breasts, upper back, and abdomen.[1] It affects 5% to 10% of women of reproductive age.[1,2]

Hirsutism should be differentiated from hypertrichosis, which can be hereditary or acquired, and which is defined as increased general hair growth in androgen-independent areas.[1]

Excess hair is cosmetically concerning for women and can significantly affect self-esteem.[3] Normal or acceptable hair growth depends on a woman's ethnicity and her perception of familial, cultural, and societal norms for the quantity and distribution of hair. Mediterranean women generally have a medium amount of body and facial hair, whereas Asian women have a minimal amount.[1,4,5]

Hirsutism can be clinically graded according to the Ferriman-Gallwey scale[2,6] and is defined as a Ferriman-Gallwey score of 8 or higher.[1]

HOW CIRCULATING ANDROGENS AFFECT HAIR FOLLICLES

In androgen-dependent areas, circulating androgens influence hair follicle characteristics. Androgens increase the size and diameter of the hair fibers in certain androgen-dependent sites, as seen in puberty with the transformation of vellus hairs (small, nonpigmented hairs) into terminal hairs (large, pigmented hairs) in the pubic and axillary regions in women, as well as the beard area in men.[2,7] Interestingly, the same circulating androgens cause miniaturization of the susceptible hair follicles of the central scalp.[7] The susceptibility of the hair follicle to the effects of the androgens may be genetically determined.[7,8]

Hirsutism is a sign of hyperandrogenism and increased action of androgens on hair follicles. In women, about half of circulating testosterone arises from the ovaries and adrenal glands; the rest originates from peripheral conversion of weaker androgens (such as androstenedione produced by the adrenals and ovaries) into testosterone.[9] Dehydroepiandrosterone sulfate (DHEAS) originates mainly in the adrenal glands.[9,10] Testosterone is converted to the more potent dihydrotestosterone (DHT) by type II 5-alpha reductase in the skin, which can then act on susceptible hair follicles.[7,11] Therefore, hirsutism can be a consequence of endogenous androgen overproduction from the ovaries or the adrenal glands (or both), of exposure to an exogenous source of androgen such as a drug, or of heightened hair follicle sensitivity and metabolism of normal circulating androgen levels (target end-organ dysfunction).[1]

'IDIOPATHIC' HIRSUTISM: A MISLEADING DIAGNOSIS

Many women with hirsutism are found to have polycystic ovary syndrome as the underlying cause, but hirsutism is also commonly labeled as idiopathic when it occurs without an obvious cause, eg, in women with regular menses and normal androgen levels and without features suspicious for other causes of hirsutism.[1,2,12,13] But while this term is commonly used,[1,12] it may be misleading, especially if the diagnosis of idiopathic hirsutism is based on standard laboratory tests, which do not always detect androgen excess.[2,13] Minor ovarian or adrenal functional hyperandrogenism,[14] increased peripheral activity of 5-alpha reductase in the hair follicle, or abnormalities in the androgen receptor have been implicated in the pathogenesis of so-called idiopathic hirsutism.[2,15]

HIRSUTISM AND POLYCYSTIC OVARY SYNDROME

Polycystic ovary syndrome, a metabolic syndrome, presents clinically with menstrual irregularities such as oligomenorrhea or amenorrhea, infertility, and signs of hyperandrogenism such as hirsutism, acne, or androgenetic alopecia.[16,17] Metabolic disturbances including insulin resistance, impaired glucose tolerance, hyperlipidemia, and obesity (body mass index > 30 kg/m^2) also can occur, thus increasing cardiovascular risk.[16–18]

The finding of polycystic ovaries is not required to make the diagnosis of polycystic ovary syndrome, and their presence does not prove the diagnosis.[16,19] Gonadotropin-dependent functional ovarian hyperandrogenism is believed to cause this syndrome; however, mild adrenocorticotropic-dependent functional adrenal hyperandrogenism also is a feature in many cases. In rare cases, polycystic ovary syndrome presents with an isolated elevation of DHEAS.[16,20]

OTHER CONDITIONS OF EXCESS ANDROGEN

The syndrome of hyperandrogenism, insulin resistance, and acanthosis nigricans, abbreviated as HAIR-AN, is separate from polycystic ovary syndrome; it characterizes a group of inherited syndromes associated with severe metabolic abnormalities of insulin and glucose metabolism and with marked clinical signs of hyperandrogenism.[12]
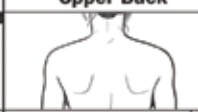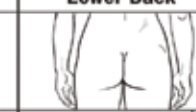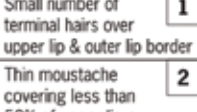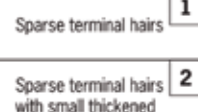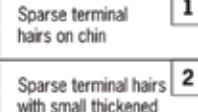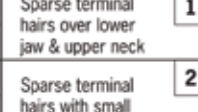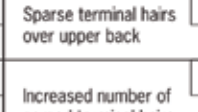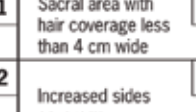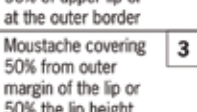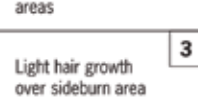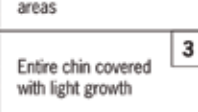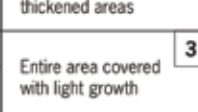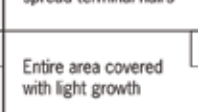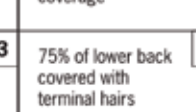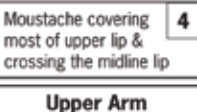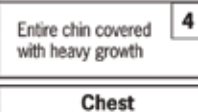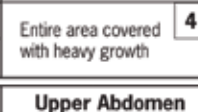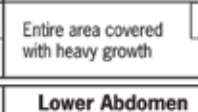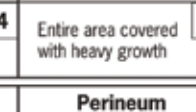
The syndrome of seborrhea, acne, hirsutism, and acanthosis nigricans, abbreviated as SAHA, while not itself a diagnosis, is a clinical spectrum of dermatologic signs and symptoms also associated with hyperandrogenism. These are signs that may present with the HAIR-AN syndrome or with another cause of excess androgens, such as idiopathic, ovarian, adrenal,
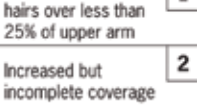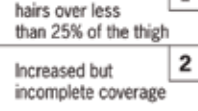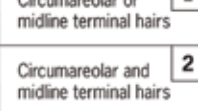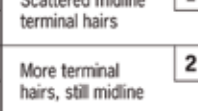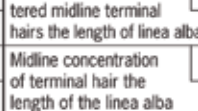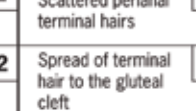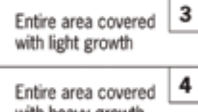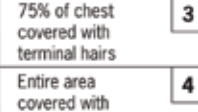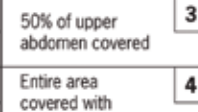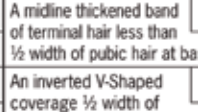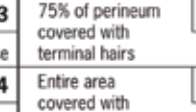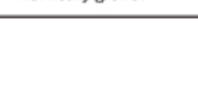
Normal or acceptable hair growth depends on ethnicity and familial, cultural, and societal norms

Age_____ Height_____ Weight_____ Body Mass Index_____ Blood Pressure_____

Caucasian ☐   African American ☐   Asian ☐   N. American Indian ☐   Mediterranean ☐

Upper Lip
1. Small number of terminal hairs over upper lip & outer lip border
2. Thin moustache covering less than 50% of upper lip or at the outer border
3. Moustache covering 50% from outer margin of the lip or 50% the lip height
4. Moustache covering most of upper lip & crossing the midline lip

Sideburn Area
1. Sparse terminal hairs
2. Sparse terminal hairs with small thickened areas
3. Light hair growth over sideburn area
4. Thick growth over sideburn area

Chin
1. Sparse terminal hairs on chin
2. Sparse terminal hairs with small thickened areas
3. Entire chin covered with light growth
4. Entire chin covered with heavy growth

Lower Jaw & Neck
1. Sparse terminal hairs over lower jaw & upper neck
2. Sparse terminal hairs with small thickened areas
3. Entire area covered with light growth
4. Entire area covered with heavy growth

Upper Back
1. Sparse terminal hairs over upper back
2. Increased number of spread terminal hairs
3. Entire area covered with light growth
4. Entire area covered with heavy growth

Lower Back
1. Sacral area with hair coverage less than 4 cm wide
2. Increased sides coverage
3. 75% of lower back covered with terminal hairs
4. Entire area covered with heavy growth

← Subtotal

Upper Arm
1. Scattered terminal hairs over less than 25% of upper arm
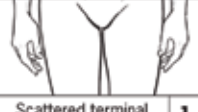2. Increased but incomplete coverage
3. Entire area covered with light growth
4. Entire area covered with heavy growth

Thigh
1. Scattered terminal hairs over less than 25% of the thigh
2. Increased but incomplete coverage
3. Entire area covered with light growth
4. Entire area covered with heavy growth

Chest
1. Circumareolar or midline terminal hairs
2. Circumareolar and midline terminal hairs
3. 75% of chest covered with terminal hairs
4. Entire area covered with terminal hair growth

Upper Abdomen
1. Scattered midline terminal hairs
2. More terminal hairs, still midline
3. 50% of upper abdomen covered
4. Entire area covered with terminal hair growth

Lower Abdomen
1. Small number of scattered midline terminal hairs the length of linea alba
2. Midline concentration of terminal hair the length of the linea alba
3. A midline thickened band of terminal hair less than ½ width of pubic hair at base
4. An inverted V-Shaped coverage ½ width of pubic hair at base

Perineum
1. Scattered perianal terminal hairs
2. Spread of terminal hair to the gluteal cleft
3. 75% of perineum covered with terminal hairs
4. Entire area covered with terminal hair growth

← Subtotal

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Total Score =

FIGURE 1. A modification of the Ferriman-Gallwey scoring system. A score of 8 or more indicates hirsutism.

or hyperprolactinemic hyperandrogenism.[21]

Thyroid disease, hyperprolactinemia, acromegaly, Cushing syndrome, exogenous factors such as androgenic drugs, and nonclassical congenital adrenal hyperplasia can also produce hirsutism.[12] In nonclassical congenital adrenal hyperplasia, which is typically caused by a deficiency of 21-hydroxylase, patients present with premature pubarche, hirsutism in the prepubertal years, and menstrual irregularities including primary amenorrhea.[22,23]

Important rare causes of hirsutism include benign and malignant androgen-secreting tumors of adrenal or ovarian origin. In such cases, hirsutism can have an acute onset or rapid progression and may be associated with features of virilization, such as deepened voice, increased muscle mass, androgenetic alopecia, clitoromegaly, and increased libido.[12]

■ A THOROUGH HISTORY IS CRITICAL TO DIAGNOSIS

A thorough medical history can provide important diagnostic clues in women with hirsutism. The clinician should elicit details about the onset and progression of the hair growth,[12,15] previous treatments, and any cutaneous signs of hyperandrogenism, such as acne, seborrhea, acanthosis nigricans, or patterned hair loss.

Also important are the menstrual history and a history of infertility. Primary amenorrhea is defined as failure to menstruate by 16

years of age if secondary sexual characteristics have developed, or by 14 years of age if no secondary sexual characteristics have developed, and it can indicate nonclassical congenital adrenal hyperplasia.

The clinician should also try to determine if the patient has a history of galactorrhea or symptoms of virilization (eg, deepened voice, clitoromegaly, increased muscle mass); a family history of hirsutism, polycystic ovary syndrome, HAIR-AN syndrome, metabolic conditions such as type 2 diabetes mellitus, or cardiovascular disease[12,15]; or a history of symptoms of any condition known to produce hirsutism, such as Cushing disease, acromegaly, or a thyroid disorder. Also important is a drug history to determine if the patient has taken drugs such as androgens, anabolic steroids, or valproic acid (Depakote).[20]

THE PHYSICAL EXAMINATION

The physical examination involves use of the Ferriman-Gallwey hirsutism scoring system or a modified Ferriman-Gallwey scoring system (**FIGURE 1**), which helps categorize the severity and distribution of excess hair growth. A Ferriman-Gallwey score of 8 to 15 (out of a possible 36) indicates moderate hirsutism, whereas a score above 15 indicates severe hirsutism.[2,15]

Another proposed predictor of hirsutism is that terminal hair on the chin or the lower abdomen (Ferriman-Gallwey score ≥ 2) is nearly 100% sensitive and 27% specific at predicting total-body hirsutism.[24]

As part of the physical examination, the clinician should also look for other cutaneous signs of hyperandrogenism, such as acne, androgenetic alopecia, and seborrhea. Acanthosis nigricans is a sign of insulin resistance. Height and weight should be measured and the body mass index calculated. Blood pressure should be recorded, as high blood pressure may be seen in Cushing syndrome and is an important cardiovascular risk factor. Signs of virilization should be identified. Indicators of Cushing disease such as striae, moon facies, fat redistribution, fragile skin, and proximal myopathy should be noted as well as signs of thyroid disease, such as textural skin changes, goiter, and hair loss. Expressible or spontaneous galactorrhea suggests hyperprolactinemia.

Acromegaly is associated with coarse facies and enlarged hands and feet. Many of the endocrinopathies can be caused by a pituitary adenoma, which can manifest as a visual field defect, so visual fields should be examined.[25] The examination should also exclude any palpable ovarian or adrenal mass.[12]

WHEN IS ADDITIONAL TESTING NEEDED?

Laboratory and radiologic testing in patients with hirsutism may be needed to confirm the diagnosis of a suspected underlying condition or to exclude serious underlying pathology (**TABLE 1**).[1,12,15–18,20,22,23,25–28]

The current Endocrine Society guidelines[20] recommend obtaining an early-morning testosterone blood level in the following patients:

- Women with moderate or severe hirsutism
- Women with hirsutism of any degree with sudden onset or rapid progression, or accompanied by signs or symptoms suggesting malignancy or polycystic ovary syndrome: eg, menstrual irregularity, infertility, central obesity, clitoromegaly, or acanthosis nigricans.[15,20]

Testing androgen levels in mild, isolated hirsutism has not been proven to be useful or to alter management.[20]

Free testosterone level

An early-morning total or free testosterone level is the initial test in the laboratory evaluation of hirsutism.[12,15] Additional specialized laboratory testing may be needed to determine the free testosterone level,[15] as the free testosterone test is not available at all laboratories. A normal total testosterone level does not exclude hyperandrogenism but can suggest the diagnosis of idiopathic hirsutism.[15]

Further testing is needed if the total testosterone level is normal or only slightly elevated, or if there is a strong clinical suspicion of an underlying condition such as endocrinopathy or tumor. It is also useful in patients whose hirsutism responds poorly to medical treatments[15] (see discussion below).

If the total testosterone level is elevated, if the hirsutism is moderate to severe, if there are associated symptoms, or if hirsutism is acute or progressive, a further endocrinologic workup is

Polycystic ovary syndrome, high prolactin, acromegaly, Cushing syndrome, and certain drugs can produce hyperandrogenism

TABLE 1

Tests suggested in the workup of hirsutism

CONDITION	CLINICAL PRESENTATION	TESTS
'Idiopathic' hirsutism	Hirsutism Regular menstrual cycle	Total and free testosterone levels
Polycystic ovary syndrome	Hirsutism Irregular menstrual cycle, infertility Weight gain Acanthosis nigricans Metabolic syndrome (obesity, insulin resistance, type 2 diabetes, lipid abnormalities, cardiovascular disease)	Total and free testosterone levels Sex hormone-binding globulin Dehydroepiandrosterone sulfate Androstenedione Transvaginal ovarian ultrasonography Metabolic screen
HAIR-AN syndrome (hyperandrogenism, insulin resistance, acanthosis nigricans)	Hirsutism Irregular menstrual cycle, infertility Weight gain Acanthosis nigricans Metabolic syndrome (obesity, insulin resistance, type 2 diabetes, lipid abnormalities, cardiovascular disease)	Total and free testosterone levels Sex hormone-binding globulin Dehydroepiandrosterone sulfate Androstenedione Transvaginal ovarian ultrasonography Metabolic screen
Nonclassical congenital adrenal hyperplasia	Hirsutism onset before puberty Menstrual irregularities or primary amenorrhea Premature pubarche	Total and free testosterone levels Sex hormone-binding globulin Dehydroepiandrosterone sulfate Androstenedione 17-hydroxyprogesterone level
Hyperprolactinemia	Hirsutism History of galactorrhea (spontaneous, expressible) Visual field defects if pituitary in origin	Serum prolactin
Acromegaly	Hirsutism Visual field defect, coarse facies, large hands and feet	Somatomedin C (insulin-like growth factor 1) level

Adrenal or ovarian tumor	Hirsutism (acute onset, severe, or progressive)
	Virilization (increased libido, deepened voice,
	  clitoromegaly, increased muscle mass)
		Total and free testosterone level
		Sex hormone-binding globulin
		Dehydroepiandrosterone sulfate
		Androstenedione
		Computed tomography or magnetic
		  resonance imaging (abdomen or pelvis)

Thyroid dysfunction	Hirsutism Hot or cold intolerance Diffuse scalp hair loss Weight change Textural skin changes	Total and free testosterone level Sex hormone-binding globulin Dehydroepiandrosterone sulfate Androstenedione Thyroid-stimulating hormone, free T4 Thyroid autoantibodies
Cushing syndrome	Hirsutism Mood or sleep disturbance Striae, bruising, fragile skin Weight gain Fat redistibution, moon facies, supraclavicular fat pad Proximal weakness, fatigue Hypertension Insulin resistance	24-hour urinary free cortisol Dexamethasone suppression test

needed,[15] possibly including measurement of free testosterone, sex hormone-binding globulin, DHEAS, and androstenedione.[15] Free testosterone, unbound to sex hormone-binding globulin, is the biologically active fraction, with the levels of binding globulin increased by drugs such as oral contraceptives[15] and decreased by high insulin levels in insulin resistance.[25]

Test in patients with mild hirsutism?

Although the guidelines suggest that no additional workup is necessary for women with mild hirsutism, we evaluate all patients with hirsutism and those with the SAHA clinical spectrum by measuring free and total testosterone and DHEAS. In our experience, even women with mild hirsutism with subtle symptoms and signs of hyperandrogenism and mild hirsutism often have elevated androgen levels.

Test in women with idiopathic hirsutism?

In women with idiopathic hirsutism, minor forms of functional ovarian and adrenal hyperandrogenism are believed to play a role and are thought to be undetectable with conventional testing.[25] The gonadotropin-releasing hormone (GnRH) analogue stimulation test may uncover occult hyperandrogenism in this setting, but it is used as a research tool and does not currently have application in routine clinical practice.[14]

It is important to remember that some women with apparent idiopathic hirsutism and a history of regular menstrual cycles are actually oligo-ovulatory or anovulatory. In these instances, another diagnosis should be considered,[13] and referral to an endocrinologist for further evaluation of ovulatory function is recommended.[13]

■ CURRENT USE OF DIAGNOSTIC IMAGING

When malignancy is suspected

A testosterone level above 200 ng/dL suggests an ovarian tumor, and a DHEAS level above 700 μg/dL suggests an adrenal tumor.[26] However, not all tumors present with such high androgen levels, and sudden onset of hirsutism, rapid progression of hirsutism, or signs of virilization suggest a tumor.[15] In such cases, transvaginal ultrasonography, computed to-mography, or magnetic resonance imaging (MRI) of the abdomen can exclude an ovarian or adrenal tumor.

When polycystic ovary syndrome is suspected

The diagnosis of polycystic ovary syndrome is confirmed by two out of three criteria:
- Oligo-ovulation or anovulation
- Clinical or laboratory signs of hyperandrogenism
- Ultrasonographic evidence of polycystic ovaries, with exclusion of other causes of hyperandrogenism.

■ ADDITIONAL LABORATORY TESTING

Tests for polycystic ovary syndrome

Assessment of polycystic ovary syndrome involves transvaginal ultrasonography, but ultrasonographic evidence of a polycystic ovary is not necessary for the diagnosis.[16] A fasting lipid profile and fasting serum glucose are recommended, and if the fasting serum glucose is normal, an oral glucose tolerance test is recommended.[17]

Some have reported measuring the ratio of luteinizing hormone to follicle-stimulating hormone in the workup of polycystic ovary syndrome, and a ratio greater than 2 has been considered indicative but not diagnostic.[16,25] The individual levels of luteinizing hormone, follicle-stimulating hormone, and estradiol are more important in the evaluation of infertility and ovulatory dysfunction. In patients with elevations of these hormones or with these symptoms, referral for infertility screening with an endocrinologist or gynecologist is recommended.[25]

Additional testing and referral for Cushing syndrome, other conditions

Cushing syndrome can be tested for with a 24-hour urine cortisol, overnight low-dose dexamethasone suppression test, and late-night salivary cortisol.[27,28] Referral to an endocrinologist for further testing can differentiate between corticotropin-dependent or corticotropin-independent Cushing syndrome.[25] Cushing syndrome is often associated with hyperandrogenism, particularly in those cases caused by adrenal tumors.[29]

Testing androgen levels in mild, isolated hirsutism has not been shown to alter management

The prolactin level and the level of somatomedin C (insulin-like growth factor 1) can be used to rule out hyperprolactinemia and acromegaly, respectively.[12] If Cushing syndrome, hyperprolactinemia, or acromegaly is diagnosed by endocrinologic testing, pituitary MRI should be performed.[12,25]

Referral to specialist centers with experience with these conditions is essential. Nonclassical congenital adrenal hyperplasia can be screened for by a serum 17-hydroxyprogesterone level measured in the follicular phase.[12] Measurement of thyroid-stimulating hormone, free thyroxine, and thyroid peroxidase antibodies screens for thyroid disease.[12] Hirsutism has been reported with the commencement of L-thyroxine therapy.[30]

■ **THE PRINCIPLES OF TREATMENT**

Patient education regarding the cause of hirsutism and reasonable treatment expectations and emotional support are important in the management of hirsutism. Also important is regular follow-up to measure and document the response to treatment; this can include repeating Ferriman-Gallwey scoring, taking photographs of affected areas, and retesting androgen levels after 3 to 6 months.[12]

Treatment must be continued for an ongoing effect, and most pharmacologic treatments can take up to 3 to 6 months to produce significant improvement.[1]

When an underlying condition is diagnosed, treatment of the condition is essential. Androgen-secreting tumors require surgical management.[12] Cushing disease, hyperprolactinemia, and acromegaly should be clinically apparent from examination and testing, and appropriate referral and standard management should be instigated. Exogenous sources of androgen such as androgenic progestins or anabolic steroids should be discontinued. Lifestyle management is important, and weight loss in obese patients with polycystic ovary syndrome can improve hirsutism as well as mitigate cardiovascular risk factors.[31]

In classic congenital adrenal hyperplasia, glucocorticoid therapy manages both ovulation induction and hirsutism.[20] However, in nonclassical congenital adrenal hyperplasia, glucocorticoid therapy supports ovulation in-

duction, but hirsutism usually requires both systemic antiandrogen and hair removal.[20]

■ **CURRENT OPTIONS FOR HAIR REMOVAL**

The mainstay of treatment of hirsutism is removing the excess hair. Options (**TABLE 2**) include inexpensive, home-based, self-care methods such as plucking, shaving, waxing, using depilatory creams, and bleaching, and more expensive clinic-based treatments such as clinic-based waxing, electrolysis, and laser hair removal. These methods can also be combined with drug therapy.[1]

The choice of method depends on patient preference, adverse effects, the degree of hirsutism, the level of distress, previous treatments, and cost.[1,15,32]

Self-care methods
Self-care methods offer only temporary reduction of excess hairs.

Plucking removes the entire hair, including the root, but it is painful and time-consuming, and it is only practical for areas where few hairs exist, such as on the face.[1]

Shaving is an easy, inexpensive, and painless choice for hair removal. Although a common belief is that shaving causes faster or thicker hair regrowth, shaving affects neither the diameter nor the rate of growth of the hair.[32] Given its masculine association, shaving is not acceptable to most women except perhaps for use on the legs and axillae.[1,32] Shaving can cause irritation, folliculitis, pseudofolliculitis, and infection.[1]

Waxing removes the entire hair. While it is more expensive than plucking, regrowth is slower, occurring over weeks. It is painful and can cause thermal burns, irritation, folliculitis, scarring, and postinflammatory dyspigmentation.[1]

Chemical depilatories, usually thioglycolic acid preparations, are inexpensive, painless, and easy to use. However, the resulting hair reduction is of short duration because the hair shafts are only removed at the level of the skin surface.[1] They can also cause irritant dermatitis.[1]

Bleaching with hydrogen peroxide is inexpensive and can camouflage dark facial hair, but it can also cause skin discoloration and irritation.[1]

Shaving is not a preferred option for most women, except for the legs and axillae

TABLE 2

Hair removal methods and their potential side effects

METHOD	SKIN IRRITATION, DERMATITIS	FOLLICULITIS, PSEUDOFOLLICULITIS	DYSPIGMENTATION	SCARRING	PAIN
Bleaching	+++	None	None	None	None
Depilatory creams	+++	+	None	None	None
Shaving	+	+++	+ [a]	+ [a]	None
Plucking	+	+	+ [a]	+ [a]	+
Waxing	++	+++	++ [a]	+ [a]	+++
Electrolysis	+	+++	++	++	+++
Laser, intense pulsed light treatment	None	Rare [b]	Rare [b]	Rare [b]	+ [c]

[a] Typically follows folliculitis.

[b] Rare if performed by a trained practitioner; dyspigmentation and scarring are more likely in skin photoypes III-VI.

[c] Pain is usually only mild if performed by a trained practitioner using a topical anesthetic and laser cooling device.

THE INFORMATION IN THIS TABLE IS BASED ON THE PERSONAL EXPERIENCE OF WILMA F. BERGFELD, MD.

Clinic-based methods

Electrolysis often results in a permanent reduction in hair growth.[1,32] A fine needle is placed into the hair follicle and an electrical current is applied. Each follicle is treated individually.[1,32] Best results are seen on darker hairs in patients with lighter skin, but it can be used on all skin types and hair colors.[1,32]

Electrolysis is operator-dependent, and there are US Food and Drug Administration (FDA) regulations regarding electrolysis techniques. It requires multiple treatments, and it is painful and can cause erythema, folliculitis, pseudofolliculitis, infection, scarring, and postinflammatory dyspigmentation.[1,32] Some reports suggest that prior waxing and plucking of hairs damages the hair by twisting the hair shaft, making electrolysis more difficult.[32]

Laser treatment uses light of certain wavelengths to damage the hair follicles. While laser hair removal does not result in complete or persistent hair removal, it is more effective than shaving, waxing, and electrolysis, producing partial hair reduction for up to 6 months; the effect is enhanced with multiple treatments.[33,34] The number of treatments required depends on the laser type and on the nature of the patient's hair follicles.[35]

Laser systems for hair removal are of various wavelengths and also include intense pulsed light systems. The choice of system depends on the patient's skin type and hair color. Women with fair skin and dark hair are ideal candidates; longer-wavelength lasers are preferred for darker or tanned skin types.

Adverse effects of laser hair removal include pain, erythema, burns, dyspigmentation, and scarring. Laser cooling devices can prevent or minimize some of these effects. Laser treatment has also been known to cause a paradoxical increase in hair growth.[1,33,34]

■ DRUG THERAPIES FOR HIRSUTISM

Another option for hair removal in patients with hirsutism is drug therapy (**TABLE 3**).[1,12,15,20,31,32,36–42] Several meta-analyses have studied drug treatments for hirsutism and treatment guidelines have been published.[20,36–38] However, the studies are limited by the heterogeneity of patients with hirsutism, small sample sizes, limited methodology,

TABLE 3

Possible side effects of drug treatments for hirsutism

Topical eflornithine cream (Vaniqa)
Mild burning sensation
Acne, pseudofolliculitis barbae
Irritant and allergic contact dermatitis
Effect reverses 8 weeks after discontinuation

Oral contraceptives (low-androgenic progestins)
Breast tenderness
Irregular periods and vaginal bleeding
Mood change, fatigue, headache
Hypertension
Weight gain
Abnormal liver function
Gastrointestinal upset
Decreased libido
Venous thromboembolism risk

Spironolactone (Aldactone)
Irregular periods and vaginal bleeding
Abnormal liver function
Gastrointestinal upset
Decreased libido
Breast tenderness, irritability pre-period
Postural hypotension
Hyperkalemia
Feminization of a male fetus

Cyproterone acetate
Irregular periods and vaginal bleeding
Weight gain
Decreased libido
Feminization of a male fetus
Venous thromboembolism risk

Finasteride (Propecia)
Hepatotoxicity
Gastrointestinal upset
Decreased libido
Feminization of a male fetus
Pregnancy category X

Flutamide
Hepatotoxicty
Feminization of a male fetus
Pregnancy category X

Gonadotropin-releasing hormone analogues
Hot flushes
Osteoporosis
Atrophic vaginitis
Pregnancy category X

Eflornithine cream treats facial hirsutism by slowing the rate of hair growth

and failure to distinguish between the types of hirsutism.

The drugs most commonly used for hirsutism are oral contraceptives (off-label use) and antiandrogenic drugs (off-label use). Topical eflornithine cream (Vaniqa) is FDA-approved for hirsutism but is less commonly used. Insulin sensitizers, GnRH analogues, and other drugs are occasionally used (off-label) to treat hirsutism.

Topical eflornithine cream

Topical eflornithine cream treats facial hirsutism by slowing the rate of hair growth; it does this by irreversibly inhibiting ornithine decarboxylase, an enzyme essential for hair growth.[39,40] Studies showed that twice-daily application reduced unwanted facial hair in women after 24 weeks of treatment.[39,40] Treatment must be continuous, since hair growth rapidly returns to the pretreatment rate by 8 weeks after discontinuing eflornithine.[39,40] White women have been shown to respond better than black women.[39] Adverse effects include a mild burning sensation, acne, pseudofolliculitis barbae, irritation, and allergic contact dermatitis.[39,40] Improved outcomes have been suggested when eflornithine cream is combined with laser hair removal.[41]

Oral contraceptives

Oral contraceptives are commonly used off-label for the management of hirsutism.[20] Oral contraceptives suppress the secretion of luteinizing hormone and, hence, the synthesis of ovarian androgen, thereby increasing levels of sex hormone-binding globulin and decreasing free plasma testosterone.[1,20] Adrenal androgen production is also slightly reduced.[20]

Oral contraceptives usually combine a synthetic estrogen and a progestin. Certain progestins are more androgenic and should be avoided.[1]

For treating hirsutism, oral contraceptives should be used that contain low-androgenic progestins such as cyproterone acetate (not available in the United States), drosperinone (eg, in Yasmin), norgestimate (eg, in Ortho Tri-Cyclen), or desogestrel (eg, in Mircette).[1,20]

Side effects of oral contraceptives include breast tenderness, gastrointestinal upset, headache, loss of libido, hypertension, and the potential risk of venous thromboembolism.[1,15,32,36]

Antiandrogenic drugs

Several antiandrogenic drugs are used off-label to treat hirsutism.

Spironolactone (Aldactone), a competitive inhibitor of the androgen receptor and 5-alpha reductase activity,[20] can be effective in the treatment of hirsutism. Monotherapy with spironolactone, without an oral contraceptive or other reliable form of contraception, is not recommended because of the teratogenic potential of all antiandrogens to feminize a developing male fetus.[20] Thus, reliable contraception should be used in females of childbearing age when starting antiandrogen therapy.

The dosage of spironolactone for hirsutism is usually 100 mg to 200 mg daily.[1,20] Hyperkalemia, polyuria, postural hypotension, irregular menses, and liver abnormalities are among the possible adverse effects (**TABLE 3**). Spironolactone was found to be tumorigenic in animal studies, although this has unknown relevance in humans.[36]

Cyproterone, an antiandrogen not available in the United States,[42] competitively inhibits the androgen receptor and 5-alpha-reductase activity.[1,20,36] It can be used for only the first 10 days of the menstrual cycle (50-mg or 100-mg dose) with an oral contraceptive pill, or in a low dose in a combined oral contraceptive pill (Diane-35 in Canada and the United Kingdom).[1]

Side effects are similar to those of oral contraceptives and include fatigue, mood change, risk of venous thromboembolism, and decreased libido.[1,15,36] Importantly, in woman of childbearing age, there is the potential risk of feminization of a male fetus, so reliable contraception must be used.[15,36]

Flutamide, an investigational antiandrogen, has shown promise in the treatment of hirsutism.[20] Flutamide is a nonsteroidal competitive inhibitor of androgen receptor binding. It carries a significant risk of hepatotoxicity.[1,15]

Finasteride (Propecia) 1 mg is only occasionally used in the treatment of hirsutism (off-label usage). It inhibits type II 5-alpha-reductase to suppress dihydrotestosterone levels.[32] It carries a risk of gastrointestinal disturbance, decreased libido, hepatotoxicity, and feminization of a male fetus (pregnancy category X), so reliable contraception is required in all females of childbearing age, as with all antiandrogens[1] (**TABLE 3**).

Dutasteride (Avodart), a type I and II 5-alpha-reductase inhibitor, has not been studied for the treatment of hirsutism (pregnancy category X).

Insulin sensitizers

Metformin (Glucophage) and other insulin sensitizers are less effective than antiandrogens at reducing hirsutism.[20,38] However, metformin is effective at inducing ovulation in patients with polycystic ovary syndrome.[38] Gastrointestinal upset is a common side effect; lactic acidosis is a serious but rare adverse effect.[1]

Gonadotropin-releasing hormone analogues

GnRH analogues are an option only if oral contraceptives and antiandrogen drugs are unsuccessful in patients with severe hyperandrogenism.[20] They suppress secretion of luteinizing hormone and the synthesis of ovarian androgen.[1,20] These drugs are given as monthly intramuscular injections, usually with some form of estrogen-progestin replacement, since GnRH analogues cause estrogen levels to fall to menopausal levels.[1]

Side effects include signs and symptoms of menopause including hot flushes, atrophic vaginitis, and osteoporosis.[1,15] These drugs completely inhibit ovulation, and some endocrinologists and gynecologists do not suggest further contraception in women of childbearing years for this reason. However, GnRH analogues are not approved as a contraceptive and are pregnancy category X.

Other drugs

Other drugs with antiandrogen activity include cimetidine and ketoconazole.[12] Cimetidine (Tagamet) is not effective for the treatment of hirsutism, and ketoconazole (Nizoral) is associated with significant risk for adrenocortical suppression[12] and hepatotoxicity in addition to multiple drug interactions, given its effect on the hepatic P450 enzyme system. ∎

Several drugs are often used off-label to treat hirsutism

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