Hirsutism

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Summary
Hirsutism is defined as the excessive growth of terminal hair on the face and body of a female in a typical male pattern distribution. Untreated, it can be associated with considerable loss of self-esteem and psychological morbidity. Hyperandrogenaemia is the key trigger for excess hair growth, but the expression and severity are modified by genetic factors. Polycystic ovary syndrome, resulting in excess ovarian androgen production, is the most common cause of hirsutism. A raised serum testosterone level of greater than 5 nmol/l should prompt further investigations to exclude adrenal pathology or an underlying androgen-secreting tumour. The treatment of hirsutism is most effective using combination therapy, including androgen suppression, peripheral androgen blockade and mechanical/cosmetic amelioration and destruction of the unwanted hairs.

Introduction
Hair follicles are found on the whole body, except the palms of the hands, soles of the feet, lips and mucosal surfaces of the external genitalia. Prior to puberty, most of the body is covered with vellus hair, which is fine and downy except on the scalp and eyebrows, these being covered with terminal hair, which is thick and pigmented. During puberty, androgens stimulate the conversion of vellus hair to sexual hair in sex-specific areas. Sexual hair develops in males on the face (beard area), chest, lower back and anterior thighs, and in both sexes in the genital area and lower abdomen.

Hirsutism is caused by increased androgen production and/or bioavailability in a woman, leading to the appearance of sexual hair in areas normally associated with a male appearance. The development of coarse dark hair on the upper lip and chin is particularly distressing and a common reason for women to seek medical advice. If the excess hair growth occurs in areas typical of men, the hair growth is androgen induced, even if serum androgen levels are normal. Conversely, a diffuse increase in long fine hairs, including areas such as the forehead and flanks, is not androgen dependent.

Hirsutism is usually of benign aetiology and must be differentiated from virilisation, in which, in
addition to excess hair growth, symptoms include increased muscle mass and libido, breast atrophy, clitoromegaly and deepening of the voice. Virilisation is usually more sinister and associated with a sudden rise in circulating androgens, for example a rapidly growing androgen-secreting tumour or exposure to androgenic drugs.

Pathophysiology of abnormal hair growth

The key modulators of sexual hair growth are androgens, promoting growth, increased thickness and pigmentation of the facial, genital and axillary hair. Paradoxically, on the scalp, they have the opposite effect in genetically predisposed individuals, producing regression of scalp hair to vellus hair (balding). Oestrogens reduce the rate of hair growth, resulting in thinner, less pigmented hair. Progestogens have a variable effect, depending on their androgenic potency. Racial and genetic factors affect the expression and perception of abnormal hair growth in women.

5α-Dihydrotestosterone is the most potent androgen in terms of abnormal hair growth. It is derived from the conversion of circulating testosterone and androstenedione within the hair follicle, a reaction catalysed by the enzyme 5α-reductase. In normal circumstances, the ovary and adrenal contribute equally to circulating testosterone and androstenedione levels. Luteinizing hormone (LH) and insulin stimulate ovarian, while adrenocorticotropic hormone (ACTH) stimulates adrenal androgen, secretion. The biological effect of androgens depends on the level of free hormone in the circulation. Both testosterone and dihydrotestosterone are bound to albumin and sex hormone-binding globulin (SHBG). SHBG production falls as circulating insulin levels and body mass index rise, producing an increase in biologically active androgen. This explains the impact of obesity, insulin resistance and hyperinsulinaemia on the development and severity of hirsutism. Oestrogens have the opposite effect, i.e. they increase SHBG production and reduce free testosterone levels, which is why oral contraceptives are an effective treatment for mild hirsutism. Table 1 summarises the key factors that can lead to the development of hirsutism.

Causes of hirsutism

The causes of hirsutism are summarised in Table 2.

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<td>• Increased adrenal androgen production</td>
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<td>• Reduced sex hormone-binding globulin levels—increased free androgen</td>
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<td>• Increased body mass index</td>
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<td>• Hyperinsulinaemia</td>
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<td>• Increased 5α-reductase activity in the hair follicle</td>
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<td>• Racial and genetic predisposition</td>
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<th>Table 2</th>
<th>Causes of hirsutism.</th>
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<td>• Polycystic ovary syndrome</td>
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<td>• Idiopathic</td>
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<td>• Late-onset congenital adrenal hyperplasia</td>
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<td>° Cushing’s disease (ACTH-secreting pituitary tumour)</td>
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<td>° Ectopic ACTH secretion by non-pituitary tumour (bronchus, thyroid)</td>
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<td>° Ectopic corticotrophin secretion by tumour (very rare)</td>
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<td>• Androgen-secreting tumours of the ovary</td>
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<td>° Adenomas</td>
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<td>° Glucocorticoids</td>
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ACTH, adrenocorticotropic hormone.

Polycystic ovary syndrome

This is by far the most common cause of hirsutism. Excess body and facial hair may occur alone or be accompanied by cycle irregularity, acne and/or male-pattern alopecia. Obesity and hyperinsulinaemia are common and exacerbate the clinical symptoms. Diagnosis rests on the finding of polycystic ovaries on pelvic ultrasound, which are
reported in 60–97% of women presenting with hirsutism. In polycystic ovary syndrome (PCOS), the ovary, rather than the adrenal gland, is the principal source of androgen excess, hence these women usually benefit from therapy targeted at ovarian and/or pituitary follicle-stimulating hormone and LH suppression.

A subgroup of women with PCOS have hyperinsulinaemia and insulin resistance, with or without obesity. Insulin augments the LH stimulation of ovarian androgen production, reduces hepatic SHBG synthesis and stimulates growth of the hair follicle. Increased body mass index reduces SHBG levels and increases free androgen levels. Obese hyperinsulinaemic women with PCOS are therefore particularly prone to hirsutism as a result of increased androgen production and bioavailability, neither of which are reflected by the total serum testosterone level. Weight loss is therefore a very important therapeutic measure, acting by promoting a fall in circulating insulin and testosterone levels. Recent therapies for hirsutism in this group of women have focused on insulin-lowering agents such as metformin and diazoxide.

About 5% of obese women with severe hyperinsulinaemia and PCOS develop acanthosis nigricans, characterised as areas of hyperpigmented papillomas typically found in the axillae, neck and groin areas. Another small subgroup of women with polycystic ovaries has an intrinsic, possibly primary, abnormality of adrenocortical steroidogenesis. This should always be considered when there is poor response to conventional antiandrogen therapy, and other adrenal pathology such as Cushing’s syndrome or late-onset congenital adrenal hyperplasia have been excluded, as glucocorticoid therapy may be beneficial in these women.

**Idiopathic hirsutism**

This is defined as hirsutism in women with regular cycles, normal ovaries on ultrasound and no other pathology to account for their symptoms. It was believed to be the most common cause of hirsutism until the true prevalence of PCOS in hirsute women was appreciated and probably only accounts for 6% of cases. Plasma testosterone levels are often within the normal range, but androstenedione levels are elevated and SHBG levels suppressed. Elevated 5α-reductase activity has been demonstrated in the hair follicles of women with idiopathic hirsutism, and excess hair growth is likely to be due to an exaggerated response of the hair follicle to normal androgen levels.

**Late-onset congenital adrenal hyperplasia**

This is the underlying pathology in 2–5% of women with hirsutism and can be easily missed as 83% of affected women also have polycystic ovaries on ultrasound. The changes in ovarian morphology are secondary to the hyperandrogenaemia. The condition results from an enzyme deficiency in the adrenal gland, leading to reduced glucocorticoid synthesis. Resultant low cortisol levels produce a rise in ACTH levels, which stimulate the excess secretion of androgen and glucocorticoid precursors, leading to hyperplasia of the adrenal cortex. Most cases are inherited in an autosomal recessive mode and a family history of hirsutism should increase suspicion.

In its most severe form, congenital adrenal hyperplasia (CAH) presents at birth with salt loss and virilisation of the female external genitalia. Late-onset CAH is a mild variant and does not usually present until childhood or early puberty. Most cases are due to partial 21-hydroxylase deficiency. Late-onset CAH should always be considered in women with polycystic ovaries on scanning but serum testosterone levels of over 5 nmol/l. Significantly elevated 17α-hydroxyprogesterone levels before and in response to a single dose of ACTH (a short synacthen test) are diagnostic.

**Cushing’s syndrome**

Excess production of cortisol by the adrenal may be due to excess ACTH secretion by the pituitary gland (Cushing’s disease), ectopic ACTH secretion by a non-pituitary tumour, the autonomous secretion of cortisol by an adrenal or ovarian tumour or, in very rare cases, ectopic corticotrophin secretion by a tumour. As with CAH, polycystic ovaries are often seen on scan as a secondary effect of the hyperandrogenaemia.

**Androgen-secreting tumours of the ovary or adrenal**

These are very rare but must be excluded in any woman who develops hirsutism or virilisation over a short time period and/or has a serum testosterone level above 5 nmol/l, i.e. more than twice the upper limit of the normal range (0.5–2.6 nmol/l). Fewer than 1% of ovarian tumours secrete androgen; these are classified into sex-cord stromal cell tumours comprising granulosa cell tumours, thecomas, Sertoli–Leydig cell and Leydig cell tumours, and adrenal-like tumours of the ovary, which
include luteomas, virilizing lipoid cell tumours, hypernephromas and adrenal rest tumours. The two most common tumours are the Sertoli–Leydig tumour and Leydig tumour. Sertoli–Leydig tumours typically present during the reproductive years. They are unilateral, palpable and benign in 90% of cases. Leydig cell tumours generally present at or beyond the menopause and are usually small, unilateral and benign.

Hirsutism presenting during pregnancy may be associated with a luteoma in which the ovarian stroma shows an exaggerated response to the high levels of human chorionic gonadotrophin. These regress spontaneously postpartum and pose little threat to the pregnancy or the fetus.

Adrenal tumours comprise benign adenomas or malignant adenocarcinomas.

**Iatrogenic**

A number of drugs may produce hirsutism in susceptible individuals. It is a common side-effect of danazol, testosterone and glucocorticoids.

**DIAGNOSIS**

Features to note in the history are:

- speed of onset and severity of hair growth (frequency of plucking, shaving, etc.);
- cycle disturbance;
- the presence of acne or alopecia;
- changes in body weight;
- current or recent medication.

Most women with benign hirsutism (PCOS or idiopathic) report symptoms dating from puberty, with a gradual worsening of hair growth over time. An increase in body weight or coming off the combined oral contraceptive is a common trigger in unmasking the hyperandrogenaemia associated with polycystic ovaries and precipitating symptoms. A sudden development of hirsutism is suggestive of more worrying pathology such as Cushing’s syndrome or an androgen-secreting tumour, particularly if there is also evidence of virilisation.

Clinical evaluation should include:

- height and weight;
- an assessment of the amount, distribution and severity of hirsutism. A score of 6 or above in a ‘modified’ Ferriman–Gallway score is used by many authors as the cut-off point for the diagnosis of hirsutism;
- pelvic examination to exclude clitoromegaly and palpate the adnexae for ovarian tumours;
- a check for markers of hyperinsulinaemia such as acanthosis nigricans;
- a check for markers of Cushing’s syndrome such as facial plethora, central obesity, hypertension, thin skin, bruising, striae and proximal muscle wasting.

Baseline investigations are:

- a pelvic scan to assess ovarian morphology and exclude tumours (day 2–5 if the cycle is regular);
- serum testosterone.

Serum testosterone is poorly correlated with severity of symptoms but is the most useful indicator of serious pathology. Levels higher than 5 nmol/l should prompt further tests of adrenal function depending on clinical symptoms. Testosterone levels may subsequently be used to monitor treatment if clinical response is poor.

Further investigations are as follows:

- CAH is diagnosed by the short synacthen test in which 17α-hydroxypregesterone and cortisol levels are measured before, and 1 h after, the administration of a single dose (250 mg intramuscularly or intravenously) of synthetic ACTH.
- Cushing’s syndrome is diagnosed by measuring 24-h urine free cortisol levels or performing an overnight, low-dose (1 mg) dexamethasone suppression test. If either is positive, diurnal serum cortisol and ACTH measurements should be made and a high-dose dexamethasone suppression test (2 mg at night for 5 days) performed.

**Treatment**

Pituitary or adrenal tumours, Cushing’s syndrome and CAH are best referred to an endocrinologist for further management. Ovarian tumours should be surgically excised, and thereafter cosmetic measures alone should suffice. The majority of cases presenting to the gynaecologist will involve benign hirsutism, i.e. PCOS or idiopathic hirsutism. Therapy is primarily pharmacological. Most women will notice a reduction in hair growth once medication is started but should be warned that this is unlikely to be apparent for 3–6 months. Cosmetic measures, directed at removing terminal hair, should be continued during this time. Furthermore, women with a genetic or racial predisposition to coarse
dark facial hair are unlikely to see a complete resolution of their symptoms.

Obesity significantly exacerbates the severity of hirsutism, and subjects with a body mass index of over 25 kg/m\(^2\) should be advised to embark on a weight loss programme at the time medical treatment is initiated. It has been shown that obese women with PCOS who manage to lose more than 5% of their initial body weight have a significant improvement in their biochemical profile, including a reduction of testosterone, an increase in SHBG and an improvement in their Ferriman–Gallway (F–G) scores.

When PCOS is diagnosed, patients should receive an adequate explanation of the condition and associated symptoms. The possibility of infertility and long-term risks of diabetes and cardiovascular disease should be discussed, particularly as the latter are to a large extent preventable with a modification of diet and lifestyle. Obese subjects should have fasting glucose and lipid levels checked on a regular basis.

**Drug therapy**

The treatment of hirsutism is most effective using combination medications and/or interventions, including androgen suppression, and peripheral androgen blockade together with mechanical/cosmetic measures and the destruction of the unwanted hairs. The goal of medical therapy should be to reduce the time spent mechanically removing unwanted hair.

Androgen suppression can be achieved with insulin-sensitising drugs or interventions, such as weight loss and metformin, as well as combined oestrogens and progestogens (e.g. oral contraceptives) and long-acting gonadotrophin-releasing hormone (GnRH) analogues. Laparoscopic ovarian drilling, which also aims to suppress androgen production, appears to have only temporary effects and is not recommended for hirsutism. In general, hirsutism responds better to medications that block androgen action than to ovarian or adrenal suppression. Once an acceptable level of hirsutism has been attained, the dose of antiandrogen can often be decreased without causing a worsening of the hirsutism. When women with PCOS are treated with antiandrogens, a better response will be obtained if ovarian androgen secretion is also suppressed.

Because it is easier to prevent worsening hirsutism than to treat existing hair growth, physicians should not be reluctant to institute medical therapy in young, mildly hirsute adolescents who have a family history of moderate to severe hirsutism. Lifelong therapy may be needed to prevent recurrence. Long-standing hair growth of the chin may be especially difficult to improve.

Four groups of drug are used to treat hirsutism, these being classified according to their mode of action (Table 3).

**Ovarian or adrenal androgen blockers**

*Combined oral contraceptive agents*, with or without the antiandrogen cyproterone acetate, are the best first-line treatment for mild to moderate hirsutism. The high-dose oestrogen suppresses pituitary follicle-stimulating hormone and LH, secretion leading to a reduction in ovarian androgen production. It also stimulates SHBG production by the liver and inhibits 5\(\alpha\)-reductase. Progestogens have also been reported to inhibit 5\(\alpha\)-reductase activity, act as an antagonist at the androgen receptor and increase the metabolic clearance rate of both testosterone and dihydrotestosterone.

The choice of progestogen is debatable as pills containing desogestrel and gestodene, which are the least androgenic, have an enhanced risk of thromboembolism. In practical terms, the best first-line pill to use is Dianette, which combines low-dose ethinyl oestradiol with a small but therapeutic dose of cyproterone acetate (see below). Because progestogens and oestrogens independently exert biological activities that improve hirsutism, their isolated use in unique situations might be warranted. Medroxyprogesterone acetate, either in the form of Depo-Provera, 150 mg intramuscularly every 3 months, or

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**Table 3** Drugs used to treat hirsutism

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<td>Combined oral contraceptive pill</td>
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<td>Gonadotrophin-releasing hormone agonists</td>
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<th>Adrenal suppression</th>
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<td>Glucocorticoids</td>
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<td>P450 enzyme inhibitors</td>
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<td>Ketoconazole</td>
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<th>Peripheral androgen blockers</th>
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<td>Androgen receptor antagonists</td>
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<td>Cyproterone acetate</td>
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<td>Spironolactone</td>
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<td>Flutamide</td>
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<td>5(\alpha)-Reductase inhibitors</td>
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<td>Finasteride</td>
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<th>Insulin-sensitising agents</th>
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<td>Metformin</td>
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<th>4. Topical agents</th>
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<td>Eflornithine</td>
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10–30 mg orally every day, has been shown to be an effective treatment against hirsutism.

**GnRH analogues** induce a more complete suppression of ovarian androgen secretion but have little role to play in clinical practice. They are expensive and have undesirable side-effects associated with oestrogen suppression, which limits the duration of treatment. They can, however, be useful in cases of severely androgenised or hyper-insulinaemic patients. For premenopausal women, they need to be combined with oestrogens and progestogens, and the treatment needs to continue for at least 3 months. In postmenopausal patients, they can be used to assess the effect on hirsutism of a ‘medical oophorectomy’ prior to bilateral oophorectomy.

**Glucocorticoids** suppress ACTH-mediated adrenal secretion. They are, however, less effective than the peripheral androgen blocker cyproterone acetate in treating hirsutism when there is adrenal component to the hyperandrogenaemia, for example late-onset CAH, although they do have a role as second-line therapy in these women. Dexamethasone 0.25–5.0 mg or prednisolone 2.5–5.0 mg taken at night is an effective dose to suppress the morning ACTH surge and adrenal androgen production. Patients should be monitored for weight gain.

**Ketoconazole** is a synthetic imidazole derivative that inhibits cytochrome P450-dependent enzymes, thereby blocking both ovarian and adrenal steroidogenesis. Although clinically effective, the drug has pronounced side-effects, including nausea, asthenia and alopecia, and carries a small risk of hepatotoxicity. The latter is a reason for regularly monitoring liver function during treatment.

**Peripheral androgen blockers**

Cyproterone acetate, flutamide and spironolactone act on the hair follicle by inhibiting the binding of testosterone and 5α-dihydrotestosterone to the androgen receptor. Finasteride is a non-steroidal competitive inhibitor of 5α-reductase. All drugs that block androgen action provide similar results, so the selection of drugs depends primarily on the side-effect profile of each drug and its tolerability. Because these drugs act through different mechanisms from those of the oral contraceptives, it is usually beneficial to combine the two. In addition, oral contraceptives will reduce the incidence of abnormal per vaginam bleeding and provide reliable contraception.

**Cyproterone acetate** is the most widely used drug in the management of hirsutism in the UK and is, in either low or high dose, first-line therapy for most women. It is a strong progestogen and results in a decrease in circulating testosterone and adrostenedione levels through a decrease in circulating LH level. It also antagonises the effect of androgens at the peripheral level. In mild to moderate hirsutism, a dose of 2 mg taken in combination with 21 days of ethinyl oestradiol 35 mg (Dianette) has been shown to improve symptoms in over 50% of cases. This is also a useful ‘maintenance’ preparation once a response has been achieved with higher doses. In more severe hirsutism, cyproterone acetate is prescribed at a dose of 25–100 mg combined with either Dianette or 30 mg ethinyl oestradiol taken for a 21-day cycle. Seventy per cent of women treated at this higher dose note an improvement in symptoms within a year.

Side-effects of cyproterone acetate include depression, fatigue, mood changes and weight gain. Liver function should be checked regularly during long-term use as hepatotoxicity, albeit a rare complication, has been reported, as have adrenal insufficiency and loss of libido. With cyproterone, there is usually a 2–3 day delay in the onset of menses in comparison with an oral contraceptive regimen alone. Because of its long duration of action and potent progestational activity, amenorrhoea is more common when cyproterone acetate is given in larger doses or for more than the first 10 days of the combined oral contraceptive. For this reason, cyproterone acetate is usually prescribed in a reversed sequential regimen for the first 10 days of a 21-day cycle with oestrogen. Contraception is mandatory when taking cyproterone acetate and is recommended for at least 3 months after stopping treatment, as the drug crosses the placenta and may produce feminisation of a male fetus.

In doses of 50–100 mg/day, combined with 30–35 μg ethinyl oestradiol, cyproterone is as effective as the combination of spironolactone (100 mg/day) and an oral contraceptive pill. Interestingly, in a dose-ranging study, Barth and colleagues noted that an oral contraceptive pill containing 35 mg ethinyl estradiol and 2 mg cyproterone acetate per day was as effective at reducing hirsutism as the same oral contraceptive pill with the addition of 20 mg/day or 100 mg/day CPA for the first 10 days of the cycle. For postmenopausal women or women over 40 years old, who do not tolerate contraceptive doses of oestrogens, the cyproterone acetate can be combined with hormone replacement therapy doses of oestradiol.

**Spironolactone** is an aldosterone antagonist with potent androgen-receptor blocking activity. Although as effective as cyproterone acetate, it is rarely used in the UK as the Committee on the Safety of Medicines has advised against its
long-term use. Side-effects include polydypsia, polyuria, nausea, headaches, fatigue and ovulatory dysfunction. The most common side-effect of spironolactone is more frequent menses, usually every 2 weeks, which occurs in 20–25% of women not using the oral contraceptive. This can be treated by adding a combined oral contraceptive (COC) or by reducing the dose of spironolactone. Because of its action as an aldosterone antagonist, spironolactone is also a diuretic and has the potential to cause hyperkalaemia. Other minor side-effects of spironolactone are gastritis/dyspepsia and dry skin. Spironolactone should be taken with food.

To minimise side-effects, a starting dose of 25 mg/day should be increased over several weeks. Doctors may wish to evaluate serum electrolytes and blood pressure 2–4 weeks after treatment has started. Most side-effects are temporary. A dose of 100 mg a day is considered appropriate for the lean hirsute woman, but a higher dose of 200–300 mg/day might be necessary for women who are severely hirsute or obese. Spironolactone should be given for at least 6 months to achieve the maximum benefit. The dose can then be dropped to 25–100 mg/day. Contraindications to spironolactone include renal insufficiency, hyperkalaemia, pregnancy and abnormal uterine bleeding. Experiments in rats have resulted in malignant mammary tumours, so spironolactone should not be given to women with a genetic predisposition to breast cancer.

The oral contraceptive Yasmin contains drospirenone and has been proved successful in the treatment of excessive hair growth in women with PCOS. Drospirenone is a progestin derived from 17α-spiroloactone and thus has antiandrogenic activity similar to that of spironolactone. In addition to blocking androgen receptors, drospirenone inhibits ovarian androgen production. As an aldosterone antagonist, it also exerts a diuretic effect that can diminish premenstrual symptomatology.

Flutamide is a useful second-line antiandrogen when cyproterone acetate is not tolerated. It is usually prescribed as a daily dose of 250 mg combined with the oral contraceptive pill and can cause a reduction of F–G score by 64% at 6 months and 71% at 12 months. It can, however, also be given alone, without the oral contraceptive pill, so far as contraception is adequate. In the light of reports of hepatotoxicity, regular checks of liver function should be carried out. In fact, no serious cases of hepatotoxicity have been reported at doses of less than 500 mg/day. Other side-effects include dryness of the skin and a greenish tint to the urine. Recent studies employing lower doses of flutamide have shown equal efficacy with 125 mg or even 52.5 mg/day. This has reduced the cost and side-effects of treatment.

Finasteride, a 5α-reductase inhibitor, inhibits the conversion of testosterone to dihydrotestosterone, which is the most active androgen in the hair follicle. At a dose of 5 mg a day, it has the fewest side-effects of all the drugs used to treat hirsutism, although it can cause teratogenicity. Side-effects with finasteride include minimal gastrointestinal disturbances, headaches, dry skin and decreased libido. In terms of effectiveness, 5 mg finasteride compare favourably with 100 mg/day spironolactone and 250 mg/day flutamide. It has recently been shown that 50% of the standard daily dose of finasteride (i.e. 2.5 mg/day) is as effective as the standard dose.

Insulin-sensitising agents
Metformin and other insulin-sensitising agents, which reduce serum insulin and testosterone levels, have been shown to be beneficial in the treatment of hirsutism, particularly in PCOS associated with hyperinsulinaemia. The drug is a biguanide commonly prescribed to individuals with diabetes. The recommended dose for the treatment of hirsutism is 850 mg twice a day or 500 mg three times daily.

Topical agents
Eflornithine hydrochloride 13.9% cream (Vaniqua) has been approved by the US Food and Drug Administration for the treatment of unwanted facial hair growth. It is a specific, irreversible inhibitor of the enzyme ornithine decarboxylase, which is involved in hair growth. Topical eflornithine is applied twice daily to affected areas of the face. Two multicentre, randomised, double-blind, controlled trials evaluated the use of eflornithine in a total of 596 hirsute women for 6 months. There were significant differences between the treatment and placebo arms. By 8 weeks of therapy, 58% of subjects had some improvement and 32% had marked improvement, compared with 32% of the placebo group who reported some improvement. Both studies confirmed that the beneficial effects of the treatment with eflornithine were transient, with hair growth returning to pre-treatment levels within 8 weeks of stopping the medication. Side-effects are few, mainly local skin erythema (2% of patients), burning, stinging and tingling (15% of patients and 5% of the placebo group).
Surgical treatment

Surgery has little place in the management of hirsutism. Laparoscopic ovarian drilling, which produces a rapid and significant fall in androgen level, should be restricted to the management of anovulatory infertility as the fall in androgens is short lived. Bilateral oophorectomy (usually combined with hysterectomy) may be a sensible option for women who have completed their family and in whom long-term medication is either not acceptable or poses a health risk. A short trial of a GnRH analogue may be useful in determining whether surgery is likely to be beneficial.

Cosmetic treatments

Mechanical methods of hair removal include bleaching, shaving, plucking, waxing, depilatory creams and electrolysis. Shaving does not lead to a worsening of hirsutism and is a good short-term solution for facial hair.

Electrolysis produces permanent destruction of the dermal papilla but, although effective, is expensive and time-consuming. The most effective form of electrolysis in the ‘blend’ technique, which combines electrolysis and thermolysis.

Selective photothermolysis of hair follicles using either normal-mode ruby or Nd-YAG laser has been shown to be effective and, unlike electrolysis, allows large areas of hair-bearing skin to be treated over a short period of time with minimal discomfort or risk of scarring. For laser therapy, it is necessary that the target has greater optical absorption than the surrounding tissues. This can be achieved either by choosing dark hair on women with light skin, or by using special stains to ‘label the target’. Repeated therapies are necessary, and permanent hair removal is rarely achieved.

Hirsutism in the menopause

There is a tendency to increased body and facial hair in postmenopausal women, but sudden-onset hirsutism in this age group should be fully investigated and an androgen-secreting tumour excluded. In postmenopausal women with PCOS or idiopathic hirsutism, cyproterone acetate can be prescribed in a reverse sequential regime, with hormone replacement doses of oestrogen. A few women with PCOS have ovarian hyperthecosis, in which both stroma and follicles within the ovaries are packed with luteinised thecal cells. Elevated LH levels, characteristic of ovarian failure, lead to increased ovarian androgen production, producing severe hirsutism.

The response to medication is usually poor, and serious consideration should be given to oophorectomy in this group of patients.

Practice points

Investigation

- Hirsutism is a distressing condition, and whenever medical advice is sought, investigation and treatment should be offered
- The majority of cases are due to PCOS
- Baseline investigations should include a pelvic ultrasound scan and serum testosterone level
- There is a universal trend towards simplifying the investigation of hirsutism
- A serum testosterone level of over 5 nmol/l should prompt further investigations to exclude adrenal pathology or an underlying ovarian tumour. Severe hirsutism or a history of recent onset and rapid progression should raise the suspicion of a tumour or other serious cause

Treatment

- For overweight women with PCOS, even a 5% weight reduction can bring about significant improvement in biochemical profile and F–G score
- The best results are achieved with combination treatment, including antiandrogens, suppression and topical treatments
- The goal of medical therapy should be to reduce the time spent mechanically removing unwanted hair
- Androgen suppression can be achieved with insulin-sensitising drugs or interventions, such as weight loss and metformin, as well as combined oestrogens and progestogens (e.g. oral contraceptives) and long-acting GnRH analogues. Laparoscopic ovarian drilling, which also aims to suppress androgen production, appears to have only temporary effects and is not recommended for hirsutism. Antiandrogens are more effective than androgen suppression
- Most antiandrogens have similar efficacy. The choice of drug depends mainly on its tolerability by each individual patient
It appears that the efficacy of most anti-androgens is as good at doses lower than the ones traditionally prescribed (e.g. cyproterone 2 mg, flutamide 52.5 mg, finasteride 2.5 mg).

The first-line management of benign hirsutism is with cyproterone acetate.

Finasteride, at a dose of 5 mg a day, seems to have fewer side-effects than flutamide and spironolactone.

Metformin is a useful second-line therapy in hyperinsulinaemic women with PCOS.

Glucocorticoids should be considered as second-line therapy if there is evidence of adrenal hyperandrogenaemia.

When medical treatment is stopped, hirsutism is likely to recur. Maintenance therapy should be continued in the form of the combined pill, with or without low-dose cyproterone acetate.

It is easier to prevent worsening hirsutism than to treat existing hair growth. Doctors should not be reluctant to start medical therapy in young, mildly hirsute adolescents who have a family history of moderate to severe hirsutism.

Shaving does not lead to a worsening of hirsutism and is a good short-term option for facial hair, especially at the chin.

Further reading


