



Excess body hair-hirsutism- causes and treatment option advice for patients and health professionals

Many women are bothered by what they feel to be excess or an undesirable distribution or amounts of body hair – about 9% of Australian women. A degree of hairiness which may be acceptable in one culture or country may not be acceptable to either the individual or general society in a different community. So the problem of body hair must be considered not only in terms of what is biologically normal or abnormal but also according to various social environments. Excess body hair may be a manifestation of an underlying hormonal disorder, which if treated may result in less hair growth. The medical term 'HIRSUTISM' is used to describe the condition of excessive thick dark hair growth in women in the androgen sensitive regions of the body in a pattern not considered normal for a woman.

Normal Body Hair

Normal body hair growth is determined genetically and differs both within and between different racial groups. The number of hair follicles one has is established before birth. Hair follicles are found all over the body except for the palms, lips and soles of the feet. Most body hair is fine and unpigmented. Body hair growth is governed by the action of sex hormones on the hair follicles. Not only are the absolute levels of sex hormones in the blood important but also the sensitivity of the hair follicles to the hormones. Thus two women with the same blood hormone levels will have different body hair growth patterns according to the number of hair follicles over their bodies and how sensitive their hair follicles are to the growth stimulating effects of the hormones.

The main hormones stimulating hair growth are called 'androgens'. Androgens are commonly called 'male hormones' but this is somewhat misleading, as androgens are normally produced by both the adrenal glands and ovaries in women and have important actions in normal healthy women.

The adrenal glands sit above the kidneys and as well as producing androgens, produce the important 'stress' hormones cortisol and adrenaline. The most well known androgen is **testosterone**. Testosterone is converted to oestrogen in the ovaries and body fat. Women cannot make oestrogen unless they can first make testosterone or adrenal androgens.

The other important hormones that are converted in cells into androgens are dehydroepiandrosterone (DHEA) and androstenedione (A). The skin and hair follicles convert DHEA and A to testosterone therefore high levels of these weak androgens can cause acne and excess hair growth.

Hair follicles in certain parts of the body are more sensitive to the influence of androgens and are called the hormone or androgen sensitive areas of the body. These areas include the upper lip, sides of the face, chin, central chest and around the nipples, lower abdomen, back, upper arms, pubic region and inner thighs. In contrast, the arms and lower legs are less sensitive to the effects of hormones. Androgens not only stimulate hair growth in the hormone sensitive areas by

increasing the speed of hair growth but also increase the pigmentation (darkening) of hair and the thickness of the hairs. Thus androgens convert fine unpigmented hair into coarser dark more rapidly growing hair.

Puberty begins with the development of underarm and pubic hair. This sexual hair starts to appear when the adrenal glands 'switch on' and produce increasing amounts of androgens at the onset of puberty. We do not know what triggers this initial phase of maturation. By the end of puberty there is considerable variation in the amount of body hair between individuals. As women age, their overall amount of coarse body hair tends to gradually increase, again with a wide range of individual variation.

Determining excess hair growth

Hair removal treatments are often used for cosmetic reasons by people with normal hair pattern. Race and ethnicity play a major role in how much body hair is considered normal. Most Asian women, for example, have little body hair whilst Mediterranean women have relatively heavy body hair. An important consideration, irrespective of background is a change in pattern of hair growth or rate of growth.

When a woman considers she has excessive facial or body hair she should seek medical assessment and advice. An underlying hormonal disorder is more likely in women who have a recent change in the amount or rate of growth of body hair, and in those who have **irregular periods** or **acne**. Other specific signs of abnormal hormone levels include deepening of the voice, loss of scalp hair in a pattern similar to balding in men and an increase in libido. Hirsutism may also be linked to obesity and diabetes in some women.

Body hair can be assessed using a scoring system devised many years ago by the researchers Ferriman and Gallway. The system is quite simple. The body is considered as nine separate regions and the extent of hair in each region is given a value ranging from zero (no hair) to 4 (complete coverage of hair equivalent to male pattern growth). A total score over 8 is said to indicate hair growth in excess of that expected for a woman, whereas the problem is described as severe when a woman is given a total body score greater than 19.

Most women with the problem of hirsutism do not have a specific hormonal abnormality and are said to have **idiopathic** hirsutism. Blood tests may reveal slightly increased levels of adrenal and ovarian androgenic hormones but usually the levels are normal. Many women with hirsutism have normal blood hormone levels and have increased androgen turnover and/or enhanced sensitivity to normal levels of circulating hormones.

Polycystic Ovarian Syndrome (PCOS) is the most commonly identified condition causing excess hair growth in women and affects up to 20% of women in some communities. PCO classically develops after puberty when girls experience irregular, infrequent periods. The progressive increase in body hair is usually associated with weight gain. Acne is also a common feature. The name of this condition 'PCOS' is misleading. The ovaries are not actually full of cysts but contain excess numbers of **follicles** which are best described as minicysts which develop as a result of failed ovulation.

In simple terms, certain cells in the ovaries of women with PCOS overproduce androgens especially testosterone. These high levels of androgens in the ovaries interfere with the development of a normal egg and instead of normal ovulation proceeding the nest of cells or the follicle containing the developing egg turns into a 'mini cyst'. These mini cysts are clearly identified by an ultrasound examination. It is essential that the diagnosis of PCOS is made by someone experienced in ultrasound of the ovaries. PCO can easily be confused with multicystic ovaries which is a biological variation of normal and does not appear to be related to hormonal imbalance. Whereas a normal ovary contains up to three small follicles; the ovaries of women with PCO contain ten or more follicles. This condition appears to affect up to twenty percent of women with varying degrees of severity.

Women who have both PCO and a problem with weight are more likely to have higher androgen levels, excess body hair and problems with infertility. Women with PCO and obesity usually have high blood insulin levels and are at significant risk of developing diabetes.

The next most common medical condition causing excessive body hair growth is Congenital Adrenal Hyperplasia (CAH). This is an inherited condition usually diagnosed in childhood. However more subtle forms of this condition may not appear until after puberty as increased body hair in women. When this occurs it is called late-onset CAH. This condition is more common in certain ethnic groups and can be diagnosed with specific blood tests.

It is rare for excess body hair growth to be caused by over production of one of the **pituitary hormones**, growth hormone, prolactin or the adrenal stimulating hormone. Usually other identifying abnormal symptoms and signs are present and specialised blood tests lead to the correct diagnosis.

Tumours which produce abnormal quantities of androgens are fortunately extremely rare. They are usually associated with a sudden and significant increase in hair growth and other signs of masculinisation.

Some **medications** can cause an increase in body hair, the most commonly prescribed one being phenytoin (Dilantin) which is used in the treatment of epilepsy.

Should hormone levels be measured?

As most women with hirsutism do have a major underlying disease causing their problem, few blood tests are necessary.

- Women with mild to moderate excess hair growth which has developed gradually and who have regular periods do not need any investigations.
- Women with more extensive hair growth (severe hirsutism) and regular periods should have their blood androgen levels measured.
- Women with increased hair growth and **irregular periods** need to have more extensive blood hormone tests done.

Women with moderate to severe hirsutism may be advised to have an ultrasound of the ovaries, especially if they have irregular menstrual cycles. The need for other specialised tests is determined by the results of the initial investigations.

Management of Hirsutism

There is no instant or permanent cure for hirsutism. Initial management is exclusion of any serious underlying pathology. For the majority of women the primary aim of treatment is to achieve a body image that is acceptable. This is generally accomplished with either cosmetic or pharmacological measures, or both.

Cosmetic Measures

Excess hair in regions that are non-androgen dependent, such as the arms and lower legs, may have an ethnic basis and cosmetic treatments are usually effective. Common cosmetic approaches include bleaching with peroxide, heavy makeup, shaving, plucking, waxing and depilatory creams. These methods are time consuming and expensive. They are effective for mild forms of hirsutism, but for patients with moderate to severe hirsutism their effects are only temporary. Problems with such treatments include skin irritation from bleaches and depilatory creams, folliculitis with plucking, burns from waxing and the development of stubble after shaving. Skin irritation or plucking rapidly induces the anagen stage and hair follicle growth, and shaving tends to reinforce a masculinised self-image. Both electrolysis and photothermolysis (eg laser) require trained personnel to provide treatment, are repetitious and expensive and practical for treating limited areas only, although electrolysis may be rapid and cost effective where the hair density is sparse. Laser therapy allows larger areas to be treated over a short time period.

Electrolysis

Electrolysis produces permanent destruction of the dermal papilla. The two basic methods of electrolysis are galvanic and thermolytic with galvanic being more common. In the galvanic method the hair follicle is destroyed using a direct current. The most effective form, the blend technique, combines thermolysis with electrolysis. Thermolysis creates heat within the follicle causing its destruction by use of an alternating current.

A benefit compared to laser treatment is that it can be used on both dark and light skinned patients and those with fair hair. It is painful. Other side effects of redness and swelling are generally temporary. Acne and ingrown hairs as well as postinflammatory pigment changes may occur, as well as scarring and keloid formation in susceptible patients. Success depends on the skill of the operator. People with pacemakers should not undergo electrolysis.

Photo thermolysis- Lasers and Intense Pulsed Light (IPL) treatment

Laser and light source treatment targets melanin (pigmentation) in the hair bulb which absorbs the light emitted by the laser or light source. This light energy changes into heat causing destruction of the hair bulb. If adjacent skin is also pigmented, however, the laser energy is absorbed into the surrounding epidermis causing damage or interference with absorption so that hair destruction is less effective. Therefore dark haired and fair skinned individuals, with relatively higher concentration of melanin in the hair compared to the epidermis, allow more selective absorption of light within the bulb. White or gray hair conversely is a poor target for laser treatment.

There is evidence to suggest that some lasers produce short-term effect of approximately 50% hair reduction up to 6 months after treatment (alexandrite and diode).

The most common side effects are redness and swelling which usually resolve within 24 hours after treatment . It can be slightly painful because of the heat energy created. Other side effects include hypopigmentation and hyperpigmentation. There have been instances of an increase in hair density, colour, coarseness or a combination of these (hypertrichosis) following laser therapy and without other explanation, however this is a rare event and definite cause and effect relationship with laser therapy has not been proven. Intense Pulsed Light generates specific wavelengths of light with the addition of filters to tailor treatment to skin type and hair colour of the patient. Most trials examined short- term effect of six months following treatment. Evidence is lacking for long-term hair removal. High quality research is required.

Weight Loss

For women with PCOS, weight loss may result in improvements in menstrual cycles, and a reduction of hair growth, although this is usually modest. Therefore obese women with high androgen levels should follow a sensible low calorie, low fat diet as well as regular exercise.

Topical pharmacological therapy

Eflornithine cream (Vaniqa) is a specific, irreversible inhibitor of ornithine decarboxylase, an enzyme involved in hair growth. It is available in Australia by prescription for delaying re-growth of unwanted facial hair in women following depilation. It is applied twice daily to affected facial areas. Studies up to 6 months indicate that eflornithine 11.5% cream significantly reduces hirsutism in women with unwanted facial hair.

Eflornithine cream is effective in 2 out of 3 women after about 6 to 8 weeks of treatment irrespective of the type of hair growth (dark or light hair) or skin colour.

Because it is effective within a few weeks it complements the use of oral therapies and is very effective when combined with other treatments.

When used in combination with laser therapy for the treatment of facial hirsutism it enhances the efficacy of laser.

Hair growth returns to pretreatment levels within 8 weeks of ceasing the treatment.

Side effects are few and include acne, local skin irritation and rash. It must not be used (contraindicated) in severe renal impairment and is not recommended in pregnancy and lactation although this should be discussed with your doctor.

Oral Pharmacological Agents

Pharmacological treatment is recommended when hirsutism is severe or when cosmetic measures have failed. Whatever therapy is used, six to twelve months of treatment is required before efficacy can be judged. Furthermore, the drugs are only effective when taken and the benefits fade when discontinued. A good measure of treatment efficacy is reduction in frequency and duration of mechanical hair removal. Medical treatment can be divided into two main categories – suppressants of androgen secretion and medications that block androgen action- these are called anti-androgens.

Oral Contraceptives

The suppression of the ovulatory cycle by the oral contraceptive pill (OCP) results in reduced androgen production. The OCP is ideal for women requiring cycle control or contraception. OCP's with non-androgenic progestins such as desogestrel or norgestrel may be effective as treatment of hirsutism. Oral contraceptive pills that contain the progestins with specific anti-androgen activity, have been shown to significantly decrease hirsutism scores when administered for six months.

Glucocorticoids

Theoretically, glucocorticoid therapy is indicated to suppress adrenal androgen production in situations of adrenal androgen excess (eg late onset CAH). However in practice, side effects are common and such women are best treated with anti-androgens.

Cyproterone acetate

Cyproterone acetate is a potent progestin and an androgen receptor blocker (antagonist). It can be administered in low dose (2mg/day) with ethinyloestradiol as an OCP or combined with oestrogen as hormone therapy. In women with acne and minimal hirsutism, low dose OCP therapy is adequate, but women with moderate to severe hirsutism usually require higher doses to achieve a satisfactory response .

In premenopausal women, it is administered in a reverse sequential manner with the oral contraceptive pill ie.cyproterone acetate 50 to 100mg daily from day 5-15 of each cycle or simply one/two tablets daily with the first ten active tablets for each OCP cycle. The initiating dose is usually 100mg, being tapered to 50mg for ten days per month after twelve months of therapy. Co-administration with an OCP is essential to avoid menstrual irregularity and prevent unwanted pregnancy and feminisation of a male fetus. In postmenopausal women cyproterone acetate is given at 25-50mg daily for the first 20 days of each month.

The most common side effects include suppressed libido, diarrhoea, nausea, weight gain, breast tenderness, and headache.

Spirolactone

Spirolactone is an aldosterone antagonist with antihypertensive properties. It is also a weak progestin and a competitive inhibitor of the androgen receptor. Spirolactone is a common first line treatment of hirsutism, being as effective as cyproterone acetate , flutamide and finasteride . The recommended starting dose is 100mg twice daily that should be maintained for at least six to twelve months to achieve a clinical response. In women with regular cycles spironolactone may induce cycle irregularity, whereas in women with infrequent cycles, menstrual regularity may be restored. If necessary, menstrual cycles can be regulated with the addition of an oral contraceptive pill. Again the need for safe contraception is recommended as spironolactone can cross the placenta and may emasculate a male fetus.

Flutamide

Flutamide is a pure non-steroidal androgen receptor antagonist, currently licensed for the treatment of prostatic carcinoma. Its efficacy in hirsutism has been demonstrated with normalisation of hirsutism scores, similar to that of cyproterone acetate and spironolactone. Flutamide has 20% affinity for the androgen receptor

compared with spironolactone, and thus has a dose equivalence of 500mg for each 100mg of spironolactone. The recommended dose is 250mg daily and is generally effective and well tolerated. The dose can be increased to 250mg bd, however with higher risk of adverse effects such as diarrhoea, fatigue, breast tenderness or decreased libido. One study demonstrated that low dose flutamide (62.5mg daily) reduced Ferriman-Gallwey scores by seventy percent after twelve months of treatment. Liver toxicity is rare but has been reported with very high dose flutamide in prostatic cancer treatment, but not with lower doses commonly used for treating hirsutism. Flutamide is not currently marketed for treatment of hirsutism in Australia.

Ketoconazole

Ketoconazole is an imidazole derivative, which inhibits cytochrome P-450 dependent enzymes. It acts by inhibiting gonadal and adrenal androgen synthesis. Its effectiveness in hirsutism has been demonstrated at 300mg daily, however its serious liver toxicity precludes its use. The liver toxicity is not duration or dose related, but more idiosyncratic.

Finasteride

Finasteride is a 5α -reductase inhibitor that blocks the conversion of testosterone to DHT and is used in the treatment of prostatic hypertrophy. In one study, a dose of 5mg daily for six months reduced hirsutism scores by forty-seven percent, and when combined with an OCP the scores were further diminished. The efficacy of finasteride compared to other anti-androgens is not clearly established with conflicting findings in different studies. Side effects with finasteride have not been commonly reported but may include headache, depression and breast tenderness and decreased libido. Women of child-bearing age must have effective contraception as the risk of feminisation of genitalia in male fetuses can occur with this agent.

Conclusion

The management of hirsutism requires thorough medical evaluation and detailed discussion of available treatments.

The primary role of the clinician is to exclude significant underlying pathology, which requires specific therapy. If cosmetic measures alone are insufficient pharmacological agents should be considered. It is essential to tailor therapy to each individual to achieve a satisfactory aesthetic result.

Women already on an OCP can be advised to take a formulation with a non-androgenic progestin. Generally, spironolactone or cyproterone acetate are appropriate first line medical treatment options. These agents can be combined with a low dose OCP to improve efficacy, to regulate periods or act as contraception to prevent the feminisation of male fetuses as seen with anti-androgens.

Agents such as flutamide and finasteride have been shown to be comparably effective in treating hirsutism, and may be appropriate second line agents should they become available in Australia for this indication.

It is important to be aware that it may take six to twelve months before any subjective or objective differences are noticed. When the response has stabilised, the regimen should be maintained for another six months before attempting to taper the dose. As most of the medical therapies display similar and often limited efficacies, the choice of which agent to use ultimately depends not only on the clinical setting of each individual but also on the drug's availability, its side effect profile and its cost.