# Androgenetic alopecia in men and women

**All men and women suffer androgenic hair loss as they age. Androgenic alopecia becomes a problem only when the hair loss is perceived as excessive, premature and distressing.**

**RODNEY SINCLAIR**
MB BS, FACD

Dr Sinclair is Clinical Associate Professor, Monash University Department of Medicine, Alfred Hospital; Senior Lecturer, University of Melbourne Department of Medicine (Dermatology), St Vincent's Hospital; and Consultant Dermatologist, Skin and Cancer Foundation of Victoria, Melbourne, Vic.

Androgenetic alopecia, the process by which common balding occurs, is an androgen mediated age-related change in hair growth over the frontal and vertex scalp. By the age of 80 years, only 2.5% of men and 45% of women will still have a full head of hair; everyone else will have developed balding to some degree. Although the age of onset of hair loss is extremely variable, once started it progresses at a rate of 5 to 10% each year. It is often difficult for patients to see hair loss over the vertex scalp and consequently many patients underestimate the extent of their hair loss.

Balding may affect patients psychologically and lower self-esteem or cause distress and anxiety. Women, in particular, may withdraw and restrict social interactions, because hair in women is considered part of gender identity and attractiveness. The patients most likely to seek treatment are those who are young, single and concerned about their physical appearance.

## The normal hair cycle

Hair growth is cyclical, in contrast to nail growth, which is continuous. The phases of the hair growth cycle are anagen, catagen and telogen (Figure 1). Anagen is the growth phase; the hair grows at a rate of about 1 cm per month during this phase. The duration of anagen is the primary determinant of ultimate hair length; the phase lasts two to five years on the scalp, two to three months on the eyebrows and eight to 12 months in the axillary and pubic regions. Catagen is a two-week involutional phase, during which the lower two-thirds of the hair follicle undergoes apoptosis. Telogen is the dormant phase and lasts three months. At the end of telogen, the entire lower

**IN SUMMARY**

- **Some degree of bitemporal recession occurs in 65% of women and 95% of men; however, neither the presence nor severity of bitemporal recession correlates with vertex or midfrontal scalp hair loss. Bitemporal recession does not respond to finasteride or oral antiandrogens.**
- **Finasteride will arrest hair loss in 90% of men and stimulate hair regrowth to some degree in over 60%.**
- **Oral antiandrogens will arrest hair loss in over 90% of women and stimulate hair regrowth to some degree in over 30%.**
- **Topical minoxidil will produce visible hair regrowth in over 50% of men and women within six months, but might not arrest further hair loss.**
- **Diagnosis of female pattern hair loss is facilitated by the use of the described clinical grading scale. Women with grade 3, 4 or 5 hair loss have androgenetic alopecia.**
- **Up to 60% of women presenting with increased hair loss but who appear to have normal hair density on examination (grade 1 or 2) will have demonstrable androgenetic alopecia on scalp biopsy. Doctors should be wary of too eagerly reassuring women who claim to be losing hair but who have little visible hair loss.**

portion of the follicle regenerates from stem cells in the hair bulge at the level of insertion of the erector pili muscle. A new hair grows from the new bulb and causes the telogen hair to be shed. About 60 to 100 telogen hairs are normally shed from the scalp daily.

## Pathogenesis of androgenetic alopecia

Androgenetic alopecia is a disorder of hair growth. Prolongation of the duration of telogen, a corresponding shortening of anagen and a reduction of the population of cells within the hair matrix correspond with increased hair shedding, reduced hair length and reduced hair diameter respectively. Long terminal hairs are converted into short, fine, unpigmented hairs (also known as vellus), leading to baldness (Figure 2). This is the reverse of the changes seen in the hair follicles of the face, axillae and pubic regions with puberty.

## Determinants of hair loss

Four factors determine the extent of hair loss due to androgenetic alopecia: the susceptibility to the condition, the age of onset of balding, the rate of progression of balding and the pattern of balding. Studies in twins suggest all four factors are genetic. Any environmental, nutritional, emotional or stress related influence can, therefore, be considered negligible. No correlation between balding and dihydrotestosterone (DHT) levels and 5α-reductase has been consistently identified.

Susceptibility to androgenetic alopecia is inherited as a polygenic trait. Current modelling suggests that at least four genes are involved in determining susceptibility. The only gene identified to date is the androgen receptor gene on the X chromosome. Association studies have shown that polymorphisms on the androgen receptor gene are necessary but not sufficient in themselves for the development of male pattern balding.

## Clinical features in men

The characteristic pattern of hair loss in androgenetic alopecia in men is described by the Norwood–Hamilton scale (see the box on page 50). Hair loss characteristically begins with bitemporal recession of the anterior hairline (types I and II), followed by thinning of the hair over the vertex, leading to a bald spot, and continuing frontal recession (types III to VI). Ultimately, when the frontal recession joins the bald vertex area, there is complete loss of hair over the entire crown (type VII).

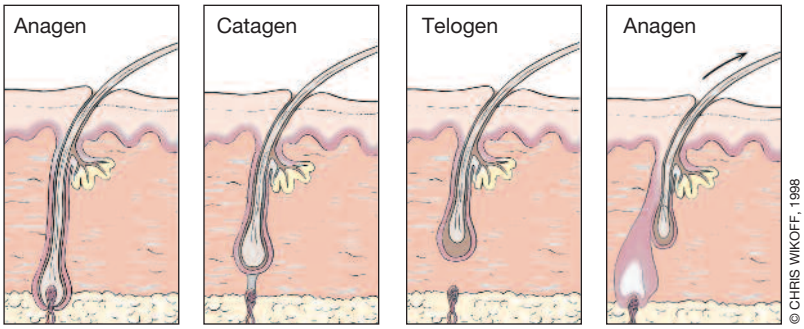



Figure 1. The normal hair cycle. Anagen is the growth phase and lasts from two to five years on the scalp. This is followed by catagen, a two-week phase during which the hair bulb undergoes apoptosis and the hair stops growing. Telogen is the dormant phase; the hair does not grow but remains attached to the follicle for about three months. Telogen is followed by the next anagen phase, in which a new hair is created and the old hair is shed.

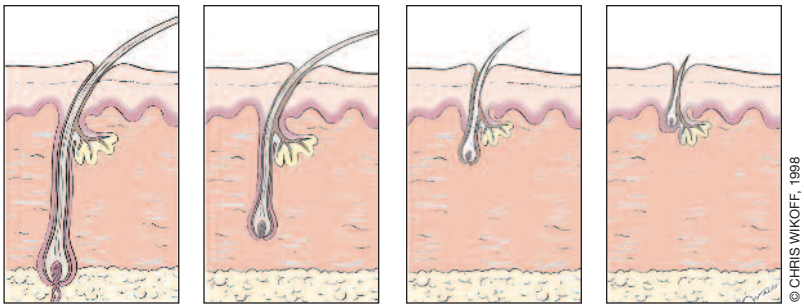


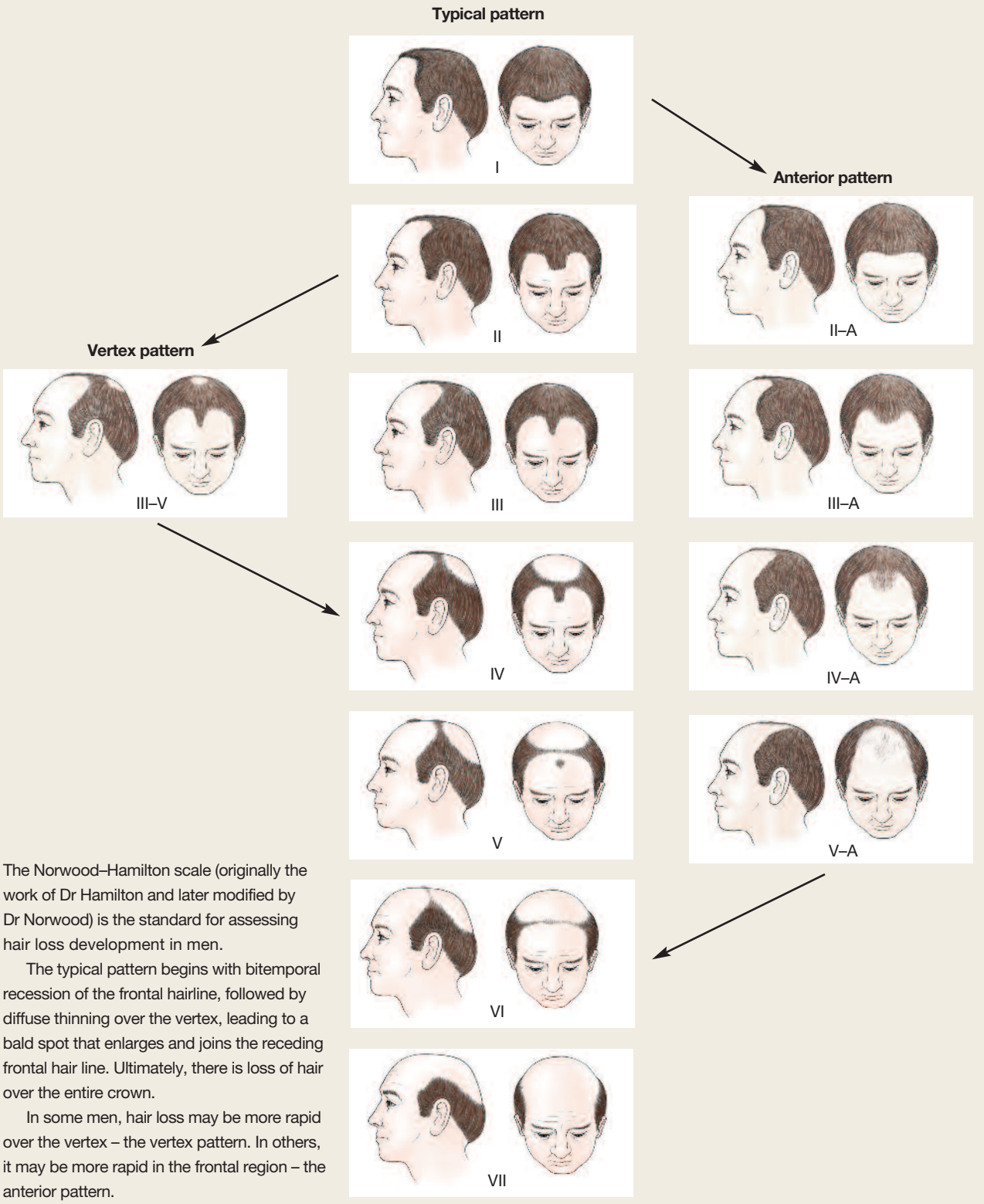

Figure 2. Androgenetic alopecia. Stepwise miniaturisation of the hair follicle, shortening of the anagen phase and diminution of hairs is mediated by androgens binding to hair follicle androgen receptors.

Recent studies have challenged this scale, in particular the lack of correlation between the presence or severity of bitemporal hair loss and the presence or severity of midfrontal or vertex hair loss. Bitemporal recession (type I) is identifiable in 96% of men by the late teens, but on its own is not a prodrome to vertex balding.

Most men develop diffuse thinning over the vertex scalp that progresses to total hair loss within the area (baldness) and extends centrifugally and anteriorly. In contrast, some men develop diffuse thinning over the midfrontal scalp. This is characterised by widening of the central part line (Figure 3), similar to the pattern of hair loss described by Ludwig in women with balding. This midfrontal hair loss pattern is most common in younger men.

**continued**

## The Norwood–Hamilton clinical grading scale for male baldness




The Norwood–Hamilton scale (originally the work of Dr Hamilton and later modified by Dr Norwood) is the standard for assessing hair loss development in men.

The typical pattern begins with bitemporal recession of the frontal hairline, followed by diffuse thinning over the vertex, leading to a bald spot that enlarges and joins the receding frontal hair line. Ultimately, there is loss of hair over the entire crown.

In some men, hair loss may be more rapid over the vertex – the vertex pattern. In others, it may be more rapid in the frontal region – the anterior pattern.

## Clinical features in women

Women only develop diffuse thinning over the midfrontal scalp, and never a bald spot over the vertex. Some degree of bitemporal hair loss is present in 65% of adult women, but it is pronounced in only 10%. Neither the presence nor severity of bitemporal hair loss indicates impending balding over the crown.

In the earliest stages, androgenetic alopecia may present with increased hair shedding alone. While many women will describe a reduction in the thickness of their ponytail, there will be no visible reduction in hair density over the scalp. These women are challenging diagnostically because it is difficult to define normal versus increased daily hair shedding. Of the up to 100 hairs normally shed each day, only about five are noticed, especially when the hair is short. The observation of an increase in the number of hairs shed may, therefore, be due to either a true increase in the number of hairs shed or anxiety about hair loss leading to increased interest in the capturing and counting of shed hairs. Furthermore, the hair shedding in early androgenetic alopecia is commonly episodic, lasting three to six months, then abating for three to 24 months before recurring. This clinical picture closely mimics acute telogen effluvium.

To help clinical diagnosis, a new validated clinical grading scale was developed – the Sinclair scale (see the box on this page). This scale was developed to enable classification of the most common type of female pattern hair loss, and has been used to determine the incidence of hair loss at various ages. Grade 1 is the normal pattern found in all girls prior to puberty but in only 45% of women aged 70 years and over. Grade 2 indicates widening of the central part; grade 3, widening of the central part with additional thinning of the hair adjacent to the part line; grade 4, emergence of a bald area in the midfrontal scalp; and grade 5, advanced hair loss. In a large case series of women

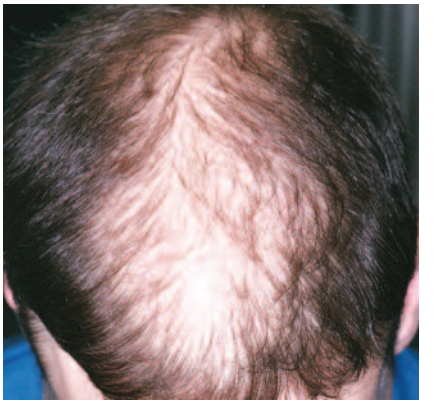
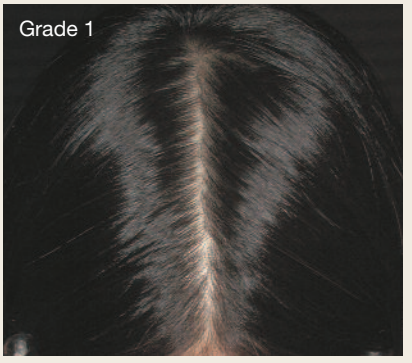
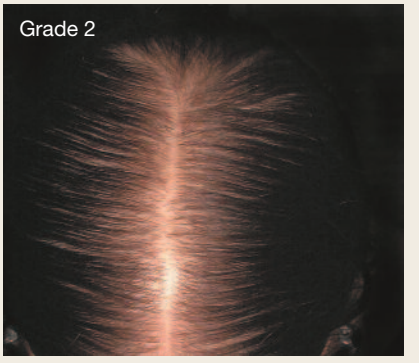
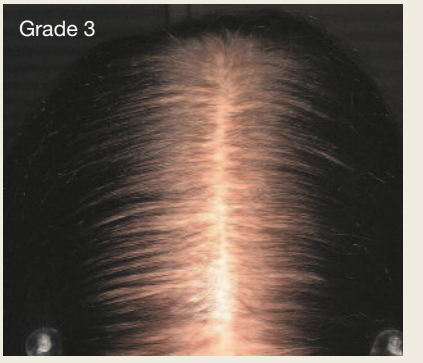


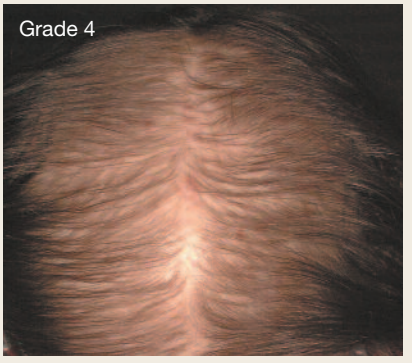
Figure 3. Diffuse thinning over the midfrontal scalp is more common in younger men than in older men.

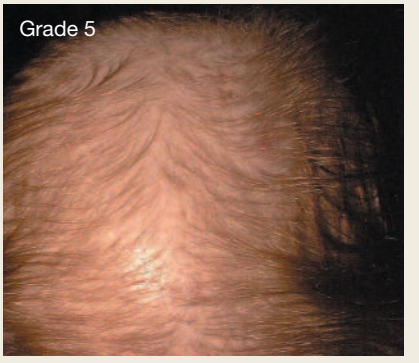
### The Sinclair scale of female pattern baldness




The Sinclair scale was developed to enable classification of the most common type of female pattern hair loss, and has been used to determine the incidence of hair loss at various ages. Grade 1 is the normal pattern, found in all girls prior to puberty, but in only 45% of women aged 70 and over. Grade 1 does not exclude androgenetic alopecia. Grades 3, 4 and 5 indicate androgenetic alopecia, while grade 2 may also be seen with other causes of hair loss.

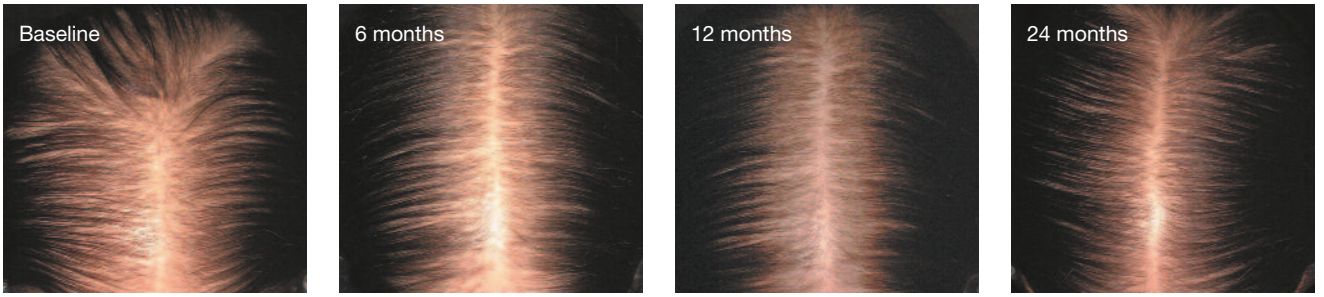



Figure 4. Hair regrowth following treatment with spironolactone 200 mg daily for 24 months.

presenting with hair loss of greater than six months' duration, 60% of women with clinical grade 1 and 2 were found to have androgenetic alopecia on scalp biopsy and 97% of women with grades 3, 4 and 5 had androgenetic alopecia.[1]

## Diagnosis

The diagnosis of common balding in men and women is usually based on the pattern of hair loss and history alone. Scalp biopsy is required only for women with grade 1 or 2 hair density who present with:

- chronic increased hair shedding as their principle symptom (more than six months' duration)
- acute increased hair shedding with no obvious trigger
- relapsing episodes of acute increased hair shedding
- incomplete recovery following an acute episode of increased hair shedding.

## Investigation

Investigations are rarely required in men as the pattern and extent of the hair loss make the diagnosis obvious. In early cases or where men present with midfrontal hair loss alone, a scalp biopsy may be required for diagnosis.

In women with increased hair shedding, alternative causes to common balding should be excluded, such as a recent febrile illness, miscarriage or childbirth, or hypo- or hyperthyroidism. It is unlikely that a low serum ferritin in the absence of iron deficiency anaemia or minor zinc deficiency causes hair loss. Fewer than 10% of women with scalp hair loss have elevated circulating androgens or evidence of an endocrine disorder. In women with associated hirsutism, menstrual irregularity, low fertility or acne, the most common diagnosis is polycystic ovary syndrome (PCOS). The diagnosis of PCOS should prompt further investigations aimed at early detection of insulin resistance and hyperlidipaemia. A virilising tumour is an unlikely cause as such tumours are exceptionally rare and balding among females is exceedingly common.

Therefore, while no investigations are required for many women, some may be indicated on clinical grounds, such as thyroid function test, full blood count and iron studies. Assessing serum testosterone, dihydroepiandosterone, sex hormone binding globulin, serum lutenising hormone and serum follicle stimulating hormone are sufficient to screen for PCOS and virilising tumours.

## Treatment

The three distinct aims in the management of androgenetic alopecia are to arrest further progression, to stimulate regrowth and to conceal the hair loss.

Topical minoxidil stimulates regrowth and may arrest further progression. Oral antiandrogens and 5α-reductase inhibitors arrest further progression and may stimulate regrowth. Coloured hair sprays and wigs (toupees) conceal the hair loss but do not stimulate regrowth or arrest further hair loss. Hair transplantation redistributes hair more evenly over the scalp.

### Drug therapy

#### Minoxidil

Topical 2% or 5% minoxidil solution (Replete, Rogaine) prolongs the duration of anagen, shortens the duration of telogen and may increase hair shaft diameter, which corresponds to a reduction in hair shedding and an increase in hair density to areas where it is applied. Maximal hair growth occurs after six months of therapy with the 5% solution and 12 months with the 2% solution. Minoxidil needs to be continued to maintain hair regrowth. Cessation of treatment leads to regression to the pretreatment state (i.e. loss of all the hair that has regrown with the minoxidil), but no additional hair is lost.

There may be a paradoxical temporary increase in hair shedding on initiation of therapy as resting telogen hairs are prematurely released from follicles.

#### Finasteride

At a daily dose of 1 mg, the 5α-reductase type II inhibitor finasteride (Propecia) reduces conversion of testosterone to DHT by approximately 70% in both the blood and the scalp tissue. In men, the medication arrests further progression of hair loss in over 90% of those who use it continuously for 24 months, and in 66% of patients it stimulates new hair growth.[2] The prospect of regrowth is greater on the vertex scalp than the midfrontal zone, and there is almost no effect on bitemporal hair loss. Cessation of finasteride results in the resumption of the balding progress rather than

regression to the pretreatment state.

There is some anecdotal evidence to suggest finasteride is also effective in the treatment of balding in women. However, finasteride is a teratogen (Australian Drug evaluation Committee [ADEC] category X) and its long biological half-life mitigates against its use in premenopausal women.

A study sponsored by the US National Institutes of Health demonstrated that men aged 55 years or older who took finasteride 5 mg daily for seven years had a 25% reduced risk of developing prostate cancer (45 cases per 100,000 men taking finasteride *v.* 60 cases per 100,000 in the placebo group).[3] However, all of the reduction appeared to be in the well differentiated group of prostate cancers (Gleeson scale 2 to 7), while poorly differentiated adenocarcinomas were marginally increased (22 cases per 100,000 *v.* 18 cases per 100,000 in the placebo group). The significance of this for young men taking 1 mg per day is unknown, and no additional data are expected for some years.

### Oral antiandrogens

Spironolactone and cyproterone acetate have been widely used for both hirsutism and common balding in women for many years. As antiandrogens have a feminising effect on men they are not an appropriate therapy for balding men.

Spironolactone (Aldactone, Spiractin) is used primarily as a potassium sparing diuretic but is also a competitive antagonist of the androgen receptor, inhibiting ovarian androgen production, and can be used to treat androgenetic alopecia. Patients with normal renal function rarely develop hyperkalaemia, even with doses of 200 mg daily. Higher doses are required for treating common balding than hirsutism. The usual dose for balding is 200 mg per day, although some women will benefit from 100 mg daily (Figure 4). Hair loss is arrested in over 90% of women, but regrowth is seen in fewer than 35%. Cessation of spironolactone results in the resumption of balding. Side effects include postural hypotension, lethargy, menstrual irregularity, urticaria and weight loss. Spironolactone is a potential teratogen (ADEC category B3) and women of childbearing age should avoid becoming pregnant while taking it.

Cyproterone acetate (Androcur, Cyprone, Cyprostat), an androgen receptor antagonist and weak progestogen, is as effective as spironolactone in the treatment of balding in women. It is another potential teratogen (ADEC category D) and women of childbearing age should avoid pregnancy while taking it. For premenopausal women, therefore,

it is usually combined with an oral contraceptive to prevent pregnancy and minimise menstrual irregularity and breakthrough bleeding (dosage, 100 mg per day for 10 days each cycle). Other side effects include mood disturbance and weight gain. Postmenopausal women may take 50 mg daily continuously.

Unfortunately, fluctuations in daily hair shedding cannot reliably be used to predict response to therapy or progression of hair loss. Many women regrowing hair with systemic antiandrogen therapy continue to report excess shedding.

### Hair transplantation

Hair transplantation is widely used for older men with stable baldness, but the role of hair transplantation in young men who are rapidly balding and in women is controversial.

As transplanted hairs retain the growth parameters of the donor site, occipital hairs placed on the vertex are not miniaturised through androgenetic alopecia.

The procedure of single follicle transplantation involves removing strips of hair-bearing skin from alopecia insensitive occipital areas. These strips are dissected into individual units of one, two or three hairs and then planted into the bald scalp in the desired orientation. The cost is around $5 to $10 per hair grafted, and three or four sessions of 300 to 600 grafts are required to convert a Norwood–Hamilton type VII to type III. The main complications include hypertrophic scarring, hyperaesthesia and haematoma. Postoperative infection is uncommon, and chronic folliculitis is rare.

## Conclusion

Androgenetic alopecia is an age-related condition that has varying emotional effects on sufferers, depending on the individual's gender, age and self-perception. The various treatments available for men and women are all palliative and need to be ongoing for sustained effect. When regrowth occurs with the available pharmacological agents, it is slow in coming and rarely dramatic. Motivated patients, however, can achieve substantial benefits over time. Many treatments for hair loss are promoted and sold over the Internet, and patients have been known to spend thousands of dollars. Patients should be warned that any treatment that sounds too good to be true probably is just that. MT

*A list of references is available on request to the editorial office.*

**DECLARATION OF INTEREST:** Professor Sinclair has acted as a consultant for GlaxoSmithKline, Merck Sharp & Dohme and Pfizer.

Medicine Today 2004; 5 (10): 48-56

# Androgenetic alopecia in men and women

**RODNEY SINCLAIR** MB BS, FACD

## References

1. Sinclair R, Jolly D, Mallari R, et al. Morphological approach to hair disorders. J Investig Dermatol Symp Proc 2003; 8: 56-64.
2. Whiting DA, Olsen EA, Savin R, et al. Efficacy and tolerability of finasteride 1 mg in men aged 41 to 60 years with male pattern hair loss. Eur J Dermatol 2003; 13: 150-160.
3. Thompson IM, Goodman PH, Tangen CM, et al. The influence of finasteride on the development of prostate cancer. N Engl J Med 2003; 349: 215-224.

## Further reading

1. Ellis JA, Sinclair R, Harrap SB. Androgenetic alopecia: pathogenesis and potential for therapy. Exp Rev Mol Med 2002; 19 November. http://www.expertreviews.org/02005112h.htm
2. Padilha MH, Saconato H, Sinclair R. Interventions for androgenic alopecia in men (Protocol in preparation). Cochrane Skin Group, 2004.
3. Sinclair R. Male pattern androgenetic alopecia. Br Med J 1998; 317: 865-869.
4. Sinclair R. There is no clear association between low serum ferritin and chronic diffuse telogen hair loss. Br J Dermatol 2002: 147: 982-984.
5. Nyholt DR, Gillespie NA, Heath AC, Martin NG. Genetic basis of male pattern baldness [letter]. J Invest Dermatol 2003; 121: 1561-1564.
6. Severi G, Sinclair R, Hopper JL, et al. Androgenetic alopecia in men aged 40-69 years: prevalence and risk factors. Br J Dermatol 2003; 149: 1207-1213.