6 Management of male androgenetic alopecia

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WEEDING OUT THE MYTHS

Alopecia is a common complaint in clinical practice, with androgenetic alopecia, also referred to as male-pattern hair loss or common baldness, representing by far the most frequent cause of hair loss in men. The first signs may occur in adolescence, leading to an age-dependent progressive, patterned, nonscarring, loss of scalp hair. Due to the frequency and the often significant impairment of life quality perceived by affected individuals, hair loss cures have been experimented on for centuries. What is remarkable about their history is that despite the more recent genuine advances in effective medical treatments, hair cosmetics, and surgical procedures, phony hair loss solutions continue to be marketed today with an amazing success. For prevention or treatment of hair loss, countless herbal solutions, oils, lotions, magic pills, and even spiritual invocations have been advanced with questionable result. With the advance of medical technologies, ultraviolet light-emitting lamps, electrical scalp simulators, and vacuum-cap machines have all been alleged to help stimulate the follicles to grow hair. Despite their outrageous claims, most lack scientifically measurable efficacy in preventing hair loss or promoting hair growth. But people are so concerned about their hair loss, they want to believe some miracle cure or some charismatic healer will help them. Therefore, competent diagnosis and treatment are particularly important in dealing with hair loss.

Exactly as the fixation on treating hair loss is not a new phenomenon, age-old myths regarding hair growth and shedding continue to exist up to this day. In the effort to find ways to prevent hair loss or to promote hair growth, many people have fallen victim to these myths. In dealing with the fear or complaint of hair loss, it is important to weed out these myths from the facts (Table 6.1).

Table 6.1 Most Frequent Layman's Myths Regarding Hair Loss in Men

- Wearing hats causes hair loss
- Frequent washing and blow drying can lead to hair loss
- Hairstyling products and dyes cause hair loss
- Brushing your hair can make it stronger and more resistant to hair loss
- Cutting your hair will make it grow back thicker
- Hair loss cannot be stopped or helped

In a community-based survey of men conducted in Switzerland in 1998 to characterize the significance of scalp hair and self-perception of hair loss, and to evaluate treatment of hair loss, of 508 men, aged 15–74 years (27% age 15–27 years, 41% age 30–49 years, and 32% age 50–74 years), 43% reported hair loss. Of these, 26% admitted to the use of hair growth-promoting agents, while 31% rejected use of hair growth-promoting agents because of no need, and 27% because they did not believe that they worked.[1]

PREREQUISITES FOR SUCCESSFUL MANAGEMENT OF HAIR LOSS

Prerequisites for a successful management of hair loss are twofold: on the psychological and on the technical levels. These require on the part of the attending physician a genuine interest in the patient's complaint on the emotional level, and a genuine interest in the problem of hair loss on the scientific level.[2]

On the psychological level, for a successful encounter at an office visit, one must be sure that the patient's key concerns have been directly and specifically solicited and addressed: acknowledge the patient's perspective on the hair loss problem, explore the patient's expectations from treatment, and educate patients in the basics of the hair cycle, and why patience is required for effective cosmetic recovery. One must recognize the psychological impact of hair loss. Physicians should recognize that alopecia goes well beyond the simple physical aspects of hair loss. Patients' psychological reactions to hair loss are less related to physicians' ratings than to patients' own perceptions. Some patients have difficulties adjusting to hair loss. The best way to alleviate the emotional distress is to eliminate the hair disorder that is causing it. Only a minority of patients suffer from true imaginary hair loss. These have varied underlying mental disorders ranging from overvalued ideas to delusional disorder. In these cases, one must aim at making a specific psychopathologic diagnosis.

On the technical level, prerequisites for success are a specific diagnosis, a profound understanding of the underlying pathophysiology, the best available evidence gained from the scientific method for clinical decision making, and regular follow-up of the patient combining standardized global photographic assessments and epiluminescence microscopic photography with or without computer-assisted image analysis.

METHOD OF RIGHTLY CONDUCTING THE REASON, AND SEEKING TRUTH IN THE SCIENCES

As with any medical problem, the patient complaining of hair loss requires a comprehensive medical and drug history, physical examination of the hair and scalp, and appropriate laboratory evaluation to identify the cause. The clinician also has a host of diagnostic techniques that enable classification of the patient's disorder as a shedding disorder or a decreased density disease, and documentation of true pathology or only perceived pathology.

With respect to the diagnosis and treatment, one must remain open minded for the possibility of a multitude of cause-relationships underlying hair loss, and therefore also for the possibility of combined treatments and multitargeted approaches to hair loss.

The diagnosis of male androgenetic alopecia is usually quite straightforward and easy. Challenges in male androgenetic alopecia are listed in Table 6.2.

By approaching the hair loss patient in a methodical way, commencing with objects the simplest and easiest to recognize, ascending step by step to the knowledge of the more complex, and making enumerations so complete and reviews so general that nothing is omitted, an individualized treatment plan can be designed that usually results in success.[3]

PATHOPHYSIOLOGICAL UNDERSTANDING OF MALE ANDROGENETIC ALOPECIA

Androgenetic alopecia affects at least 50% of men by the age of 50 years, and up to 70% of all males in later life.[4] The hair loss is heritable, androgen dependent, and occurs in a defined pattern. It is assumed that the genetically predisposed hair follicles are the target for androgen-stimulated hair follicle miniaturization, leading to gradual replacement of large, pigmented hairs (terminal hairs) by barely visible, depigmented hairs (vellus hairs) in affected areas.[5] The result is a progressive decline in visible scalp hair density. Male-pattern androgenetic alopecia is characterized by its typical bitemporal recession of hair and balding vertex, while diffuse thinning of the crown area with an intact hairline is referred to as female-pattern androgenetic alopecia. Although the majority of men present with the male pattern, the female pattern is observed in children with premature alopecia, and in an estimated 4% of adult men with androgenetic alopecia.

Table 6.2 Challenges in Male Androgenetic Alopecia

- Premature alopecia
- Unusual patterns of androgenetic alopecia
- Androgenetic alopecia with comorbidities
- Androgenetic alopecia with follicular microinflammation and fibrosis

Although the genetic involvement is pronounced but poorly understood, major advances have been achieved in understanding principal elements of the androgen metabolism involved.[6] Androgen-dependent processes are predominantly due to the binding of dihydrotestosterone (DHT) to the androgen receptor (AR). The DHT-dependent cell functions depend on the availability of weak androgens, their conversion to more potent androgens via the action of 5α-reductase, low enzymatic activity of androgen-inactivating enzymes, and functionally active AR present in high numbers. The predisposed scalp exhibits high levels of DHT and increased expression of the AR. Conversion of testosterone to DHT within the dermal papilla plays a central role, while androgen-regulated factors deriving from dermal papilla cells are believed to influence growth of other components of the hair follicle.

Finally, the limited success rate of treatment of androgenetic alopecia with modulators of androgen metabolism, such as oral finasteride, and of hair growth promoters, such as topical minoxidil solution, means that further pathogenic pathways must be taken into account.[7] Among these, the role of oxidative stress, and of follicular microinflammation and fibrosis have gained more recent attention.

Naito et al.[8] analyzed the effect of the lipid peroxides on hair follicles and observed that the topical application of linolein hydroperoxides, one of the lipid peroxides, leads to the early onset of the catagen phase in murine hair cycles. Furthermore, they found that lipid peroxides induced apoptosis of hair follicle cells. They also induced apoptosis in human epidermal keratinocytes by upregulating apoptosis-related genes. These results indicate that lipid peroxides, which can cause free radicals, induce the apoptosis of hair follicle cells, and this is followed by early onset of the catagen phase. Ultimately, Bahta et al.[9] cultured dermal hair papilla cells (DPCs) from balding and nonbalding scalp and demonstrated that balding DPCs grow slower in vitro than nonbalding DPCs. Loss of proliferative capacity of balding DPCs was associated with changes in cell morphology, expression of senescence-associated beta-galactosidase, decreased expression of proliferating cell nuclear antigen and Bmi-1, upregulation of p16(INK4a)/pRb, and nuclear expression of markers of oxidative stress and DNA damage, including heat shock protein-27, super oxide dismutase catalase, ataxia-telangiectasia-mutated (ATM) kinase, and ATM- and Rad3-related protein. The finding of premature senescence of balding DPC in vitro, in association with expression of markers of oxidative stress and DNA damage, suggests that balding DPCs are particularly sensitive to environmental stress, such as cigarette smoking or ultraviolet radiation (UVR).

Eventually, a population-based cross-sectional survey among Asian men 40 years or older showed statistically significant positive associations between moderate or

severe androgenetic alopecia and smoking status, current cigarette smoking of 20 cigarettes or more per day, and smoking intensity.[10] The odds ratio of early onset history for androgenetic alopecia grades increased in a dose–response pattern. Risk for moderate or severe androgenetic alopecia increased for family history of first-degree and second-degree relatives, as well as for paternal relatives.

Even though the consequences of yet another environmental stress, namely, sustained UVR on unprotected skin, are well appreciated, mainly photocarcinogenesis and solar elastosis, the effects of UVR on the evolution of androgenetic alopecia have only recently found attention.[11] However, some clinical and morphological observations suggest that UVR has some negative effect on hair growth. Histopathologically, elastosis is regularly found in scalp biopsies, especially in alopecic conditions, but so far has largely been ignored. To date, no controlled study has been performed on the degree of scalp elastosis in relation to the pace of development, duration, or grade of androgenetic alopecia, though it would seem to be a good marker for exposure to UVR penetrating the skin.

The implication of microscopic follicular inflammation in the pathogenesis of androgenetic alopecia has emerged from several independent studies[12–14]; an early study referred to an inflammatory infiltrate of activated T cells and macrophages in the upper third of the hair follicles, associated with an enlargement of the follicular dermal sheath composed of collagen bundles (perifollicular fibrosis), in regions of actively progressing alopecia. Horizontal section studies of scalp biopsies indicated that the perifollicular fibrosis is generally mild, consisting of loose, concentric layers of collagen that must be distinguished from cicatricial alopecia. The term *microinflammation* has been proposed,[13] because the process involves a slow, subtle, and indolent course, in contrast to the inflammatory and destructive process in the classical inflammatory scarring alopecias. The significance of these findings has remained controversial. However, morphometric studies in patients with male androgenetic alopecia treated with minoxidil showed that 55% of those with microinflammation had regrowth in response to treatment, in comparison to 77% in those patients without inflammation and fibrosis.[14] Surprisingly, so far, the inflammatory component has not been included in treatment protocols for male androgenetic alopecia.

EVIDENCE-BASED MEDICINE-GUIDED TREATMENT OF MALE ANDROGENETIC ALOPECIA

Although testing medical interventions for efficacy has existed since the time of Avicenna's (980–1037) "The Canon of Medicine" in the eleventh century, it was only in the twentieth century with the works of Alvan R. Feinstein (1925–2001) and Archie Cochrane (1909–1988) that this effort evolved to impact almost all fields of health care and policy.[15,16] Evidence-based medicine (EBM) aims for the ideal that healthcare professionals should make conscientious, explicit, and judicious use of the best available evidence gained from the scientific method in clinical decision making. It seeks to assess the strength of the evidence of risks and benefi s of diagnostic tests and treatments, using techniques from science, engineering, and statistics, such as the systematic review of medical literature, meta-analysis, risk-benefit analysis, and randomized controlled trials.

As EBM guidelines on hair loss are rare, a European consensus group recently developed guidelines for treatment of androgenetic alopecia. It conducted a systematic literature review of Medline, Embase, and Cochrane databases upto August 2008.[17] There were 1370 publications found; 51 were added by hand search. Eight-five publications fulfilled the following inclusion criteria for the guideline: prospective study with a number of patients ≥20 (no minimal patient number required in twin studies), age ≥12 years, with confirmed diagnosis of androgenetic alopecia (diagnosis either clinically or by further diagnostic evaluations, e.g., trichogram, TrichoScan, or biopsy). Objective outcome measures of efficacy described for drug therapy were mean change from baseline hair count in target area or measurement of hair growth/loss in target area by global photography.

The guideline revealed excellent evidence levels (randomized, double-blind, comparative clinical studies of high quality, e.g., sample size calculation, flowchart of patient inclusion, intent-to-treat [ITT] analysis, sufficient size, or meta-analysis, which includes at least one randomized double-blind, comparative clinical study of high quality) for the therapeutic use of topical minoxidil solution and for oral finasteride, low evidence levels (little to missing systematic evidence) for hormonal or surgical treatments, and insufficient, respectively, lacking, evidence for a broad panel of miscellaneous treatments available claiming effectiveness. Table 6.3 summarizes the EBM-guided recommendations for treatment of male androgenetic alopecia, and Table 6.4 lists miscellaneous treatments with insufficient or lacking evidence for efficacy.

Finasteride is a competitive inhibitor of type 2 5α-reductase and inhibits the conversion of testosterone to DHT. The rationale for the use of finasteride to treat AGA in men is based on the absence of androgenetic alopecia in men with congenital deficiency of type 2 5α-reductase, and the presence of increased 5α-reductase activity and DHT levels in balding scalp.[18]

Minoxidil promotes hair growth through increasing the duration of anagen. It causes hair follicles at rest to grow, and enlarges suboptimal follicles. Minoxidil was developed for treatment of hypertension, and this feature of the drug's action is best understood; its mechanism of

Table 6.3 Treatment Recommendations for Male Androgenetic Alopecia

Topical minoxidil solution

- Topical minoxidil 2%–5% solution 1 mL twice daily is recommended to improve or to prevent progression of androgenetic alopecia in male patients older than 18 years with mild to moderate androgenetic alopecia (Hamilton-Norwoo IIv-V).
- Use of 5% solution is suggested for greater efficacy.
- There is not enough data to recommend the 5% minoxidil foam instead of the 5% solution.
- The response to treatment should be assessed at 6 months. If successful, treatment needs to be continued to maintain efficacy.

Oral finasteride

- Oral finasteride 1 mg a day is recommended to improve or to prevent progression of androgenetic alopecia in male patients older than 18 years with mild to moderate androgenetic alopecia (Norwood–Hamilton IIv–V).
- The response to treatment should be assessed at 6 months, although in some men it may not become evident until 12 months. If successful, treatment needs to be continued to maintain efficacy.
- There is insufficient evidence to support the use of topical finasteride.
- For greater efficacy, the combination of oral finaseride 1 mg/1 × /d and topical minoxidil 2%–5% solution, 2 × /d can be considered.

Hormonal treatments

- The use of oral estrogens or androgen-receptor-antagonists is inappropriate to improve or prevent progression of androgenetic alopecia in male patients.
- There is insufficient evidence to support the use of topical alfatradiol to improve or prevent progression of androgenetic alopecia in male patients.
- It is suggested that topical fluridil or topical fulvestrant should not be used in male patients with androgenetic alopecia.

Surgical treatments

- Surgery, especially follicular unit transplantation (FUT), can be considered in male patients with sufficient donor hair.
- It is suggested that FUT to be combined with finasteride 1 mg daily to achieve a better clinical outcome.

Source: Adapted from Blumeyer A, Tosti A, Messenger A et al. *J Dtsch Dermatol*. 2011;Ges;9 Suppl 6:S1–S57.

Table 6.4 Miscellaneous Treatments with Insufficient or Lacking Evidence for Efficacy and Proposed Mechanisms of Action in Treatment of Androgenetic Alopecia

Promotion of hair regrowth

- Amino acids
- Iron supplements in absence of efficacy
- Vitamins (biotin, niacin derivates)
- Proanthocyanidines
- Millet seed (silic acid, amino acids, vitamins, minerals)
- Marine extract and silicea component
- Chinese herbals
- Ginkgo biloba
- Aloe vera
- Ginseng
- Bergamot
- Hibiscus
- Sorphora
- Caffeine
- Melatonin
- Retinoids
- Ciclosporine
- Electromagnetic/electrostatic field
- Low-level laser

Improved perifollicular vascularization

- Prostaglandins (viprostol, latanoprost)
- Aminexil
- Glyceroloxyesters and silicium
- Minerals
- Niacin derivatives
- Mesotherapy

DHT-inhibitory activity

- Saw palmetto
- ß-sitosterol
- Polysorbate 60
- Green tea
- *Cimicifuga racemosa*

Anti-inflammatory activity

- Ketoconazol
- Zinc pyrithione
- Corticosteroids

Improved hair nutrition

- Vitamins (biotin, niacin derivates)
- Trace elements (zinc, copper)

Others

- Botulinum toxin

Source: Adapted from Blumeyer A, Tosti A, Messenger A et al. *J Dtsch Dermatol*. 2011;Ges;9 Suppl 6:S1–S57.

action on hair growth is poorly understood. Minoxidil is a potassium-channel opener and vasodilator, and it has been reported to stimulate the production of vascular endothelial growth factor (VEGF) in cultured dermal papilla cells.[19] There is evidence that this effect is mediated by adenosine and sulfonylurea receptors, which are well-known target receptors for adenosine-triphosphate-sensitive potassium channel openers.[20]

Autologous hair transplantation represents the only treatment that can produce substantial improvement in patients with advanced hair loss and can give satisfactory results, as long as the patient has a realistic expectation

regarding the treatment results.[21] Hair line design, evaluation of the donor and recipient areas, as well as discussion of graft numbers, are basic parts of the hair transplant consultation. There are two donor hair harvesting techniques that are performed under local anesthesia: in one technique, a strip of scalp skin is taken from the occipital area, which then is divided into mini- or micrografts, each containing 1–4 hairs. The grafts are then planted into tiny slits in the desired recipient area. The other technique is follicular unit extraction (FUE): multiple follicles are harvested with small 1-mm punches and planted in the target area, avoiding the occipital linear scar of the strip technique. However, FUE is more labor intensive and therefore usually more expensive. A natural looking result can be achieved with both procedures. One or two sessions usually provide good coverage of a balding recipient area. Final results are usually seen 6–8 months after the surgery.

BEYOND EVIDENCE-BASED MEDICINE

Although EBM has become the gold standard for clinical practice, there are a number of limitations of its use (summarized in Table 6.5).

In EBM, the expert opinion is considered to be the least valid form of evidence. Nevertheless, knowledge gained from clinical research does not directly answer the primary clinical question of what is best for the patient at hand, and suggests that EBM should not discount the value of clinical experience. Good medical practice means integrating individual clinical expertise with the best available external clinical evidence from EBM.

For successful management of male androgenetic alopecia, one must remain open-minded for the possibility of a multitude of cause-relationships underlying hair loss, and accordingly for the potential of combination treatments.[22] It is important to manage male androgenetic alopecia strategically, with the variety of current therapeutic options depending on the individual's needs. Ultimately, combination treatments with topical minoxidil, oral finasteride, nutritional supplements, surgery, low-level laser therapy, and appropriate scalp care may act synergistically. The scientific rationale for such an approach is given, but—again—there is a need for clinical studies to establish an increase in efficacy of combination regimens and adjuvant treatments.

Table 6.5 Limitations of EBM

- EBM guidelines do not remove the problem of extrapolation to different populations or longer time frames
- Even if several top-quality studies are available, questions always remain about how far, and to which populations, their results may be generalized
- Certain groups have been historically underresearched, such as racial minorities and people with comorbid diseases, and thus the literature is sparse in areas that do not allow for generalizing
- EBM applies to groups of people, but this does not preclude clinicians from using their personal experience in deciding how to treat an individual subject

Finally, the influence of the prescribing physician should be kept in mind, because inspiring confidence versus skepticism and fear clearly impacts the outcome of treatment.[22] Treatment success relies on patient compliance that, on its part, relies on comprehension of treatment benefi , confidence, and motivation. A positive physician–patient relationship and regular follow-up visits (at 3, 6, 12, and 24 months; Figure 6.1a–e), including standardized photographic assessments, are the most important factors in determining the degree of patient compliance. The overall goal is to gain short-term compliance as a prerequisite to long-term adherence to treatment. Recommendations for improvement of patient compliance are summarized in Table 6.6.

More recently, the post-finasteride syndrome has been claimed to occur in men who have taken oral finasteride to treat either hair loss or benign prostatic hyperplasia. Reported symptoms include persistent loss of libido, erectile dysfunction, reduction in penis size, penile curvature or reduced sensation, gynecomastia, muscle atrophy, cognitive impairment, severely dry skin, and depression. The condition allegedly may have a life-altering impact on sufferers and their families, such as job loss and the break-up of romantic relationships or marriages, while also being linked to suicides.[23] As yet, the condition is not recognized by the scientific community, although individuals who suffer from the syndrome do present with distinctive and relatively homogenous symptoms. Even though the incidence of persistent sexual, mental, and physical side effects which continue despite quitting finasteride is unknown, it is likely that over 1000 men worldwide are experiencing the effects. This estimate is based on the number of registered users on the Internet forum www.propeciahelp.com. The Post-Finasteride Syndrome Foundation (www.pfsfoundation.org) is a nonprofit organization dedicated to helping fund research on the characterization, underlying biologic mechanisms, and treatments of the post-finasteride syndrome, while improving public awareness of the condition.

There are no predictive factors for the risk of development of post-finasteride syndrome, and there are no known treatments for the disorder. Preliminary recommendations for the prescription of oral finasteride in the treatment of male androgenetic alopecia are summarized in Table 6.7.

HAIR CARE

A majority of current treatments associated with thinning hair, such as androgenetic alopecia and aging hair,

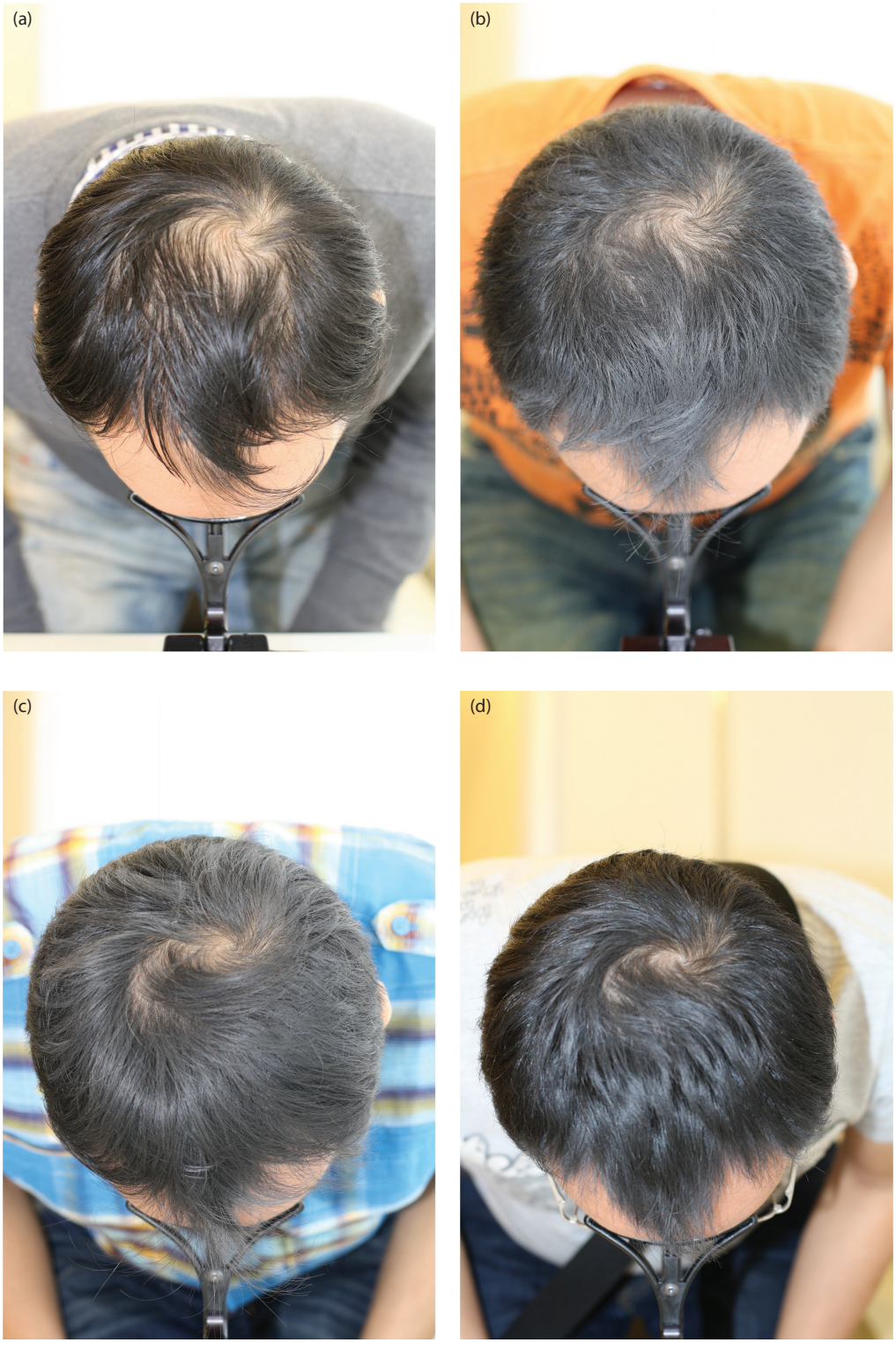

Figure 6.1 **(a–e) Photographic documentation of successful combination treatment in a 45-year-old male with 1-mg oral finasteride and topical 5% minoxidil solution bid, (a) before, (b) after 3 months, (c) 6 months, (d) 12 months, and (e) 24 months.** *(Continued)*

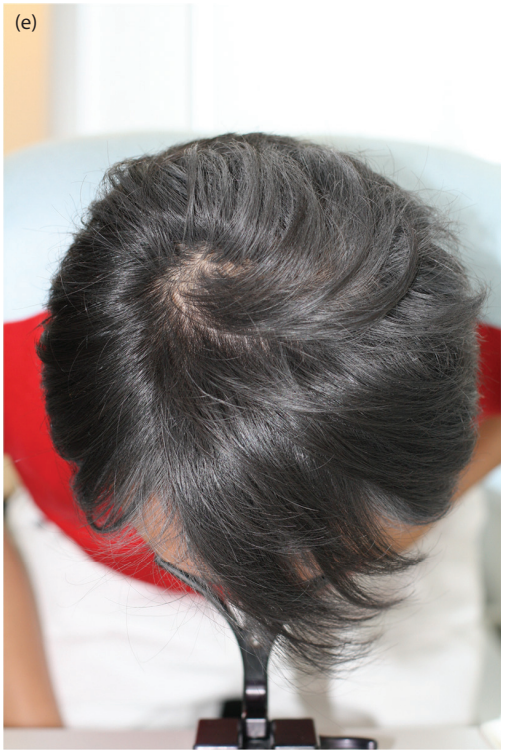

***Figure 6.1 (Continued)* (a–e) Photographic documentation of successful combination treatment in a 45-year-old male with 1-mg oral finasteride and topical 5% minoxidil solution bid, (a) before, (b) after 3 months, (c) 6 months, (d) 12 months, and (e) 24 months.**

are focused on improving scalp hair density, and on preventing further damage of the hair fiber. The efficacy of hair growth-promoting agents in shampoo form is questionable, given their dilution with water and short contact time, unless they can be absorbed in effective quantities. Nevertheless, since hair fiber diameter has been recognized to represent another key contributor to hair thinning, a novel leave-on technology has been developed that combines caffeine, niacinamide, panthenol, dimethicone, and an acrylate polymer (CNPDA) to affect the diameter and behavior of individual scalp hair fibers as an approach to improve decreasing fiber diameter. Utilizing a laser scan micrometer for assessment of fiber diameter measures, and tensile break stress and torsion pendulum testing for assessment of behavioral properties, it was found that CNPDA significantly increased the diameter of individual terminal scalp hair fibers by 2–5 µm, which yields an increase in the cross-sectional area of approximately 10. Beyond the increase in hair fiber diameter, the CNPDA-thickened fibers demonstrated enhanced mechanical properties characteristic of thicker fibers, such as increased suppleness/

Table 6.6 Recommendations for Improvement of Patient Compliance

- Only recommend treatments that are effective in circumstances when they are required
- Prescribe the minimum number of different medications (e.g., combining active ingredients into a single compound)
- Simplify dosage regimen by selecting different treatment or using a preparation that needs fewer doses during the day
- Select treatments with lower levels of side effects or fewer concerns for long-term risks
- Discuss possible side effects, and whether it is important to continue medication regardless of those effects
- Advise on minimizing or coping with side effects
- Provide regular follow-up for reassurance on drug safety and treatment benefits
- Develop trust so patients do not fear embarrassment or anger if unable to take a particular drug, allowing the doctor to propose a more acceptable alternative

Source: With kind permission from Springer Science+Business Media: *Male Alopecia. Guide to Successful Management*, Cham, 2014, Switzerland: Springer International Publishing, Trüeb RM, Lee W-S.

Table 6.7 Recommendations for Prescription of Oral Finasteride in Treatment of Male Androgenetic Alopecia

- Note that efficacy and safety of oral fi asteride for treatment of male androgenetic alopecia in men aged 18 through 40 with mild to moderate androgenetic alopecia (Hamilton–Norwood IIv–V) have been demonstrated.[a]
- Refrain from prescribing oral fi asteride to a patient with a personal history of depression, sexual dysfunction, or fertility problems.
- When fertility is an issue, consider performing a sperm count before and during treatment with oral fi asteride.
- In any case of adverse effects, immediately stop oral fi asteride treatment.
- In all men 45 and over, perform PSA before starting therapy with oral fi asteride, after starting therapy, and thereafter on a twice-yearly basis. The level should drop by ca. 50% upon initiation of therapy. In case of increase >0.4 ng/mL per year, refer to a urologist to check prostate condition.
- Note that for men who choose regular prostate-cancer screening, the use of oral fi asteride meaningfully reduces the risk of prostate cancer.[b]

Source: With kind permission from Springer Science+Business Media: *Male Alopecia. Guide to Successful Management*, Cham, 2014, Switzerland: Springer International Publishing, Trüeb RM, Lee W-S.

[a] See also Finasteride Male Pattern Hair Loss Study Group. *Eur J Dermatol*. 2002;12:38–49.

[b] See also LeFevre A. *N Engl J Med*. 2013;369:670–671.

pliability and better ability to withstand force without breaking.[24]

In summary, although cosmetic treatments will not reverse the process of androgenetic alopecia, new technologies help to mitigate the effects of androgenetic alopecia-related thinning of hair.

CONCLUDING REMARKS

Mainstream scientists are currently working on gene polymorphisms diagnostics for prediction of risk, prevention, diagnosis, and targeted treatment development for male androgenetic alopecia, on stem cell technologies, and on bioengineering of the hair follicle. Meanwhile, healthcare providers are becoming increasingly aware of a more holistic approach toward successful treatment of hair loss in men, to include awareness, lifestyle, environmental factors, nutrition, EBM-guided pharmacotherapy and medical devices, surgery, and hair care.

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7 Management of female androgenetic alopecia

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Female androgenetic alopecia (AGA) is the most common form of alopecia in women, occurring in up to 50% of women in the course of their life.[1] It appears in most cases after the age of 60, but onset in young adult females is not rare.[2] Rapid appearance of patterned thinning in a premenopausal woman should always suggest a possible hormonal disease. Progression is also slower than in males, with generally a more diffuse involvement of the scalp. Patients usually complain of progressive hair thinning, and/or loss of hair volume, or about a continuous or intermittent hair shedding.

In women three different patterns[3] can be observed: (1) diffuse thinning of the crown region with maintenance of the frontal hairline (Ludwig type) (Figure 7.1); (2) thinning and widening of the central part of the scalp with breach in the frontal hairline (Christmas tree pattern) (Figure 7.2); (3) more rare, thinning associated with bitemporal recession (Hamilton type) (Figure 7.3), usually observed in postmenopausal women and in women with hyperandrogenism.

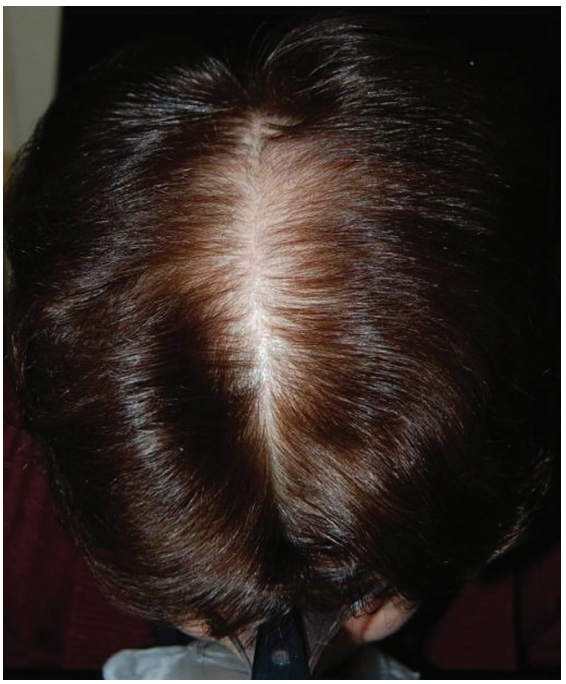

Figure 7.1 **Ludwig-type androgenetic alopecia: widening of the medial hairline.**

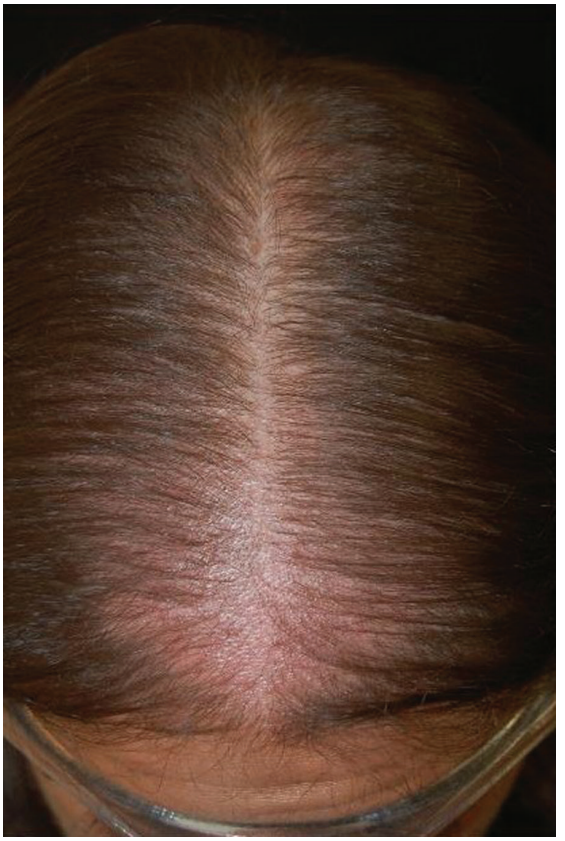

Figure 7.2 **Christmas tree pattern: widening of the central line from the back to the frontal area.**

Involvement of the parietal and occipital scalp with diffuse alopecia can be seen as well.

The hairs of the affected regions are both decreased in number, and reduced in diameter, length, and pigmentation; they are less evident and therefore no more able to cover the scalp adequately. Complete miniaturization only affects a percentage of the hair, which assumes the appearance defined as *vellus*, while the majority of hair acquires border-line characters, keeping the pigment and reaching partially intermediate thickness, between vellus hairs and normal ones.

Hair thinning has an important impact on a woman's quality of life, and a treatment should always be advised.[4]

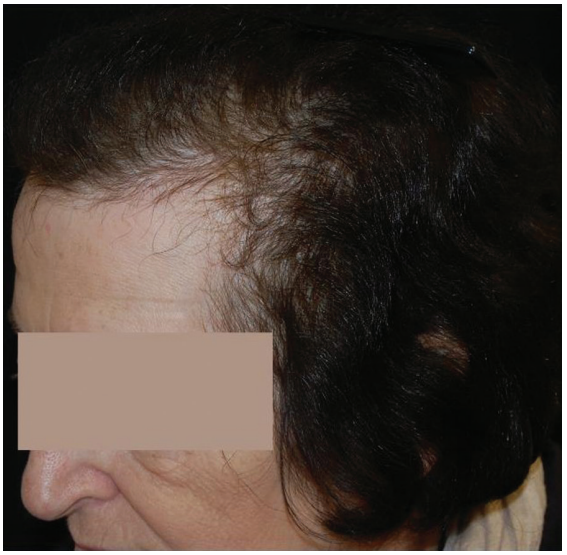

Figure 7.3 **Androgenetic alopecia in a female with a male pattern: receding frontotemporal hairline.**

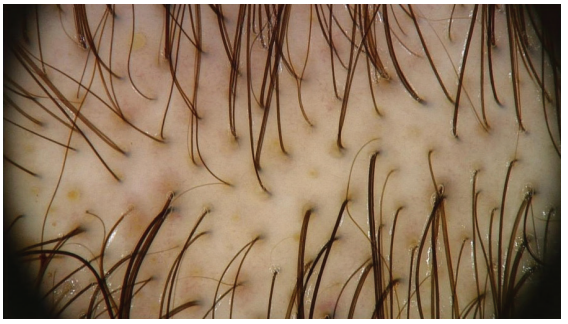

Figure 7.4 **Scalp videodermoscopy of female androgenetic alopecia: hair diameter variability, yellow dots, and perifollicular halos.**

FIRST STEP FOR CORRECT MANAGEMENT OF FEMALE ANDROGENETIC ALOPECIA (AGA): ESTABLISH THE DIAGNOSIS

Diagnosis of AGA is simple in most cases. The patient complains of a slowly progressive hair thinning, which is not generally associated with increased hair shedding. Patients usually report a change in consistency and thickness of the hair, which appears thinner. The history of acute hair shedding is indicative of an associated acute telogen effluvium. Telogen effluvium may in fact be associated with AGA, and in some cases it may induce the onset of the condition or its worsening. It is therefore important to understand if the patient complains of thinning alone or of an associated hair shedding. Causes of this acute telogen effluvium may include drugs, crush diets, systemic disease, and childbirth.

Clinical examination should start with evaluation of the density of hair in the different areas of the scalp. Comparing the density of hair in the crown region with that of the occipital region can be very helpful to differentiate mild forms of AGA from diffuse hair loss. The pull test may be negative or may reveal an increased telogen shedding. The presence of telogen hairs, shorter than 3 cm, representing the telogen phase of miniaturized follicles, is diagnostic for AGA. Variation in the hair shaft diameter is typical of AGA and is an important feature for early diagnosis of the disease. This can be better visualized using scalp dermoscopy[5] (Figure 7.4). The dermoscopic features of AGA are variation of the hair shaft diameter, empty follicles phenomenon, peripilar depressions, pigmentation, and inflammation of the scalp. (1) Variation of the diameter of the hair is diagnostic of AGA. A variation in diameter affecting >20% of hair in androgen regions is seen. Under the effect of androgens, hair follicles undergo a progressive miniaturization and produce a hair shaft that is gradually thinner and less pigmented. Follicular miniaturization initially involves the adjacent follicles in a different extent: in the initial forms of androgenetic alopecia, using scalp dermoscopy, we can see in the same area hair of normal diameter, hair slightly thinner, and very thin and short hair (diameter <0.3 mm). A diagnosis of early forms, which are not recognized by clinical examination alone, is then possible. In the most severe forms of AGA, the miniaturization affects follicles diffusely, and the hair shafts are uniformly thin. (2) The empty follicle phenomenon is another pathogenetic factor of AGA. Empty follicles appear as yellow spots (yellow dots) on the scalp. The yellow color is due to the fact that the follicular ostium, more or less dilated, contains sebum produced by sebaceous glands associated with the follicle. They can be seen especially in the frontal area. (3) Peripilar depressions, also called *peripilar halos*, appear as dark halos extended approximately 1 mm around the follicular ostium from which the hair emerges. They are specific and characteristic of androgenetic alopecia and occur more often in patients with mild forms of androgenetic alopecia, with a high density of hair.

A scalp biopsy is very useful in doubtful cases: in longitudinal sections the detection of the miniaturized follicles is diagnostic. Important findings are a decrease of terminal hairs, anagen hairs, and an increase of vellus-like hairs, telogen hairs, and fibrous streamers. A mild to moderately dense perifollicular lymphohistiocytic inflammatory infiltrate may be seen around the infundibulum.

SECOND STEP FOR CORRECT MANAGEMENT OF FEMALE AGA: DEFINE SEVERITY OF DISEASE

According to the classification proposed by Ludwig, female AGA can be divided into three grades of severity.[6] The first grade is characterized by a slight thinning of