Guidelines for Male and Female Androgenetic Alopecia

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I have performed clinical studies, given lectures, received honoraria, or had consulting activities for the following companies (in order of alphabet):

- Apomedica (Switzerland)
- Asatona (Switzerland)
- Biolab (Brazil)
- Cipla (India)
- Johnson & Johnson
- Lexington
- Merz Pharma (Germany)
- MSD
- Permed (Switzerland)
- Procter & Gamble
- Rausch (Switzerland)
- Spirig (Switzerland)
- Vichy
- Wolff (Germany)
Androgenetic alopecia is the most common hair loss disorder, affecting both men and women.

First signs often occur in adolescence, leading to progressive alopecia typically with a pattern distribution.

Due to the frequency and the often significant impairment of life quality perceived by affected individual, competent diagnosis and treatment are particularly important.
Andro(chrono)genetic Alopecia (Definition)

Genetically determined, androgen-induced, age-dependent, progressive hair loss with sex-dependent differences in incidence, pattern, and severity

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<thead>
<tr>
<th>Age Range</th>
<th>Men (%)</th>
<th>Women (%)</th>
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<tbody>
<tr>
<td>18 - 29</td>
<td>12%</td>
<td>3%</td>
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<td>30 - 39</td>
<td>38%</td>
<td>17%</td>
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<td>40 - 49</td>
<td>45%</td>
<td>16%</td>
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<td>50 - 59</td>
<td>52%</td>
<td>23%</td>
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<td>60 - 69</td>
<td>65%</td>
<td>25%</td>
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<td>70 - 79</td>
<td>64%</td>
<td>28%</td>
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<td>&gt; 80</td>
<td>70%</td>
<td>32%</td>
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</tbody>
</table>

Men:

[Images of hair loss stages from Hamilton-Norwood I-VII]

Women:

[Images of hair loss stages from Ludwig I-III]

Androgens + Androgen metabolism

Polygenic Trait

Progressive shortening of anagen phase + Reduction of volume of dermal papilla

Hair follicle miniaturization

Histopathology

Increased shedding of hair: Telogen effluvium

Trichogram

Decreased hair growth: Terminal-to-vellus hair transformation

Trichoscopy
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 dealing with the fear or complaint of hair loss, it is important to weed out these myths from the facts:

- Wearing hats causes hair loss
- Frequent washing and blow drying can lead to hair loss
- Hair styling 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

Don‘t Believe Everything you Hear About Hair: Layman‘s Myths
While the popular or layman’s myths are usually easy to dismiss, the physician’s myths root deeper in the conception of primary care physicians. Among the most prevalent among physician’s myths standing in the way to successful management of hair loss are:

- The majority of women complaining of hair loss are suffering of imaginary hair loss
- Losing 100 strands of hair per day is normal
- The most frequent disorder associated with hair loss in women is iron deficiency
- The first line therapy for androgenetic alopecia in women are antiandrogens
- Hair loss in men can’t be stopped or helped
Evidence-based medicine (EBM) is a relatively young discipline that aims to apply the best available evidence gained from the scientific method to clinical decision making.

It seeks to assess the strength of the evidence of risks and benefits of treatments and diagnostic tests.

Using techniques from science, engineering and statistics such as:
- the systematic review of medical literature
- meta-analysis
- risk-benefit analysis
- and randomized controlled trials (RCTs)

EBM aims for the ideal that healthcare professionals should make conscientious, explicit, and judicious use of current best evidence in their everyday practice.
Guidelines for Male and Female Androgenetic Alopecia

As evidence-based guidelines on hair disorders are rare, a European consensus group was constituted to develop guidelines for

• **diagnostic evaluation** of AGA

• **treatment** of AGA


Guidelines for Diagnostic Evaluation of Androgenetic Alopecia

AGA is diagnosed by clinical hair and scalp inspection, incl. dermoscopy, where a patterned, non-scarring, progressive alopecia with diversity of hair shaft diameters is observed.

A pull test and examination of scalp, facial and body hair and nails, should be included to exclude differential diagnoses, particularly diffuse telogen effluvium, alopecia areata, and inflammatory or scarring alopecias.

The S1 guideline for diagnostic evaluation in AGA provides more detailed information.


Remain open-minded for the possibility of a multitude of cause-relationships underlying hair loss, including: seasonality of hair growth and shedding, hormonal factors, nutrition, and medications, ultimately in the elderly the problems of co-morbidities and multimorbiditiy must be taken into account.

The greater the number of different tests done, the greater the risk of getting false-positive or irrelevant leads. Therefore, laboratory testing must be kept sharply focused.

Clinical suspicion is the determinant, and knowledge of clinical dermatology is prerequisite for combining medical sense with economic sense in requesting laboratory tests.
Diagnosis of Androgenetic Alopecia

Family and personal history:
- Polygenic trait
- History of hair loss in relation to life-time events

Clinical inspection:
- Pattern recognition (male, female, mixed, diffuse)
- Pull test

Trichoscopic examination:
- > 20% anisotrichosis proposed
- Diagnostic criteria

Trichogram (pluck test):
- Confirm diagnosis
- Exclude diffuse telogen effluvium

Laboratory work-up:
- Identify co-morbidities (e.g. iron deficiency, thyroid dysfunction)
- As indicated
Diagnosis of Female Androgenetic Alopecia (FAGA)

**Background:** Standard diagnostic methods for diagnosis of FAGA are clinical inspection, pull test, and trichogram. It has been suggested that scalp dermoscopy (trichoscopy) revealing diversity of hair shaft diameter >20% is diagnostic of FAGA.

**Objective:** To evaluate the value of trichoscopy as compared to the trichogram for the diagnosis of FAGA.

**Patients and Methods:** Retrospective case study of 162 women with the complaint of hair loss who underwent trichoscopic examination and trichograms.

**Results:** Of all women diagnosed FAGA (55%), 62% were diagnosed by trichogram, 72% by trichoscopy with a cut-off point of 20%, and 100% irrespective of the degree of diversity of hair shaft diameter.

**Conclusions:** Trichoscopy is a valuable and superior method to the trichogram for diagnosis of FAGA, especially in early cases with the highest yield irrespective of the suggested cut-off of 20% diversity of hair shaft.

Diagnostic Criteria for Female Androgenetic Alopecia

Major criteria:
1. Ratio of > 4 empty follicles in 4 images (70x) in frontal area
2. Lower average thickness in frontal area compared to occiput
3. > 10% of thin hairs (< 0.03 mm diameter) in frontal area

Minor criteria:
1. Increased frontal to occipital ratio of single-hair pilosebaceous unit
2. Vellus hairs
3. Peripilar signs

Fulfillment of 2 major criteria or of one major and 2 minor criteria allow diagnosis of FAGA with 98% specificity.

Guidelines for Treatment of Androgenetic Alopecia

A **systematic literature search** was conducted in Medline, Embase and Cochrane databases until August 2008. 1370 publications were found, 51 added by hand search. 85 publications fulfilled the following **inclusion criteria** for the guideline:

**Prospective study**
Number of patients ≥20 (no minimal patient number required in twin studies)

**Age ≥12 years**

**Confirmed diagnosis of androgenetic alopecia** male/female pattern (diagnosis either clinically or by further diagnostic evaluations e.g. trichogram, TrichoScan, biopsy)

**Objective outcome measure of efficacy described for drug therapy:**
Mean change from baseline hair count in target area or
Measurement of hair growth/loss in target area by global photography

**For surgical therapy:**
Mean change from baseline hair count in target area or
Measurement of hair growth/loss in target area by global photography or
Graft survival and global photography

Guidelines for Treatment of Androgenetic Alopecia

The guideline revealed:

**excellent evidence levels** (either randomized, double-blind, comparative clinical studies of high-quality, e.g. sample size calculation, flow chart of patient inclusion, ITT-analysis, sufficient size, or meta-analysis, which includes at least one randomized double-blind, comparative clinical studies of high-quality) for the therapeutic use of **topical minoxidil** in men and women and **oral finasteride** in men exists,

**low evidence levels** (little to missing systematic evidence) for **hormonal** and **surgical treatments**

**insufficient respectively lacking evidence** to the broad panel of **miscelaneous treatments** available claiming to be efficient too.

Recommendations for Topical Minoxidil in MAGA

**Therapeutic recommendation: Male**

↑↑ Topical Minoxidil 2 to 5% solution 1ml twice daily is recommended to improve or to prevent progression of AGA in male patients above 18 years with mild to moderate AGA (Hamilton-Norwood IIv -V).

↑ We suggest using 5% solution 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.

Topical 5% Minoxidil in MAGA

Male androgenetic alopecia, M, 70 years old, after 6 months treatment with topical 5% minoxidil lotion

(Personal observation)
Recommendations for Topical Minoxidil in FAGA

**Therapeutic recommendation: Female**

↑↑ Topical minoxidil 2% solution 1ml twice daily is recommended to improve or to prevent progression of AGA in female patients above 18 years with AGA.

→ There is not enough data to recommend the 5% minoxidil solution instead of the 2% solution.

↑ The response to treatment should be assessed at 6 months. If successful, treatment needs to be continued to maintain efficacy.

Topical 2% Minoxidil in FAGA

Female androgenetic alopecia, F, 84 years old, after 3 and 6 months treatment with topical 2% minoxidil lotion

(Personal observation)
Recommendations for Oral Finasteride in MAGA

**Therapeutic recommendation: Male**

**Finasteride**

↑↑ Oral finasteride 1mg a day is recommended to improve or to prevent progression of AGA in male patients above 18 years with mild to moderate AGA (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 finasteride 1mg, 1x/d and topical minoxidil 2% to 5% solution, 2x/d can be considered.

Androgenetic alopecia, M, 61 years old, 3 months after adding on 1 mg oral finasteride to preexisting topical minoxidil

(Personal observation)
# Recommendations for Hormonal Treatments (Topical/Oral)

**Therapeutic recommendation: Female**

- There is no or insufficient evidence to support the use of oral antiandrogens (chlormadinone acetate, cyproterone acetate (CPA), drosperinone, spironolactone, flutamide) to improve or prevent progression of AGA in female patients.

- Oral CPA can be considered in women with clinical or biochemical evidence of hyperandrogenism.

- There is insufficient evidence to support the use of topical alfatradiol to improve or prevent progression of AGA in female patients.

- There is no evidence to support the use of topical natural oestrogens or progesterones to improve or prevent progression of AGA in female patients.

- There is no evidence to support the use of topical fluridil to improve or prevent progression of AGA in female patients.

- We suggest that topical Fulvestrant should not be used in female patients with AGA.

Recommendations for Hormonal Treatments (Topical/Oral)

**Therapeutic recommendation: Male**

↓↓ The use of oral oestrogens or androgen-receptor-antagonists is inappropriate to improve or prevent progression of AGA in male patients.

→ There is insufficient evidence to support the use of topical alfatradiol to improve or prevent progression of AGA in male patients.

↓ We suggest that topical Fluridil should not be used in male patients with AGA.

↓ We suggest that topical Fulvestrant should not be used in male patients with AGA.

Recommendations for Surgical Treatments

Therapeutic recommendation: Male
→ Surgery, especially follicular unit transplantation (FUT) can be considered in male patients with sufficient donor hair.

↑ We suggest follicular unit transplantation (FUT) to be combined with finasteride 1mg daily to achieve a better clinical outcome.

Therapeutic recommendation: Female
→ Surgery, especially follicular unit transplantation (FUT) can be considered in female patients with sufficient donor hair.

## Miscellaneous Treatments with Insufficient or Lack of Evidence

<table>
<thead>
<tr>
<th>Promotion of hair regrowth</th>
<th>Improved perifollicular vascularisation</th>
<th>DHT-inhibitory activity</th>
<th>Anti-inflammatory activity</th>
<th>Improved hair nutrition</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Aminoacids</td>
<td>1 Prostaglandines (viprostol, latanoprost)</td>
<td>7 Saw palmetto</td>
<td>12 Ketoconazol</td>
<td>15 Vitamines (biotin, niacin derivates)</td>
<td>- Botulinum toxin</td>
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<td>2 Iron supplements in absence of iron deficiency</td>
<td>2 Aminexil</td>
<td>8 §-sitosterol</td>
<td>13 Zinc pyrithione</td>
<td>16 Trace elements (zinc, copper)</td>
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<tr>
<td>3 Vitamines (biotin, niacin derivates)</td>
<td>3 Glyceroloxystes and silidum</td>
<td>9 Polysorbate 60</td>
<td>14 Corticosteroids</td>
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<tr>
<td>4 Proanthocyanidines</td>
<td>4 Minerals</td>
<td>10 Green tea</td>
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<tr>
<td>5 Millet seed (silic acid, aminoacids, vitamins, minerals)</td>
<td>5 Niacinderivates</td>
<td>11 Cimifuga racemosa</td>
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<td>6 Marine extract and silic acid component</td>
<td>6 Mesotherapy</td>
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<td>7 Chinese herbals</td>
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<td>8 Ginkgo bibboa</td>
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<td>9 Aloe vera</td>
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<td>10 Ginseng</td>
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<td>11 Bergamot</td>
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<td>12 Hibiscus</td>
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<td>13 Sorphora</td>
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<td>14 Caffeine</td>
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<td>15 Melatonin</td>
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<td>16 Retinoids</td>
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<td>17 Ciclosporine</td>
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<tr>
<td>18 Electromagnetic/static field</td>
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<tr>
<td>19 Low level laser</td>
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Limitations of Evidence-Based Medicine

EBM guidelines do not remove the problem of extrapolation to different populations or longer timeframes. 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 under-researched such as racial minorities and people with many co-morbid 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 each patient.

*Ex cathedra* statements by the medical expert are 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.
Concept of Multitargeted Treatment

Ultimately, combination treatments with topical minoxidil, oral finasteride, nutritional supplements, low-level laser therapy, and appropriate scalp care may act synergistic to enhance hair growth. The scientific rationale for such an approach is given, but there is a need for clinical studies to establish increase in efficacy of combination regimes and adjuvant treatments.

Finally, the influence of the prescribing physician should be kept in mind, since inspiring confidence versus scepticism and fear clearly impacts the outcome of treatment.

Treatment success relies on patient compliance that, on its part, relies on comprehension of treatment benefit, confidence, and motivation.

A positive physician-patient relationship and regular follow-up visits are the most important factor in determining the degree of patient compliance.

Only recommend treatments that are effective in circumstances they are required.

The overall goal is to gain short-term compliance as a prerequisite to long-term adherence to treatment!
Concept of Multitargeted Therapy, Integrating LLLT

1 mg oral finasteride daily + 5% topical minoxidil b.i.d. + LLLT

9 months 12 months

(Personal observation)
Ensuring Patient Compliance

**Simplifying dosage regimen** by selecting different treatment or using a preparation that needs fewer doses during the day, e.g.


Selecting treatments with lower levels of side effects or fewer concerns for long-term risks

Discussing possible side effects, and whether it is important to continue medication regardless of those effects, e.g. finasteride issues

**Advice on minimising or coping with side effects**

Regular follow-up for reassurance on drug safety and treatment benefits

Finally, patients should be aware of **seasonal fluctuations in hair growth and shedding** at times complicating the assessment of pharmacological effects. Awareness of these fluctuations is prerequisite to providing the correct cause and prognosis to the patient, ensuring patient adherence

Finasteride, Persistent Sexual Dysfunction, and Depression

Refrain from prescribing oral finasteride to a patient with a personal history of depression, sexual dysfunction, or fertility problems.

When fertility is an issue, may consider performing a sperm count before during treatment with oral finasteride!

In all men 45 years and over, perform PSA before, after starting therapy with oral finasteride, and thereafter on twice yearly basis. The level should drop by ca. 50% upon initiation of therapy. In case of increase > 0.4 ng/ml per year check prostate!


Irwig MS, Kolukula S. Persistent sexual side effects of finasteride for male pattern hair loss. J Sex Med. 2011;8:1747-53


Fluctuations in frontal telogen rates (n = 823) in relation to the day of the year:

Telogen rates showed an overall annual periodicity manifested by a maximal proportion of telogen hair in July.

A second telogen peak seems to exist, although less pronounced, in April.

Seasonality of Hair Growth and Shedding in Women

Seasonal fluctuations in telogen rates may be significant enough to be clinically apparent in women with female androgenetic alopecia!

Thank you for your attention!