Hair Loss: New Insights and Implications in Clinical Practice

(Queda de cabelo: Novos insights e implicação na prática clínica)

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Hair Loss: To Be or Not to Be?

Don‘t believe everything you hear about hair:

1. The majority of women complaining of hair loss are suffering of imaginary hair loss
2. Losing 100 strands of hair per day is normal
3. The most frequent disorder associated with hair loss in women is iron deficiency
4. The first line treatment for androgenetic alopecia in women are antiandrogens
5. Nutritional supplements have no significant effect on hair growth
The Facts Are:

1. Every woman complaining of hair loss has a right to be investigated adequately.

2. The **number of hair lost per day** depends on the amount of hair on the scalp, the pathologic dynamics of hair loss, and seasonal effects.

3. **Iron deficiency** is overestimated as a single cause of hair loss in women.

4. The **role of antiandrogens** is overestimated in the treatment of femal pattern hair loss.

5. There is growing evidence for the modes of action and efficacy of **nutritional supplements** for promoting hair growth in both **telogen effluvium** and **female androgenetic alopecia**.
Hair loss is frequent

Hair loss causes considerable distress

Treatment options are available, though limited, both in terms of indications and of efficacy

Success depends on unpatronizing sympathy from the side of the physician and comprehension of the underlying pathophysiology

Treatment must meet patients‘ expectations, otherwise patients must be informed on what to expect
Prerequisites for Successful Treatment of Hair Loss

Technical Level

Psychological Level
Technical Level:

Diagnosis:
- A diagnosis is prerequisite to treatment!
- Remain open-minded for the possibility of a multitude of cause-relationships underlying hair loss

Pathophysiological Understanding:
- Causal treatment wherever possible!
- Remain open-minded for the possibility of combined treatments and multitargeted approaches to hair loss
- Ultimately, in the elderly the problems of co-morbidities and multimorbidity must be taken into account

Evidence Based Medicine (EBM):
- Apply best available evidence gained from the scientific method to clinical decision making!
- Remember, GMP means integrating individual clinical expertise with best available external evidence from EBM

Regular Follow-Up:
- Standardized global photographic assessments
- Epiluminiscence microscopic photography
For a successful encounter at an office visit, be sure that the patient’s key concerns have been directly and specifically solicited and addressed!

- Acknowledge the patient’s perspective on her hair loss problem
- Recognize the psychological impact of hair loss, especially adjustment disorders with depressed mood, anxiety, and/or disturbance of conduct, somatic and/or sexual dysfunction, and feelings of guilt and/or obsession
- Explore patient’s expectations from treatment
- Educate patients into the basics of the hair cycle, and why patience is required for effective cosmetic recovery
Adjustment Disorders to Hair Loss (Frequent)

Prolonged depressive reaction (ICD-10 F43.21)

Mixed anxiety and depressive reaction (ICD-10 F43.22)

With predominant disturbance of conduct (ICD-10 F43.24)

With mixed disturbance of emotions and conduct (ICD-10 F43.25)

The best way to treat the adjustment disorder is to effectively treat the underlying hair disorder!
Fact # 2:
The Number of Hair Lost per Day Depends on the Amount of Hair on the Scalp, the Pathologic Dynamics of Hair Loss, and Seasonal Effects

- **Anagen** (2-6 years)
- **Telogen** (3 months)
- **Catagen** (2 weeks)
- **Teloptosis**

**Daily telogen shedding:** 35-100

**Hair cycling** in a random mosaic pattern

Control of hair cycling within the hair follicle itself

Influence of systemic and external factors:
- hormones
- cytokines
- toxins
- deficiencies (nutrients, vitamins, energy)
Telogen Effluvium

**Definition:**
Disruption of the hair cycle resulting in increased proportion (> 20%) and shedding of telogen hair.

Hair loss < 50% of scalp hair: Diffuse thinning of hair, most conspicuous at the temples.

Positive pull test of telogen club hairs.

< 6 months: acute telogen effluvium:
- Fever: postfebrile telogen effluvium
- Childbirth: postpartum telogen effluvium
- etc.

> 6 months: chronic telogen effluvium:
- Primary disorder
- Secondary to a variety of systemic disorders

Kligman. Arch Dermatol 1961;83:175-198
Chronic Telogen Effluvium

Diffuse shedding of telogen hair > 6 months

Secondary to a variety of systemic disorders:
• iron deficiency, other dietary deficiencies
• thyroid disease, other metabolic diseases
• systemic lupus erythematosus, other connective tissue disorders
• syphilis, HIV
• drug-induced hair loss

Primary disorder:
• First described 1960 as „Diffuse cyclic hair loss in women“
  Guy and Edmundson. Arch Dermatol 1960;81:205-227
• Revived in 1996, since then focus of interest again
• Diagnosis of exclusion!

Treatment:
• Causal treatment whenever possible!
• Role of nutritional supplement?
Androgenetic Alopecia

Genetically determined, androgen induced, age-dependent progressive loss of hair with sex-dependent differences in pattern of alopecia

Men:
- 18 - 29: 12%
- 30 - 39: 38%
- 40 - 49: 45%
- 50 - 59: 52%
- 60 - 69: 65%
- 70 - 79: 64%
- > 80: 70%

Women:
- 20 - 29: 3%
- 30 - 39: 17%
- 40 - 49: 16%
- 50 - 59: 23%
- 60 - 69: 25%
- 70 - 79: 28%
- 80 - 89: 32%

Hamilton-Norwood I-VII
Ludwig I-III

Current Treatment for Androgenetic Alopecia

Kaufman et al. Long-term treatment with finasteride 1 mg decreases the likelihood of developing further visible hair loss in men with androgenetic alopecia (male pattern hair loss). Eur J Dermatol 2008;18:400-6

Price et al. Changes in hair weight and hair count in men with androgenetic alopecia, after application of 5% and 2% topical minoxidil, placebo, or no treatment. J Am Acad Dermatol 1999;41:717-21
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.

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

Seasonality of Hair Growth and Shedding in Women

Subsequent images taken in January 2007, August 2007, and February 2008

Fact # 3:  
Iron Deficiency is Overestimated as a Single Cause of Hair Loss in Women

Decreased serum ferritin is associated with alopecia in women ("Rushtonians"):  


There is no clear association between low serum ferritin and chronic diffuse telogen hair loss ("Sinclairians"):  

- Aydingoz et al. 1999;13:65-7
- Sinclair R. Br J Dermatol 2002;147:982-4

No association between serum ferritin levels >10 microg/L and hair loss activity in women (trichogram).  

- Bregy and Trüeb. Dermatology 2008;217:1-6
**Fact # 4:**
The Role of Antiandrogens is Overestimated in the Treatment of Female Pattern Hair Loss

Androgenetic alopecia (female pattern) **can develop in the absence of androgens**, i.e. before onset of puberty, with hypogonadism


Female androgenetic alopecia in normoandrogenic women **does not respond to antiandrogen therapy** with cyproterone acetate or 1 mg oral finasteride

- Price et al. JAAD 2000;43:768-776

**Gestagens with androgenic action (norethisterone, levonorgestrel, tibolone)** precipitate hair loss in female androgenetic alopecia!

Male pattern hair loss is more frequent in **postmenopausal women** than in premenopausal women

- Venning and Dawver. JAAD 1988;18:1073-1077

Under **pathologic conditions with high levels of androgens**, women develop male pattern androgenetic alopecia
Fact # 5: There is Growing Evidence for the Modes of Action and Efficacy of Nutritional Supplements for Promoting Hair Growth

Pharmacy aisles and Internet drugstores are full of vitamins promising full, thick, luscious hair -- for prices that range from suspiciously cheap to dishearteningly exorbitant.

What are the facts?

• Unless the hair is falling out due to a vitamin deficiency, there’s only so much that vitamins can do to increase the size of individual hairs. This is because hair thickness is largely genetic.

• Nevertheless, there are external factors that influence hair health to a great degree, and vitamins can boost hair that’s suffering from these problems.
Role for Nutritional Treatments

Hair production is determined by 4 factors:

**Follicles**: Number and size genetically predetermined

**Protein Intake**: Because hair shaft is composed almost entirely of protein, protein component of diet critical for production of normal healthy hair:

- Hair keratin contains 15.9% **L-cystine**
- Cysteine is limiting factor in biosynthesis of the **natural antioxidant glutathione**

**Energy Intake**: Rate of mitosis sensitive to calorific value of diet, provided mainly by carbohydrates stored as glycogen in the ORS of follicle

**Vitamins and Trace Metals**: Related to the biosynthetic and energetic metabolism of follicle
Nutrition and Hair Growth

**Inborn errors of metabolism (rare):**
- Homocystinuria
- Biotinidase deficiency
- Menkes kinky hair disease

**Acquired deficiency disorders:**
- Undernutrition/Protein-Calorie-Malnutrition
- Specific deficiency disorders:
  - Vitamins
  - Trace metals
  - Aminoacids

**Oral supplementation studies:**
- Animals (sheep, mice)
- Humans
Amino Acids: Supplementation Studies

**Sheep (Methionine, Cysteine, Cystine, Vitamin B):**
- Effect on production of wool (given per abomasum)
  - Gillespie and Reis. Biochem J 1966;98:669

**Human (CYP-complex):**
- Effect on hair quality (biophysical parameters)
- Effect on hair colour (colorimetric)
- Effect on hair growth (anagen rate)
  - Petri et al. Schweiz Rundsch Med Prax 1990;79:1457
  - Budde et al. Hautarzt 1993;44:380
  - Lengg et al. Therapy 2007;4:59

**Mouse (L-cystine and Vit. B6):**
- Chemoprevention of smoke-induced alopecia in mice
  - D'Agostini et al. Toxicol Lett 2000;3;114:117-23
Smoking and Hair Loss

There are significant positive associations between premature hair loss and smoking


- effect on microcirculation
- direct (geno-) toxic effect
- imbalance in the follicular protease/antiprotease systems involved in tissue remodelling and the hair follicle cycle
- oxidative stress
- inhibition of aromatase, hydroxylation of E2, relative hypoestrogenic state

Trüeb RM. Association between smoking and hair loss: another opportunity for health education against smoking? Dermatology 2003;206:189-191

Su LS, Chen THH. Association of androgenetic alopecia with smoking and ist prevalence among Asian men. Arch Dermatol 2007;143:1401-1406

Premature senescence of balding DPC in vitro in association with expression of p16(INK4a)/pRB suggests that balding DPC are sensitive to environmental stress and identifies alternative pathways that could lead to novel therapeutic strategies for treatment of AGA.

Metanalysis of Studies Performed with Oral Combination of Cystine, Yeast and Pantothenic Acid (CYP)

Anagen rates – average difference between baseline and close-out
Verum vs. Placebo: 3.83 absolute points improvement in anagen rates (n = 180)

Analysis was carried out using the full analysis set with a fixed-effect model, p-value from test of overall difference between verum and placebo.
Error bars represent standard error of the mean.

From: Finner A. Poster, EHRS 2011 Jerusalem
Double-Blinded, Placebo-Controlled Study in Healthy Women with Hair Loss Using Oral Combination of Cystine, Yeast and Pantothenic Acid (CYP)

Active compound led to statistically significant improvement and normalization of mean anagen hair rates within 6 months of treatment, independent of age and presence of female androgenetic alopecia

From: Lengg et al. Dietary supplement increases anagen hair rate in women with telogen effluvium: results of a double-blind placebo-controlled trial. Therapy 2007;4:59
Implications for Treatment of Telogen Effluvium and Female Androgenetic Alopecia

The study endpoint was defined as change of anagen hair rate from abnormal at baseline to normal (> 80%) at close-out (6 months). Women assigned to active treatment (with CYP-complex) reached the study endpoint, while those with placebo did not.

The active compound did not have an impact on hair count, hair density, and cumulative hair diameter thickness. This can be interpreted as such, that its therapeutic effect probably results from an induction of anagen phase.

CYP-complex is thus indicated for any form of telogen effluvium due to synchronization of cyclic hair growth in telogen:
- symptomatic diffuse telogen effluvium, e.g. postfebrile
- postpartal effluvium
- seasonal telogen effluvium
- diffuse cyclic hair loss in women/chronic telogen effluvium

CYP-complex may be of additional benefit to minoxidil in androgenetic alopecia, especially in smokers, and senescent alopecia, where synchronization phenomena and oxidative stress complicate the course. This is underlined by the fact that regression analysis failed to show any influence on outcome of: age, presence of androgenetic alopecia, and tissue iron status in the normal range > 10 microgram/Liter.
Trust me.
I’m a doctor.

Another Success Story
Ensuring Patient Compliance

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.

Short term compliance issues addressed by the physician within the first three months of therapy are: winning the patient’s confidence in the diagnosis and treatment plan, and detecting problems relating to the prescribed treatment regimen, or drug tolerance.

Long term compliance issues addressed at 6, 12 months of follow up and thereafter are: treatment efficacy and sustainability, long term toxicities, and treatment costs.

Patients should be aware of the existence 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 to therapy.
Thank you for your attention!