Telogen Effluvium
(Old Myths and New Insights into Hair Loss in Women)

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A Definition of Myth

1. A traditional sacred story, typically revolving around the activities of gods and heroes, which purports to explain a natural phenomenon or cultural practice.

2. A fiction or half-truth, especially one that forms part of an ideology:
   - Religious myth
   - Historical myth
   - Popular (layman‘s) myths
   - Physician‘s myths
According to tradition, St. Agnes was a member of the Roman nobility and raised in a Christian family. She suffered martyrdom at the age of 12 during the reign of Roman Emperor Diocletian in 304.

The Prefect Sempronius wished Agnes to marry his son, and on Agnes' refusal he condemned her to death.

As Roman law did not permit the execution of virgins, Sempronius had a naked Agnes dragged through the streets to a brothel. Various versions of the legend give different methods of escape from this predicament. In one, as she prayed, her hair grew and covered her body.
Hair loss cures have been experimented for centuries:

The great Greek doctor Hippocrates handled his patients’ yearning for hair loss cures by applying pigeon droppings on their head.

Renowned bald philosopher Aristotle used goat’s urine to cure baldness.

Cleopatra applied a mixture of ground horse teeth and deer marrow to help out Julius Caesar’s receding hairline. She did this to save her beloved from being ridiculed since his name “Caesar” means “abundant hair” in Latin.
Age Old Myths: Popular or Layman‘s Myths

- 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
- Hair loss can't be stopped or helped
Don‘t Believe Everything You Hear About Hair:  Physician‘s Myths

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 treatment for androgenetic alopecia in women are antiandrogens

Nutritional supplements have no significant effect on hair growth

Ageing of hair and androgenetic alopecia are basically the same
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 pathology**

Treatment must meet **patients‘ expectations**, otherwise patients must be informed on what to expect
Psychocutaneous Disorders Related to the Hair

- Imaginary Hair Loss (Psychogenic Pseudoeffluvium)
- Adjustment Disorders
- Feeling of Disfigurement (Body Dysmorphic Syndrome)
- Abnormal Scalp Sensations (Cutaneous Sensory Disorder)
- Self-Induced Injury (Trichotillomania, Factitious Disorder)

Adjustment Disorders to Hair Loss

- 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!
Anagen (2-6 years)

Catagen (2 weeks)

Telogen (3 months)

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)

Daily telogen shedding: 35-100 depending on amount of hair on the head!
Diffuse Alopecia: Dystrophic Anagen Effluvium

Direct insult to the rapidly dividing bulb matrix cells

LM: Tapered proximal end and lack of root sheath

Within days to few weeks loss of 90% of scalp hair

- **antineoplastic drugs:** chemotherapy-induced alopecia
- **x-ray:** radiation-induced alopecia:
  - *temporary* > 3-4 Gy
  - *permanent* > 30 Gy deep x-rays, > 50 Gy soft x-rays

- **environmental or occupational toxin exposure:** toxic alopecia

- **immunologic injury:** alopecia areata

Alopecia Areata

Most frequent cause of hair loss in childhood. Before age 2 <2%, before age 20 32.5-63 %, and **after age 40** 20% of cases

May cause diffuse hair loss (2% of patients, women > 40 years)!

Organ specific autoimmune disease of hair follicle with usually focal alopecia and unpredictable course with tendency to recurrence or chronicity, depending on age of onset, disease associations, duration of disease, and extent of hair loss

**Diagnosis:**
- Non-cicatrizsing alopecia with **dystrophic hairs** and **empty follicles**: typical dermascopic findings
- **Nail changes** in 20-40% (more frequent in children)
- **Trichogram**: telogen or dystrophic anagen effluvium
- **Histology**: peribulbar lymphocytic infiltration
- **Immune serology**: Frequently circulating autoantibodies (thyroid, intrinsic factor)
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
Pathologic Dynamics of Telogen Effluvium

With synchronization:

- **Diffuse Telogen effluvium:**
  - Immediate anagen release
  - Delayed anagen release
  - Immediate telogen release
  - Delayed telogen release

Without synchronization:

- Short anagen:
  - **Androgenetic alopecia**
  - **Senescent alopecia**

Seasonality of Hair Growth and Shedding

Reports **3 women** in New York who experienced maximum hair loss in November


Demonstrate in **14 men** over a period of 18 months that the proportion of telogen hair and of hair shedding were maximal in September


Demonstrate in **10 men** with or without alopecia during a period of 8-14 years a maximal proportion of telogen hairs at the end of summer

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.

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!

Differential diagnosis:
- Diffuse alopecia areata („alopecia areata incognita“)
- Androgenetic alopecia/Female pattern hair loss (FPHL)
## Androgenetic Alopecia

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

<table>
<thead>
<tr>
<th>Age Range</th>
<th>Percentage</th>
<th>Age Range</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>18-29</td>
<td>12%</td>
<td>20-29</td>
<td>3%</td>
</tr>
<tr>
<td>30-39</td>
<td>38%</td>
<td>30-39</td>
<td>17%</td>
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<tr>
<td>40-49</td>
<td>45%</td>
<td>40-49</td>
<td>16%</td>
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<tr>
<td>50-59</td>
<td>52%</td>
<td>50-59</td>
<td>23%</td>
</tr>
<tr>
<td>60-69</td>
<td>65%</td>
<td>60-69</td>
<td>25%</td>
</tr>
<tr>
<td>70-79</td>
<td>64%</td>
<td>70-79</td>
<td>28%</td>
</tr>
<tr>
<td>&gt;80</td>
<td>70%</td>
<td>80-89</td>
<td>32%</td>
</tr>
</tbody>
</table>

**Hamilton-Norwood I-VII**


**Ludwig I-III**

Androgens + Androgen metabolism

Genetics

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

Follicular microinflammation → Perifollicular fibrosis

Hair follicle miniaturization/hair growth arrest

Increased shedding of hair: Telogen effluvium

Decreased hair growth: Terminal-to-vellus hair transformation
Value of Scalp Dermoscopy (Trichoscopy)

Normal finding

Diversity of hair shaft diameter > 20% in androgenetic alopecia


Yellow dots typical for alopecia areata

Dermoscopy of Scalp (Trichoscopy)

Tosti A. Dermoscopy of Hair and Scalp Disorders with clinical and pathological correlations. Informa healthcare UK 2007


Zinkernagel MS, Trüeb RM. Fibrosing alopecia in a pattern distribution: patterned lichen planopilaris or androgenetic alopecia with a lichenoid tissue reaction pattern? Arch Dermatol 2000;136:205-11
Inflammatory Phenomena and Fibrosis

Follicular microinflammation and fibrosis:
Whiting D. Diagnostic and predictive value of horizontal sections of scalp biopsy specimens in male pattern androgenetic alopecia. JAAD 1993;28:755-763

Kossard S. Postmenopausal frontal fibrosing alopecia. Scarring alopecia in a pattern distribution. Arch Dermatol. 1994;130:770-4


Zinkernagel MS, Trüeb RM. Fibrosing alopecia in a pattern distribution: patterned lichen planopilaris or androgenetic alopecia with a lichenoid tissue reaction pattern? Arch Dermatol 2000;136:205-11
Investigating Diffuse Hair Loss

Family history of hair loss

Personal history:
• of hair loss
• of medical problems and drug intake
• of diet habits

Clinical examination:
• hair loss pattern
• hair loss activity (pull test)
• dermoscopy

Biochemical investigations:
• for hematinic deficiencies (CRP, ferritin, vitamin B12, folic acid)
• thyroid stimulating hormone
• estradiol (in menopausal), extended hormonal studies as indicated
• extended biochemical studies as indicated

Trichogram and scalp biopsy as indicated:
• CTE versus FPHL (trichogram)
• Loss of follicular orifices (biopsy)
Managing Diffuse Hair Loss

Trichological and biochemical characterization of hair loss

Quantitating hair loss:
- Daily count
- Wash test
- Combining epiluminiscence microscopy with digital imaging (TrichoScan)

Causal treatment, wherever possible!

Specific treatments for the scarring alopecias

Specific treatments for alopecia areata:
- Acute: Corticosteroids (pulse therapy, intralesional)
- Chronic: Topical immunotherapy

Specific treatments for androgenetic alopecia:
- Topical 2-5% minoxidil
- 5-alpha reductase inhibition

Role for hormonal and nutritional treatments?
Efficacy of Corticosteroid Pulse Therapy in Diffuse Alopecia Areata

3 x 500 mg i.v. methylprednisolone on 3 consecutive days


Efficacy of Topical Minoxidil in Androgenetic Alopecia/FPHL

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
Effect of estrogen therapy on postmenopausal women?

Antiandrogen therapy not effective in normoandrogenic women


Gestagens with androgenic action may precipitate hair loss in women: norethisterone, levonorgestrel, tibolone contraindicated!

DHEA may cause hair loss in women in a dose-dependent manner!
Finasteride in Postmenopausal Women

Randomized, double-blind, placebo-controlled study with 1 mg oral finasteride during 12 months in 137 postmenopausal age 41-60 Y.

Study endpoints:
- Hair count
- Global photographic assessment
- Biopsy (morphometric)

Results: For all endpoints no difference in comparison to placebo


5 normoandrogenic postmenopausal women treated with 2.5 – 5 mg oral finasteride for up to 18 months showed improvement on global photographic assessments.

Trüeb et al. Dermatology 2004;209:202-207

Iorizzo et al. Arch Dermatol 2006;142:298-302
Role for Nutritional Treatments in Diffuse Hair Loss

Pharmacy aisles and Internet drugstores are full of nutrients 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 **nutritional deficiency**, there's only so much that nutrients 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 nutrients can boost hair that's suffering from these problems.
Role of Nutritional Deficiency: Iron

**Iron deficiency most common nutritional deficiency:** 12-16% prevalence in adolescent girls and women of childbearing age (16-49 years of age) and 6-9% in women 50 years of age and older in the USA

Most laboratories use **10 - 15 µg/l as lower limit of normal for menstruating women, and 30 µg/l for children, men and non-menstruating women.** In women of childbearing age, a cutoff of 10-15 µg/l yields a sensitivity of 75% and specificity of 98%, a cutoff of 30 µg/l yields a sensitivity of 92% and a specificity of 98%

**Most common causes of iron deficiency:**
- in premenopausal women: menstrual blood loss, pregnancy and lactation
- in postmenopausal women: decreased absorption and gastrointestinal loss.
- **Risk factors:** heavy menstrual bleeding (> 80 ml per month), use of an IUD, history of iron deficiency anemia, insufficient dietary iron intake.

From: Bregy and Trüeb. Dermatology 2008;217:1-6
Role for Iron Supplementation

Decreased serum ferritin is associated with alopecia in women ("Rushtonians"):  
Hard S. Acta Derm Venereol 1963;43:562-569  

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).

From: Bregy and Trüeb. Dermatology 2008;217:1-6
<table>
<thead>
<tr>
<th></th>
<th>Androgenetic alopecia</th>
<th>Senescent alopecia</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Onset</strong></td>
<td>Early (teens, twens)</td>
<td>Late (60 years +)</td>
</tr>
<tr>
<td><strong>Distribution</strong></td>
<td>Patterned</td>
<td>Diffuse</td>
</tr>
<tr>
<td><strong>Pathophysiology</strong></td>
<td>Increased activity of 5-α reductase (DHT) in men</td>
<td>Senescence (decreased activity of 5-α reductase )</td>
</tr>
<tr>
<td><strong>Genetics</strong></td>
<td>Polygenic</td>
<td>Unknown</td>
</tr>
<tr>
<td><strong>Association or risk factor for other diseases</strong></td>
<td>Cardiovascular diseases Benign prostatic hyperplasia Prostate cancer</td>
<td>Age-related disorders?</td>
</tr>
<tr>
<td><strong>Gene expression profiles</strong></td>
<td>Decreased expression of genes required for anagen onset and maintenance / increased expression of catagen and telogen inducers</td>
<td>Increased expression of markers for mitochondrial dysfunction and oxidative stress</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>Minoxidil, Finasteride, Estrogens (anecdotal)</td>
<td>Minoxidil, Nutritional supplements, hGH (anecdotal)</td>
</tr>
</tbody>
</table>

Efficacy of Topical Minoxidil in Senescent Alopecia

Before treatment

After 6 months of treatment

Personal observation
Biology of Hair Aging

Intrinsic (Chronologic) Aging:
- **Genetic**: AGA, familial premature graying (AD), progerias (rare)
- **Hormones und hormone metabolism**: AGA
- **Replicative senescence**: Graying, senescent alopecia?
- **Oxidative metabolism** (melanogenesis): Graying

Extrinsic (Accelerated) Aging:
- **Oxidative stress from UV-R**
- **Oxidative stress from tobacco smoking**
- **Others**?

Trüeb RM. Is androgenetic alopecia a photaggravated dermatosis? Dermatology 2003;207:343-348

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


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.

Value of Nutritional Intervention in Aging Hair

**Structural Ageing of Skin:**
- Atrophy
- Degeneration
- Functional impairment

**Immune Ageing of Skin:**
- Decrease in immunocompetence

**Photoageing of Skin:**
- Cumulation of genotoxic and oxidative damage to
- Exhaustion of antioxidative defense network

**Skin:**
- Vulnerability
- Impaired wound healing
- Decreased hydration
- Pruritus
- Eczema
- Infections
- Carcinogenesis

**Hair:**
- Hair loss
- Hair greying
- Hair weathering

**Nutritional Intervention?**
Double-Blinded, Placebo-Controlled Study in Healthy Women with Hair Loss Using Oral Combination of Cystine and B-Vitamins

Active compound led to **statistically significant improvement and normalization of mean anagen hair rates within 6 months of treatment**, independent of age (smoking status not examined)

Hair count and cumulative hair shaft diameter did not show any change in both groups (as opposed to studies with topical minoxidil)
Summary and Conclusions

The complaint of hair loss is frequent in women and causes considerable distress.

In a minority of patients hair loss is imaginary.

The number of hair lost per day depends on the amount of hair on the scalp and seasonal effects.

There are effective therapies of hair loss, though with limitations with respect to indications and efficacy.

The role of nutrition is overemphasized by the lay and underestimated by physicians.

Iron deficiency is overestimated as a single cause of hair loss in women, as well as the role of antiandrogens in the treatment of female pattern hair loss.

Androgenetic alopecia and ageing of hair are two distinct entities, though with some common denominators.

Treatment should target multiple factors responsible for hair loss.

Treatment success depends on comprehension of the underlying pathology and unpatronizing sympathy on the part of the physician.
References:


www.derma-haarcenter.ch