

Let it grow again – on actives and active systems to stimulate hair growth

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Beautiful hair is considered as an expression of vitality. Yet, what can be done if a hormone-related hair loss strikes at an early age already? Since ages people have used tricks and tinctures to reactivate its growth – to no avail though. Now, there are new findings that may raise hope.

Just as the skin, also the human hair is influenced by internal and external factors. Colour, hair thickness, hair density, length growth and hair quality change in the course of life – although in a rather different way depending on whether we deal with the head hair, pubic hair, eyelashes or the downy hair (vellus hair) of the body. Increased hair growth can occur in the form of hypertrichosis or hirsutism while a reduced growth can appear as hypotrichosis, effluvium or alopecia.

Various factors either positively or negatively influence the growth of hair:

Individual somatic causes

- androgenetic factors
- hormonal changes (puberty, menopause, hormonal variations)
- autoimmune reactions
- enzyme defects
- hypothyroidism

Disease-related causes

- diseases that affect the metabolism
- skin diseases (hereditary/acquired)
- mycoses, frequently identifiable by scaling
- bacterial infections
- parasite infestation (e.g. mites)
- cancer (including radiation damages)
- mental diseases (including stress or depressions)

Orally or externally active substances

- contraceptives
- pharmaceuticals (e.g. beta blockers, retinoids, gold salts, immunostimulants)
- chemotherapeutics (mitotic inhibitors, cytostatic antibiotics, alkylating cytostatics),
- harmful substances (toxic substances) in occupational and natural environment, nutrition

Malnutrition

- trace elements such as iron, selenium, zinc
- vitamins
- essential fatty acids
- diets

Cosmetics, hygiene & Co

- hair cleansing: washing, blow drying, combing
- treatments: perms, dyeing, straightening
- cosmetic actives

Needless to say that in disease-related hair growth disorders the primary disease has to be treated first. The same applies for orally and externally active substances which only cause a temporary hair loss though. Malnutrition can largely be excluded today and, in line with expectations, food supplements do not enhance the hair growth in the case of a varied diet.

Individual somatic causes have to be considered in a different way and there are interesting approaches in this context. It is estimated that nearly 20 percent of the German male population is affected by hormone-related hair loss – triggered by testosterone which, on the contrary, stimulates the hair growth on other parts of the body such as breast and pubic area. The reason for the loss of head hair is the enzymatic conversion of testosterone into dihydrotestosterone (DHT) respectively androstanolone through steroid-5 α -reductase. It cooperates with the locally acting prostaglandin D₂¹⁾ and thus inhibits the hair growth. Resulting are two concepts to correct the defect:

- to inhibit the steroid-5 α -reductase
- to use PGD₂-antagonists

Combating hair loss...

Inhibiting the steroid-5 α -reductase: Finasteride (INN)² is a selective inhibitor of the steroid-5 α -reductase. The synthetic steroid only is available on prescription and also used to treat the enlarged prostate (prostate hyperplasia). The substance is reported to inhibit the hair loss in men and even an increase of hair density has been observed³. However, the substance has adverse effects in the urogenital area such as erectile dysfunction. The substance is available under several names.

PGD₂-antagonists: Prostaglandins are tissue hormones developing from omega-3 and omega-6 fatty acids; already minor concentrations locally control various body functions. Almost every prostaglandin has a natural receptor antagonist, at least as far as parts of its effects are concerned. In the case of PGD₂ it is the prostaglandin F_{2 α} (PGF_{2 α}) which already had been analyzed a while ago. Synthetic structural analogues of PGF_{2 α} are used in the glaucoma treatment in the form of eye drops that increase the discharge of intraocular fluid and thus reduce the intraocular pressure. The following PGF_{2 α} -analogues are reported to show an interesting side effect – i.e. an increased growth of eyelashes:

- **Bimatoprost** (INN): In specific countries this ethyl amide is licensed for the treatment of hypotrichosis of eyelashes
- **Latanoprost** (INN): Besides the improved growth of eyelashes, the isopropyl ester also is effective against androgenetic alopecia and alopecia areata⁴.
- **Tafluprost** (INN): Characteristic for this isopropyl ester is the lacking hydroxyl group in the carbon chain that otherwise is typical for PGF_{2 α} . Instead it contains two fluorine atoms at this place.
- **Travoprost** (INN): The isopropyl ester is a cloprostenol analogue however instead of its 3-Chlorphenoxy it contains a 4-Trifluoromethylphenoxy group.

There are further compounds, also isopropyl esters or ethyl amides, derived from prostanoid acid or synthetic analogues such as cloprostenol which are better reabsorbed than free acids. The technical terms given to the substances frequently are somehow elusive even for professionals and partly even faulty. The side effects described for the glaucoma treatment such as itching, headaches, and red eyes also apply for hair growth treatments, particularly if larger areas are treated. Cloprostenol is used in veterinary medicine because of its luteolytic effects. Since toxic effects on unborn

babies cannot be excluded, PGF_{2 α} -analogues are labelled with health warnings for women of childbearing age. In 2011, the FDA, in other words the supreme public health authority of the US, warned against the use of isopropyl cloprostenate. Adverse effects can also originate from additives such as benzalkonium chloride.

Hormone therapy

Estrogens such as 17 β -Estradiol are locally applied in the form of solutions to treat **androgenic alopecia** in women.

Cyproterone (INN), a steroidal testosterone antagonist, inhibits the androgenic hair loss. However, the substance also reduces the body hair. In the form of cyproterone acetate (pills or lotion) the substance is prescribed to treat the female alopecia. Also combinations with estrogens such as ethinyl estradiol (INN) are reported. This particular therapy however is not recommended for men since the substances will find their way into the body even with topical treatments, and hence may cause adverse hormonal effects. As regards women, it is recommended to pay particular attention to safe contraception.

Alternatively to cyproterone, other synthetic gestagens such as drospirenone (INN), chlormadinone (INN), and dienogest (INN) are therapeutically administered.

Autoimmune reactions

Autoimmune reactions are assumed in the case of **circular hair loss** (alopecia areata). The therapy applied is rather different though and consists of inducing a contact allergy. Allergenic chemical compounds such as diphenylcyclopropanone and squaric acid dibutylester serve as triggering substances in this case. The strategy behind is that the immune reactions of the body will now concentrate on the foreign substances instead of the own hair and that the hair will restart to grow⁵.

Substances to stimulate the blood flow

Minoxidil (INN; 2,6-Diamino-4-piperidino-pyrimidine-1-oxide), a pharmaceutical to treat hypertension, has vasodilating effects on the capillaries, hence it stimulates the circulation and can slow down androgenetic alopecia. Isolated cases of new hair growth have been observed. Its mechanism of action has not yet been clarified in detail. The topical treatment with a 2-5% solution or foam to be applied 1 to 2 times a day^{6,7} is a prolonged procedure though and its potential success can only be evaluated after a year. Frequently an adjuvant

treatment with **finasteride** is recommended. Also the combination of minoxidil with **alfatradiol** (17α -Estradiol), a substance that inhibits the steroid- 5α -reductase (see above) but has no estrogen activity, has been reported⁹⁾. As yet, no striking success could be achieved. As far as circulation-enhancing effects are concerned, also liposomal solutions are employed. Until now, no evidence-based studies have been carried out in this context.

Cosmetics, hygiene & Co

Similar to the skin, also the hair and hair growth are affected or even permanently damaged by excess hygiene or inadequate products and procedures. The daily shampooed, blow-dried, straightened and on top of it also gelled hair will sooner or later probably end up in the hair brush. The proverb "less is more" holds true also in this particular context. Frequent hair dying, straightening and perms stress the scalp, hair and hair follicles. The individual sensitivity may vary though and effects will only show after a certain time.

Cosmetics offer a whole variety of active agents:

- **Biotin** (vitamin B₇ alias vitamin H): Deficiency symptoms are brittle nails and hair loss.
- **Cystine**: Hair contains more than 10% of this amino acid – bound to keratin.
- **Caffeine**: The alkaloid improves the microcirculation in the surface capillaries of the scalp.
- **Green tea**: Epicatechin-3-gallate und epigallocatechin-3-gallate, the main ingredients inhibit the steroid- 5α -reductase (see above). It is assumed that this also applies to several essential fatty acids such as α -linolenic acid⁹⁾ and to isoflavones (phyto-hormones). Isoflavones occur in soybeans and in red clover. Also zinc salts are described in this context.
- **D-Panthenol**, the precursor of the natural pantothenic acid of the body also is a typical ingredient of caring lotions for the scalp.
- **Pyridine-2,4-dicarboxylic acid diethyl-ester** (lutidine diethylester) protects the hypoxia induced factor (HIF- 1α), which is involved in the control of the oxygen requirement of the cells. The hair density will improve after about 3 months.

Compounds of these active agents in the form of lotions are on the market or can be combined in the form of sera. In addition, a wide

range of extracts with appropriate effects is offered to the customers.

References

1. Garza LA et al., Prostaglandin D₂ Inhibits Hair Growth and Is Elevated in Bald Scalp of Men with Androgenetic Alopecia, *Sci Transl Med* 2012;4(126):126ra34
2. INN = International Nonproprietary Name
3. Whiting DA, Efficacy and tolerability of finasteride 1 mg in men aged 41 to 60 years with male pattern hair loss, *European Journal of Dermatology* 2003;13:150-60
4. Blume-Peytavi U, Lönnfors S, Hillmann K, Garcia Bartels N, A randomized double-blind placebo-controlled pilot study to assess the efficacy of a 24-week topical treatment by latanoprost 0.1% on hair growth and pigmentation in healthy volunteers with androgenetic alopecia, *J Am Acad Dermatol* 2012;66(5):794-800
5. Freyschmidt-Paul P, Happle R, Hoffmann R, Alopecia areata - Klinik, Pathogenese und rationale Therapie einer T-Zell-vermittelten Autoimmunerkrankung, *Der Hautarzt* 2003;54:713-722
6. Blumeyer A et al., Evidence-based (S3) guideline for the treatment of androgenetic alopecia in women and in men. *JDDG* 2011;9(suppl 6):1-57
7. Blume-Peytavi U, Hillmann K, Dietz E, Canfield D, Bartels NG, A randomized, single-blind trial of 5% minoxidil foam once daily versus 2% minoxidil solution twice daily in the treatment of androgenetic alopecia in women, *J Am Acad Dermatol* 2011;65(6):1126-1134
8. Blume-Peytavi U, Kunte C, Krisp A, Bartels NG, Ellwanger U, Hoffmann R, Comparison of the efficacy and safety of topical minoxidil and topical alfatradiol in the treatment of androgenetic alopecia in women *JDDG* 2007;5(5):391-395
9. Azzouni F, Godoy A, Li Y, Mohler J, The 5 alpha-reductase isozyme family: a review of basic biology and their role in human diseases, *Adv Urol* 2012: 530121

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