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

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-5α-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-5α-reductase
- to use PGD₂-antagonists

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Combating hair loss...

**Inhibiting the steroid-5α-reductase:** Finasteride (INN) is a selective inhibitor of the steroid-5α-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 observed. 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 F₂α (PGF₂α) which already had been analyzed a while ago. Synthetic structural analogues of PGF₂α 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 PGF₂α-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 areata.
- **Tafluprost (INN):** Characteristic for this isopropyl ester is the lacking hydroxyl group in the carbon chain that otherwise is typical for PGF₂α. Instead it contains two fluorine atoms at this place.
- **Travoprost (INN):** The isopropyl ester is a cloprostenolate analogue instead of its 3-Chlorophenoxo it contains a 4-Trifluormethylphenoxo 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, PGF₂α-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 17β-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), chloromadinone (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 diphenylcyclopropenone 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 grow.

**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 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 alfatra-
diol (17α-Estradiol), a substance that inhibits the steroid-5α-reductase (see above) but has no estrogen activity, has been reported>. As yet, no striking success could be achieved. As far as circulation-enhancing effects are con-
cerned, 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 sham-
pooed, 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 ef-
fects will only show after a certain time.

Cosmetics offer a whole variety of active
agents:

- **Biotin** (vitamin B7 alias vitamin H): Defi-
ciency 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 micro-
circulation in the surface capillaries of the
scalp.
- **Green tea**: Epicatechin-3-gallate und epi-
gallocatechin-3-gallate, the main ingre-
dients inhibit the steroid-5α-reductase (see
above). It is assumed that this also applies to
several essential fatty acids such as ω-
linolenic acid and to isoflavones (phyto-
hormones). Isoflavones occur in soybeans
and in red clover. Also zinc salts are de-
scribed in this context.
- **D-Panthenol**, the precursor of the natural
pantothenic acid of the body also is a typi-
cal 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 re-
quirement 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 com-
bined in the form of sera. In addition, a wide
range of extracts with appropriate effects is
offered to the customers.

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