The type of hair loss known in dermatology as alopecia has been a problem throughout human history, regardless of gender or age. Hair loss could be the symptom of a skin disease or a complementary symptom of other internal illness. Hair loss is very visible and a blurred line between health and illness.

It is a well-known fact that female (picture 1) and male (picture 2) pattern hair loss are different in their etiological and physiological processes, except in regards to the androgenic factor, clinical symptoms, and progression of symptoms. We specially avoid using the words illness or disease, because, often, hair loss is a condition of the person’s general appearance. On the other hand, such conditions could develop into an illness easily and suddenly, a fact that may instigate impressive and dramatic changes in psychological status of the people. Based on the scientific research available for our analyses we could present the common view on the classification of hair loss. Different classification forms of alopecia (hair loss) are reported in the literature, most of them are based on androgenic and non-androgenic types. Testosterone activity is the most known and well-studied etiopathology of hair loss. The hormone testosterone plays an important role, seemingly independent of genetic predisposition. Androgenic alopecia (AGA) is an androgen-mediated disorder that causes hair thinning in a defined pattern. In the hair follicle cells, testosterone converts into the biologically more active metabolite dihydrotestosterone (DHT) catalysed by the enzyme 5-alpha reductase. This hormone binds to androgenic receptors in the hair follicle and the specific bond triggers cellular processes which reduce the anagen phase of the hair cycle. For this reason the hair passes earlier into the telogen phase and falls out. Gradually, over succeeding cycles, large, thick, pigmented terminal hair converts into thinner, shorter, indeterminate hairs and finally to short, wispy, non-pigmented vellus hair (i.e. the retrograde phase of the cycle) and the hair follicle becomes minute (picture 3). The density of the androgenic receptors in the hair follicles varies according to location in a manner that is genetically determined. However, the pathogenetic mechanisms underlying AGA are not fully understood. Age factors too play an important role in AGA. The first manifestation usually occurs in the third decade. The prevalence of AGA increases with ageing, from 31% at age 40–55 years to 53% at age 65–69 years.

Female pattern hair loss (FPHL), or female patterned alopecia, is a form of non-scarring alopecia that might also be linked with androgen dysfunction. Androgenic alopecia

**Hair loss is very visible and a blurred line between health and illness.**

**The hormone testosterone plays an important role, seemingly independent of genetic predisposition.**
in women is less frequent, though the etiology is in principle the same as in men.

The actual statistic of female pattern hair loss (FPHL) does not reflect the actual state of the problem, as complaints of “hair loss” or “thinning hair” are not a priority for the patients compared to other diseases detected at the same time.

Diffuse, rapid onset, non-scarring alopecia is not common in patterned alopecia and should raise suspicion to the existence of iron deficiency, thyroid disease or other endocrine disorders such as polycystic ovarian syndrome, medication exposure; or an autoimmune etiology. The relationship of FPHL with pregnancy and maternity is by now widely known.

FPHL that occurs commonly in postmenopausal adult women is characterized by a progressive reduction in hair density on the crown of the scalp with sparing of the frontal hairline (Ludwig scale). Temporal recession occurs to a lesser degree in females compared to than in males.

After extensive research on PubMed, we were surprised not to find any information about “the aging process of hair”, which can be explained as genetically determined shortening of the anagen phase of growth with a constant telogen phase leading to a gradual conversion of terminal hairs into vellus hairs.

Who is suffering more?

Despite a significantly large prevalence, many women feel the condition is rare and are affected socially and psychologically.

Relative to control subjects, women with FPHL completing a standardized questionnaire possessed a more negative body image and a pattern of less adaptive functioning. FPHL is solely a cosmetic concern which fosters psychological distress for patients, as it has a notable impact on quality of life; thus, women seeking evaluation want successful treatments that can minimize further hair loss while also stimulating new hair growth or regrowth of previously lost hairs.

Therapy

Unfortunately, no current therapy is curative and only one FDA-approved treatment is available at this time. Heightened interest and demand for improved, successful treatments have stimulated an expansion of treatments. When presenting the existing treatments we specify: pharmacological activity (PhA), legal status (LS) of pharmacological substances, well known commercial name (CN) of the product(s), negative information & side effects (NISE).

Minoxidil - vasodilator through the stimulation of potassium channels (PhA), medication (LS), approved FDA.
- Topical minoxidil 2% (Rogaine, Johnson and Johnson, New Brunswick, NJ, USA) (CN)
- Clinical effects are unpredictable. Facial hypertrichosis (picture 4), allergy contact dermatitis (picture 5) (NISE)

Finasteride - specific inhibitor of type II 5-reductase (PhA).
- Finasteride 1 mg daily dose (Propecia, Merck and Co, Inc, White House Station, NJ, USA) (CN)
- MPHL: Erectile dysfunction (NISE)
- FPHL: Off-label treatment (LS)

Dutasteride - inhibitor of both types I and II 5-reductase (PhA).
- Dutasteride (Avodart, GlaxoSmithKline, Research Triangle Park, NC, USA) (CN)
MPHL: Erectile dysfunction [NISE]
FPHL: Off-label treatment [LS], teratogenicity [NISE]

Spironolactone reduces adrenal androgen production and exerts competitive blockade on androgen receptors in target tissues [PhA]. Spironolactone (Aldactone, Pfizer Inc, New York, NY, USA) [CN]

Unfortunately, no current therapy is curative and only one FDA-approved treatment is available at this time.

MPPH: Teratogenicity, menstrual irregularities. [NISE]

Side effects of spironolactone are dose-dependent, primarily resulting from aldosterone effects on the renal system, and include hypotension, hyperkalemia, fatigue, headache, weight loss, increased urinary frequency, and dry skin. [NISE]

Off-label treatment for both genders [LS]

Cyproterone acetate - synthetic steroid with antiandrogen and antigonadotropic properties with weak progesterone activity [PhA]. Androcure (Schering GmbH und Co. Produktions KG, Weimar, Germany) [CN]

Weight gain, menstrual irregularities, decreased libido, breast tenderness, feminization of a male fetus [NISE]

Off-label treatment for both genders [LS]

Prostaglandin analogs (PGAs) - induction of the anagen phase in telogen hair follicles through targeting the dermal papilla [PhA].

Latanoprost (Xalatan, Pfizer Inc), Travoprost (Travatan, Alcon Laborato-ries Inc, Fort Worth, TX, USA) [CN]

Folliculitis, erythema, and burning sensation [NISE]

Off-label treatment for both genders [LS]

Bimatoprost (Latisse, Allergan Inc) is the only FDA-approved topical treatment for hypotrichosis of the eyelashes.

Ketoconazole - imidazole antifungal agent with anti-inflammatory effects, antiandrogen effects, inhibits steroid biosynthesis of testicular and adrenal androgens [PhA]. Off-label treatment for both genders [LS]

Estrogens decrease the duration of the telogen phase and increase the duration of the anagen phase in the human scalp [PhA].

FPPLH: the estrogen receptor beta and the polymorphism in the gene encoding aromatase [CYP19A1] in hair suggest estrogen’s influence on the hair follicle growth cycles [PhA].

Europe: topical estrogens are available for FPHL treatment [LS]

Hair transplant surgery Surgical treatment of alopecia has been successfully performed for the past 4 decades [LS].

The main problem is covering the bald area with donor plugs (or follicles) sufficient in number to be effective [NISE] Micro-grafting produces a more natural appearance than the old technique of transplanting plugs.

Scalp reduction has been attempted to decrease the size of the scalp to be covered by transplanted hair.

Transplantation procedures are often time consuming, uncomfortable, and expensive, and may not give an ultimate cure even after multiple treatments [NISE] (Table 1) (picture 6/7)

Micropigmentation - pigment implantation into the area of hair loss with decorative & camouflage functions [picture 8] Micro pigmentation is not a medical procedure [LS]

Infection, folliculitis, and allergic dermatitis [NISE]

Table 1. Side effect after hair transplant surgery

<table>
<thead>
<tr>
<th>Side effects of hair transplant surgery</th>
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<tbody>
<tr>
<td>Scars</td>
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<tr>
<td>Folliculitis</td>
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<tr>
<td>Post treatment pain</td>
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<tr>
<td>Irregular or uneven or delayed hair growth</td>
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<tr>
<td>Numbness of the scalp</td>
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Side effects after hair transplant surgery
Hair loss is a cosmetically and psychologically distressing problem.

It is important to diagnose early and start treatment immediately. It has always been problematic deciding who is to treat patients experiencing hair loss, especially because a lot of cases are due to hormonal dysfunction falling under the purview of gynecologists, urologists, endocrinologists, and dermatologists. Although few medications are currently approved for the medical treatment of both genders, there are not many other options that can be utilized with relatively minimal side effects.

New medical approach

One of the new potential treatments for hair loss (androgenic and non-androgenic) is to use medical devices CE class III for injections into the scalp area or applying it using microneedling devices. The main medical proposal for the new therapeutic approach is to be safe, minimize side effects during long-term therapy, and be effective.

XL Hair® is a new opportunity for the treatment of different baldness patterns and symptomatic hair loss made in conformity with EU Regulation (picture 9). The product is tested as being implantable, non-allergenic, non-teratogenic, non-cytotoxic, non-carcinogenic.

XL Hair® formula, designed for superficial and deep dermal injections, are based on the purest and most effective ingredients, with synergistic actions. Non cross-linked HA from biotechnological non-animal origin provides: antioxidant effect, turnover stimulation & matrix reorganization. Hyaluronic acid 3,0 mg/ml is associated in XL Hair® with active biorevitalization solution (BS, 52, 38 mg/ml) and helps to improving the transport function of the actives from BS. The complex actives of BS are: growth factors GF (Rh-Polypeptide-1, Copper peptide), deoxyribonucleic acid, amino acids (Alanine, Folic Acid, Leucine, Valine, Tyrosine, Glycine, Histidine, Isoleucine, Lysine, Methionine, Phenylalanine, Proline, Serine, Threonine and etc), trace elements (Ca, Fe, K, Mg, Mn, Na, P, Se and etc), vitamins (Vit A, PP, B, H and etc), terpenes (Quercetin), fatty acids (Oleic Acid, Linoleic Acid), flavonoids (Rutin, Kaempferol), antioxidants (Quercetin, Citric Acid, Ginkgolides A, B, C, M), NAD, NADP. The final target of the actives is to repair and to stimulate hair growth, increase the thickness of hair by improving skin nutrition and skin defence against internal & external stress and damage factors. Fibroblast growth factors (FGFs) and their receptors control a wide range of biological functions, regulating cellular proliferation, survival, migration and differentiation. Added to this is the delivery of copper peptide to the base of follicles, which helps strengthen hair while stimulating hair follicles to produce a strong hair shaft, help...
informative function (membrane receptors, intracellular signals) Trace elements [XL Hair® content: Ca, Fe, K, Mg, Mn, Na, P, Se and etc] have an influence on the binding, transport and release of oxygen, donate or accept electrons in reaction of reduction or oxidation, compensate cells nutrition and play the structural role to important biological molecules. The biggest group of bioreviatilization solution of XL Hair® is antioxidants. The mechanisms by which these antioxidants act at the molecular and cellular level include roles in gene expression and regulation, apoptosis, and signal transduction. Antioxidants are involved in fundamental metabolic and homeostatic processes and help repairing damaged biomolecules and defend antioxidant enzymes, which are mostly intracellular. Thanks to their unique formula, the products XL Hair® & Reparestim Hair® & AD daily care Hair® are capillary regenerators which revitalize and strengthen capillary fiber via a greater contribution of essential nutrients for capillary growth and a stimulating action of hair growth factors. The topical (Reparestim Hair®) and daily care (AD daily care Hair®) are analogs (similarly formulated) of injectable XL Hair®, recommended for use as complementary products for the treatment of hair loss.

Clinical study

A multi-center, open label, non-comparative pilot study was performed in medical clinics in Spain, the Netherlands, and Romania, with 47 patients (32 women and 15 men) who had sought medical attention for hair loss. The diagnosis of alopecia is a combination of a detailed inquiry into the patient’s history, including family, social, and medical histories, as well as a comprehensive physical examination with appropriate testing. Hamilton referred to the mutual interplay of androgens, genetic and age factors in the origin of AGA and elaborated a precise method for the clinical assessment of alopecia. Hamilton’s classification was later modified by Norwood and was used during the examination. The pull test and non-invasive method of microscopic hair examination on portable video system [Menard] was included in the study. Exclusion criteria included history of severe allergic disorders, cutaneous infection or skin alteration affecting the scalp, known hypersensitivity or allergy, history of autoimmune disease, cortical or immunosuppressant therapy, acute joint rheumatics, repetitive angina, endocarditis, use of anticoagulant therapy, cicatricial alopecia, pregnancy and lactation. The patients signed consent forms and authorized the use of before and after pictures.

XL Hair® (Aesthetic Dermal, Spain) injectable CE class III medical device for scalp area, 3 ml per vial, single use; Reparestim Hair® (Aesthetic Dermal, Spain) 3ml sterile solution for topical application by using sterile microneedling medical device Class IIa AD Roll TD® + Stamp (Aesthetic Dermal, Spain) 0,5 mm, 600 needles by roll, 12 needles by stamp, single use; and AD Daily Care Hair® (Aesthetic Dermal, Spain) solution 100 ml for personal use.

XL Hair® injections and Reparestim Hair application with microneedling device AD Roll TD® + Stamp repeated once a week on the area of hair loss, total 8 sessions (8 weeks) Spray AD Daily Care Hair® recommended for use directly onto the scalp and with light massage ensuring the product is well distributed over the problematic area. Spray applied
twice a day, 3 times a week, during minimum 12 to 24 weeks. Efficacy was determined at the 3rd and 6th months. Possible side effects were assessed as well.

Patients and physicians rated their satisfaction with the results of the procedure at the end of the treatment on a 4-point scale (1=non satisfactory, 2=satisfactory, 3=good, 4=excellent).

Results

During clinical study we enrolled 47 patients (32 women and 15 men), 35-50 years old, who required hair loss treatment targeting moderate-to-severe non-cicatricial alopecia affecting different areas, i.e. vertex, frontal and temporal. Inclusion criteria for the study were clinical evidence of moderate-to-severe non-cicatricial alopecia rated for men as grade IIa to V using the Norwood-Hamilton classification and rated for women as grade I to III using the Ludwig classification. Duration of progressive hair loss was from 5 to 10 years. 50% of the patients previously received different treatments, including 2% Minoxidil (Rogaine), Finasteride, nutrition supplements or other daily care without satisfactory results.

After analyses of the anamnestic data, the results are as follows: more than 50 % of the patients have genetically related hair problems, 32 % of the patients claim about a stressful life, 16% related the problem to pregnancy and 10 % were postmenopausal hair loss, one patient has hypertension.

30 % of the patients from the women’s group have anemia of varying grades. 50 % of the patients from the women’s group are using and hormonal contraception for more than 6 months, 40% of women more than 2 years. 60 % of women’s group had a special diet or a nutritional deficit during 6 months/one year.

In both groups 0% of patients had contact with any known toxin or radiation.

More than 10% from both groups had attacks of seborrhoeic dermatitis more than once, but only 5 % confirmed the diagnosis by dermatological consultation.

All patients concluded the study.

In the female group, aesthetic improvement was significant, starting at 8 to 12 weeks if compared to before the treatment (picture 10/11) At 12 weeks 61% of female group stopped losing hair. New hair growth was significantly increased within 24 weeks in 73% of the female group (picture 12/13).

In the male group 41% stopped active hair loss in 12 weeks.

New hair growth was significantly increased in 24 weeks in 63% of the male group (pictures 14/15/16/17/18/19/20/21)

60 % of both groups achieved a high rate mark of satisfaction, from good to excellent. Surprisingly, more than 85% [only 61% achieved good clinical results!] of the male group declaraed to be highly satisfied by the treatment included injections technique and daily care application, and are motivated to continue or repeat the treatment course.

SIDE EFFECTS

Some patients presented untoward effects like swelling and ecchymosis that resolved within 24 and 48 hours.

Conclusion

The results of the study indicate that injections of XL Hair® and Reparestim Hair TD® applied with
a microneedling device (AD Roll TD® + Stamp) and combined with AD Daily Care Hair® are an efficient treatment for hair loss in different baldness patterns. The results indicate that intradermal injections of XL Hair® and microneedling with Reparestim® Hair TD combined with AD Daily Care Hair® induce the activation of the hair follicle which promotes an enlargement of the anagen phase and a shortening of the telogen phase, reversing the miniaturization of the hair follicles, stopping hair loss and promoting new hair growth. The protocol of application and frequency of treatment have been adapted by gender. To optimize results, the application of AD Daily Care Hair® cannot be less than 6 months in duration, which means regular home daily care is very important for maintaining results. The best efficacy was observed in case of symptomatic hair loss in female pattern: after pregnancy, nursing period, stress, or died. In the male pattern, which is related to androgenic alopecia, results are satisfactory but require further investigation. Patient with androgenic alopecia should be treated longer: once every one to two weeks for a 12 weeks duration, at minimum. 60% of the patients from both groups were satisfied with the results after 24 weeks of treatment. The biological and pharmacological functions of XL HAIR® (Reparestim® Hair) have not yet been fully investigated.