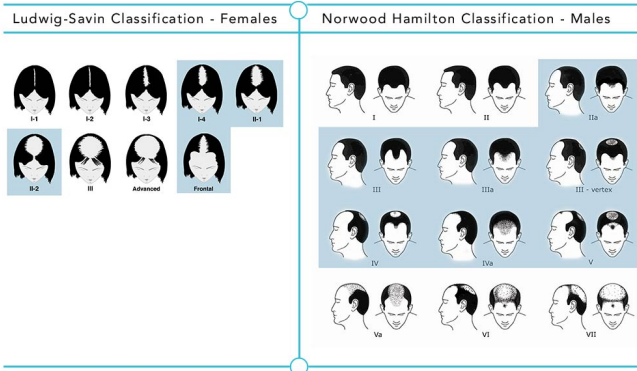


# Hair Regrowth using Human & Botanical Bio-signaling

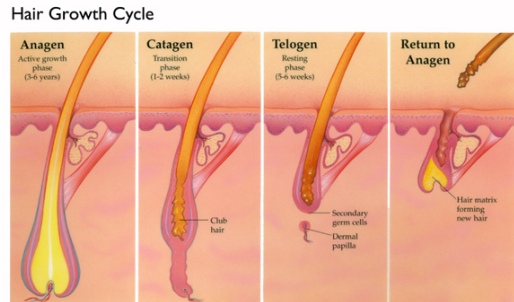
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The major cause of hair loss in both sexes is androgenetic alopecia. One-quarter of men show signs of male pattern baldness by age 21. At age 35 that number is 2/3 and 85% by age 50. Although fewer women are affected, one-half notice thinning hair by age 50 with those who are more hirsute in youth more likely to develop female pattern baldness.



hair bearing organ, the follicle, is complex and undergoes cyclical transitions throughout life.

Hair cycles consist of three phases: *Anagen* - the active growth phase which can last years. *Catagen* - the 1-2 week phase during which the follicle transitions into the resting phase, called *telogen*. About 5% to 10% of scalp hair is in the telogen phase at any given time.



Hair loss is strongly influenced by ethnicity and genetic heritage, which dictates degree of loss and age of onset. Because the primary baldness gene is found on the "x" chromosome, inheritance, especially in men, is strongly influenced by the maternal parent's family.

## PHYSIOLOGY of ANDROGENETIC ALOPECIA

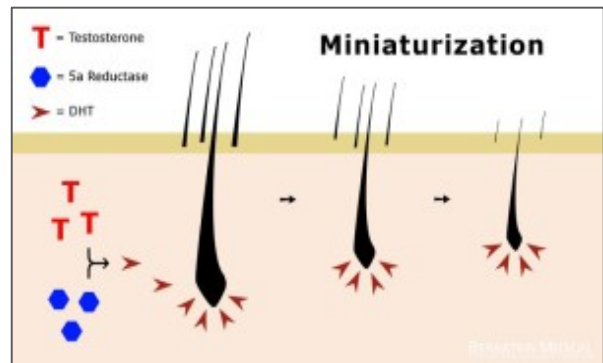
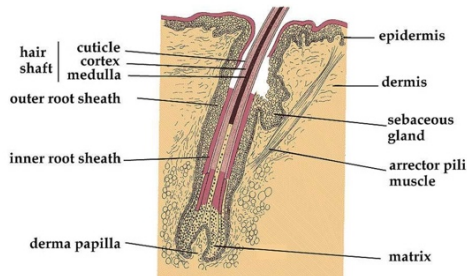
The culprit hormone in androgenetic alopecia is dihydrotestosterone (DHT), a derivative hormone of testosterone when it is acted upon by the enzyme 5-alpha-reductase. In men, the hair at the temples and mid-anterior scalp are most sensitive, with the pattern eventually progressing in many men to affect all but a horseshoe pattern of remaining hair.

Many people with hair loss experience lowered self-esteem. For some, this can lead to depression, anxiety, and other emotional issues. The psychological damage caused by hair loss can be as devastating as serious disease, with an emotional toll that affects physical health. It is not surprising then that Americans spend well over one billion dollars annually on hair loss products and treatments.

The process of androgenetic alopecia is not completely understood, Scientists do know that DHT shrinks hair follicles by shortening the growth window, causing them to become smaller and smaller with each cycle. The miniaturization makes the hair become thinner and wispy. Eventually, the follicle may disappear altogether.

## HAIR ANATOMY AND PHYSIOLOGY

The average person has 100,000 to 150,000 hairs on their scalp at any given time, with each strand comprised of multiple microscopic components. The physiology and structure of the



## OTHER TYPES OF HAIR LOSS

*Effluviums* (“outflow”) are mystifying losses of hair that occur during the telogen or anagen phases. Telogen, the “resting” phase, usually lead to an anagen phase, when vigorous hair growth renews within several weeks. In *telogen effluvium*, the anticipated regrowth does not occur and there is a reduction in the number of follicles growing hair. *Anagen effluvium* occurs when there is an insult that interrupts the active cellular division that occurs during hair growth. The most familiar example of anagen effluvium is acute hair loss in cancer patients treated with chemotherapy. Other causes are certain skin diseases and inflammatory insults.

*Alopecia areata* occurs when there is autoimmune destruction of hair follicles in localized areas of the skin. Hair loss can also be due to metabolic causes such as thyroid disease, anemia, and protein & vitamin deficiency.

## TREATMENT OPTIONS for ANDROGENETIC ALOPECIA

*Pharmaceutical* - Finasteride (Propecia®) and minoxidil (Rogain®) are FDA approved medications for topical use. Finasteride, originally developed to treat benign prostatic hyperplasia is an inhibitor of 5-alpha-reductase. There are undesirable sexual side effects associated with finasteride and a disturbing incidence of breast cancer. Hundreds of lawsuits have been filed against its makers. Minoxidil, originally developed as a treatment for hypertension, helps promote blood flow. It also promotes hair shedding during telogen, accelerating entry into anagen, which it prolongs. Both drugs are better at retaining hair than re-growing it.

*Surgical* – Hair transplantation is effective treatment although a “shock period” frequently affects transplanted follicles for a period of time. The traditional way is to harvest a strip of DHT “resistant” hair from the back of the head, dissect the individual follicle from the strip, and implant them into small stab incisions in the bald areas. Newer robotic technologies with optical sensors can harvest hair follicles in a “scattered” manner from an area of permanent hair, eliminating the scar and recovery associated with the strip removal.

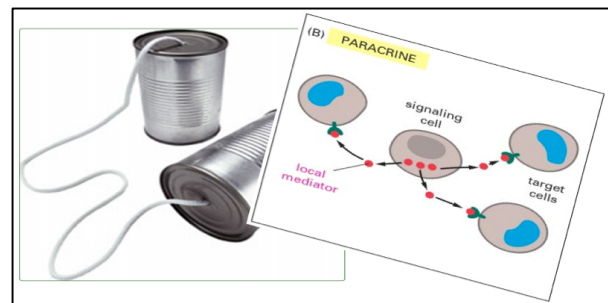
*Light* – LLLT (Low-level Laser Therapy) is hypothesized to stimulate the epidermal stem cells in the hair follicle bulge, shifting the follicles into anagen phase. It is administered with wearable caps, stationary panels, and hand-held wands and brushes with red-light emitting diodes. Infrared radiation has also been employed.

*Using bio-signals to influence follicle stem cell behavior* - Scientists have long thought people with hair loss had a depletion of hair follicles and follicle stem cells, which are necessary to grow hair. We now know bald people have the same number of follicle stem cells as those with hair. An

inability of stem cells in the scalp to develop into the type of cells that make hair follicles may be an underlying cause of pattern baldness. Scientists know that these follicle stem cells need bio-signals (biological signals) from within the skin to grow hair.

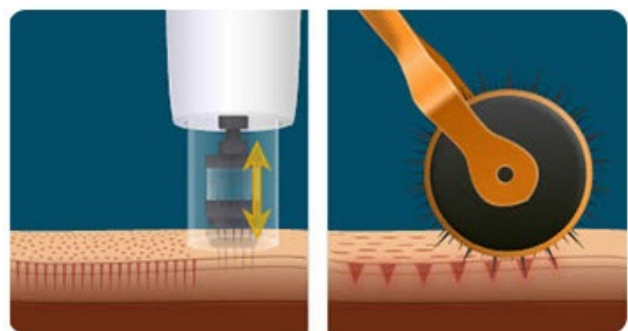
In an effort to provide the necessary biological signals, platelet rich plasma (derived from the patient’s own blood after centrifugation and activation) has been injected into the scalp with varying degrees of success in hair regrowth. Other promising techniques include microneedling, with or without topical application of bio-signals (cytokines and growth factors) derived from laboratory culture of specific types of human cells.

## BIO-SIGNALS as HAIR REGROWTH STIMULANTS



*Cellular communication* -The adult human has more than two hundred types of cells, whose numbers total in the trillions. All of them, except red blood cells, are constantly interacting by “speaking” with, or “listening” to, growth factors and cytokines. This highly complicated communication process is termed paracrine signaling.

Topical application of cytokines and growth factors enhances paracrine signaling. Bio-signals applied to the skin augment what the body is already doing...or not doing. The bio-signals that “turn on” hair follicles, which are missing in pattern baldness, can theoretically be topically applied, thereby inducing hair regrowth in quiescent follicles. Microneedling serves two functions felt to be of benefit in follicle stimulation.



*Microneedling* – is a simple yet effective therapy developed to rejuvenate skin and reduce the visibility of scars and abnormal pigmentation. The procedure employs a handheld roller, stamp, or electrical oscillating device that creates many thousands of shallow perforations in the skin. For stimulation of hair regrowth, shallow perforations (0.5 mm) are used to avoid direct damage to hair follicles, which extend 3 or 4 mm into the scalp.

Aside from the minor trauma created, the perforations greatly enhance the penetration of products applied to the skin during and immediately after treatment. In the case of hair restoration, the primary interest is enhanced penetration of bio-signals although the trauma caused is helpful in increasing localized blood flow (part of the reason that PRP and minoxidil are felt to be useful in promoting hair regrowth.)

***Caution: It is important to keep in mind that during and for several hours after microneedling, only substances that are intrinsic and inherent to human physiology should be applied to the skin. In other microneedling settings, applied substances not naturally found within the skin have been linked to adverse outcomes when applied during or within hours after microneedling.***

#### A THREE-PART HAIR REGROWTH SYSTEM

Professional microneedling treatments using a hair regrowth specific microneedling solution are one part of a three-part system intended to be used over a period of several months. The other two components include a similar take-home solution to be used, preferably with but can also be used without, 0.2 – 0.25 mm home-use dermal stamps or rollers, and a botanical lotion that is used without microneedling. The home use products are intended for use two to three times each per week.

The composition of each of these system components is unique and combinatorial, exploiting a number of cellular signaling pathways not addressed by any other product. Each ingredient in each of the three-part system is natural and with abundant peer reviewed literature confirming its value in stimulating hairs follicles and promoting hair regrowth.

#### **1, Hair Regrowth Microneedling Solution.**

This hair regrowth product is similar to the microneedling products currently produced by Cellese for skin rejuvenation, except special culture techniques in the laboratory “coax” bone marrow mesenchymal stem cells to focus on fair follicle bio-signals, specifically the Wnt/ $\beta$ -catenin signaling pathway. This pathway is important for hair matrix cell proliferation, and promotes bulge stem cell proliferation and survival,

Additional synthetic cytokines and growth factors, each molecularly identical to natural bio-signals and each with proven efficacy in promoting hair regrowth are additional ingredients.

Current studies are underway to determine the optimal frequency of use of Hair Regrowth Microneedling Solution.

**2. Home Bio-signal Lotion** – This lotion contains the same bio-signal combination as is used in Hair Regrowth Microneedling Solution (number 1, above), along with other ingredients that enhance penetration of bio-signals into hair follicles. It is intended to provide ongoing bio-signal stimulation to the follicles between professional microneedling sessions, and be used as a maintenance treatment. Home Bio-signal Lotion can be used at home in conjunction with short needle (0.2 – 0.25 mm) dermal stamps or rollers.

**3. Botanical Actives Lotion** – Through the years, a great deal of scientific work has been devoted to finding ways to stimulate hair regrowth, including examining the potential benefits of plant derived active ingredients. Our comprehensive approach to hair regrowth, therefore, incorporates those that have scientific proof of efficacy. This at-home lotion is used in alternating fashion with Home Bio-signal Lotion. It contains active ingredients extracted from more than two dozen botanical sources. Botanical Actives Lotion ***is not intended or recommended to be used in conjunction with dermal needling.***

#### SAFETY

The application of cell culture derived bio-signals to skin (including the scalp) dates back a decade and a half. Our scientifically selected cell of choice to culture for bio-signals is the bone marrow mesenchymal stem cell. Other cell types cultured by others for skin products include fat derived stem cells and fibroblasts. The physician/scientists of Cellese are pioneers in using bone marrow stem cells for this purpose, and chose them because from birth to death, these are the cells that act as command and control of healing in all tissues of the body. They are the only cells that play this role. Like other cellular elements in the blood (red & white cells and platelets), bone marrow stem cells migrate from the bone to the bloodstream where they gain access to all parts of the body. They are on constant patrol in people of all ages, gender or race. Their numbers, however, drop dramatically with advancing age, leading to less robust healing and increased and prolonged inflammatory responses.

All individuals produce exactly the same bio-signaling molecules throughout life, which makes allergic response impossible. (All cells and cell remnants are filtered out before conditioned media is used as an ingredient in any product.)

All Cellese products have a proven record of safety in topical skincare and microneedling. Our two-part anti-aging skincare systems have been used many tens of thousands of times by consumers without report of a significant adverse event. More than 100,000 unit doses of our skin microneedling solution have been used without a reported adverse event.

Topical skin application of cell culture-derived bio-signals is proven to be exceedingly safe, no matter what the type of cell being cultured. Searching PubMed, Google Scholar, and FDA databases reveals no instances of a significant health issue resulting from topical cytokines and growth factors.

The botanical bio-signals are derived from extracts of more than two-dozen different plants, each of which has a long history of use as food, herbal medication, or spice

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