

# HAIR LOSS MARKET ANALYSIS

## A. HAIR PROGRESSION

A common form of hair loss in both men and women is called androgenetic alopecia. In men, this condition is also known as male-pattern baldness. Male-pattern baldness is thought to occur in varying forms in about 66% of adult males are affected by male pattern baldness by age 50, and baldness treatments is estimated to be US \$1.5 billion per year industry.<sup>[1]</sup> Hair is lost in a well-defined pattern, beginning above both temples. Over time, the hairline recedes to form a characteristic "M" shape. Hair also thins at the crown (near the top of the head), often progressing to partial or complete baldness. The trigger for this type of baldness (called androgenic alopecia because it is caused by male hormones or androgens). Researchers have determined that this form of hair loss is related to hormones called androgens particularly an androgen called dihydrotestosterone (DHT), a metabolite of testosterone, a powerful sex hormone. In genetically-prone scalp, DHT initiates a process of hair follicle miniaturization. Through the process of follicular miniaturization, hair shaft width is progressively decreased until scalp hair resembles fragile vellus hair commonly known as "peach fuzz" or else becomes non-existent. Onset of hair loss sometimes begins as early as end of puberty, and is mostly genetically determined due to DHT hormone productions.

The pattern of hair loss in women differs from male-pattern baldness. Female pattern baldness, in which the midline parting of the hair appears broadened, is less common. It is believed to result from a decrease in estrogen, a hormone that normally counteracts the balding effect of testosterone, which normally occurs in women's blood. In women, the hair becomes thinner all over the head, and the hairline does not recede. Androgenetic alopecia in women rarely leads to total baldness. Men with androgenic alopecia typically have lower levels of total testosterone, higher levels of unbound/free testosterone, and higher levels of total free androgens including DHT.<sup>[2]</sup>

Hair growth life cycles of various phases: **anagen** is the growing phase; **catagen** is the involuting or regressing phase; and **telogen**, the resting or quiescent phase. Each phase has several morphologically and histologically distinguishable sub-phases. Prior to the start of cycling is a phase of **follicular morphogenesis** (formation of the hair follicle). There is also a shedding phase (**exogen**), that is independent of anagen and telogen in which one of several hairs that might arise from a single follicle exits. Normally up to 90% of the hair follicles are in anagen phase while, 10–14% are in telogen and 1–2% in catagen. The cycle's length varies on different parts of the body. For eyebrows, the cycle is completed in around 4-7 months, while it takes the scalp 2–4 years to finish; this is the reason eyebrow hairs have a fixed length, while hairs on the head seem to have no length limit. Growth cycles are controlled by a chemical signal like epidermal growth factor (EGF).

### SEE PICTURE ON THE ILLUSTRATION OF HAIR GROWTH

Body Site	% Anagen (growing) hairs	% Telogen (resting) hairs	Duration of Telogen	Follicle Density	Depth of Follicle
Scalp	85%	15%	3 months	350/sq.cm	5-7 mm
Facial	70%	30%	10 weeks	500/sq.cm.	2-4 mm
Upper Lip	65%	35%	6 weeks	500/sq.cm.	1-2.5 mm
Axilla (Armpit)	30%	70%	3 months	65/sq.cm.	4-5mm
Chest/Abdomen/Back	30%	70%	3 months	70/sq.cm.	2-5mm
Breasts	30%	70%	4 months	70/sq.cm.	2-4mm
Arms	20%	80%	5 months	80/sq.cm	2-4mm
Legs	20%	80%	6 months	60/sq.cm	2-4.5 mm
Pubic	30%	70%	3 months	70/sq.cm.	4-5 mm

Medical Treatments for Balding in Men," April 1999, American Family Physician (medical journal)  
 K. S. Stern and R. Paus (2001). "Controls of Hair Follicle Cycling". *Physiological Reviews* 81 (1): 449–494.  
 PMID 11152763. (comprehensive topic review, successor to landmark review of 1954 by HB Chase)

## B. STUDIES ON LASER THERAPY FOR HAIR RESTORATION

Thousands of controlled clinical scientific studies have shown that most middle-aged and younger males with typical male pattern baldness re-grow hair when the scalp is irradiated with Low-Level-Laser therapy for 3 to 5 minutes twice a week for 6 weeks. Studies also show that this works with women with thinning hair.

- International Journal of Cosmetic Surgery and Aesthetic Dermatology
  - Showed a 93% increase in hair among the respondents using LLLT
  - 90% of users achieve positive benefits
  - 44% see noticeable indications of benefits within the first 6 weeks
  - Another 45% see results within 6 to 12 weeks
  - The rest see subtle improvements after 12 weeks
- Budapest Study, 1967
 

In 1967, a few years after the first working Laser was invented, Endre Mester in Semmelweis University Budapest, Hungary wanted to find out if Laser might cause cancer. He took some mice, shaved the hair off their backs, divided them into two groups and gave a Laser treatment with a low powered ruby Laser to one group. They did not get cancer and to his surprise the hair on the treated group grew back more quickly than the untreated group. That was how "Laser biostimulation" was discovered.

Original paper published in Hungarian: Effect of Laser on hair Growth of mice. Mester, E. Szende, B. and Tota, J.G. (1967). Kiserl Orvostud 19. 628-631

- Leever Research Clinical Study of 375 LLLT Hair Therapy Participants
  - 78% had an appearance of thicker hair
  - 76% had an appearance of fuller hair
  - 64% had an appearance of shinier hair
  - 86% had an appearance of healthier hair
  - 85% perceived that their hair looked better
  - 84% were pleased with the progress
- Medical Laser Research Center Study, Dankook University, College of Medicine, Cheonan, South Korea
  - LLLT irradiation increased hair growing speed by 30%
  - Hair started to grow on the 13<sup>th</sup> day of test
  - Normal level of hair growth on the 25<sup>th</sup> day

- Double Blind Placebo Study
 

A double blind placebo study was conducted to evaluate the effect of Laser light therapy by comparing it with a placebo Laser. Here are the results:

  - All patients, with the exception of one in the Laser group, showed a complete stop of hair loss . All patients, except three, showed a clear re-growth of hair
  - Out of 18 patients, 14 showed an increase in hair thickness and all 18 showed improvements in the general hair shaft quality. The results showed no improvement in the placebo group or any adverse effect of the treatment.

- International Laser Research Group Association, 1986
 

Included in their trial report on "cold beam" Laser: "If we start from a normal quantity of hair bulbs per square cm of the various subjects involved, we can state that there was strengthening of hair bulbs...hair growth could be actually ascertained – also it being darker than before."
- Dateline NBC Study
 

The Dateline TV Show on NBC aired the conclusion of a 12-month study on five hair loss products on July 31, 2005.

The treatments studies included hair transplant surgery, Propecia, Minoxidil, Viviscal and the HairMax LaserComb.

Dr. Paolo Romanelli of the University of Miami Dermatology Department validated hair re-growth with Low-Level-Laser therapy devices (such as the HairRejuvenator® and HairMax).

- Canadian Government
 

Laser hair treatment using LLLT has received certification by the Canadian government to claim and indicate that it strengthens hair, prevents hair loss and stimulates re-growth of hair in men and women.

## C. DEMOGRAPHICS OF BALDNESS

According to the American Hair Loss Association:

- About 25% of males have hair loss by the age of 21.
- By age 35, two-thirds of males will experience hair loss.
- By age 50, approximately 85% of men have significant hair loss.
- It is estimated that 20 to 25% of women experience hereditary hair loss.
- In the US, 25 to 30 million women suffer from hair loss.

### United States Hair Loss Market

- Total hair loss population 86,954,338
- Innovators – 2.5% 2,173,858
- Early Adopters – 13.5% 11,738,835
- Early Majority – 34% 29,564,475

## D. MARKET FOR HAIR LOSS PRODUCTS

The Company's HairRejuvenator® handheld device will tap a large and growing hair restoration market segment. There are 2.7 million men and women in the US alone annually purchasing hair loss drugs, such as Rogaine, Propecia and Avacor which are reported to have side effects.

According to the American Academy of Dermatology, the baldness treatment industry is estimated to be a US \$1.5 billion per year industry.

### Handheld Laser Therapy for Hair Loss

Lexington's LaserComb for hair loss (non-coherent)  
 HairMax – 40,000 units sold in 2005  
 HairMax – 15% of "innovators" market share (estimate)

### Medications for Hair Loss

- Rogaine (Minoxidil)
  - \$300 million annual sales
  - Estimate \$360 per person, per year
  - Equal 833,333 persons annually
- Propecia (Finasteride)
  - \$292 million annual sales
  - Estimate \$916 per person, per year
  - Equals 318,777 persons annually

HAIR LOSS TARGET CONSUMER POPULATION					
Country	Males with Thinning Hair	Females with Thinning Hair	Total Thinning Hair Population	Innovators 2.5%	Early Adopters 13.5%
US	60,665,471	26,278,867	86,954,338	2,173,858	11,738,835
Canada	6,454,997	2,876,193	9,331,190	233,279	1,259,710
UK	12,795,975	5,749,792	18,545,767	463,644	2,503,678
Australia	3,554,416	1,827,382	5,381,798	134,544	726,542
<b>Total</b>	<b>83,470,859</b>	<b>36,752,234</b>	<b>120,223,093</b>	<b>3,005,325</b>	<b>16,228,765</b>

Assumptions: According to American Hair Loss Association

1. Females: 25% have thinning hair
2. 25% of males age 21 have hair loss
3. Age 35 to 50, two-thirds have hair loss
4. Age 50, 85%

## E. BALDNESS

The most common form of baldness is a progressive hair thinning condition called androgenic alopecia or 'male pattern baldness' that occurs in adult human males and some primate species. The severity and nature of baldness can vary greatly; it ranges from male and female pattern alopecia (androgenetic alopecia, also called androgenic alopecia or alopecia androgenetica), alopecia areata, which involves the loss of some of the hair from the head, and alopecia totalis, which involves the loss of all head hair, to the most extreme form, alopecia universalis, which involves the loss of all hair from the head and the body. Treatment for alopecia has limited success. The more hair lost, the less successful the treatment will be.

Male pattern baldness is characterized by hair receding from the lateral sides of the forehead, known as "receding hairline" or "receding brow." An additional bald patch may develop on top (vertex). The trigger for this type of baldness (called androgenic alopecia because it is caused by male hormones or androgens) is DHT, a powerful sex hormone. The mechanism by which DHT accomplishes this is not yet understood. In genetically prone scalps, DHT initiates a process of follicular miniaturization. Through the process of follicular miniaturization, hair shaft width is progressively decreased until scalp hair resembles fragile vellus hair or "peach fuzz" or else becomes non-existent. Onset of hair loss sometimes begins as early as end of puberty, and is mostly genetically determined.

Female pattern baldness, in which the midline parting of the hair appears broadened, is less common. It is believed to result from a decrease in estrogen, a hormone that normally counteracts the balding effect of testosterone, which normally occurs in women's blood.

## F. BALDNESS TREATMENTS

Since the 1980s, drug therapy has increasingly become a realistic management option for baldness for men and women. Increased understanding of the importance of dihydrotestosterone in male and female pattern baldness has led to targeted intervention to prevent this hormone from acting on receptors in the scalp. Coupled with chance discoveries and the ever-present lure of a breakthrough involving stem cells and hair multiplication, scientifically proven baldness treatments continue to be an area of research that receives a large amount of funding.

Baldness treatment alternatives available to men and women include:

- Low-Level-Laser therapy
- Hair transplant surgery
- Hair weaves
- Hair wigs
- Diet and lifestyle
- Herbal medicine
- Saw palmetto
- Pumpkin seed
- Propecia
- Minoxidil
- Revivogen
- Antiandrogens
- Copper peptides
- Ketoconazole
- Hair multiplication (future treatment)

It is easier to prevent the aging and falling out of healthy hairs than to regrow hair in follicles that are already dormant. There are products that have good success rates with regrowth, including the scientifically proven finasteride (marketed in the U.S. as Propecia) and minoxidil (marketed in the U.S. as Rogaine, and some places as Regaine). Without preventive treatment, in three double blind, placebo-controlled, randomized studies, 72% of the balding men on placebo had lost hair compared to baseline by 24 months. This is compared to 83% of participants on Propecia experiencing either no more hair loss or regrowth.

The prospective treatment of hair multiplication/hair cloning, which extracts self-replenishing follicle stem cells, multiplies them many times over in the lab, and microinjects them into the scalp, has been shown to work in mice, and is currently under development, expected by some scientists to be available to the public in 2009-2015. Subsequent versions of the treatment are expected by some scientists to be able to cause these follicle stem cells to simply signal the surrounding hair follicles to rejuvenate.

The average hair loss treatment takes a minimum of 6 months to begin working, and sometimes up to 24 months to truly see optimal results. Treating hair loss takes time because of hair cycles. The process of hair loss is the process of "miniaturization," which takes many years. Hairs grow in, cycle into dormancy, and then grow in again several months later. Each time they re-emerge, they do so thinner, shorter, and less pigmented. In time, they become so small that they are no longer noticeable. This can take many years. New hairs only grow in 2 or 3 a year, which is why it can take a year or more to be able to detect the success of a treatment.

This difficulty can be increased because many (scientifically proven) treatments often cause initial periods of shedding, as some resting hair follicles are ejected and a new cycle of growth begins, hopefully with a thicker follicle. Discontinuing treatments can also cause periods of shedding, though this hair loss is generally considered to be temporary, not affecting the baseline.

### 1. Propecia

Propecia, also called by its non-brand name Finasteride, is a "DHT inhibitor" pill that is FDA approved to inhibit production of DHT through the entire body (called systemic) It accomplishes this by inhibiting 5-alpha-reductase, the enzyme responsible for the conversion of free testosterone to DHT. Finasteride is taken orally and has a reported 29-68% success rate (vs 17-45% in patients receiving a placebo). It is effective only for as long as it is taken; the hair gained or maintained is lost within 6-12 months of ceasing therapy. In clinical studies, Propecia, like Minoxidil, was shown to work on both the crown area and the hairline, but is most successful in the crown area.

Propecia is the same as the oral prescription drug, Proscar, used in higher doses to treat an enlarged prostate. Some users save money by buying Proscar instead of Propecia , and split the pills in quarters using a pill-splitter to ensure the same amount as is present in Propecia is taken.

Propecia has been shown to be ineffective for treating hair loss in women, and shouldn't even be touched by pregnant or potentially pregnant women, as it has been speculated that it could cause severe birth defects in male fetuses.

### 2. Revivogen

Revivogen is a non-FDA approved topical DHT inhibitor treatment applied to the scalp, with many ingredients, such as types of fatty acids that are thought, though not proven, to inhibit DHT levels in the scalp and have a positive influence in combating hair loss. Revivogen also contains ingredients that are thought, though not proven, to function as an antiandrogen that has a positive influence in combating hair loss. Clinical trials are reportedly underway.

Revivogen uses simple mixtures of fatty acids (gamma Linolenic acid, alpha Linolenic acid, Linolenic acid, and a few others, which are thought to be potent inhibitors of 5AR, both type I and type II), in their free form, that come from the bulk de-esterification of natural oils like borage and flaxseed. This methodology is considered just as effective as using purified fatty acids, but saves considerable expense. There are other products that contain fatty acids from natural oils, such as black currant oil and emu oil, but virtually all-natural oils, including these two, contain only insignificant amounts of free fatty acids.

### 3. Antiandrogens

Antiandrogens block DHT already produced and present in the blood stream from binding with hair follicles. Their specificity varies greatly from specific antiandrogens such as finasteride, which inhibit the conversion of testosterone to DHT by interfering with 5-alpha-reductase to more broad-spectrum antiandrogens (fluzonazole, spironolactone, etc.), which can have serious side effects including gynecomastia. Ketoconazole, (often sold as Nizoral Shampoo) and Neutrogena T-Gel can have been clinically shown to have antiandrogen properties and are prescribed by medical professionals or available over the counter depending on the product, concentration and country.

### 4. Minoxidil

Minoxidil dilates blood vessels, and is a "potassium channel agonist." Minoxidil is a derivative of the physiological blood vessel dilator nitric oxide and this may also explain minoxidil's ability to stimulate hair growth and thicken hair. In the brand name Rogaine, it is FDA approved to stimulate regrowth and thicken hairs. Minoxidil is applied topically to the scalp, and has been shown to promote hair growth in about 25% of men and women, though it may take several months to work. New hair is usually thinner and lighter, like baby hair, and grows mostly on the top of the head, not at the hairline. Its effects may fade with time. Skin irritation is the most commonly reported side effect. Dizziness and increased heart rate have also been reported, but rarely.

### 5. Copper peptides

Copper peptides are topical, and shorten the resting phase of hairs, resulting in more hair follicles on the scalp being in the growing phase (as opposed to the resting or falling out phase) at one time. Copper Peptides generally have superoxide dismutase activity. They likely work by destroying superoxide, the antagonist to Nitric Oxide (NO), the natural miNOxidil.

### 6. Ketoconazole

Because Ketoconazole is both an anti-fungal and also a 5-alpha reductase inhibitor, it can help to slow the balding process. There is some suggestion that ketoconazole could inhibit testosterone synthesis in utero, which could potentially inhibit genital development of a male fetus. However, this has not been documented in any controlled studies.

### 7. Saw Palmetto

Saw Palmetto (Serenoa repens) is an herbal DHT inhibitor, which is cheaper than most commercial drugs and claimed to have fewer side effects than finasteride and dutasteride. Unlike other 5-alpha-reductase inhibitors, Saw Palmetto extract inhibits the conversion of testosterone to DHT without interfering with the cellular finasteride, which only inhibits the (predominant) type 2 isoenzyme of alpha-5-reductase. A preliminary study of saw palmetto extract for treating hair loss noted improvement in six of ten subjects. Dosages and length of study were not reported.

### 8. Pumpkin Seeds

Used to aid in the breakdown of DHT by the liver. An extract is often used, as unprocessed pumpkin seeds are high in fat, which can exacerbate hair loss in susceptible patients.

### 9. Diet and Lifestyle

While there are a number of genetic factors which determine a person's susceptibility to androgenic alopecia including androgen receptor polymorphisms, 5-alpha-reductase levels in the scalp, androgen receptor density and distribution in the scalp and other factors some of which may not have been discovered yet the dramatic increase in baldness in the population of Japan after World War II demonstrates that hair loss can be influenced by diet and lifestyle. Increased fat or caloric intake, decrease in aerobic exercise and general "westernization" was accompanied by a dramatic increase in incidence of male pattern baldness.

Daily, vigorous aerobic exercise (as opposed to short workout periods designed to raise androgen levels and build muscle or more sporadic exercise) and a diet which is adequate yet more moderate in terms of fat/total calorie intake have been shown to reduce baseline insulin levels as well as baseline total and free testosterone, significantly lowering testosterone DHT.

Lower insulin levels and reduced stress both result in raised levels of Sex Hormone Binding Globulin. SHBG binds to testosterone, and prevents it from circulating free in the blood. Only free testosterone is converted to DHT. It is the level of free androgens and not total androgens, which is relevant to the levels of DHT in the scalp and the progression of MPB. In short, aerobic exercise is capable of significantly lowering DHT.

Androgenic alopecia has been shown to correlate with metabolic syndrome. Medically increasing androgen levels does not worsen this condition, demonstrating that androgens do not cause metabolic syndrome. Instead, high insulin levels (and possibly chronic inflammation) seem the likely link in the demonstrated correlation between baldness and metabolic syndrome. This reinforces the notion that behaviors, which help to keep insulin levels low and reduce chronic inflammation, might also help to preserve hair.

### 10. Hair Transplant

Surgery is another method of reversing hair loss and baldness, although it may be considered an extreme measure. The surgical methods used include hair transplantation, where patches of skin with hair are moved from one part of the head to another. Another method is scalp reduction, where parts of the scalp are removed, the skin is stretched over the area that had been removed, and everything is stitched back together. Hair transplants generally cause scarring, sometimes severe, which may be especially visible if hair loss continues over the rest of the scalp.

### 11. Hair Multiplication (Future Treatment)

Stem cells have been discovered in hair follicles and some researchers predict research on these follicle stem cells may lead to successes in treating baldness through hair multiplication, also called hair cloning within three or four years (as of November 2004). This treatment is expected to initially work through taking stem cells from existing follicles, multiplying them in cultures, and implanting the new follicles into the scalp. Later treatments may be able to simply signal follicle stem cells to transmit chemical signals to nearby follicle cells, which have shrunk during the aging process, which respond to these signals by regenerating and once again making healthy hair.

Unfortunately, this new approach to treating baldness appears to be taking longer than expected. The first products are now expected to hit the market in 2009/2010. However, it remains unclear how effective they are going to be. It has been suggested that only future generations of HM will allow patients to grow as much hair as they want.

HM is being developed by two independent companies: ARI (Aderans Research Institute, a Japanese owned company in the USA) and Intercytex, a company in Manchester (UK).

### 12. Others

- Azelaic acid - promoters claim it is "Proven to inhibit up to 100% of DHT where applied." The evidence for this claim is uncertain. A study titled "Inhibition of 5a-reductase activity in human skin by zinc and azelaic acid" found a 90% inhibition of 5a-reductase activity in vitro with an azelaic acid and zinc combination. There was an additive effect between the two compounds.
- Spironolactone
- Retin-A (Retinoic acid; chemical peel stimulation of scalp)
- Avacor – discredited. Not to be confused with Avodart.
- LLT or Low-level Laser Therapy; Not FDA approved for hair regrowth, but only as a cosmetic hair enhancer. Treatments are administered at either a clinic or salon (most of which are in Europe), or by the individual user via a home-based portable system. For example, "The Laser Comb". No official results have been proven or published in regards to hair regrowth.
- Stinging nettle
- Zinc - While oral zinc supplementation may help prevent the conversion of testosterone to DHT, it also increases total testosterone levels.