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The Bald Truth about Androgenetic Alopecia

Mention the word “disease” and several severe sicknesses arise in one’s mind: diabetes, heart disease, cancer, HIV/AIDS, to mention just a few. But there is one malady that studies have shown to affect 50% of men and 6% of women by the age of 50, and at least 70% of men and 30-40% of women by the age of 70 (Trueb, 2002). It is a disease that elicits a wide range of psychological reactions, has treatments with limited results at best, and yet still manages to cost patients thousands of dollars in lifetime treatments. Unlike most diseases – which chew away at the body from the inside – this disease makes its presence known for the world to see, a threat constantly looming over its victims’ heads. It is Androgenetic Alopecia (AGA), otherwise known as male or female pattern baldness.

The process behind balding is actually quite complex: hair doesn’t simply float away in the wind. As Ralph M. Trueb (cited earlier) explains extensively in his 2002 article “Molecular Mechanisms of Androgenetic Alopecia” from *Experimental Gerontology*, normal hair follicle cells go through a continuous cycle of growth, death, and shedding. Anagen, the growing phase, is a 2-7 year period of time in which not only does the hair shaft grow, but the entire follicular unit (consisting of epithelial cells and keratinocytes in the hair matrix) undergoes rapid proliferation. Anagen is followed by Catagen, a two week period in which the follicle experiences apoptosis. Finally, in the approximately 100-day period of Telogen, the hair shaft matures and is then shed before the cycle begins anew.

However, in victims of AGA, the hair follicle actually miniaturizes, and as a result the amount of time spent in Anagen progressively shortens and the time spent in Telogen proportionally increases. This offset ratio results in a gradual thinning of the scalp, characterized by Trueb as a “bitemporal recession of hair and balding vertex” in men, and a “diffuse thinning of the crown and intact frontal hairline” in women. At the end of its progression, AGA leaves men with a horseshoe-like spread of hair on the scalp, while women are left (in the most severe cases) with a circular gap in the center of their scalp.

What makes AGA so very interesting is that the mechanism behind the follicular miniaturization remains to this day largely a mystery. The extent of our knowledge is reflected in the name of the disease itself, “andro” referring to the hormonal side of its etiology, and “genetic” referring to the genetic aspect of the disease pathway. Our understanding of the genes influencing AGA is limited. There is a common saying that the likelihood of balding increases if an individual’s maternal grandfather is bald, but based on the high concurrence of similar balding patterns between fathers and sons, it is evident that the gene is heritable from both sides of the family. Based on the difficulty of pinpointing its exact locus, Trueb has reported that “We probably deal with a polygenic inheritance, dependent on a combination of mutations,” (Trueb, 2002, Subsection: “Genetic Involvement”).

The hormonal side of AGA, however, we understand significantly better than its genetic side. In fact, humans first stumbled upon the truth as far back as 2000 years ago, as Rama Musa in his historically oriented “Folk Remedies for Alopecia” article writes, “Hippocrates…noted that children and eunuchs did not go bald,” and additionally, “The balding Aristotle (384 BCE – 322 BCE) believed that hair was nurtured by a ‘mysterious secretion which in libidinous men is dissipated too rapidly.”’ As it turns out, both of these ancient men were on the right path, as the hormonal culprit behind AGA is a sex hormone known as Dihydrogen Testosterone (DHT).

DHT is a metabolized version of testosterone via the enzyme 5-alpha-reductase, and it is five times more potent for the Androgen Receptor in our cells. So potent, in fact, that DHT is able to enter the follicles within the scalp and cause them to miniaturize. However, the mechanism behind this miniaturization – short of magic – remains unknown. All that is known at this point is that people suffering from AGA have a greater concentration of DHT than people who are not, and the reason women display a lower incidence of AGA is due to the higher concentrations of the enzyme aromatase, which converts testosterone to estradiol before 5-alpha-reductase can convert it to DHT (which also explains why post-menopausal women develop thinner hair, as aromatase and estradiol concentrations decrease). To cause further confusion to our already lack of understanding, Evelyn Y. Chin notes the paradoxical effect of DHT in the body in which it actually “influences the growth of deeply pigmented terminal hairs on the legs, arms, underarms, chest, back, and pubic area”. There is clearly still a ways to go until scientists can fully understand why pattern baldness occurs.

This lack of understanding is reflected in the treatments available for the condition, most of which were not tailored specifically for balding, nor do we fully understand how they work. The two drugs that are currently FDA approved to treat AGA are topical Minoxidil (Rogaine) and oral Finasteride. Minoxidil is a miracle drug in the sense that it was originally intended as an anti-hypertensive that had the miraculous effect of promoting hair growth. Finasteride similarly is commonly used to treat benign prostate cancer by targeting the enzyme 5-alpha-reductase and preventing it from converting testosterone to DHT (which causes both benign prostate cancer and AGA). Our lack of understanding of how AGA occurs is evident in these medications which were not originally intended to treat balding. And even when we do intend to treat balding, we still do not always fully understand how we are treating it. Take for example the Low-Level Laser Light Therapy, administered through a comb, which has multiple proposed mechanisms but no definitive one. There are several other topical solutions being tested at this time, such as solutions containing Prostaglandins, Estrogens, Ketoconazole, and Melatonin, which are aimed at targeting either regulating the hair cycle (inducing Anagen) or regulating hormone/enzyme activity within the scalp.

There are several major issues with these treatments: first, that their effects are short term, and second, that they have limited regenerative effects. Really, to call them “treatments” would be taking a great deal of liberty with the term, since “treatment” implies the eventuality of a cure: “management” is better suited for AGA. In an article for *Medscape*, Dr. Robert Feinstein writes that, “Continuing topical treatment with the drug [Minoxidil] is necessary indefinitely because discontinuation of treatment produces a rapid reversion to the pretreatment balding pattern.” This holds true for Finasteride as well and really any drug that is currently available, and it becomes a problem because insurance companies view AGA as a cosmetic concern, so all these managements have to be purchased with out-of-pocket costs. Over the course of a lifetime, continuously purchasing these medications piles up into a hefty sum of money. Short of getting transplant surgery (which is still surgery and thus still quite a bit of money), there is no permanent cure for AGA.

However, even transplant surgery – despite being a permanent solution – has its limitations, as do all these managements. On transplant surgery, Dr. Robin Unger in her article “Female Hair Restoration” states that, “The main focus should be how much of an illusion of density can be created by using the lowest number of grafts in any given area, so as to enable the treatment of the most cosmetically important regions in one surgery.” “Illusion” is the key word here, as it cements the notion of there being no miracle cure. Transplant surgery is limited by the amount of donor area available, and since it is such a meticulous surgery (upon harvesting the graft, all the hair is separated into follicular units and then individually implanted into the desired area) there is only so much that can be done at one time. Minoxidil – the most popular management drug for men and women – works in a limited capacity as well, as Dr.’s Shamsaldeen, Mubki, and Shapiro report that, “The average increase in target area hair count is about 8% with minoxidil 2% lotion and 10-12% with the 5% formulation.” This is true of all treatments for AGA: regeneration is limited. This is why most physicians are advised to “manage expectations”. With multiple treatments used concurrently and effective combing, hair can give the “illusion” of being thick, but as of now there is no way in which a full, healthy head of hair can be regenerated.

This poses a huge problem for the victims of AGA. In our society, balding is seen as a sign of aging or growing, and those of us that do go bald are told to just “deal with it”. But our society is demanding, for while it scorns those individuals that cannot accept their balding, it simultaneously mocks all bald individuals for the way they look; image is everything in our society, and while there was a time thousands of years ago when balding was considered the epitome of manliness, that same does not hold true today. In fact, in a study conducted by Dr.’s Tabolli, Sampogna, Pietro, Mannooranparampil, Ribuffo, and Abeni, it was shown that 78% of men suffering from AGA also suffered from some sort of anxiety. 22% of the men in the study were more prone towards hostility, irritability, and even violence. And of all the bald women in the study, a staggering 55% were understandably depressed to some degree. Almost all patients suffering from AGA come to their physicians with concerns about their condition, but find that most physicians display a great deal of “disinterest discussing hair loss” (Chin, 2013). At the end of the day, AGA is not a life threatening disease and so it is understandable that physicians would not give it much weight, but the fact of the matter is that AGA elicits an astounding psychological effect on patients, and physicians need to take that into account for the sake of the patient’s overall wellbeing.

But this wellbeing may not just be limited to mental wellbeing: AGA has been linked to several serious physical illnesses as well. As mentioned earlier, Finasteride is commonly used to treat both AGA and benign prostate cancer since DHT is the root of both diseases. Studies have shown that “Bald men, regardless of hair loss type, had a 69% greater risk of prostate cancer, and young men with frontal hair loss were six times more likely than those without such baldness to get advanced prostate cancer by age 60 years,” (Fillon, 2013). If physicians are disinterested in AGA, they should be interested in prostate cancer. It is clear that the two diseases are linked, and as such researchers should make a push for understanding how DHT functions either in the cells or how it can be prevented from being produced. But as mentioned earlier, simply stopping DHT would probably not prevent hair loss: the disease pathway for AGA is simply too complex. And that complexity has become evident in a study recently published by *JAMA,* as “Moderate or severe AGA was associated with a 2.01-fold higher risk of mortality from DM and heart disease compared with normal or mild AGA… our results showed a significant relationship between AGA and mortality from DM and heart disease in both sexes,” (Su, 2013). While the authors of this study note that the results do not indicate that curing AGA would cure either DM or heart disease (or vice versa), AGA can be used as a diagnostic tool or risk factor for these diseases. More important, I think, is the fact that AGA shows up within the context of DM and heart disease at all, indicating once again how complex its etiology is.

That complexity provides even more of a reason to research it. This disease is not merely a cosmetic concern, but one that has been proven to possess links to other serious ailments, and whether or not researching AGA further can shed light on those more serious diseases hinges upon whether more research on AGA is done at all. The research would be worth it, if not to cure those more serious diseases, then at least to address AGA’s immense psychological impact on its victims, the lack of more effective treatments (rather than “managements”), and the monetary and social strain placed upon its victims. It is easy to laugh this issue away or simply ignore it in the light of other more pressing concerns, but the fact of matter is, in a world of rapid medical advancements and scientific discovery, our lack of understanding of something as benign as balding is pitiful at best.

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