The Connection between Diet, Lifestyle and Androgenic Alopecia

If it looks like a duck, swims like a duck and quacks like a duck…

Version 0.4
Author: RF
Date: 30 October 2023

Proof of authorship (SHA256): c4bd5d4b079ca2ef229b653f4643988e78cfd30995818b4a30d20b3ab0acfb61
Preimage will be released with next version to prove authorship.
Preimage for version 0.3.2: suMQ1635!2MALnq-;.A2Maoy

Table of contents

Abstract

In this document I am presenting an explanation of how and why male pattern baldness, also known as androgenetic alopecia or androgenic alopecia (AGA), occurs. Such an explanation is also known as a pathogenesis model. As the explanations are quite long and I want you to know the rough direction where this is going beforehand. This is the short version:

Statistical correlation with other diseases

AGA is statistically strongly correlated with metabolic syndrome (MetS – a set of metabolic changes that ultimately lead to diabetes type 2) and cardiovascular disease (CVD). The main risk factor for **both** MetS and CVD are issues with carbohydrates, sugar and insulin – directly (diet and exercise) or indirectly (inflammatory diet, stress, lack of sleep, meat overconsumption). Additionally, the hormone profile of individuals who lose hair from AGA is hyperandrogenic – meaning androgens like DHT are very high – and resembles that of polycystic ovary syndrome (PCOS). This is a disease afflicting women that is known to be caused by the same reasons as MetS and CVD and leads to hair loss in women.

My main argument is that AGA is not only statistically strongly correlated to MetS, CVD and PCOS – all of which are known to be caused by direct or indirect issues related to carbohydrates, sugar and insulin. It is my hypothesis that the root causes are the same.

Pathogenesis model in short

The pathogenesis model is in short as follows:

1. Direct and/or indirect issues with carbohydrates, sugar and insulin lead to (a) DHT overproduction and (b) vascular damage
    1. Direct causes: Overconsumption of carbs/sugars and/or too little exercise
    2. Indirect causes: Inflammatory foods, stress, lack of sleep, too little muscle mass, endurance overexercise, magnesium insufficiency, smoking, meat overconsumption
2. The scalp is highly vascularized (filled with blood vessels) but mostly with very fine and thin ones that can be more easily damaged; carb/sugar/insulin issues cause vascular damage
3. High androgen levels (like DHT) accelerate vascular damage of the scalp vasculature
4. Scalp vascular damage has two effects:
    1. Blood, oxygen and nutrient supply becomes weaker and weaker, starving follicles
    2. In trying to repair the vascular damage, the body summons pro-inflammatory and pro-fibrotic mediators like calcium and TGF-β which spill over into the scalp dermis and cause dermal inflammation and fibrosis. This mechanism is identical to hair loss in scleroderma, the dermal presentation of systemic sclerosis.
5. Certain factors common in AGA patients accelerate dermal fibrosis.
6. The combination of vascular damage and dermal fibrosis creates an environment where hair can no longer grow. The pro-fibrotic agents also keep hair follicles in a resting phase as inflammatory mediators are part of hair follicles' natural life cycle.

Introduction

For decades already, there's a truthism in hair loss research that is barely examined more closely or questioned: "It's the DHT/androgens!"

But no one really seems to bother where these androgens come from, why they are elevated in the first place, and what exactly the mechanism of action is in which they damage our hair. Instead, people resort to another superficial mantra: "It's genetic!"

In this document I want to challenge the status quo. I want to point out correlations with other diseases that hint at a common root cause that is not primarily genetic. I want to elucidate where the elevated androgen levels come from and how they cause damage. And lastly, I want to cover how hair loss can be slowed down to a full halt.
However, full disclosure: At this point I do not know how to reverse hair loss.

Is it all genetic and predetermined?

There are two very good data points which show that androgenetic alopecia is not all genetic and predetermined: two studies done on identical twins (one in Japan, one in the USA) and one in China on the demographics of hair loss.

Chinese demographics of AGA study

This idea is supported by a study from China[1] on the demographics of AGA. It showed that only 40% of hair loss sufferers had a family history of hair loss. In other words, for 60% of hair loss sufferers they were the **first** in 3 generations (them, their parents, their grandparents) to experience hair loss.

> *"A family history was present in 39.74% of men and 36.78% of women with AGA."*

If AGA was truly genetic, the percentages would have been much higher. How come almost two thirds of balding people had no family history of balding?

The study having been conducted in China is very enlightening because, unlike in the west where dietary and lifestyle changes happened over centuries, changes in lifestyle in China were very rapid so their effects on the human body will show pronounced differences in different generations. The different generations grew up in vastly different worlds regarding diet and lifestyle.

Another data point coming from China is a study[2] finding that higher consumption of sugary

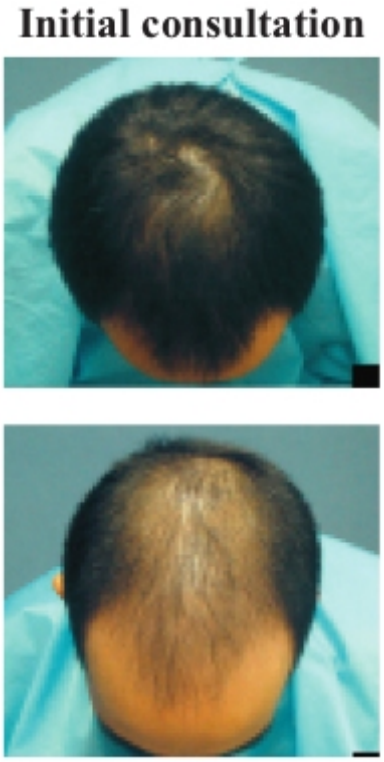
1 C. Yang et al.: “Epidemiological survey of androgenetic alopecia in Golmud area of Qinghai province”

2 X. Shi et al: “The Association between Sugar-Sweetened Beverages and Male Pattern Hair Loss in Young Men”

beverages is linked with earlier onset and more severe progression of androgenetic alopecia.

Japanese twins study

The following photo is taken from the Japanese study[3] and shows the hair loss situation of two brothers - identical twins at the same age.

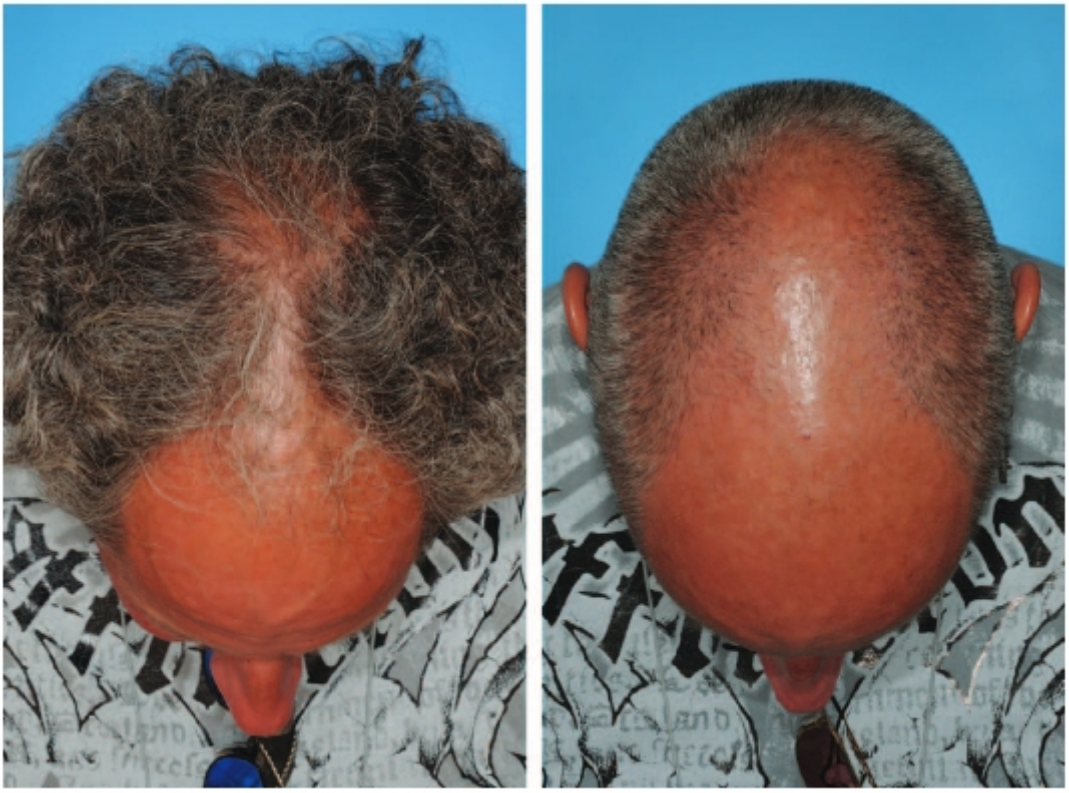


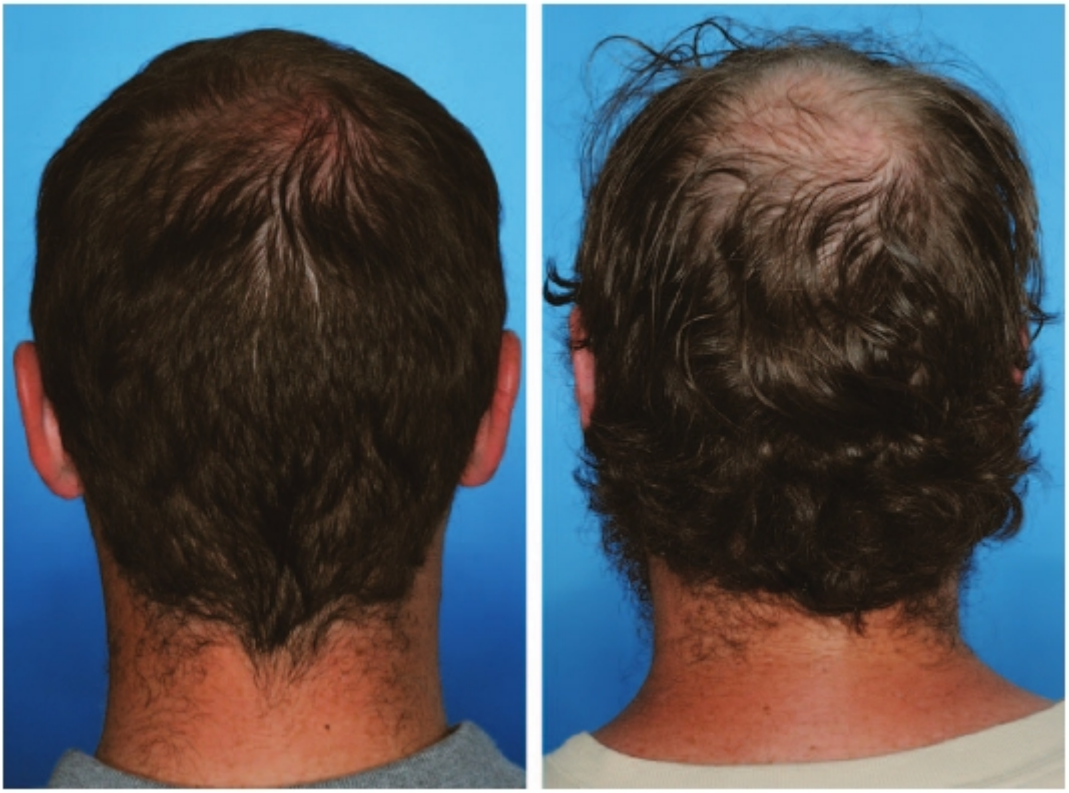
Exogenous factors in alopecia study

Another study[4] looked at different endogenous factors that influence androgenic alopecia severity. Taken into account were factors such as stress, smoking, alcohol consumption, and exercise duration. In this study, as well, significant differences were found between monozygotic, i.e. genetically identical, twins:

3 Koyama et al.: “Eleven pairs of Japanese male twins suggest the role of epigenetic differences in androgenetic alopecia”, DOI: 10.1684/ejd.2012.1898

4 Gatherwright et al.: “The contribution of endogenous and exogenous factors to male alopecia: a study of identical twins”, DOI: 10.1097/PRS.0b013e3182865ca9





As you can see, their hair loss situation is in vastly different stages of progress. As their genes and age are fully identical, this necessarily means that there were environmental or lifestyle factors that impacted the speed of progress.

What if the twins had known what these factors were? Could they have avoided hair loss almost completely or showed it down significantly, if they had just known what to do? I think so.

Prior work

Full disclosure: I am not the first person on the planet linking carbohydrates/glucose/insulin and androgenetic alopecia (AGA). There were others before me who also thought that hair loss is ultimately caused by the same dietary and lifestyle behaviors that also cause metabolic syndrome, diabetes type 2 and cardiovascular disease. To name just a few:

- Nicholas Sadgrove: "The 'bald' phenotype (androgenetic alopecia) is caused by the high glycaemic, high cholesterol and low mineral 'western diet'"
- Two research papers that link insulin resistance to a variety of diseases, including AGA:
  - "Skin Manifestations of Insulin Resistance: From a Biochemical Stance to a Clinical Diagnosis and Management"
  - "Hyperinsulinemic diseases of civilization: More than just Syndrome X"
- TuitNutrition, in her posts on Insulin and Skin and "Is There a Male Equivalent to PCOS? (a.k.a. The Detrimental Effects of Hyperinsulinemia on Men's Health)"
- healthy diet paradise

The value of this document is putting it all in one place into one coherent, extended explanation. This document also presents, for the first time, a full pathogenesis model of AGA building upon the assumption that carb/sugar/insulin or indirect causes (like stress, lack of sleep, smoking and a pro-inflammatory diet) and AGA are connected. Especially I will be including three aspects that have been largely overlooked so far in the context of AGA

1. How diet and lifestyle cause high levels of DHT ("hyperandrogenism")
2. That androgens accelerate vascular damage
3. How vascular damage and its mediators (like calcium and TGF-β) spill over into the adjacent dermis (skin); this mechanism is known from scleroderma, the dermal presentation of systemic sclerosis, which also leads to hair loss in affected areas

The document will also be describing what can be done to stop hair loss. Though, for the sake of transparency and completeness, I do not know how to reverse androgenetic alopecia – only how to stop it.

The Correlations

There are four major disease clusters that AGA is either statistically highly correlated to or very similar to in diagnostic manifestation. If they are so similar, maybe the root causes are similar or even identical? I believe so. These four are:

1. Metabolic syndrome and diabetes type 2
2. Cardiovascular disease
3. Polycystic ovary syndrome (PCOS)
4. Prostate hyperplasia

Metabolic syndrome

Metabolic syndrome (MetS) is a group of changes in human metabolism which ultimately lead to diabetes. MetS manifests as one or more of the following:

- Unhealthy lipid profile (increased triglycerides and lowered HDL - a sign for increased fat export from the liver which the liver creates through so-called de-novo lipogenesis (DNL) from carbs and sugar)
- Increased blood pressure
- Weight gain
- Increased blood sugar levels

At the core of MetS lies insulin resistance - a state in which the body's cells show resistance to the hormone insulin which instructs them to store glucose. Over time, blood sugar rises, causing damage to the vasculature and organs. Evolutionary programs related to energy conservation also lead to a rise in blood pressure and mechanic stress (and ultimately injury) to the vasculature. Metabolic syndrome thus leads to diabetes type 2 and also to cardiovascular disease (CVD).

Metabolic syndrome and androgenic alopecia are statistically significantly correlated. The following is a list of studies that support this correlation, though there are more:

Title	**Link**
Association of Androgenetic Alopecia with Metabolic Syndrome: A Case–control Study on 100 Patients in a Tertiary Care Hospital in South India	link
Early androgenetic alopecia as a marker of insulin resistance	link
Androgenetic alopecia, metabolic syndrome, and insulin resistance: Is there any association? A case–control study	link
Androgenetic alopecia as an indicator of metabolic syndrome and cardiovascular risk	link
Severe androgenetic alopecia as a maker of metabolic syndrome in male patients of androgenetic alopecia: a hospital based case control study	link
Risks for metabolic syndrome and cardiovascular diseases in both male and female patients with androgenetic alopecia	link

Study of prevalence of metabolic syndrome in androgenetic alopecia	link
Alopecia and the metabolic syndrome	link
The association of insulin resistance and metabolic syndrome in early androgenetic alopecia	link
Is early onset androgenic alopecia a marker of metabolic syndrome and carotid artery atherosclerosis in young Indian male patients?	link
Association of Androgenetic Alopecia With Mortality From Diabetes Mellitus and Heart Disease	link

To summarize: There is a plethora of studies out there that support a statistical correlation between androgenetic alopecia and metabolic syndrome. Metabolic syndrome is a cluster of presentations that result from insulin resistance. Insulin resistance is caused primarily (but not only) by an intake of carbs and sugar that is too high for an individual‘s activity levels.

A very strong data point that also links insulin resistance/metabolic syndrome and androgenetic alopecia is the fact that a genetic mutation present in some Amish people confers immunity against both diabetes and adrogenetic alopecia (source). I propose that the immunity to diabetes is primary, and to AGA secondary – meaning that they are immune to AGA **because** they are immune to blood sugar and insulin issues.

Cardiovascular disease

It is still not perfectly understood how exactly elevated blood sugar causes CVD. It is likely a mix of several kinds of damage: glycation causes the vasculature‘s endothelium (potentially including its so-called glycocalyx) to degrade. The endothelium can be understood like a lubricant lining of your blood supply system. Without the endothelium, arterial wall damage is much more likely and frequent. Secondly, through an old evolutionary adaptation that is intended to hold onto nutrients (specifically when sugar levels are high, which the body sees as a sign of approaching winter because before industrial sugar production humans only got high sugar loads when ripe fruit was abundant), blood pressure goes up and arteries stiffen, also known as vasoconstriction. This leads to increased mechanical stress on arterial walls and on smaller vascular components like capillaries. Both of these - endothelial damage and increased pressure and stiffness - ultimately lead to mechanical damage to the vascular system. Lastly, elevated blood glucose also seems to generate physical damage to arterial walls and generally increased inflammation levels. The statistics are clear: Increased blood sugar, insulin resistance and metabolic syndrome are the main risk factors for developing cardiovascular disease.

The human body tries to repair this damage by first marking the damaged components for recycling and then sending in agents to destroy and clean up. This process is known as inflammation. It is followed by a repair process. In humans, there are various conditions under which the tissue that is rebuilt as part of the repair process is not identical to the pre-damage tissue. Rather, the body uses "hardened" components to build back stronger. On the skin this is known as scar tissue. When repairing the cardiovascular system, atherosclerotic plaques form which consist of fat and calcium. (It is not quite sure if the fat

accumulations are there on purpose or as a side effect of blood lipid content; calcium, on the other hand, is generally part of the healing process and summoned by the body on purpose.)

Excess calcium, however, increases mechanical stiffness and also degrades nutrient supply. The scalps of people with androgenetic alopecia have indeed been found to be calcified (source: Baldness and Calcification of the "Ivory Dome" by F. Hoelzel). The presence of calcium deposits in AGA scalp at least hints at the possibility of vascular injury and repair happening in AGA scalps. (I will later introduce a model that explains how and why this happens to AGA scalp. Ultimately, AGA scalp vasculature receives identical damage to that which causes CVD in the central blood supply.)

Regardless of the exact mechanisms behind blood glucose and insulin resistance leading to CVD, there is a multitude of studies which have found significant statistical correlation between CVD and AGA:

Title	**Link**
Androgenetic alopecia as an indicator of metabolic syndrome and cardiovascular risk	link
Risks for metabolic syndrome and cardiovascular diseases in both male and female patients with androgenetic alopecia	link
Is early onset androgenic alopecia a marker of metabolic syndrome and carotid artery atherosclerosis in young Indian male patients?	link
Androgenetic alopecia and risk of coronary artery disease	link
Association of Androgenetic Alopecia With Mortality From Diabetes Mellitus and Heart Disease	link
Male pattern baldness and its association with coronary heart disease: a meta-analysis	link
Male-pattern baldness and incident coronary heart disease and risk factors in the Heinz Nixdorf Recall Study	link
Is there any relationship between cardiovascular disease and androgenetic alopecia in men and women?	link
Updated meta-analysis of the relation between heart disease and androgenic alopecia or alopecia areata	link
A Study on Association between Androgenetic Alopecia and Cardiovascular Risk Factors in Males with History of Hair Fall	link
Early Onset of Androgenetic Alopecia Associated With Early Severe Coronary Heart Disease: A Population-Based, Case-Control Study	link
Is androgenetic alopecia a risk for atherosclerosis?	link

Again, the genetic mutation in some Amish mentioned above also confers immunity to atherosclerosis and androgenetic alopecia at the same time (source). To repeat, I am suggesting that the primary effect is immunity to blood sugar and insulin issues, and as a

consequence immunity against CVD and AGA is conferred.

The interaction between androgens and glucose/insulin in CVD

Men are affected by CVD and related ailments like heart attacks 20 years earlier on average than women. Sex hormones seem to play a role here: androgens seem to be harmful, estrogens protective, or both.

As the hormonal profile of women changes with menopause, this is also when (non-PCOS) women first start experiencing hair loss. The role of sex hormones in CVD risks (women before menopause are spared, men are at a higher risk) is also, I believe, the exact same reason why men and their hormonal profile predisposes them to a higher hair loss risk. If we take the statistical correlations (1: male sex hormones and hair loss, and 2: hair loss and cardiovascular disease), the connection between cardiovascular disease and hair loss is not proven, but becomes more likely.

There are several studies which cover the increased CVD risk for men compared to women. Depending on the study, men develop CVD between 7 and 20 years earlier than women.

Prostate hyperplasia (BPH)

(Benign) prostate hyperplasia or BPH for short is quite widespread among older men. Like metabolic syndrome and CVD it is statistically strongly correlated with AGA. It has also, just like MetS and CVD, been shown to be caused by insulin resistance and high blood sugar level.

It is hence no coincidence that the drugs which are used to treat BPH are - at least in their mode of action but in some cases also in their active ingredients - identical to the drugs used to treat AGA. Again, the reason is that the root causes are the same: Insulin resistance and increased blood sugar levels.

The drugs are:

- 5 alpha reductase inhibitors (finasteride and dutasteride)
- Blood pressure lowering medication (minoxidil for AGA, Viagra for BPH)

My reasoning here is as follows: If the drugs used to treat BPH are identical to those for treating AGA, and the root causes for BPH are known to be elevated blood glucose and insulin resistance, then it is quite likely that AGA has the same root causes.

PCOS

Polycystic ovary syndrome is a disease state in women where in many (but not all) cases the ovaries become cystic. It has been named after these cysts because they were the first symptoms recorded of this syndrome but it is a bit of a misnomer because they do not always occur.

PCOS is rather well studied. It is known to be ultimately caused by insulin resistance and

elevated blood sugar. There are four main root causes or types of PCOS:

- **Insulin resistant PCOS,** caused by too much carb and sugar intake and too little exercise. The most common.
- **Adrenal PCOS**, caused by chronic stress. The stress hormone cortisol has a suppressive effect on insulin, thus causing or contributing to insulin resistance and blood sugar increases. This is by evolution, as cortisol is supposed to make energy available, whereas insulin is supposed to store energy. Chronic lack of sleep also falls into this category.
- **Inflammatory PCOS**. There is some mutual effect between a body's general level of inflammation and its level of insulin resistance. This is often caused by a diet high in omega-6 fatty acids, trans fats and oxidized fats (e.g. from frying or BBQing). Meat consumption is another cause due to mixed factors (inflammatory substances in meat, omega-6 content, purines). Smoking also contributes to this, as do high levels of carbohydrate and sugar consumption (which however are already the main cause behind insulin resistant PCOS).
- **Pregnancy or pill related PCOS**. Not relevant for men.

As you can see, three out of four of these forms of PCOS are either directly (insulin resistant PCOS) or indirectly (action of stress hormones on insulin and sugar metabolism & inflammation on insulin resistance) related to sugar, carbohydrates, and insulin.

In general, PCOS leads to a state of highly elevated androgen levels in women. This is an important lead for later: High carb and sugar intake and insulin resistance seem to increase androgen levels - not only in women.

Why does PCOS matter - apart from the fact that it leads to high androgen levels and androgens are part of the AGA disease cascade?

Because multiple studies have already noticed that the hormonal profile of male AGA patients strongly resembles that of female PCOS patients. Two examples:

- Glycolipid and Hormonal Profiles in Young Men with Early-Onset Androgenetic Alopecia: A meta-analysis
- A Comparison of the Hormonal Profile of Early Androgenetic Alopecia in Men With the Phenotypic Equivalent of Polycystic Ovarian Syndrome in Women

Citing from the second paper:
"Men with early AGA could be considered as male phenotypic equivalents of women with PCOS."

It would thus not be far fetched to assume that the same hormonal profile found in AGA and PCOS sufferers was also caused by the same root causes. And, luckily for us, the root causes of PCOS are well known. Three of them (those pertaining to men) are repeated here because it is important to remember them for the pathogenesis model to be introduced later:

1. Insulin resistant PCOS, caused by too much carb/sugar intake and too little exercise
2. Adrenal PCOS, caused by stress and lack of sleep
3. Inflammatory PCOS, caused by certain fats (omega-6, trans fats), fried food, and

smoking

Unsurprisingly, female PCOS patients often also suffer from androgenetic hair loss!

Additionally, treatments against PCOS often follow the same avenue as those against AGA:

- Spironolactone (which lowers blood pressure, like minoxidil)
- Birth control pills (which alter the sex hormone profile – like finasteride and dutasteride in males)

However, and this is important, there are treatments that are also effective against PCOS which are not currently used against AGA. They target blood sugar and insulin: metformin and inositol. Interestingly there are many accounts in PCOS forums of metformin and inositol leading to hair regrowth. The effectiveness of these two drugs in treating female PCOS and female androgenic hair loss also points at the root cause of male hair loss: carbs and sugars.

To summarize PCOS: We know that PCOS causes high androgen levels and hair loss in women. We also know that it is caused by issues with carbs/sugar/insulin – directly ("insulin resistant PCOS") or indirectly ("adrenal/stress PCOS" and "inflammatory PCOS"). Two papers noted that the hormonal profiles of PCOS and AGA are very similar. The drugs used to treat PCOS are similar in their mode of action to drugs used for treatment of AGA; in addition PCOS patients also use drugs to lower blood sugar and improve insulin sensitivity. I am thus suggesting that the root causes of PCOS are also the root causes of AGA.

Connection between drugs

It is no coincidence that the two approved hair loss medications (finasteride and minoxidil) work if we assume that the root cause of hair loss are blood sugar issues.

As we have seen above, cardiovascular disease is a common downstream complication of metabolic syndrome. One of the aspects of CVD is increased blood pressure. Minoxidil is a blood pressure medication. Through vasodilation it reduces blood pressure.

We have also seen that PCOS leads to highly increased androgen levels. PCOS is also caused by insulin resistance and high blood sugar. The other approved hair loss medication, finasteride, counters the more potent of the two main androgens, DHT.

As we can see, the two hair loss medications that are approved by the FDA and EMA target issues that are downstream of carb/sugar/insulin issues (and their secondary contributors like cortisol and inflammation). This is no coincidence. But it should also mean that fixing what is upstream - carbohydrate and sugar intake as well as exercise (or blood sugar levels through medication), stress (in different forms!) and inflammatory diet - will likely stop hair loss. This is supported by two blood sugar medications, inositol and metformin, having been reported to lead to hair growth in PCOS patients who experienced hair loss.

The following diagram contains the main drugs used to counter PCOS, AGA and BPH and

shows on which physical manifestation of the underlying issues they work:

The question marks in the above diagram will be resolved later in this document.

The fact that medications with identical downstream targets (blood pressure, androgens) work for both PCOS and AGA implies that the medications that target upstream aspects in PCOS (inositol and metformin) should also work for AGA. In addition the fact that they work specifically on blood sugar and insulin should point us in the right direction: That AGA is caused by issues with blood sugar and insulin.

This is also strongly supported by a study which found that berberine, known as “nature’s metformin”, led to reduced levels of 5 alpha reductase in the prostate.[5] Just to reiterate: A drug that has insulin sensitizing and blood sugar lowering effects was specifically shown to decrease 5 alpha reductase, the enzyme that converts testosterone into the much stronger DHT.

Summary of correlations

If it looks like a duck, swims like a duck and quacks like a duck, it likely is a duck.

There are three disease states that are statistically strongly correlated with AGA: metabolic

5 Youn et al.: Berberine Improves Benign Prostatic Hyperplasia via Suppression of 5 Alpha Reductase and Extracellular Signal-Regulated Kinase *in Vivo* and *in Vitro*

syndrome/diabetes type 2, cardiovascular disease (CVD) and prostate hyperplasia (BPH). Those three are all known to be caused by glucose/carbs/insulin. I am suggesting that the root cause of these three diseases (that are correlated with AGA) is the same as the root cause of AGA.

There's also female PCOS - which has an identical hormonal profile to male AGA and also leads to hair loss in women. This hormonal profile is most often caused by 1) insulin resistance, 2) carbohydrate and sugar intake, and 3) lack of (right) exercise. These three factors are the factors of primary insulin resistance. Sometimes, it is also caused by stress – cortisol, the stress hormone, leads to insulin resistance. Please note however that there are less common forms of stress as well, like crash dieting, overexercising, and lack of sleep. The same applies to inflammatory PCOS, which also is known to cause insulin resistance, though it is not perfectly understood how exactly. Inflammatory PCOS is caused by inflammatory diet (high omega-6 content, lots of fried foods, consumption of a lot of meat, smoking). Stress-related and inflammatory insulin resistance can be considered secondary or indirect insulin resistance.
In all cases, however, it boils down to insulin (the modulator of carb/sugar storage) and carb/sugar levels.

Let us summarize all this in table form:

Metabolic syndrome & diabetes type 2	**Cardiovascular disease**	**Prostate hyperplasia**	**Polycistic ovary syndrome (PCOS)**
• Statistically strongly correlated with AGA • Caused by insulin resistance, too much carbs/sugar intake, too little physical exercise, stress, lack of sleep	• Statistically strongly correlated with AGA • Known downstream risk of the same risk factors as MetS and diabetes type 2	• Statistically strongly correlated with AGA • Known downstream risk of the same risk factors as MetS and diabetes type 2	• The hormone profiles of AGA and PCOS resemble one another • Hair loss is a common symptom of PCOS • The known root causes of PCOS are: 1. Mismatch between carb/glucose intake and physical activity levels 2. Inflammation (e.g. through diet or smoking)

			3. Stress/cortisol and lack of sleep

One of the central hypotheses of this document, although this is not an original thought and has been expressed by other researchers before, is that the root causes of AGA and PCOS are identical. (Or, more precisely, three of the four root causes of PCOS are the root causes for AGA, because PCOS cause 4, hormonal pill or pregnancy related PCOS, does not apply to men.)

Special mention #1: Scleroderma/systemic sclerosis

For the sake of completeness I am also mentioning scleroderma, the dermal presentation of systemic sclerosis, here. This disease is as far as I know not statistically correlated with AGA. However, I am mentioning it here shortly because it shares one mechanism with AGA: Infiltration of the dermis by pro-inflammatory substances (like TGF-β) and repair agents (like calcium) that stem from vascular damage. This will be elaborated later on in this document. The mechanism of vascular-to-dermal inflammatory substance spillover is, according to my hypothesis, part of the pathogenesis of AGA.

Special mention #2: Sebum and oily scalp skin

Many people losing their hair report having an oily scalp or shiny forehead. This is no coincidence. There are two connections between factors already mentioned before in this chapter and sebum (skin fat/oil) production rate: Diet and lifestyle. The connection between diet and sebum production speed and amount is well established in the literature. The link between lifestyle and sebum, on the other hand, not as much.

Aspect 1: Diet

It is well established in the scientific literature that the most important factor in high levels of sebum production is diet. Out of the dietary factors, the glycemic load plays the biggest role, although other dietary components like dairy can also play a part. In the following I will provide excerpts from several scientific papers that highlight this connection.

S. Vora et al.[6] note that there is a direct correlation between the amount and speed of sebum excretion and the levels of IGF-1. IGF-1 is elevated due to high carb/sugar or high protein intake:

> *"It was seen that there was a positive correlation between the amount of MFSE and serum IGF-1 (Fig. 1; R2 = 0.69; P = 0.0001). Moreover, this was true in both men and women (Table 1). It has recently been shown that IGF-1 can increase lipid production in sebocytes in vitro via the activation of IGF-1 receptor through multiple pathways. 8 Together, our data suggest that increased IGF-1 could lead to increased sebum secretion."*

6 S. Vora et al.: "Correlation of facial sebum to serum insulin-like growth factor-1 in patients with acne", DOI: https://doi.org/10.1111/j.1365-2133.2008.08764.x

Okoro et al.[7] noticed that insulin, which gets released into the blood stream in response to carbohydrate or sugar intake, increases the number and size of sebocytes as well as the amount of sebum produced:

> *"Insulin induces an increase in the size and number of sebocytes, as well as lipogenesis and inflammatory response."*

A study from Korea by Lim et al.[8] tested different dietary patterns to see if they lead to different rates of sebum production, and they did:

> *"In conclusion, we demonstrated that specific dietary patterns were associated with sebum content, skin hydration and pH in healthy Korean adults and that those associations were affected by sex."*

One specific study[9] came to the conclusion that a low-glycemic load diet is able to significantly decrease sebum production:

> *"Low glycemic load diet has been demonstrated to be able to correct the increased sebum production [...] All these findings suggest that dietary habits, supplying substrates for the sebaceous lipid synthesis, can be involved in the sebum production mechanism. [...] Caloric restriction has been shown to dramatically decrease the sebum secretion rate."*

While sebum production is not a disease like the other correlations in this chapter, it still points in the same direction: Diet. Many hair loss sufferers wonder why they have shiny foreheads and oily scalp skin. The cited studies provide an explanation.

Aspect 2: Lifestyle

The second aspect in sebum production is, I believe, exercise, stress and sleep – summed up as "lifestyle". However, unlike with diet, I cannot provide scientific sources for this, but only my own experimentation.

I have performed three experiments and checked, although not properly or scientifically quantified, my own sebum production for lack of proper tools.

For 10 days each, I have followed one of three different lifestyles:

1. High-carb diet, mostly consisting of white rice and potatoes, and no exercise (less than 2,000 steps a day, no sports).
2. Medium-carb balanced diet (meaning also lots of vegetables) with plenty of exercise (3 sessions of strength exercise in a gym of 1 hour each, 2 runs of 30 minutes each, so 5 exercise sessions in ten days for a total of about 5 hours of exercise in one week)
3. 10 days of sleep deprivation (between 3 and 4 hours per night), no exercise (less

7 Okoro et al.: "Insulin and the sebaceous gland function", DOI: https://doi.org/10.3389/fphys.2023.1252972

8 S. Lim et al.: "Dietary Patterns Associated with Sebum Content, Skin Hydration and pH, and Their Sex-Dependent Differences in Healthy Korean Adults", DOI: 10.3390/nu11030619

9 M. Picardo et al.: "Sebaceous gland lipids", DOI: 10.4161/derm.1.2.8472

than 2,000 steps a day, no sports), balanced medium-carb diet.

In settings 1 and 3, my sebum production picked drastically up within three to four days after starting the experiment run. After the third or fourth day, every afternoon my forehead would be very shiny. When wiping my forehead with my palms, they would be sticky from sebum.

In setting 2, on the other hand, my skin remained completely free from sebum for the whole 10 days. Even in the evenings, right before going to bed, my forehead skin was not oily in the slightest.

These three short experiments should show that the sebum issue is not about diet per se, but about the balance of carb/sugar intake and its burn through physical exercise. (Experiment 3, with sleep deprivation, can be explained though cortisol raising blood sugar). I am quite aware that the study population size of n=1 (only me) is far from good practice but unfortunately there is only little literature on the connection between exercise and sebum production. This is in contrast to diet where literature support for the connection is very strong.

Hereditary components of AGA

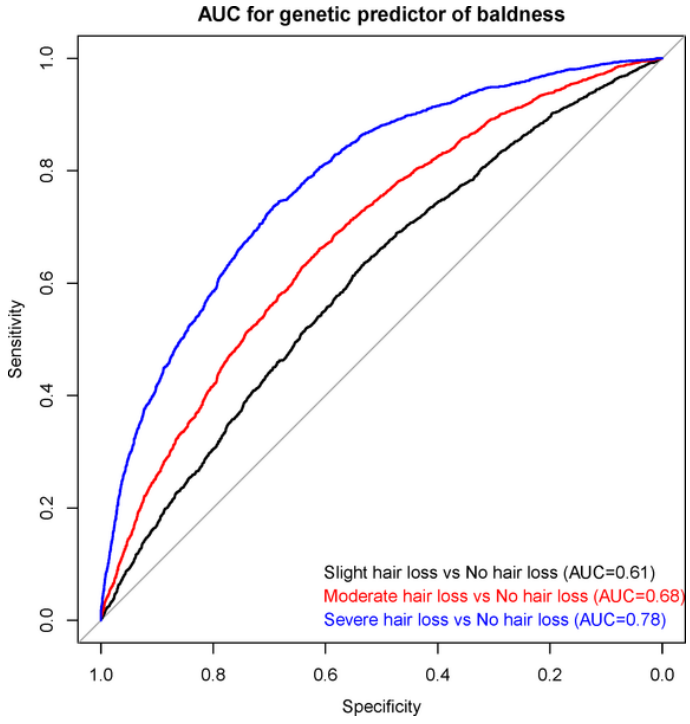
While AGA is not genetic destiny (as should be clear from the two studies cited in the introduction), there is a genetic and epigenetic component to it. Possibly there is also a hereditary but non-genetic component to it as well.

Epigenetics

In terms of epigenetics, a study found that daughters of women with PCOS also have higher 5-alpha reductase activity in early childhood[10]. This might either hint at a higher baseline 5ar level or at a greater propensity to less efficient glucose metabolism. Either way a tendency towards hyperandrogenism seems to be passed on from mothers to daughters. This might also be passed on from mothers (or both parents) to sons too. If so, it would mean that your mother's metabolic health has impact on your metabolic health as well.

Genetics

In the paper "Genetic prediction of male pattern baldness"[11], Hagenaars et al. performed a genome-wide association study (GWAS) to identify all statistical predictor genes that indicate added hair loss risk. While they do manage to identify various genetic variations that confer increased likelihood, they do not prove genetic destiny.



10 L. C. Torchen et al.: Evidence for Increased 5α-Reductase Activity During Early Childhood in Daughters of Women With Polycystic Ovary Syndrome

11 Hagenaars et al.: Genetic prediction of male pattern baldness

There is a prediction gap here: As 0.5 means no correlation and 1.0 (or -1.0) means full correlation, the predictive power of, for example, distinction between severe and no hair loss is only 56% (distance at 0.78 between 0.5 and 1.0). This means that there is a prediction gap of 44% - almost half the risk is not predicted by the genes identified by the researchers.

This prediction gap can be explained by various issues:

1. Hair loss degree was self-reported, which allows for a margin of error based on self-identification of hair loss degree
2. Maybe not all mutations were identified
3. The remaining risk is explained by epigenetic factors
4. Non-genetic factors explain the prediction gap

After reading this document, it should be evident that this author's document favors the fourth interpretation.

I assume there to be a parallel to a genetic disease that occurs only on Iceland called Hereditary Cystatin C Amyloid Angiopathy (HCCAA)[12]: This disease confers a vulnerability that only gets activated when people consume higher amounts of glucose or carbohydrates. When they do, they die much younger. When they consume only low amounts of glucose or carbohydrates, nothing happens.

I believe AGA to be the same. The AGA genes confer a vulnerability. This vulnerability only gets activated by insulinogenic factors. If you have genes that increase the risk for AGA but do not follow a diet, exercise regimen or lifestyle described as risky in this document, your hair loss does not progress. If you do not have pro-AGA genes but have any of the risk factors, you are lucky and also do not lose your hair. This is represented in the following table:

	Hair loss risk factors (diet, lifestyle, exercise) not present	**Hair loss risk factors (diet, lifestyle, exercise) present**
No AGA genes present	No hair loss	No hair loss
AGA genes present	No hair loss	Hair loss

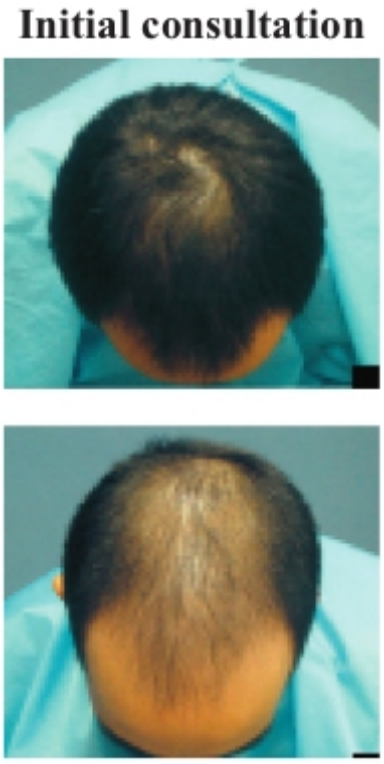
Of course, in reality this is not actually only a binary case of hair loss occurring or not occurring. In fact, there are two linear dependencies: The more pro-AGA genes you have the quicker your hair loss will be, and the more controllable risk factors (diet, exercise, stress, inflammation) are present the quicker your hair loss will be.

12 23andme blog, June 21, 2008: “Iceland’s Deadly Disease Mystery”

A more realistic model might look like this:

AGA genes\ Lifestyle risk factors	No controllable risk factors	Few controllable risk factors	Medium controllable risk factors	Many controllable risk factors
No AGA genes	No hair loss	No hair loss	No hair loss	No hair loss
Few AGA genes	No hair loss	Slow hair loss	Medium hair loss	Medium hair loss
Medium AGA genes	No hair loss	Medium hair loss	Medium hair loss	Rapid hair loss
Many AGA genes	No hair loss	Medium hair loss	Rapid hair loss	Rapid hair loss

This still means that, at the very least, we can control the speed of hair loss. May I remind the reader of the photo comparison presented at the beginning of this document:



As stated, this shows that – while both twins are prone to balding – there are ways in which the speed of balding can be drastically changed.

Non-genetic hereditary factors: Behavior

There is something that is passed on from parents to children that is neither genetic nor epigenetic: Behavior. This includes for example education, exercise and diet. If your parents cook or eat a high-carb or processed food diet which you eat for your childhood and

adolescence at home, you are more likely to cook and eat high-carb or processed food afterwards too. The same applies to exercise habits. Children of parents with bad exercise habits are also much less likely to exercise on a regular basis.

Summary on heritable traits

There are three ways in which people can inherit balding risks from their parents:

- Epigenetics
- Genetics
- Behavior and socialization

Genetics only explain part of the balding risk. The remainder is, in all likelihood, controllable by each individual through diet, exercise, and lifestyle (like stress, sleep, etc.).

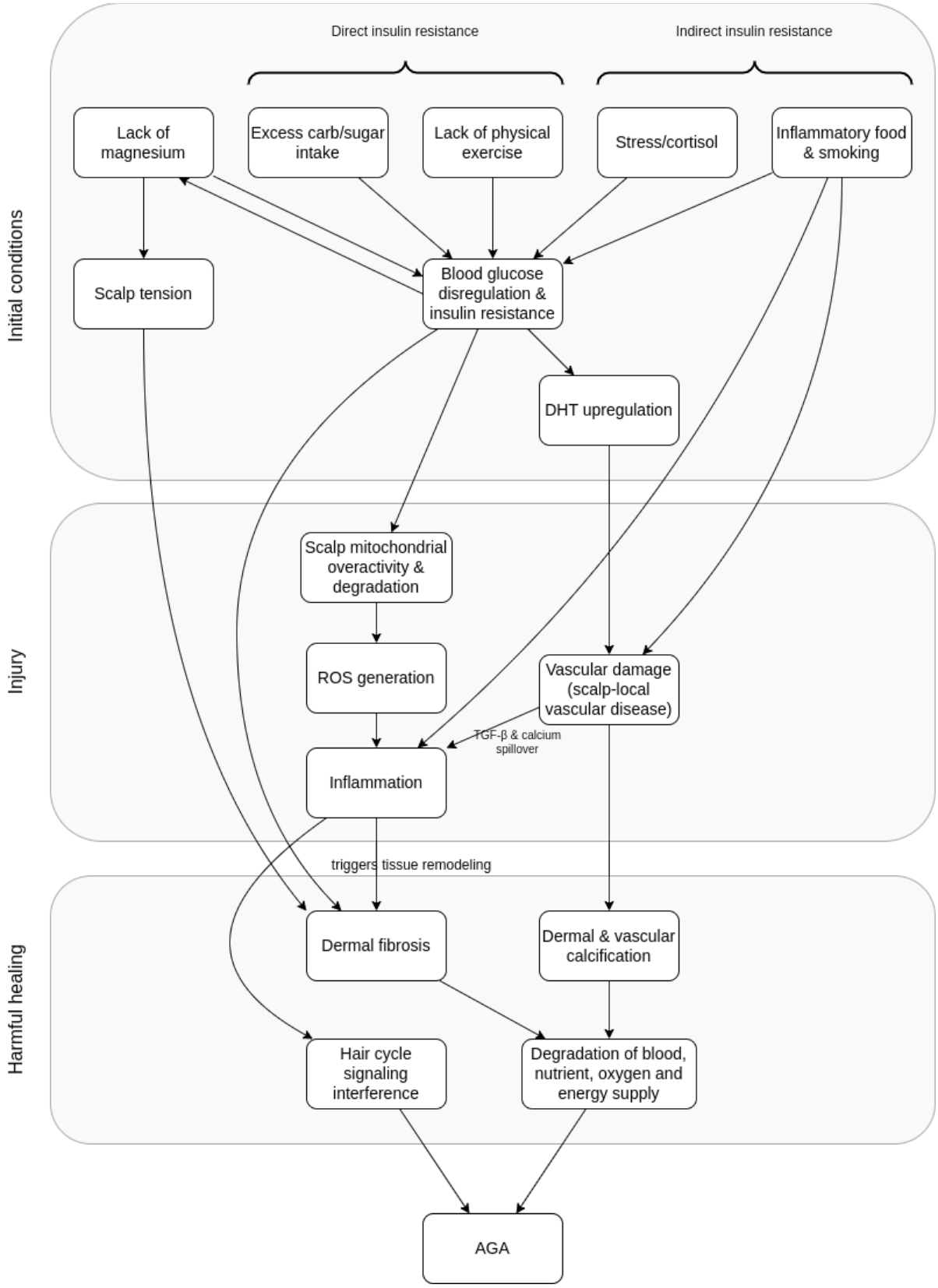
The Process (Pathogenesis Model)

In this chapter I want to propose a full chain of events from root cause all the way to hair follicle damage.
I am splitting this section into three parts:

1. **Preconditions**: The "kickstarter" and continuous fuel supply in the form of excess carbs and sugar, which starts and maintains high DHT levels on the one hand and causes vascular damage on the other. This is amplified by secondary insulin resistance contributors (stress, lack of sleep, inflammatory diet, meat over-consumption, magnesium insufficiency).
2. **Damage**: The damage that is being caused by these androgens in interaction with glucose. This includes most importantly damages to the scalp vasculature and inflammation spillover into adjacent dermis.
3. **Harmful healing**: The degenerative healing process which alters the scalp environment that makes it harder and ultimately impossible for hair to continue growing. This affects both the vasculature (which becomes calcified and impaired) as well as the dermis (which becomes fibrotic).

Please bear in mind that, as long as you do not interrupt the process, all three phases are active at the same time, just progressing in different areas of the scalp. They also act simultaneously even in the same area – because AGA is a case of chronic inflammation. That means that all phases are working simultaneously. It is not the case that you (or your scalp) is first in Phase 1 and when that is finished in Phase 2, followed by Phase 3. Rather, it is very tiny areas that can be said to be in a certain phase at any moment.

So as to give you an overview of where I am going with this, the process and pathogenesis model is summarized in the following diagram:


Direct insulin resistance
Indirect insulin resistance
Lack of magnesium
Excess carb/sugar intake
Lack of physical exercise
Stress/cortisol
Inflammatory food & smoking
Initial conditions
Scalp tension
Blood glucose disregulation & insulin resistance
DHT upregulation
Injury
Scalp mitochondrial overactivity & degradation
ROS generation
Vascular damage (scalp-local vascular disease)
TGF-β & calcium spillover
Inflammation
triggers tissue remodeling
Harmful healing
Dermal fibrosis
Dermal & vascular calcification
Hair cycle signaling interference
Degradation of blood, nutrient, oxygen and energy supply
AGA

Phase 1: The conditions for androgen elevation

How sugar and carbs lead to androgen overproduction

Why would our bodies increase androgens (like DHT) in response to elevated blood sugar to begin with?

The answer consists of two parts:

1. Androgens are increased in response to energy surplus
2. Androgens help the body deal with excess energy and are protective against excess carbs/sugar

As this chapter is supposed to deal with correlations and not with basic human endocrinology, I will keep it short.

How food intake is related to androgen levels

Step 1: Testosterone

Androgen production depends on having the basic building blocks for androgens available (fat) and on the body sensing sufficient energy. Our body has two sensor-controller sites that impact testosterone levels:

1. The pituitary gland which senses blood glucose levels and releases, depending on blood glucose levels, LH (luteinizing hormone) and FSH (follicle stimulating hormone). They travel through the blood stream to our gonads (in the case of men: testes), where they trigger the production of testosterone.
2. The liver releases SHBG in response to its own levels of stored glucose (in glycogen form) and fat (created from sugar through de-novo lipogenesis). SHBG determines how much of our testosterone is free.

So we have two sensor-controllers: The pituitary gland in the brain which controls how much testosterone is produced and the liver which controls how much of that testosterone is "free", which means bio-available.

Step 2: DHT

Testosterone is mostly a systemic hormone: It is released into the blood stream where it cruises around and has a base level that is largely identical throughout the body.

DHT on the other hand is used for "locally amplified" androgenic effects: It is produced locally wherever more androgenic action is needed. The need for locally stronger effects is also reflected in the fact that DHT is 5 to 8 times stronger than testosterone.

Production happens locally through an enzyme called 5-alpha reductase (or 5ar for short). This is the enzyme that is decreased by dutasteride and finasteride.

The question in the context of AGA is, however: What increases 5ar activity such that DHT

becomes elevated in our scalps? The answer to this is: Excessively or chronically elevated androgen levels (like testosterone or DHT). 5ar is elevated in response to high androgen levels – in other words, the activator, fuel and product of 5ar are all the same. It is a self-sustaining feedback loop that only dies down if the fuel supply is lowered or interrupted.

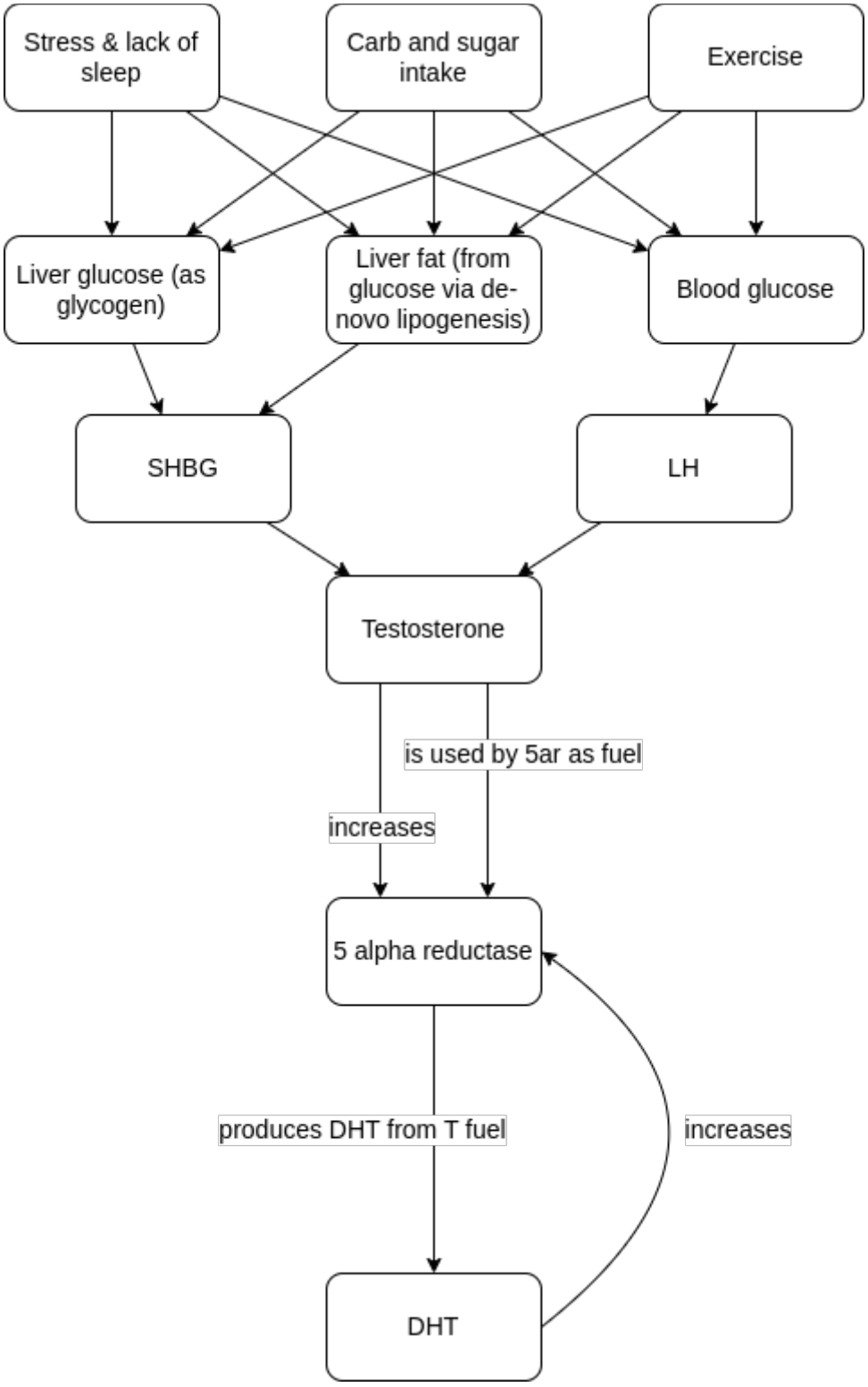
(Note for completeness and references on the androgen-5ar feedback loop: The androgen-5ar amplifying feedback loop is cell type dependent and is not present in all cell types. In general, androgen receptor activation leads to lower 5ar levels in some cells, to higher 5ar levels in others, and to no change in 5ar levels in yet others. The positive feedback loop where androgen receptor activation leads to higher 5ar levels has been confirmed in at least the following cell types: brain[13] (some), prostate[14] and pubic skin[15]. Out of these three cell types, two are relevant and likely similar to our scalp: Pubic skin and prostate. The prostate because of the known parallels in treatment, pubic skin because hair growth there is androgen dependent. A strong supporting fact for the feedback loop also being present in the human scalp is that sebum production depends on glucose intake and blood glucose levels. Sebum production rate is determined by androgens too: People with complete androgen deprivation syndrome no longer produce sebum – even with high-glycemic diets. Thus it stands to reason that glucose triggers sebum production via local androgen production. The root cause is likely glucose and/or insulin, the mediating agent is androgens, the result is increased sebum production.)

The following diagram illustrates the androgen production chain with the feedback loop between androgens and 5-alpha reductase:

13 J. Li et al: Androgen Regulation of 5α-Reductase Isoenzymes in Prostate Cancer: Implications for Prostate Cancer Prevention

14 Torres and Ortega: Differential regulation of steroid 5a reductase isozymes expression by androgens in the adult rat brain

15 Mowszowicz et al: Dihydrotestosterone stimulates 5 alpha-reductase activity in pubic skin fibroblasts and Mauvais-Jarvis: Regulation of androgen receptor and 5 alpha-reductase in the skin of normal and hirsute wome


Stress & lack of sleep
Carb and sugar intake
Exercise
Liver glucose (as glycogen)
Liver fat (from glucose via de-novo lipogenesis)
Blood glucose
SHBG
LH
Testosterone
is used by 5ar as fuel
increases
5 alpha reductase
produces DHT from T fuel
increases
DHT

How androgens help the body deal with excess glucose

Several studies have shown that androgens play a role in lowering blood sugar. It is not known if this is a protective mechanism or just a "side effect" of androgens usually being elevated when more energy (glucose) is present and enabling processes that require and burn more of that energy.

Some studies supporting this:

- A study in rats showed that resistance training alleviated diabetes. However, once a 5 alpha reductase inhibitor was administered, the positive effects were diminished. This supports the view that DHT is part of a chain that clears glucose. In another study this was confirmed to happen in cultured muscle cells.
- Another study in rats showed that DHT increased insulin levels and reduced glucose levels. Insulin is the main hormone for glucose clearance. Limitation here: This study was in female rats and in pancreatic beta cells. The cells that are more relevant for hair loss would be peripheral soft tissue (skin) or muscle (galea). Interesting nonetheless. It was also confirmed in humans.

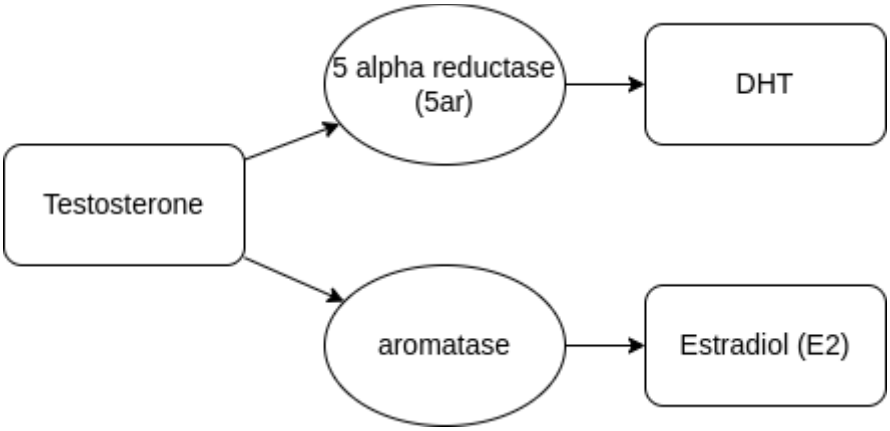
Now we know that DHT in at least two cell types (pancreatic and muscle) leads to better glucose clearance. The assumption that it does so in other cell types isn't far fetched then, like skin/hair.

What happens if we deprive humans of DHT? Their risk for diabetes goes up! This shows that DHT's effects on glucose clearance aren't only small local effects but play a role for the body as a whole.

Systemic androgen levels

While higher glucose intake and blood glucose levels lead to higher testosterone production in the short term, other aspects related to insulin resistance and MetS may lead to lower systemic testosterone levels in the long term in some individuals. The reason for this is obesity. Fat tissue is metabolically active. One of its effects is the production of aromatase – an enzyme which converts testosterone to estradiol (E2), an estrogen. In individuals who are overweight or obese, the levels of aromatase may be so high that systemic testosterone levels are below average and estrogen levels above average. (This is, by the way, one of the main reasons for "man boobs".)

The following diagram shows how estradiol and DHT are produced from testosterone:



Thus, aromatase and 5ar compete for testosterone.

You may be wondering now how lower systemic testosterone levels can still lead to hair loss. There are two reasons to this:

1. As explained before, testosterone is systemically evenly distributed but DHT is locally elevated. Testosterone may be systemically below average (by male standards, not female standards), but DHT can still be above average locally, e.g. in the scalp.
2. Androgens are protective against blood sugar issues, but if blood sugar issues are present, androgens confer higher CVD risks. As I will explain later, CVD is part of AGA pathogenesis.

Generally, when it comes to MetS and CVD, there seem to be added risks both for underweight and overweight. Underweight individuals suffer from risks of too little estrogens (which would help protect a) against CVD and b) against elevated DHT because all testosterone converted to estrogen cannot be converted to DHT). Overweight individuals suffer from risks related to too little systemic testosterone and too much systemic estrogen. The healthiest range in regards to MetS and CVD risks seems to be a BMI between 21 and 23.

The special role of fructose and sucrose

Fructose is another sugar. Without going into too much detail, fructose works a bit differently in the body than glucose but the effects are comparable.

Fructose does not directly hit the blood stream like glucose does. Instead, it has two effects:

1. Activating the so-called polyol pathway
2. Priming the body towards energy saving. Two of the mechanisms for this are insulin resistance and increased blood pressure.

For the sake of brevity, these two mechanisms will not be explained here for now. Just remember that fructose is maybe as bad as glucose, if not worse, when it comes to metabolic health.

Sucrose, which you may know as table sugar, consists of 50% glucose and 50% fructose.

The special role of alcohol

Alcohol has similar effects to sugars in your body and is metabolized in similar ways. It should thus be treated similarly in the context of AGA.

How exercise relates to androgen levels

Above I explained how blood glucose levels depend on diet. They also depend on another factor: Exercise.

Exercise lowers the glycogen and fat stores in the liver. These control SHBG production which in turn controls how much of your testosterone is "free", or bio-available.

Additionally, your body‘s energy stores have a maximum capacity. Basically, your body has three main stores:

- Liver: Glycogen and fat
- Muscles: Glycogen
- Adipose tissue

There is an order to how these stores are filled and emptied.

The first line is your liver‘s glycogen. When that is full, additional glucose gets partially converted to fat and stored in the liver. When liver capacity is full, more energy gets sent to the body: Glucose gets soaked up by empty muscle glycogen stores (and that that does not fit anymore once glycogen stores are full cruises the blood stream). Fat that does not fit into the liver anymore gets stored in adipose tissue.

The issue is that once liver and muscle glycogen stores are both full, any excess glucose needs to be either converted into fat or cruise around in the blood stream. Glucose to fat conversion is actually slow in many individuals. This means that having full glycogen stores almost always means increased blood glucose. And this, in turn, means increased androgen production – please remember that the pituitary gland senses blood glucose to determine how much LH to produce. LH controls testosterone production. And elevated blood glucose also means that liver glycogen stores must have been mostly full – meaning that the liver allows more testosterone to be free (by producing less SHBG).

How does exercise now come into play? Exercise first burns glycogen and only once glycogen is empty, starts burning fat. Liver glycogen fuels endurance exercise and the needs of the body as a whole: Brain, heart, respiration, and so on. Muscle glycogen stores are present in the main muscle groups like your legs, arms, and back. They get used up when the specific muscles are engaged. For example, strength exercises for your arms will deplete primarily arm muscle glycogen stores. Running or cycling will deplete liver glycogen stores (because of their endurance aspect) and leg muscle glycogen (because of muscle engagement).

Regular exercise empties glycogen stores. This also means that these empty glycogen stores will have free capacity to soak up glucose hitting the blood stream. Total glycogen

capacity depends on the individual and their muscle mass but typically ranges between 2000 and 3500 kcal – basically a day‘s worth of energy. There is a clear consequence here: Regular exercise, by freeing up glycogen capacity, is the best way to prevent excess blood glucose apart from limiting carb/sugar intake.

Now you understand how diet and exercise interact to determine your body‘s glucose levels: Carbs and sugar fill up glycogen stores. Exercise empties glycogen stores. When glycogen stores are full, excess glucose hits the blood stream. Excess blood glucose elevates androgens.

(The reverse is also true, by the way: Having too little glucose means that your androgen levels will drop and issues with libido, motivation and erections can follow. However, having too little glucose is usually not the problem of people dealing with AGA, as you should know by now. More commonly, when people with AGA have too low androgen levels, it is because of too much aromatase stemming from too much fat tissue. There is another issue related to overexercise, however: Cortisol, which causes insulin resistance. We will get to this soon.)

A note on body weight and AGA

By now you could think that AGA is mostly a problem for people who are overweight or obese. While this group is affected above average, normal or even underweight men can also be affected by AGA. There are three potential reasons for this:

1. Lack of muscle glycogen stores due to low muscle mass
2. Lean phenotype (caused by a slow de-novo lipogenesis rate, little adipocyte capacity, or both)
3. Presence of other risk factors (like stress, lack of sleep, overexercise, inflammatory diet)

The first reason is a lack of muscle glycogen stores. This applies especially to lean or underweight AGA sufferers. Remember that glycogen soaks up excess glucose in the blood stream? When you have very little muscle mass, you also have very little muscle glycogen capacity. You simply have less capacity that can buffer incoming glucose and which would soak excess out of the blood stream. Muscle mass is actually protective against blood glucose issues (including MetS and diabetes type 2).

The second reason is genetic. There is a part of the population which belongs to the so-called "lean phenotype". Depending on ethnicity it is estimated that these comprise about 10% of the population. These are people who cannot easily gain weight even when eating copious amounts of food. There can be two genetic causes for this: One is that genetically they have a very slow conversion rate from glucose to fat (called de-novo lipogenesis). The second is that adipocytes cannot grow or multiply. Some individuals have one of these genetic components, some both. In either case they cannot really gain weight as fat tissue. This automatically means that excess energy hits the liver and blood stream as excess glucose. The most important countermeasure against AGA these individuals can take is exercise (to burn off the liver glycogen and fat) – but not too much so as not to lose the body’s fat reserves and so as not to cause cortisol issues.

The third and last reason is that the other risk factors (stress, inflammatory diet, smoking, overexercise...) are independent of body fat.

In general however it is very well possible to have blood sugar issues and/or insulin resistance even without any extra weight or even while underweight.

In fact, underweight people have been found to suffer from blood sugar issues and related downstream diseases like cardiovascular disease at higher rates than normal weight individuals. Their rates are lower than those of overweight or obese, but still elevated. The order of CVD risk is:

1. Obese
2. Overweight
3. Lean or underweight
4. Normal weight

This risk hierarchy should also translate to AGA prevalence rates and onset ages.

I recommend keeping your BMI in the range between 21 and 23 (if you are very muscular, up to 24). If you are lean, prioritize muscle mass increases over endurance exercise. Due to cortisol reasons and muscle catabolism (leading to glycogen capacity reduction), endurance exercise may even contribute to hair loss in lean individuals.

Stress and lack of sleep

Without going into too much detail here, the main culprit here is cortisol.

You may know cortisol as the "stress hormone". It is released by your body as a response to stress: Physical or mental. The purpose of cortisol is to mobilize energy that may be needed in stressful situations. Think, for example, being pursued by an attacker or a preying animal that wants to eat you. Cortisol gets raised to give your body the energy it needs to fight or flee.

Insulin has the opposite effect: Your body uses it as an energy storage hormone. It opens "store doors" and lets energy (like glucose) inside. This is obviously not want you want in a stressful and potentially threatening situation. You want that energy to be available to you, not stored as glycogen or fat.

As such, cortisol suppresses the effects of insulin – it is "insulin resistance by evolutionary design". It prevents your body from putting glucose away in glycogen or fat stores and instead keeps it cruising around your blood stream. This is where it causes damage (we will get to that soon) and leads to androgens increasing.

Special stress: Lack of sleep

Lack of sleep or a bad circadian rhythm is a special case of this because our bodies actually use cortisol for waking us up and mobilizing energy in the morning. Why would we need to mobilize energy in the mornings? Because we just did not have any food for about 7 hours or more. Energy needs to come from stores (preferably glycogen or alternatively fat). Cortisol helps release that energy we need before we get external energy from breakfast. Lack of sleep or a misaligned circadian rhythm messes with the cortisol release curve. This leads to similar effects as stress.

Special stress: Overexercise

For the sake of completeness and because it applies to some lean people with AGA, I will shortly cover the topic of overexercise here. This mostly relates to endurance overexercise.

Remember that your body depletes glycogen stores during exercise. What happens, however, when your glycogen stores are empty and you continue exercising? Your body needs to mobilize energy somehow. Again it uses cortisol for this.

The science on when (and how much and how quickly) cortisol rises once glycogen stores are empty during exercise is not yet settled. This obviously also depends on how much your glycogen stores were filled when you started exercising. It also depends on exercise intensity – the more intense, the sooner glycogen will be depleted and the sooner cortisol will rise. Some studies found cortisol to rise after as early as 30 minutes of continuous endurance exercise, some after one hour. The truth is probably somewhere in the middle.

Additionally, having body fat seems to have some protective effects. Your body gets some energy from fat being burned so cortisol does not increase too much; the longer the energy deficit persists, the more cortisol will rise. Being lean and performing endurance exercise, however, leads to rather quick and strong increases in cortisol. If your body cannot burn enough fat quickly enough to fulfill its energy requirements, it may even catabolize muscle – which would decrease your maximum glycogen capacity. All in all, overexercise has at least two negative effects on your carb/sugar/insulin metabolism: through cortisol increase and through muscle catabolism. The latter only affects people with insufficient fat reserves.

In terms of total exercise per week, 7 hours of total exercise (endurance and strength combined) seems to be the absolute upper limit above which cortisol is almost guaranteed to be released.

Strength exercise seems to carry a lower risk of leading to cortisol increases. There are two reasons for this:

- Strength exercise increases muscle glycogen stores
- Strength exercise is not as continuous as endurance exercise, allowing your body to replete some of its energy stores before running completely on empty

I personally believe that endurance exercise should not be performed for more than 40 minutes in one go to prevent by averaging the findings of different papers. This is not a

proper metastudy however so take this with a grain of salt. And remember that there are individual factors at play here.

Inflammatory foods and smoking

Through mechanisms not entirely understood by science, inflammatory processes and ROS (reactive oxygen species) contribute to insulin resistance. As the science on this matter is currently, to the best of my knowledge, not settled, I will not elaborate on the hypotheses here for the sake of brevity.

However, I will line out the risk factors here:

- Too much omega-6, too little omega-3 intake
- Fried, deep friend and BBQed food (because of oxidized fats)
- Trans fats
- Meat
- Smoking

There were three major developments that pushed modern diets into PUFA imbalance, nowadays leaning heavily towards omega-6 dominance:

1. The development of industrial (mostly heat and chemical based) oil extraction techniques and the advent of seed and vegetable oils
2. Factory farming with grain and soy based feed instead of grazing, for meat, dairy and butter production
3. Processed foods and junk food becoming widely available and consumed - they make heavy use of seed and vegetable oils (see 1.)

While historically, the omega-6 to omega-3 ratio was between 3:1 and 1:1, in many industrialized and post-industrialized countries, the ratio is now closer to 20:1. This pushes our bodies' inflammation levels to a much higher, aggressive baseline.

One country has mostly resisted this change: Japan. Japan still consumes higher relative amounts of omega-3 and lower relative amounts of omega-6. It is assumed that this is a major contributor to lower levels of CVD and other diseases with a strong inflammatory component in Japan.

The heavy use of "vegetable oils" and seed oils (like sunflower oil, canola oil and others) on the one hand, and grain feeding practices of livestock on the other, have led to a large increase in omega-6 intake in the last few decades. Omega-6 oils are used copiously at home, in restaurants and in industrialized/processed food. Animals that eat grains rather than leafy greens or grass/hey store omega-6 rather than omega-3 in their meat. Most meat nowadays comes from grain-fed animals. In combination, these two factors lead to a large increase in omega-6 consumption. Omega-3 and omega-6 work together to determine the body‘s base level of inflammation. Omega-3 lowers it, omega-6 increases it.

Fried, deep fried and BBQed food is usually fried or BBQed with oil or fat. No matter which kind of oil or fat is used for this, strong heat will oxidize it – just at different rates. PUFAs like

omega-6 and omega-3 oxidize the quickest, MUFAs like olive oil oxidize rather quickly, and SFAs like butter, ghee, cheese or coconut oil oxidize slowly under heat. You should prefer to boil, steam or bake your food – food heating methods that evenly distribute heat are better than those that apply a lot of heat in a concentrated fashion. Also use fats that do not oxidize when heated, like butter, ghee or coconut. Oxidized fat turns into radicals (and hence inflammation) in the body.

Trans fats act mostly "erratically" and in different ways. In some ways they act like free radicals, in others they destabilize cell walls. The topic of trans fats is complicated and out of scope.

Meat and fish have a number of pro-inflammatory and insulinogenic effects that depend on a variety of factors. Some of these are always present, some of these depend on how to animals were fed and raised. Two factors that are always present in the case of meat is that their consumption leads to an increase in purines and IGF-1. Both of these can contribute to insulin resistance. Depending on how the animals are raised (e.g. in factory farms), their meat contains pro-inflammatory substances that are deposited there because the animal grew up in a stressful and potentially more pathogenic environment. If the animal has been fed with grains or soy (rather than with grass) its meat will be rich in omega-6, which is a pro-inflammatory kind of PUFA. All in all, a lot of the risk factors of meat can be avoided by buying only pasture-raised and grass-fed meat while avoiding factory-farmed and grain- or soy-fed meat. The remaining risk factors (IGF-1 and purines) can be reduced by eating less meat.

Smoking has two effects:

- Damage to the vascular endothelium and thus direct contribution to cardiovascular disease
- Direct creation of reactive oxygen species (ROS)

The first of these two consequences of smoking directly contributes towards cardiovascular disease. The second one contributes to higher baseline inflammation levels in the body. Both thus accelerate AGA.

Lack of magnesium

Magnesium plays a special role that is a little different from the broader risk factors outlined before. It is a mineral like calcium – and its intake has drastically decreased over the last few decades. One reason is a change in diets which are now less diverse, the other is the degradation of soil which simply contains less magnesium than it did a few decades ago.

Magnesium plays two roles in AGA:

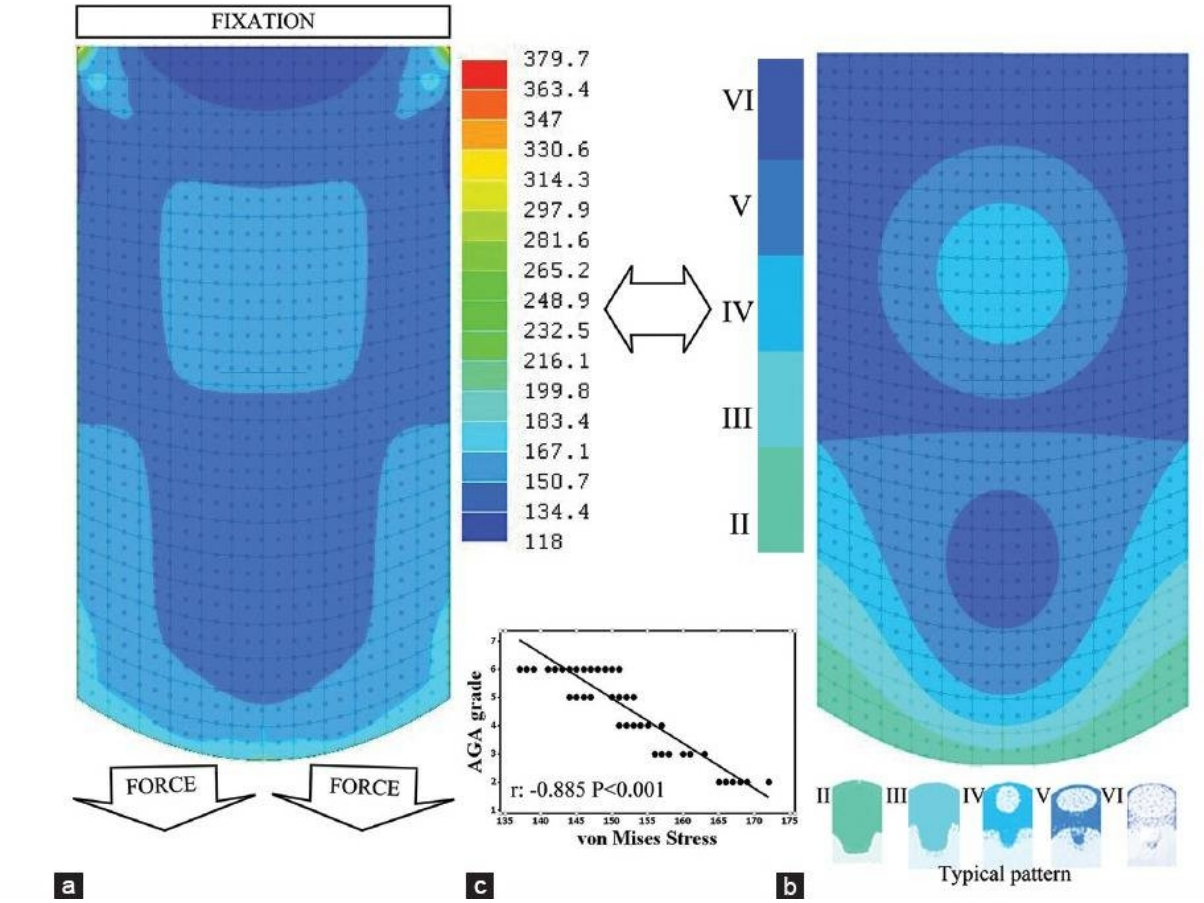
1. Glucose control and insulin resistance
2. Scalp muscle tension

The first aspect is controlled by two mechanisms which I will only mention here for completeness, but not elaborate on: Polyol pathway suppression and ATP production.

Magnesium is needed for both. Please also note that carb and sugar metabolism requires magnesium too – meaning that consuming too much of these will deplete magnesium.

The second aspect has been pioneered by two people: Rafael Tellez-Segura and Robert English.

Tellez-Segura noted in his paper "Involvement of Mechanical Stress in Androgenetic Alopecia" that a von Mises stress stretch model predicts balding patterns. This is an image of such von Mises stress models:



As you can see, they closely resemble balding patterns.

Building upon this work, Robert English developed a pathogenesis model (R. English: A hypothetical pathogenesis model for androgenic alopecia: clarifying the dihydrotestosterone paradox and rate-limiting recovery factors) and a therapy approach using a protocol of standardized scalp massages (R. English: Self-Assessments of Standardized Scalp Massages for Androgenic Alopecia: Survey Results). Some people have even used Botox to relax scalp muscles (R. English: Use of Botulinum Toxin for Androgenic Alopecia: A Systematic Review).

My personal hypothesis why scalp tension stress matters has mostly to do with Phase 3, the

healing phase, which will be covered later. In the healing phase, the body needs to decide how to build back damaged tissue. When it comes to dermal tissue, there are at least three factors at play:

1. Glucose levels
2. Tension
3. Sex hormones

Factors 1 and 2 are both related to magnesium: Magnesium helps with glucose control as mentioned above. Magnesium insufficiency also directly contributes to muscle tension – insufficient levels can lead to chronic tension. I hypothesize that this tension plays a role in the healing phase and determines, along with other factors, if dermal tissue becomes fibrotic.

It was Nicholas Sadgrove who first put magnesium in the spotlight of AGA and who gave me the idea of its involvement. He covered magnesium and its role in AGA in great length in his paper "The ‘bald’ phenotype (androgenetic alopecia) is caused by the high glycaemic, high cholesterol and low mineral ‘western diet’".

Phase 2: Injury

We have now covered the basic risk factors in Phase 1 and can move on to Phase 2: Where the conditions created in Phase 1 lead to injuries which ultimately lead to a healing process in Phase 3. The healing process in Phase 3 remodels our scalp dermis in ways that prevent future hair growth.

Vascular damage and dermis spillover

As covered in some detail before, insulin resistance and excess carb/sugar intake that are in mismatch with physical exercise are the main risk factors for cardiovascular disease. Secondary factors like cortisol (through stress, lack of sleep or overexercise) and inflammation (through diet or smoking) ultimately work by also influencing carbs/sugar/insulin. The statistical correlation between carbs/sugar/insulin and cardiovascular disease is as strong as it gets. The mechanisms how cars/sugar/insulin cause cardiovascular disease have mostly been elucidated.

One important aspect to bear in mind for the following paragraphs is that androgens seem to accelerate cardiovascular damages, as evidenced by much earlier onset and generally heavier presentation of CVD in men than women. Also keep in mind that DHT is much more powerful that testosterone.

The question is now, however, how cardiovascular disease and androgens (like T and DHT) are connected to hair loss. There are two sides to this:

1. Actual vascular damage
2. Dermis spillover

Before I go into detail on these two aspects, I want to credit the papers that gave me the inspiration for pursuing these ideas:

1. Deng et al.: Androgen Receptor-Mediated Paracrine Signaling Induces Regression of Blood Vessels in the Dermal Papilla in Androgenetic Alopecia
2. B.A Caleb Santiago Hernandez: Is androgenic alopecia a result of endocrine effects on the vasculature?
3. Fleming et al.: Is Scleroderma a Vasculopathy?
4. Pattanaik et al.: Vascular involvement in systemic sclerosis (scleroderma)

Vascular damage: Accelerated by diet and androgens

The scalp is one of the most heavily vascularized dermal tissues of the human body. There is a very fine capillary network underlying the whole scalp (which in areas without AGA works well and, according to my hypothesis, in areas with AGA does not work anymore). These fine and ubiquitous capillaries connect every single hair to the body‘s blood supply.

Finer and smaller blood vessels have one issue, however: Injury makes them dysfunctional much earlier than bigger blood vessels. They are more vulnerable to rupture from elevated blood pressure due to thinner walls and smaller diameter. Damages in their walls (from

inflammation and blood glucose) are more likely to lead to a larger relative reduction in diameter due to repair (with calcium and fat) – because they are so small. This then even smaller diameter leads to less blood flow and even greater vulnerability to future damages from mechanical pressure. Just like arteries can be completely blocked from arteriosclerotic plaque, so can finer blood vessels like those in the scalp – but because their diameter is much smaller and their walls are thinner, they will become blocked much earlier. They become “congested” or can even rupture.

In addition to the fine network that is already present, hair follicles "dock" to these capillaries using their own little capillaries that they create themselves during their early growth phase called anagen phase. This process of creating their own connection to the greater blood supply is called angiogenesis or neoangiogenesis.

As covered earlier, androgens accelerate the onset and increase damage to vasculature compared to a more feminine sex hormone profile. This means that in men who have the preconditions for cardiovascular damages met, elevated androgen levels cause such damages earlier and quicker. Several studies confirmed the connection between androgens – especially DHT – and vascular damage:

- Androgen receptors, 5 alpha-reductase activity and androgen-dependent proliferation of vascular smooth muscle cells
- Take androgens away, endothelial function becomes better: Androgen Deprivation Is Associated With Enhanced Endothelium-Dependent Dilatation in Adult Men
- Androgens and Androgen Receptors as Determinants of Vascular Sex Differences Across the Lifespan

As outlined right above, smaller and finer blood vessels will receive such damages first, while the bigger central blood vessels (that are affected in CVD) are affected later.

As specific evidence that scalp hair capillaries are affected in this way by androgens, one paper confirms this mechanism: Deng et al.: Androgen Receptor-Mediated Paracrine Signaling Induces Regression of Blood Vessels in the Dermal Papilla in Androgenetic Alopecia.

But the damage caused to the vasculature itself is not all that happens in AGA due to the combination of elevated androgens and pro-CVD risk factors (carbs/sugars/insulin, stress and inflammatory diet). This damage seems to spill over into the dermis – a mechanism known from scleroderma.

Dermis spillover

Those who have read hair loss research in the past may be familiar with a little molecule called TGF-β. TGF-β is a pro-inflammatory substance that is known to be present in AGA scalp and is one of the agents ultimately leading to degradation of the scalp of those with AGA. But where does it come from?

We can find an explanation in a seemingly unrelated disease with partially similar symptoms: Scleroderma, the dermal version of systemic sclerosis. One of the hallmarks of many

(though not all) cases of scleroderma is a loss of hair in areas that have been affected by scleroderma.

Two papers argue that scleroderma is actually a vasculopathy – a disease of the blood supply. They have noticed that agents involved in vascular damages spill over into the surrounding dermis:

- Fleming et al.: Is Scleroderma a Vasculopathy?
- Pattanaik et al.: Vascular involvement in systemic sclerosis (scleroderma)

It is my hypothesis that it is exactly this that also happens in androgenetic alopecia: The damage of the scalp's vasculature causes inflammatory processes whose agents spill over into the scalp dermis.

We know that elevated androgens combined with elevated carbs/sugar/insulin lead to cardiovascular damages. We know from other research that the 5 alpha reductase enzyme converting testosterone to DHT leads to very high levels of DHT in the scalps of those with AGA (which led to the use of finasteride and dutasteride to treat AGA). And we have practical evidence from at least one paper linked above that androgens damage the blood supply of hair follicles.

This is one of the main theses of this document: Androgens (which are also elevated from carbs/sugar/insulin/lack of exercise), especially DHT, and carb/sugar/insulin-derived cardiovascular risk factors, cause vascular damage in the scalp which also spills its agents like TGF-β and calcium over into the surrounding dermis. The subsequent healing process, presented in Phase 3, makes the scalp an unviable environment for hair growth.

Inflammation, mitochondriae, prostaglandins and hair cycling

Another issue that results from chronic inflammation, apart from the remodeling of tissue that will be described in Phase 3, is that hairs are permanently kept in a dead state because of hair cycling mechanisms.

Hair follicles actually have a life cycle consisting of several stages: early anagen (preparation, including angiogenesis), anagen (growth), catagen (transition phase – nothing much happens here), telogen (resting phase), exogen (shedding phase). Then, for a healthy hair follicle, the cycle repeats.

Part of this process is also the voluntary killing of big parts of a hair follicle's cell population. Afterwards, in a healthy follicle surrounded by healthy scalp skin, these cells are then recreated from the follicle's stem cells. The hair follicle uses pro- and anti-inflammatory markers, called prostaglandins and resolvins, to mark its own cells for destruction and to later stop (resolve) the inflammation.

And herein lies the issue: If pro-inflammatory substances are what keeps the hair follicle in one of its destructive life cycle stages that does not create hair, the follicle will remain there

as long as its environment remains inflammatory – even if it was not the natural hair cycle that caused this inflammation in the first place. For example, it has been noted that AGA scalp is high in PGD2 – a pro-inflammatory prostaglandin.

PGD2 is an activator of PPAR-γ, which is basically a growth controller. In a pro-inflammatory environment, PPAR-γ pushes so-called fibroblasts to create a fibrotic extracellular matrix – basically, fibrotic skin tissue. PPAR-γ activation also increases local glucose absorption into cells which overloads mitochondriae. Overloaded mitochondriae generate free radicals – reactive oxygen species (ROS) – that create inflammation and damage surrounding cells. Some researchers argue that mitochondrial damage plays a bigger role in AGA as well.

One of the main precursors of PGD2 are the pro-inflammatory omega-6 fats. There seem to be glucose-dependent activation mechanisms as well, however.

Phase 3: Harmful healing

In Phase 2 we have covered how the conditions from phase 1 – namely, increased androgens like DHT on the one hand and increased blood glucose and insulin on the other – create damages in the scalp‘s vasculature (blood supply) and dermis (skin). Our bodies have repair programs though – so why do these damages then lead to hair loss? This will be covered in this last phase, Phase 3: Harmful healing. In short, it is because in adult humans, healing processes do not recreate the damaged tissue as it was before.

Vasculature: Destruction - Bursting and thickening of walls, calcium deposits

The increased blood pressure and abrasion of the endothelial layer leads to physical damages in the vasculature: from rips in the walls to complete bursts and death.

In the repair process, the body deploys calcium and, though it is not sure if this is by design or not, fat. The calcium and fat mixture known as plaque leads to a shrinking of diameters of blood vessels which increases pressure forces even further. Additionally, they become more stiff, making them even more prone to more injuries in the future - a vicious cycle. After several iterations of this process, blood supply is diminished greatly and the vasculature basically dysfunctional. No more blood, nutrients and oxygen flow to follicles.

There is another peculiarity about scalp vasculature that might play a role in AGA and has been mentioned before: angiogenesis. Each follicle‘s "last mile" of the blood supply is constantly torn down and rebuilt as part of hair cycles. During anagen phase, hair follicles create their own capillaries and dock them to the body's blood supply network underneath. During telogen, these blood vessels get destroyed and reabsorbed. However, as we know, the vessels that have been damaged by blood pressure and increased sugar levels were repaired with calcium - where does the calcium go? There are strong indicators that the calcium remains in the scalp dermal tissue after the vasculature disappears. It has been noted through biopsies that the scalps of hair loss patients are calcified. This means that the dermis gets infiltrated with calcium and ostensibly hardens/stiffens.

All in all, we now have a compromised blood supply that has been filled up with calcium and is insufficient to deliver blood, nutrients and oxygen to hair follicles.

Dermis: Scarring (Fibrosis)

Now that there is damage in the vasculature of the scalp the body tries to repair it. As you may know from visible injuries you got yourself, wounds can heal in two ways: with or without a scar. Unfortunately, in AGA sufferers, it is much more likely most regenerated tissue will be fibrotic. Fibrosis hardens the scalp and makes some processes that are needed for hair growth more difficult. These processes include, for example, angiogenesis and the migration of the hair follicle up and down through the dermis in its different lifecycle phases.

There are various factors that determine how a wound heals, meaning if tissue is rebuilt as good as new or with at least some scarring. There are at least the following three:

1. Mechanical tension on the tissue
2. Whether the cells building the tissue are fueled by sugar or fat
3. Sex hormone levels

We will cover each of these separately in the following.

Mechanical tension

In general, mechanical tension is one of the factors which pushes fibroblasts towards creating fibrotic (scar) tissue[16]. In most AGA sufferer‘s scalps, tension will be high, for several reasons. One, because magnesium supply is low (caused by lack of intake on the one hand and depletion by ATP production on the other). Two, because male skulls actually grow after puberty – this effect is stronger in those with higher androgen or insulin levels. Continued growth of male skulls also explains the pattern of male hair loss: While women with PCOS or after menopause also develop hair loss, their hair loss is usually not patterned but evenly distributed. Men, however, due to their different skull shape and bigger size have more mechanical tension working on the scalp‘s dermis. The stretch force is greatest where predicted by the von Mises models shown earlier.

Substrate use (sugar or fat)

Another factor that contributes to the decision whether recreated dermal tissue becomes fibrotic or soft is whether the surrounding fibroblast cells – the cells that create the so-called extracellular matrix which is, among other things, composed of collagen – currently generate their energy from glucose or fat[17]. Generally, as long as there is sufficient glucose around, cells prefer glucose. When local glucose stores are empty, they switch into fat burn mode. Being in sugar burn mode makes it more likely for new skin tissue to be fibrotic. Being in fat burn mode makes it more likely that recreated dermal tissue is not fibrotic.

Sex hormones

The sex hormone balance seems to play a role in pro- and anti-fibrotic tendencies as well. This brings us back to the topic of 5 alpha reductase and DHT elevation. DHT and androgens seem to push the needle slightly in favor of pro-fibrotic tissue creation, while estrogens seem to be protective against fibrosis. One study[18] even found specific anti-fibrotic effects of estrogens counteracting fibrosis induced by TGF-β which may be another factor in why women are much less likely to suffer from androgenic alopecia than men.

Summing up

The scalp skin is inflamed for two reasons: On the one hand, pro-inflammatory signaling substances like TGF-β and vascular repair agents like calcium invade the skin from damaged vasculature. On the other, dietary factors increase the scalp‘s base level of

16 Wang et al.: Extracellular matrix stiffness – The central cue for skin fibrosis

17 Zhao et al.: Metabolic regulation of dermal fibroblasts contributes to skin extracellular matrix homeostasis and fibrosis

18 Avouac et al.: Estrogens Counteract the Profibrotic Effects of TGF-β and their Inhibition Exacerbates Experimental Dermal Fibrosis

inflammation. This inflammation leads to the destruction of skin tissue which needs to be recreated after clean-up. Due to three factors, the scalp skin tissue in AGA sufferers is not rebuilt the way it was, but as scar (fibrotic) tissue. These three factors are tension, substrate/fuel (glucose or fat), and sex hormone balance. This fibrotic tissue is not conductive to hair health but actually prevents two processes needed for hair growth.

Overview of Consequences of Harmful Healing

We have now covered how a healing process which fails to build back damaged vasculature and dermal tissue in its original form, instead building back "stronger" through calcification and fibrosis, creates a changed environment: stiffened, with increased mechanical tension, internally scarred, with calcium infiltration and a dysfunctional blood supply.

The consequences of these changes are manifold:

- Compromised blood supply means less nutrient supply
- Compromised blood supply also leads to lower oxygen levels (hypoxia). Hypoxic environments lead to two things:
  - Polyol pathway activation preference
  - 5ar preference, leading to even more DHT production
- Fibrosis and calcium accumulation making it harder for follicles to move up and down in the dermis as they naturally do in their life cycle
- Fibrosis and calcium accumulation also make it harder to perform angiogenesis
- Chronic inflammation keeps hair follicles in catagen or telogen because of inflammation‘s role in hair cycling

Summary

We now know that there is a healing process which destroys the healthy environment that hair follicles need to grow. On the one hand, vasculature is destroyed. On the other, dermal tissue grows back with a lot of fibrotic collagen and hard calcium deposits. There is now a tightened, fibrotic, calcified and inflamed environment that is also low in oxygen. The inflammation (which is part of a healthy hair lifecycle as well but only temporarily) keeps follicles in catagen or telogen. The tightened low oxygen environment makes it more difficult to perform angiogenesis thus preventing anagen. Blood and nutrient supply is compromised.

These tissue changes are part of a healing process that responds to vascular damages and its inflammatory processes, as well as inflammatory processes happening independently of the vascular damage. The vascular damages are caused by an interplay between androgens and vascular risk factors (like endothelial damage and increased blood pressure). Both of these are downstream effects of issues with carbs/sugar/insulin.

Recap: The AGA disease process

This chapter was a lot, so let us recap.

The process that leads to hair loss consists of three phases.

In **Phase 1**, there are preconditions that lead to issues with carb/sugar/insulin metabolism:

- Consumption of too much carbs/sugar paired with an insufficient amount of physical exercise (equivalent to insulin resistant PCOS)
- Stress in different forms (mental stress, physical stress like crash dieting or overexercise, lack of sleep)
- Inflammatory diet (like friend and processed foods, high omega-6 intake, meat consumption) and smoking

Additionally, lack of magnesium plays a special role related both to carb/sugar metabolism and to a downstream (phase 3) aspect: Scalp muscle tension.

These preconditions lead to two main outcomes:

- Production of very high levels of androgens, especially DHT
- Vulnerability to vascular damages – the very delicate and dense scalp vasculature is especially prone – because of downstream effects of insulin resistance and high blood glucose levels (like increased blood pressure and damages to the vascular endothelium)

Once these preconditions are met, there is the actual damage in **Phase 2**: Very high androgen levels and vascular risk factors combine to cause the actual injury to the scalp's vasculature. At the same time, inflammatory factors (e.g. from diet or smoking) contribute to vascular and dermal damage. The vascular damage and inflammation causes a spillover of substances like TGF-β and calcium into the adjacent dermis. TGF-β causes inflammation there as well. The spillover is identical to how it happens in scleroderma.

In **Phase 3**, the body attempts to repair the damage in the scalp's vasculature and dermis. However, in adult humans, healing processes do not recreate the damaged tissue as it was. In the case of the vasculature, calcification and plaques lead to increased stiffness and decreased diameters. These not only lead to worse nutrient supply but make the vasculature even more prone to future damages: The increased stiffness and reduced diameter mean greater pressure forces from blood pressure. The dermis grows back in a fibrotic fashion. Pro-inflammatory infiltrates also influence hair follicle cycling and keep follicles out of anagen. A lack of oxygen supply (hypoxia) seems to contribute to 5 alpha reductase upregulation.

Ultimately, the altered environment (impaired blood, nutrient and oxygen supply), inflammation (and its effects on hair cycling) and the fibrotic dermis prevent hair from growing: Pattern baldness, otherwise known as AGA.

Solutions

By now you should know most of the root causes and how they interact with each other to create the three-phase process that ultimately causes AGA. In this chapter I want to revisit the causes, some of them in more detail, and add a few that have not been covered yet – like animal protein and its effects on uric acid and IGF-1. The goal is to show you how you can halt hair loss naturally, purely through changes in diet and lifestyle.

Unfortunately, while there are hypotheses on how hair regrowth can be achieved, they are not consistently successful. I might cover them only shortly in the future because there is sufficient information about them on the internet.

Taking stock & setting expectations

As you should know by now, AGA can be traced back to primary (carbs/sugar/exercise) or secondary (inflammation/stress) insulin resistance. The question now is how to reliably track your level of insulin resistance and when to expect additional hair loss to stop.

Measuring insulin resistance

Unfortunately, GPs (and even endocrinologists without a focus of MetS/diabetes) have too little knowledge about insulin resistance to properly diagnose it. They mostly rely on fasting blood glucose and HbA1c. Fasting blood glucose is the level of glucose in your blood in a fasted state – usually in the morning before any food (breakfast or snacks) and after having skipped dinner. HbA1c is the amount of glycated (sugar-degraded) hemoglobin in your blood and roughly indicates average blood glucose over the last two to three months.

Unfortunately, both of these values are very unreliable. While their false positive rate is low, their false negative rate is high. That means: Elevated fasting blood glucose and/or elevated HbA1c each are a (rather) reliable indicator of insulin resistance. Them being normal or low, however, is not an indicator of not having insulin resistance. In the case of HbA1c the reasons are mostly genetic. In the case of fasting blood glucose, the reason is that your body is capable of controlling glucose by increasing insulin through the roof. Your blood sugar thus may look completely fine – but without measuring insulin it is not possible to see that a very high amount of insulin was needed to keep blood glucose in check. Additionally, untypical dietary or exercise behavior (or even lack of sleep) can influence your glucose level on the day your blood was taken.

So how can insulin resistance be reliably measured?

The best option is a so-called OGTT (oral glucose tolerance test) that measures glucose and insulin simultaneously. This OGTT should include as a minimum three measurements, better five. In such an OGTT test, you will consume a standardized amount of glucose and at three, four or five points in time after glucose intake, blood will be drawn. From these three, four or better five blood samples, blood glucose and insulin measurements will be made. This will

provide you and your doctor with two things:

1. HOMA-IR values. HOMA-IR is calculated from glucose and insulin and shows the ratio between them. It basically indicates how much insulin your body needs to achieve a certain blood glucose level. Having a time series of measurements also shows how much insulin rises and how quickly.
2. Your glucose curve. Depending on how well your body can still store glucose, the curve will look different: Both in how much it rises (maximum value) and how long it stays elevated. That is also why I recommend taking 5 measurements: 3 are not enough to really approximate a curve.

You or your doctor may also use a CGM (continuous glucose monitor) to get a precise glucose curve. Insulin, however, needs to be determined from blood samples.

An OGTT consisting of five measurements that simultaneously take glucose and insulin (to calculate HOMA-IR) is the gold standard for identifying insulin resistance. I strongly recommend it. It should be supported by other measurements which I will introduce in more detail below:

- LDL
- HDL
- Triglycerides
- HbA1c
- SHBG
- Blood pressure

Having an OGTT as described with these six measurements will give you a reliable indicator of whether you are insulin resistant and by how much.

The next best option is taking a single blood test that measures both fasting glucose and fasting insulin. This would also allow you or your medical professional to calculate HOMA-IR. Unfortunately it also suffers from inaccuracies caused by e.g. untypical eating or exercise behavior the day before or too little sleep. It should also be augmented with the six measurements listed above: LDL, HDL, triglycerides, HbA1c, SHBG and blood pressure.

Another option are so-called proxy indicators. The six values above (LDL, HDL, triglycerides, HbA1c, SHBG, blood pressure) change in response to insulin resistance. LDL, triglycerides and blood pressure usually increase. HbA1c increases but only in some individuals. HDL usually decreases. Additionally, liver enzymes (AST and ALT, also known as GOT and GPT) sometimes increase as well – mostly if there is too much stored energy in your liver – but this does not happen in all cases. By putting these proxy values into relation to one another, one can get a better estimate of whether insulin resistance is present than through fasting blood glucose and HbA1c alone. For example, triglycerides/HDL should be less than 1.2. But in general even all proxy values combined are less reliable than a properly done OGTT that measures HOMA-IR at five points in time.

To summarize, I strongly suggest getting a 5-measurement OGTT that captures HOMA-IR at these five points in time. As a second-best option, get a single HOMA-IR in fasted state. In both cases, augment the HOMA-IR measurement(s) by the six supportive readings: LDL, HDL, triglycerides, HbA1c, SHBG and blood pressure. Optionally, also get AST/ALT (also

known as GOT/GPT) to check your liver – the more data you can get, the better. Do not rely only on blood glucose and/or HbA1c on their own. Blood glucose and HbA1c are insufficient to detect insulin resistance because of their high false negative rates.

How long for hair loss to stop

The question is basically how long it takes to resolve insulin resistance and get your body back into an insulin sensitive state. The unfortunate answer to this is that it takes long. In the case of this document's author, it took almost two years of having a good diet and exercise regimen for glucose to reach healthy levels again. Please bear in mind that you may still lose additional hair while the insulin resistance recovery is in progress. Hair loss will only stop once a good degree of insulin sensitivity has been achieved again.

How to achieve and maintain that insulin sensitivity will be explained in the following section.

Halting hair loss

Halting hair loss ultimately consists of counteracting the main risk factors that have been introduced at the very beginning of this document:

- Diet
  - Carbohydrates and sugars
    - Supplements to help insulin and glucose control (risky!)
  - Pro-inflammatory foods
  - Usage of the right oils and fats for the right purposes
  - Animal protein
  - Food heating techniques
- Exercise
  - Not too much, not too little
- Smoking
- Stress
  - Sleep
  - Mental
  - Physical
- Lack of magnesium

Additionally, there are things you can do to slow down or even halt the "harmful healing" phase:

- Supplements to counteract calcification, reduce inflammation and improve glucose metabolism
- Reducing tension through massages

Diet

There are various aspects about diet which I will do my best to cover below.

Carbohydrates and sugar

There are a few general rules you can follow to avoid most damage. In general, avoid all sugary drinks. This includes sodas, fruit juices, sugary cocktails, sweet teas (like bubble tea or ice tea with added sugar) and the like. Also avoid all sugary or doughy desserts or those that include sweet cream: Cake, cookies, pastry and the like. Candy is obviously off-limits too. Jams/marmalade and other sweet breakfast spreads are a bad choice too. Generally, try to avoid everything that has added sugar (table sugar/sucrose), no matter if liquid or solid.

Unfortunately, sweeteners are not necessarily a good solution if you want to go for sweet drinks (like diet coke or coke zero): Several sweeteners like for example sorbitol actually get metabolized in the body into sugar. Their usage by companies is an advertising trick.

There is another class of food items you should avoid or strongly limit: Processed or

industrial carbs. This includes things like pasta and white bread. Instead, use whole grain pasta and whole grain bread. While white rice is not quite as bad, brown rice is preferable. In general, when it comes to the typical "carby side component" that is commonly used in most western meals I would recommend beans, lentils, brown rice or whole grain pasta.

Another group of foods that should be fully avoided are starchy snacks: Chips, pretzel pieces and the like. Anything in a supermarket‘s snack section is off limits.

Alcohol is metabolized similarly to sugar, so alcohol intake should be limited as much as possible.

Two hidden sources of sugar are breakfast cereals and sauces (like ketchup, BBQ sauce but many more). Avoid breakfast cereals and only buy those whose sugar comes from natural ingredients like dried fruit. Speaking of dry fruit – needs to be heavily limited. Fresh fruit is no problem.

If all these rules seem complicated, there is a way to measure and compare foods regarding their glucose-like effects in your body. These two measures are called the Glycemic Index (GI) and Glycemic Load (GL). Generally, avoid all foods with a GI of 70 or more (except fresh fruit) – foods with a GI of 70 or more are considered high GI. Limit your intake of foods in the medium GI category (GI between 55 and 69). A GI below 55 is usually not an issue.

The following table is intended to summarize the most important culprits in this category:

Food item	Harm level	Recommendation
Fructose	9	Only consume as part of fresh fruit, never consume fruit juice
Sugary or otherwise sweet drinks like sodas, fruit juices, bubble tea, ice tea with added sugar, tea with added sugar, sugary cocktails – even "diet" or "zero" versions	9	Avoid completely
Sorbitol	9	Considered a sweetener but acts in the body like fructose. Avoid completely.
Sucrose (table sugar)	8	Avoid completely
Foods with a GI of 70 or more	7	Avoid completely
Glucose	7	Avoid completely
Sweet baked items (cake, cookies, pastry)	7	Avoid completely

Starchy snacks (chips, pretzel pieces, etc.)	7	Avoid completely
Breakfast cereals with added sugar	7	Avoid completely
Processed sauces	7	Avoid completely
Foods with a GI between 55 and 69	6	Limit consumption

Non-exhaustive list of examples for some good alternatives:

Food item	Replaces
Brown rice, whole grain pasta, brown rice, lentils, beans	Mashed potatoes, white or yellow pasta, white rice
Whole grain bread	White bread or toast
Muesli or oat meal with nuts	Breakfast cereals
Sliced bell peppers with hummus dip	Potato chips

Oils and fats

Oils and fats are a rather complicated topic. There is the aspect of basic fatty acid type ut also of heat stability.

In general, the following applies:

- Do not use any cooking or frying oils ("vegetable oils" or seed oils) that primarily consist of omega-6
- Avoid "stabilized" fats like margarine completely; instead, natural saturated fats like butter, ghee, cheese or coconut may be used
- Never heat PUFA oils (like omega-6, e.g. sunflower, canola or rapeseed oil) or MUFAs (like olive oil). The only oils and fats that can be heated are natural saturated fats like butter, ghee, cheese or coconut.
- Do not eat factory farmed meat. Only eat meat from animals that grazed outside or were exclusively fed grass and hey. Grain feeding practices in factory farming mean high omega-6 content in meat.
- Do not buy baked items from supermarkets – they were usually baked with omega-6 oils like canola, rapeseed or sunflower oil.

Food item	Harm level	Recommendation
Trans fats aka hydrogenated fats	9	Avoid completely
Stabilized oils/fats like margarine	8	Avoid completely

Oxidized fats	8	Avoid completely
Seed and vegetable oils (sunflower oil, canola oil, rapeseed oil)	8	Avoid completely
Any oils which were not produced using a mechanical cold press process	8	Avoid completely

Instead, I recommend you use only the following:

Oil/fat	Recommended use
Butter	Frying, cooking, baking, cold use
Coconut oil or coconut fat	Frying, cooking, baking, cold use
Olive oil (extra virgin and cold pressed)	Cold use only

Food heating methods

Different food heating methods can make foods pro-inflammatory – because of the oils or fats used for frying, because of the heat concentrating in small spaces leading to fat oxidation, or both.

As stated before, some oils are generally unfit for heating. This mostly applies to "vegetable oils" and seed oils that often consist mostly of omega-6 PUFAs. They oxidize very quickly under heat. You should only fry or bake with SFAs like butter, ghee or coconut because they are stable against oxidation from heat.

The heat concentration methods of food preparation you should avoid are the following:

- Frying
- Deep frying
- Grilling/barbecuing/roasting

Instead, use these methods that evenly distribute heat:

- Baking
- Boiling
- Steaming

Animal proteins and meat

Meat has, regardless of its quality and where it comes from, insulin-like effects on the human body. This is because of two aspects:

- IGF-1 acts like insulin and is released when consuming animal protein

- Purines stimulate uric acid production which impairs glucose metabolism in the body

Additionally, depending on feeding practices, meat might be high in omega-6 PUFA content. This applies to almost all factory farmed meat because of grain feeding and is, as such, pro-inflammatory. This does not apply to meat of animals that were purely grass-fed or grazed outside.

Lastly, the living conditions determine if meat is pro-inflammatory: A high stress environment leaves pro-inflammatory messenger molecules in the meat which you consume when eating the meat.

The issue of animal meat, though only treated quite late into this document, is far from a minor one: It has been shown that in individuals suffering from AGA, IGF-1 is above average and IGF binding proteins are below average. This is a typical hallmark of increased meat consumption in the AGA cohort compared to healthy controls.

Some people follow a carnivore diet in order to improve their overall metabolic health. Some people have even seen improvements in their speed of AGA progression. The reason for this is that a carnivore diet is healthier than the standard western diet from a carb/sugar/insulin point of view. However, it is still less effective than a diet based on whole foods that is low in animal protein.

Putting a name on it: Whole-food plant-based

The diet I am suggesting is very close to one that already exists: Whole-food plant-based (WFPB). If you need recommendations for recipes or ingredients, google for that diet‘s name. Specifically, I am advocating for a low- to medium-carb, zero-added-sugar WFPB diet that also limits oils and meats according to the guidance in this document.

Supplements

Supplements can be used to at least slow down some of the harmful effects explained in the Process chapter. They target different phases, some even several at the same time.

Glucose metabolism and polyol pathway counteraction

These supplements help with sugar/carb metabolism.

Supplement	Effect	Recommended dose
Magnesium	Counteracts insulin resistance and aids glucose clearance (by improving ATP production and counteracting the polyol pathway)	360 to 400 mg daily (180 to 200 mg in the am, 180 to 200 mg in the pm)
Vitamin C	Counteracts the polyol pathway and is a strong anti-oxidant, helping with ROS in inflammatory processes	

Calcium metabolism

As you have learned, there is calcification happening in the AGA process. There are some supplements that can help slow this calcification down or even halt it. Some research indicates that very high doses of these supplements combined can even reverse calcification in the body‘s main arteries and veins. However, it is unknown whether this would also work in the scalp vasculature.

There are a few cases on the Internet of people regrowing hair just by supplementing vitamin D3, though all of them were very mild cases of hair loss.

Supplement	Effect	Recommended dose
Vitamin K2	Helps dissolve calcium deposits	Minimum dose 150 mcg, probably no upper dose limit
Vitamin D3	Helps dissolve calcium deposits	4000 to 6000 IU daily
Magnesium	Helps dissolve calcium deposits	360 to 400 mg daily (180 to 200 mg in the am, 180 to 200 mg in the pm)

Scalp tension

Magnesium can help with scalp tension as well:

Supplement	Effect	Recommended dose
Magnesium	Relaxes chronic muscle tension, including in the scalp.	360 to 400 mg daily (180 to 200 mg in the am, 180 to 200 mg in the pm)

Inflammation reduction

I strongly recommend algae-based omega-3 oil over fish oil because most fish oil is high in oxidized fats. Oxidized fats, as we have learned, are pro-inflammatory – which defeats the purpose of taking omega-3 supplements as they are supposed to be anti-inflammatory.

Supplement	Effect	Recommended dose
Algae-based Omega 3 oil	Helps balance the omega-6 to omega-3 ratio and thus reduces the body‘s base inflammation level	At least 1.7 g (1700 mg) per day

Blood sugar control

Be very careful with the below supplements. Once your blood sugar reaches a healthy range, they can be dangerous because at that point they can cause hypoglycemia. I recommend using those only after talking to a doctor and only if you can get regular OGTTs (oral glucose tolerance tests).

Supplement	Effect	Recommended dose
Inositol	Lowers blood sugar and improves insulin resistance	TBD by medical professional
Metformin	Lowers blood sugar and improves insulin resistance	TBD by medical professional

Combined recommended supplement list

Combining all of the above, we arrive at the following list:

Supplement	Recommended dose
Magnesium	360 to 400 mg daily (180 to 200 mg in the am, 180 to 200 mg in the pm)
Vitamin C	
Vitamin K2	Minimum dose 150 mcg, probably no upper dose limit
Vitamin D3	4000 to 6000 IU daily
Algae-based omega-3 oil	At least 1.7 g (1700 mg) per day

Exercise

First off, let us define some desirable physical traits we want for our body to protect against bad glucose control, insulin spikes or hyperinsulinemia, and metabolic syndrome:

- We want to maximize our glycogen storage capacity.
    - Keeping visceral (liver) glycogen stores empty: through regular exercise, preferably daily or almost daily
    - Increasing muscle glycogen stores capacity by performing resistance training focused on muscle hypertrophy
- We want to increase mitochondrial health and numbers
    - Endurance training in zone 2 for at least 60 minutes straight (source: Nature wants us to be fat

You can already see that we require a mix of resistance (aka strength) and endurance exercise.

There are also several things we want to avoid:

- Cortisol release. Never perform endurance training for more than 60 minutes; if your BMI is too low (below 21), do not perform endurance exercise for more than 40

minutes. Also try to stay in zone 2 as much as possible. Also don't have "total weekly overexercise", which seems to be around 7 hours per week (endurance and strength combined) that should not be exceeded.
- Muscle catabolism (which removes both glucose burning capacity and glycogen storage capacity): Never perform endurance training for more than 60 minutes; if your BMI is too low (below 21), do not perform endurance exercise for more than 40 minutes. If your BMI is below 19.5, drop endurance training temporarily until you got your BMI above 19.5.
- Loss of fat buffer capacity
    - You can lose fat buffer capacity by simply having full adipocytes. Make sure you are not in overweight territory with your BMI.
- Caloric deficit as this will drop testosterone levels (which has impact on nutrient partitioning)
- Sex steroid or growth hormone use: This will undo the positive benefits of exercise for MetS/insulin/glucose

This leaves us at an **optimal** exercise regimen that would roughly look as follows; total weekly exercise time will be between 5 and 7 hours:

1. Day 1: Full body strength workout optimized for hypertrophy
2. Day 2: Around 40 to 60 minutes of endurance exercise, depending on BMI
3. Day 3: Full body strength workout optimized for hypertrophy
4. Day 4: Around 40 to 60 minutes of endurance exercise, depending on BMI
5. Day 5: Full body strength workout optimized for hypertrophy
6. Day 6: Around 40 to 60 minutes of endurance exercise, depending on BMI
7. Day 7: Rest

This optimum is obviously not achievable for many people because of time constraints. However, you can also simply reduce the number of workouts per week - less is better than nothing. In the following example, total weekly exercise time will be between 3.5 and 4.5 hours:

1. Day 1: Full body strength workout optimized for hypertrophy
2. Day 2: Around 40 to 60 minutes of endurance exercise, depending on BMI
3. Day 3: Rest
4. Day 4: Full body strength workout optimized for hypertrophy
5. Day 5: Rest
6. Day 6: Around 40 to 60 minutes of endurance exercise, depending on BMI
7. Day 7: Rest

Stress & Lifestyle

Stress

I assume this is sort of self-explanatory. Try to avoid stress as much as possible, as stress releases cortisol which contributes to insulin resistance and worsens sugar/carb metabolism.

This includes both mental stress (like stress at work or depression) but also physical stress (like overexercising or crash dieting).

Sleep

Try to get at least 7 to 8 hours of sleep every night. Try to adjust your sleeping and waking hours with a healthy circadian rhythm, for example going to bed around 11 pm and waking up around 7 or 7:30 am.

Crash diets

Do not perform crash diets.

Overexercise

I am mentioning it here again because it is related to cortisol: Avoid overexercise. This holds especially true if you are lean and intend to perform endurance training.

Scalp massages

There is an excellent resource on the Internet on everything related to massages called Perfect Hair Health (PHH). The owner of PHH also published a paper and videos detailing these massage practices.

Summary on Halting Hair Loss Naturally

Ultimately, you want to achieve a lifestyle that prioritizes carb/sugar metabolism and insulin sensitivity while also avoiding inflammation. This means a number of things: A diet that is not high in concentrated or processed carbs, zero added sugar, minding oils and fats, eating little and only healthy forms of meat, reducing stress, and having a healthy sleep routine. Exercise is also essential, though overexercise should also be avoided. All this together should halt your hair loss completely.

Maybe, if you are very lucky, you might also get a bit of regrowth. After adopting all the changes outlined in this document I had some vertex regrowth but zero in the temples.

Reversal & regrowth

At this point in time I do not know how to reliably achieve cosmetically significant regrowth, if it is even possible at all. I want to cover both known and experimental treatments for two reasons:

- Known treatments: I want to cover these for the sake of completeness and so this document can serve as a reference and starting point for readers to do their research. This section will not be detailed on purpose.
- Experimental treatments: These are covered because these are, while not as established or effective as the known treatment, closer to the root causes. It is my intention that others can pick up from there (especially experimental approaches that aim at fibrosis reversal or calcification reversal) and maybe come at with protocols that work.

Known treatments

This category is only here for completeness. I am not covering these treatments in detail at all. They are mostly established forms of treatment. Use this section as a reference for further research on your own.

My personal stance on the treatments in this section is that they do not address the underlying issues – issues of primary insulin resistance (carbs/sugars intake and exercise) or secondary insulin resistance (inflammatory diet and smoking, stressors like stress, crash dieting, lack of sleep and overexercise). They focus on downstream effects of insulin resistance issues, like blood pressure and hyperandrogenism. That does not mean that they are ineffective. However, I personally prefer tackling the root cause (see the chapter Halting hair loss in this document) rather than downstream effects.

Minoxidil (Rogaine)

Minoxidil, sold under the brand name Rogaine but also available from other companies as a cheaper no-name product, is a vasodilator – basically, a blood pressure medication. You can apply it topically (as liquid or foam) or take it orally as pills. May provide limited regrowth. Hair that was regrown with minoxidil seems to be dependent on it, meaning that once you stop applying minoxidil, the hair you gained from it falls out again within a few weeks to months.

Some studies have found that minoxidil regrowth is strongly enhanced by microneedling (see below).

Finasteride (Propecia)

Finasteride is a 5-alpha reductase inhibitor. As such it lowers DHT levels. It was originally developed as a drug against prostate hyperplasia (BPH). One of the main issues with finasteride is that it may lead to sexual side effects (reduction in libido, erection problems). It can also lead to motivational issues (lowered ambition or depression). In some individuals, these side effects seem to persist even after stopping finasteride. One study found side

effects that remained even a few months after discontinuing finasteride in about 17% of study participants though other studies report lower rates. Finasteride may regrow some hair after a few months of taking it, but not in all individuals.

Finasteride is usually taken as a pill and thus has systemic effects (and side effects). It is also possible to use it topically in order to reduce systemic absorption and thus side effects. At this point it is unclear just how much systemic absorption can be reduced this way.

Dutasteride

Dutasteride is, like finasteride, a 5-alpha reductase inhibitor. It is stronger than finasteride – both in terms of effects and side effects. Like finasteride, it is usually taken orally as a pill but can also be applied topically.

Ketoconazole shampoos

Ketoconazole was originally an anti-fungal. It seems to have positive effects on hair loss as well. It is not known whether this is because of its anti-inflammatory properties, anti-fungal properties, anti-androgenic properties, or all three. It is usually applied topically as a shampoo.

RU-58841

RU-58841 is an anti-androgen that does not work like finasteride or dutasteride. Finasteride and dutasteride work by blocking 5-alpha reductase and hence prevent the conversion of testosterone to DHT. RU-58841, on the other hand, does not inhibit 5-alpha reductase. As far as is currently known, its mode of action is that it binds to cells' androgen receptors without activating them. By "squatting" on the androgen receptors it prevents DHT from binding and activating them.

The great theoretical advantage of RU-58841 is that, if applied topically on the scalp, it can exert its effects locally. Its propensity to spread systemically seems to be lower than that of topical finasteride or topical dutasteride. I am not aware of proper studies that have tested this assumption in practice, however.

Please note, however, that RU-58841 has not been approved by the FDA or EMA for treatment of hair loss.

Fluridil/Topilutamide, flutamide and bicalutamide

Fluridil, flutamide and bicalutamide are, like RU-58841, receptor antagonists. In other words, they block androgen receptors by binding to them without activating them.

Bimatoprost and latanoprost

Bimatoprost and latanoprost are as indicated by their names related to prostaglandins. Specifically, they are analogs of PGF2a. As prostaglandins control the inflammatory process, there are two hypotheses how PGF2a (and its analogs) help with hair growth:

- PGF2a counteracts PGD2
- PGF2a causes hair follicles to enter another stage of the hair cycle, getting them out

of the stage they are stuck in due to the chronic expression of PGD2

Spironolactone

Spironolactone is not completely understood regarding its mechanism of action but seems to have a dual effect: It is both an anti-androgen and lowers blood pressure. Thus it attacks two issues that cause androgenetic alopecia at once. It has been successfully used by women suffering from PCOS for the long time and has reportedly led to hair regrowth in women with PCOS.

Experimental treatments

In this section, experimental treatments with limited evidence are covered. I hope that researchers will, in the future, explore these in more depth.

Microneedling

Microneedling is the act of pushing a lot of very thin needles into your skin to cause fine wounds. The correct set of parameters for microneedling (wound/needle diameter, needle/wound depth, wound density, wounding frequency, healing time) seems to trigger non-fibrotic healing that also rejuvenates hair follicles. This parameter combination was researched by a company called Follica and they plan to offer it through an in-office treatment.

Some people have also reported success with microneedling by following other published protocols (i.e. not Follica's). Others, however, have had no success at all – from the same protocols.

I am mentioning microneedling here specifically because until now there is public confusion among people with AGA why some people regrow hair from some microneedling parameters (also known as protocols) and others do not – from the same parameters.

It might be because of the three criteria that determine how skin heals – with or without fibrosis. These three criteria are tension, substrate use (glucose or fat) and sex hormone balance. I have not experimented with this and have no definitive answer to whether these three factors play a role but want to raise the possibility that they do.

However, I consider microneedling to be promising because resolving fibrosis is likely a requirement for hair regrowth. Perhaps, when the three factors (tension, substrate, sex hormone balance) are right and if a correct protocol (needle length and diameter, needle spacing, needling frequency) is used, microneedling can be effective in most individuals to trigger regrowth by reliably resolving fibrosis.

Vascular calcification reversal

There are some studies that have attempted to study if it is possible to reverse vascular calcification. The context and target of these studies is central CVD in order to reduce risks like heart attacks or strokes. Central calcification can be measured with a technique called a CAC scan.

The below table contains some of these studies and their approaches:

Title	Link	Pop. size	Protocol	Improvement (%)	Duration (months)	Notes
Stop Stenting; Start Reversing Atherosclerosis	link	?	reduce smoking, hypertension, diabetes; improve dislipidemia	?	24	Meta study
Calcification in coronary artery disease can be reversed by EDTA-tetracycline long-term chemotherapy	link	77	EDTA-tetracycline chelation therapy plus nutraceutical (Vitamin C, Vitamin B6, Niacin, Folic Acid, Selenium, EDTA, l-Arginine, l-Lysine, l-Ornithine, Bromelain, Trypsin, CoQ10, Grapeseed Extract, Hawthorn Berry, Papain)	14	4	100 started, 23 dropped out; no placebo control or randomization
Reversing coronary artery calcium using a functional medicine protocol	link	1	Diet of raw veggies with zero refined carbs and low total carbs, zero grains, no dairy, little animal products (only grass-fed free-range), fasting, exercise, vitamin K2, vitamin D3, magnesium, vitamin C, omega-3 supplement, EDTA	46	12	Very small study population size, very aggressive protocol
Sugar drug reverses atherosclerosis	link	?	cyclodextrin	?	?	Mouse study

A clinical study on the effect of nattokinase on carotid artery atherosclerosis and hyperlipidaemia	link	76	3 x 100 mg nattokinase	36	6	-
A Vegan Diet Rich in Fats of Plant Origin May Reverse Coronary Artery Disease	link	1	Plant-based diet with plant-sourced fats (nuts, olive oil, avocados)	100	27	Primary endpoint was not CAC but arterial stenosis
The Relationship Between Nutrition and Atherosclerosis	link	?	B vitamins, omega-3 PUFAs	?	?	Review article
Plant-based diets and cardiovascular health	link	?	Plant-based diet	?	?	Review article
Effect of a combined therapeutic approach of intensive lipid management, omega-3 fatty acid supplementation, and increased serum 25 (OH) vitamin D on coronary calcium scores in asymptomatic adults	link	45	Supplements; Niacin, vitamin D, omega-3; low carb low sugar diet;	15	18	-

What can we learn from these studies?

First off, that there is agreement on certain factors that are definitely beneficial:

- Low-carb and low-sugar diets
- Elimination of non-fish meat
- Niacin aka vitamin B3

- Omega-3
- Vitamin D
- Plant-based diets
- Plant-based oils and fat (note: **not** seed oils aka "vegetable" oils! we are talking nuts, avocado, coconut and olive oil, **not** sunflower, canola, rapeseed oil etc.)

I wouldn't count natto (nattoinase) among the factors listed above that are broadly agreed upon because it is still rather "avantgarde", though I believe natto is probably beneficial for two major reasons: nattokinase and vitamin K2. Vitamin K2 is also not widely used in studies so far but I believe that is because the science around K2 is rather young. Only one study (with a pop size of 1) used K2. Given that K2 is very powerful for getting calcium where it is supposed to be, I assume it would be very helpful.

Magnesium was also missing except for one of the above studies though according to multiple of its actions (aid in glucose metabolism, calcium dissolution) it should definitely be beneficial.

My personal opinion is that the following substances are the most promising in reversing calcification:

- Magnesium
- Vitamin D3
- Vitamin K2
- Omega-3
- Nattokinase

In addition to that, lifestyle and diet changes as laid out in this document are also essential.

Another aspect that is very important to note: The time frames. 15% improvement after 18 months means that the recovery **process is extremely slow**.

In any case I am mentioning these studies here because the approaches used to successfully reverse central calcification might also be helpful in reversing scalp vasculature calcification. There have been no studies on this yet so this would be experimental.

Electric stimulation

A very new approach to hair loss reversal is using electric microcurrents. I am uncertain about the mode of action. While small-scale study results were promising, my main concern with this approach is that at this point it is uncertain if these microcurrents only aid in recovery of hair follicles themselves or also of the surrounding environment (vasculature and dermis). In my opinion, treatments targeting only the hair follicles without the surrounding dermis and vasculature might not be as successful in the long run. However, due to its novelty and at least some potential for good results as indicated by its initial small-scale study I am mentioning it here too. The only company currently selling such devices is Niostem.

Inositol, metformin and berberine

These were already mentioned in the supplements section above. Both inositol and metformin are blood sugar lowering and insulin sensitizing drugs. However, I am mentioning these two here again for completeness reasons because many women with PCOS noticed noticeable hair regrowth from using one of these two. They might also help with acceleration of insulin resistance reversal compared to going only a natural route.

Scalp massages

As discussed before, scalp tension is one of the three factors that determines if scalp dermis is rebuilt with fibrotic or regular tissue. As a consequence scalp massages may at least help halt or slow hair loss by slowing the rate of fibrosis. Very intense massages may also help rip apart fibrotic tissue, thus reducing the level of fibrosis. Again I am referring the reader to the website Perfect Hair Health (PHH) for information on scalp massages. The study for scalp massages can be found here: R. English: Self-Assessments of Standardized Scalp Massages for Androgenic Alopecia: Survey Results.

Summary & conclusion

Let us finally summarize the core hypotheses of this document.

On the problem side, we have found the following:

- AGA's root causes are primary insulin resistance (too much sugar/carb intake for a given physical activity level) and secondary insulin resistance (inflammatory diet, stress, lack of sleep, overexercise, crash diets, smoking...). These root causes are the same as those of PCOS (except for PCOS type 4 which is caused by birth control pills or pregnancy).
- AGA is statistically strongly correlated with metabolic syndrome, cardiovascular disease and benign prostate hyperplasia. All three are known to be caused by issues with carb/sugar over-consumption for a given activity level and insulin. The hormonal profile of men with AGA and that of women with PCOS is very similar. Three out of the four types of PCOS are primary and two types of secondary insulin resistance.
- These root causes lead to two effects:
    - In men, like in women, they lead to hyperandrogenism: Overproduction of androgens, especially DHT.
    - Carb/sugar excess and insulin issues also lead to cardiovascular disease. Carb/sugar overconsumption for a given activity level as well as secondary factors are known as the main risk factors for CVD. The damages caused include, for example, hypertension and endothelial degradation. There is also stiffening of the arterial walls due to atherosclerosis and VSMC infiltration.
- What manifests systemically as CVD disease manifests locally, in the scalp, as vascular damage. The scalp is highly vascularized – mostly with very small and thin blood vessels. Such vessels are much more vulnerable vascular damages (hypertension, calcium deposits, stiffening, endothelial injury). Hair follicles depend on angiogenesis to dock onto the body's blood supply.
- Androgens, especially DHT, are known as accelerators of vascular damage.
- Inflammatory agents (like TGF-β) and repair substances (like calcium) spill over from the damaged vasculature into the adjacent dermis. This causes inflammation of the dermis as well, triggering the body to destroy tissue which then needs to be rebuilt afterwards. This spillover is also known from scleroderma.
- Several factors present in men in general (like scalp tension) and especially men with AGA (increased scalp tension from lack of magnesium, glucose rather than fat substrate dominance, sex hormone balance) cause the body to recreate the scalp dermis as fibrotic tissue, rather than as healthy non-fibrotic tissue. This is also known from scleroderma: After the spillover from the vasculature causes the surrounding skin to be inflamed, skin is recreated in a fibrotic way.
- These two effects combined – vascular damage and dermal fibrosis as a consequence of vascular damage spillover – change the scalp dermis in a way that follicles can no longer grow. Energy, oxygen and nutrient supply is comprised.
- Additionally, inflammatory factors keep hair follicles miniaturizing and dormant because follicle's use inflammation in order to cycle through their life cycle stages. The presence of pro-inflammatory factors keeps them from entering growth stages.

Regarding the impact of genes we have found, through one study, that genes do have predictive power for hair loss – but only to a limited degree. The author of this document believes that genes only **confer a vulnerability to hair loss**. This vulnerability to hair loss only manifests if dietary, exercise or lifestyle factors are present. If the risk factors laid out in this document are avoided, hair loss will not manifest or, at the very least, will be slowed down.

On the solution side, we have concluded:

- In order to stop AGA, we need to eliminate primary and secondary insulin resistance factors. We need to match our glucose/sugar intake with activity levels. We also need to eliminate stressors (like lack of sleep, stress, overexercise, crash dieting and a few others) and inflammatory factors (like certain oils and fats, certain kids of meat and smoking). This corresponds to three of the four known root causes of PCOS. The fourth root cause of PCOS is related to hormonal changes in women (like birth control pills and pregnancy) and hence does not apply to men.
- How long it takes to achieve insulin sensitivity depends on the degree of resistance present. It might however take many months or upwards of a year.
- Measuring insulin resistance reliably requires HOMA-IR, preferably in a 3 to 5 measurement OGTT which determines HOMA-IR at 3 to 5 points in time alongside with glucose and insulin response curves. Some blood values (like LDL, HDL, triglycerides and SHBG) may serve as support.
- Established drugs like finasteride or minoxidil counter downstream effects of insulin resistance: Hyperandrogenism and hypertension. It would be more effective to tackle upstream factors, especially root causes.
- While diet, exercise and lifestyle changes should halt AGA, it is not known as of now how regrowth can reliably be achieved. There are experimental approaches but none of them are proven to work reliably for most individuals:
    - We need to eliminate fibrosis in the scalp. Two approaches to this are microneedling and massages. We have identified three factors (tension, glucose rather than fat as dominant substrate, and sex hormone balance) that determine how injured dermal tissue is recreated. Perhaps, if all those three factors are right, tissue disrupted by microneedling will be recreated without fibrosis. As of now, this is just a hypothesis and unconfirmed.
    - We need to heal the vasculature, e.g. through calcification reversal. Calcification reversal protocols are known for CVD. However, it is not known if they would also help with reversing damages in the scalp vasculature. They are also extremely slow.

You need to identify which of the three PCOS risk factors apply to you and eliminate them:

- Issues with too much carb or sugar consumption for your given level of physical activity. This corresponds to type 1 PCOS ("insulin resistant PCOS"). Unfortunately, fixing insulin resistance takes, even with a clean diet and good exercise regimen, many months. Hence you will only see androgen reduction after months as well.
- Issues with inflammation. This can be due to diet and/or smoking. Corresponds to "inflammatory PCOS".

- Issues with cortisol (the "stress hormone"). At its core, the body uses cortisol to provide the body with energy in times of need. Such times of need can be related to what you feel as stress but also what the body perceives as stress without you noticing. The cause(s) can vary a lot between individuals. In some cases it is simply what is commonly known as chronic stress, e.g. from work or in interpersonal relationships. In other cases it can be chronic sleep deprivation or a messed up sleep cycle. In lean individuals it can be due to overexercise. It can be due to crash dieting or being way too skinny. Corresponds to "adrenal PCOS".

An individual with AGA can be affected by one, two or all three of these root causes. Everyone needs to figure out for themselves which one(s) apply to them.

PS: Musings

Implications for your health

Everything we have covered so far has a few implications for your health if you suffer from AGA. These are, most importantly, that the more hair you have already lost, the more metabolic syndrome and insulin resistance, as well as their downstream effects like cardiovascular disease, likely have progressed. This also has implications for your general health risks and life expectancy.

If you are in advanced stages of AGA, meaning NW 4 or higher, I'd suggest getting a CAC scan. This is a scan to assess the progress of CVD in your body as a whole. Very likely you will have a score that will show some calcification.

You should also get some diagnostics for metabolic syndrome and prediabetes. The problem with these is that reliable diagnostics for these are quite difficult and doctors are not very educated on them. Most doctors only look at fasting blood glucose which is, on its own, a tremendously unreliable marker.

What you can do instead is either a so-called OGTT (oral glucose tolerance test) that simultaneously measures blood glucose and insulin – at at least 3 points in time, better 5. Measuring insulin simultaneously is important so you (or your doctor) can calculate HOMA-IR for these 3 to 5 points in time. Alternatively, you can get a CGM (continuous glucose monitor) and have your glucose response curves interpreted by an experienced professional.

You will also be at an increased risk for benign prostate hyperplasia (BPH).

Basically, have a look at all the diseases in the Correlations chapter of this document – your risk for having them is increased.

Why does androgenetic alopecia exist?

The whole topic of AGA makes me believe that the reasons why humans have scalp hair even though the rest of our bodies are furless might be because hair is an honest costly signal. The fact that disorders in several metabolic pathways (mineral, inflammation from diet, sugar/carbs) and CVD (blood pressure, atherosclerosis) all seem to have an impact on hair might be by evolutionary selection and hence "on purpose". That would also explain why various other diseases correlate with baldness (CVD, diabetes/MetS, PCOS, prostate hyperplasia) and even manifest in different visible ways (acne, for example). Scalp hair might be a signal for general internal health and chances of long-term survival. In animals fur is the same: Shiny, thick, long fur communicates generally good health status. Infection, disease, poisoning (think chemotherapy), age and nutrient deficiencies all show in fur. Maybe humans kept hair on their heads as the last remnant of that signaling mechanism.

Human scalp hair might be the equivalent of the peacock's tail. And this might be the reason why baldness, in many cases, takes a big measurable toll on perceived attractiveness.

Don‘t overdo the androgen reduction

Androgens have positive effects as well, especially on males. They are responsible for libido and drive. Androgen deprivation can even lead to depression. AGA sufferers may have high DHT levels in their scalp, but nuking your testosterone through eating too little carbs and exercising too much is actually possible. As often in life, you need to find a healthy middle ground.

Shiny or oily forehead or scalp

A lot of people who experience AGA notice that their scalps or their forehead close to their hair lines is shiny or oily. The reason for this is that elevated blood glucose accelerates sebum production. Sebum production is the strongest where hair follicles exist (or existed) because of the sebaceous glands that are located right next to every hair follicle and are even considered a part of hair follicles.

Reiteration on the connection of body weight and AGA

I have mentioned it before in this document but want to stress this point again: Just because primary insulin resistance (carb/sugar intake vs activity levels) or secondary insulin resistance (stress, inflammation) are at the root of AGA this does not mean that AGA only afflicts men with a few extra pounds. You can be lean and still be insulin resistant. The reasons for this are manifold:

- Secondary insulin resistance (like stress, overexercise, lack of sleep, smoking) does not necessarily translate to extra weight
- Lean people have smaller glycogen and adipose capacity and thus can buffer glucose not as well
- People can belong to the lean phenotype and gain visceral fat without gaining adipose fat

In short: It is not only people with above-average weight that will suffer from AGA. It can affect lean individuals as well.

FAQ

Until now, several questions in the context of AGA were unanswered which I believe are answered by the suggested pathogenesis model. Some of them are addressed below.

Q1: Why is DHT elevated in balding men?
A1: Because insulin resistance (both in its primary/direct form, i.e. due to too much intake of carbs and sugar for a given level of physical activity, and its two indirect forms, stress/cortisol and inflammation) leads to hyperandrogenism. This is known to happen in women with PCOS and, this document argues, also in men. The reasons for female PCOS-related hyperandrogenism and male hyperandrogenism are the same.

Q2: Why is 5 alpha reductase upregulated in the scalps of balding men?
A2: Because of a feedback loop between androgens (testosterone and DHT) and 5 alpha reductase (5ar). In some cell types, androgens upregulate the expression of 5ar and this likely also happens in the scalp.

A3: Why does balding follow a pattern that starts in the temples and vertex, as described by von Mises mechanical tension models[19]?
Q3: Because inflammation in the scalp causes the destruction of previously present non-fibrotic tissue and forces the body to recreate it. This is known as tissue remodeling. Depending on at least three different factors, fibroblasts decide whether to recreate tissue in a fibrotic or non-fibrotic fashion. One of these factors is mechanical tension. Mechanical tension pushes fibroblasts towards creation of fibrotic tissue. This happens downstream of vascular damages (and their acceleration by androgens) which summon pro-fibrotic substances into the dermis in the first place.

Q4: Why do finasteride and other 5ar inhibitors and DHT blockers work if scalp tension causes balding?
A4: Because the tension only comes into play after vascular damages and repair processes that are vastly accelerated by androgens. First, androgens accelerate vascular damages in the scalp vasculature. Then, the pro-inflammatory agents like TGF-β spill over from the vasculature into the scalp skin. Only then, tissue remodeling is triggered. Without tissue remodeling (that follows tissue destruction because of TGF-β-mediated inflammation) tension does not play a role.

Q5: Why do male and female balding patterns differ?
A5: Male skulls continue to grow past puberty. They develop a shape that concentrates stretch forces in specific places: The temples and the vertex. Male skulls are also larger than female skulls. As a consequence stretch forces on male scalps are higher than on female scalps. Additionally, women have more subcutaneous fat. Subcutaneous fat reduces stretch forces and produces aromatase, which reduces DHT production and increases estradiol levels. This has protective effects on the vasculature.

19 R. Tellez-Segura: Involvement of Mechanical Stress in Androgenetic Alopecia

Q6: How is it possible that DHT leads to beard hair growth but scalp hair loss (otherwise known as the DHT paradox)?
A6: Again, stretch/tension forces are the factor that set these two apart. Stretch forces on the scalp are high, in the face low.

Q7: Why do some men with "chubby" faces seem to be resistant to hair loss?
Q7: The "chubby" look with more facial fat is due to more subcutaneous adipose tissue. More subcutaneous adipose tissue, which is not only present in the face but usually also on the forehead and around the scalp, reduces stretch/tension forces. Additionally, fat tissue is metabolically active: It produces aromatase which converts testosterone to estradiol. This conversion has two effects: The testosterone is no longer available for conversion to DHT and less DHT is produced. Secondly, estradiol has protective effects on the vasculature. Subcutaneous fat, however, only confers protective effects if it is not overpowered by negative effects on the vasculature and hormone levels by obesity. Obesity does not confer protection against AGA because it is usually (but not always) accompanied by insulin resistance.

Q8: Why are cardiovascular disease (CVD) and androgenetic alopecia (AGA) correlated?
A8: Because AGA and CVD share steps of their pathogenesis. Vascular damage (such as: VSMC conversion or infiltration, vasoconstriction and increased blood pressure, endothelial damage) is an important step in both.

Q9: Why is there calcium in the scalp of men with AGA[20]?
A9: Because the vascular damage in the scalp, which the body tries to repair with calcium, spills over into the dermis (skin).

Q10: Why are the hormonal profiles of women with PCOS and men with AGA similar?
A10: Because they share the same root causes. These root causes (primary/direct and two types of secondary/indirect insulin resistance) cause overproduction of androgens, known as hyperandrogenism.

Q11: Why are androgenetic alopecia (AGA) and metabolic syndrome (metS)/diabetes type 2 correlated?
A11: Because they share the same root causes. These root causes are primary/direct insulin resistance and two types of secondary/indirect insulin resistance.

Q12: Why do men have cardiovascular disease between 7 and 20 years earlier than women?
A12: Because androgens seem to accelerate vascular damages. This is also the reason why women are usually only affected by scalp hair loss after menopause when their hormonal profile changes.

20 F. Hoelzel: Baldness and Calcification of the "Ivory dome"

Q13: Where does TGF-β in androgenetic alopecia come from?
A13: TGF-β enters the balding scalp from damaged scalp vasculature. The vascular damages cause TGF-β upregulation. This mechanism is known from scleroderma.

Q14: How are androgenetic alopecia (AGA) and scleroderma connected?
A14: They share an important step in their pathogenesis: Spillover of vascular inflammatory substances from the vasculature into the surrounding dermis (skin).

Q15: Why can skinny, lean or normal weight men lose their hair even if hair loss is tied to insulin resistance?
A15: Insulin resistance can be present in lean, skinny or normal weight men as well, for two reasons: The so-called lean phenotype, which is estimated to affect around 10% of the population, stores energy primarily around the liver instead of storing it in visible fat tissue. In this case, excess carb/sugar intake paired with insufficient exercise leads to glycogen and fat overaccumulation in the liver which pushes the body towards diabetic/metS metabolism. The second reason is that insulin resistance can also be caused by indirect causes such as inflammation (through diet and smoking) or cortisol (through stress, lack of sleep, bad sleeping patterns, crash diets, overexercise, being underweight). On top of the reasons that can lead to insulin resistance, skinny/lean/underweight men also miss protective factors: Subcutaneous adipose tissue in the face and on the scalp reduces tension forces and hence reduces fibrosis. It also produces aromatase which lowers DHT levels and produces estradiol. Having some subcutaneous fat stores also prevents cortisol increases in times of energy need (e.g. during exercise or after not having eaten for a longer time). Being too skinny is hence damaging.

Q16: Why do women not go bald?
A16: Because the regular female hormonal profile confers protection against vascular damages compared to a more androgenic hormonal profile. This is the same reason why men are affected by cardiovascular disease between 7 and 20 years earlier than women. Women can however lose their hair, under two circumstances:

1. If they acquire PCOS. PCOS is caused by direct insulin resistance or two kinds of indirect insulin resistance (related to stress/cortisol and inflammation). (In women, it can also be caused by hormonal birth control pills or pregnancy, both of which do not apply to men.) PCOS changes the typical female hormonal profile to become more androgenic. This is known as hyperandrogenism. Women with PCOS also have a higher cardiovascular disease risk[21].
2. Past menopause. Menopause changes the hormonal profile of women.

21 P. Scicchitano et al.: Cardiovascular Risk in Women With PCOS

Glossary

Term	Explanation
5ar	S. 5-alpha reductase
5-alpha reductase	Enzyme that converts the androgen testosterone into the much stronger androgen DHT
AGA	Androgenetic alopecia, sometimes also called androgenic alopecia
Androgen	Male sex hormone (but present in both males and females)
Androgen receptor	Receptor in cells where androgens dock to exert effects. Without androgen receptors, androgens have an effect. The androgen receptor is targeted by some drugs which, instead of working on androgen production, focus on androgen receptors to remove androgens' target site.
AR	S. Androgen receptor
Aromatase	An enzyme converting the androgen testosterone into the estrogen estradiol (E2)
Arteriosclerosis	Hardening of the arteries because of vascular damage. This damage is repaired using "plaque", a mixture of fat and calcium.
Atherosclerosis	Hardening of the plaques that line the vasculature after damages.
BPH	Benign prostate hyperplasia. The growth of the prostate beyond normal size.
Cortisol	One of the body's stress hormones (the other well-known one is adrenaline) and also one of the body's energy balance hormones. Causes energy release from stores and prevents energy storage. Hence causes insulin resistance "by design".
CVD	Cardiovascular disease
De-novo lipogenesis	Process that converts fat from sugars or carbs
DNL	S. de-novo lipogenesis
DHT	S. Dihydrotestosterone
Dihydrotestosterone	An androgen and a much stronger version of testosterone
Dutasteride	A 5ar inhibitor that lowers DHT levels.
E2	Estradiol, an estrogen
Estrogen	Female sex hormone (but present in both males and females)
Finasteride	A 5ar inhibitor that lowers DHT levels. Originally developed to treat BPH. One of two FDA-approved drugs to treat AGA.
Fructose	One of the most common forms of sugar (the other common ones are glucose and sucrose)
Glucose	One of the most common forms of sugar (the other common ones

	are fructose and sucrose). The body converts carbohydrates into glucose.
Glycogen	Stored form of glucose. The body's biggest stores are found in the liver and the muscles. Muscle mass determines total glycogen capacity. Carbohydrates and sugar consumption fills glycogen, exercise empties glycogen.
Inositol	A blood sugar lowering and insulin sensitivity improving drug
Insulin	Opens cells in order to take in and store energy. One of the body's energy balance hormones. Can be disabled by cortisol.
LH	S. luteinizing hormone
Luteinizing hormone	Produced in the brain, more specifically the pituitary gland. Controls how much testosterone is produced in the testes.
Metformin	A blood sugar lowering and insulin sensitivity improving drug
MetS	Metabolic syndrome. A series of metabolic changes causes by direct and indirect issues with carb/sugar metabolism and insulin.
Minoxidil	A blood pressure lowering drug. One of two FDA-approved drugs to treat AGA. Sold under the brand name Rogaine.
MUFA	Mono-unsaturated fatty acid (contained e.g. in olive oil)
Omega-6	Part of the PUFA kinds of fats, mostly pro-inflammatory
Omega-3	Part of the PUFA kinds of fats, mostly anti-inflammatory
PCOS	Polycystic ovary syndrome
PGD2	A pro-inflammatory prostaglandin
Prostaglandins	Inflammation controlling signaling molecules
PUFA	Poly-unsaturated fatty acid. The two main types are omega-6 (e.g. contained in sunflower oil, canola oil, rapeseed oil) and omega-3 (e.g. contained in flax seed, some nuts, meat of grass-fed animals, algae, some fatty fish)
ROS	Reactive oxygen species. A form of free radical. Causes inflammation and general damage.
Sex hormone biding globulin	Transport molecule produced by the liver. Levels depend on liver energy storage balance. Determines which relative share of sex hormones (like testosterone, DHT and so on) is "free" and hence bio-available. Higher SHBG levels bind more hormones and mean lower free share. Lower SHBG levels mean higher free share.
SFA	Saturated fatty acid (contained e.g. in butter, cheese, ghee or coconut fat/oil)
SHBG	S. sex hormone biding globulin
Sucrose	Consists of 50% glucose and 50% fructose. One of the most common forms of sugar (the other common ones are fructose and glucose)

Vasculature	The totality of all of the body’s blood vessels
Vasoconstriction	The tightening of blood vessels. Leads to increased blood pressure and increased mechanical force on the vasculature. Increases likelihood of damage.
Vasodilation	The relaxation of blood vessels. Leads to decreased blood pressure and decreased mechanical force on the vasculature. Decreases likelihood of damage.