HIGH SCHOOL EDITION
Journal of Student Research
Volume 12 Issue 3 (2023)

Alopecia: An Overall review including causes, COVID-19, diet, and treatments

Rizan Khan Muhammad

Tesoro High School

ABSTRACT

Despite the hopes of many, the autoimmune disease alopecia is not a curable disease. Fortunately, there is lots of information and research about the disease, its underlying mechanisms, as well as old and new treatments including light therapies, injectables, hair transplantation, and even supplements and OTCs. Furthermore, this paper will explore the various side effects, cost, and effectiveness of these therapies based on experiments done with them. This paper will introduce various non-scarring alopecias such as alopecia areata, androgenetic alopecia, and telogen effluvium and describe what makes them occur. This paper will also explain the large impact of diets as well as different types and components of each diet that can contribute to controlling and preventing alopecia. Explore the underlying mechanism of the effects of COVID-19 and the COVID-19 vaccine on the body that can cause alopecia.

Introduction

Alopecia is an autoimmune disease that occurs when the standard hair growth cycle is slowed or interrupted which can lead to a loss of hair in various patterns. There are many different forms of Alopecia that can be scarring and non scarring. This research paper will focus primarily on non scarring alopecias such as alopecia areata, androgenetic alopecia, telogen effluvium, and tinea capitis. Alopecia affects between 50 to 75 percent of persons over 50 and many children experience their first case at around 16 years old. There is no singular cause for alopecia, but there are a number of things that have a correlation with alopecia and autoimmune diseases that could be the cause for alopecia. In this paper we will be covering the topics that have a correlation with alopecia, what happens within the body that creates the underlying mechanism that causes alopecia, as well as the treatment options and how effective they are for the amount of side effects they give. A trigger that has been shown to cause alopecia is COVID-19 and the COVID-19 vaccine. After having COVID or receiving the COVID vaccine rates of Alopecia have increased. Inflammation and diet have shown a correlation with alopecia. Genetic susceptibility is also a major factor in contracting alopecia and for any of the previously listed causes to take effect. Finally, some of the treatment options for treating alopecia that already exist and will be discussed are therapies such as topical, oral, light, and hormonal therapies, this will also cover new and upcoming therapies such as JAK inhibitors and clascoterone.

Different types of alopecia and what makes them occur

Alopecia areata

Alopecia areata is characterized through patchy hair loss all over the head. It includes having short hairs, black and yellow dots, as well as broken hair shafts. This condition can also lead to total hair loss. Alopecia areata is an auto-immune disease in which T lymphocytes interact with a follicular auto-antigen presented by a perifollicular or follicular cell (Mahmud et al). The T lymphocytes then create inflammatory cytokines which makes the anagen phase of hair growth unable to continue, which results in hair loss.

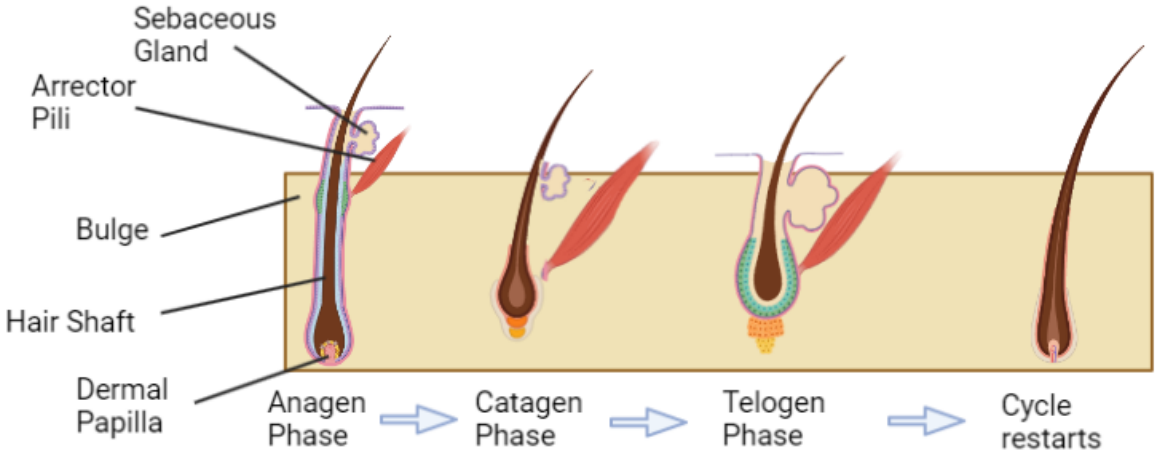
Androgenetic alopecia

Androgenetic alopecia is categorized in men as thinning of frontal and vertex of the scalp or hair loss of the entirety of the scalp except for some hair remaining at the occiput and temporal fringes. In women it is categorized by hair thinning of the vertex with hair remaining at the front of the scalp. In this condition hair follicles grow smaller over time which leads to a bald appearance. This happens because the anagen phase of the hair growth cycle gradually gets smaller and the telogen phase grows longer. This means that the resting phase of the hair grows longer. The

anagen phase determines the length of the hair so the maximum length of the newly grown anagen hair becomes shorter than the hair that grew before it, leading to miniaturization of the hair and eventually a bald look (Sheth).

Telogen Effluvium

Telogen Effluvium is categorized by clumps of hair falling out when using a hairbrush or when in the shower. This type of alopecia usually occurs during or following physiologic or emotional stress. There are five different types of mechanisms in which hair is shed in telogen effluvium. The first is immediate anagen release in which the hair follicles exit the anagen phase of hair growth and enter the telogen phase too early which leads to increased shedding. The second mechanism is delayed anagen release in which the anagen phase of the hair growth cycle is extended leading to heavy telogen shedding(Asghar et al). The third mechanism is short anagen syndrome, in which the anagen phase is shortened. Short anagen syndrome is known to be behind most chronic telogen effluvium cases. The fourth mechanism is immediate telogen release, in which the telogen phase is shortened which results in a massive release of club hair (Asghar et al). The fifth mechanism is delayed telogen release, in which the telogen phase is extended and the anagen phase has a delayed transition.



Copyrighted by Rizan Khan Muhammad
Figure 1. Shows the various structures of hair follicles as well as the hair growth cycle starting with the anagen phase and eventually restarting the entire cycle.

Tinea Capitis

Tinea Capitis is categorized by dermatophyte infection of the hair shaft and follicles, people with tinea capitis usually have a patchy pattern of hair loss (Phillips et al). This disease mostly affects children. Tinea capitis is a dermatophyte infection of the hair follicles and hair shaft which means that the hair follicles and hair shafts are infected by fungi which may have come in contact with them from people, animals, and soil.

Diet and inflammation in regards to alopecia

Anti-inflammatory diets have gained much interest in recent years as they have been shown to reduce inflammation, which can be particularly helpful in autoimmune diseases. Chronic flammation can cause the overproduction of inflammatory cells into places that they do not belong within the body, which can contribute to the symptoms of various autoimmune conditions. The gut microbiota has become of interest in alopecia areata, with changes in diet having an effect on the health of the gut microbiota.

Diet And Its Effects on Androgenetic Alopecia

For androgenetic alopecia there were various diets tested such as vegan/vegetarian, paleo, hCG diet, protein rich breakfast, or consumption of fruits, vegetables, soy and alcohol. One study was conducted on 354 Taiwanese males that were given soybean drinks 3 days a week and this showed a 77% decrease in androgenetic alopecia. The conclusion of the study showed that this habit may allow protective effects against moderate to severe androgenetic alopecia (Pham et al). Another study in androgenetic alopecia was conducted on 351 caucasian subjects. The majority of these subjects reported a low consumption of fruits, vegetables, protein, and wine. Androgenetic alopecia severity was not linked with the consumption of fruits, vegetables, and protein. However, severity of androgenetic alopecia did show a correlation with a high amount of wine consumed. The mediterranean diet was also studied and showed that a high consumption of raw vegetables, cooked vegetables, cruciferous vegetables, leafy green vegetables, and tomatoes showed protective effects for androgenetic alopecia (Pham et al). This diet has many antioxidant, anti-inflammatory, and estrogenic properties so it contains many phytochemicals with anti-inflammatory and antioxidant properties (Pham et al). Therefore, it has the capacity to lower the generation of reactive oxygen species in dermal papilla cells, resulting in a reduction in the secretion of transforming growth factor B1 and promotion of hair growth (Pham et al). Furthermore, polyphenols can inhibit 5a-reductase activity. Another study also showed the importance of routine and protein intake on androgenetic alopecia with patients that ate breakfast would have a higher amount of protein intake and less hair issues while people that missed breakfast or ate their breakfast later increased their chances of getting androgenetic alopecia as well as the severity of it.

Diet and its effects on alopecia areata and telogen effluvium

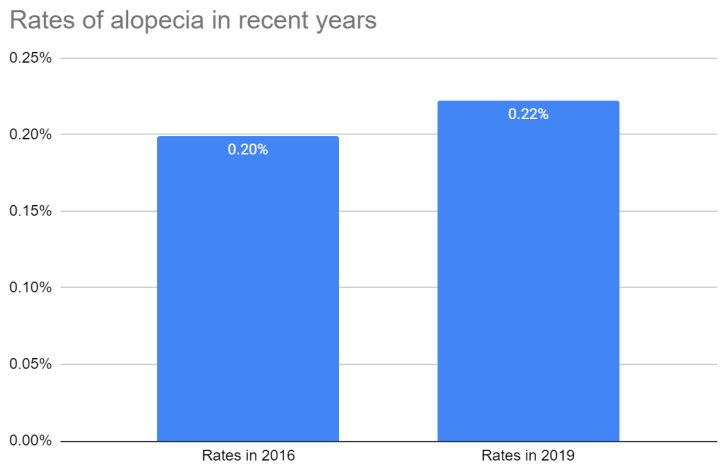
Among alopecia areata patients, a gluten free diet showed positive results. Hair regrowth occurred on parts of the body such as scalp, eyebrows, and eyelashes within two months of starting the diet. There was no recurrence of alopecia areata for up to three years after the study was conducted. A lactose free diet was also given temporarily to a 6 month-old female and a 18 month-old male but no significant improvements were made to their status of hair loss until they started a gluten free diet (Pham et al).
In telogen effluvium, many of the patients have lower levels of protein and protein is a major part of hair, so a higher intake of protein within a diet is recommended. Another link to alopecia overall was the consumption of fish. And in some cases, discontinuing the consumption of fish led to improvements in hair growth.

The Gut

Short-chain fatty acids control T cells and interleukin-10 which has anti-inflammatory properties. In the west, most diets consist of large amounts of processed foods and fats. This coupled with lower fiber content leads to smaller amounts of short-chain fatty acids and altered gut bacteria (Pham et al). Celiac disease was found in many patients with Alopecia areata. A study showed that a short-chain fatty acid pattern normalized after a gluten free diet. This diet calmed down inflammation and improved hair regrowth on the scalp (Pham et al).

COVID-19, the COVID-19 vaccine, and stressful situations effect on alopecia

Due to the recent COVID-19 pandemic cases of alopecia have shown an increase. Dermatology clinics are seeing a rise in patients with alopecia after that patient has had COVID-19. After contracting COVID-19, hair loss occurs in about 60% of patients. This is usually in telogen effluvium. When patients contract COVID-19, it is accompanied by stress, various medications, weight loss, and even nutritional deficiency(Aryanian et al). These are all factors that are linked to hair loss, and specifically telogen effluvium. It should be noted that TE usually occurs in women when they already have androgenic alopecia which could account for the emotional stress that is experienced even after a less severe case of COVID-19. Furthermore, more thyroid disorders have been found after a COVID-19 infection, and a lack of thyroid has been linked to hair loss. A vitamin D deficiency has also been linked to hair loss following a COVID-19 infection. Acute TE which lasts for less than six months, usually eases and disappears by itself. While in cases exceeding six months the hair loss becomes more chronic.



Copyrighted by Rizan Khan Muhammad

Fig 2. Shows cases of alopecia in recent years based on percentages of the world's population. Cases of alopecia are increasing as a whole.

Another type of alopecia called alopecia areata is a recurrent autoimmune disease. This type of hair loss has also shown a significant increase since the COVID-19 pandemic. Genetic factors, atopy, autoimmunity, stress, nutrient deficiency, hormonal changes, vaccination, and infections have all contributed to the evolution of this disease (Aryanian et al). Alopecia areata occurs in cycles due to stressful conditions. Alopecia areata may occur during the COVID-19 infection due to a cross reaction between viral and self antigens which, leading to a hyperimmune reaction which targets the hair follicles resulting in hair loss (Aryanian et al). Some other mechanisms are the cytokine storm which is when the body releases too many substances that are created by certain cells in the immune system which tend to have an effect on other cells. This leads to an elevation of IL-6, therefore keeping the hair shafts from elongating and the matrix cells (proteins that support and give structure to cells and tissues in the body) from growing rapidly in numbers.

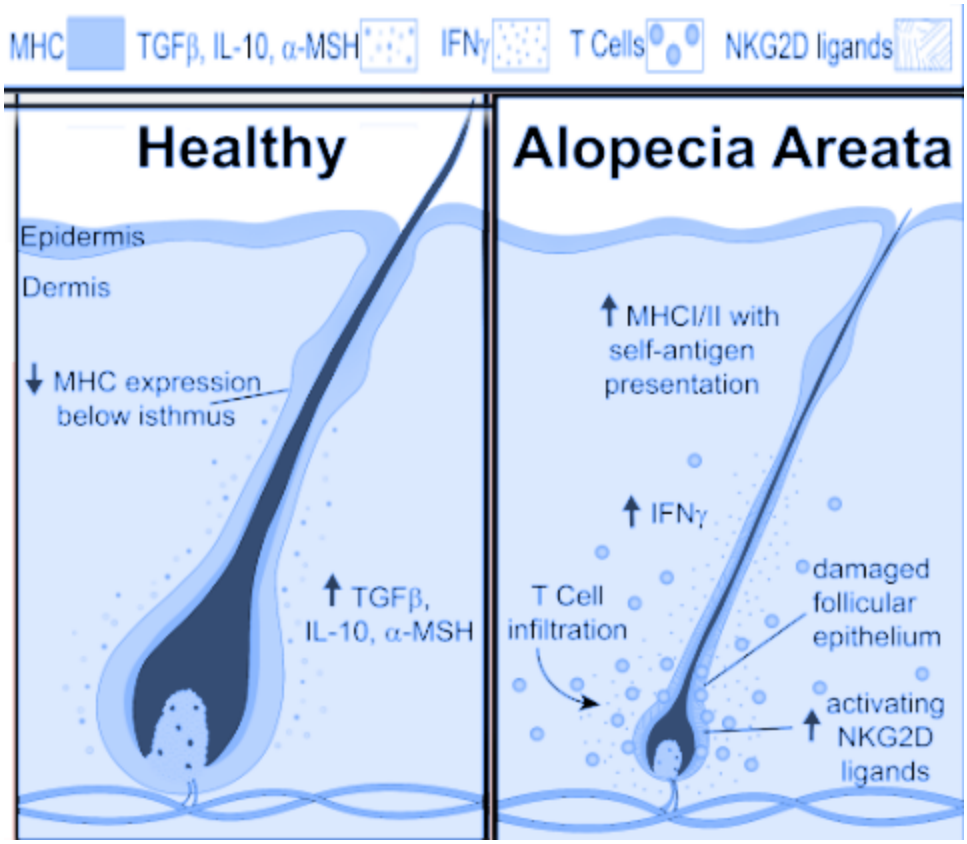


Fig 3. Shows the differences between regular hair follicles and hair follicles that are affected by alopecia areata. Some noticeable differences are the T-cell infiltration towards the dermal papilla of the hair follicle and the damaged follicular epithelium.

The COVID-19 vaccine and its role in alopecia

The COVID-19 vaccines have also shown a correlation with Alopecia. Following the vaccine, alopecia areata and its variants have been particularly high, this is either because of new cases or recurrence of previous cases (Aryanian et al). Molecular mimicry and the creation of pathological autoantibodies, could be the underlying mechanism of the COVID-19 vaccine's side effects (Aryanian et al). The vaccine may create an autoimmune/inflammatory syndrome which may lead to alopecia, but this usually occurs in patients that have genetic predisposition.

Exploring Treatments For Alopecia

There are many treatment options for alopecia such as topical therapies, oral therapies, hormonal therapies, light therapies, and injectables. For topical therapies two common treatments are, topical minoxidil and topical finasteride. These therapies are usually used for people that have mild or moderate hair loss because other methods of treatment have significantly higher side effects. The vertex and frontal parts of the scalp is where minoxidil has been shown to have the most noticeable effects. It reduces the pace of which the hair loss occurs by extending the anagen phase. Minoxidil also increases hair growth through increasing the diameter and density of the hair.(author citation). Some side effects of this treatment include scalp irritation, pruritus, and dermatitis. It should be noted that these side effects are much more commonly seen with patients that used the 5% version of the topical rather than the 2% version. Topical finasteride has been demonstrated to drastically lower plasma and scalp DHT levels.(author citation). It showed great results in hair growth and less balding. cutaneous erythema, contact dermatitis, elevated liver enzymes, nocturnal enuresis, testicular pain, headaches, presyncope, and oropharyngeal pain are some of the symptoms that may be experienced (Caserini et al).

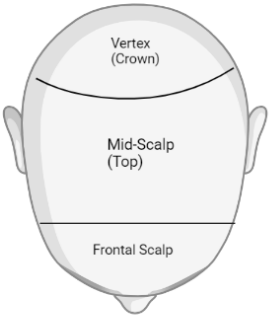


Fig 4. Shows the main sections of the scalp mentioned in the treatments section starting with vertex towards the top of the scalp, the mid-scalp towards the middle of the scalp, and the frontal scalp at the front of the scalp.

Finasteride can also be taken orally. It inhibits type 2 5-alpha-reductase enzyme which blocks the conversion of testosterone to DHT. This is a tablet that is able to be purchased over the counter which makes it very cost effective for patients that need to use oral finasteride over a long period of time. This treatment is successful in treating hair loss at the vertex, as opposed to the frontal scalp. This is why it is suggested to continue this treatment indefinitely so that any hair that is left after treatment can continue to grow safely (Nestor et al). There are a variety of side effects involving this treatment such as hypertension and dizziness, but there also a variety of sexual disorders that can arise from the consistent use of finasteride such as erectile dysfunction, decreased libido, and ejaculatory dysfunction. Furthermore, there have also been some studies that have shown a decreased sperm count after the use of finasteride. All of these side effects have also been shown to cause depression among patients, therefore physicians should exercise caution when prescribing this oral therapy.

Oral dutasteride is another oral therapy and it is a second generation 5-alpha-reductase inhibitor. It is said to be much more potent at blocking the type 1 and type 2 isoenzymes of 5-alpha-reductase (Nestor et al). It is important to note that if patients are not responding as well to other oral treatments such as oral finasteride, dutasteride may dramatically help the patient and have much more effective results in blocking DHT and encouraging hair growth. The side effects for this oral therapy are very similar to the side effects experienced by patients using oral finasteride.

Hormonal Therapies

Spironolactone is a hormonal therapy used to treat female pattern hair loss because of its antiandrogenic properties. It decreases the amount of testosterone produced in the adrenal gland and it does this through affecting 17a-hydroxylase and desmolase. Spironolactone is not the most effective of all treatments but depending on the patient, you will see a positive impact through hair regrowth and the thickening of the hair. Some side effects of spironolactone are electrolyte imbalance, weakening of renal function, and hypotension.

A therapy that is not used very frequently is flutamide. This therapy showed a decrease in hair loss. Another therapy that is not used very frequently is bicalutamide. This treatment also showed positive results when treating alopecia. Out of these two hormonal therapies flutamide was shown to have a higher number of serious side effects. It had the potential to cause hepatic injury and hepatic failure. Bicalutamide on the other hand, is much safer and has more mild side effects such as a higher amount of liver enzymes.

Light Therapies

Low-level laser therapy has been being researched for decades. It has finally started being used for treating alopecia. This type of therapy is usually taken by patients through devices that are capable of being used at home. This therapy works because red light intake by cytochrome c oxidase in the mitochondria leads to photodissociation

of inhibitory factor induction. This leads to more protein synthesis and the downstream effects of No-related vasodilation (Nestor et al). This treatment on its own showed improvements in hair count. But when combined with other therapies such as Finasteride or minoxidil it showed even greater improvements in the patients level of hair. There were very low amounts of side effects from this low-level laser therapy. Side effects included acne, dry skin, headaches, mild paresthesia, and pruritus. Patients may have had to use this treatment several times a week, but it was made easier because they were able to receive the treatment at home.

Light-emitting diode devices emit small wavelengths. These light-emitting diode devices increase blood flow to the affected area, reduce inflammation, and hinder DHT via 5-AR downregulation (Nestor et al). This light therapy also showed positive results and increased hair growth. There were no prevalent side effects in this treatment. But it is important to note that in order to maximize results from this therapy other treatment options must be being used simultaneously. This type of treatment is best for patients that do not want invasive therapies and intensive side effects. The devices that administer this treatment can be used at home but patients must be flexible and willing to come into the office for treatments. An issue that arises with this treatment is that it can be expensive.

Injectables

Platelet-rich plasma is an injectable treatment that is used on patients with early stage androgenetic alopecia, and a great advantage of this treatment is that it is performed without any responsibilities being taken on from the patient. In the procedure, 10-30 mL of blood is taken from a patient's vein and then centrifuged for 10 minutes. This is done in order to extract the plasma from red blood cells. This plasma is rich in platelets and contains many things that contribute to growth. This is then injected into deep dermis or subcutaneous tissue (Nestor et al). This treatment requires no pain relievers and there are only mild side effects. These side effects include scalp pain, headaches, and a mild burning sensation. These side effects subside within a short period of time. This treatment increases hair count and shaft quality. Unfortunately, this treatment does not cure alopecia and must be used consistently in order for effects of the treatment to be maintained. A notable issue with this treatment is that platelet-rich plasma is not suitable for people with bleeding disorders, autoimmune disease, and active infection, as well as people that are taking an anticoagulant medication (Nestor et al). Lastly, this treatment is very expensive so over a long period of time, many people may not be able to afford it.

Adjuvant Therapy

Microneedling releases growth factors and stem cells which trigger mechanisms that regenerate wounds, and creates ways to enhance topical penetration (Nestor et al). Microneedling is used in conjunction with other treatments. Patients that do not respond to traditional therapies have seen improvements after the addition of microneedling into their treatments. Some side effects of microneedling are pain, bruising, and folliculitis. This treatment is expensive and painful.

Supplements and OTC Treatments

Oral nutraceutical supplement containing Synergen Complex® is created through a blend of “saw palmetto, ashwagandha, curcumin, hydrolyzed marine collagen type 1 and 3, palm extract, horsetail, amino acids, black pepper fruit extract, Japanese knotweed, hyaluronic acid, and biotin”(Nestor et al). Through these ingredients the body experiences lower cortisol levels, less inflammation, and even more time spent in homeostasis. This supplement showed improved hair growth and hair quality. A major advantage of this treatment is that there are no side effects that were reported.

Another supplement that shows increased hair growth in patients with alopecia is the marine complex supplement. This supplement is created by making a blend of the extracellular matrix components of shark and mollusks, vitamin C, horsetail extract, and flax seed extract (Nestor et al). This supplement can be taken orally or through various products such as shampoos, creams, and conditioners. There have been no side effects seen in clinical trials, but due to the nature of the ingredients used to create this supplement some potential side effects are constipation, diarrhea, nausea, and arthralgias.

Plant based oils are also a viable source of treatment for alopecia. Using plant based oils on one’s scalp has been very common in many parts of the world for hundreds of years. In fact, a study was carried out that showed a set of

patients using rosemary oil and another set of patients using minoxidil 2% to help treat their androgenetic alopecia over the course of six months. Both groups were able to have a large increase in hair count, but the group that was assigned rosemary oil proved to have less itching in the scalp area(Nestor et al). Another few plant based oils that proved, through various studies, that they were beneficial in treating alopecia were pumpkin oil, tea tree oil, coconut oil, and even castor oil. There were very few side effects when using these oils, but the most common side effect caused by these treatments was scalp irritation.

Ketoconazole is a topical applicant and should be used long term when treating alopecia. It has antifungal and anti-inflammatory properties as well as antiandrogenic properties and DHT inhibition(Nestor et al). The improvements that ketoconazole brought was elongated diameter of the hair shaft. Ketoconazole is usually applied at home through the form of a shampoo. This treatment has no side effects and is not very costly.

Hair Transplantation

This form of treatment is most common among patients that have had no noticeable beneficial effects through medical therapy or among patients that have lost a very large amount of hair, and that portion of their hair can only be replaced through hair transplantation. The procedure for hair transplantation requires anesthesia. If hair is continuously lost even after hair transplantation the density and cosmetic appearance of the hair transplantation(Nestor et al). That is why it is best to combine a hair transplantation with other forms of medical therapy. Possible side effects of hair transplantation are poor reaction to anesthesia, bleeding, pain, edema, intraoperative or postoperative pain, problems with healing of the wound, and scars(Nestor et al).

New Treatment Options

A recently approved treatment option for alopecia is clascoterone, it gained FDA approval in 2020 and is the first topical antiandrogen agent that has the ability to treat hormonal acne. This treatment works through “antagonizing androgen receptors on dermal papillae and inhibiting DHT’s effect on hair miniaturization and dermal inflammation” (Nestor et al).

JAK inhibitors are another treatment option used to treat alopecia areata. This treatment works by disrupting the mechanism by which alopecia areata actually occurs. This treatment stops the body's autoimmune attack on the hair follicles with IL-15 creation as a response to interferon-y secretion(Nestor et al). JAK inhibitors reset the cycle of hair growth back to the anagen phase which allows hair to continue growing.

Conclusion:

In conclusion, alopecia is an autoimmune disorder that can cause hair loss on the scalp and all across the body. There are many different types of alopecia which are usually caused by interruptions or delays to the hair growth cycle. In recent years, cases of alopecia have increased, and this can be linked to both increasingly stressful situations and both the COVID-19 vaccine and COVID-19 infections creating mechanisms within the body such as crosses between viral and self antigens and cytokine storms. There have also been studies linking diet to cause alopecia and even to cause regrowth of hair when changed due to effects to the dermal papilla cells, which would eventually promote hair regrowth. Diets all ultimately play into the role of the gut in alopecia, where most diets have large amounts of processed foods and fats which can lower short-chained fatty acid counts and alter gut bacteria. There are also many treatment options for alopecia, although there is no cure. Some of these treatment options have been around for a long time, and others have been newly created or use advanced technologies to deliver results and all of them have varying side effects. This research paper was designed to give an overview about various aspects of this disease to help broaden the understanding and give new insights on the various aspects covered. The study of alopecia has progressed a lot and there are still organizations and researchers working on improving our understanding of alopecia and helping patients deal with this disease.

Acknowledgements

I would like to extend my heartfelt gratitude to Dr. Rajagopal Appavu Ph.D. and Ms. Jothsna Kethar for their guidance in helping me compose this research paper.

References

Aryanian, Z., Balighi, K., Hatami, P., Afshar, Z. M., & Mohandesi, N. A. (2022, April 1). *The role of SARS-COV-2 infection and its vaccines in various types of hair loss*. Dermatologic therapy. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9111640/

Asghar, F., Shamim, N., Farooque, U., Sheikh, H., & Aqeel, R. (2020, May 27). *Telogen effluvium: A review of the literature*. Cureus. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7320655/

Caserini, M., Radicioni, M., Leuratti, C., Iorizzo, E., & Palmieri, R. (2016, January). *Effects of a novel finasteride 0.25% topical solution on scalp and serum dihydrotestosterone in healthy men with Androgenetic Alopecia*. International journal of clinical pharmacology and therapeutics. https://pubmed.ncbi.nlm.nih.gov/26636418/

Mahmud, M. R., Akter, S., Tamanna, S. K., Mazumder, L., Esti, I. Z., Banerjee, S., Akter, S., Hasan, M. R., Acharjee, M., Hossain, M. S., & Pirttilä, A. M. (2022, July 22). *Impact of gut microbiome on skin health: Gut-skin axis observed through the lenses of Therapeutics and skin diseases*. Gut microbes. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9311318/

Nestor, M. S., Ablon, G., Gade, A., Han, H., & Fischer, D. L. (2021, November 6). *Treatment options for androgenetic alopecia: Efficacy, side effects, compliance, financial considerations, and Ethics*. Journal of cosmetic dermatology. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9298335/

Pham, C. T., Romero, K., Almohanna, H. M., Griggs, J., Ahmed, A., & Tosti, A. (2020, January 7). *The role of Diet as an adjuvant treatment in scarring and nonscarring alopecia*. Skin appendage disorders. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7109385/

Phillips, T. G., Slomiany, W. P., & Allison, R. (2017, September 15). *Hair loss: Common causes and treatment*. American Family Physician. https://www.aafp.org/pubs/afp/issues/2017/0915/p371.html

Sheth, P. (2013, August 31). *Androgenetic alopecia: An update*. Indian Journal of Dermatology, Venereology and Leprology. https://ijdvl.com/androgenetic-alopecia-an-update/