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Review Article

A pathophysiological and clinical review of androgenetic , areata, anagen effluvium, telogen effluvium and traction alopecia's

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Abstract

This article summarizes the pathophysiological processes and clinical manifestations of the five most prevalent types of alopecia: traction alopecia, anagen effluvium, telogen effluvium, and androgenetic alopecia. Terminal hairs gradually shrink in a certain way in androgenetic alopecia, a hereditary, androgen-mediated condition. Loss of immunological privilege and a T-cell-mediated attack on the hair follicle cause alopecia areata, an autoimmune disease that causes abrupt, non-scarring, and frequently patchy hair loss. The rapid and widespread losing of hair caused by the acute, direct poisoning of anagen hair follicle matrices by poisons or chemotherapeutic drugs is known as anagen effluvium. The reactive process known as telogen effluvium occurs when a major systemic or psychological stressor triggers the early, coordinated transition of a large number of anagen follicles into the telogen phase, which leads to dispersed shedding months later. Lastly, traction alopecia is a mechanical, avoidable disorder that can lead to permanent hair loss if left untreated. It is brought on by long-term tension on hair follicles from specific haircuts. For proper diagnosis, suitable research, and efficient treatment, a thorough grasp of these various etiologies is essential.

Keywords: Pathophysiological, Clinical manifestations, Traction alopecia, Anagen effluvium, Telogen effluvium, Androgenetic alopecia

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1. Introduction

Baldness is a serious problem for patients in terms of its effect on self-esteem, particularly causing great distress.[1] From a clinical perspective, it is essential to distinguish between effluvium (active shedding of >100 hairs/day) and alopecia (visible 30% loss of hair density) The normal scalp cycle has 100,000 hairs, with 100-150 lost per day; 85-90% in the growth (anagen) phase, 10% in resting (telogen), and 1% in catagen, controlled by molecules such as Wnt and Sonic Hedgehog.[1-3]

Anagen Effluvium**:** refers to sudden hair loss of anagen hairs through impairment of the follicle's mitotic or metabolic activity.[12] It is usually induced by radiotherapy or chemotherapeutic agents (antimetabolites, alkylating agents), with the shedding usually commencing 1 to 3 weeks following the insult.[4-5] The loss is sudden and diffuse, but subsequent growth is often feasible once the precipitant is discontinued.

Alopecia Areata**:** is a non-scarring, autoimmune condition in which the hair follicle becomes weakened and sheds.[6] It may occur as patchy scalp baldness or affect facial hair (beard, eyebrows).[7,8] The course is one of spontaneous remission and recurrent attacks.[9] There is also a diffuse form, which is a clinically important cause of hair loss.[10]

Telogen Effluvium (TE): which is characterized by Kligman, is a stress response in which anagen follicles abnormally enter the telogen stage. It results in a diffuse, massive shedding 2-3 months following a precipitating event such as illness, surgery, or childbirth.[11] It is typically self-limiting if the precipitant is removed.

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Traction Alopecia (TA): is caused by repeated tension on the hair due to particular hairstyles and cultural habits, rather than hair type.[1] Its prevalence in the general population has not been well documented.[3] If the tension is continued, it can lead to permanent scarring. Androgenetic Alopecia (AGA): Or male/female pattern baldness, is the most prevalent, occurring in the majority of the population by age 70.[1,2] It is an autosomal dominant condition involving follicular miniaturization, in which terminal hairs become vellus hairs, the anagen phase decreases, and the telogen phase increases.[5,12] Topical minoxidil, oral finasteride, and low-level light therapy are FDA-approved treatments currently available.[20](**Figure 1**)

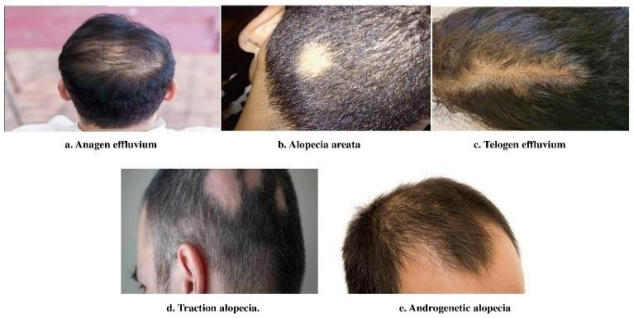

Figure 1: Kinds of hair loss caused by pathophysiological factors

2. Etiopathogenesis

Alopecia areata (AA) pathogenesis is rooted in immune dysregulation, genetic predisposition, and environmental pressures. The core event is the breakdown of the immune privilege of the hair follicle, making self-antigens accessible to the immune system. This initiates an autoimmune attack, dominated by CD8+NKG2D+ T cells that concentrate around the follicle.[24-27] These cells secrete IFN-γ through JAK1/2, activating epithelial cells to secrete IL-15, which subsequently reactivates the T cells through JAK1/3, forming a pathogenic cycle.[22,27] CD4+ T cells, seen as perifollicular infiltrates, regulate the immune response and can cause systemic AA.[26,32-35]

Others involved are iNKT cells connecting innate and adaptive immunity [39, 40] and defective Tregs, whose defective suppression could accelerate the attack.[37-39] The resulting inflammation compels follicles into the telogen phase, thus leading to hair loss. Tissue-resident memory T (TRM) cells, CD69+ and CD103+, are resident in skin tissue continuously and are ready for speedy reaction.[40,41] The IFN-γ-producing TRM1 cells take part in local inflammation and may underlie the chronic, recurrent course of AA since T cell clones remain at sites of lesions.[42,43]

Lastly, dendritic epidermal T cells (DETCs), a distinct subpopulation of γδ T cells, are also involved. They express features common to pathogenic CD8+ T cells, like elevated NKG2D expression and the ability to secrete IFN-γ. DETCs are normally absent in healthy skin but are greatly elevated in AA patients and potentially play a role in depleting hair follicle immune privilege.[44,45] In short, AA pathogenesis is fuelled by a multifaceted interaction of multiple immune cells, such as CD8+ and CD4+ T cells, iNKT cells, Tregs, TRM cells, and DETCs, which together destroy the hair cycle and lead to hair loss.

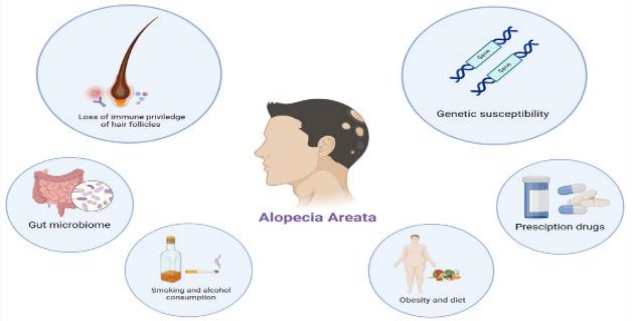

Figure 2: An overview of the elements that affect the pathophysiology of alopecia areata.

Alopecia areata (AA) pathogenesis is characterized by immune privilege breakdown in the hair follicle. CD8+NKG2D+ T cells are central effectors, piling up at the bulb and creating a pathogenic circuit with IFN-γ and IL-15 through JAK/STAT pathways.[22,24-27] CD4+ T cells modulate the process and can induce systemic AA.[32-35] Additional players are iNKT cells,[35,36] deranged Tregs,[37-39] long-term TRM cells that lead to recurrence,[40-43] and DETCs,[44,45] building a multifaceted autoimmune attack. In conclusion, AA pathogenesis is the result of a complicated interplay among various immune cell populations, such as CD8+ and CD4+ T cells, iNKT cells, Tregs, TRM cells, and DETCs, which together interfere with the hair cycle and lead to hair loss.(**Figure 2**)

2.1. Cytokines

Cytokines are the pivot of alopecia areata (AA). IFN-γ is a major perpetrator, breaking hair follicle immune privilege and inducing MHC-I upregulation.[52-56] IL-17 and IL-15 are also crucial, with the latter creating a pathogenic feedback loop with CD8+ T cells.[22,56,57] IL-10 and TGF-β, on the other hand, are "security guards".[21,36] Other immune cells enhance the inflammation: mast cells degranulate and engage with T cells,[46-48] and eosinophils are present in enlarging lesions.[48-51] The melanocyte antigens also stimulate the autoimmune attack, further complicating AA.

2.1.1. Signalling pathways

Several inflammatory signalling pathways are responsible for the pathogenesis of alopecia areata (AA). Both Th1 and Th17 pathways are involved, with their respective signature cytokines (IFN-γ, TNF-α, and IL-17A) being higher in patient sera and associated with the severity of the disease.[56]

The JAK-STAT pathway plays a pivotal role in AA pathogenesis, since most implicated cytokines are signalling-dependent on it. A critical pathogenic positive feedback

occurs when IFN-γ produced by CD8+NKG2D+ T cells interacts with follicular epithelial cells, leading to activation of the JAK1/2–STAT1 pathway and increasing IL-15 secretion. IL-15 subsequently activates CD8+NKG2D+ T cell receptors.

In addition, IL-23 also activates the JAK2–STAT3 and TYK2–STAT4 pathways that induce Th17 cells to secrete IL-17A, IL-17F, and IL-22. Likewise, IL-12 also activates the TYK2–STAT4 pathway that induces Th1 cells to secrete IFN-γ. Other cytokines such as IL-2, IL-7, and IL-21 also utilize the JAK-STAT pathway to speed up hair follicles into the degenerative phase that leads to hair loss.

The pathogenesis of alopecia areata (AA) involves an intricate interaction between signalling pathways, environmental stimuli, epigenetic changes, disruption of the hair cycle, and genetic predisposition. The JAK-STAT pathway is a key signalling cascade in AA. A vital positive feedback mechanism is initiated when activating factors stimulate CD8+NKG2D+ T cells to secrete IFN-γ through JAK1 and JAK3. This IFN-γ increases IL-15 production in follicular epithelial cells via JAK1 and JAK2 signals. The secreted IL-15 acts on CD8+NKG2D+ T cells, leading to subsequent production of IFN-γ and increased inflammatory response. Furthermore, binding of IL-23 to its receptor activates the JAK2–STAT3 and TYK2–STAT4 pathways, causing Th17 cells to release IL-17A, IL-17F, and IL-22. Likewise, binding to IL-12 triggers the TYK2–STAT4 and JAK2–STAT4 signalling pathways, which induce Th1 cells to secrete copious amounts of IFN-γ.

2.1.2. Environmental factors

Environmental stimuli have an intimate interaction with epigenetic pathways to modulate AA development. Chronic mental stress, a major trigger, can result in abnormal activation of the hypothalamic-pituitary-adrenal axis and extended cortisol elevation. This dysregulation of hormones suppresses the hair follicle stem cells and interferes with immune homeostasis by compromising the immune privilege of the follicle and inducing pro-inflammatory cytokine release.

This is supported by epidemiological data, with almost 80% of participants describing severe psychological trauma preceding disease development. Some medical interventions, such as hepatitis B vaccination and highly active antiretroviral therapy, are also recognized triggers. Dietary patterns come into play; deficiencies in micronutrients impair the physiology of the follicles, whereas diets rich in fats and hyperglycemia associated with Western diets can diminish microcirculation, compromise hormone homeostasis, and induce chronic inflammation.

2.1.3. Epigenetic factors

Epigenetic control, which adjusts gene expression without changing the DNA sequence, is an area of major interest. In AA, DNA methylation, histone modification, and microRNAs (miRNAs) regulate the expression of immune response genes. Aberrant patterns of DNA methylation and epigenetic regulator dysregulation, such as DNMT1 and HDAC2, occur in AA patients. Certain miRNA profiles have been identified: miR-1246 and miR-210 differentiate AA patients from healthy controls, whereas miR-185-5p, miR-125b-5p, and miR-186-5p are overexpressed during severe disease. Epigenetics serves as a bridge, transducing environmental stressors such as viral infections into lasting disruptions that counter immune tolerance.

3. Disruption of Hair Follicle Cycle

A key pathological hallmark of AA is the interruption of the cycle of hair follicles with a severely abbreviated anagen phase, early catagen, and extended telogen. The JAK-STAT signalling pathway and pro- inflammatory cytokines such as TNF-α produce an inflammatory local microenvironment that not only worsens the immune assault but directly kills anagen hair follicle epithelial cells and suppresses differentiation of hair follicle stem cells. Oxidative stress enhances the process; excessive production of reactive oxygen species initiates aberrant expression of NKG2D ligands, activating immune cells while disrupting antioxidant enzymes and establishing a pro-oxidative microenvironment. Single-cell sequencing indicates dynamic alterations within immune subsets such as macrophages and mast cells during this cycle disruption. Epigenetic dysregulations have the potential to transform environmental stressors into irreversible causes of hair follicle cycle disruption.

3.1. Genetic susceptibility

Genetic predisposition is a foundation of AA pathogenesis. The HLA gene complex, specifically some subtypes of HLA-DQ and HLA-DR, is significantly linked with susceptibility. Genome-wide association (GWA) studies have implicated 14 genomic loci associated with the disease. These involve genes for immune regulation, including those for production of IFN-γ (IL2), T cell expansion and activation (CTLA4, IL2RA, ICOS), and cytotoxicity (ULBP3/6). Hair follicle-associated genes such as STX17, PRDX5 (implying a function of oxidative stress), and CCHCR1 (implying keratinization disorders) are also implicated. The interaction of these genetic determinants with environmental stimuli, including infections and stress, is a predominant element of AA's genetic susceptibility, with family history still being an important risk factor.

Anagen effluvium is marked by direct injury to the highly proliferative matrix keratinocytes in the hair bulb that occurs when in active growth (anagen) phase. This most frequently results from cytotoxic chemotherapy drugs, whose mode of action is to destroy rapidly dividing cells. The extent of hair loss varies with the toxicity of the offending agent; lesser toxicity leads to dystrophic anagen effluvium with retarded regrowth, whereas more toxicity leads to

massive loss but possibly faster regrowth. The condition is usually reversible since the resting stem cells in the bulge of the follicle, the ones responsible for re-initiation of growth, are usually spared. Signalling pathways such as sonic hedgehog are involved in follicle cycling, and modulation of the same is promising for the prevention of this form of alopecia.[59,63-65]

Telogen effluvium**,** on the other hand, is induced when a severe physiological stressor—e.g., medication, emotional stress, or pregnancy—induces a large cohort of anagen hairs to shift earlier than usual into the resting (telogen) phase. Following a 1-6 month lag phase, these telogen hairs are lost as new anagen hairs form. At a molecular level, this transition is mediated by perturbations to growth factors, neuroendocrine signals, and cytokines that cause perturbations to follicular homeostasis, leading to premature induction of the catagen phase.[66]

Traction alopecia is a consequence of repeated and sustained tension on follicles, leading to mechanical trauma of the dermal papilla. Risk is increased with tension on previously compromised hair by chemical relaxers or heat-styling. Although it may occur in anyone, it is particularly common in those with tightly curled hair textures, frequently appearing along the frontotemporal hairline.[67]

Androgenetic alopecia (AGA) is androgen-driven, which triggers receptors within the follicle to increasingly shorten the anagen phase. This results in follicular miniaturization, where terminal hairs become shorter, thinner, and potentially do not even reach the epidermis. A characteristic of AGA is the pathological alteration in the anagen-to-telogen ratio from a typical 12:1 to 5:1.[68,69] Alopecia includes a range of conditions with varied causes and presentations.

4. Chemotherapy

Chemotherapy-induced alopecia is a more severe manifestation of anagen effluvium that involves cytotoxic medications causing damage to dividing matrix keratinocytes during the anagen (growth) phase. This results in sudden breakage of hair shafts and diffuse, sometimes complete, hair loss. It is usually reversible, with regrowth 3-6 months following discontinuation of therapy, although texture or pigmentation of the hair may temporarily be altered.[70,71]

Contrastingly, alopecia areata is an autoimmune condition in which cytotoxic T lymphocytes target anagen hair follicles following a loss of immune privilege. This leads to discrete, circular patches of nonscarring hair loss, often with pathognomonic "exclamation mark hairs." Its behaviour is unpredictable, varying from spontaneous remission to extension to complete loss of scalp or body hair (alopecia totalis/universalis).[72]

Telogen effluvium is a reactive, diffuse alopecia precipitated by major emotional or physiological stress, e.g., surgery, illness, or childbirth. The stressor shocks a high percentage of anagen hairs into prematurely going into the telogen (resting) phase. After a latent period of 2-3 months, this results in an apparent increase in daily shedding. It is self-limiting if the precipitant is resolved, with improvement normally in 6-9 months.[73]

Traction alopecia is an avoidable condition due to chronic mechanical tension of recurrent hairstyles such as tight ponytails, braids, or extensions. The chronic pulling causes inflammation, hair breaking, and folliculitis, mainly at the temples and hairline. With continued tension, permanent scarring and irreversible hair loss can occur, with early intervention and patient education being essential.[74]

Androgenetic alopecia (AGA) is the most prevalent condition of hair loss, fueled by genetic and hormonal factors. The responsible hormone is dihydrotestosterone (DHT), a highly active testosterone derivative. In genetically predisposed hair follicles, DHT binding progressively miniaturizes the follicle, decreases the anagen phase, and grows finer, more limited hairs. The result is patterned thinning: bitemporal recession and vertex balding in males, and diffuse central thinning in females. Unlike transient alopecias, AGA is chronic and progressive, though treatments like minoxidil and anti-androgens (e.g., finasteride) can slow or partially reverse its course.[75]

5. Clinical Finding

Alopecia includes separate diseases with specific diagnosis. Alopecia Areata (AA) is characterized by abrupt, round, non-scarring hair loss from T-cell-mediated follicle damage.[76] Diagnosis includes "exclamation mark" hairs and thermoscopic yellow/black dots.[77] Treatment varies from intralesional steroids to JAK inhibitors.[78] Anagen Effluvium is characterized by rapid, widespread loss from chemotherapy-induced damage to anagen matrix cells with resultant fractured shafts. Regrowth resumes once the insult is ceased.[79,80] Telogen Effluvium (TE) is diffuse shedding caused by stress (e.g., surgery, childbirth), forcing anagen hairs into telogen. Shedding follows after a 2-3 month delay; it is self-limiting with removal of the trigger.[78,81] Traction Alopecia occurs due to chronic tension from hairstyles, leading to hairline thinning and breakage.

Cessation of tension early on leads to recovery; scarring is irreversible.[77,82] Androgenetic Alopecia (AGA) the most prevalent form, is patterned thinning due to follicular miniaturization. Bitemporal recession in men and diffuse central thinning in women. Topical minoxidil as first-line treatment, oral finasteride in men.[78,83,84](**Table 1)**

Table 1: Diagnosis of androgenetic , areata, anagen effluvium, telogen effluvium and traction alopecia's,

Feature	Androgenic alopecia (male/female pattern hair loss)	Alopecia areata	Telogen effluvium	Anagen effluvium	Traction alopecia
Primary cause	Genetic sensitivity of hair follicles to androgens (like DHT).	Autoimmune disorder; body's immune system attacks hair follicles.	A physiological Shift in the hair growth cycle, pushing a large number of hairs into shedding (telogen) phase.	Direct injury to the metabolically active hair bulb in the anagen (growth) phase.	Physical, prolonged tension on the hair shaft over a long period.
Pattern of loss	Men: Receding temples, crown thinning, vertex balding. Women: Diffuse thinning over the crown With preserved frontal hairline.	Patchy, well-circumscribed, round or oval bald patches. Can progress to total scalp (alopecia totalis) or body hair loss (alopecia universalis).	Diffuse, non-patterned thinning across the entire scalp. Shedding is widespread.	Diffuse, rapid, and severe hair loss across the entire scalp. Often complete.	Localized to areas under tension. Commonly hairline, temples, part lines (based on hairstyle).
Hair shaft & roots	Hair miniaturization (hairs become progressively finer and shorter).	Exclamation mark hairs: short hairs tapering at the base. Broken hairs.	Telogen clubs: white bulbs at the end of the shed hairs.	Dystrophic anagen roots: tapered, fractured, or pigmented roots (no bulb).	Broken hairs of varying lengths.[74-77,85]
Is it scarring?	Non-scarring (follicular openings preserved).	Non-scarring (hair follicles are dormant, not destroyed).	Non-scarring.	Non-scarring (if the insult is removed, regrowth is possible).	Can become scarring if tension is prolonged and chronic, destroying the follicle.
Key diagnostic clues	Family history, classic pattern, presence of miniaturization on dermoscopy.	Sudden onset of round patches, exclamation mark hairs, associated nail pitting.	History of a trigger (e.g., surgery, illness, stress, childbirth, crash diet) 3 months prior.	History of a trigger (e.g., surgery, illness, stress, childbirth, crash diet) 3 months prior.	History of tight hairstyles (braids, ponytails, weaves, extensions). Pattern follows hairstyle.
Regrowth potential	Miniaturized follicles may be permanently damaged. Treatment can slow progression and stimulate some regrowth.	Excellent potential for spontaneous regrowth, but episodes can recur. Hair may regrow white initially			

6. Investigation

This article outlines the diagnostic strategy for frequent alopecias. Anagen effluvium is diagnosed on the basis of Trichogramma/ hair pull test, which reveals tapered hair shaft breaks. Confirmation comes with biopsy demonstrating a normal anagen-to-telogen ratio (<15% telogen follicles) and no inflammation.[86,87] Traction alopecia diagnosis is based on a thorough history and clinical examination, with the use of questionnaires to record hairstyling habits, symptoms, and patient characteristics.[88,89]

Alopecia areata (AA) is mostly clinical but confirmed by dermoscopy (yellow dots, exclamation mark hairs).[90] A biopsy demonstrates a lymphocytic infiltrate around the bulb and elevated catagen/telogen follicles in active disease. Telogen Effluvium (TE) investigation seeks to establish diagnosis and identify the trigger. A positive hair pull test and trichoscopy with empty follicles and upright regrowing hairs are definitive. Labs (CBC, ferritin, TSH) detect underlying etiologies, and a biopsy reveals >15-20% telogen follicles without miniaturization.[91]

Androgenetic alopecia (AGA) is diagnosed based on patterned hair loss clinically. Trichoscopy is crucial, showing

hair diameter heterogeneity (>20%) and miniaturization.[92] A negative hair pull test differentiates it from TE. Labs exclude other conditions in difficult cases, and a biopsy establishes miniaturization and an abnormal terminal-to-vellus hair ratio.(**Table 2**)

Table 2: Treatment for androgenetic, areata, anagen effluvium, telogen effluvium and traction alopecia's.

Type of alopecia	Primary cause	First-line & Common treatments
Alopecia areata	Autoimmune	1. Intralesional corticosteroids (triamcinolone) 2. Topical corticosteroids 3. JAK inhibitors (e.g., Baricitinib, Ritlecitinib) 4. Topical immunotherapy (DPCP)
Telogen effluvium	Reaction to a physiological stressor	1. Identify & address trigger (stress, deficiency, illness) 2. Reassurance and time 3. Correct nutritional deficiencies (if present)
Anagen effluvium	Cytotoxic insult (e.g., chemo)	1. Prevention with scalp cooling 2. Supportive care (wigs, gentle handling) 3. Spontaneous regrowth after insult ends
Traction alopecia	Physical tension on hair	1. Behavior modification: Stop tight hairstyles 2. Topical/intralesional steroids (early stage) 3. Hair transplantation (late-stage scarring)
Androgenic alopecia	Genetic sensitivity to DHT	Men: Topical Minoxidil, Oral Finasteride/Dutasteride Women: Topical Minoxidil, Anti-androgens (e.g., Spironolactone) Both: LLLT, PRP, Hair Transplantation

7. Conclusion

All of the main types of alopecia androgenetic, areata, traction, telogen effluvium, and anagen effluvium present with distinctive patterns of hair loss, although having different pathophysiologies. Whereas alopecia areata is an autoimmune disease that results in patchy loss, androgenetic alopecia is a progressive hereditary condition. Anagen effluvium and telogen are usually temporary disorders caused by stress or chemotherapy, but traction alopecia is a preventable condition caused by mechanical stress. Given the range of potential reasons, a precise diagnosis is essential for developing a successful, customized treatment strategy that incorporates lifestyle and medication changes.

8. Source of Funding

None.

9. Conflict of Interest

None.

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