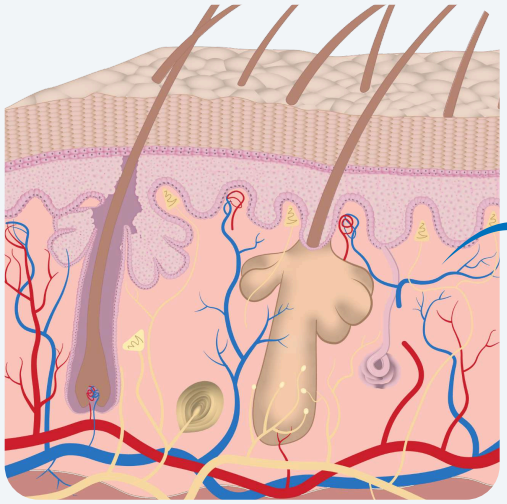
ALOPECIA AREATA

HAIR LOSS CAUSED BY AUTOIMMUNE DISORDER

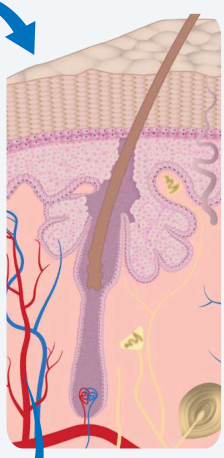
Alopecia Areata (AA) is an autoimmune disorer where the body attacks its own hair follicles. AA can damage the hair roots, resulting in hair loss. The hair may or may not regrow by itself.

NORMAL HAIR GROWTH



ANAGEN

- Growth Phrase
- 3-8 years
- A pigment Hair Shaft is Generated

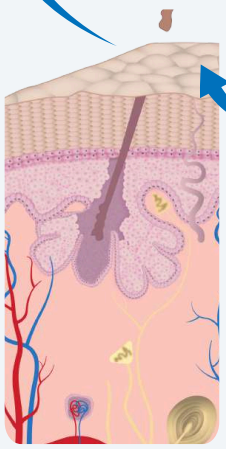


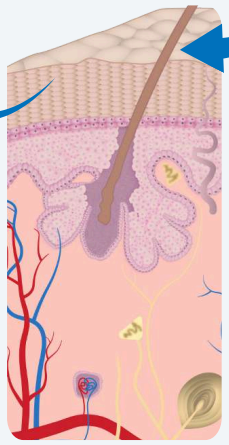
CATAGEN

- Transition Phrase
- 1-2 weeks
- Hair stops growing and becomes detached from the base of the follicle

TALOGEN

- Resting Phrase
- 5-6 weeks
- Hair does not grow but stay attached to the follicle.

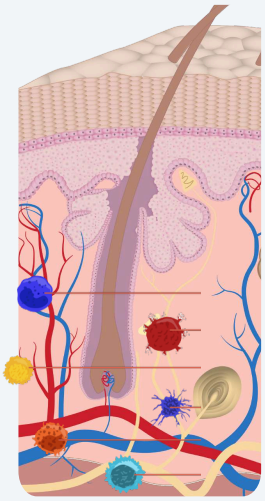




Return to ANAGEN

ALOPECIA AREATA ANAGEN PHASE in AA

Premature Induction of Catagen



The Hair Follicle is an immune-Privileged Site (where selected immune responses are suppressed or excluded.

The breakdown of immune privilege of the hair follicle has been thought to be a major driver of AA.

PREVALENCE OF AA

2%

of the general population at some point during their lifetime was affected by AA.

40 Y/O

Most patients (82.6-88%) develop the onset of AA before 40 years of age, with the mean age of onset between 25-36 years.

39.5%

of children and 11% of adults with AA were associated with atopic dermatitis. Several studies also reported a significant percentage of AA patients had an associated personal and family history of atopy.

74%

of the AA patients had experienced the lifetime prevalence of psychiatric disorders. the disorders include major depression, generalized anxiety disorder, social phobias and paranoid disorder.

CLASSIFICATION BY EXTEND

PATCHY ALOPECIA AREATA
Round and oval patches on the scalp or other places in the body that grow hair. it is seen in 75% of the patients

ALOPECIA TOTALIS
Total or near-total-loss of all scalp hair

ALOPECIA UNIVERSALIS
Hair loss across the entire scalp, face (including eyebrows and eyelashes), and the rest of the body (including pubic hair).

BALDNESS

ATOPY DISEASES

Atopy is defined as a personal/ or familial tendency to become sensitized and produced IgE antibodies in response to ordinary exposure to allergens.

CARDIOVASCULAR DISEASES

AA, in many studies, is associated with increased metabolic syndrome and cardiovascular diseases.

THYROID DISEASES

Through the hormones it produces, the thyroid gland influences almost all of the metabolic processes in your body.

PSYCHIATRIC DISEASES

Psychiatric disorder are a heterogenous group of mental disorders, manifesting as unusual mental or behavioural patterns that cause distress or disability to the individuals.

THE HIGHEST PREVALENCE the DISEASES in AA PATIENTS

17.7%
Allergic Rhinitis

37.3%
Metabolic Syndrome

13.9%
Autoimmune Thyroid Diseases

52.9%
Alexithymia

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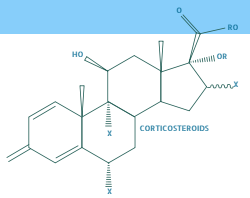
LOCALIZED THERAPIES

Treatment that is directed to a targeted area of the body.



INTRALESIONAL CORTICOSTEROIDS

Intralestional corticosteroid treatments have been used to treat AA for over 45 years. For adult patients with limited involvement, ILCS are considered first -line therapy. Despite their common use, there are no randomized controlled trials. Current reported cases showed 64% to 97% of hair regrowth of AA sites after treatment.

ADVERSE EFFECT

SIde effects include transient atrophy and telangiectasia, which can be prevented by use of smaller concentrations and volumes, minimizing the number of injection per site, and avoiding injecting too superficially.

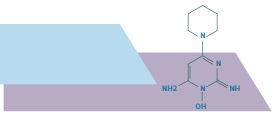
TOPICAL CORTICOSTEROIDS

Midpotent and potent topical corticosteroids are widely used in the treatment of AA. The evidence for their efficacy is limited.

ADVERSE EFFECT

Side effects include folliculitis (more with ointment compares with foam formulations) and rarely skin atrophy and telangiectasia. The relapse rate varies from 37% to 63% after tropical corticosteroid treatment has. stopped and even with continuation of theraphy.

MONOXIDIL

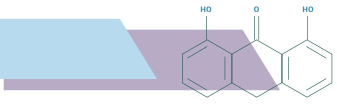


Minoxidil was first introduced as antihypertensive agent. It directly affects follicles by stimulating proliferation at the base of the bulb and differentiation above the dermal papilla, independent of its vascular influences.

ADVERSE EFFECT

Contact dermatitis and hypertrichosis are the most common side effects. Contact dermatitis can be minimized by using minoxidil foam, Which does not contain propylene glycol.

ANTHRALIN



Anthralin is presumed to elicit hair growth through its irritant contact properties. Patients are instructed to gradually increase daily exposure to anthralin cream to avoid severe cosmetic response. Response rates of 75% in patients with patchy AA and 25% in patients with AT have been reported.

ADVERSE EFFECT

Adverse effects include: pruritus, local erythema, scaling staining of treated skin fabrics, folliculitis, and regional lymphadenopathy.

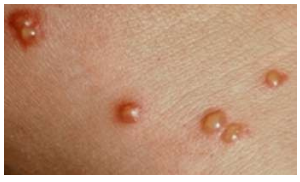
TOPICAL IMMUNOTHERAPY

Topical immunotherapy is defined as the induction of periodic elicitation of allergic contact dermatitis (ACD) by applying potent contact allergens to the affected skin.

DPCP

For example, Diphenylcyclopropenone (DPCP): This agent is a potent contact sensitizer, including an allergic response on the scalp in 98-99% of AA patients. Factors such as disease severity, age of onset, atopy and family history will affect the treatment efficiacy.

ADVERSE EFFECT



Vesicular rash can be one of the adverse effects, it may be suggestive of local or disseminated infection with various pathogens or signal a serious drug reaction.

SYSTEMIC THERAPIES

Treatment using substances that travel through the bloodstream, Reaching and affecting cells over the body

SYSTEMIC CORTICOSTEROIDS

Systemic corticosteroids have been used for decades in patients with extensive AA. In a randomized placebo-controlled study on oral corticosteroid (prednisolone) for a 3-month treatment, significant hair regrowth was noted in 35% of patients in the treatment group,

ADVERSE EFFECT

The side effects of systemic steroids include hyperglycemia, osteoporosis, cataracts, immunosuppression, mood changes, obesity, dysmenorrhea, acne, and cushing syndrome [disorder that occurs when your body have too much cortisols over time].

SULFASALAZINE

Sulfasalazine has both immunomodulatory and immunosuppressive actions, including inhibition of T-cell proliferation study, cosmetically acceptabble hair regrowth was noted in 23% of patients with severe AA.

ADVERSE EFFECT

Adverse effects include gastroinstestinal distress rash, headache and laboratory abnormalities.

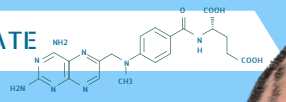
CYCLOSPORINE

Cyclosporine is a common immunosuppressant agent used in post-transplantation patients which exerts its effect via inhibition of T-cell activation. The success rates for AA treatment ranges from25% to 76.7%.

ADVERSE EFFECT

Cyclosporine is not a preferred option in AA because of high side effect profile and relapse rate. Side effects include nephrotoxicity, immune suppression, hypertension, and hypertrichosis of body hair.

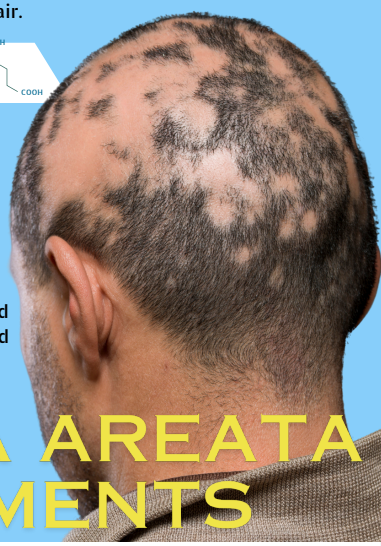
METHOTREXATE



Methotrexate is an immunosuppressant agent and is commonly used to treat cancer and autoimmune disease. The response rates for AA treatment range from 38% to 57%.

ADVERSE EFFECT

Adverse effects include transient elevated transaminases, persistent nausea, and lymphocytopenia.



ALOPECIA AREATA TREATMENTS

PROSTAGLANDIN ANALOGS

Prostaglandin analogs, such as latanoprost and bimatoprost, showed stimulatory effects on murine hair follicles and follicular melanocytes in both the telogen and anagen stages and stimulated conversion from the telogen (resting) to the anagen (growth) phrase.

However, a few clinical trials failed to show the hair regrowth or significant differences between treated and non-treated areas. Only recent non-blind, non-randomized trial showed a 45% response rates of latanoprost-treated group.

ADVERSE EFFECT

Side effects include transient mild eye irritation or hyperemia.

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REGENERATIVE THERAPY AND ALOPECIA AREATA

THE EMERGING THERAPIES FOR AA

Regenerative medicine has the potential to heal or replace tissues and organs damaged by age, disease, or trauma, as well as to normalize congenital defects. Promising preclinical and clinical data to date support the possibility for treating both chronic diseases and acute insults across a wide range of diseases.

Current treatments for hair loss are relatively limited. Hair additionally plays a central role in maintaining psychosocial well-being, and the loss of hair can have profound psychological consequences, particularly in women where it is most often devastating, Regenerative medicine, as the emerging therapy for many diseases, is also considered by researchers for their anti-inflammation mechanism to target autoimmune-related disorders.

MESENCHYMAL STEM CELLS (MSCs)

- Anti-inflammatory Effect

MSCs may prevent further inflammation and possible damage to hair follicles through the enhancement of anti-oxidate and anti-inflammatory mechanisms.

MSCc are able to inhibit the proliferation of B cells and their capacity to produce antibodies.

- Growth Factors

The paracrine characteristics of MSCs to secrete specifics factors to the neighbouring cells, including VEGF, HGF, IGF, and PDGF, that have possible effects on hair regeneration.

- Angiogenesis

Findings presented that adipose-derived MSCs may induce new blood vessel growth around and into the fat graft by releasing significant amounts of angiogenic growth factors such as VEGF, HGF, BFGF.

MSC-DERIVED EXOSOMES

- The Crosstalk

The MSC-derived exosomes do have the adaptability and capability to communicate with multiple cell types within the immediate vicinity and some remote areas to generate appropriate cell responses. Currently, the use of stem cell-derived extracellular vesicles (microvesicles and exosomes) as vectors for delivering compounds or regulating cell function in vivo is an emerging application in regeneration medicine.

- Mimicking Parental Effects

The released exosomes known to mimic the effects of the parental MSCs by orchestrating the principle mechanisms of MSC's action infusion.

Findings also suggest that exosomes carry hydrophobic Wnt proteins on their surface to induce β-catenin activation over a distance. This is a key signaling pathway involved in the hair morphogenesis and regeneration.

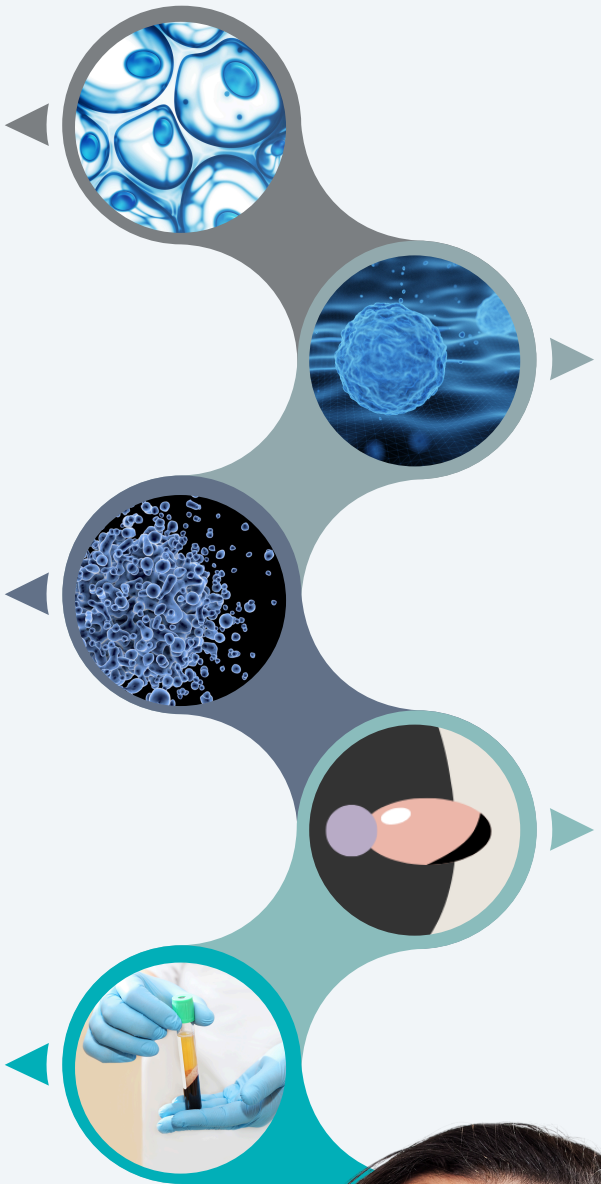
Platelet-rich Plasma (PRP)

The concentrated plasma enrich with platelets provided autologous growth factors that enhanced angiogenesis, extracellular matrix remodeling, and celllular proliferation and differentiation.

In patchy type and ophiasis-type steroid-resistance AA, PRP induced hair regrowth and reduced the amount of vellus and dystrophic hairs, with complete remission in 60% of patients.

- Growth Factors

The growth factors released (plateletderived growth factor, TGF-b, vascular endothelial growth factor, IGF, and FGF) encouraged the telegen-to-anagen transition by direct stimulation of the DP, indirect activation of Wnt and growth factor pathways, and prevention of apoptosis.



HAIR FOLLICULAR STEM CELLS (HFSC)

- Hair Follicle Homeostasis

Adult stem cells have the innate ability to regenerate damaged or senescent cells. HSFCs found in the bulge region of hair follicle, they are mostly dormant but they have the innate ability to migrate, proliferate and differentiate in order to maintain homeostasis.

- HFSC Differentiation

Hair follicles are known to contain a well-characterized niche for adult stem cells: the bulge, which contains epithelial and melanocytic stem cells. Stem cells in the hair bulge can generate the interfollicular epidermis, hair follicle structures, and sebaceous glands.

JAK Inhibitors

Janus kinase (JAK) are a group of medications that inhibit the activity of one or more of the Janus kinase enzymes (JAK1, JAK2, JAK3, and TYK2). These enzymes normally promote inflammation, and they are involved in some diseases.

- Hair Follicle Regeneration

The role of JAK inhibitors in hair follicle regeneration and epidermal pigmentation include promoting the telogen-to-anagen transition and stimulating Wnt and Sonic Hedgehog signalling. Activation of Wnt signalling induces proliferation, migration, and differentiation of melanocyte precursors needed for epidermal melanocyte regeneration, JAK inhibitors stimulate hair elongation and hair pigmentation by direct effects on melanocyte precursors in the hair follicle bulge and bulb.

- Anti-inflammatory Effect

JAK inhibitors can block the cytokines that promotes inflammation and calm down the over-reactive immune system to prevent further damage of immune response to the hair follicle.

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