Alopecias

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alopecias

- Non scarring alopecias
- Scarring alopecias
- Hair shaft abnormalities

biphasic pattern of alopecia

- A few hair diseases demonstrate a biphasic pattern, where non-scarring hair loss is seen early in the course of the disease, and permanent hair loss becomes apparent in the later stages of the disease.
- Examples include
- androgenetic alopecia
- alopecia areata
- traction alopecia
- where after many years or decades of continuous active disease, permanent dropout of follicles may occur.

Normal scalp

- In the normal scalp, there are ~100 000 hair follicles of which ~90% will be in the anagen phase, and the remaining 10% in telogen
- Daily, ~50–200 hairs undergo exogen and are shed

life cycle of hair follicle

A hair follicle has a three-phase life cycle. It consists of a growing phase (anagen), an involuting phase (catagen), and a resting phase (telogen).

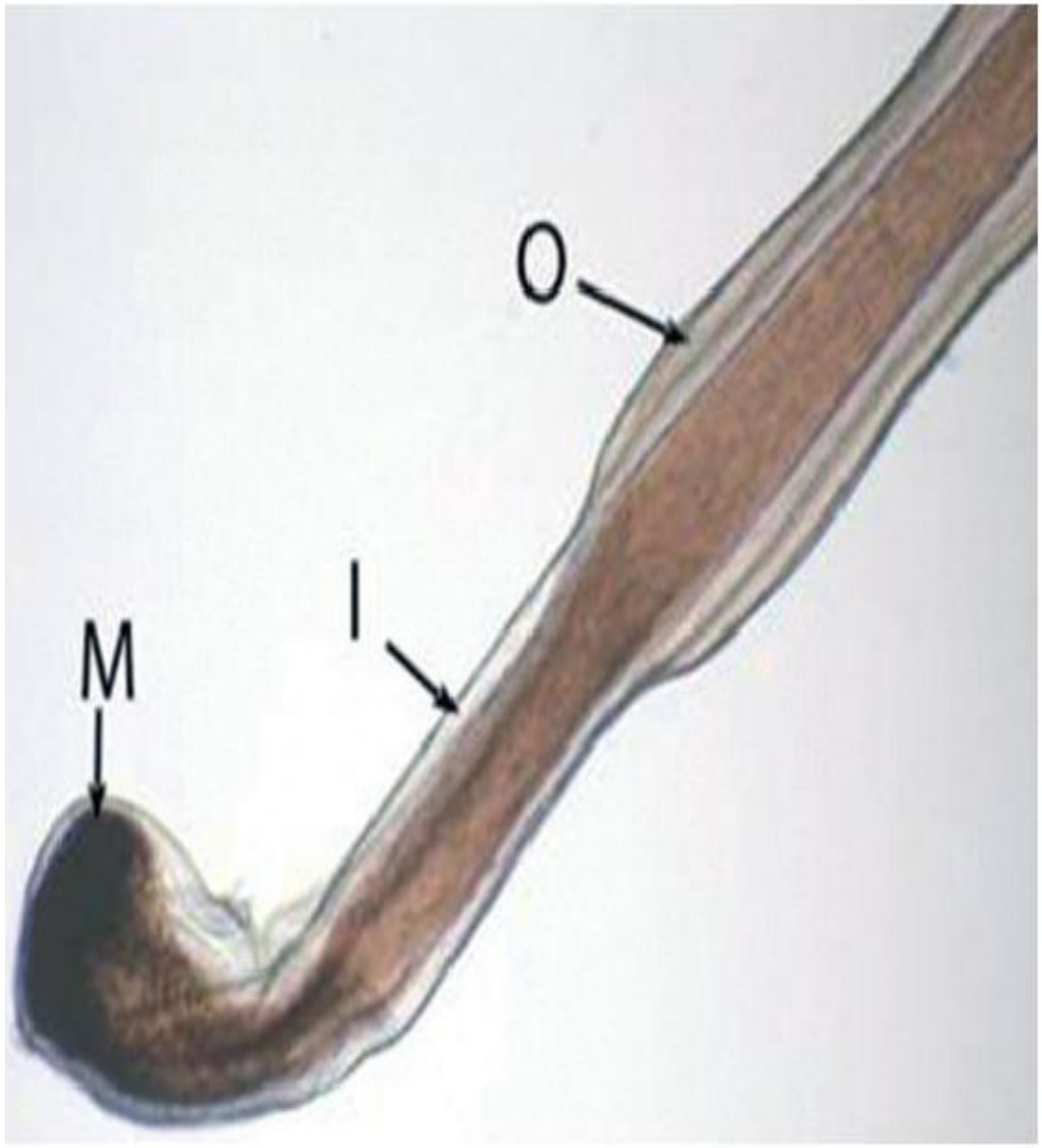
- The anagen phase can last for about two to five years, and around 90% of scalp hair is in this phase .
- The catagen phase is a much shorter phase, lasting three to six weeks. During this phase, the hair follicles go through a process of programmed cell death (apoptosis) .
- Finally, the telogen phase lasts for around three to five months, and 10% of the scalp hair are in this phase. During this phase, the hair shaft matures into a club hair, which is eventually shed from the follicle

Telogen shaft showing a club-shaped bulb

Anagen shaft with attached root sheaths,

demonstrating a pigmented and distorted bulb . M, matrix; I, inner root sheath;

O, outer root sheath .



Clinical assessment of alopecia

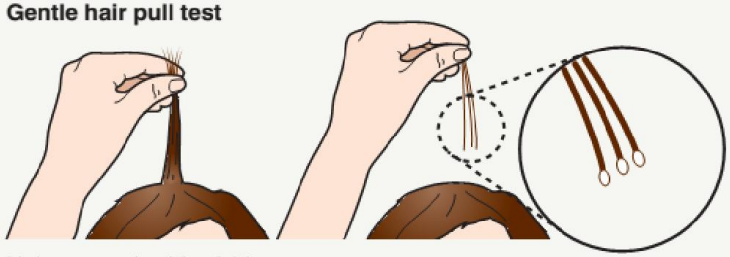
- Determine if patient has increased hair shedding (suggestive of telogen effluvium) or a reduction in hair density with visible balding or both; the latter is suggestive of patterned hair loss
- If increased hair shedding, is the hair "coming out by the roots"?

(suggestive of telogen effluvium) vs breaking near the scalp?
(suggestive of acute alopecia areata, anagen effluvium) vs breaking near the ends?
(suggestive of hair shaft abnormalities such as trichorrhexis nodosa)

- • If increased hair shedding and hair “coming out by the roots”, a duration <3 months suggests acute telogen effluvium whereas >6 months is diagnostic of chronic telogen effluvium;
- recurrent episodes of acute telogen effluvium without a clear trigger is a common prodrome to female pattern hair loss

BEDSIDE DIAGNOSTIC TESTS FOR THE ASSESSMENT OF ALOPECIA

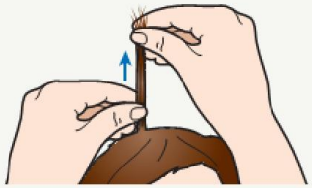
Gentle hair pull test



Hair not washed for 24 hours

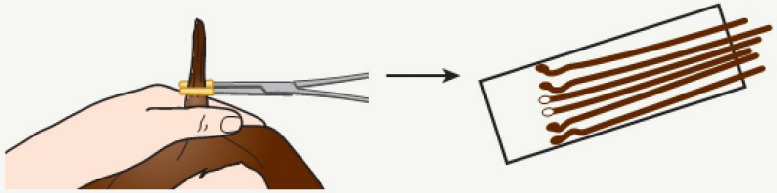
Telogen hairs

"Tug" test



Assessment for hair shaft fragility

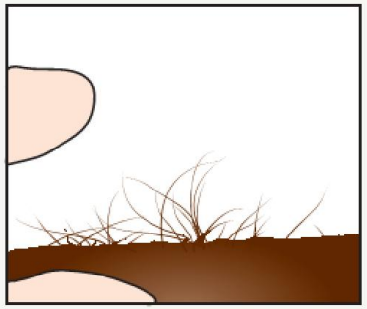
Unit area trichogram



Plucking of hairs within defined area (e.g. 60 mm^2)

Determine ratio of anagen:telogen hairs

Hair card test



Assessment of hair ends (e.g. broken vs tapered), diameters, and growth

Trichoscopy

Visualization of hair shafts, follicular openings, and interfollicular skin (10×; see Fig. 69.7)

Computerized trichometric analysis

In addition to trichoscopy (50×), measures and records density/cm^2 and average hair shaft diameters

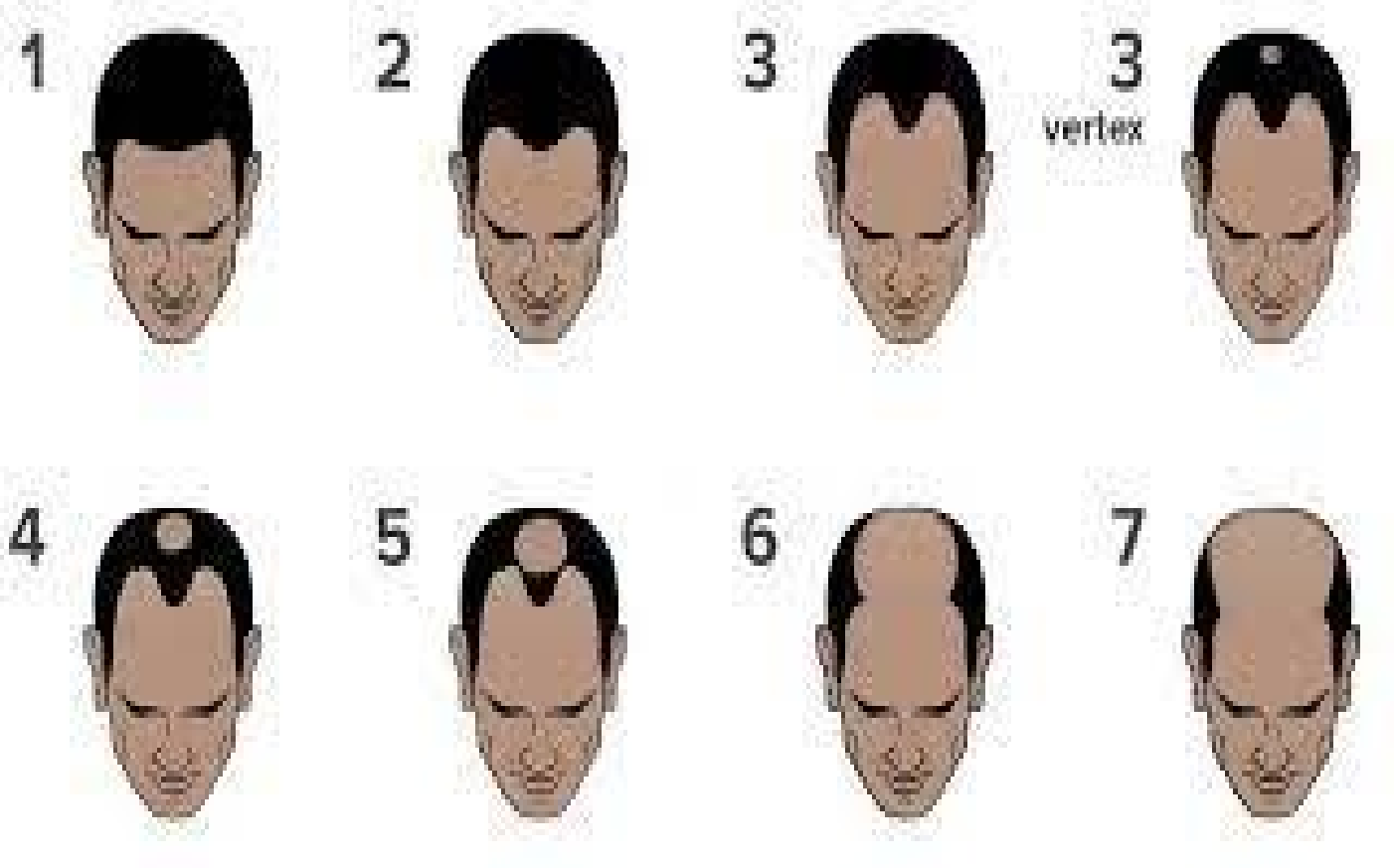
ANDROGENETIC ALOPECIA

Androgenetic alopecia (AGA) is an androgen-dependent, hereditary physical trait resulting from the conversion of scalp terminal hairs into miniaturized vellus hairs in a characteristic pattern. Androgenetic alopecia is the most common form of progressive hair loss in humans. A genetic predisposition and hormonal status are considered as major risk factors for this condition.

- The frequency and severity increase with age, and at least 80% of Caucasian men and ~50% of women show evidence of AGA by age 70 year

- Androgenetic alopecia is the most common form of hair loss in humans affecting 80% of Caucasian men and 50% of Caucasian women.
- The Hamilton–Norwood scale is used to assess the extent and severity of androgenetic alopecia in men, whereas the Ludwig scale is preferred for women.
- Both men and women have higher levels of androgen receptors and alpha-reductase type I and II activities in the frontal area of the scalp as compared to hair follicles located in the occipital area which have higher aromatase levels.
- The alpha-reductase type I and II activity in frontal hair follicles is three times greater in men than in women. Thus, male androgenetic alopecia is considered an androgen dependent condition, but the role of androgen signaling in women remains uncertain.

Hamilton–Norwood scale



Ludwig scale

Type I - Minimal thinning that can be camouflaged with hair styling techniques

Type II - Characterized by decreased volume and noticeable widening of the mid-line part

Type III - Describes diffuse thinning, with see-through appearance on the top of scalp

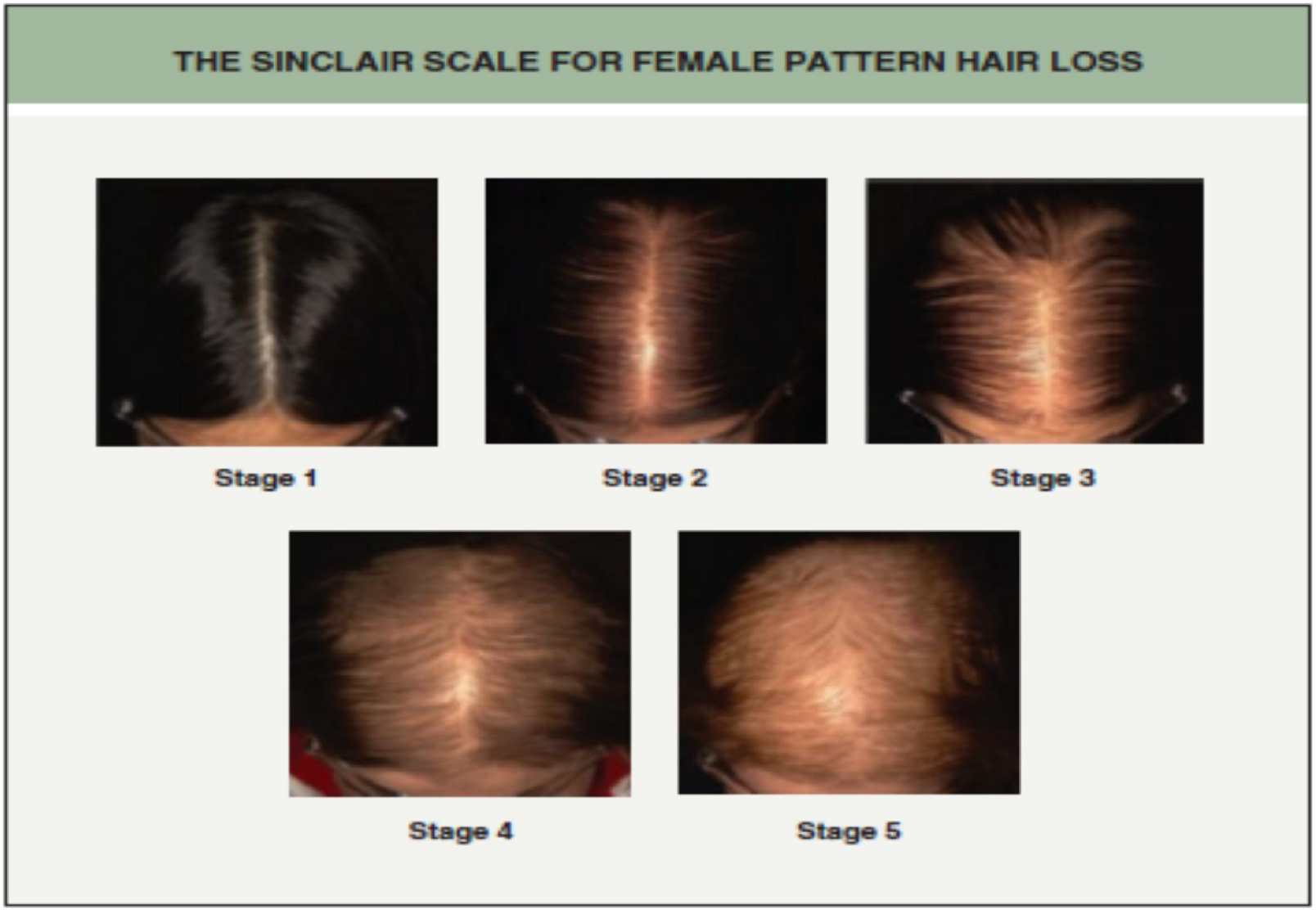


Fig. 69.5 The Sinclair scale for female pattern hair loss. Stage 1 – normal; Stage 2 – widening of the central part line; Stage 3 – widening of the part line with translucency of the hairs at its border; Stage 4 – development of a bald area anteriorly along the part line; and Stage 5 – advanced hair loss.

treatment

- Topical formulations of minoxidil (2% solution, 5% solution, 5% foam) and oral finasteride have been approved by the US Food and Drug Administration (FDA) for the treatment of men with male AGA.

minoxidil

Originally developed as an antihypertensive agent, minoxidil has been known for decades to promote hair growth.

Minoxidil causes premature termination of the telogen phase, lengthens the anagen phase, and can increase follicle size, particularly of miniaturized follicles.

Stimulation of vascular endothelial growth factor and prostaglandin synthesis may also play a role.

Although oral minoxidil relaxes vascular smooth muscle by opening ATP-dependent potassium channels, this mechanism has not been definitively linked to stimulation of hair growth

The most frequently reported adverse reactions are mild scalp dryness and irritation, and, rarely, allergic contact dermatitis.

Minoxidil-induced hair growth is commonly associated with shedding of telogen hairs and a paradoxical worsening of hair loss ~4 to 6 weeks following initiation of treatment. This resolves with continued treatment

- The main side-effect of topical minoxidil is hypertrichosis, most probably due to local spreading or excessive continuous topical application, sometimes also due to individual sensitivity. Irritant and allergic contact dermatitis may also occur. Irritation is more common with the 5% solution due to its higher content in propylene glycol.
- It is recommended to pause topical minoxidil use during pregnancy and lactation, due to lack of data during this period.(category C)

finasteride

Oral finasteride e (1 mg daily), a type II 5α-reductase inhibitor has been found to be effective in the treatment of balding in men[16].

It halts hair loss in 90% of patients, and partial hair regrowth occurs in 65% of those receiving finasteride.

The response to treatment should be assessed at 6–12 months. If successful, treatment needs to be continued to maintain efficacy. In case of ineffective treatment with 1 mg finasteride over 12 months, the off-label use of dutasteride 0.5 mg/day can be considered.

Side effects

- Possible finasteride side effects include reversible loss of libido, reduced volume of ejaculate fluid, and erectile dysfunction, which occurs in ~2% of men.
- There are reports of long-lasting sexual dysfunction (post-finasteride syndrome), but its incidence is unknown.
- In patients with active depression or current sexual dysfunction, finasteride is therefore contraindicated.
- The level of finasteride in the semen of treated man is very low, even with regular intake of finasteride 5 mg/day, and there is no risk in case of sexual relation with pregnant women.

- While the overall incidence of prostatic carcinoma is reduced among elderly men who take finasteride 5 mg daily for benign prostatic hypertrophy, patients should be informed that this higher dose has been associated with an increased risk of the diagnosis of high-grade prostatic carcinoma.
- It is uncertain if the latter represents overdiagnosis due to enhanced screening or whether it is predictive of an increased risk of metastasis and a higher mortality rate.
- With regard to the effects of finasteride (1 mg/day) on lowering serum concentrations of prostatespecific
- antigen (PSA), the recommendation is to adjust the measured serum PSA concentrations upwards by 40–50% for the purposes of prostate cancer screening

Female pattern hair loss

- In the US, topical minoxidil (2% solution, 5% foam) is approved for the management of FPHL.
- FPHL can develop in the setting of hyperandrogenemia, and women may benefit from oral contraceptives (to suppress ovarian androgen production), spironolactone or, if appropriate, finasteride therapy.

- While finasteride (1 mg per day) appears to be ineffective in postmenopausal women, when given at higher daily doses of 2.5 and 5 mg, it can improve FPHL.

- Dutasteride is a combined type I and type II 5α-reductase inhibitor.
- A dose of 0.5 mg/day leads to a greater reduction in serum and scalp DHT levels than does finasteride at 5 mg/day.
- This suggests that dutasteride may be a more effective therapy.
- While there are case reports of dutasteride leading to improvement of FPHL, the potential teratogenicity and prolonged biologic half-life preclude its use in women of childbearing age

A Systematic Review of Topical Finasteride in the Treatment of Androgenetic Alopecia in Men and Women

- Seven articles were included in this systematic review. In all studies, there was significant decrease in the rate of hair loss, increase in total and terminal hair counts, and positive hair growth assessment with topical FNS. Both scalp and plasma DHT significantly decreased with application of topical FNS; no changes in serum testosterone were noted.

Oral minoxidil treatment for hair loss: A review of efficacy and safety-2020

- A total of 17 studies with 634 patients were found discussing the use of oral minoxidil as the primary treatment modality for hair loss. Androgenetic alopecia was the most studied condition, but other conditions included telogen effluvium, lichen planopilaris, loose anagen hair syndrome, monilethrix, alopecia areata, and permanent chemotherapy-induced alopecia.
- Oral minoxidil was found to be an effective and well-tolerated treatment alternative for healthy patients having difficulty with topical formulations.

Adverse Sexual Effects of Treatment with Finasteride or Dutasteride for Male Androgenetic Alopecia: A Systematic Review and Meta-analysis

- The overall use of 5-ARIs for male AGA increased the risk of adverse sexual effects, especially erectile dysfunction and decreased libido.
- Use of 5α-reductase inhibitors carried a 1.57-fold risk of sexual dysfunction .The relative risk was 1.66 (95% CI 1.20–2.30) for finasteride and 1.37 (95% CI 0.81–2.32) for dutasteride. Both drugs were associated with an increased risk, although the increase was not statistically significant for dutasteride. As studies into dutasteride were limited, further trials are required.

The Efficacy of Platelet-Rich Plasma in the Field of Hair Restoration and Facial Aesthetics-A Systematic Review and Meta-analysis-2019

- In androgenetic alopecia (AGA) patients, 3 monthly PRP injections (1 session administered every month for 3 months) exhibited greater efficacy over placebo as measured by change in total hair density .
- to achieve an improvement in hair restoration in patients with mild AGA, 3 initial monthly PRP injections should be given.

Comparative Study between Mesotherapy and Topical 5% Minoxidil by Dermoscopic Evaluation for Androgenic Alopecia in Male: A Randomized Controlled Trial-2019

- There is no significant improvement of mesotherapy in male AGA over minoxidil.

Comparing the Efficacy of Mesotherapy to Topical Minoxidil in the Treatment of Female Pattern Hair Loss Using Ultrasound Biomicroscopy: A Randomized Controlled Trial

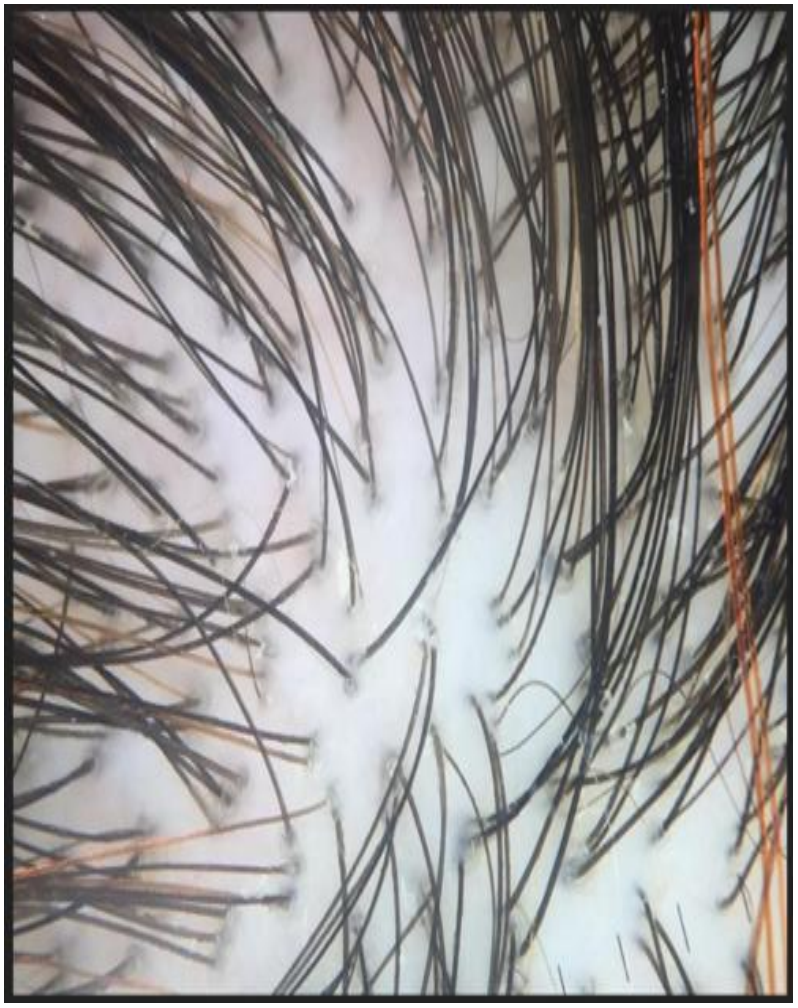
- 30 patients with FPHL were randomly classified into two equal groups: Group A applied minoxidil 5% lotion twice daily; Group B was injected with mesotherapy once weekly.
- The mesotherapy group showed more improvement with regard to the increase in the number of the hair follicles after treatment

TELOGEN EFFLUVIUM

Telogen effluvium is by far the most common form of hair loss due to medications or in association with systemic diseases or altered physiologic states.

If there is a definable precipitating event, hair loss begins approximately 3 months after this event, since it takes that amount of time for a hair follicle to progress through the telogen phase and then finally be shed. There is neither clinical nor histologic evidence of inflammation in “pure” telogen effluvium.

it affects both males and females, with a higher incidence rate in females. Elderly women are known to be more susceptible to acute telogen effluvium .



CAUSES OF TELOGEN EFFLUVIUM

- Shedding of the newborn (physiologic)
- Postpartum (physiologic)
- Chronic telogen effluvium[29] (no attributable cause or illness)
- Postfebrile (extremely high fevers, e.g. malaria)
- Severe infection
- Severe chronic illness (e.g. HIV disease[137], systemic lupus erythematosus)
- Severe, prolonged psychological stress
- Postsurgical (implies major surgical procedure)
- Hypothyroidism and other endocrinopathies (e.g. hyperparathyroidism, hyperthyroidism)
- Crash or liquid protein diets; starvation/malnutrition
- Drugs:
  - discontinuation of oral contraceptives
  - retinoids (acitretin, isotretinoin) and vitamin A excess
  - anticoagulants (especially heparin)
  - antithyroid (propylthiouracil, methimazole)
  - anticonvulsants (e.g. phenytoin, valproic acid, carbamazepine)
  - interferon-α-2b
  - heavy metals
  - β-blockers (e.g. propranolol)

chronic telogen effluvium

This chronic telogen effluvium primarily affects women between the ages of 30 and 60 years and is a diagnosis of exclusion.

Computer modeling of hair cycle kinetics has suggested that chronic telogen effluvium results from a reduced variance in the duration of anagen rather than a shortened anagen phase

Clinical features

- Telogen effluvium can present as acute or chronic hair fall with symptoms such as trichodynia .
- Thinning of the hair involves the entire scalp and may also be noted on other hairy regions of the body (e.g. pubic and axillary hair).
- A gentle hair pull may be positive for two or more normal telogen hairs
- In an active telogen effluvium, a 60-second timed hair count will usually be in excess of 100 hairs (the mean normal value is 10 hairs). This method, can be used to follow the progression and eventual resolution of a telogen effluvium
- While a telogen count of 15–20% is suggestive of abnormal shedding, >20% is diagnostic.

LAB. TESTS

- When the cause is unclear, the evaluation of a patient with telogen effluvium includes
- thyroid and chemistry panels,
- sedimentation rate,
- Hematocrit
- ferritin (as a reflection of total body iron storage).
- According to literature recommendations, ferritin levels should be at least 40 ng/dl, but the significance of abnormal values is uncertain

prognosis

- Eventually complete hair regrowth is expected. The prognosis for women with chronic telogen effluvium is relatively good, for although hair shedding can continue for many years, this does not appear to lead to baldness.
- he prognosis for telogen effluvium associated with systemic disease is excellent if the precipitating cause is eliminated.

- In persistent cases of telogen effluvium, i.e. those lasting beyond 6 months, a scalp biopsy specimen submitted for horizontal sectioning can prove useful in excluding early AGA

Management and treatment

- Acute telogen effluvium becomes self-limited if the triggering factor is identified and removed.
- Patient education is important in disease management. Disease correlation with triggers, and the timing of hair loss should be explained and frustrations addressed.

nutritional component

In idiopathic TE, the nutritional component should be suspected; the supplementation of an association of nutrients in recommended daily intake can lead to significant improvement of the condition from the first trimester of use. The use of an association with proven efficacy and a safety profile and posologic convenience facilitate its indication and patient adherence.

biotin

- Vitamin B7: an essential co-enzyme for 5 carboxylases involved in fatty acid synthesis, amino acid catabolsm, and glucogenesis.
- Frank biotin deficiency is rare.
- Marginal biotin deficiency may be encountered in: pregnancy ,smoking , and with long term anticonvulsant use.

- Biotin therapy was shown to promote normal hair growth in 2 case series of familial uncombable hair syndrome.
- In a series of patients experiencing alopecia after valproic acid treatment, biotin resulted in subjective improvement of alopecia.
- Studies found that nail thickness increased significantly after biotin therapy in patient with brittle nails.

- Adequate intake for biotin is 30 µg/day for adults , which is easily achieved through a well-balanced diet including biotin-containing foods, such as meat,eggs,fish,nuts,seeds and certain vegetables.
- Biotin toxicity has not been reported at doses up to 200 mg orally and 20 mg intravenously.
- Biotin supplementation has benn shown to interfere with routin immuno-assays: troponin T and TSH .

Serum levels of biotin

Serum levels of biotin were optimal in patients and control groups with no significant difference between the groups.

Insignificantly lower biotin levels in elderly patients, smokers, athletes, those with a history of recurrent infections, and women who were pregnant and/or lactating were observed. There was also an insignificant positive correlation between the serum level of biotin and patient age and an insignificant negative correlation between disease duration and patient body mass index.

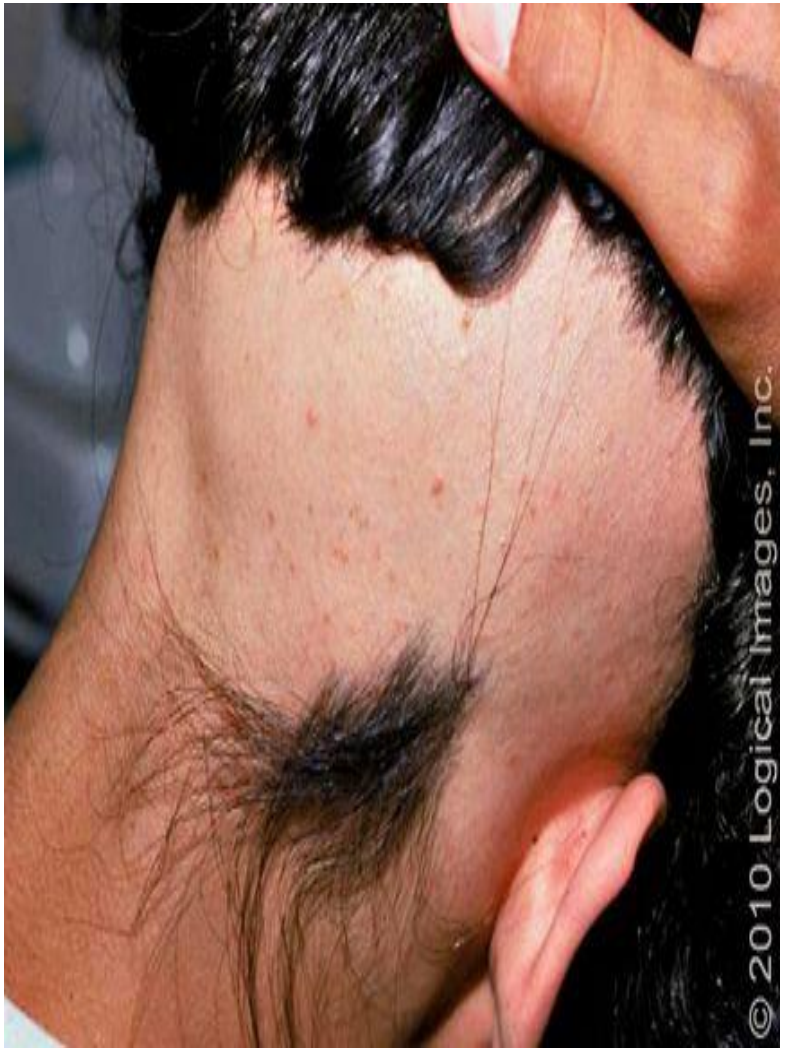
There was no significant difference in serum biotin levels between cases and controls or between those with acute or chronic telogen effluvium.

ALOPECIA AREATA

- Alopecia areata is a non-cicatricial alopecia that is postulated to be a hair-specific autoimmune disease, with genetic factors playing a role in disease susceptibility and severity.
- The prevalence of alopecia areata in the US is ~0.1% to 0.2% of the population

Clinical features

- Alopecia areata commonly presents as round or oval patches of nonscarring hair loss. Other presentations include alopecia totalis (loss of all scalp hair), alopecia universalis (loss of all scalp and body hair. an ophiasis pattern (band-like pattern) of hair loss along the periphery of the temporal and occipital scalp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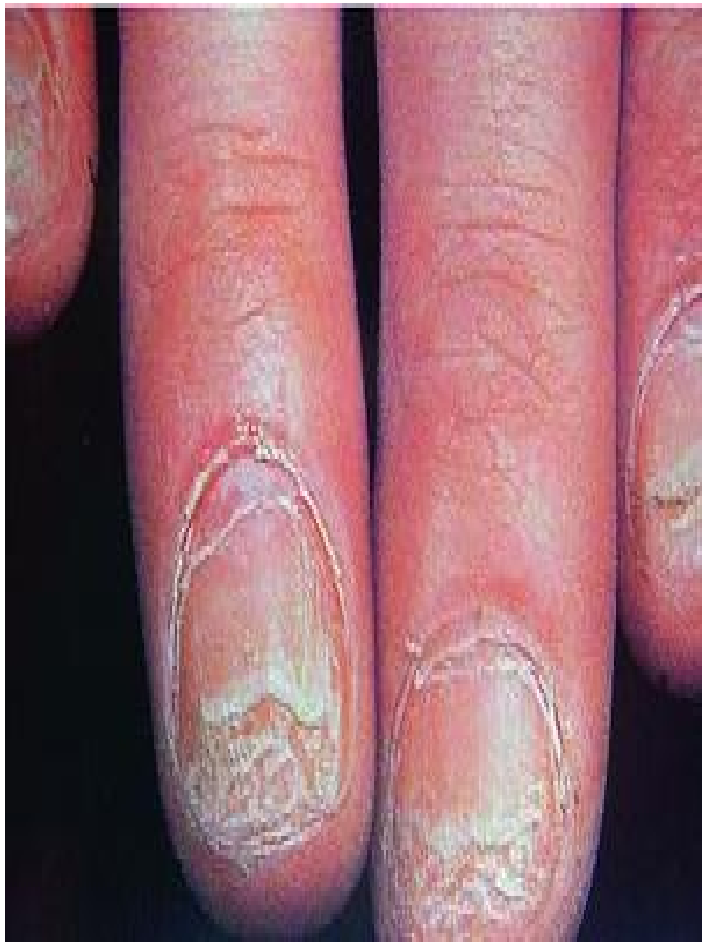
Nail involvement

- Nail abnormalities are present in ~20% of adults and 50% of children with alopecia areata.
- Signs that are characteristic of nail alopecia areata include geometric pitting and trachyonychia. The pits are small, superficial, and regularly distributed in a geometric pattern (grid-like).
- Trachyonychia is more common in children and most frequently seen in male patients with alopecia totalis or universalis.
- Additional nail abnormalities observed in alopecia areata include punctate leukonychia, erythema of the lunula, and onychomadesis.



ALOPECIA AREATA: DISEASE AND GENETIC ASSOCIATIONS

Associated diseases

- Atopy (allergic rhinitis, atopic dermatitis, asthma); >40% in some studies
- Autoimmune thyroid disease (e.g. Hashimoto thyroiditis), vitiligo, inflammatory bowel disease
- Autoimmune polyendocrinopathy syndrome type 1 (autosomal recessive; due to mutations in the autoimmune regulator gene [*AIRE*]; up to 30% of patients have alopecia areata)
- Type 1 diabetes increased in *relatives* of patients with alopecia areata

HLA associations

- HLA-DQB1*0301 (DQ7), HLA-DQB1*03 (DQ3), and HLA-DRB1*1104 (DR11); HLA-DQB1*03 appears to be a susceptibility HLA marker for all forms of alopecia areata, whereas the HLA alleles DRB1*0401 (DR4) and HLA-DQB1*0301 (DQ7) are considered markers for severe longstanding alopecia totalis/universalis

Additional genome-wide associations[138]

- Function of Treg cells: *CTLA4, IL-2/IL-21, IL2RA, Eos, LLRC32/GARP*
- Expressed within the hair follicle: *PRDX5, STX17, BCL2L11* (*BIM*)
- *ULBP* gene cluster – encodes activating ligands of NK cell receptor NKG2D

treatment

The treatment of patchy alopecia areata may include topical or intralesional corticosteroids, topical minoxidil (2% or 5%), topical anthralin (0.5–1% cream applied daily;), and combination therapy.

The concentration of intralesional corticosteroid is usually 2.5–5 mg/ ml of triamcinolone acetonide, and injections can be repeated every 4–8 weeks. This medication should be injected at the level of the mid dermis to target the diseased, miniaturized hair bulbs.

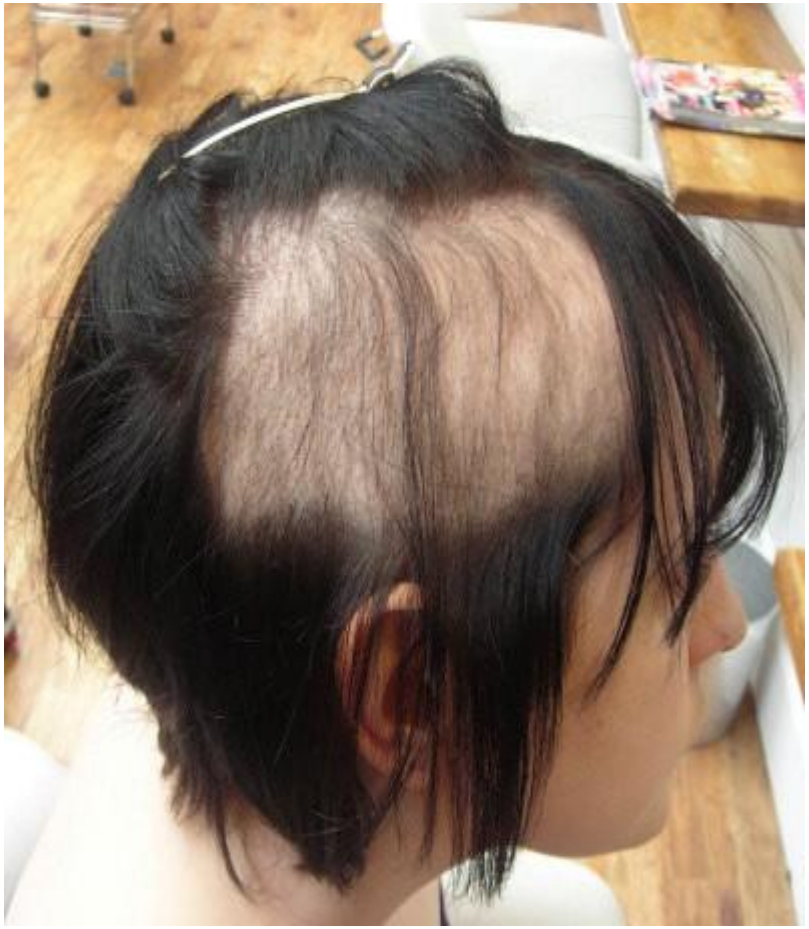
- for extensive disease:
- Approximately 80% of patients will respond to high-dose systemic corticosteroids (e.g. 40 mg triamcinolone intramuscularly monthly, or daily oral prednisolone or dexamethasone tapered over 6–8 weeks); however ~50% will relapse with dose reduction or cessation of therapy.
- Topical immunotherapy (with diphencyprone or squaric acid dibutyl ester) is a non-FDA-approved treatment for extensive disease.

- More recently, promising results with oral JAK/STAT pathway inhibitors (e.g. tofacitinib, ruxolitinib) have been reported, but relapse following discontinuation is an issue.

TREATMENT OPTIONS FOR THE MANAGEMENT OF ALOPECIA AREATA
Topical and intralesional corticosteroids (1)
Topical irritants (e.g. anthralin, tazarotene, azelaic acid) (2)
Topical minoxidil (2)
Topical immunotherapy (e.g. squaric acid dibutyl ester, diphencyprone) (1)
Systemic corticosteroids, pulsed dosing* (especially if rapidly progressive) (2)
Systemic JAK/STAT pathway inhibitors: tofacitinib (2), ruxolitinib (3)
Topical or oral photochemotherapy (PUVA) (2)
Excimer laser (3)
Systemic corticosteroids, chronic (2)
Systemic cyclosporine (3)
*e.g. oral prednisolone 300 mg (5 mg/kg for children) monthly for a minimum of three doses.

TRICHOTILLOMANIA

- Individuals with trichotillomania usually pluck scalp hair, resulting in patchy or full alopecia of the scalp
- Patches of alopecia often have bizarre shapes, irregular borders, erosions, and contain hairs of varying lengths
- In severe cases, hairs in the occiput tend to be spared.
- The clinical diagnosis can be supported by creating a "hair growth window" by repeatedly (weekly) shaving a small area of involved scalp to demonstrate normal, dense regrowth.



Treatment

No specific treatment approach has been established as effective in any large controlled study.

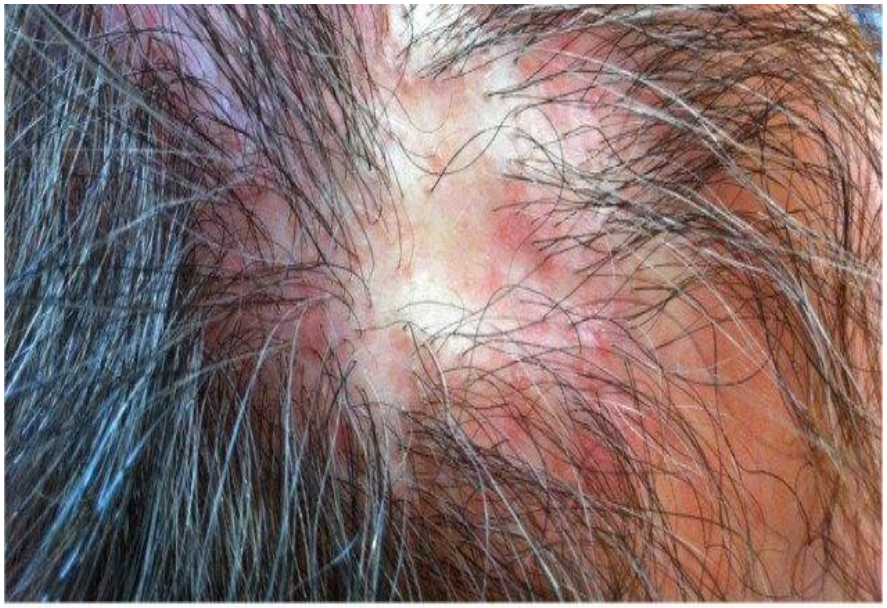
Hypnosis, behavioral modification therapy, insight-oriented psychotherapy, and pharmacologic therapy have all been tried, but success rates are low.

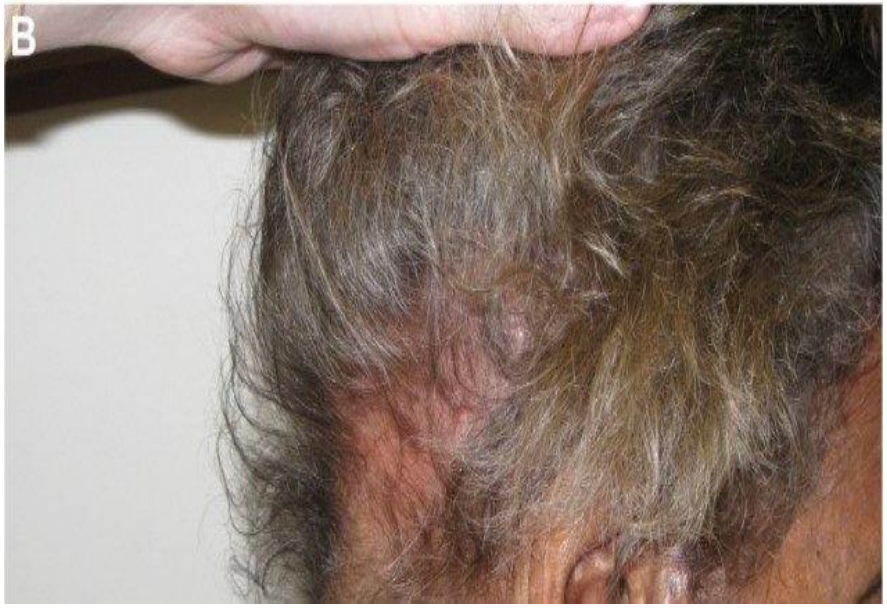
If pharmacological therapy is considered, the recommended first-line medication is clomipramine.

Selective serotonin reuptake inhibitors (SSRIs) have been tried without convincing success

Lichen Planopilaris

- Lichen planopilaris (LPP) affects women more often than men.
- Fewer than 30% of patients develop lesions of lichen planus on the skin.
- Most commonly, there are several scattered foci of partial hair loss with associated perifollicular erythema, follicular spines, and scarring

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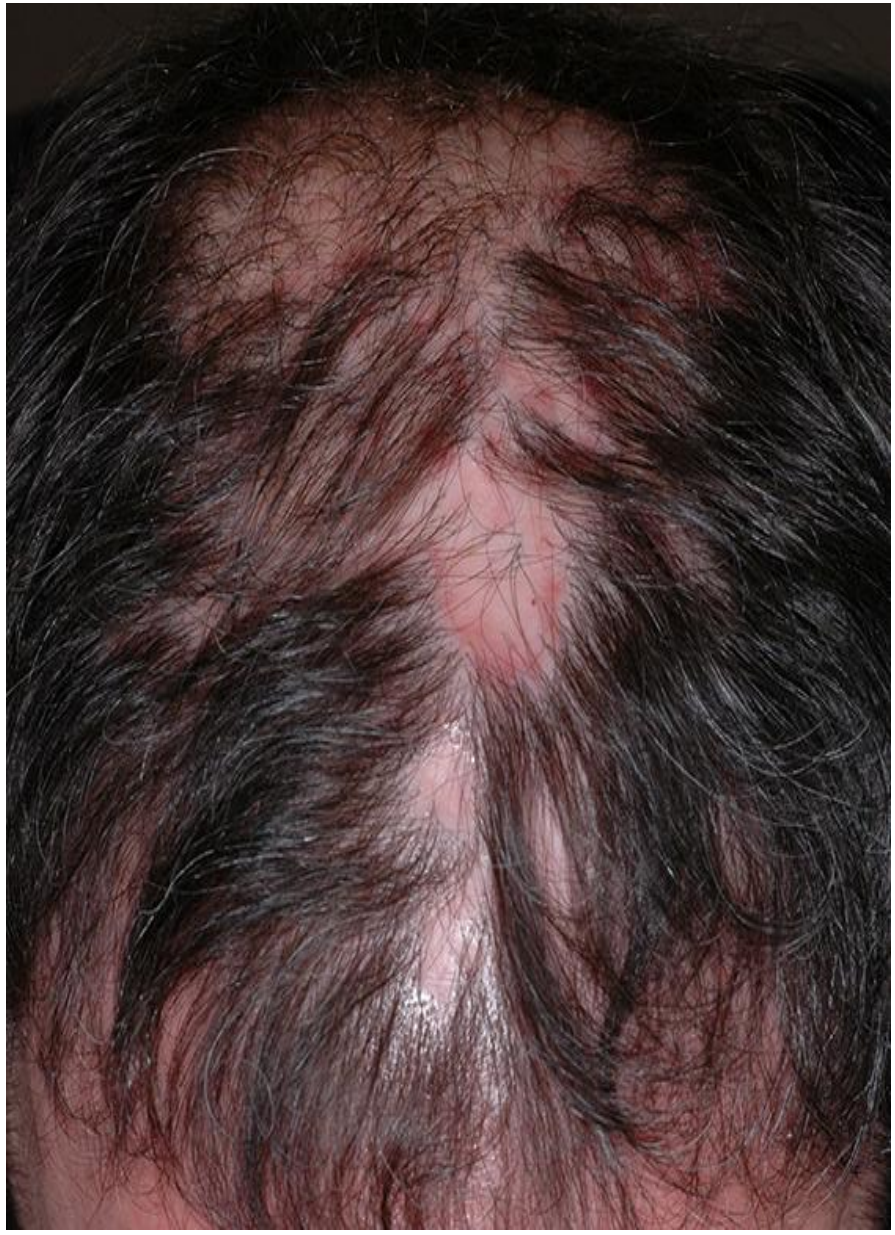


Treatment

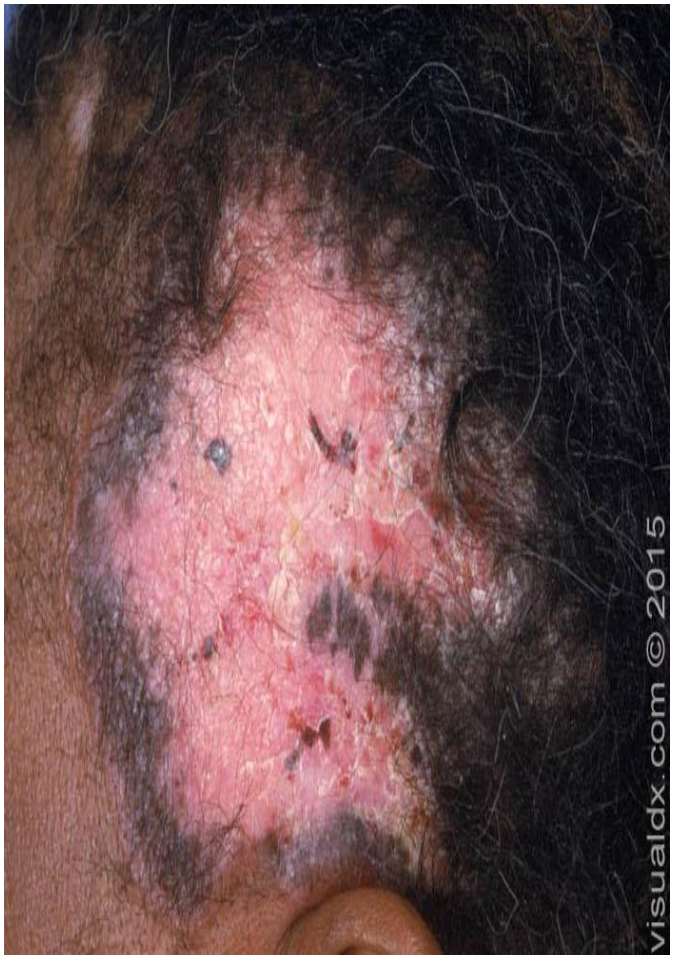
- LPP can be difficult to treat.
- Therapeutic recommendations include oral antimalarial drugs (e.g. hydroxychloroquine) and corticosteroids (topical, intralesional, and oral).
- Pioglitazone hydrochloride (a PPAR-γ agonist) was used with reported success.
- Various other anecdotal or uncontrolled studies have reported that oral cyclosporine, mycophenolate mofetil, retinoids, or low-dose weekly methotrexate may be effective in some patients.

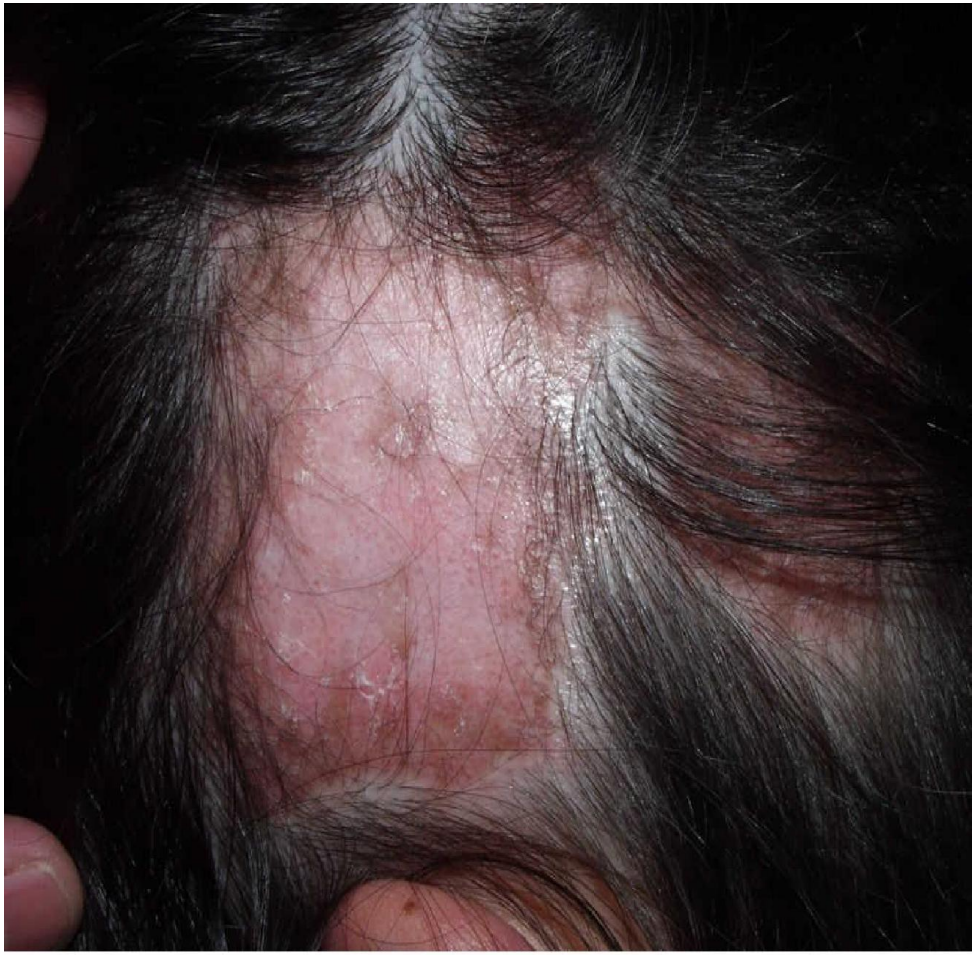
Discoid Lupus Erythematosus

- Although DLE is seen in patients with systemic LE, the majority of patients do not have systemic disease.
- Discoid LE (DLE) usually occurs in adults and is more common in women.
- The diagnosis of DLE and LPP requires histologic confirmation and cannot be based solely on the clinical appearance of scalp lesions.

Clinical feature

- They may resemble classic discoid lesions elsewhere ,with erythema, epidermal atrophy, and dilated, plugged follicular ostia in addition to alopecia. Central hypopigmentation and peripheral hyperpigmentation are commonly seen in dark-skinned individuals.





Actas Dermosifiliogr. 2012;103:376-87

Treatment

- Discoid lesions usually respond to oral antimalarial drugs (e.g. hydroxychloroquine) and corticosteroids (topical, intralesional, and oral).
- If initiated early, a surprising amount of regrowth can occur.
- Various anecdotal or uncontrolled studies have reported that oral medications including mycophenolate mofetil, retinoids, thalidomide, azathioprine, low-dose weekly methotrexate, cyclosporine, and TNF-α inhibitors may be effective in some patients

با تشکر از توجه شما