A REVIEW ON ETIOLOGY, TYPES AND TREATMENT OF PSORIASIS

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Summary

Psoriasis is an inflammatory Papulo-squamous disease that generally appears as patches of raised red skin covered by a flaky white build up in many different forms. It is the result of overreaction of the immune system which gives faulty signals resulting in acceleration of the growth cycle in skin cells which pile up on the surface where the body cannot shed them fast enough. Psoriasis is a disorder in which factors in immune system, enzyme and other biochemical substances that regulate skin cell division become impaired, probably because of one or more genetic defects, this cause rapid keratinocytes proliferation and inflammation. Thus the immune system is somehow triggered, which in turn speeds up the growth cycle of skin cells. A normal skin cell matures in 28 to 30 days & is shed from the skin's surface unnoticed. But a psoriatic skin cell takes only 3 to 4 days to mature and more to the surface, and the cells pile up & form the elevated red lesions. More than 7 million in U.S. and 25 million in India are the victims of Psoriasis, that's not only leads to physical disorder but also affect emotional make up and the social status of the victim. The exact cause of psoriasis is still unknown. Several treatments are available, each specifically related to certain factors but none of these have curative effects. However, some treatments are usually effective and will control the condition by clearing or reducing the patches of psoriasis.

Key words: Psoriasis, Papulo - squamous, Keratinocytes

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Introduction

Various forms of psoriasis exist. Some can occur independently or at the same time as other variants, or one may follow another. Psoriasis is a chronic skin disorder marked by periodic flare-ups of sharply defined red patches covered by a silvery, flaky surface. The primary disease activity leading to psoriasis occurs in the epidermis (a hyper proliferative skin disease with a markedly increased 5-6 times normal rate of epidermal turnover).The process starts in the basal (bottom) layer of the epidermis. Here, Keratinocytes are immature skin cells that produce keratin, a tough protein that helps to form hair and nails as well as skin. In normal cell growth, keratinocytes mature and migrate from the bottom (basal) layer to the surface and are shed unobtrusively. This process takes about a month. In psoriasis, however, the keratinocytes proliferate very rapidly and travel from the basal layer to the surface in only about four days. The skin cannot shed these cells quickly enough so they accumulate in thick, dry patches, or plaques. Silvery, flaky areas of dead skin build up on the surface of the plaques and are shed. The underlying skin layer, the dermis, is red and inflamed. The dermis contains nerves and blood and lymphatic vessels, which supply the abnormally multiplying keratinocytes with their blood supply and also transport potent immune factors that cause the underlying inflammation and redness [1-2].

Causes of psoriasis

The exact cause remains unknown. There may a combination of factors, including genetic predisposition and environmental factors. The immune system is thought to play a major role. Despite research over the past 30 years looking at many triggers, the "master switch" that turns on psoriasis is still a mystery.

There are two main hypotheses about process that occurs in development of the disease. The first considers psoriasis as primarily a disorder of excessive growth and reproduction of skin cells. The problem is simply seen as a fault of the epidermis and its keratinocytes. The second hypothesis sees the disease as being an immune-mediated disorder in which the excessive reproduction of skin cells is secondary to factors produced by the immune system. T cells (which normally help protect the body against infection) become active, migrate to the dermis and trigger the release of cytokines (tumor necrosis factor-alpha TNFα, in particular) which cause inflammation and the rapid production of skin cells. It is not known what initiates the activation of the T cells.

Some Genetic Factors, Environmental factors and some other triggers are also involved in inducing Psoriasis [2-6].

Genetic Factors:-

A combination of genes is involved with increasing a person's susceptibility to the conditions leading to psoriasis

(1) HLA Molecules: The processes leading to all autoimmune disease involve the human leukocyte antigen (HLA) system, which is genetically regulated. HLA molecules are designed to pick off parts of antigens and present them on the surface of a cell so that the various infection-fighting factors in the immune system can recognize and destroy them. Malfunction of this system is at the root of most immune disorders, including psoriatic arthritis. For example, psoriasis patients with a specific HLA genetic factor called HLA-CW6 tend to develop psoriasis at an earlier than average age. It should be noted, however, that only 10% of people who harbor these genes develop psoriasis.

(2) PSORs: Researchers have now identified four key genes (named PSORs 1-4) that are involved with psoriasis. Of particular interest are the genes located in regions on specific chromosomes that are linked to HLA and tumor necrosis factor, an immune component strongly associated with psoriasis.

Environmental and Other Triggers:-

Outside factors, including weather, stress, injury, and infection, while not direct causes, are often important in triggering the disease process leading to onset and worsening of psoriasis.

(1) Weather: Weather is a strong factor in psoriasis:
- Cold, dry weather is a common precipitant of psoriasis flare-ups.
- Hot, damp, sunny weather helps relieve the problem in most patients.
- To confuse matters, some people have photosensitive psoriasis, which actually improves in winter and worsens in summer when skin is exposed to sunlight.

(2) Stress and Strong Emotions: Stress, unexpressed anger, and emotional disorders, including depression and anxiety, are strongly associated with psoriasis flare-ups. In one study, nearly 40% of patients remembered a specific stressful event that occurred within a month of a psoriasis flare. A 2001 study suggested that stress can trigger specific immune factors associated with psoriasis flares. Some evidence indicated that people with psoriasis may respond to stress differently from those without the skin disease. In one study, psoriasis patients had fewer aggressive verbal responses than others did when confronted with hostile situations.

(3) Infection: Infections caused by viruses or bacteria can trigger some cases of psoriasis. Some examples include the following:
- Streptococcal infections in the upper respiratory tract, such as tonsillitis, sinusitis, and so-called "strep" throat, are known to trigger guttate psoriasis in children and young adults. The infections may also worsen ordinary plaque psoriasis.
- The human immunodeficiency virus (HIV) is also associated with psoriasis.
- An uncommon form of human papillomaviruses (HPV) called EV-HPV has been associated with psoriasis. Although EV-HPV is probably not a direct cause, it may play an indirect role in the perpetuation of psoriasis. (This HPV form is not the virus associated with cervical cancer and genital warts.)
- Helicobacter pylori (H.pylori) infection, a major cause of peptic ulcers, has been proposed as a possible cause of psoriasis. Research in 2001 indicated that this is highly unlikely, at least in children.

It seems reasonable to assume that pustular psoriasis, which resembles an infection, is caused by some organism, but none to date have been identified.

(4) Skin Injuries and the Köbner Response: The Köbner response is a delayed response to skin injuries, in which psoriasis develops later on at the site. In some cases, even mild abrasions can cause an eruption, which may be a factor in the frequency of psoriasis on the elbows or knees. (It should be noted that psoriasis can develop in areas with no history of skin disruption.)

(5) Drugs: A number of drugs can worsen or induce pre-existing latent psoriasis, including the following:
- The anti-malarial drug chloroquine.
- Certain drugs used for hypertension and heart problems, including angiotensin-converting enzyme

(ACE) inhibitors. Beta-blockers may actually trigger the onset of psoriasis and produce flare-ups in people who already have it.
● Progesterone used in female hormone therapies.
● Lithium, which is used in bipolar disorder. (It may trigger the onset of the who already have psoriasis.)
● Indomethacin, a non-steroidal anti-inflammatory drug (NSAID), can cause or worsen psoriasis.
(It should be noted that other NSAIDs, such as meclofenamate, may actually improve the condition.)
● Withdrawing from oral steroids or high-potency steroid ointments that cover wide skin areas can cause flare-ups of severe psoriasis, including guttate, pustular, and erythrodermic psoriasis. Because these drugs are also used to treat psoriasis, this rebound effect is of particular concern.

Types of Psoriasis

Psoriasis typically looks like red or pink areas of thickened, raised, and dry skin. It classically affects areas over the elbows, knees, and scalp. Essentially anybody area may be involved. It tends to be more common in areas of trauma, repeat rubbing, use, or abrasions.

Psoriasis has many different appearances. It may be small flattened bumps, large thick plaques of raised skin, red patches, and pink mildly dry skin to big flakes of dry skin that flake off.

There are several different types of psoriasis as described below [7-9].

(1) Plaque Psoriasis

Description of Plaque Psoriasis Patches: Plaque psoriasis is the most common form and causes skin patches with the following characteristics:
● The patches start off in small areas, about one-eighth of an inch in diameter. They usually appear symmetrically, that is, in the same areas on opposite sides of the body.
● The patches gradually enlarge and develop thick, dry plaque. If the plaque is scratched or scraped, bleeding spots the size of pinheads appears underneath (known as the Auspitz sign).
● Some patches may become ring shaped (annular) with a clear center and scaly raised borders that may be wavy and snake-like.
● Eventually separate patches may join together to form larger areas as the disorder develop. In some cases, the patches can become very large and cover wide areas of the back or chest (known as geographic plaques because they resemble maps).

Location of Plaque Psoriasis:
● Patches most often occur on the elbows, knees, and the lower back.
● About half of patients develop psoriasis on the scalp. Many patients have only a few patches in this location. In some cases, however, psoriasis can cover the scalp with thick plaques that may even extend down from the hairline to the forehead. It rarely affects the face in adulthood, however.
● Patches also can appear on the palms and soles, in the genital areas of both men and women, above the pelvic bone, and on the thighs and calves of the legs.

In children, psoriasis is most likely to start in the scalp and spread to other parts of the body; unlike in adults, it also may occur on the face and ears.

Course of Plaque Psoriasis: Plaque psoriasis may persist for long periods. More often it flares up periodically, triggered by certain factors, such as cold weather, infection, or stress.

(2) Psoriatic Arthritis

Description of Psoriatic Arthritis**:** Psoriatic arthritis (PsA) is an inflammatory condition characterized by stiff, tender, and inflamed joints. About 80% of PsA patients have psoriasis in the nails. Arthritic and skin flare-ups tend to occur at the same time. It is not clear whether psoriatic arthritis is a unique disease or a genuine variation of psoriasis, though evidence suggests they are both caused by the same immune system dysfunction.

Location of Joint Pain Psoriatic Arthritis: Some experts define five forms of PsA as determined by the location and severity of the joint involvement:

● Symmetric PsA. Symmetric arthritis occurs in the same location on both sides of the body. It usually affects multiple pairs of joints and in about half of the cases, the condition will progress. The condition is very similar to but less disabling than rheumatoid arthritis. The psoriasis itself is often severe.

● Asymmetric PsA. Asymmetric PsA involves periodic joint pain and redness, usually only in one to three joints, which can be in the knee, hip ankle wrist, or one or more fingers. The pain does not occur in symmetric locations.

● Distal Interphalangeal Predominant (DIP). DIP involves the joints of the fingers and toes closest to the nail and occurs in about 5% of PsA cases.

● PsA in the Spine. Inflammation in the spinal column (spondylitis) is the primary symptoms in about 5% of PsA cases. Such patients may experience stiffness and burning sensations in the neck, lower back, sacroiliac, or spinal vertebrae.

● Arthritis Mutilans. This is a severe, deforming and progressive arthritis that affects less than 5% of PsA cases. It principally affects the small joints of the hands and feet, but it also frequently affects the neck and lower back. Arthritic and skin flares and remissions tend to coincide.

Course of Psoriatic Arthritis: Although patients with psoriatic arthritis tend to have mild skin manifestations, the disease is systemic; that is, it affects the body as a whole. PsA, therefore, is more serious than the more common plaque psoriasis.

(3) Guttate Psoriasis

Description of Guttate Psoriasis: Psoriasis is named after the French word for drop"goutte" since the lesions are multiple, small (5-15 mm), round, or oval and drop-like in shape. This form of psoriasis is seen mainly in children and young adults after a Streptococcal throat infection

Location of Guttate Psoriasis: They will typically cover your trunk, arms, legs, face and scalp.

Course of Guttate Psoriasis: It is the presenting form of psoriasis in approximately 15% of people and often goes away on its own within a few weeks or months.

(4) Pustular Psoriasis

Pustular psoriasis may be found in one localized area or spread over many areas of your body. Although pustules are seen in this form, they do not represent an infection and are not contagious.

a) Localized pustular psoriasis

One or more patches of psoriasis spontaneously develop small pustules. Irritation and aggressive over treatment may also induce this form of psoriasis.

b) Palmoplantar pustulosis

It occurs on the palms of your hands and the soles of your feet. It is chronic, persistent, symmetrical and difficult to treat, it typically affects middle-aged women.

c) Acropustulosis

Acropustulosis is a localized form of pustular psoriasis that affects fingers, thumbs and toes. Pustules appear then burst leaving bright red areas that may ooze, become scaly and/or crusty. The nails are often abnormal, crumbly and may lift up because of underlying lakes of pus.

d) Generalized (von zumbusch) pustular psoriasis

This type of psoriasis usually reflects a worsening of the psoriasis. The skin becomes sore and red. Pin-point pustules develop and spread forming large patches. The skin folds and groin area are commonly involved. People with this rare type of psoriasis usually feel unwell, they may have a fever and a high white blood cell count, and occasionally die from this condition.

(5) Inverse Psoriasis

Inverse psoriasis refers to psoriasis that occurs in the creases and folds of your skin for example, armpits, and groin and under the breasts. The lesions are well defined red patches, but scaling is often not present or is minimal.

(6) Nail Psoriasis

Nail changes occur in 25-50% of people who have psoriasis. They are more common in people who also have psoriatic arthritis. Small indents in the nails (“pitting”) are the most common nail changes, other changes include lifting up of the nails (“onycholysis”), discoloration, thickening and crumbling.

(7) SeborrheicPsoriasis

Patches appear as red scaly areas on the scalp, behind the ears, above the shoulder blades, in the armpits or groin, or in the center of the face.

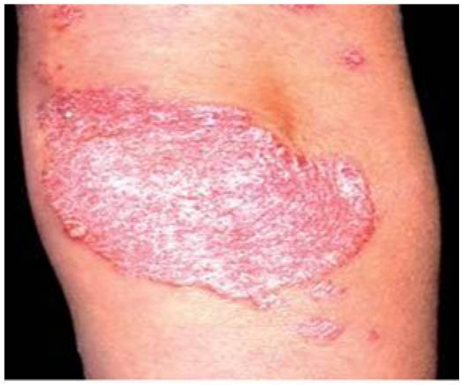
(8) Generalized Erythrodermic Psoriasis

This is a rare severe and form, in which the skin surface becomes scaly and red. The disease covers all or nearly all of the body.

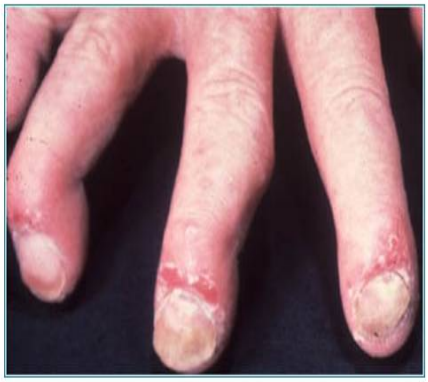
Different types of psoriasis are shown in **figure 1(A) and 1(B).**

Figure no: 1(A) Different types of Psoriasis

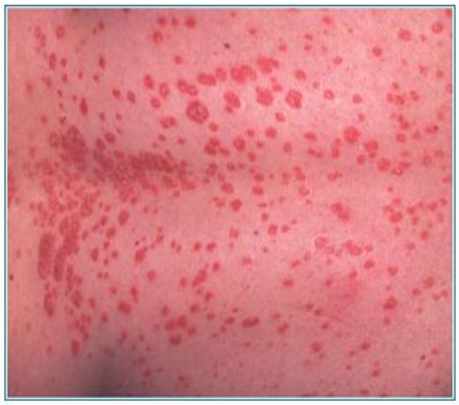
(1) Plaque psoriasis



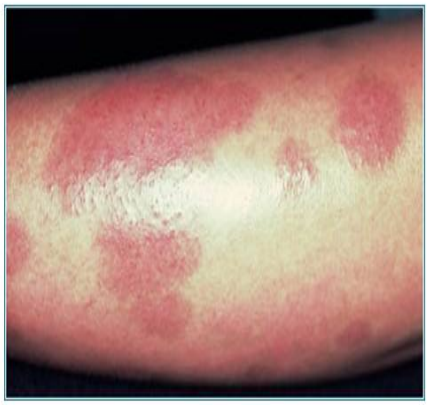
(2) Psoriatic arthritis



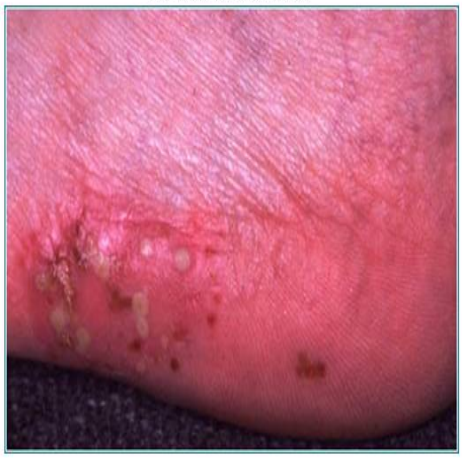
(3) Guttate psoriasis-on the back



(4) a. Localized pustular psoriasis



(4) b. Palmoplantar pustulosis on the sole of foot



(4) c. Acropustulosis - Pustular psoriasis involving the nail bed

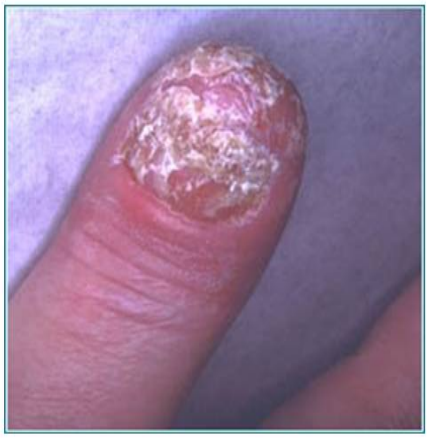
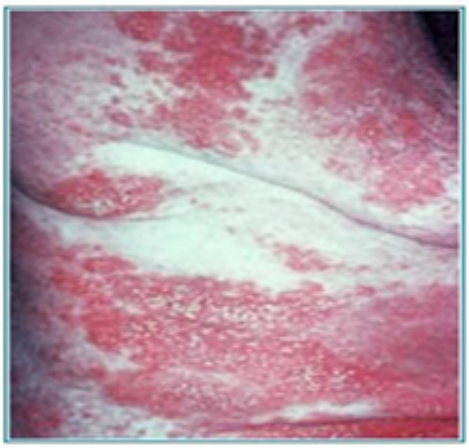
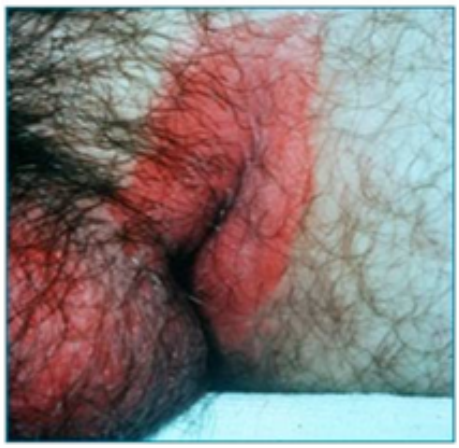


Figure no: 1(B) Different types of Psoriasis

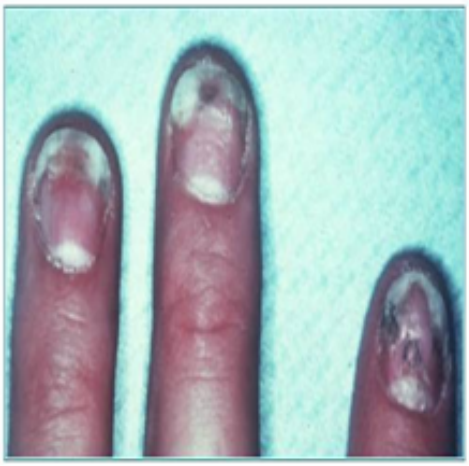
(4) d. Generalized pustularpsoriasis



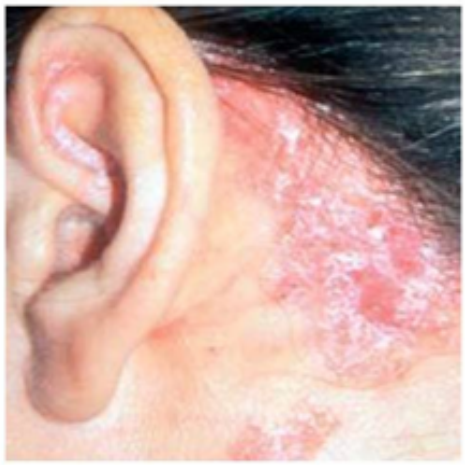
(5) Inverse psoriasis



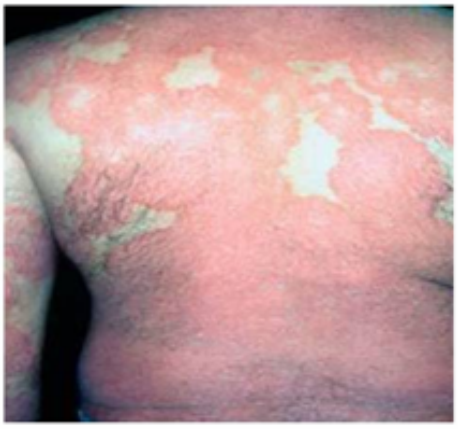
(6) Nail Psoriasis



(7) Scalp psoriasis



(8) Erythrodermic psoriasis



Treatment of Psoriasis:

Unfortunately, none of the available treatments for psoriasis is a cure. Treatment can often control the disease for long periods, but the disease can come back when treatment stops. But new biological therapies in development should offer better control while reducing the number of side effects.

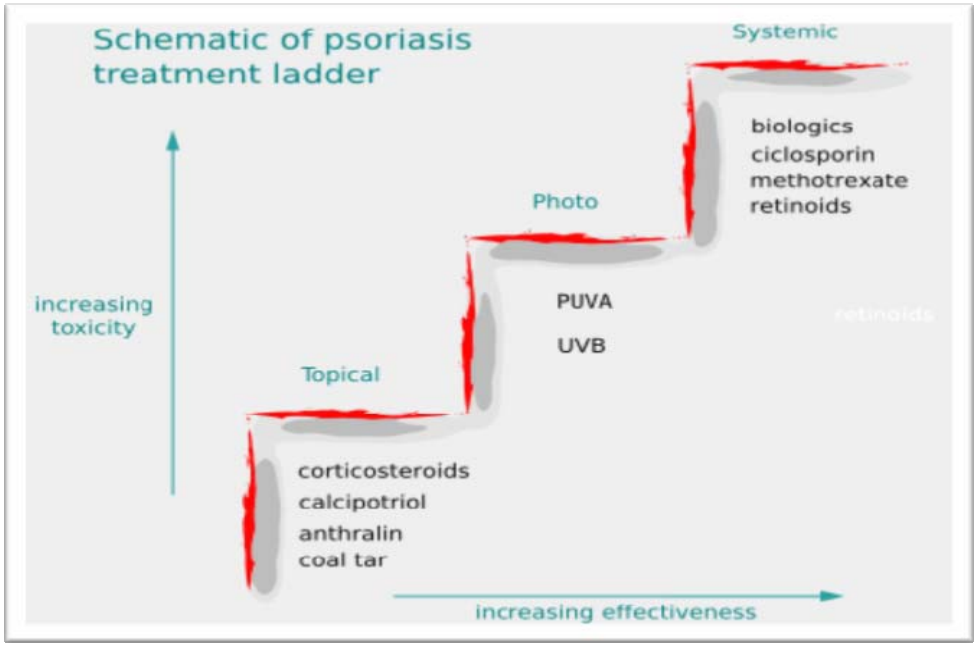
Treatment for psoriasis varies depending on:
- The type of psoriasis
- The extent and severity of the disease (how much of the skin is affected and how badly)
- The age, sex, and lifestyle of the affected person
- How the affected person has responded to treatment in the past.

In general, doctors treat psoriasis in three steps.
Step 1: Medications applied to the skin (**topical therapy**)
Topical steroids, Calcipotriol, Coal tar, Tazarotene, Emollients, Anthralin, Methotrexate

Step 2: Treatments that use light (**photo therapy**)
Sunshine. Ultraviolet therapy. UVB therapy. PUVA.

Step 3: Medications given as a pill or injection (**systemic therapy**)
Alefacept. Methotrexate. Retinoids. Cyclosporine. Hydroxyurea.

Figure 2 Schematic of psoriasis treatment ladder [10]



These treatments can be combined in various ways to try to get the best outcome. Finding the most effective treatment for an affected individual can involve a lot of trial and error. What works for one person may not work for someone else. People with severe and extensive psoriasis may get the most relief and avoid or reduce side effects when treatments are rotated.

Treatments for psoriasis can often control the disease for long periods. However, none of the available treatments is a cure. The disease can come back when treatment stops.

Biologic agents are being introduced for the treatment of psoriasis and have substantial advantages over previously used systemic therapies because they have fewer risks and side effects. Two of the therapies currently being used, etanercept and remicade, are already available for the treatment of rheumatoid arthritis and Cohn's disease. Both therapies are tumor necrosis factor (TNF) blockers, which work by interfering with specific immune responses that are responsible for psoriasis. Alefacept was approved in Jan. 2003 and works by interfering with the T cell process.

Step 1: Medications applied to the skin (topical therapy)

Topical treatments of psoriasis are a mainstay in its management. Topicals are particularly indicated in patients with mild disease, although those with more widespread psoriasis may benefit as well.

In general, objective dermatological assessments such as the Psoriasis Area and Severity Index (PASI), the body surface area involved, is used in most clinical trials.

Topical agents are effective, convenient to use, and are relatively free of the serious side effects associated with systemic therapy. They are most effective when used to treat localized plaque psoriasis covering <20% of the BSA [10].

Different Topical Agents [11-29]

Topical steroids: Topical steroid medications are one of the most common treatments for mild to moderate psoriasis. They reduce redness (inflammation) and itching and stop the rapid build-up of dead skin cells. They come in varying strengths, from weak to highly potent and are available as creams, gels, lotions, ointments, or solutions. Generally stronger preparations are used on the scalp, knees, palms and feet while weaker creams or ointments are used on the face and other sensitive areas. New foam for scalp psoriasis called clobetasol propionate has recently been approved. In foam form, it penetrates the skin easily - enhancing the effectiveness of the treatment.

Some Topical Corticosteroids used for Psoriasis is shown in **table 1**.

Table 1: Some Topical Corticosteroids Used for Psoriasis

Low potency (Some are available over the counter)	Hydrocortisone low potency (Hytone, Penecort, Synacort, Cort-Dome, Nutracort, Westcort). Desonide (Tridesilon, DesOwen). Flumethasone pivalate (Locorten). Fluocinolone acetonide (Synalar, Derma-Smoothe). Triamcinolone acetonide (Aristocort)
Low to medium potency	Alclometasone dipropionate (Aclovate). Hydrocortisone low to medium potency (Locoid, Pandel). Hydrocortisone valerate (Westcort). Prednicarbate (Dermatop).
Medium to upper-mid potency	Clocortolone pivalate (Cloderm). Fluticasone propionate (Cutivate). A low-dose ointment (0.005%) is proving to be effective for psoriasis on the face and in folds of the skin, but not in other areas. Mometasone furoate (Elocon). (Only needs to be administered once a day. May be as or more effective than corticosteroids at the same strength while having a lower risk for severe side effects.) Triamcinolone acetonide (Aureocort, Tri-Adcortyl, Kenalog). Available as a topical cream or as an injectable agent to treat nail psoriasis.
High potency	Betamethasone (Diprosone) (Also available in lower potencies) Amcinonide (Cyclocort) Desoximetasone (Topicort) Diflorason (Florone, Maxiflor) Fluocinonide (Lidex) Halcinonide (Halog)
Very high potency	Halobetasol propionate (Ultravate). Betamethasone (Diprolene). Available as a foam (Luxiq), which was developed for the scalp but patients are finding it preferable for trunk and extremities as well. In one study, 72% of patients were clear or almost clear of disease after 28 days of treatment, compared with 47% who were clear after using the lotion. The foam turns to liquid on the trunk or extremities and is a cosmetically preferred option for many patients. Clobetasol propionate (Temovate). Also available as a foam. Diflorasone diacetate (Florone, Maxiflor, Psorcon). Psorcon is a gel form that may be particularly helpful.

Calcipotriol and **tacalcitol** belong to a group of medicines known as **Vitamin D analogues** (which are chemically related to vitamin A). Calcipotriol is available as a cream or ointment to treat plaque psoriasis and as a lotion for scalp psoriasis. It is also available in combination with betamethasone, a potent topical steroid. Tacalcitol is available as an ointment to treat plaque psoriasis. Calcitriol is a form of **Vitamin D** and is available as an ointment for the treatment of mild to moderate plaque psoriasis. These are effective treatments and usually well tolerated but sometimes cause irritation. Using topical calcipotriene in combination with topical corticosteroids facilitates more rapid improvement in the psoriasis and prevents the side effect of irritation [30-32].

Tazarotene is a retinoid (a substance chemically similar to **vitamin A**). It is available as an ointment, gel and cream is an effective treatment. It does not smell or stain. It is only used on areas affected by psoriasis and not on normal skin and it can cause irritation. You can protect the surrounding normal skin with yellow or white soft paraffin.

Coal tar helps to reduce inflammation and also helps to remove loose scales from the patches of psoriasis. Coal tar can be applied to or allowed to come into contact with normal skin. Some tar products can be used on the face and in the flexures (behind elbows/knees and on the shins). Tar baths and shampoos can also be helpful. Higher strengths of coal tar may be needed to treat the thicker patches of psoriasis. The disadvantages of coal tar preparations are that they can cause skin irritation, they can also stain clothing and sheets or pillowcases.

Emollients hydrate and sooth the skin and soften the plaques of psoriasis. For mild psoriasis, treatment with an emollient may be all that is needed. You can also use emollients in addition to any other treatment, to keep the skin moist and supple.

Anthralin (or dithranol) has been known for its anti-psoriatic properties for almost a century. It is commercially available in concentrations ranging from 0.1% to 3% in cream, ointment, and lotion vehicles. Anthralin is most commonly used for chronic recalcitrant plaques or in association with UVB phototherapy. The classical regimen starts with low concentrations of 0.1% in an ointment or paste applied daily or overnight with weekly increase in concentration until plaques resolve. Alternatively, the short-contact method using concentrations as high as 1%±3% can be applied daily or every other day for 10±20 minutes and then washed off with increased duration of application on a weekly basis to avoid irritation. Side effects include irritation as well as discoloration of hair, skin, and nails. Staining of clothes, bed sheets, and furniture is also a major disadvantage.

Other treatments, the keratolytic properties of salicylic acid are often used for scalp psoriasis to reduce scaling and enhance transcutaneous penetration of other therapeutic agents. The topical use of macrolide immunomodulators, including cyclosporine, tacrolimus, ascomycin and rapamycin, is limited by their poor percutaneous absorption. Topical tacrolimus ointment was reported ineffective in a pilot study but was found to decrease erythema, in epidermal thickness when applied under occlusion in a microplaque assay. Improvement of facial psoriasis was also reported in 11 patients treated with 0.1% ointment bid for 2 ±4 weeks.

A topical preparation of **Methotrexate** was recently shown to be superior to vehicle in patients with plaque-type psoriasis. (Rextop Topical gel from systopic laboratories)

Some Topical therapies used for psoriasis are listed in **table 2**.

Table 2: Topical therapies for psoriasis

Therapy	Formulation	Efficacy	Duration of remission	Adverse effects
Cortico-steroids	Multiple gels, lotions, creams, ointments, solutions, foams grouped by relative strength (classes 1-7)	Thinning of plaques, Decreased symptoms in first 2 wk of treatment, with improvement in subsequent weeks	Mean duration of 2 mo with betamethasone Propionate ointment; Rebound phenomenon may occur if abruptly ceased	**Local:** atrophy, striae, telangiectasis, among others **Systemic:** risk of HPA axis suppression with excessive, prolonged use
Vitamin D analogs	Calcipotriene ointment, cream, scalp solution	As effective as class 2 cortico-steroids, but often take 6-8 wk for full effect	Mean of 43.3 days; long-term therapy necessary	**Irritation;** risk of hypercalciuria And hypercalcemia at >100 g/wk
Retinoid	Tazarotene 0.05%, 0.1% gel or cream	As effective as class 2 cortico-steroids; improvement noted in first 1-2 wk of therapy	Prolonged compared With fluocinonide (class 2 corticosteroid)	**Irritation;** must be used with extreme caution in women of Childbearing age (category X)
Tar	Crude coal tar, liquor carbonis detergens, tar shampoos	Thinning of plaques, decreased symptoms in 2-4 weeks	Prolonged, particularly When combined with UVB	Irritation, folliculitis, photosensitivity
Anthralin	Commercial formulations, compounded formulations	Thinning of plaques, decreased symptoms in 2-4 wk	Prolonged	Extremely irritating; must avoid contact With surrounding skin
Salicylic acid	Compounded by pharmacist in concentrations of 2%-10% in white petrolatum or other base; OTCscalp solutions, shampoos	Typically does not result in clearance as monotherapy; used in combination with corticosteroids to decrease amount of scale	Not applicable	Risk of salicylate toxicity with application to > 20% body surface area

Step 2: Treatments that use light therapy (phototherapy) [33-35]

Natural sunlight contains ultraviolet (UV) light. UV light kills T cells in skin, reducing redness and slowing the overproduction of skin cells that causes scaling.

Sunshine: Brief, regular periods of exposure to natural sunlight can improve or clear psoriasis in some people. This approach to treating psoriasis is called **climatotherapy**. Sunburn should be avoided because it can make psoriasis worse.

Exposure to sunlight is not recommended for people who are sun-sensitive. Sun exposure can cause aging of the skin. An annual medical checkup is advised because sun exposure can increase the chance of skin cancer.

Ultraviolet therapy: Exposing the skin to UV light in carefully controlled doses is called phototherapy. Sunlight contains two kinds of UV light, known as UVA and UVB. Both can be used to treat psoriasis. In phototherapy, the affected person sits or lies inside a "light box," a booth fitted with special light-emitting tubes. Usually, people go to a doctor's office to receive phototherapy. Sometimes a light box can be purchased with a doctor's prescription for use at home.

UVB therapy: Treatment with UVB light is the safest form of phototherapy for widespread psoriasis or psoriasis that has not responded to medications applied to the skin. Usually three to five treatments a week are recommended, with a gradual increase in UV exposure depending on skin type. Significant clearing of psoriasis can be expected in one to three months. There are some risks of causing phototoxicity, but the sunburn reactions of UVB typically are not severe. Chronic adverse effects include photoaging, so the face should not be treated if there is no psoriasis there. Skin cancer is another potential risk, but this risk must be small because the long-term studies of patients who received Goeckerman (UVB + tar) for years were unable to detect an increased risk [36-37].

Exposure to UVB light must be carefully monitored to prevent sunburn. During treatment, the eyes must be shielded with goggles to guard against the possible formation of cataracts. Skin aging, wrinkling and eye damage may be a side effect of UVB treatment.

UVB phototherapy may be combined with tar, Anthralin, topical steroids, or other medications applied to the skin. The Goeckerman regimen, developed at the Mayo Clinic, uses crude coal tar, tar baths, and UVB treatment to treat widespread psoriasis. The Ingram regimen uses coal tar baths, Anthralin paste, and UVB therapy.

PUVA: PUVA is used for widespread psoriasis or when other treatments have not been effective. It combines a medication called psoralen with careful exposure to UVA light. (PUVA stands for Psoralen plus UVA.) Psoralen may be taken by mouth or applied to the skin. It makes the skin more sensitive to light. Treatment is given two or three times a week, up to about 25 treatments. The amount of UV exposure may be gradually increased, depending on skin type. As with UVB therapy, significant clearing of psoriasis can be expected in one to three months.

Compared with UVB therapy, PUVA clears skin more consistently with fewer treatments. However, PUVA has more short-term side effects, such as nausea, headache, fatigue, burning, and itching.

When psoralen is taken by mouth, nausea may be avoided by taking food at the same time. As with UVB therapy, the eyes must be shielded with goggles during UVA exposure to guard against the formation of cataracts.

Psoralen can be applied to the skin in the form of a cream, lotion, gel, or solution.

- **Paint PUVA:** Psoralen is painted onto skin plaques such as those on the palms of the hands or soles of the feet.
- **Soak PUVA:** The affected areas, such as the hands or feet, are immersed in a basin of water containing psoralen.
- **Bath PUVA**: The body is immersed in a tub of water containing psoralen.

After the paint, soak, or bath routine, the person is exposed to UVA light in a light box. UVA light is the same kind used in commercial tanning salons. Treating psoriasis in tanning salons is not recommended because attendants are untrained and the dose of UVA is not controlled. UVA therapy must be given in carefully controlled doses and supervised by a doctor.

PUVA is recommended for people with moderate to severe psoriasis or who have not improved with other treatments. . Also, because Psoralen remains in the lens of the eye, patients must wear UVA blocking eyeglasses when exposed to sunlight from the time of exposure to psoralen until sunset that day. PUVA can be combined with some oral medications (Retinoids and Hydroxyurea) to increase its effectiveness. Simultaneous use of drugs that suppress the immune system, such as cyclosporine, have little beneficial effect and increase the risk of cancer. Long-term use of PUVA increases the risk of developing both squamous cell skin cancer and melanoma. Regular medical examinations are advised to check for signs of skin cancer.

Step 3: Medications given as a pill or injection (systemic therapy) [38-39]

Doctors may prescribe medications that are given as a pill or an injection for severe psoriasis that does not respond to other treatments. Several new experimental biological therapies in development target specific steps in the pathogenesis of psoriasis. The first biological therapy was approved in January 2003. Initial data suggest improved safety over older agents such as Methotrexate and ciclosporin, but more research is necessary.

Alefacept [40-42]**:** In January 2003, the U.S. Food and Drug Administration approved Amevive (alefacept), the first biological therapy for psoriasis. The injected medication is used to treat adults with moderate to severe plaque psoriasis. Amevive treats plaque psoriasis through a unique immunosuppressive mechanism of action. Specifically, Amevive is believed to work by simultaneously blocking and reducing the cellular component of the immune system that is thought to play a significant role in the disease process.

Patients taking this medication should have regular monitoring of white blood cell counts during therapy. Amevive must be administered under the supervision of a physician. The medication works by suppressing the immune system, which could potentially increase their chances of developing an infection or malignancy. Patients should inform their physician promptly if they develop any signs of an infection or malignancy while undergoing a course of treatment with Amevive. Because the effect of Amevive on pregnancy and fetal development, including immune system development, is not known, women who become pregnant while taking the medication are urged to register in the drug manufacturer registry.

Methotrexate: This medication slows down the build-up of dead skin cells by interfering with DNA and by suppressing the immune system and can have a dramatic effect on psoriasis. Methotrexate is also used to treat cancer. The doses used to treat psoriasis are much smaller than those used in cancer treatment. The drug is usually taken by mouth once a week, either in a single dose or in three doses taken 12 hours apart. A supplement of folic acid (a B vitamin) may be taken at the same time. This therapy should be limited to patients with refractory, disabling psoriasis [43]. Methotrexate is very effective for people with widespread psoriasis that does not respond to ultraviolet light treatment or to medications applied to the skin. It is also effective for psoriatic arthritis. Skin improvement usually begins within several weeks of starting treatment. Maximum improvement is usually seen within two to three months. Medications applied to the skin may be used to treat any remaining plaques. If psoriasis still does not clear completely, or if the drug dose must be lowered to reduce side effects, Methotrexate may be combined with UVB or PUVA phototherapy or with another medication, such as a retinoid.

People taking Methotrexate must be closely monitored. The drug can cause liver damage. It can also decrease the body's production of red and white blood cells and platelets. Chest x-rays, as well as regular blood tests, should be done to check the blood count and liver and kidney function. A periodic liver biopsy may also be recommended because the drug's effects on the liver may not show up on blood tests. People who have liver disease or anemia should not take Methotrexate. Methotrexate can cause birth defects. It cannot be used by pregnant women, women planning to become pregnant, or their male partners. We chose fixed 15mg oral methotrexate schedule to treat our patients. It is possible that incidence of side effects may be less with lower dosage or with parenteral route as reported in some studies [44]. However dosage lowers than 15mg/week may not achieve the desired control of psoriasis. Intracellular accumulation of methotrexate and its metabolites result in depletion of folate store [45-46].

Retinoids: These drugs are related to Vitamin A. They normalize the growth of skin cells in psoriasis. Acitretin and isotretinoin are systemic vitamin A derivatives used in treatment of psoriasis. They are useful in treating severe forms of psoriasis, such as erythrodermic and pustular psoriasis that do not respond to other therapies.

Retinoids cannot be used by pregnant women, women planning to become pregnant, or their male partners. Women who take Acitretin must avoid pregnancy for up to three years after they stop taking the drug. Women also must not drink alcohol while they are taking Acitretin and for two months after they stop taking it.

Other possible side effects include dry skin, chapped lips, dryness of the eyes and nasal passages, hair thinning, sun sensitivity, and bone spurs of the long bones or spine. The drugs may also increase blood levels of both liver enzymes and triglycerides, a type of fat found in the blood. Reducing the dose of the drug usually reduces these side effects.

Cyclosporine [47-51]**:** This drug is widely used to prevent the rejection of transplanted organs. It is used to treat severe, disabling psoriasis in people who cannot tolerate other therapies or for whom other therapies have not been effective. In addition to being highly effective therapy for psoriasis, cyclosporine has been instrumental in shifting the focus of psoriasis research and treatment from keratinocyte abnormalities to immune perturbations, including the development of biologic therapies targeted at modulating immune function in psoriasis patients.

Cyclosporine works by suppressing the immune system in a way that slows the build-up of dead skin cells. Depending on the daily dose, the drug can clear most or all skin plaques within several weeks to a month. However, when a person stops taking the drug, the disease can come back.

People taking cyclosporine must be closely monitored by a doctor. The drug can cause high blood pressure and damage kidney function. It is not recommended for people who have a weak immune system or by people who have used ultraviolet light treatment a lot. Women who are pregnant, planning to become pregnant, or breast-feeding also must not use it.

Cyclosporine may also be used as a short-term crisis therapy. Other therapies with different side effects are then used to maintain the clearing of skin plaques.

Hydroxyurea: This drug reduces the build-up of dead skin cells by interfering with DNA. Like Methotrexate, Hydroxyurea is also used to treat cancer. In psoriasis, it may have fewer side effects than Methotrexate or cyclosporine but it is also less effective. It is sometimes used in combination with ultraviolet light treatment.

Possible side effects of Hydroxyurea include anemia and a decrease in white blood cells and platelets. Like Methotrexate and cyclosporine, it must not be used by women who are pregnant or planning to become pregnant.

Rotating Treatments

All of the treatments used for widespread, severe psoriasis have side effects when used for a long time. One way to reduce side effects is to use one treatment (or combination of treatments) for one to two years, then switch to another treatment, and continue in this fashion through a series of different treatments. This is called rotational therapy. If the skin clears up, treatment is stopped until psoriasis reappears. Then the cycle of rotating treatments begins again. In some cases, patients may be rotated from one therapy to another because the efficacy of the initial treatment has diminished with time, there is an increase in cutaneous side effects, or in the case of a person being treated with topical agents for mild disease there is an increase in the percentage of body surface area involved [52].

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