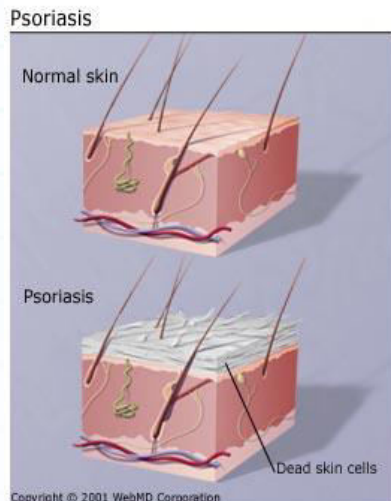


# Psoriasis



Psoriasis is a common, chronic, relapsing/remitting, immune-mediated systemic disease characterized by skin lesions including red, scaly patches, papules, and plaques, which usually itch. The skin lesions seen in psoriasis may vary in severity from minor localized patches to complete body coverage.

The five main types of psoriasis are plaque, guttate, inverse, pustular, and erythrodermic. Plaque psoriasis, the most common form, typically manifests as red and white scaly patches on the top layer of the skin. Skin cells rapidly accumulate at these plaque sites and create a silvery-white appearance.

Plaques frequently occur on the skin of the elbows and knees, but can affect any area, including the scalp, palms of hands, and soles of feet, and genitals. In contrast to eczema, psoriasis is more likely to be found on the outer side of the joint. Fingernails and toenails are frequently affected (psoriatic nail dystrophy) and can be seen as an isolated sign. Inflammation of the joints, known as psoriatic arthritis, affects up to 30% of individuals with psoriasis.

The causes of psoriasis are not fully understood. It is not purely a skin disorder and can have a negative impact on many organ systems. Psoriasis has been associated with an increased risk of certain cancers, cardiovascular disease, and other immune-mediated disorders such as Crohn's disease and ulcerative colitis. It is generally considered a genetic disease, thought to be triggered or influenced by environmental factors. Psoriasis develops when the immune system mistakes a normal skin cell for a pathogen, and sends out faulty signals that cause overproduction of new skin cells. It is not contagious. Oxidative stress, stress, and withdrawal of a systemic corticosteroid have each been suggested as a trigger for psoriasis. Injury to the skin can trigger local psoriatic skin changes known as the Koebner phenomenon.

No cure is available for psoriasis, but various treatments can help to control the symptoms. The effectiveness and safety of targeted immune therapies is being studied, and several have been approved (or rejected for safety concerns) by regulatory authorities. The disease affects 2–4% of the general population

## Causes of Psoriasis

The cause of psoriasis isn't fully known, but it's thought to be related to an immune system problem with cells in your body. More specifically, one key cell is a type of white blood cell called a T lymphocyte or T cell. Normally, T cells travel throughout the body to detect and fight off foreign substances, such as viruses or bacteria. If you have psoriasis, however, the T cells attack healthy skin cells by mistake, as if to heal a wound or to fight an infection.

Overactive T cells trigger other immune responses. The effects include dilation of blood vessels in the skin around the plaques and an increase in other white blood cells that can enter the outer layer of skin. These changes result in an increased production of both healthy skin cells and more T cells and other white blood cells. This causes an ongoing cycle in which new skin cells move to the outermost layer of skin too quickly — in days rather than weeks. Dead skin and white blood cells can't slough off quickly enough and build up in thick, scaly patches on the skin's surface. This usually does not stop unless treatment interrupts the cycle.

Just what causes T cells to malfunction in people with psoriasis isn't entirely clear. Researchers have found genes that are linked to the development of psoriasis, but environmental factors also play a role.

### **Psoriasis triggers**

Psoriasis typically starts or worsens because of a trigger that you may be able to identify and avoid. Factors that may trigger psoriasis include:

- Infections, such as strep throat or skin infections
- Injury to the skin, such as a cut or scrape, bug bite, or a severe sunburn
- Stress
- Cold weather
- Smoking
- Heavy alcohol consumption
- Certain medications — including lithium, which is prescribed for bipolar disorder; high blood pressure medications such as beta blockers; antimalarial drugs; and iodides.

### **Symptoms of Psoriasis**

There are several types of psoriasis. Symptoms for each type may vary, but the major symptoms are:

- Raised, bright red patches of skin, often covered with loose, silvery scales, usually on the knees, elbows, or low back
- Tiny areas of bleeding when skin scales are picked or scraped off (Auspitz's sign)
- Mild scaling to thick, crusted plaques on the scalp
- Itching, especially during sudden flare-ups or when the psoriasis patches are in body folds, such as under the breasts or buttocks
- Discoloured or pitted nails

#### **Other symptoms of psoriasis may include:**

- Similar plaques in the same area on both sides of the body (for example, both knees or both elbows)
- Flare-ups of many raindrop-shaped patches (guttate psoriasis)
- Joint swelling, tenderness, and pain (psoriatic arthritis)
- Psoriasis patches that appear after an injury, such as a cut, a burn, or too much sun is called Koebner's phenomenon. Because this response is common, it's important for people with psoriasis to avoid irritating or injuring their skin

Several other skin conditions have symptoms similar to psoriasis. And some medicine reactions can cause symptoms (such as reddened skin) similar to psoriasis.

#### **Diagnosis of Psoriasis**

In most cases, diagnosis of psoriasis is fairly straight forward.

- Physical exam and medical history: Your doctor usually can diagnose psoriasis by taking your medical history and examining your skin, scalp and nails.
- Skin biopsy: Rarely, your doctor may take a small sample of skin (biopsy) that's examined under a microscope to determine the exact type of psoriasis and to rule out other disorders. A skin biopsy can generally be done in a doctor's office after application of a local anesthetic.

#### **Conditions that can look like psoriasis**

Other conditions that may look like psoriasis or may occur at the same time as psoriasis include:

- Seborrheic dermatitis:** This type of dermatitis is characterized by greasy, scaly, itchy, red skin. It's often found on oily areas of the body, such as the face, upper chest and back. Seborrheic dermatitis can also appear on the scalp as stubborn, itchy dandruff.
- Lichen planus:** This is an inflammatory, itchy skin condition that appears as rows of itchy, flat-topped bumps (lesions) on the arms and legs.
- Ringworm of the body (tinea corporis):** Ringworm is caused by a fungal infection on the top layer of your skin. The infection often causes a red, scaly ring or circle of rash.
- Pityriasis rosea:** This common skin condition usually begins as one large spot (herald patch) on your chest, abdomen or back, which then spreads. The rash of pityriasis rosea often extends from the middle of the body, and its shape resembles drooping pine tree branches.

### **Treatment of Psoriasis**

Psoriasis treatments aim to:

- Stop the skin cells from growing so quickly, which reduces inflammation and plaque formation
- Remove scales and smooth the skin, which is particularly true of topical treatments that you apply to your skin
- Psoriasis treatments can be divided into three main types: topical treatments, light therapy and systemic medications.

### **Topical treatments**

Used alone, creams and ointments that you apply to your skin can effectively treat mild to moderate psoriasis. When the disease is more severe, creams are likely to be combined with oral medications or light therapy. Topical psoriasis treatments include:

- Topical corticosteroids :** These powerful anti-inflammatory drugs are the most frequently prescribed medications for treating mild to moderate psoriasis. They slow cell turnover by suppressing the immune system, which reduces inflammation and relieves associated itching. Topical corticosteroids range in strength, from mild to very strong.

Low-potency corticosteroid ointments are usually recommended for sensitive areas, such as your face or skin folds, and for treating widespread patches of damaged skin. Your doctor may prescribe stronger corticosteroid ointment for small areas of your skin, for persistent plaques on your hands or feet, or when other treatments have failed, Medicated foams and scalp solutions are available to treat psoriasis patches on the scalp.

Long-term use or overuse of strong corticosteroids can cause thinning of the skin and resistance to the treatment's benefits. To minimize side effects and to increase effectiveness, topical corticosteroids are generally used on active outbreaks until they're under control.

- Vitamin D analogues** : These synthetic forms of vitamin D slow down the growth of skin cells. Calcipotriene (Dovonex) is a prescription cream or solution containing a vitamin D analogue that may be used alone to treat mild to moderate psoriasis or in combination with other topical medications or phototherapy. This treatment can irritate the skin. Calcitriol (Rocaltrol) is expensive but may be equally effective and possibly less irritating than calcipotriene.

- Anthralin** : This medication is believed to normalize DNA activity in skin cells. Anthralin (Dritho-Scalp) also can remove scale, making the skin smoother. However, anthralin can irritate skin, and it stains virtually anything it touches, including skin, clothing, countertops and bedding. For that reason, doctors often recommend short-contact treatment — allowing the cream to stay on your skin for a brief time before washing it off.

- Topical retinoids**: These are commonly used to treat acne and sun-damaged skin, but tazarotene (Tazorac, Avage) was developed specifically for the treatment of psoriasis. Like other vitamin A derivatives, it normalizes DNA activity in skin cells and may decrease inflammation. The most common side effect is skin irritation. It may also increase sensitivity to sunlight, so sunscreen should be applied while using the medication. Although the risk of birth defects is far lower for topical retinoids than for oral retinoids, tazarotene isn't recommended when you're pregnant or breast-feeding or if you intend to become pregnant.

- Calcineurin inhibitors**: Currently, calcineurin inhibitors — tacrolimus (Prograf) and pimecrolimus (Elidel) — are approved only for the treatment of atopic dermatitis, but studies have shown them to be effective at times in the treatment of psoriasis. Calcineurin inhibitors are thought to disrupt the activation of T cells, which, in turn, reduces inflammation and plaque buildup.

Calcineurin inhibitors are not recommended for long-term or continuous use because of a potential increased risk of skin cancer and lymphoma. They may be especially helpful in areas of thin skin, such as around the eyes, where steroid creams or retinoids are too irritating or may cause harmful effects.

- Salicylic acid**: Available over-the-counter (nonprescription) and by prescription, salicylic acid promotes sloughing of dead skin cells and reduces scaling. Sometimes it's combined with other medications, such as topical corticosteroids or coal tar, to increase its effectiveness. Salicylic acid is available in medicated shampoos and scalp solutions to treat scalp psoriasis.

- **Coal tar** : A thick, black byproduct of the manufacture of petroleum products and coal, coal tar is probably the oldest treatment for psoriasis. It reduces scaling, itching and inflammation. Exactly how it works is not known. Coal tar has few known side effects, but it's messy, stains clothing and bedding, and has a strong odor.

Coal tar is available in over-the-counter shampoos, creams and oils. It's also available in higher concentrations by prescription. This treatment isn't recommended for women who are pregnant or breast-feeding.

- **Moisturizers**: By themselves, moisturizing creams won't heal psoriasis, but they can reduce itching and scaling and can help combat the dryness that results from other therapies. Moisturizers in an ointment base are usually more effective than are lighter creams and lotions.

### **Light therapy (phototherapy)**

As the name suggests, this psoriasis treatment uses natural or artificial ultraviolet light. The simplest and easiest form of phototherapy involves exposing your skin to controlled amounts of natural sunlight. Other forms of light therapy include the use of artificial ultraviolet A (UVA) or ultraviolet B (UVB) light either alone or in combination with medications.

- **Sunlight**: Ultraviolet (UV) light is a wavelength of light in a range too short for the human eye to see. When exposed to UV rays in sunlight or artificial light, the activated T cells in the skin die. This slows skin cell turnover and reduces scaling and inflammation. Brief, daily exposures to small amounts of sunlight may improve psoriasis, but intense sun exposure can worsen symptoms and cause skin damage. Before beginning a sunlight regimen, ask your doctor about the safest way to use natural sunlight for psoriasis treatment.

- **UVB phototherapy**: Controlled doses of UVB light from an artificial light source may improve mild to moderate psoriasis symptoms. UVB phototherapy, also called broadband UVB, can be used to treat single patches, widespread psoriasis and psoriasis that resists topical treatments. Short-term side effects may include redness, itching and dry skin. Using a moisturizer may help decrease these side effects.

- **Narrow band UVB therapy** : A newer type of psoriasis treatment, narrow band UVB therapy may be more effective than broadband UVB treatment. It's usually administered two or three times a week until the skin improves, then maintenance may require only weekly sessions. Narrow band UVB therapy may cause more severe and longer lasting burns, however.

- **Goeckerman therapy** : Some doctors combine UVB treatment and coal tar treatment, which is known as Goeckerman treatment. The two therapies together are more effective than either alone because coal tar makes skin more receptive to UVB light. Once requiring a

three-week hospital stay, a modification of the original treatment can be performed in a doctor's office.

- **Photochemotherapy or psoralen plus ultraviolet A (PUVA):** Photochemotherapy involves taking a light-sensitizing medication (psoralen) before exposure to UVA light. UVA light penetrates deeper into the skin than does UVB light, and psoralen makes the skin more responsive to UVA exposure. This more aggressive treatment consistently improves skin and is often used for more-severe cases of psoriasis. PUVA involves two or three treatments a week for a prescribed number of weeks. Short-term side effects include nausea, headache, burning and itching. Long-term side effects include dry and wrinkled skin, freckles, and increased risk of skin cancer, including melanoma, the most serious form of skin cancer. Because this treatment makes you more sensitive to sunlight, it's important to avoid sun exposure when possible and to wear a broad-spectrum sunscreen with an SPF of at least 30. To protect your eyes, wear UVA-protective sunglasses.

- **Excimer laser :** This form of light therapy, used for mild to moderate psoriasis, treats only the involved skin. A controlled beam of UVB light of a specific wavelength is directed to the psoriasis plaques to control scaling and inflammation. Healthy skin surrounding the patches isn't harmed. Excimer laser therapy requires fewer sessions than does traditional phototherapy because more powerful UVB light is used. Side effects can include redness and blistering.

### **Oral or injected medications**

If you have severe psoriasis or it's resistant to other types of treatment, your doctor may prescribe oral or injected drugs. Because of severe side effects, some of these medications are used for only brief periods and may be alternated with other forms of treatment.

- **Retinoids.** Related to vitamin A, this group of drugs may reduce the production of skin cells if you have severe psoriasis that doesn't respond to other therapies. Signs and symptoms usually return once therapy is discontinued, however. Side effects may include lip inflammation and hair loss. And because retinoids such as acitretin (Soriatane) can cause severe birth defects, women must avoid pregnancy for at least three years after taking the medication.

- **Methotrexate.** Taken orally, methotrexate helps psoriasis by decreasing the production of skin cells and suppressing inflammation. It may also slow the progression of psoriatic arthritis in some people. Methotrexate is generally well-tolerated in low doses but may cause upset stomach, loss of appetite and fatigue. When used for long periods, it can cause a number of serious side effects, including severe liver damage and decreased production of red and white blood cells and platelets.

- **Cyclosporine.** Cyclosporine suppresses the immune system and is similar to methotrexate in effectiveness. Like other immunosuppressant drugs, cyclosporine increases your risk of

infection and other health problems, including cancer. Cyclosporine also makes you more susceptible to kidney problems and high blood pressure — the risk increases with higher dosages and long-term therapy.

- **Drugs that alter the immune system (biologics).** Several immunomodulator drugs are approved for the treatment of moderate to severe psoriasis. They include etanercept (Enbrel), infliximab (Remicade), adalimumab (Humira) and ustekinumab (Stelara). These drugs are given by intravenous infusion, intramuscular injection or subcutaneous injection and are usually used for people who have failed to respond to traditional therapy or who have associated psoriatic arthritis. Biologics work by blocking interactions between certain immune system cells and particular inflammatory pathways. Although they're derived from natural sources rather than chemical ones, they must be used with caution because they have strong effects on the immune system and may permit life-threatening infections. In particular, people taking these treatments must be screened for tuberculosis.

- **Other medications.** Thioguanine and hydroxyurea (Droxia, Hydrea) are medications that can be used when other drugs can't be given.

- **Experimental medications.** There are a number of new medications currently being researched that have the potential to improve psoriasis treatment. Some of the treatments being looked at include A3 adenosine receptor agonists; anti-interleukin-17, anti-interleukin-12/23 and anti-interleukin-17 receptor agents; Janus kinase (JAK) inhibitors; and phosphodiesterase 4 inhibitors.

### **Treatment considerations**

Although doctors choose treatments based on the type and severity of psoriasis and the areas of skin affected, the traditional approach is to start with the mildest treatments — topical creams and ultraviolet light therapy (phototherapy) — and then progress to stronger ones only if necessary. The goal is to find the most effective way to slow cell turnover with the fewest possible side effects.

In spite of a range of options, effective treatment of psoriasis can be challenging. The disease is unpredictable, going through cycles of improvement and worsening, seemingly at random. Effects of psoriasis treatments also can be unpredictable; what works well for one person might be ineffective for someone else. Your skin also can become resistant to various treatments over time, and the most potent psoriasis treatments can have serious side effects.

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