

Psoriasis:

Information for the Pharmacist

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Goals and Objectives

Goals:

To provide the pharmacist with information dealing with psoriasis, including its characteristics, pathology and treatment.

Objectives:

After completing this article, the pharmacist should be able to:

1. Discuss the characteristics of psoriasis.
2. Explain the normal structure of the skin and the alterations associated with psoriasis.
3. Describe the various treatment options for psoriasis.
4. Counsel patients with regard to their prescribed drug therapy program for psoriasis.

Recognized as a specific skin disorder two centuries ago, psoriasis is a common inflammatory skin condition characterized by frequent episodes of redness, itching, and thick, dry, silvery scales on the skin. Although psoriasis causes little, if any, mortality, there is significant morbidity associated with this incurable dermatologic disease.

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General Features of Psoriasis

Approximately two percent of the population in the United States is affected with psoriasis. The onset may be acute or insidious and the disease is characterized by remissions and recurrences. Psoriasis occurs most often in Caucasians and equally in men and women. Although psoriasis can occur at any age, it most frequently begins between the ages of 15 and 35 years.

Psoriasis is characterized by abnormalities in the cycle of epidermal development. These abnormalities include altered maturation of the skin, inflammation, vascular changes, and a hyperproliferation of the epidermis. These result in the characteristic lesions that may be painful, itch, and/or bleed and are located in a few areas or anywhere on the body.

Pathology of Psoriasis

In order to discuss the pathology of psoriasis, a review of the certain aspects of the skin is needed. The primary function of the skin is to provide protection, which is accomplished via the epidermal layer. The epidermal layer is composed of five layers, which are, from deepest to most superficial, the stratum basale, the stratum spinosum, the stratum granulosum, the stratum lucidum, and the stratum corneum. Four types of cells compose these layers: keratinocytes (90% of the cells), melanocytes (8%), Langerhans' cells, and tactile dendrites (also known as Merkel cells). During the epidermal cell cycle, new cells formed in the stratum basale migrate toward the stratum corneum. As cells move toward the surface, they accumulate keratin and their organelles disappear. By the time the cells reach the stratum corneum, they have died and been completely filled with keratin. This smooth, keratinous external layer is what offers the skin its protection. The surface cells slough off (exfoliate) and are replaced by the underlying cells. The epidermal cell cycle normally takes about four weeks. Keratinocytes in the basal layer divide approximately once every two weeks.

In psoriatic skin, the epidermal cell cycle is accelerated. Cell division in the basal layer occurs every 1.5 days, and the migration of keratinocytes to the stratum corneum occurs within about four days. Since the cells move to the surface so rapidly, they do not differentiate and mature properly. The stratum corneum is not fully keratinized, and epidermal cells build up abnormally and become scaly. The epidermis in psoriatic lesions is three to five times thicker than normal. Blood vessels in the papillary layer of the dermis dilate in psoriasis, and inflammatory cells, such as neutrophils, infiltrate the epidermis.

There are several theories regarding the etiology of psoriasis. Several involve immunological processes which include various T lymphocytes altering the development of appropriate epidermal skin layer. Other theories are related to injury to the area which triggers an abnormal process for development of the epidermal skin layer. Exacerbations of psoriasis are associated with similar factors, such as injury or irritation to the skin (e.g., cuts, burns), immunosuppression (e.g., infection, AIDS), and/or autoimmune disorders. There may be a genetic predisposition to the development of psoriasis. Approximately one-third of the cases of psoriasis are attributed to heredity. For example, if both parents have psoriasis, then their children have an approximately fifty percent chance of developing psoriasis.

Types of Psoriasis

There are a variety of types of psoriasis. The most common form is plaque psoriasis, which occurs in about 90% of patients. The lesions in plaque psoriasis begin as small papules that develop and form large plaques that have a scaly appearance and are the well-known silver color.

Another type of psoriasis is known as guttate psoriasis. This form of psoriasis is usually preceded by a streptococcal throat infection and occurs in individuals in their teens. Guttate psoriasis is an acute condition that responds to ultraviolet therapies and is characterized by drop-like pink dots that become scaly.

Erythrodermic psoriasis is a severe form of psoriasis that may occur on its own or as a complication of another form of psoriasis. Erythrodermic psoriasis is usually widespread with severe symptoms. It must be treated aggressively and may be complicated by infections.

Another severe form of psoriasis is pustular psoriasis. This form is characterized by pus-like, non-infectious blisters which are usually located on the palms and soles. These lesions are often difficult to treat and recur often. The generalized form of pustular psoriasis is usually associated with fever and malaise and is often treated on an inpatient basis.

Psoriatic arthritis occurs in somewhat less than 20% of individuals with psoriasis and usually affects the peripheral interphalangeal joints. Inflammation, swelling, and joint destruction are typical symptoms.

Nail psoriasis is found on toenails and fingernails. Initially, it begins as pits, then progresses to a thickened nail that may be yellow and brittle. These nail changes occur frequently in patients with psoriasis.

General Treatment of Psoriasis

There are a variety of treatments for psoriasis. In general, the therapeutic approach to treating psoriasis will be dependent on the severity of the disease and the type(s) of psoriasis.

Tars

Tars have been used to treat skin diseases for many years. They are obtained from organic materials and coal tar is the primary product used.

Coal tar is a viscous liquid that is composed of numerous materials, including phenols, nitrogen compounds, sulfur compounds, and hydrocarbons. Although the mechanism of action is not known, coal tar preparations have anti-inflammatory activity, reduce the amount of sebum, and decrease epidermal cell scaling. Coal tar is useful in psoriasis that is associated with severe itching, but not as desirable for treating pustular psoriasis as irritation may result in Koebner's phenomenon (a psoriatic event that occurs on traumatized skin). Problems associated with the use of coal tar are skin irritation and patient acceptance. With regard to skin irritations, this problem may be reduced by using coal tar on small areas that have fewer groups of lesions. Since tar preparations are usually greasy, have an odor, and can stain material, many individuals will not use them. However, tar products can be useful in the treatment of mild psoriasis.

Anthralin

Anthralin has been used as a topical treatment for mild psoriasis for many years. Anthralin, a derivative of chrysarobin, is an effective and safe topical treatment for psoriasis. However, it does stain skin and material; therefore, patient acceptance is not good. Anthralin decreases inflammation and increases cellular differentiation in psoriasis, but may irritate nonpsoriatic skin. Anthralin is applied topically to the skin in concentrations of 0.1% to 1% at bedtime. In the morning, the skin is washed and an emollient (e.g., bath oil) is used.

Corticosteroids

Topically corticosteroids are the most frequently used medications for treating mild to moderate psoriasis in the United States. These drugs reduce inflammation, scaling, and itching and have high patient acceptance. Formulations of topical corticosteroids include ointments, creams, lotions, and gels. The formulation used is dependent on the type of psoriatic lesion and the base components of the formulation. Lotions and gels are useful for scalp psoriasis because they are less viscous and easily applied. Creams can be applied to all areas, while ointments, which are oily, are useful in small areas that are dry and scaly and need to retain moisture. In many instances, mild plaque psoriasis can be treated with topical corticosteroids in a twice-daily application. Once the psoriasis is controlled, then adjustments can be made to determine a maintenance therapeutic plan. Topical corticosteroids may cause skin atrophy after several weeks of therapy. In addition, allergic contact dermatitis, fine hair growth, and hypopigmentation can occur. For specific treatment of a localized lesion that is not responsive to initial therapy, direct injection of a corticosteroid to the area may be useful.

Vitamin D Analogues

Vitamin D₃ or cholecalciferol receptors are located in several areas of the body, including the skin. The active form of vitamin D₃ is calcitriol, which is an active metabolite of vitamin D₃. Calcitriol increases cellular differentiation and inhibits cellular proliferation. These activities make calcitriol a useful drug for treating psoriasis. Adverse effects associated with the use of calcitriol make it less desirable to treat psoriasis. The primary adverse effects are hypercalcemia and hypercalciuria. These adverse effects can result in renal stones and calcification of soft tissue, including the blood vessels and heart.

Another analog of vitamin D₃ is calcipotriol. Calcipotriol provides similar activity to that of calcitriol, but has a modest effect on calcium activity; therefore, it is less likely to produce abnormalities in calcium function. Calcipotriol is used in a 50 ug/ml ointment or cream and a 50 ug/ml solution. The maximum weekly dose is 5 mg, which is 100 milliliters of solution or 100 grams ointment or cream base. Calcipotriol may be applied once or twice daily and usually achieves maximum effects within two months. The major side effect associated with the use of calcipotriol is skin irritation. Calcipotriol is contraindicated in pregnancy and lactation and its safety in children has not been determined.

Retinoids

Retinoids are biological derivatives of vitamin A, but have a significantly higher therapeutic index than the parent compound. Retinoids exert their effects after binding to specific retinoid receptors in the cytoplasm and nucleus. The retinoid receptors in the skin, known as retinoic acid receptors, are specific to this area. When the retinoid compounds bind to these receptors, it results in processes that impede the abnormal skin formation that occurs in psoriasis.

Tazarotene is a retinoid that is used topically in an emollient gel that is water soluble. Tazarotene is used to treat plaque psoriasis and facial psoriasis. Tazarotene exerts its effects via its selective binding to specific retinoic acid receptors. Tazarotene reduces inflammation and hinders abnormal keratinocyte function. Tazarotene is used in a 0.05% and/or 0.1% gel that is usually applied twice a day. Tazarotene gel should be used in very small amounts and thoroughly massaged into the lesion, such that there is no residue. The gel should not be applied to surrounding normal skin and should be removed with water, if normal skin is involved. Tazarotene can cause retinoid erythema.

Oral retinoids, such as acitretin, are used to treat severe forms of psoriasis. Oral retinoids are not as effective as monotherapy for plaque psoriasis as they are for pustular psoriasis. Acitretin is administered twice a day in a dose of 0.125 to 0.4 mg/kg/day depending on the type of psoriasis. Symptoms usually improved within a month. After the lesions have cleared, the therapy may be maintained for six months. The addition of topical corticosteroids may be useful during the maintenance period. Adverse effects associated with the use of acitretin include dry and/or peeling skin, alopecia, and nail changes. In addition, acitretin has potential teratogenic effects, may be enhanced by alcohol ingestion, and should not be used in patients with severe liver or kidney disease.

Phototherapy

Phototherapy has been used in treating dermatologic disorders for more than a century and is useful in moderate to severe psoriasis. Photochemotherapy uses a combination of ultraviolet light and drugs. For treatment of psoriasis, the typical regimen is ultraviolet A light and psoralen, a skin sensitizer. The combination, which is known as PUVA, causes anti-inflammatory, immunosuppressive, and antiproliferative effects.

PUVA therapy may be oral or topical. With regard to oral therapy, methoxsalen is taken orally two hours prior to the use of ultraviolet A light. The dosage of ultraviolet light will depend on the patient's skin type with darker skin requiring greater dosages. The toxicity of PUVA is related to the amount of the psoralen in the skin and the amount of ultraviolet light applied. Phototoxicity reactions peak within three days; therefore, treatments must be spaced such that there is at least three days between treatments. Side effects encountered with oral psoralens include GI tract dysfunction, pruritus and erythema. Patients should not be exposed to the sun for six hours after treatment.

Patients who receive PUVA may have several long term adverse effects. These include premature cutaneous aging, cataracts, and skin cancers. However, these effects are related in part to the duration and number of PUVA treatments.

PUVA is usually administered two to four times a week. Approximately 20 treatments are required before lesions clear. In many instances, dosages will need to be increased because exposure to ultraviolet light will result in tanning.

Topical PUVA therapy uses a psoralen in a cream, lotion, ointment, or aqueous bath vehicle. The psoralen is applied topically or placed in an aqueous bath. The aqueous bath provides complete coverage with the psoralen, while the topical preparations must be applied to the lesions. The aqueous bath does not appear to be as effective as the topical preparations, particularly if the lesions are confined to specific areas of the body. Since the psoralen is not ingested, gastrointestinal effects and cataract formation do not occur. However, topical PUVA therapy usually cannot provide the consistent full body therapy that is seen with oral PUVA therapy.

Methotrexate

If response to topical treatment is not acceptable, then methotrexate can be used to treat moderate to severe psoriasis. Methotrexate is a folic acid inhibitor, which eventually results in the inhibition of the synthesis of pyrimidine, an essential component in the cell formation process. Although the exact mechanism of action of methotrexate in the treatment of psoriasis is not known, methotrexate appears to impede the proliferation of epidermal cells as well as affect immune processes. Methotrexate should be used in those patients who are not responsive to other conventional therapies and have lesions involving more than 20% of the body surface. Methotrexate should not be used in patients with renal or liver disorders, pregnant patients, patients with infections, blood abnormalities, or alcoholic patients. Dosing of methotrexate varies, but the usual regimen is 2.5 mg to 5 mg orally taken at 12-hour intervals for a total of three doses each week. The total dose should not be more than 30 mg per week and increases in doses should be in 2.5 mg weekly increments, if liver function tests and blood counts are acceptable. Adverse effects associated with the use of methotrexate include headache, chills, fever, fatigue, dizziness, and GI tract dysfunction.

Cyclosporine & Related Drugs

Cyclosporine has immunomodulating properties that provide its activity for treatment of resistant psoriatic lesions. The complex immunosuppressive activity of cyclosporine eventually results in altering the functions of keratinocytes and other related cells that can be precursors to psoriatic lesions. The usual oral dose for cyclosporine is 3 mg/kg daily. If no improvement occurs within a month, then the daily dose may be increased by 1 mg/kg. The maximum dosage should not exceed 5 mg/kg daily. Remission will normally occur within three months. At that time, a reduction in dose of 0.5 mg/kg every two weeks can be initiated and another drug may be added to control plaque formation. Adverse effects associated with the use of cyclosporin include flu-like symptoms, paresthesia, increased blood pressure, GI discomfort, and URI.

Tacrolimus is a macrolide antibiotic that is similar to cyclosporine, but has significantly greater immunosuppressive activity. Tacrolimus has been effective in treating psoriasis in a dose of 0.1 to 0.15 mg/kg/day. Adverse effects include GI distress, hypertension, tremor, and paresthesia.

Mycophenolate is used to prevent acute rejection after cardiac and renal transplantation. Mycophenolate blocks the synthesis of guanine nucleotides required for RNA and DNA synthesis and has a specific lymphocyte antiproliferative effect. Adverse effects of mycophenolate include gastrointestinal toxicity, increased potential for infections, and hematologic effects. The usual dose for mycophenolate is 400 mg four times a day.

Biologic Therapy

There are several new and costly drugs that are part of this group.

Infliximab is a chimeric monoclonal antibody directed against TNF-alpha, which is suspected to be a culprit in psoriasis. Adverse effects associated with the use of infliximab include headache, fever, chills, fatigue, diarrhea, increased infections, and hypersensitivity reactions. Infliximab has not been associated with specific organ toxicity. Infliximab is administered in three doses at weeks 0, 2, and 6 in a dose of mg/kg via slow intravenous drip.

Alefacept, an inhibitor of T-cell activation, is used parenterally for treatment of adults with moderate to severe chronic plaque psoriasis. Alefacept is approximately 63 percent bioavailable and has a mean elimination half-life of about ten days. Adverse effects

associated with the use of alefacept includes chills, dizziness, increased cough, nausea, injection site discomfort, and myalgia. The usual dose for alefacept is 7.5 milligrams given once a week as an intravenous bolus or 15 milligrams given once a weekly as an intramuscular injection. The regimen should be continued for twelve weeks.

Efalizumab, a humanized monoclonal antibody that inhibits T-cell activation, is used for treatment in adults with moderate to severe chronic plaque psoriasis. Adverse effects associated with the use of efalizumab have been mild and include headache, chills, fever, nausea and myalgia. As with the other drugs in this group, serious acute infections and reactivation of latent chronic infections may occur. The usual does for efalizumab is one mg/kg administered subcutaneously once a week. The maximum recommended dose is 200 milligrams. Platelet counts should be monitored before and during therapy.

Conclusion

Psoriasis is a complex dermatologic disease that is treated primarily with drugs. The exact therapeutic regimen will vary from patient to patient. The drugs with the fewest adverse effects used at the lowest dose should be the initial choice of therapy. In many instances, psoriasis will require complex therapy with several drugs. Consequently, the pharmacist is the health care practitioner who will be required to counsel patients regarding their prescribed drug therapy programs.

Bibliography

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Examples of Drugs Used to Treat Psoriasis

Generic Name	Example of Brand Name
Coal Tar	Estar
Anthralin	Dritho
Calcipotriol	Dovonex
Tazarotene	Tazorac
Betamethasone	Diprolene
Halobetasol	Ultravate
Clobetasol	Temovate
Methoxsalen	Oxsoralen
Methotrexate	Rheumatrex
Acitretin	Soriatane
Cyclosporine	Neoral
Tacrolimus	Prograf
Mycophenolate	CellCept
Infliximab	Remicade
Alefacept	Amevive
Efalizumab	Raptiva