PSORIASIS AND PSORIATIC ARTHRITIS

A Treatment Guide for the Health Insurance Industry

NATIONAL PSORIASIS FOUNDATION®

Connect. Control. Cure.

REACHING NEW LEVELS OF SUCCESS AFTER 35 YEARS

It may be hard to believe that the National Psoriasis Foundation began with a tiny classified ad, especially looking back at all the organization has accomplished, but small, individual efforts can lead to great things.

In 1966, Beverly Foster, of Portland, Ore., was suffering from severe psoriasis. Understanding her pain, Foster's husband placed an ad on her 30th birthday in a local newspaper asking people with psoriasis to call and share their own experiences. Within a week, Foster had received more than 100 calls from fellow psoriasis sufferers. After holding regular meetings with the people she met, Foster formed the Psoriasis Society of Oregon. Soon after, a far greater mission beckoned, as the group realized it needed to reach out to others suffering in silence. In October 1968, they established the National Psoriasis Foundation.

Personal Messages 40

Business Personals 42

In the intervening years, the Psoriasis Foundation's accomplishments have been many, including getting psoriasis recognized as a disabling disease by the Social Security Administration, securing the first federally mandated funding of skin disease research and establishing the National Psoriasis Tissue Bank.

Today the Psoriasis Foundation reaches millions of people a year. We are the leading national and international organization serving the psoriasis community.

INCLUSIVENESS

Ultimately, we are who we serve, and we serve the psoriasis community. We want people with psoriasis to represent the Psoriasis Foundation. Early in 2003, we held a photo shoot, and invited members of the Foundation to volunteer to represent the community on the pages of our magazine, on the Web site and in our printed materials.

CHAMPION

One of our most important tasks is to serve as an advocate for people with psoriasis and psoriatic arthritis. We make sure that safe, effective treatments are available, doctors and nurses are educated about psoriasis, and research into new treatments is properly funded. This past year, our commitment to advocacy was strengthened as we expanded our advocacy department and set new goals.

CONNECT. CONTROL. CURE.

We use "Connect. Control. Cure." to describe what we do. We connect people who have psoriasis and psoriatic arthritis with others who have the diseases through educational meetings, our Web site, a Peer Network and support groups, among other ways. We help people with psoriasis and psoriatic arthritis gain control over their diseases by providing them with educational resources and access to treatments. We work for a cure by funding research and bringing psoriasis researchers together.

ABOUT THIS GUIDE

More than 5 million people in the U.S. are diagnosed with psoriasis and/or psoriatic arthritis. The *Treatment Guide for the Health Insurance Industry* was developed by the National Psoriasis Foundation in collaboration with several members of our eminent Medical Board to provide the insurance industry with information about psoriasis and psoriatic arthritis, quality of life issues and various treatment modalities. The *Guide* is designed to assist insurers in making appropriate decisions regarding reimbursement and access to care for patients with these often emotionally devastating and physically disabling diseases.

Although there are a variety of highly effective treatments for psoriasis and psoriatic arthritis, the Foundation believes patients need and deserve more therapy options such as those provided by the recent advances in biologic medications. We know patients give up on therapies that do not work and/or have intolerable or dangerous short- or long-term side effects. Our research shows that 78% of patients with moderate to severe psoriasis are not using aggressive therapies because of concerns about side effects and effectiveness. We also know patients make choices—weighing carefully a therapy's effectiveness, safety, complexity, cost, and ease of use. Finding what works is challenging, so having choices is critical.

The Psoriasis Foundation welcomes comments and questions about this guide. Please direct inquiries to the Advocacy Department by calling 503.244.7404 or 800.723.9166 or via e-mail at *advocacy@psoriasis.org.*

National Psoriasis Foundation

6600 SW 92nd Avenue, Suite 300
Portland, Oregon 97223-7195 USA
Tel: 503.244.7404, 800.723.9166
Fax: 503.245.0626
E-mail: *getinfo@psoriasis.org*
Web site: *www.psoriasis.org*

© 2004

Executives

Leslie Holsinger, Ph.D.
Chairman, Board of Trustees
Belmont, Calif.

Gail M. Zimmerman
President and CEO
Portland, Ore.

Leslie Holsinger, Ph.D.

Gail M. Zimmerman

NATIONAL PSORIASIS FOUNDATION MISSION STATEMENT

Our mission is to improve the quality of life of people who have psoriasis and psoriatic arthritis. Through education and advocacy, we promote awareness and understanding, ensure access to treatment, and support research that will lead to effective management and, ultimately, a cure.

BOARD OF TRUSTEES

The Board of Trustees approves and evaluates the National Psoriasis Foundation's long-term plans and goals, provides financial oversight and works with the president to fulfill the Foundation's mission. The Board comprises volunteers from the community who share two things—psoriasis or psoriatic arthritis, either individually or through a loved one, and a deep personal commitment to directing the Foundation toward finding a cause and, ultimately, a cure.

Leslie Holsinger, Ph.D.
Chairman
Belmont, Calif.

Dale White
Vice Chairman
Poolesville, Md.

Mary Beth Cicero
Treasurer
Hingham, Mass.

Mara Kelly
Secretary
Phoenix, Ariz.

Edward M. Feigeles
New York, N.Y.

Andrew Henschel
North Miami Beach, Fla.

Benjamin Isenberg
Lake Oswego, Ore.

Pamela Naylor
McMinnville, Ore.

Edward Reiss
San Francisco, Calif.

Richard Seiden
Los Angeles, Calif.

Teresa Theisen
Atlanta, Ga.

Peter Tiedemann
Sacramento, Calif.

Jana Wessels
North Liberty, Iowa

Gail M. Zimmerman
Ex officio
Portland, Ore.

MEDICAL BOARD

The Medical Board advises the National Psoriasis Foundation on matters of a technical or scientific nature and provides guidance about the effective application of its resources toward improvement of the medical treatment and control of psoriasis and psoriatic arthritis.

Mark Lebwohl, M.D., *Chairman*
Mount Sinai School of Medicine of NYU
New York, N.Y.

Jerry Bagel, M.D.
Psoriasis Treatment Center of Central New Jersey
East Windsor, N.J.

Andrew Blauvelt, M.D.
National Institutes of Health
Bethesda, Md.

Robert M. Day, Ph.D.
National Psoriasis Foundation Board of Trustees
Newtown, Pa.

Steven Feldman, M.D., Ph.D.
The Bowman Gray School of Medicine
Winston-Salem, N.C.

Dafna Gladman, M.D., FRCPC
Toronto Western Hospital
Toronto, Ont.

Kenneth B. Gordon, M.D.
Loyola University Medical Center
Maywood, Ill.

Alice B. Gottlieb, M.D., Ph.D.
UMDNJ–Robert Wood Johnson Medical School
New Brunswick, N.J.

John Y.M. Koo, M.D.
University of California–San Francisco
San Francisco, Calif.

Gerald G. Krueger, M.D.
Chairman emeritus
University of Utah Medical School
Salt Lake City, Utah

Craig Leonardi, M.D.
Central Dermatology
St. Louis, Mo.

Philip Mease, M.D.
University of Washington School of Medicine
Seattle, Wash.

Warwick Morison, M.D.
Johns Hopkins University
Lutherville, Md.

Amy Paller, M.D.
Northwestern University Medical School
Chicago, Ill.

David Pariser, M.D.
Pariser Dermatology Specialists
Norfolk, Va.

Daniel Sauder, M.D.
Johns Hopkins University
Baltimore, Md.

Robert Stern, M.D.
Beth Israel Deaconess Medical Center
Boston, Mass.

Gerald D. Weinstein, M.D.
Chairman emeritus
University of California–Irvine
Irvine, Calif.

Melodie Young, M.S.N., R.N., A.N.P.
Texas Dermatology Associates
Dallas, Texas

Michael Zanolli, M.D.
Dermatology Consultants
Nashville, Tenn.

GLOSSARY OF COMMONLY USED TERMS

Antibody: specialized blood protein synthesized in response to the presence of a particular antigen in order to attack it and render it harmless.

Antigen: any substance that the body considers foreign or dangerous, against which it produces an antibody.

Arthritis mutilans: a form of chronic arthritis characterized by extensive destruction of the joint cartilage and bony surfaces, resulting in pronounced deformities, usually in the hands and feet, that can occur in psoriatic arthritis.

Arthropathy: any disease or disorder involving a joint.

Atrophy: wasting away of a normally developed organ or tissue because of cell degeneration, which can be caused by aging, undernourishment or lack of use.

Autoimmunity: a disorder of the body's defense mechanisms in which antibodies are produced against components or products of the body's own tissues, treating them as foreign and attacking them.

Chimera: tissue or medication that contains material from an organism that has received a transplant of genetically and immunologically different tissue.

Crohn's disease: disease in which segments of the digestive tract become inflamed, thickened and ulcerated.

Dermis: the thick layer of skin lying beneath the epidermis; the "true skin."

Dimer: a compound produced by the combination of two like molecules.

Epidermis: outer layer of the skin.

Erythema: flushing of the skin due to widening of the blood capillaries in the dermis.

Erythroderma: abnormal reddening, flaking and thickening of the skin; can result from eczema or psoriasis or be caused by drugs.

Genome: the total genetic material of an organism.

Guttate: A type of psoriasis that often presents in young adults or children with a prior history of streptococcal throat infection. Guttate lesions usually appear on the arms, legs and trunk in the form of small, red dots on the skin.

Hepatotoxic: capable of damaging or destroying liver cells.

Human lymphocyte antigen (HLA): series of four gene families that code for proteins expressed on the surface of most cells.

Immune system: network of organs, cells and glands that protect the body from infection.

Immunogenic: capable of provoking an immune response.

Immunoglobulin: any of the five antibodies that block the effects of antigens in the body.

Immunosuppessive: a drug that reduces the body's resistance to infection and other foreign bodies by suppressing the immune system; used to maintain transplants and to treat autoimmune diseases, such as rheumatoid arthritis.

Incidence: the number of new episodes of a disease arising in a population over a given period of time, e.g., 1 year.

Infusion: slow injection of a substance, usually into a vein.

Interphalangeal: between the bones of the fingers or toes.

Lymphocyte: type of white blood cell present in the lymph nodes, spleen, thymus and bone marrow, in addition to the blood.

Monoclonal antibody: antibody produced artificially from a cell clone, consisting of a single type of immunoglobulin.

Murine: relating to mice.

Nephrotoxic: capable of damaging or destroying kidney cells.

Oligoarthritis: arthritis in which only a few joints are involved.

Palmar-plantar: relating to the palms of the hands and the soles of the feet.

Papule: a small raised spot on the skin less than 5mm in diameter.

Phototherapy: treatment of disease by means of ultraviolet light.

Plaque: a raised patch on the skin, formed by papules enlarging or coalescing to form an area an inch or more across.

Polyarthritis: rheumatic disease involving several or many joints.

Prevalence: the number of episodes of a disease in a population at any given point in time or over a period of time.

Psoriasis: An immune-mediated, genetic, chronic skin disease that is characterized by thickened, red areas of skin covered by silvery scales. The extent of skin involvement can range from discrete, localized areas to generalized body involvement. The joints, nails and mucous membranes may also be affected with the disease.

Psoriatic arthritis: A chronic, progressive, inflammatory arthritis often accompanied by the skin lesions of psoriasis. It is associated with pain, swelling and stiffness in the joints of the fingers and toes as well as the neck, lower back, knees, ankles and other joints.

Pustule: a small blister containing pus found on the skin.

Refractory: failing to respond satisfactorily to a treatment.

Rheumatoid arthritis: a disease of the synovial lining of joints, causing pain, stiffness and swelling of the joints.

Salicylic acid: a drug that causes the skin to peel and destroys bacteria and fungi; it is applied to the skin to treat psoriasis, eczema, dandruff, warts and corns.

Spondylitis: inflammation of the synovial joints of the backbone.

Synovium (synovial membrane): membrane that forms the sac enclosing a freely moveable joint, such as the knee or elbow; it secretes the lubricating synovial fluid.

Tachyphylaxis: a falling-off of the effects produced by a drug during continuous use.

T cell: a type of white blood cell involved in immunity; a type of lymphocyte.

Teratogen: any substance, agent or process that induces the formation of developmental abnormalities in a fetus; teratogenic.

Tumor necrosis factor (TNF): either of two proteins, TNF-alpha or TNF-beta, that destroy tumor cells and can stimulate proliferation of skin cells.

PSORIASIS AND PSORIATIC ARTHRITIS TREATMENT

Psoriasis and psoriatic arthritis are chronic, immune-mediated diseases of the skin and joints. They typically require ongoing treatment to restore function, maintain health and prevent disability. There is no universally effective therapy or therapy combination for psoriasis and psoriatic arthritis. All treatment must be individually tailored to each patient's needs and the type of disease being addressed.

KEY POINTS TO REMEMBER

- Patients should not be forced to fail one therapy in order to qualify for a more appropriate therapy.
- Ongoing therapy is often required to maintain remission.
- Life factors such as employment, childbearing potential, alcohol intake, access to therapies, concomitant conditions such as arthritis or diabetes, response to sunlight, and response to prior therapies must be considered in selecting the ideal treatment for a patient.
- Psoriasis can cause as much disability as cancer, diabetes and other major diseases.

Epidemiology

Psoriasis is an immune-mediated, genetic and chronic skin disease that is characterized by thickened, red areas of skin covered by silvery scales. The extent of skin involvement can range from discrete, localized areas to generalized body involvement. The joints, nails and mucous membranes may also be affected with the disease. Psoriasis affects more than 4.5 million U.S. adults and approximately 1.5 million have moderate to severe psoriasis. 150,000 to 260,000 new cases are diagnosed annually.[1] Psoriasis can cause as much disability as cancer, diabetes and other major diseases.[2]

Approximately 1 million Americans have psoriatic arthritis.[3] Like rheumatoid arthritis, it can frequently lead to disability and may require surgery to help people whose joint destruction limits motion and function.

Psoriasis appears in people of all ages, genders and ethnic groups. Although the disease may have genetic roots that are present at birth, its signs and symptoms may not show up for many years.[5] Studies show that the most common age for the onset of psoriasis is between 15 and 35, although children and infants can also develop the disease. Disease onset occurs before age 20 in 31% to 45% of adults with psoriasis.[4-6] In addition, a recent study indicates that people who have early-onset psoriasis tend to have more extensive disease and a more severe treatment course.[7]

Clinical Manifestations

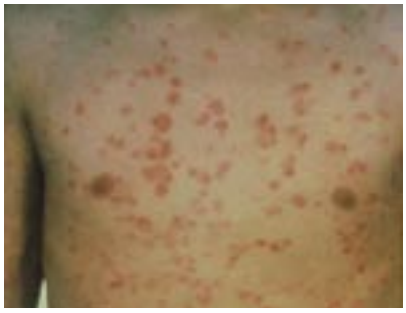
Psoriasis is a highly varied and diverse disease that appears in several different forms. Disease types include plaque psoriasis, guttate psoriasis, pustular psoriasis, inverse psoriasis and erythrodermic psoriasis. Most individuals have only one type of disease, although in some cases, two or more forms of the disease appear simultaneously. Occasionally, one form of the disease changes to another—from plaque to guttate or erythrodermic, for example. This change can be caused by a number of trigger factors, including the rapid discontinuation of systemic therapy.[8]

Figure 1

Plaque Psoriasis: Plaque psoriasis is the most prevalent form of psoriasis, occurring in 80% of patients with the disease. Plaque psoriasis is characterized by raised, inflamed, red lesions covered by a silvery white scale. Lesions can present on any part of the body, although they are most commonly found on the elbows, knees, scalp and the lower back (Figure 1).

Because plaque psoriasis is the most common form, most studies examine drugs used for plaque psoriasis. The same treatments for plaque psoriasis are usually effective for other forms of the disease.

Figure 2



Guttate psoriasis: This form of disease commonly affects children and young adults and is characterized by small, red spots on the skin, usually on the trunk, limbs and scalp (Figure 2).

Figure 3

Pustular psoriasis: Pustular psoriasis affects only 5% of all people with the disease. It is characterized by white pustules surrounded by red skin. The pustules contain noninfectious pus consisting of white blood cells. Pustular psoriasis may be localized to certain areas of the body such as hands or feet, or it may be generalized to the entire body. Patients with generalized pustular psoriasis lose the protective functions of their skin, including protection against infection, loss of fluids and nutrients, and control of body temperature. Patients may also suffer from high-output cardiac heart failure. Pustular psoriasis often requires hospitalization and can be fatal. Subtypes of this form of psoriasis include von Zumbusch, palmar-plantar pustulosis and acropustulosis (Figure 3).

Figure 4

Inverse psoriasis: This form is found in the armpits, groin, under the breasts or in other skin folds around the genitals or buttocks. More common in obese patients, inverse psoriasis shows as smooth, dry, very red, unscaly lesions that are subject to irritation from rubbing and sweating (Figure 4).

Figure 5

Erythrodermic psoriasis: A particularly inflammatory form of psoriasis that often affects most of the body surface, erythrodermic psoriasis is the least common form of the disease and may occur in association with von Zumbusch pustular psoriasis. Erythrodermic psoriasis is characterized by periodic widespread redness and shedding of the skin that is associated with severe itching and pain (Figure 5). Other symptoms include protein and fluid loss. Edema, infection, pneumonia, congestive heart failure and dysregulation of body temperature may also occur. It is important to differentiate erythrodermic psoriasis from other forms of erythroderma, such as eczema, cutaneous T-cell lymphoma (CTCL) and other drug-related causes. Often, a biopsy is indicated if edema is a first presentation. Erythrodermic psoriasis can be life-threatening and often requires hospitalization.

Psoriatic Arthritis

Psoriatic arthritis (PsA) is a chronic, progressive, inflammatory arthritis often accompanied by the skin lesions of psoriasis. It is associated with pain, swelling and stiffness in the joints of the fingers and toes as well as the neck, lower back, knees, ankles and other joints. Approximately 1 million Americans have psoriatic arthritis.[3] In most cases, cutaneous psoriasis lesions precede the joint involvement by months or even years. Among the forms of arthritis seen in PsA are oligoarthritis, distal interphalangeal joint involvement, spondylitis and symmetric polyarthritis. A rapidly destructive form of PsA, arthritis mutilans, affects only about 4% of patients with the disease but is sometimes associated with premature death. It has also been shown that those afflicted with PsA are at an increased risk of death compared to the general population.[9] About 20% of patients have more than five totally damaged joints and as a result have significantly impaired function and quality of life.[10]

Disease Severity

Psoriasis is an individualized disease, varying by location on the body and the amount of skin affected. In some people, the symptoms of the disease are virtually unnoticeable. In others, the raised, reddened plaques of skin psoriasis can be widespread.

Figure 6

Figure 7

Figure 8

Occasionally, skin lesions can crack and bleed. Psoriasis in these patients may be debilitating.

Psoriasis severity is most frequently categorized by the amount of body surface area (BSA) involved.[11]

- Mild: up to 3% of the body (Figure 6)
- Moderate: 3% to 10% of the body (Figure 7)
- Severe: more than 10% of the body (Figure 8)

The National Psoriasis Foundation defines severity based on the amount of skin affected, the location and severity of the plaques, and the psychosocial and physical impact of the psoriasis on the individual. When psoriasis involves the palms, soles, face or scalp, the disease is likely to cause significant functional impairment, disfigurement and emotional distress. Psoriasis has been further defined as severe when it alters the patient's quality of life.[12]

Factors Affecting Remissions and Flares

Psoriasis tends to occur in episodes, with occasional relapses that are unpredictable. The natural evolution of psoriasis varies for each individual, depending on the type and severity of the disease. Some people have disease that is constant and unremitting, while some may experience relapses within weeks or months following treatment, and others can go years between episodes. People with frequent relapses tend to develop more severe forms of the disease, with rapidly spreading lesions covering significant portions of the body. In addition, people with early onset psoriasis are more likely to show widespread and recurrent disease than those whose onset occurs later in life.[6] Although there are no specific treatments for extending remission periods, most psoriasis patients are continued on maintenance therapy following improvement of their disease to prevent recurrences.

Quality of Life for the Psoriasis Patient

Regardless of the type of psoriasis a patient has or the severity of disease, it is likely to have a profound impact on his or her quality of life. Several studies have documented the anguish, stress, anxiety and low self-esteem people with psoriasis experience in their daily lives and their relationships with others.[13-16] Moreover, suicide ideation is three times higher for people with psoriasis as compared to the general population.[17-18] In 1998, the Psoriasis Foundation conducted a survey of its members to gain their perspectives on the impact of psoriasis on their lifestyle, emotional well-being, employment and social conditions.[19] Interacting in the workplace and with family/spouse, establishing and keeping friends, exclusion from public facilities, gaining employment, sexual activities and suicide were among the issues reported by respondents.

In a follow-up telephone survey with respondents who reported they had severe psoriasis, 79% reported that severe psoriasis had an overall negative impact on their lives. Moreover, 78% reported frustration with the effectiveness of their treatments. Employed respondents

reported missing work because of their psoriasis, and 6% reported discrimination at work. Approximately 31% of respondents said they had suffered some degree of financial difficulty from their psoriasis, with those earning less than $30,000 a year citing the highest level (42%) of financial difficulty. A study revealed that the annual costs of psoriasis are similar to other diseases such as emphysema, atopic dermatitis/eczema and epilepsy. Psoriasis is a costly disease, with third-party payer costs ranging from $1.9-$3.9 billion compared to $2.9 billion for emphysema, $0.9-$3.9 billion for atopic dermatitis/eczema and epilepsy at $1.8 billion.[20]

Etiology

As a result of intensive research into the cause of psoriasis, investigators have determined that psoriasis is a common, chronic, immune-mediated inflammatory disease affecting the skin and the joints. The disease is characterized by rapid, exaggerated skin cell growth triggered by faulty activation of the immune system. Although environmental factors such as stress or infection are known to contribute to outbreaks of psoriasis, a genetic susceptibility for the disease has been identified as a key contributor in its etiology.

Role of the Immune System in Psoriasis and Psoriatic Arthritis

Research during the last two decades has resulted in evidence of an immunological component in the pathogenesis of psoriasis. This concept was supported and expanded by the observation that transplant patients receiving the immunosuppressive drug cyclosporine (who also had psoriasis) experienced a clearing of their disease.

Psoriasis is now recognized as one of several immune-mediated inflammatory disorders (IMIDs) such as multiple sclerosis, Crohn's disease and rheumatoid arthritis. A key factor in the initiation and maintenance of psoriasis is T-cell activation in which CD4+ (helper) and CD8+ (suppressor/cytotoxic) cells stimulate the hyperproliferation of skin cells and the lesions seen in psoriasis patients.[21-22]

It has been shown that inhibition of T-cell activation, T-cell migration and proinflammatory cytokines such as tumor necrosis factor-alpha (TNF-alpha) have significant positive effects on psoriasis and psoriatic arthritis. Improved understanding of the cause of psoriatic skin and joint disease has led to the development of new, targeted therapies with improved efficacy and safety profiles.

Therapy

Psoriasis is a currently incurable disease subject to unpredictable flares and remissions. Vigorous initial therapy is required to bring the disease under control. Like diabetes, arthritis and heart disease, psoriasis requires lifelong treatment. If a patient cannot sustain a treatment-free remission, continuing maintenance therapy is required.

The goals of psoriasis therapy are as follows:

- Gain initial rapid control of the disease
- Decrease the involvement of body surface area (BSA)
- Decrease erythema, scaling and the thickness of plaque lesions
- Maintain long-term remission and avoid relapse
- Avoid adverse events
- Improve patient quality of life without producing undue harm medically, financially or emotionally
- Control signs and symptoms and inhibit the progression of psoriatic arthritis.

Maintenance Therapy Minimizes Risk

Lack of access to appropriate and effective maintenance therapy may lead to increased frequency of psoriasis flares and possible conversion of mild psoriasis to a more severe form. Just as diabetic patients require insulin, dietary adjustments and regular physician evaluations, psoriasis patients require maintenance therapy. No one would claim that insulin is "useless" or "ineffective" for diabetes because it is necessary to maintain control of the disease. Likewise, psoriasis patients are likely to have flares if they are denied access to effective maintenance therapy, whether it is topical or systemic medication, phototherapy, biologic therapy, or a combination thereof. Patients who are denied access to available therapies will experience needless pain and suffering and decreased quality of life. Therefore, patient access to maintenance therapy should not be withheld.

It is the opinion of the Medical Board of the Psoriasis Foundation that patients are candidates for phototherapy or systemic treatment if any of the following are true:

- 5% or greater BSA involvement
- the psoriasis is disabling
- significant impact on quality of life
- concomitant psoriatic arthritis

Overview of Psoriasis Therapies

A physician treating psoriasis will develop a treatment plan based on the patient's prior medical history, including compliance with previous treatment, body surface involvement, location of lesions, type of disease and degree of inflammation. There are many options available to treat the disease, according to a variety of strategies, including:

- Monotherapy: using a single agent
- Combination therapy: using two or more agents per course of therapy
- Rotation therapy: using an agent for a year or two, then switching to another agent or agents
- Sequential therapy: using a strong agent to clear psoriasis, then a milder agent for maintenance

Table 1. Overview of Treatment Options for Psoriasis and Psoriatic Arthritis

Topical Therapy	Phototherapy	Systemic Therapy
Anthralin • Psoriatec* **Coal tar*** **Retinoids** • Tazarotene* (Tazorac) **Salicylic Acid*** **Corticosteroids** **Topical Immunomodulators** • Pimecrolimus (Elidel) • Tacrolimus (Protopic 0.1%) **Vitamin D Analogs** • Calcipotriene* (Dovonex)	**Goeckerman Regimen (tar and UVB)** **Home Phototherapy** **Laser** • Pulsed Dye* • Xtrac* • EX-308* **PUVA** • Psoralen* (Oxsoralen-Ultra/ 8-MOP) **UVB** **NB-UVB**	**Biologics** • Adalimumab (Humira) • Alefacept (Amevive)* • Efalizumab (Raptiva)* • Infliximab (Remicade) • Etanercept (Enbrel)** **Disease Modifying Anti-Rheumatic Drugs (DMARDs)** • Cyclosporine (Neoral)* • Hydroxyurea (Hydrea) • Methotrexate* (Rheumatrex/Trexall) • Sulfasalazine (Azulfidine) **Immunosuppressants** • Mycophenolate Mofetil (CellCept) **Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)** **Purine Analogs** • 6-Thioguanine **Retinoids** • Acitretin (Soriatane)* • Isotretinoin (Accutane)

Legend: * = FDA approved for psoriasis
** = FDA approved for psoriatic arthritis

Note: This table includes drugs not currently FDA approved that are used off-label for treating psoriasis and psoriatic arthritis.

Physicians and patients need to weigh carefully the advantages and disadvantages of a particular therapy or treatment regimen. The use of combination, rotation or sequential therapy for psoriasis patients optimizes efficacy while minimizing the risk of side effects. The current range of treatment options is summarized in Table 1. For further information on treatment options, contact the Psoriasis Foundation to request a *Psoriasis and Psoriatic Arthritis Treatment Guide*.

Topical Therapies

Anthralin: a synthetic substitute for chrysarobin, found in Goa powder from the bark of the araroba tree. Anthralin is effective for moderate to severe psoriasis in combination with ultraviolet light and is usually administered in the hospital or daycare setting. Its exact mechanism of action in psoriasis remains unknown. Anthralin can enhance the efficacy of many agents when used in combination and is most effective when given as short contact therapy as a single agent. It does not work as quickly or as thoroughly as superpotent topical steroids, but it has no known long-term side effects. Anthralin can produce extended treatment-free remissions of four to six months in some patients.

Coal tar: tar used for medicinal purposes is derived from both coal and wood. However, coal tar is the type used most commonly to treat mild, moderate and severe psoriasis. Tar can help reduce itching, scaling and inflammation and can help slow down the rapid proliferation of skin cells and return the skin to a normal appearance. Improvement may be seen within two weeks of starting tar therapy, although it may take up to two months to obtain the maximum benefit. The best candidates for tar monotherapy are patients with limited psoriasis on the knees, elbows, scalp and shins, or those with well-defined lesions. Tar can also be used in combination with UVB, although it can cause stinging to burning when combined with UV therapy or sunlight.

Corticosteroids: topical corticosteroids are the gold standard of topical treatments for mild to moderate psoriasis. Corticosteroids are formulated as lotions, creams, foams, ointments, gels, tape and sprays. Corticosteroids work via anti-inflammatory, immunosuppressive and antiproliferative properties. Used as monotherapy, superpotent (Class I) corticosteroids have the best potential to temporarily clear or nearly clear plaque psoriasis more effectively than other topical therapies. These agents may also be used

in combination with systemic therapies or phototherapy to treat severe disease. The side effects of corticosteroids are well known. Cutaneous side effects are the most common and usually occur when corticosteroids are used with excessive frequency, excessive duration or when applied on the face or intertriginous areas. Systemically, corticosteroids can cause hypothalamic-pituitary-adrenal (HPA) suppression, Cushing Syndrome and glaucoma.

Retinoids: tazarotene is a vitamin A derivative topical retinoid. It is available as a 0.1% and 0.05% gel and cream. Its mechanism of action is thought to include the reduction of lymphocytes in the dermis, decreased expression of inflammatory markers and modification of abnormal keratinocyte differentiation and proliferation. Tazarotene is effective as monotherapy and may be used in combination with topical corticosteroids to increase efficacy and decrease irritation. It may also be used with UVB therapy for a more rapid response, to increase efficacy and to reduce the cumulative UVB dose. Tazarotene can cause itching, burning, stinging and erythema at application sites and is potentially teratogenic.

Topical immunomodulators: tacrolimus ointment is the topical formulation of FK-506, an immunomodulatory agent first used as an oral drug in patients undergoing organ transplantation. It inhibits the activation and proliferation of T cells and the synthesis and expression of cytokines. Tacrolimus is very effective in treating atopic dermatitis and is being investigated in the treatment of psoriasis. It has shown effectiveness for facial plaques[23] and inverse psoriasis.

Vitamin D analogues: calcipotriene is the structural analog of calcitriol (1,25-dihydrox vitamin D_3). It is the most commonly prescribed therapy for psoriasis in the U.S. Although its mechanism of action is not completely understood, calcipotriene has been shown to inhibit the proliferation of keratinocytes and may modulate the proliferation of T lymphocytes. Calcipotriene is less effective than superpotent topical corticosteroids when used as monotherapy, however it can be combined with topical steroids to provide enhanced efficacy that either agent alone. It also provides rapid clearance in lower doses when combined with systemic agents such as cyclosporine and acitretin and with phototherapy. Side effects are minimal and generally involve skin irritation.

Phototherapy

Goeckerman regimen: this therapy consists of concentrated treatment with UVB and topical coal tar for at least three to four weeks in a hospital or psoriasis day treatment center. The regimen can be supplemented with steroid medications and keratolytics (scale removers), particularly in the early stages of treatment. The Ingram regimen is a modification of the Goeckerman regimen in which anthralin is used instead of coal tar. Goeckerman regimen patients have reported average remission times of 6 to 12 months. The remission time and relative safety of the Goeckerman regimen are major reasons why it remains a treatment for moderate to severe psoriasis, particularly for patients who have not responded to PUVA and UVB therapy. The regimen is also well suited for patients with generalized, recalcitrant psoriasis who are not candidates for systemic therapy. Despite its safety and efficacy, the regimen is available only at a few locations in the U.S. due to reimbursement constraints. It is widely available in Canada and Europe, and new centers are opening in the Middle East.

Home phototherapy: treating psoriasis with a UVB light unit at home can be an economical and convenient choice for patients who live too far away from their physician's office to maintain a frequent phototherapy treatment schedule. Home phototherapy requires a physician's prescription, and the patient must continue with regular check-ups.

Lasers: *excimer lasers* (such as Xtrac and EX-308) emit high-intensity UV light that is similar to narrow-band UVB units. A small diameter beam can be targeted at selected areas of the skin and is used to treat patients with mild to moderate plaque psoriasis. Although significant improvements in plaque psoriasis have been reported, there is little long-term data to indicate the efficacy of remissions. The only adverse reactions include mild sunburn.

Pulsed dye lasers emit high-intensity yellow light to treat chronic localized plaque lesions. They destroy the tiny blood vessels that contribute to and support the formation of lesions. Side effects include a small risk of scarring. The most common side effect is a bruise that remains after treatment for a week to 10 days.

Narrow-band UVB (NB-UVB): NB-UVB light therapy consists of high-intensity light ranging from 311-313 nm. NB-UVB provides efficacy without the high-energy, shorter wavelengths that can cause burning, premature aging, and increased incidence of skin cancer. Several studies indicate that NB-UVB clears psoriasis faster and produces longer remissions than broad-band UVB. It is effective with two or three treatments per week, while in some cases, broad-band must be administered more frequently to be effective. NB-UVB is also emerging as an alternative to PUVA. Although not as effective as PUVA, NB-UVB is easier for patients to undergo and may be safer over the long term.

PUVA (Psoralen plus UVA): PUVA is an acronym for psoralen (a light-sensitizing medication) combined with exposure to UVA. PUVA, like other phototherapy options, works by inhibiting the excessive cell reproduction of psoriasis. PUVA is considered for patients who have been resistant to other types of treatment, in patients who are physically or emotionally disabled because of psoriasis, and in older patients as a primary therapy. Stable, plaque psoriasis, guttate psoriasis and psoriasis of the palms and soles are especially responsive to PUVA treatments. Studies show that PUVA clears psoriasis for more than 85 percent who use it and it induces long remission times without maintenance treatment. The skin clearance PUVA provides can last from a few months to more than a year. The most common short-term effects are nausea, itching and erythema. The primary long-term risk of PUVA therapy is a higher risk of skin cancer, particularly non-aggressive forms like squamous cell carcinoma (SCC) and basal cell carcinoma (BCC).

UVA (ultraviolet A): UVA is only mildly effective as monotherapy; its chief value is as a component of PUVA.

UVB (ultraviolet B): UVB phototherapy consists of treatment in a light box lined with UVB lamps. UVB radiation works by penetrating the skin to slow the abnormally rapid growth of skin cells involved in psoriasis. UVB treatment involves exposing the skin to UVB light for a set length of time on a regular schedule, either under a physician's direction in a medical setting or with a home unit purchased with a physician's prescription. There are two types of UVB treatments, broad-band and narrow-band (see above). Broad-band is most commonly used in the U.S. although narrow-band is gaining acceptance. The primary difference between broad-band and narrow-band is that narrow-band emits a more specific range of UV wavelengths. UVB treatments will be effective for at least two-thirds of patients who have thin plaques, moderate to severe disease and are responsive to sunlight. UVB is appropriate when topical medications are not effective. It may be used as monotherapy or in combination with topical treatments such as anthralin, coal tar, vitamin D analogs and retinoids and with systemic agents such as methotrexate and Soriatane. Drawbacks include the need for frequent visits and access to a nearby phototherapy unit.

Systemic Therapies

Disease Modifying Anti-Rheumatic Drugs (DMARDs)

Cyclosporine: a systemic medication approved by the FDA in 1997 for the treatment of severe, recalcitrant psoriasis in adults with non-compromised immune systems. Approved in 1995 to prevent organ rejection in transplant patients, cyclosporine works by suppressing the immune system and preventing actions of certain immune cells. By preventing this immune activity, cyclosporine slows the growth of skin cells. Cyclosporine can provide fairly rapid relief from symptoms and patients may see improvement after two weeks of treatment, particularly if stronger doses are used. However, it may take 12 to 16 weeks to reach a more complete level of control. Most patients experience the reappearance of their psoriasis upon discontinuation of therapy, thus physicians often recommend alternating cyclosporine with other forms of treatment in order to manage psoriasis successfully. Extended use of cyclosporine by transplant patients is well established, but long-term experience as a treatment for psoriasis is limited. Therefore, the FDA recommends treatment with cyclosporine not exceed 1 year.

Hydroxyurea: a systemic oral cancer systemic agent that can be used to enhance UVB or PUVA phototherapy. It can produce significant improvement in plaque psoriasis and is well suited for patients who have less than adequate responses to phototherapy. The primary advantage of hydroxyurea is the minimal risk of hepatotoxicity with long-term use, however, it also has potentially dangerous side effects, including bone marrow suppression, nephrotoxicity and skin cancer. Hydroxyurea may be an alternative to methotrexate for those unwilling to undergo a liver biopsy.

Methotrexate (MTX): a systemic medication used for the treatment of patients with moderate to extensive plaque lesions as well as erythrodermic psoriasis, acute pustular psoriasis (von Zumbusch), psoriatic arthritis and localized pustular psoriasis. MTX binds to an enzyme involved in the rapid growth of cells and in psoriasis slows down the rate of skin-cell growth. In most psoriasis patients, improvement will begin within four to six weeks. More than 80 percent of patients see some improvement within two or three months of starting treatment. MTX is sometimes rotated with other therapies such as PUVA, acitretin and cyclosporine in order to decrease side effects. MTX can also be used in combination with PUVA or UVB to reduce the amount of light need to clear the skin. The primary long-term risk of MTX therapy is the potential for liver damage. Most physicians will perform a liver biopsy when a patient reaches a cumulative dose of 1 to 1.5 grams. Other risks include teratogenicity and immunosuppression. Death from bone marrow toxicity can occur in rare severe cases.

Sulfasalazine: an oral medication reported to be effective for some patients with psoriasis and psoriatic arthritis. It is significantly less effective than MTX but tends to have less dangerous side effects. However, many patients cannot tolerate sulfasalazine because of allergies or side effects, including nausea, vomiting and loss of appetite.

Immunosuppressants

Mycophenolate mofetil: used for the prevention of organ transplant rejection and for the treatment of several inflammatory or autoimmune skin diseases. It can be used to administer or taper treatment with cyclosporine.

Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)

Used to treat mild joint disease through analgesia and anti-inflammatory activity. There are many NSAIDs and no particular agent is considered superior to the others. NSAIDs can occasionally exacerbate psoriasis, which is why patients need to be evaluated by both a dermatologist and a rheumatologist.[24]

Purine Analogues

6-Thioguanine: an oral medication approved for treating certain types of leukemia. It has been reported to be effective for psoriasis in some cases, particularly pustular psoriasis. However, 6-thioguanine must be used under close medical supervision due to the potential side effects associated with bone marrow suppression.

Retinoids

Acitretin: may be used alone or in combination with PUVA, UVB or other psoriasis treatments. Acitretin may also be used sequentially with cyclosporine. This type of combination therapy can speed clearing and help to reduce the amount of the drug and/or light needed, thereby reducing risks and side effects.

Isotretinoin: approved to treat severe acne and has been used to treat severe psoriasis. Generally, it is not as effective as acitretin. Isotretinoin may also be combined with UVB or PUVA for plaque or pustular psoriasis.

Biologics

Many of the more than 4.5 million adults in the United States with psoriasis have psoriasis that is refractory to topical therapies and/or severe enough to require systemic therapy, such as cyclosporine, methotrexate and psoralen plus ultraviolet light A (PUVA). Although these conventional systemic therapies are effective as short-term options to reduce disease severity, the long-term use of these drugs may be limited by severe toxicities, such as malignancy, teratogenicity, hepatic and renal dysfunction, and drug interactions.

Biologics are a subset of systemic medications. They are made from living sources, such as viruses, animals and people. Biologics are injected or infused into the body rather than taken orally. Biologics work in a variety of ways, such as reducing the number of overactive T cells involved in psoriasis, inhibiting T-cell activation, blocking the inflammatory process and/or decreasing the production of inflammatory cytokines.

The availability of biologic therapies has the potential to offer psoriasis and psoriatic arthritis patients safe, effective and long-term control of their disease and significantly improve daily functioning and quality of life. Because they are new for patients with psoriasis, however, long-term side effects are unknown.

Adalimumab: a recombinant human IgG1 monoclonal antibody specific for tumor necrosis factor (TNF). Adalimumab is approved as monotherapy or in combination with methotrexate for reducing the signs and symptoms and inhibiting the progression of structural damage in adult patients with moderately to severely active rheumatoid arthritis who have had inadequate response to one or more DMARDs.

Adalimumab binds to TNF-alpha and blocks its interaction with specific cell surface TNF receptors. It also lyses surface TNF expressing cells in vitro in the presence of complement and modulates biological responses that are induced or regulated by TNF, including molecules responsible for leukocyte migration.

Adalimumab is being evaluated in clinical trials to assess its safety and efficacy in adult patients with chronic moderate to severe plaque psoriasis, psoriatic arthritis, juvenile rheumatoid arthritis and Crohn's disease.

Alefacept: a lymphocyte function-associated antigen-3 (LFA-3)- IgG1 humanized fusion protein that interferes with the CD2/LFA-3 interaction that mediates T-cell recruitment and T-cell activation. The U.S. Food and Drug Administration (FDA) approved alefacept in 2003 for the treatment of moderate to severe chronic plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy.

Alefacept inhibits T-cell activation and proliferation by binding to CD2 on T cells and blocking the LFA-3/CD2 interaction and facilitates apoptosis (programmed cell death) of T cells.[25-27] Treatment with alefacept leads to transient and reversible reductions in activated memory T cells without significant impairment of vital immune functions.[28]

One or more courses of alefacept significantly improves psoriasis.[29] Repeated courses of the drug provide increased efficacy, supporting use as an intermittment therapy. Alefacept has been shown to be a safe, effective and remitting therapy, continuing to provide relief to patients following course completion.

Efalizumab: a humanized IgG monoclonal antibody that targets the alpha chain of LFA-1 (CD-11a), a marker on the surface of T cells. The FDA approved efalizumab in 2003 for the treatment of moderate to severe chronic plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy.

Efalizumab inhibits binding of T cells to endothelial cells, decreases the trafficking of T cells from the circulation into the dermis and prevents activation of T cells involved in the inflammatory cascade that ultimately lead to chronic plaque psoriasis.[25, 26, 27, 29, 30]

Studies completed to date demonstrate that efalizumab is a safe and effective treatment with a rapid onset of action and persistent efficacy when administered continuously, thus providing the rationale for long-term administration.[31]

Etanercept: a recombinant dimer composed of two soluble TNF receptor molecules fused to the Fc fragment of human IgG1. It is currently FDA-approved for the treatment of psoriatic arthritis, rheumatoid arthritis, juvenile rheumatoid arthritis and ankylosing spondylitis.

Etanercept inhibits the activity of TNF by binding to this inflammatory cytokine and preventing interactions with its cell-surface receptors. Elevated levels of TNF have been found in psoriatic skin lesions and in synovial fluid from patients with psoriatic arthritis and/or rheumatoid arthritis.[30,32,33]

Studies completed to date demonstrate that etanercept is an effective treatment with a rapid onset of action and consistent efficacy.[34] Etanercept is well tolerated by both the adult and pediatric patient populations and long-term data show an excellent safety profile. On July 8, 2003, etanercept was filed for approval by the FDA for the treatment of mild to severe psoriasis.

Infliximab: a chimeric IgG1 anti-TNF-alpha monoclonal antibody that binds to transmembrane-bound and soluble TNF-alpha. In addition, infliximab may lyse TNF-producing cells and may lead to the apoptosis of T cells.[35-38] Infliximab is approved for rheumatoid arthritis and Crohn's disease.

The potential benefits of infliximab therapy has led to its evaluation in the treatment of a number of diseases. It is in clinical development for the treatment of psoriasis.[38]

Psoriasis begins to improve quickly using infliximab and remissions of six months or longer can occur. While early trials have yielded promising results, additional studies are ongoing and will be required to define the appropriate dose and schedule.

Case Studies: Psoriasis and Psoriatic Arthritis Treatment

Acitretin

This 32-year-old male patient had psoriasis for six years. Although topical medications were usually sufficient to keep his psoriasis under control, he was experiencing a flare of severe plaque psoriasis that covered more than half his body surface. He had unsuccessfully tried many treatments in the past. When his disease progressed beyond areas that were normally hidden by clothes, it would impair his ability to perform his job. He was treated with acitretin. Clearing was gradual, but within eight weeks there was good improvement. After six months of once-daily oral acitretin, his psoriasis cleared dramatically.

Figure 9

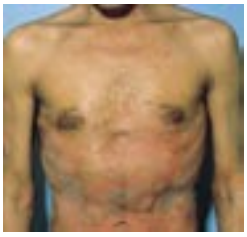


Figure 10

Clearing of psoriasis with oral acitretin

Biologic Agents

A 32-year-old female has psoriasis on 22% of her body surface area. She has had difficulty conceiving and does not use contraception. She is treated for frequent headaches and may be embarking on a course of therapy prescribed by a fertility specialist. Her physician discusses the possibility of treatment with oral cyclosporine or biologic agents. He discusses the side effects of cyclosporine including its many drug interactions and nephrotoxicity. She therefore eliminates this as a possibility and decides to consider treatment with a biologic agent.

Notes:

- **Both methotrexate and acitretin are teratogenic and would not be options for therapy in this patient who would like to conceive.**
- Cyclosporine is rated as pregnancy category C, and several of the biologic agents are rated pregnancy category B. Nevertheless, this patient's concerns about the side effects of cyclosporine and the potential of its drug interactions with many medications she may use are appropriate reasons to consider alternative therapies.
- Because the patient has Fitzpatrick skin type 1, she is not a good candidate for phototherapy, and has not responded to sun exposure in the past, making it unlikely that phototherapy would be effective.

Alefacept (Biologic Agent)

A 20-year-old male with psoriasis affecting 12% of his body surface area experiences marked improvement with narrow-band UVB, but his condition recurs as soon as he stops therapy. He is a full-time student and also has an evening job as a bartender. Because of his rigorous work and study schedule, he is unable to continue phototherapy. He is not a candidate for methotrexate because he is unable to give up limited drinking due to social pressures at school and work. The following therapeutic options are discussed with him: oral cyclosporine, oral acitretin, alefacept, etanercept, infliximab or efalizumab.

Because the patient is concerned about the nephrotoxicity of cyclosporine, and because his busy work and school schedule precludes having phototherapy with acitretin, he decides against those two choices. He refuses to consider any treatment where he has to inject himself. Ideally, he wants a treatment that will give him long periods of remission without requiring continuous therapy, so he agrees to a course of alefacept.

Figure 11

Figure 12

These photographs are representative of treatment success using alefacept.

Notes:

A. **Fortunately, most insurers do not restrict the administration of systemic medications to psoriasis patients on the basis of body surface area.** For many patients, involvement of 10% or more of body surface area will have a profound impact on their lives, and it is the impact on their lives that makes their disease severe. Few patients who consider their disease to be mild or minor would consider taking medications that require repeated injections (such as all of the biologic agents) or repeated blood monitoring (such as acitretin, cyclosporine and methotrexate) or even liver biopsy (such as methotrexate).

- **This patient's busy work and study schedule does not allow him the time commitment required for phototherapy, even if it were available nearby.**
- This patient who works as a bartender is not a candidate for methotrexate because he would find it difficult to give up even occasional drinking.

Efalizumab (Biologic Agent)

A 53-year-old male salesman complains of psoriasis on his palms and soles. Following treatment with acitretin and topical medications, he develops desquamation of the palms and soles with only slight improvement in his psoriasis. He is started on methotrexate, but develops severe nausea, and also complains that he is unable to give up social drinking because of his job. He is therefore switched to oral cyclosporine with which he clears for eight months. During that time he develops hypertension requiring treatment with amlodipine, and he now complains of leg swelling as a result of the amlodipine. He discusses treatment with biologic agents with his physician and together they decide on treatment with efalizumab.

Figure 13

Figure 14

These photographs are representative of treatment success using efalizumab.

Notes:

- **Methotrexate is associated with a number of side effects such as nausea or severe aphthous stomatitis, which often requires discontinuation.**
- **Many patients are unable or unwilling to give up even limited drinking because of social or work pressures, and there is a high frequency of hepatic fibrosis in patients on methotrexate who continue alcohol intake.**
- This patient could have tried other anti-hypertensives, although calcium channel blockers are ideal in patients on cyclosporine because of evidence that they protect against nephrotoxicity. However, because of cyclosporine's nephrotoxicity, its use has been limited to one year according to the package insert and according to published guidelines. The patient therefore appropriately looked for an alternative treatment.
- Acitretin can be helpful as monotherapy in patients with palm and sole psoriasis, but wasn't in this instance. It is often combined with PUVA or UVB, but because this patient travels for work, those treatments would have been impractical. Moreover, UVB is seldom effective for palm and sole psoriasis.

Figure 15

Figure 16

Psoriasis limited to the palms or soles can be debilitating despite the small percentage body surface area affected. Patients with psoriasis of the palms may have difficulty performing day-to-day functions such as buttoning their clothing, and are often embarrassed to shake hands or allow their hands to be seen by others. Psoriasis of the soles can result in pain on walking.

Figure 17

Figure 18

Figure 19

Psoriasis on visible parts of the body such as the neck (Fig. 17), forehead (Fig. 18), or scalp (Fig. 19) can also be debilitating even though the percentage body surface area affected is small.

Figure 20

Psoriatic arthritis can be debilitating and deforming, and progresses despite treatment with non-steroidal anti-inflammatory drugs and methotrexate.

Etanercept (Biologic Agent)

A woman with severe psoriasis and psoriatic arthritis develops some relief of her cutaneous and joint symptoms with methotrexate, but develops liver biopsy changes. Her physician prescribes etanercept 25 mg subcutaneously twice per week.

Figure 21

Figure 22

These photographs are representative of treatment success using etanercept.

Notes:

- **Methotrexate and NSAIDs are effective for treating the pain of psoriatic arthritis but do not prevent progression of joint damage.** Only etanercept has been shown to prevent progression of joint disease effectively.
- Etanercept is the only drug approved for the treatment of psoriatic arthritis.

Infliximab (Biologic Agent)

A 23-year-old female with erythrodermic psoriasis requiring hospitalization in the past failed to respond to methotrexate. Cyclosporine resulted in partial improvement, but she has been on the drug for 18 months. Her physician prescribes treatment with infliximab given at weeks zero, two and six, and every eight weeks thereafter.

Figure 23

Figure 24

These photographs are representative of treatment success using infliximab.

Notes:

- Because this patient is a woman of childbearing age, she is not a candidate for oral acitretin.
- Cyclosporine therapy is recommended for only up to one year because of the nephrotoxicity that commonly occurs in psoriasis patients treated for longer periods.
- This patient has severe disease that requires a treatment that works most of the time and that works quickly—two characteristics of infliximab.
- Continued infusions of infliximab at 8-week intervals have been shown to reduce the formation of anti-infliximab antibodies.

Figure 25

Erythrodermic psoriasis is a life-threatening form of the disease. Patients lose all of the protective functions of the skin and may become hypothermic due to loss of heat, hypovolemic due to loss of fluid, and septic because of loss of the skin's barrier against infectious agents. Loss of nutrients and fluids through the skin may render the patients anemic and may result in electrolyte imbalances.

Figure 26

Generalized pustular psoriasis can be a life-threatening condition because of loss of cutaneous function.

PUVA

An 80-year-old man had severe generalized plaque psoriasis that began approximately 10 years prior to his visit. His condition failed to respond to treatment with numerous topical steroids, tars, anthralin and UVB phototherapy. Scaling erythematous papules and plaques covered 70% of his trunk, buttocks and extremities. He also had extensive scalp involvement and isolated plaques on the face near the hairline. PUVA treatment, continued two to three times per week, produced complete clearing in three months.

Figure 27

Sitting down, a simple activity often taken for granted, can be painful and can result in cracking and bleeding of thick plaques on the buttocks.

UVB

This girl presented with new onset of psoriasis several months prior to her visit. She was treated with numerous topical steroids and tars to no avail. Her psoriasis was so severe that other children were unwilling to play with her, and she was becoming increasingly reluctant to attend school. Psoriasis affected more than 80% of her skin. She was treated with UVB phototherapy three times per week. Within four months she experienced complete clearing. She remained clear without treatment for two years, at which time the psoriasis recurred. She again cleared with a course of UVB phototherapy.

Figure 28

Figure 29

Clearing of psoriasis in a child using UVB.

UVB and acitretin

A 38-year-old white male executive has a long history of psoriasis that has been refractory to numerous topical medications. Psoriasis generally affects approximately 10% of his body surface area but clears completely upon treatment with the combination of acitretin 25 mg daily and broad-band UVB. As soon as he stops or reduces either of those treatments, his condition recurs. Other treatment options have been reviewed with this patient, but he prefers to maintain three weekly phototherapy treatments in combination with acitretin as this regimen has been effective for him for several years without significant side effects.

Note:
Psoriasis is a chronic condition. As with other chronic conditions, such as diabetes, therapy often must be maintained to prevent recurrence or flare of the disease. Just as diabetics must continue to treat themselves with insulin, many psoriasis patients require maintenance therapies to maintain remission of their disease.

UVB and coal tar

This 23-year-old patient developed psoriasis at age 14. His psoriasis seriously worsened during the previous year. He had large painful red patches of psoriasis over the arms, trunk and legs, and areas of the skin folds that were extremely painful. He was treated with a combination of coal tar and ultraviolet phototherapy at a psoriasis treatment center. At three weeks, significant improvement was noted. Access to skilled psoriasis treatment made this safe, effective treatment available to this young patient.

Figure 30

Even when psoriasis is localized to limited areas such as the legs, it can be refractory to topical therapy. Lesions are often so inflammatory, or troublesome because of cracking and bleeding, that systemic therapy is justified.

REFERENCES

1. Weiss S, Kimball A, Liewehr D, et al. Quantifying the harmful effect of psoriasis on health-related quality of life. J Am Acad Dermatol 2002;47:512-518.

2. Rapp SR, Feldman SR, Exum ML, et al. Psoriasis causes as much disability as other major medical diseases. J Am Acad Dermatol 1999;41:401-407.

3. Understanding Psoriatic Arthritis. National Psoriasis Foundation booklet 2003.

4. Raychaudhiri SP, Gross J. A comparative study of pediatric onset psoriasis with adult onset psoriasis. Pediatric Dermatology 2000;17: 174-8.

5. Farber EM, Nall ML. The natural history of psoriasis in 5600 patients. Dermatologica 1974;109:207-11.

6. Nyfors A, Lemholt K. Psoriasis in children. A short review and a survey of 245 cases. Br J Dermatol 1975;92:437-42.

7. Fernandiz C, Pujol RM, Garcia-Patos V, Bordas X, Smandia JA. Psoriasis of early and late-onset: a clinical and epidemiologic study from Spain. J Am Acad Dermatol 2002;46:867-873.

8. Bandow G, Batter M. Callis K, et al. *Therapy of Moderate-to-Severe Psoriasis: Second Edition, Revised and Expanded*. New York, N.Y.: Marcel Dekker, Inc; 2003:10.

9. Wong K, Gladman DD, Husted J, Long J, Farewell VT. Mortality studies in psoriatic arthritis. Results from a single centre. I. Risk and causes of death. Arthritis Rheum 1997;40:1868-1872.

10. Gladman DD. The natural history of psoriatic arthritis. Baillières Clin Rhematol 1994;8:379-394.

11. Understanding Psoriasis. National Psoriasis Foundation booklet 2003.

12. Krueger GG, Feldman SR, Camisa C, et al. Two considerations for patients with psoriasis and their clinicians: what defines mild, moderate, and severe psoriasis? What constitutes a clinically significant improvement when treating psoriasis? J Am Acad Dermatol 2000;43: 281-285.

13. Gupta MA, Gupta AK. Age and gender differences in the impact of psoriasis on quality of life. Int J Dermatol 1995;34:700-703.

14. Barankin B, DeKoven J. Psychosocial effect of common skin diseases. Can Fam Physician 2002;48:712-716.

15. Finlay AY, Coles EC. The effect of severe psoriasis on the quality of life of 369 patients. Br J Dermatol 1995;132:236-244.

16. Koo J. Population-based epidemiologic study of psoriasis with emphasis on quality of life assessment. Dermatol Clin 1996;14:485-496.

17. Gupta MA, Gupta AK. Depression and suicidal ideation in dermatology patients with acne, alopecia areata, atopic dermatitis and psoriasis. Br J Dermatol 1998;139(5):846-850.

18. Gupta MA, Schork NJ, Gupta AK, et al. Suicidal ideation in psoriasis. Int J Dermatol 1993;32(3):188-190.

19. Krueger G, Koo J, Lebwohl M, et al. The impact of psoriasis on quality of life. Arch Dermatol 2001;137:280-284.

20. Ellis CN, Drake LA, Prendergast MM et al. Cost of atopic dermatitis and eczema in the United States. J Am Acad Dermatol 2002;46:361-370.

21. Friedrich M et al. Flow cytometric characterization of lesional T-cells in psoriasis: intracellular cytokine and surface antigen expression indicates an activated, memory/effector type 1 immunophenotype. Arch Dermatol Res 2000;292(10):519-521.

22. Bos JD, De Rie MA. The pathogenesis of psoriasis: immunological facts and speculations. Immunol Today 1999;20(1):40-46.

23. Yamamoto T, Nishioka K. Topical tacrolimus is effective for facial lesions of psoriasis. Acta Derm Venereol 2000;80(6):451.

24. Griffiths CE. Therapy for psoriatic arthritis: sometimes a conflict for psoriasis. Br J Rheumatol 1997;36:409-410.

25. Werther WA, Gonzalez TN, O'Connor SJ, et al. Humanization of an anti-lymphocyte function-associated antigen (LFA)-1 monoclonal antibody and reengineering of the humanized antibody for binding to rhesus LFA-1. J Immunol 1996;157:4986-4995.

26. Krueger J, Gottlieb A, Miller B, et al. Anti CD-11a treatment of psoriasis concurrently increases circulating T-cells and decreases plaque T-cells, consistent with inhibition of cutaneous T-cell trafficking. J Invest Dermatol 2000;115:333.

27. Lowe J, Stefanich E, Rangell L, Pippig S. Efalizumab (anti CD11a) inhibits transendothelial migration of T-cells. Poster. Presented at Soc of Investigative Derm, Los Angeles, Calif., May 15-18, 2002.

28. Gottlieb AB, Casale TB, Frankel E et al. CD4+ T-cell-directed antibody responses are maintained in patients with psoriasis receiving alefacept: results of a randomized study. J Am Acad Dermatol. 2003 Nov;49(5):816-25.

29. Bandow G, Batter M. Callis K, et al. *Therapy of Moderate-to-Severe Psoriasis: Second Edition, Revised and Expanded*. New York, N.Y.: Marcel Dekker, Inc; 2003:305.

30. Ritchlin C, Haas-Smith SA, Hicks D, Cappuccio J, Osterland CK, Looney RJ. Patterns of cytokine production in psoriatic synovium. J Rheumatol 1998;25:1544-1552.

31. Lebwohl M, Tyring SK, Hamilton TK et al. A novel targeted T-cell modulator, efalizumab, for plaque psoriasis. N Engl J Med. 2003 Nov;349(21):2004-13.

32. Partsch F, Steiner G, Leeb BF, Dunky A, Broll H, Smolen JS. Highly increased levels of tumor necrosis factor-alpha and other proinflammatory cytokines in psoriatic arthritis synovial fluid. J Rheumatol 1007;24:518-523.

33. Ettehadi P, Greaves MW, Wallach D, Aderka D, Camp RD. Elevated tumour necrosis factor-alpha (TNF-alpha) biological activity in psoriatic skin lesions. Clin Exp Immunol 1994;9(1):146-151.

34. Leonardi CL, Powers JL, Matheson RT et al. Etanercept as Monotherapy in Patients with Psoriasis. 2003 Nov;349:2014-2022.

35. Scallon B, Cai A, Solowski N, Rosenberg A, Song X, Shealy D, Wagner C. Binding and functional comparisons of two types of tumor necrosis factor antagonists. J Pharmacol Exp Ther 2002;301:418-426.

36. Scallon B, Moore MA, Trinh H, Knight DM, Ghrayeb J. Chimeric anti-TNF monoclonal antibody cA2 binds recombinant transmembrane TNFa and activates immune effector functions. Cytokine 1995;7:251-259.

37. Choy EHS, Panayi GS. Cytokine pathways and joint inflammation in rheumatoid arthritis. N Engl J Med 2001;344:907-916.

38. Chaudhari U, Romano P, Mulcahy LD, Dooley LT, Baker DG, Gottlieb AB. Efficacy and safety of infliximab monotherapy for plaque-type psoriasis: a randomized trial. Lancet 2001;357:1942-1947.

National Psoriasis Foundation
6600 SW 92nd Avenue, Suite 300
Portland, Oregon 97223-7195
Toll Free 800.723.9166
www.psoriasis.org