A Red, Scaly Rash: How to Recognize and Treat Psoriasis

Case Study and Commentary, Kimberly A. Cayce, MD, Christie L. Carroll, MD, Daniel J. Pearce, MD, and Steven R. Feldman, MD, PhD

Abstract

- **Objective:** To review the diagnosis and treatment of psoriasis.
- **Methods:** Qualitative assessment of the literature.
- **Results:** Psoriasis is a common, chronic cutaneous disorder distinguished by erythematous, scaling plaques characteristically distributed in the scalp and the extensor surfaces of the elbows and knees. Inflammation and hyperproliferation are key findings along with associated symptoms of pruritus, pain, and in 10% to 30% of patients, a form of arthritis. Psoriasis has negative effects on quality of life as great as those seen with other major medical disorders. The pathogenesis of psoriasis is considered to be multifactorial with a known genetic predisposition; evidence for the prominent role of T cells recently has emerged. Treatment modalities include topical, oral, or injectable medications and phototherapy or lasers. Localized disease usually can be controlled with topical medications and can easily be managed by primary care providers. For patients with generalized disease or those with associated psoriatic arthritis, evaluation and management by a dermatologist is recommended. All patients with psoriasis (and the physicians who care for them) should be encouraged to use the resources of the National Psoriasis Foundation (www.psoriasis.org) to help address both psychosocial and educational issues.

- **Conclusion:** Patients with psoriasis are likely to present in the primary care setting. Physicians should be able to recognize psoriasis and manage localized disease.

Psoriasis is a common, chronic skin disease with an estimated U.S. prevalence of approximately 2% to 5% [1–3]. Psoriasis affects men and women equally and occurs in all races, although it occurs most frequently in whites. There are 2 peaks in age of onset, one between 20 and 30 years of age and another between 50 and 60 years [4]. However, psoriasis can begin at any age.

Plaque-type psoriasis is the most common form, representing 80% of cases. Itching, burning, and soreness may be associated with the lesions, and up to one third of patients may experience joint pains or arthritis [5]. Psoriasis has negative effects on quality of life that are as great as those seen with other major medical disorders. Triggering factors such as infection, winter weather, stress, and certain drugs along with a genetic predisposition have long been known to play a role in the pathogenesis of psoriasis. However, advancements have been made in our understanding of the immunologic factors involved in the development of psoriasis, particularly the role of T cells. These advances have led to the development of biological medications that interfere with specific steps in the pathogenesis of the disease. Topical therapies remain effective modalities for localized disease and such treatment can be managed by a primary care physician. For patients with generalized disease or those with associated psoriatic arthritis, referral to a dermatologist or rheumatologist is warranted. Primary care physicians are likely to encounter patients with psoriasis and should know how to recognize it, how to manage localized disease, and when to refer.

**CASE STUDY**

**Initial Presentation**

A 21-year-old white male athlete presents to his primary care physician for his annual sports physical exam. The patient asks the physician to examine a rash that he recently developed on his elbows and knees. He says that his teammates are concerned about his “contagiousness,” which is making him feel self-conscious. The patient also complains of a dry, flaky, itchy scalp.

- **What are the clinical presentations of psoriasis?**
- **What other entities might be considered in the differential diagnosis?**

*From the Center for Dermatology Research, Wake Forest University School of Medicine, Winston-Salem, NC.*
Clinical Features

In most cases, the diagnosis of psoriasis is based solely on clinical history and examination, and only rarely is biopsy required. There are 5 forms of psoriasis: plaque-type, guttate, inverse, erythrodermic, and pustular. Plaque-type psoriasis is the most common form (Figure 1), occurring in more than 80% of the psoriatic population [6]. This variant presents with the classic well-demarcated, erythematous, thick papules and plaques with overlying silvery scale. The scalp, elbows, knees, and intergluteal cleft are most commonly involved, although the palms, soles, and nails also may be affected. Characteristic nail changes that can occur with any form of psoriasis include pitting of the nail plate and the nail plate lifting up from the nail bed (onycholysis).

Guttate psoriasis (Figure 2) is seen most commonly in children and accounts for 10% of cases [6]. It often occurs following an upper respiratory tract infection, especially streptococcal pharyngitis. The lesions appear as numerous, small, scaly, erythematous papules and plaques widely distributed over the trunk and extremities. Inverse psoriasis occurs on the flexural surfaces, armpit, and groin, under the breast, and in the skin folds and is characterized by smooth, inflamed lesions without scaling. The other 2 forms of psoriasis, erythrodermic (Figure 3) and pustular (Figure 4), each account for less than 3% of cases [6]. Erythrodermic psoriasis is characterized by generalized erythema and scaling covering up to 100% of the body surface area. This serious form of psoriasis decreases the skin’s innate ability to protect from infection and loss of fluids and to control temperature. Pustular psoriasis involves the development of sterile pustules, and it can be generalized or localized. Severe cases of
generalized pustular psoriasis can cause loss of the skin’s protective functions as well. The localized variant typically involves the hands and feet and can be quite debilitating due to pain and functional disability.

### Differential Diagnosis

The clinical manifestations of several skin disorders are similar to those seen in psoriasis and should be considered in the differential. These disorders include seborrheic dermatitis, lichen simplex chronicus, tinea corporis, lichen planus, subacute cutaneous lupus erythematosus (SCLE), pityriasis rosea, pityriasis rubra pilaris, and mycosis fungoides (Table 1).

Seborrheic dermatitis (Figure 5) often presents in the scalp as a yellowish, greasy scale over an erythematous base and can be confused with the plaques of psoriasis. Other body surfaces characteristically affected in seborrheic dermatitis include the eyebrows, beard, forehead, nasolabial fold, glabella, retroauricular region, concha of the ear and ear canal, axilla, groin, sternum, submammary areas, and umbilicus. Differentiating between the 2 diseases can be difficult, but close inspection of the nails can provide clues to the diagnosis. Nail abnormalities such as pitting, onycholysis, and discoloration are present in up to 50% of psoriasis patients but are not a feature of seborrheic dermatitis. It is not uncommon for psoriasis and seborrheic dermatitis to coexist.

Lichen simplex chronicus (Figure 6) also may be associated with psoriasis, but it can accompany any pruritic cutaneous disease, such as atopic dermatitis, xerosis, and venous insufficiency. The condition results from chronic scratching or rubbing and appears as thickened, often scaly, leathery, red to brown colored plaques in areas that are easily reached by scratching. The lesions of tinea corporis (Figure 7) are usually erythematous and configured in an annular pattern with central clearing and peripheral scale. The fungus may affect any part of the body. When the diagnosis is unclear by visual inspection, microscopic examination of a potassium hydroxide preparation of skin scrapings to identify hyphae is a quick and simple aid to diagnosis. Lichen planus (Figure 8)
presents as pruritic, reddish-purple, flat-topped papules or plaques most commonly located on the wrists and ankles; however, the lower back, neck, legs, and genitals can be involved. While oral involvement is rare in psoriasis, oral lesions are common in lichen planus and appear as patches of fine white lines (Wickham’s striae). Wickham’s striae also are present on the surface of the skin lesions.

The lesions of SCLE (Figure 9) typically are distributed in areas of sun exposure. They initially appear as erythematous papules and plaques with slight scale. As the lesions progress, they can become more psoriasiform with increased scale (less common), although more often the lesions take on an annular configuration. Patients with SCLE may have systemic symptoms such as fatigue or arthralgias, and serologic abnormalities are common [7]. In fact, tests for antinuclear antibody (ANA) are positive in most patients with SCLE. Anti-Ro (SS-A) antibodies occur in 80% to 95% of these patients, while anti-La (SS-B) antibodies occur less frequently [7]. The presence of anti-double-stranded DNA antibodies usually reflects systemic disease.

The history of pityriasis rosea (Figure 10) helps differentiate it from psoriasis. The initial lesion (herald patch) erupts
Pityriasis rosea occurs acutely as an oval or circular, salmon-colored plaque with a collarette of fine scale. Within 1 to 2 weeks, a more generalized rash consisting of multiple, smaller, symmetrical lesions similar to the primary plaque appears in a “Christmas tree” pattern, primarily on the trunk. Pityriasis rosea typically resolves spontaneously in approximately 6 weeks, unlike psoriasis, which has a chronic course.

Pityriasis rubra pilaris (Figure 11) is a rare condition that presents as a pruritic, patchy, salmon-colored rash, characteristically with follicular papules, and first affects the scalp, face, or chest. Often the rash eventually extends downward covering most of the body, although it may affect only the elbows and knees. The palms and soles also become thickened with a yellow to orange hue (palmoplantar keratoderma). Small areas of unaffected skin (islands of sparing) are characteristic.

Mycosis fungoides (Figure 12) is an uncommon, slowly progressive, cutaneous lymphoma of T-cell origin. The disease usually affects adults over age 50 years but can occur in childhood and adolescence. It appears in 3 forms (patches, plaques, and tumors) and often is mistaken for other cutaneous diseases in the initial phases. The patches (flat) and plaques (raised) are erythematous, fine-scaling lesions with irregular borders. Annular or serpiginous patterns are common. Any area of the body can be affected, but the hips, buttocks, groin, lower trunk, axillae, and breasts are frequently involved. Tumors are red-violet nodules that may be dome-shaped, exophytic, or ulcerated. Other systems, such as the lymph nodes, liver, and lungs, also can be affected in later stages.

Further Evaluation

Upon further questioning, the patient says that the rash has been present for approximately 3 to 4 weeks and is getting worse. He notices that the rash becomes worse particularly after he has scraped his elbow on the football field. He has tried some over-the-counter moisturizers, but these have not helped. The patient uses “whatever shampoo is around the house.” He is otherwise healthy and does not take any medications. He denies any other complaints or family history of skin disease.

Physical examination reveals large, erythematosus plaques with thick, white, silvery scale in the scalp and on the bilateral elbows and knees. The remainder of the skin examination is normal. No oral lesions are found, and the nails appear normal. The rest of the physical examination is within normal limits.
Diagnosis

Based on these findings, the physician makes a diagnosis of psoriasis. She informs the patient that he has psoriasis and reassures him that his skin condition is not contagious. The patient wants to know how he got this disease.

- What factors are known to lead to the development of psoriasis?

Pathogenesis

Multiple factors are involved in the pathogenesis of psoriasis. A genetic predisposition combined with environmental triggers appears to play a part in disease development. The complex genetics of psoriasis are not yet fully understood but are best described as a polygenic inheritance model. PSORS1, a human leukocyte antigen (HLA)-associated allele, is considered to be a major component of the genetic basis of psoriasis [8]. However, many other genes and HLA antigens have been associated with psoriasis (Tables 2 and 3). Environmental triggers such as mechanical, ultraviolet (UV), and chemical injury can trigger the onset of psoriasis or worsen an existing case. Koebner’s phenomenon, in which psoriatic lesions manifest at a site of injury to the skin, occurs in approximately 25% of patients [9]. Various infections (particularly streptococcal pharyngitis), psychological stress, smoking, and certain medications (ie, lithium, β blockers, antimalarials, and interferon) also are known triggers for the disease [10].

The important role of T cells in the pathogenesis of psoriasis has become more evident in recent years. The T lymphocyte is the predominant cell in the infiltrate of psoriatic lesions, and it is already present in early pinpoint lesions [9]. CD4+ cells predominate in the dermis and are most prevalent in early lesions, whereas CD8+ cells predominate in the epidermis and are most prevalent in resolving lesions [9]. In the presence of unidentified antigens, antigen-presenting cells mature and interact with naive T cells, causing T-cell activation. This process requires at least 2 signals: (1) recognition of the antigen on the antigen-presenting cell by the T-cell receptor and (2) a costimulatory signal from the antigen-presenting cell to the T cell. Following this signaling, the T cells proliferate, and some become memory T cells [6]. Through the interaction between lymphocyte function-associated antigen-1 (LFA-1) on the T cell and intercellular adhesion molecule-1 on the endothelium, T cells migrate to the site of inflamed skin. Binding of T cells to endothelial cells also is facilitated by the interaction between cutaneous lymphocyte-associated antigen on T cells and E-selectin on endothelial cells. Once in the inflamed skin, T cells encounter the initiating antigen and secrete type-1 cytokines (Th1), particularly interferon-α and interleukin (IL)-2, as well as tumor necrosis factor-α (TNF-α), leading to proliferation and decreased maturation of epithelial keratinocytes [6]. IL-8, produced by most cells of the body, also plays a role in psoriasis by attracting neutrophils and T cells and promoting epidermal proliferation [9].

Further Discussion with Patient

The physician explains the causes of psoriasis and its triggering factors to the patient. The patient

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**Table 2. Susceptibility Loci Identified in Psoriasis**

<table>
<thead>
<tr>
<th>Locus Name</th>
<th>Location</th>
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<tbody>
<tr>
<td>PSORS1</td>
<td>6p21.3</td>
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<tr>
<td></td>
<td>6q</td>
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<tr>
<td></td>
<td>7</td>
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<td></td>
<td>8q24</td>
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<td>10q22–q23</td>
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<td>11p13</td>
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<td>14q31–q32</td>
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<td>17q24–q25</td>
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<td>4q21</td>
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<tr>
<td>PSORS7</td>
<td>1p35–p34</td>
</tr>
<tr>
<td>PSORS8</td>
<td>16q12–q13</td>
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</tbody>
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**Table 3. Human Leukocyte Antigens Associated with Psoriasis**

<table>
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<tr>
<td>HLA-B13</td>
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<tr>
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<tr>
<td>HLA-B37</td>
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<tr>
<td>HLA-Bw16</td>
</tr>
<tr>
<td>HLA-Cw6</td>
</tr>
<tr>
<td>HLA-DR7</td>
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<tr>
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<tr>
<td>HLA-Aw19</td>
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<tr>
<td>HLA-Bw35</td>
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<tr>
<td>HLA-DRB1*0701</td>
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Information from reference 8.
Psoriasis is a chronic condition, although complete remissions do occur. Approximately 5% of patients have reported remission times of 5 or more years [9]. In the absence of such remission, many patients experience periods of well-controlled disease with episodic flares as they cycle through various treatments. Some patients who achieve treatment success can flare when therapy is tapered or discontinued; maintenance therapy is the norm. The disease itself, along with the therapies used to treat it, can have a dramatic effect on patients’ lives, including career, finances, leisure activities, relationships, and physical intimacy [4]. For patients with psoriasis, the appearance of their skin is the most concerning aspect of having the disease [11]. Other commonly cited bothersome features of psoriasis include pruritus, physical irritation, and physical pain or soreness [4]. The severity of psoriasis is correlated with the disease’s negative impact on health-related quality of life [12,13]. Physicians frequently underestimate the psychological morbidity associated with skin disease [14]. The physical and mental functioning of psoriasis patients are comparable to patients with other chronic diseases, such as cancer, arthritis, hypertension, heart disease, diabetes, and depression [15].

Management of the psychosocial aspects of psoriasis is just as important as management of the physical disease. Various coping strategies have been reported in the literature, including educating others, covering lesions, and social avoidance [16]. Telling others that the disease is not contagious may lessen the negative impact of psoriasis [16]. In addition to talking with the patient, it is imperative for the physician to use body language that conveys openness and acceptance. Physically touching the skin lesions can be particularly beneficial and communicates to the patient that the psoriasis is not contagious. One of the most important aspects of psoriasis management is patient referral to the National Psoriasis Foundation (NPF), which offers great psychosocial support and educational resources to patients suffering from psoriasis. The NPF’s goal is to improve the quality of life of those with psoriasis and promote psoriasis research. The organization provides brief, topic-specific brochures to address patients’ most commonly asked questions, and more information can be found on their Web site at www.psoriasis.org. The foundation can be contacted by mail (6600 SW 92nd Ave., Suite 300, Portland, OR 97223-7195), phone (800-723-9166), fax (503-245-0626), or e-mail (getinfo@psoriasis.org).

**What is the impact of psoriasis on patients’ quality of life?**

The impact of the disease on the patient’s quality of life should factor into treatment planning. For example, if a patient with 7% BSA involvement is devastated and is not able to carry out her activities of daily living, aggressive therapy with a systemic agent may be warranted. Conversely, some patients with relatively extensive disease are impacted very little, and it may be appropriate to spare them exposure to potentially toxic agents. Another instance when BSAdoes not appear to be a helpful indicator is with patients who have localized disease. For such patients, systemic agents or phototherapy is likely more appropriate. This strategy essentially creates 2 classes of disease severity based on the appropriateness of topical versus systemic treatment (mild versus moderate-to-severe). The BSA can be estimated using the palm rule—1 palm equals about 1% BSA. Objective measures for assessing psoriasis severity such as the Psoriasis Area and Severity Index (PASI) and Physician Global Assessment have been developed; however, these measures can be cumbersome and subject to significant intraevaluator variability if not used frequently. These measures are most useful in clinical trials.

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**What is the approach to selecting therapy for psoriasis patients?**

**Definitions of Psoriasis Severity**

A first step in treatment planning for a psoriasis patient is evaluation of the extent and impact of disease. There are 2 major arms in psoriasis therapy: (1) localized therapy with topical agents and (2) phototherapy or systemic therapy, which is considered a more aggressive approach. For patients with mild or localized psoriasis, topicals are the first-line of treatment. Practically all topical medications available for psoriasis are safe and have efficacy when used appropriately. A good rule of thumb is that if a patient has greater than 10% body surface area (BSA) involved, application of topicals may be cumbersome and poor adherence is almost guaranteed. For such patients, systemic agents or phototherapy is likely more appropriate. This strategy essentially creates 2 classes of disease severity based on the appropriateness of topical versus systemic treatment (mild versus moderate-to-severe). The BSA can be estimated using the palm rule—1 palm equals about 1% BSA. Objective measures for assessing psoriasis severity such as the Psoriasis Area and Severity Index (PASI) and Physician Global Assessment have been developed; however, these measures can be cumbersome and subject to significant intraevaluator variability if not used frequently. These measures are most useful in clinical trials.

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**What therapies are used to treat localized disease?**

**Treatment of Localized Disease**

The case patient has localized disease and would likely benefit from treatment with topical therapy, an approach that...
avoids some of the risks associated with systemic treatment. Topical corticosteroids have been a long-standing treatment modality for psoriasis. Superpotent steroids (class I) such as clobetasol, halobetasol, and betamethasone (optimized vehicle) sometimes are used initially to penetrate through the scaly, thickened lesions. As a class, these medications have similar efficacy and often are applied twice daily. To further enhance penetration, application of occlusive dressings (even plastic kitchen wrap) is sometimes beneficial. Ointments or creams work well for lesions on the body, but solution or foam formulations generally are preferred for scalp involvement [17]. Lesion improvement in the form of decreased scale and erythema may prompt substitution of a lower-potency steroid in order to avoid long-term sequelae associated with high-potency steroid use. The high-potency steroids should be avoided on the face, axilla, and groin region because of the increased risk of skin atrophy and permanent changes in dermal blood vessels, although low-strength steroids are acceptable. Combination or sequential therapy often is preferred to minimize steroid use.

Topical calcipotriol, a vitamin D analogue, is a safe and effective treatment alternative for mild-to-moderate psoriasis and often is used in combination with topical corticosteroids or other treatment modalities, even in severe cases. The combination of calcipotriol and corticosteroid has been shown to be more effective in the treatment of psoriasis than either agent used alone [18]. Calcipotriol is usually applied twice daily. Common steroid-sparing schedules include application of each medication once daily (eg, calcipotriol in the morning and the corticosteroid at night), or use of calcipotriol during the week and corticosteroid on the weekends. Calcitriol and tacalcitol are other vitamin D analogues available in ointment formulations for the treatment of psoriasis. Fewer studies have been performed with these agents, but efficacy has been demonstrated in placebo-controlled trials [19,20]. As a class, the vitamin D analogues can clear approximately 50% of psoriasis plaques when used twice daily [19–21]. If a vitamin D analogue is combined with phototherapy, it should be applied after UV exposure because the drug is inactivated by UV light [22]. Additionally, products that contain acid, such as salicylic acid, inactivate vitamin D analogues [23]. Skin irritation is the most common side effect reported with the use of these agents.

Topical agents that are used less frequently for the treatment of psoriasis include coal tar, anthralin, and tazarotene. Coal tar exhibits anti-inflammatory properties and is particularly effective for the pruritus associated with psoriasis; however, many patients will not tolerate its unpleasant smell and messiness. Anthralin and tazarotene also have disadvantages and are second-line treatment options. Anthralin is messy and stains nearly everything with which it comes in contact. Clinical trials have demonstrated modest improvement of psoriasis with the use of tazarotene, although it may be slow to work [9]. Furthermore, the drug can be irritating, often limiting its use [5].

Another approach to localized psoriasis therapy is UV light. Light can be delivered via specialized hand and foot units for disease of the palms and soles. For other locations, delivery of UV light can be done with specialized laser devices. Laser delivery systems are able to deliver light of a limited wavelength in order to maximize UV efficacy. The 308-nm excimer laser has shown promise in the treatment of localized disease [24,25].

- **What steps can be taken to improve patient adherence to treatment?**

A major challenge in treating localized psoriasis is patient adherence to the recommended treatment regimens. Low adherence is related to use of topical therapies, which can be messy and irritating as well as time consuming to apply [26]. Studies evaluating patient compliance have reported a 40% nonadherence rate with topical therapy for psoriasis [27]. Additionally, highly motivated patients participating in a clinical trial had only about a 50% adherence rate after 8 weeks of treatment [28]. Because reduced adherence is associated with poorer outcomes, physicians must be very aggressive in promoting adherence to the topical therapies, especially over the chronic course of psoriasis. Educational materials from the NPF help encourage patients to be more adherent to recommended treatment regimens. In addition, vehicle choice is an important factor in improving patient adherence [29]. Patients generally prefer less messy topical formulations such as solutions, foams, and lotions [30]. Choosing the topical therapies or vehicles that are most appealing to patients can improve adherence and therefore improve treatment outcomes. Additionally, investigation into the patient's use of the medications is important, as changes in the regimen can be made to improve adherence.

**Initiation of Topical Therapy**

Because the patient has localized disease, the physician prescribes him sequential therapy with a topical steroid and calcipotriol. She advises him of the benefits and risks of sun exposure and refers him to the NPF for additional information and support. On follow-up visits, the patient is asked about his ability to comply with the current regimen. He reports that he misses a dose a few times a week. Importantly, he is pleased overall with his response to treatment and no alterations in his regimen are needed. The patient improves over the first 6 weeks and is scheduled for
twice-yearly visits for medication refills and monitoring for adverse events. For the next several years, he is able to control his psoriasis; there are periods of waxing and waning, but increases in his dosing regimen effectively combat the flares.

- What therapies are used for generalized disease?

**Therapeutic Options for Generalized Disease**

Topical therapies alone will not suffice for the management of generalized psoriasis. Adherence is likely a major reason that extensive psoriasis cannot be treated with topical agents. Time commitment, messiness, and the ability to reach certain plaques are important factors when considering the suitability of a topical regimen. Referral to a dermatologist is appropriate for treatment of generalized disease as screening and regular laboratory tests are required with systemic therapies. Blood counts, liver function, and lipid levels have to be monitored; at times liver biopsy is required even in the absence of laboratory abnormalities. Furthermore, adverse events, both clinically significant and occult, must be closely monitored.

**Phototherapy**

Ultraviolet B (UVB) light is a reasonably safe therapy that can lead to prolonged remissions. Treatments typically are administered 3 to 5 times per week. Patients may receive the light treatments in the office or obtain a home UVB device. In fact, sunlight itself can be highly effective and is often recommended. If patients do not respond to UVB therapy, higher-risk therapies may be employed. A combination of UVA light with an oral or topical psoralen medication (PUVA therapy) is a classic treatment for psoriasis patients. The psoralen sensitizes the patient to UVA light, intensifying the treatment. However, use of psoralen increases the risk of severe burns as well as nonmelanoma skin cancer [31]. These risks must be considered prior to initiation of treatment, and precautions must be taken to avoid treatment in areas of chronic sun exposure.

**Systemic Agents**

Systemic medications can be highly effective for the treatment of psoriasis but often are accompanied by side effects. Oral medication options include acitretin, methotrexate, and cyclosporine. Acitretin is a retinoid and works by inhibiting epidermal proliferation [9]. It is particularly useful in the treatment of generalized pustular psoriasis, with rapid resolution of lesions usually achieved within 10 days [32]. When acitretin is used as monotherapy for other forms of psoriasis, including chronic plaque-type, response time is generally slower [33]. In a study of patients with plaque-type psoriasis, 70% of subjects on acitretin monotherapy achieved an approximately 50% reduction in severity measures [9]; however, efficacy rates are typically lower in clinical practice. Combination therapy with UV light or vitamin D₃ analogues has been shown to be substantially more effective [9]. Acitretin is highly teratogenic, and this must be carefully considered before this drug is prescribed to women with childbearing potential. The half-life of acitretin is extremely long, and pregnancy must be avoided for 3 years after discontinuation of the drug. Additional possible side effects include mucocutaneous dryness, alopecia, increased serum triglycerides, and rarely hepatotoxicity. Despite the potential side effects of acitretin, the drug has been shown to be effective and generally well-tolerated as maintenance therapy [34]. Regular monitoring with serum chemistries, measurement of triglycerides, and liver function tests must be done throughout the treatment period. Prior to initiating therapy in women, a pregnancy test should be performed and definitive birth control measures initiated.

Methotrexate is a folic acid antagonist and primarily works by reducing cutaneous inflammation [5]. In a clinical trial involving 248 patients, 90% of the patients on methotrexate had at least a 75% reduction in disease severity [35]. In addition, long-term therapy with methotrexate has been shown to result in prolonged remissions [36]. Although methotrexate is highly efficacious in the management of psoriasis, adverse events typically limit its use to moderate-to-severe disease resistant to topical medications and/or UV light therapy or situations in which these therapies are contraindicated. The most worrisome side effects associated with methotrexate are its potential for bone marrow and liver toxicity. Because methotrexate can suppress the bone marrow, complete blood counts should be monitored while on therapy. Liver function tests also should be performed every 1 to 2 months, and liver biopsies are required periodically to screen for subclinical hepatotoxicity. Patients may also complain of nausea, vomiting, abdominal pain, fatigue, and headache. Administration of folic acid once daily (except on methotrexate days) may reduce these subjective symptoms as well as the risk of hematologic adverse events.

Cyclosporine is a cyclic undecapeptide that ultimately works by inhibiting the activity of T cells [9]. Efficacy rates are high and results are seen rapidly. Within 4 weeks, a reduction of 60% to 70% in severity and area of involvement has been achieved [37]. However, treatment with the drug is recommended for no longer than 1 year because of potential adverse events, most importantly, renal impairment. Other associated adverse events include hypertension, hyperkalemia, hypomagnesemia, hyperuricemia, and elevated cholesterol and triglycerides. Thus, regular monitoring of
inhibitors are available for managing psoriasis. Engineered from proteins produced by living cells, these drugs target key steps in the pathogenesis of psoriasis.

Alefacept was approved by the U.S. Food and Drug Administration (FDA) for treating psoriasis in 2003. It is a fusion protein of the CD2 binding domain of LFA-3 and the Fc portion of human immunoglobulin G1. Alefacept blocks the costimulatory pathway between LFA-3 on the antigen presenting cell and CD2 on the T lymphocyte, inhibiting T-cell activation and proliferation [38]. A selective reduction in memory T cells occurs because CD2 expression is higher on activated memory T cells than on naive T cells [38]. It is administered as a weekly intramuscular injection in the office over a 12-week period; this regimen may be repeated after a 12-week treatment-free period, if necessary. Clinical trials have demonstrated a 75% reduction in disease severity as measured by the PASI in 21% of patients treated with alefacept versus 5% with placebo [39]. The drug appears to be relatively safe with no increased risk of infection; however, routine laboratory monitoring of lymphocytes is recommended [38]. Also, there is no long-term safety data available for alefacept or any of the biologicals.

Three TNF-α inhibitors are available for managing psoriasis; only etanercept is FDA-approved for psoriasis. Etanercept is a recombinant human protein that competitively binds to TNF-α, preventing interactions with its cell surface receptors [40]. In efficacy trials, nearly 30% of treated patients achieved a 75% reduction in PASI scores [41]. It is administered at home as a twice-weekly subcutaneous injection. Injection site reactions were the most frequently cited adverse events in clinical trials [40]. Infections and central nervous system demyelinating disorders are potential concerns with the use of etanercept and patients should be screened appropriately.

Infliximab is a chimeric monoclonal antibody that binds to soluble and transmembrane TNF-α molecules in the plasma and diseased tissue, disabling activation of the TNF-α receptor [42]. In fact, some authors speculate that infliximab also could bind to TNF-α that is already bound to the receptor, turning off the activated cell [40,43]. Most experience with infliximab has come from its use in patients with Crohn’s disease and rheumatoid arthritis, but infliximab has proved to be efficacious in the treatment of psoriasis as well. Up to 88% of patients in phase 2 clinical trials achieved a 75% improvement in severity [44]. The drug is administered via intravenous infusion over 2 to 3 hours. The most common adverse events reported in clinical trials were infusion-related reactions (dyspnea, urticaria, hypotension, flushing, and headache) [42]. Patients should be screened for tuberculosis prior to treatment initiation and also should be monitored for infections during and after treatment [42]. Patients with moderate to severe congestive heart failure should not receive infliximab, and those with mild disease should be monitored carefully with discontinuation at the first signs of worsening heart failure. Careful monitoring also is advised in patients with preexisting or recent-onset central nervous system demyelinating or seizure disorders and those with renal or hepatic insufficiency [42].

Adalimumab is the third and newest TNF inhibitor introduced and is given by subcutaneous injection. Approved for rheumatoid arthritis, preliminary data have shown efficacy in psoriasis [45]. A humanized monoclonal antibody, adalimumab may have less immunogenicity (ie, development of autoantibodies to the non-native proteins) than infliximab. Adalimumab carries the same black-box warning as infliximab regarding tuberculosis, and a tuberculin skin test screen is recommended.

Efaluzimab is a humanized form of a murine antibody directed against CD11a, the α subunit of LFA-1. By binding to CD11a, it inhibits T-cell activation, cutaneous T-cell trafficking, and T-cell adhesion to keratinocytes [46]. In phase 3 trials, 30% of subjects achieved a 75% reduction in PASI scores [45]. It is administered via subcutaneous injection weekly at home. However, significant disease flares have been reported in psoriasis patients after starting or abruptly discontinuing the medication [47]. Thrombocytopenia was rare in clinical trials; therefore, occasional monitoring of platelet counts (2 to 4 times per year) is recommended. Side effects most frequently reported include headache, nonspecific infection (ie, common cold), nausea, chills, pain, and fever [46].

Case Patient: 10 Years Later

The patient arrives for an office visit 10 years after the psoriasis diagnosis was made. He has been seen 1 or 2 times per year for refills, flares, and adverse event monitoring. He states that he has noticed new lesions arising within normal limits, although there is boggy edema involving the second and third digits of the right hand.

Blood pressure, renal function, liver function, cholesterol, triglyceride, and uric acid levels, and serum chemistries is needed. Additionally, cyclosporine may cause gastrointestinal discomfort, hypertrichosis, paresthesias, gingival hyperplasia, headache, vertigo, muscle cramps, and tremor [9].

**Biological Agents**

A new category of injectable medications known as biologic response modifiers, or biologicals, recently has been used in the treatment of psoriasis. Engineered from proteins produced by living cells, these drugs target key steps in the pathogenesis of psoriasis.

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This patient now appears to have psoriatic arthritis, an erosive, debilitating arthritis found in an estimated 10% to 30% of all psoriasis patients [1]. Although cutaneous lesions generally appear well before the arthritis, 10% to 15% of patients report the arthritis developed first [47]. The clinical manifestations of psoriatic arthritis are similar to rheumatoid arthritis, but serologic testing can be negative in psoriatic arthritis. The arthritis is an asymmetrical oligoarthritis and most commonly affects the interphalangeal joints. The spine may also be involved. However, unlike rheumatoid arthritis, the metacarpophalangeal joint typically is spared in psoriatic arthritis. Nail involvement and skin lesions adjacent to the affected joints are almost always present. Radiologic findings vary by patient and stage of disease but characteristically demonstrate erosion and mutilation of the distal finger joints and of the interphalangeal joints of the toes [48]. As with cutaneous psoriasis, T cells play a prominent role in psoriatic arthritis, particularly the Th1 cytokines, interferon-α and IL-2, as well as the macrophage cytokines, TNF and IL-1β [49].

A crucial aspect of treatment for psoriatic arthritis is early identification and aggressive intervention to avoid or minimize joint damage. All patients with psoriasis should be asked about joint pains. Referral to a dermatologist and/or a rheumatologist should be prompt if symptoms are uncovered.

**Conclusion**

Psoriasis is a common, chronic cutaneous condition affecting both men and women of all ages and races. The classic lesions present as sharply demarcated, erythematous papules and plaques with a silvery scale distributed on the scalp, elbows and knees, and commonly the intergluteal cleft. Patients frequently experience a decrease in quality of life, not only because of the physical appearance of the lesions, but also because of the associated pruritus and pain. Although a genetic predisposition exists, the genetics are not yet completely understood. Advancements in the understanding of the important role of T cells, particularly Th1 cytokines, have improved the outlook for psoriasis patients, with new therapies that target specific steps in the pathogenesis. Topical therapies remain effective treatment modalities for localized disease and can easily be managed by a primary care physician. For patients with generalized disease or those with associated psoriatic arthritis, referral to a dermatologist or rheumatologist is warranted.

**References**

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