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The authors reported no potential conflict of interest relevant to this article.

Managing psoriasis: What's best for your patient?

Whether the symptoms are mild, moderate, or severe, the optimal treatment plan is the one the patient is most likely to follow.

PRACTICE RECOMMENDATIONS

> Prescribe high-potency (Class 1) topical steroids for use on thicker, chronic plaques and low-potency (Class 7) steroids for the face, intertriginous areas, and the groin. (A)

> Recommend folate supplementation (1-5 mg/d) for patients being treated with methotrexate, as it may reduce the drug's hematologic and gastrointestinal adverse effects without decreasing efficacy. (A)

> Advise patients scheduled to begin biologic therapy to get standard vaccinations—eg, pneumococcal, influenza, hepatitis A and B—before treatment is initiated and to avoid live and live-attenuated vaccines thereafter. C

Strength of recommendation (SOR)

- Good-quality patient-oriented evidence
- B Inconsistent or limited-quality patient-oriented evidence
- C Consensus, usual practice, opinion, disease-oriented evidence, case series

CASE ► Tom D, a 48-year-old white man, has a 3-year history of plaque psoriasis covering approximately 25% of his body. He also complains of joint pain and stiffness in his fingers and ankles, particularly in the morning.

Tom is obese and has a history of coronary artery disease, hypertension, hypercholesterolemia, nonalcoholic fatty liver disease (he drinks 4 or 5 beers per week), and occasional migraines. He has tried numerous topical corticosteroids and vitamin D creams for psoriasis, with minimal relief.

P soriasis is a systemic inflammatory disorder altered by environmental and genetic factors that presents as scaly erythematous plaques and affects 2% to 3% of the population.¹ Eighty percent have mild-to-moderate cutaneous disease; disabling arthritis occurs in as many as 42% of cases.^{1,2} The devastating effects on quality of life including social stigmatization, pain, physical disability, and psychological distress—are comparable to the effects of conditions like cancer and depression.² There is no definitive cure, and patients are left with a lifetime of waxing and waning symptoms.

Helping to create an individualized treatment plan tailored to disease type and extent, comorbidities, and needs of the patient can directly impact the quality of his or her life.³ For those with localized disease, topical therapy is a suitable first choice. Phototherapy is generally the first-line treatment for patients with extensive psoriasis or disabling symptoms. When phototherapy is not feasible or is ineffective, systemic treatments with conventional oral agents or biologics are indicated.

Discussions about therapeutic options should include expected results and duration of remission, cost, convenience, adverse effects, insurance coverage, and safety concerns. The patient's preferences should be taken into account in the treatment plan you create.³ A guiding principle: The



The devastating effects of psoriasis on quality of life are comparable to the effects of conditions like cancer and depression.

optimal protocol is the one the patient is motivated to adhere to.

The limits of topical therapy

Topical treatments are safe and effective when used properly, as monotherapy for localized disease and adjunctive therapy for resistant lesions. Monotherapy with topical agents is not recommended for sites that have a significant impact on quality of life, such as the palms and soles, and is not practical for patients with extensive disease (>10% of body surface).⁴

More potent topicals, such as corticosteroids, are recommended for acute flares; less potent agents with fewer adverse effects, such as calcipotriene, are typically used for maintenance (TABLE 1).⁵⁻⁸ Topical agents can be used either long term or intermittently. Here, too, the most effective treatment is the one the patient will actually apply.⁵

Steroid selection is based on site, severity

Corticosteroids are antiproliferative, immunosuppressive, anti-inflammatory, and vasoconstrictive, and divided into 7 classes. Low-potency agents (Class 7) are used on thinner skin like the face, intertriginous areas, and groin; high-potency steroids (Class 1) are reserved for thicker, chronic plaques.⁹ As a general rule, Class 1 steroids can be safely used for 2 to 4 weeks, with increased risk of both cutaneous effects and systemic absorption if used continuously for longer periods.⁵ The optimal end point for less potent agents is not known.

Cutaneous adverse effects are more common than systemic ones and include skin atrophy, telangiectasia, striae distensae, acne, folliculitis, and purpura.

■ Systemic adverse effects include Cushing's syndrome, osteonecrosis of the femoral head, cataracts, and glaucoma.⁵ The greatest risk of systemic effects is associated with prolonged use of high-potency corticosteroids over large surfaces or under occlusion with dressings or plastic wrap. Patients should be transitioned to the lowest potency possible to maintain efficacy, use corticosteroids intermittently, or combine them with nonsteroidal agents to avoid unwanted effects.

Topicals aren't working? Move on to phototherapy

Phototherapy is an option for patients with

TABLE 1 A look at nonsteroidal topical treatments⁵⁻⁸

Class	Examples	Adverse effects	Comments
Vitamin D analogues	Calcipotriol (calcipotriene), calcitriol	Burning, pruritus, edema, peeling, dryness, erythema	Combining with beta- methasone dipropionate increases efficacy
Retinoids	Tazarotene, tretinoin	Teratogenic, photosensitivity, irritation	Increased efficacy when combined with NB-UVB (and less UV exposure); increased efficacy, duration of remission, and reduction in steroid- induced atrophy when used with steroids
Calcineurin inhibitors	Tacrolimus, pimecrolimus	Burning and pruritus Black box warning for risk of malignancies*	No clinical evidence of increased cancer risk
Others	Emollients, salicylic acid, anthralin, coal tar	Severe skin irritation, staining of clothes, odor with anthralin and tar	Salicylic acid works well with steroids and topical immunomodulators, but is not compatible with calcipotriene

*Lymphoma seen with oral therapy.

UVB, ultraviolet B; NB-UVB, narrow-band ultraviolet B.

extensive disease or skin manifestations that are recalcitrant to topicals. It is efficacious, cost-effective, and lacks systemic immunosuppression. Ultraviolet (UV) A and B act on Langerhans cells, cytokines, and adhesion molecules, inhibiting epidermal proliferation and angiogenesis.¹⁰

Broadband UVB (BB-UVB) was first used during the 1950s, with crude tar or an-thralin, but is rarely used today.

I Narrow-band UVB (NB-UVB) (311-313 nm), developed in the 1980s, has largely replaced BB-UVB. In addition to providing more rapid clearing and resolution of psoriasis compared with BB-UVB, NB-UVB may have less phototoxicity.¹¹Between 20 and 25 NB-UVB treatments, 2 to 3 times a week (in the office or at home) are usually required for significant improvement.

Photocarcinogenesis is a concern but numerous studies, including a review of 3867 patients treated with NB-UVB with a median 5.5-year follow-up, found no significant association with cutaneous malignancies.¹² NB-UVB is considered safe during pregnancy and used as first-line therapy for pregnant patients.¹³

Targeted UVB therapy using a 308-nm excimer laser, another option, selec-

tively targets psoriatic lesions, leaving normal skin untreated. This makes supraerythemogenic doses possible, which increases UVB's efficacy. Long-term adverse effects and duration of remission have not been clearly established.¹⁴

I Psoralen and UVA (PUVA), which uses oral or topical psoralens to sensitize the skin to UVA, has a slightly higher efficacy than NB-UVB, but with increased risk of squamous cell carcinoma (SCC) and possibly melanoma.¹⁵ Clearing can occur within 24 treatments, with remissions lasting 3 to 6 months;¹⁶ monthly maintenance has not been found to lengthen remission.¹³

Common adverse effects include erythema that peaks 48 to 96 hours after a treatment, pruritus, xerosis, irregular pigmentation, and gastrointestinal symptoms that can be reduced by decreasing psoralen and/or UVA doses.¹³ High cumulative doses of oral PUVA (>200 treatments) is associated with a dose-related increased risk of nonmelanoma skin cancer, particularly SCC, in the Caucasian population. This increased risk has not been demonstrated in patients treated with PUVA bath therapy, which is more common in Scandinavian countries.¹⁷

Patients using topical corticosteroids should be transitioned to the lowest potency possible to maintain efficacy.

TABLE 2 Traditional systemic therapy²¹⁻²⁴

	Methotrexate (MTX)	Cyclosporine (CSA)*	Acitretin
Dosing	≤30 mg in one weekly dose (PO, IM, or SC)	2.5-5.0 mg/kg/d in 2 divided doses for 12 wk, then 12-wk nontreatment period Dose decreased (by 0.5-1.0 mg/kg) with disease clearance or when hypertension or nephrotoxicity are detected	10-50 mg/d given as a single dose Lower doses (25 mg/d) used to minimize adverse effects and in combination regimens When added to UV, light dose should be reduced 30%-50%
Contraindications	 Pregnancy and nursing Alcoholism Chronic liver disease Immunodeficiency Bone marrow hypoplasia, leukopenia, thrombocytopenia, significant anemia Hypersensitivity to MTX 	 Concomitant PUVA, UVB, MTX, or other immunosuppressant or coal tar History of >200 PUVA treatments or radiation therapy Abnormal renal function Uncontrolled hypertension Malignancy Hypersensitivity to CSA 	 Women with childbearing potential Severely impaired liver or kidney function Chronically elevated lipid levels
Baseline monitoring [†]	 H&P, BUN, CBC, CR, LFTs Liver biopsy in patients with history of significant liver disease Pregnancy test HIV test in selected patients Consider: PPD, chest x-ray for patients with underly- ing pulmonary disease 	 H&P BP, BUN, and CR (twice) Urinalysis LFTs, CBC, lipid profile, lab tests for magnesium, uric acid, and potassium Pregnancy test¹ Consider: PPD 	 H&P, CBC, LFTs Lipid profile Renal function test Pregnancy test

Narrow-band UVB therapy is a safe and effective option for patients with diffuse psoriasis.

BP, blood pressure; BUN, blood urea nitrogen; CBC, complete blood cell count; CR, creatinine; H&P, history and physical; IM, intramuscular; LFTs, liver function tests; PO, by mouth; PPD, purified protein derivative; PUVA, psoralen and ultraviolet A; SC, subcutaneous; UV, ultraviolet; UVB, ultraviolet B.

*Avoid live vaccinations; caution required with major infection and poorly controlled diabetes.

[†]Ongoing monitoring for **MTX:** BUN, CBC, CR, LFTs; possible liver biopsy (for high-risk patients or cumulative dose >3.5-4 g); **CSA:** BP, BUN, CBC, CR, LFTs; lipid profile; magnesium, uric acid, potassium tests; pregnancy testing; **Acitretin:** CBC, LFTs, lipid profile, renal function test, pregnancy testing.

There is no consensus regarding the risk of melanoma.¹⁵

A careful risk-benefit analysis is needed before initiating phototherapy in patients who take photosensitizing drugs, are immunosuppressed, or have a photosensitivity disorder or a history of melanoma, atypical nevi, multiple melanoma risk factors, or multiple nonmelanoma skin cancers.¹³ Regardless of the type of UV therapy administered, eye protection with goggles is required to decrease the risk of UV-related cataract formation, and genital shielding is needed to prevent increased risk of tumors.¹³ Photoaging is a long-term effect.

CASE ► When questioned further about the challenges that Tom has had with controlling his

symptoms, he admitted to being noncompliant. As a busy executive, he said he didn't have time to use the topical corticosteroids regularly. Phototherapy could alleviate his cutaneous symptoms, but would not address his symptoms that were consistent with psoriatic arthritis.

Pairing therapeutic modalities decreases exposure

Combining therapeutic modalities like emollients and topical or oral retinoids with NB-UVB improves efficacy while reducing the number of treatment sessions and cumulative UVB dosage. If calcipotriene is used, it should be applied *after* phototherapy because it is degraded upon UVB exposure.¹⁸ Acitretin should be started 2 weeks prior to initiation of phototherapy, and its use accompanied by a 25% reduction in initial UV dosage.¹³

PUVA may also be combined with topical calcipotriene or retinoids.¹⁹ In both cases, the addition of the other agent typically decreases the duration of phototherapy, improves the clinical response, and reduces the risk of cancer.^{13,20}

Extensive disease? Consider a traditional systemic agent

Traditional systemic therapy is used to treat extensive disease (**FIGURE**), psoriasis refractory to topical agents, and debilitating disease on the palms, soles, or scalp. Biologics are a recent alternative, but traditional systemics have been utilized longer and have a more longstanding adverse effect and safety profile, are administered orally, and are much less expensive than biologics. Monitoring patients on systemic therapy is necessary (TABLE 2).²¹⁻²⁴

■ Methotrexate (MTX), a competitive inhibitor of dihydrofolate reductase, is the most commonly prescribed traditional systemic psoriasis treatment.²¹ It is administered in a single weekly dose via tablet, parenteral solution, or intramuscular (IM) or subcutaneous (SC) injection.²⁵ A test dose (2.5 or 5 mg) is given initially and complete blood cell count is monitored within one week to evaluate for potential bone marrow toxicity. If none is observed, the dose may be increased to control the disease while minimizing adverse effects.²¹ Common adverse effects of MTX, such as nausea, vomiting, stomatitis, and fatigue, may be minimized by IM or SC administration, splitting the dose, or providing folate supplementation.²¹⁻²⁴ Given in doses of 1 to 5 mg/d, folate may reduce adverse hematologic, gastrointestinal, and hepatic effects without decreasing efficacy.²²

The major severe toxicities are myelosuppression, hepatotoxicity, and pulmonary fibrosis.²⁴ MTX-induced hepatotoxicity is similar to nonalcoholic fatty liver disease (NAFLD) and is thought to exacerbate preexisting NAFLD, which is common in patients with metabolic syndrome. A liver biopsy or serum assays for liver fibrosis (aminoterminal peptide of pro-collagen III) may be warranted during therapy.²⁴

MTX is an abortifacient and teratogen, so contraception during treatment and for up to 3 months thereafter is mandatory for women of childbearing age.²⁶ Men should be advised that MTX decreases sperm count. (For more on methotrexate, see: "When a fetus survives methotrexate exposure," at http://www.jfponline.com/Pages.asp?AID=10299).

Cyclosporine (CSA), an oral calcineurin inhibitor, is a potent immunosuppressant that rapidly clears psoriasis.²⁷ Because duration of use correlates with permanent nephrotoxicity, hypertension, and potential increased risk of SCC and lymphoma, intermittent 12-week courses are recommended. Calcium channel blockers are the preferred treatment for CSA-induced hypertension because of their effect on smooth muscle vasodilation.²¹

■ Oral retinoids. Acitretin modulates epidermal proliferation and is antiinflammatory. Because it lacks immunosuppression, acitretin is generally considered the treatment of choice in HIV patients with severe psoriasis.²⁸ Acitretin is teratogenic and contraindicated in women who plan to become pregnant or who are unwilling to use adequate contraception for 3 years after discontinuing the drug.²¹

CASE ► Given the significant percentage of body surface area involved and symptoms consistent with psoriatic arthritis, Tom required an aggressive therapeutic regimen. His history of nonalcoholic fatty liver and social

Folate supplementation may reduce the adverse hematologic, GI, and hepatic effects associated with methotrexate, without reducing efficacy.

FIGURE 4 psoriasis patients, 4 different presentations







A. The linear erythematous, scaly plaque along this patient's cardiac bypass scar demonstrates koebnerization of plaque psoriasis.

B. Diffuse erythematous scaly papules coalesce into plaques on this patient's anterior chest, arms, abdomen, and periumbilicus.

C. The pinpoint pustules on an erythematous base on this patient's lateral neck, shoulders, and upper back are characteristic of pustular psoriasis.

D. This patient has erythematous plaques with overlying silvery scale on the elbow—a classic location for plaque psoriasis.

drinking precluded the use of methotrexate. A biologic therapy was the next therapeutic choice that could relieve both his cutaneous and joint symptoms.

Biologics require lab work and a detailed medication list

Before beginning biologic therapy for a patient, the National Psoriasis Foundation²⁹ recommends obtaining a complete history, physical, medication list, future plans (ie, pregnancy or travel to locations requiring vaccinations), and baseline labs to identify possible risk factors and/ or contraindications. Periodic evaluation to monitor development of new symptoms, including infection and malignancy (TABLE 3),^{24,30-33} is needed, as well.

Biologic therapy is contraindicated in patients with active serious infection. If patients develop infections requiring antibiotics while being treated, holding the biologic until infection resolution is advised.³⁴ Standard vaccinations (eg, pneumococcal, hepatitis A and B, influenza, diphtheria, tetanus) are

TABLE 3Is your patient a candidate for biologics?24,30-33

Agent	Alefacept	Adalimumab	Etanercept	Infliximab	Ustekinumab
(Drug class)	(T-cell inhibitor)	(TNF-inhibitor)	(TNF-inhibitor)	(TNF-inhibitor)	(IL-12/23 inhibitor)
Dosing	15 mg IM/wk for 12 wk, then 12-wk nontreatment period	80 mg SC the first wk, 40 mg the 2nd wk, followed by 40 mg every other wk	50 mg SC twice/wk for 3 mo, then 50 mg/wk	5 mg/kg IV infusion to start, repeat at 2 and 6 wk, then q6-8 wk	45 mg SC (for patients <100 kg); 90 mg (for patients >100 kg) to start, repeat at 4 wk, followed by q12 wk for maintenance
Contra- indications	HIV	 First-degree relative with MS or personal history of MS or other demyelin- ating disease Hepatitis B Active TB 	 First-degree relative with MS or personal history of MS or other demyelin- ating disease Hepatitis B Active TB Sepsis 	 First-degree relative with MS or personal history of MS or other demyelin- ating disease Hepatitis B Active TB Doses >5 mg/kg should not be given to patients with NYHA Class III or IV CHF* 	Active TB
Baseline monitoring	CD4 count	PPDLFT, CBCHepatitis profile	• PPD • LFT, CBC	PPDLFT, CBCHepatitis profile	PPD
Ongoing monitoring	Biweekly CD4 count; hold dose for counts <250	 Periodic H&P Consider a yearly PPD and peri- odic CBC & LFT 	 Periodic H&P Consider a yearly PPD and peri- odic CBC & LFT 	 Periodic H&P Consider a yearly PPD and periodic CBC & LFT 	Consider a yearly PPD

CBC, complete blood cell count; CHF, congestive heart failure; HIV, human immunodeficiency virus; H&P, history and physical; IL-12/23, interleukin-12, interleukin-23; LFTs, liver function test; MS, multiple sclerosis; NYHA, New York Heart Association; PPD, purified protein derivative; TB, tuberculosis; TNF, tumor necrosis factor. *For this patient population, adalimumab and etanercept have a (theoretical) risk.

> recommended before initiation of immunosuppressive therapy. After therapy starts, patients should avoid live and live-attenuated vaccines (varicella, mumps, measles, and rubella, oral typhoid, yellow fever, herpes zoster, intranasal influenza).³⁵

> Currently, none of the biologics are indicated for use in children or adolescents with psoriasis, despite epidemiologic data suggesting that one-third of adults with psoriasis developed it during childhood, in a form severe enough to warrant the use of systemic medications.³⁴ The FDA is currently reviewing the possibility of indicating etanercept for pediatric psoriasis patients. All biologics are

category B for pregnancy as there is no evidence that they negatively affect pregnancy.²⁴

T-cell inhibitor. Alefacept binds CD2 on memory-effector T lymphocytes, inhibiting activation. Weekly intramuscular injections of alefacept for 12 weeks can clear lesions with long remissions.³⁰

TNF-inhibitors. The TNF-inhibitors have been available for more than 10 years, predominantly for inflammatory bowel disease (IBD) and rheumatoid arthritis (RA), and more than 1.5 million patients have used adalimumab, etanercept, and infliximab for these disorders. Safety data, especially long term, are mostly derived from patients with

IBD or RA, who have often combined TNFinhibitors with additional immunosuppressive therapies. Thus, for psoriasis patients, who typically use biologics as monotherapy, the risk may be overestimated.²⁴

TNF-inhibitors increase the risk for infection, most commonly of the upper respiratory tract, and, rarely, have been associated with opportunistic infections. Numerous cases of TB reactivation and an increased incidence of disseminated cases have been associated with TNF-inhibitors, so screening is recommended.²⁴

The impact of TNF inhibition on congestive heart failure (CHF) is not well understood. Studies have variously shown that TNF-inhibitors have no effect on CHF morbidity or mortality, increase CHF mortality, or improve left ventricular function. TNF-inhibitors should be avoided in patients with severe CHF (New York Heart Association class III or IV). In milder CHF patients with worsening of symptoms, treatment should be discontinued.³⁶

The increased risk of malignancy, especially lymphoma, is a concern, as there have been numerous case reports of lymphoma occurring with TNF-inhibitors. Psoriasis patients in general have an increased risk of lymphoma that confounds data interpretation.³¹ A number of case reports and a large observational study have shown patients receiving TNF-inhibitors may be at a greater risk for developing melanoma and nonmelanoma skin cancer.³²

Ustekinumab, an interleukin 12/23 inhibitor, is a human monoclonal antibody that is absorbed and eliminated slowly, making dosing injections every 12 weeks convenient with efficacy maintained for at least one year.³³ Because of its relative novelty, few studies are published regarding long-term safety. A recent head-to-head trial compared the efficacy and safety of ustekinumab with etanercept and found superior efficacy with ustekinumab, with comparable adverse events.^{37,38} Similar concerns exist with ustekinumab as with TNF-inhibitors, including infection, malignancy, CHF, and TB.³³

CASE ► Tom denied having a personal family history of multiple sclerosis, or any demyelinating disorder. Nor did he have a history of cancer, tuberculosis exposure, CHF, or hepatitis. A purified protein derivative (PPD) was negative, as was his hepatitis panel, and his complete blood count with differential and metabolic panel were within normal limits.

Tom was started on the TNF-inhibitor adalimumab, after undergoing patient education and training and receiving instructions to stop the medication if he developed a major illness or infection. He received a loading dose of 80 mg SC, followed by 40 mg every other week. He tolerated the treatment well and 70% of his cutaneous symptoms cleared after 12 weeks of therapy; his joint pain also was reduced.

Tom is followed regularly in the clinic, with labs every 4 to 6 months. He is maintained on the injections and happy with the results. At each visit, weight loss and decreased beer intake are encouraged, both of which have been shown to reduce psoriasis severity. Although the beta-blockers and ACE inhibitors he takes are known to exacerbate psoriasis, the medications are necessary to treat Tom's coronary artery disease.

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Advise patients who are candidates for biologic therapy to get any standard vaccinations they need before treatment begins.

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